



MINISTERUL EDUCAȚIEI  
ȘI CERCETĂRII  
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NICOLAE TESTEMITANU STATE UNIVERSITY  
OF MEDICINE AND PHARMACY  
OF THE REPUBLIC OF MOLDOVA

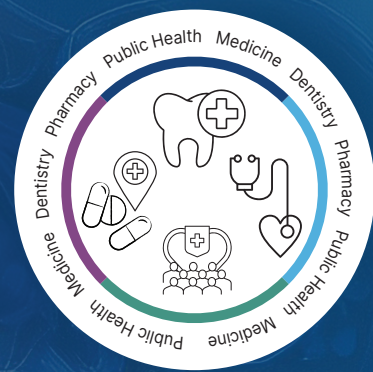


MINISTERUL SĂNĂTĂȚII  
AL REPUBLICII MOLDOVA

 **Med  
spera**

# ABSTRACT BOOK

# 10<sup>th</sup>



International Medical Congress  
for Students and Young Doctors

24-27 April 2024



Chisinau,  
Republic of Moldova

POWERED BY



ASSOCIATION OF MEDICAL  
STUDENTS AND RESIDENTS





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# Abstract Book

*MedEspera 2024*

**The 10<sup>th</sup> International Medical Congress  
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## ***BRIEF HISTORY***

*Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova is a national leader and the only higher education institution in the country that trains doctors, pharmacists and specialists for the health system, gaining international recognition as well.

The university was established based on the Institute of Medicine No. 1, Institute of Medicine No. 2, the Institute of Pediatrics of Leningrad (today Saint Petersburg) and representatives of other USSR institutions that had been evacuated during World War II to Kislovodsk and later transferred to the Moldavian Soviet Socialist Republic with their students and entire teaching staff. Thus, Chisinau State Institute of Medicine (CSIM) was founded. On October 20, 1945, the Institute started its activity with the only faculty – that of General Medicine, which had 32 departments. About 1000 students studied here, the teaching process being ensured by 130 professors.

The Faculty of Pediatrics was created in 1954, the Faculty of Stomatology – in 1959, the Faculty of Preventive Medicine – in 1963, and the Faculty of Pharmacy – one year later.

Starting from 1990, the institution has borne the name of Nicolae Testemitanu (1927-1986) – Professor Emeritus, Rector, Minister of Health, famous scientist and eminent organizer of healthcare. In the following year, the Institute was reorganized into a university.

In 1992, a more advanced higher education form – postgraduate training of future medical specialists and pharmacists through residency – was introduced, and in 2000, the Faculty of Residency and Clinical Fellowship was opened. In 2010, the Faculty of Medicine No. 2 was established to provide training in English for international students.

Currently, undergraduate studies (cycle I) are offered for Public Health, Optometry, Nursing, Radiological Technology, Physical therapy and Rehabilitation specialties; integrated higher education (cycle I and II) is provided for Medicine, Stomatology and Pharmacy specialties; and master's studies (cycle II) take place under the following programs: Management in Public Health, Molecular Technologies in Health, Human Nutrition, Clinical Optometry and Public Mental Health. All study programs are accredited at national level, and the integrated ones – at international level, as well, according to the standards of the World Federation for Medical Education (WFME), and the Stomatology Program has also been accredited by the Dental Board of California.

Starting from November 2015, higher doctoral studies (cycle III) are organized at the Doctoral School in Health Sciences, under 46 doctoral programs, while advanced fundamental and applied scientific research is being conducted within the framework of postdoctoral programs.

Postgraduate studies through residency can be done in 50 disciplines. Since 2016, the process of continuing professional training of doctors and pharmacists has been managed by the Department of Continuing Medical Education, the University providing over 428 medical education programs.

The noble mission of training specialists for the health system is being fulfilled by

approximately 1200 academic staff members and scientists (academicians and corresponding members of the Academy of Sciences of Moldova, full and honorary members of the academies of other states, PhDs and Doctor of Sciences, laureates of the State Prize in the field of science and technology).

In 2019, *Nicolae Testemitanu* University obtained the status of an internationally accredited institution according to WFME standards. During 78 years of activity, the University has trained over 49,000 doctors and pharmacists. As a sign of high appreciation of special merits in the development of healthcare and medical sciences and for the substantial contribution to the training of highly qualified specialists, the University was awarded the Order of *Labor Glory* in 2005 and the *Order of the Republic* in 2015.

*Nicolae Testemitanu* University aspires to continuous development, quality, excellence in all its activities, and members of the academic community strive to ensure its upward path by implementing modern methods of training, research and medical practice, and adjusting all curricula to international standards of higher medical and pharmaceutical education.



## MESSAGE OF THE RECTOR



Dear students and young doctors,

We invite you to *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova: we always encourage young people in their initiatives. It is our duty to inspire them to create, develop and overcome their own limits. The *MedEspera* International Congress of Students and Young Doctors is a proof of our commitment to this endeavor. The Association of Students and Residents in Medicine organizes it twice a year. We appreciate them for their inexhaustible energy and commitment to do their best.

This year, *Nicolae Testemitanu* University will host the 10th edition of the Congress. We hope it will be a great opportunity for students and young doctors to exchange ideas in research and academic activities. The number of foreign participants in *MedEspera* emphasizes the fact that medicine has no borders. We hope that this year will not be an exception and our foreign colleagues will attend the congress and be fully satisfied with the results and experience gained.

We wish all of you good luck! Don't forget to follow your dreams and work hard to achieve your goals. Take full advantage of this event and feel free to share your experiences and adopt best practices from renowned teachers and your colleagues.

I sincerely hope that your impressions of *Nicolae Testemitanu* University and Moldova will be unforgettable!



Rector  
Emil Ceban,  
MD, PhD, Professor, CM of ASM

## ***WELCOME MESSAGE OF THE ORGANIZING COMMITTEE***

Dear Esteemed Participants,

On behalf of the Organizing Committee, we are delighted and eagerly welcome all participants to the 10th edition of the MedEspera International Congress for Students and Young Doctors that takes place in Chisinau, Moldova, at *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova! We are immensely grateful for your commitment to advancing medical knowledge, fostering collaboration, and driving innovation in the field of medicine.

Since the very 1st edition, MedEspera became popular among medical students and young doctors from the Republic of Moldova and abroad. Our purpose is to contribute and maintain the development of brilliant young minds by bringing the latest information at keynotes and workshops we've prepared. The Congress' program includes all possibilities to develop new abilities, discover different medical fields and spend unforgettable time in Chisinau.

As we embark on this journey together, let us seize the opportunity to learn from one another, forge lasting connections, and collectively shape the future of medicine. Your participation and contributions are integral to the success of this congress, and we look forward to experiencing this transformative event with each and every one of you. We sincerely wish you to take the best of MedEspera 2022!



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# **I. ANATOMY SECTION**



***„Anatomia zilelor noastre, ca și a mileniului următor este și va fi din ce în ce mai mult o anatomie a substratului morfofuncțional al Sănătății, o anatomie preventivă. Și nimeni nu poate refuza Anatomiei privilegiul de a fi punctul de plecare al artei de prevenire și vindecare. Anatomia este cheia și volanul medicinei.“***

***„The anatomy of our days, as well as of the next millennium, is and will be more and more an anatomy of the morphofunctional substrate of Health, a preventive anatomy. And no one can deny Anatomy the privilege of being the starting point of the art of prevention and healing. Anatomy is the key and steering wheel of medicine.“***

***Mihail Stefanet,***

*Professor, MD, PhD,*

*Department of Anatomy and Clinical Anatomy,*

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*Chisinau, Republic of Moldova.*





## 1. ANATOMICAL VARIANTS OF THE MEDIAN SACRAL ARTERY

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**Scientific advisor:** Zinovia Zorina, MD, PhD, Associate Professor, Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Knowing the anatomical variants of the median sacral artery has the applied significance, since it is necessary for the surgeons when choosing the operational techniques, in order to ensure the safe access to the presacral space structures. The median sacral artery (hereinafter referred to as the ‘MSA’) is an azygos blood vessel, which is located in the midline, is of small calibre, begins at the dorsal semi-circumference of the abdominal aorta, at the level of the bifurcation thereof, and ends in glomus coccygeum. The MSA is a continuation of the abdominal aorta and a source of vascularisation for the coccyx region of the human organism.

**Aim of study.** Assessing the anatomical variants of the median sacral artery, based on the morphological and topographical criteria, which were found in different reference sources.

**Methods and materials.** The information on this topic was selected from 15 reference sources, and the specified data were analyzed, from the point of view of morphological and topographical variations of the median sacral artery.

**Results.** It has been stated, based on the information as provided in the specialized references, that median sacral artery arises, in the majority of cases, in the dorsal part of the aorta, over the bifurcation thereof, at a distance of 5 to 18 mm, and more seldom directly at the bifurcation level. In reference to the posterior midline, the MSA is more frequently located on the left side of the midline, in case – right on the midline, and in the remaining cases, on the right side of the midline. It has been also stated that in those cases when the abdominal aorta bifurcation is over the level of inferior vena cava formation, then the median sacral artery has a descending rectilinear pathway, and only sometimes – a descending sinuous pathway. In reference to the left/right common iliac veins, there have been identified the following locations of the MSA: its location in the midline, as correlated to both veins, has been stated in 40.9% of cases; its deviation to the left, next to the left common iliac vein has been stated in 31.2% of cases; its direction to the right common iliac vein has been stated in 27.3% of cases. Several authors mention the cases of rare occurrence, when the median sacral artery priorly intersects the left common iliac vein, on its pathway.

**Conclusion.** The point of origin of the median sacral artery varies, and it may have different pathways, both rectilinear and sinuous ones. Topographically, the MSA is located differently, in reference to blood vessels and adjacent formations. Knowing the anatomical variants of the median sacral artery, as pertaining to its morphological and topographical peculiarities, will be a great benefit for the practical medicine and it has a major importance when carrying on surgical interventions at the presacral space level, or various gynecological procedures.

## 2. ANATOMO CLINICAL ARGUMENTATION OF REFLEXOGENIC ZONES



**Author:** Zaharco Daniela

**Scientific advisor:** Turchin Radu Tudor, MD, Associate Professor, Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** A reflexogenic zone can be defined as a specific region of the human body that, through stimulation or pressure, can influence or trigger responses in other parts of the organism. These can be considered true "mirrors" of internal organs or systems, reflecting their condition, whether it is one of health or imbalance.

**Aim of study.** Determining the importance of reflexogenic zones in the medical and therapeutic context, including their role in diagnosis, as well as illustrating how these areas can influence the health of the human body.

**Methods and materials.** The presented work was created through a literature review using articles published in databases such as PubMed, NCBI, and Science Direct, as well as anatomy textbooks and international literature on alternative medicine.

**Results.** The state of internal organs can influence the appearance of external projection areas, for example, the appearance of moles, papillomas, keratomas, and condylomas, the emergence of vascular patterns on the facial skin, reddening or cyanosis of the lips and nails in the case of chronic pathology. Also, it can manifest with pain in the skin, muscles, periosteum, blood vessels, and fascia, which represents its projection. It was proven that a chronic kidney disease can lead to shoulder elevation on the same side of the body. Chronic lung diseases are often accompanied by kyphosis in the thoracic region of the spine. These aspects are based on visceral sensitivity, viscerovisceral, somatovisceral and viscerosomatic connections. For visceral sensitivity are responsible afferent visceral fibers that transmit information about the internal state of the body to the central nervous system (CNS). This information is processed unconsciously and contributes to the automatic regulation of vital functions, such as blood pressure, blood chemical composition, heart rate, respiratory rate, and vascular resistance. Viscerovisceral connections describe the interactions where one viscus can influence the functioning of another. Somatovisceral and viscerosomatic connections illustrate the interaction between internal organs and somatic structures. Stimulation of a somatic area can have effects on the functioning of a visceral organ. Conversely, dysfunctions of visceral organs can lead to manifestations in somatic areas, such as referred pain, a phenomenon in which pain from a visceral organ is felt in a superficial area of the body. It is explained by the dermatomal law, according to which visceral pain radiates to the cutaneous zones, also known as Zaharin-Head zones. Dermatomes correspond to the spinal segment at which the respective organ developed during embryonic development. An illustrative example is cardiac pain, which can be felt in the dermatomes C8-T1, also renal, ureteral, or testicular pain is referred to the dermatomes L1-L2. In the case of angina pectoris pain appears in the left shoulder and arm, in the case of gastric ulcer disease – in the interscapular region, and in the case of appendicitis – in the right inguinal region.

**Conclusion.** Knowing and studying reflexogenic areas is important to understanding the human body's complexity and developing effective therapies such as reflexology, acupuncture, acupressure, physiotherapy, kinesiotherapy, hirudotherapy, cupping therapy, and others, which are components of traditional medicine, and as alternative treatment methods are proven to be effective and with fewer side effects.



### 3. CONGENITAL ANOMALIES IN NEWBORNS: SYNDACTYLY

**Author:** Zveaghinteva Ludmila

**Scientific advisor:** Turchin Radu Tudor, MD, Associate Professor, Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

**Introduction.** The name of „hand” comes from the Latin „manus”, derived from „manipulus”. The hand is the most perfected segment of the human locomotor system and is a complex organ made up of 27 bones, 27 joints and 19 muscles. Any congenital defect negatively affects its function, but also affects its cosmetic appearance. , from this deriving other roles due to the wide range of movements and the high precision of which the hand is capable.

**Aim of study.** Study of the characteristics of the birth defect syndactyly, including its causes and manifestations.

**Methods and materials.** A literature search was conducted to identify and evaluate birth defects specifically associated with “neonatal syndactyly.” The most relevant and recent articles were selected such as “Orthopedic Journal of Sports Medicine,” “Orthopedics and Related Research,” “Kraus R, Pavlidis T, Heiss C, et al. Arthroscopic treatment of post-traumatic shoulder instability in children and adolescents.” Basic textbooks on “Congenital pathologies of the musculoskeletal system,” Shvedovchenko I.V. Congenital hand defects in children”, “Erofeeva G.I., Goryunov O.F. Long-term results of surgical treatment of syndactyly”, “Shvedovchenko I.V. Congenital malformations in children.”

**Results.** Syndactyly occurs when the digits fail to fully separate into individual fingers and toes, is a congenital malformation that is becoming more common lately. About 10 to 40 percent of children with syndactyly inherit the condition from a parent. Syndactyly is formed during pregnancy, more precisely during the gestation period. Syndactyly begins in week 6-8 of pregnancy, without affecting vital functions. Syndactyly is the most common malformation of the hand, present in 1 in 2000 births. It affects the male sex more frequently in a ratio of 2/1. The only symptom of syndactyly is your child having two or more fingers or toes fused together. The fused digits will be visible at their birth. In most cases, there is nothing a mother or father did to cause this abnormality and there was nothing that he or she could have done to prevent it. But sometimes, syndactyly happens as part of a genetic syndrome.

**Conclusion.** Syndactyly itself is not an indication for surgery if the only problem is its awkward appearance. However, syndactyly that interferes with daily movements requires surgery. To make your fingers lighter and more functional.



#### 4. CORPUS CALLOSUM AGENESIS IN MORPHOCLINICAL ASPECT



**Author:** Rotaras Arina

**Scientific advisor:** Zinovia Zorina, MD, PhD, Associate Professor, Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Agenesis of the corpus callosum (ACC) is a congenital brain anomaly, characterized by the absence of commissural fibers connecting the two large hemispheres of the brain. This can be partial or total and can appear in isolation or in association with genetic abnormalities/syndromes, having a reserved evolution and prognosis. The ACC presents the most cerebral malformation, associated with over 250 genetic syndromes, the incidence being 1:300 newborns, in about 80% of cases the neurological manifestations, being quite severe, which leads to a high morbidity, mortality and neuropsychological invalidation of these children.

**Aim of study.** Studying the morphoclinical aspects of corpus callosum agenesis according to the data elucidated in the bibliographic sources.

**Methods and materials.** 12 bibliographic sources were studied in which the morphological appearance and clinical manifestations of corpus callosum agenesis were mentioned.

**Results.** In no. 12 of sources was indicated that agenesis of the corpus callosum from a morphological point of view is divided into total and partial agenesis, in which usually the splenium (posterior part) is absent. The clinical aspect of this anomaly is based on the neurological disorders, as well as the symptoms related to the anomalies with which ACC is associated, all of which are mentioned in no. 12 of sources. Most of the bibliographic sources mention the methods of investigation of this malformation, the main one being the ultrasound of pregnant women which needs to be performed no later than on the 20th -22nd weeks of gestation.

**Conclusion.** Total corpus callosum agenesis is much more common than partial agenesis. Agenesis of the corpus callosum is most commonly associated with other intracranial anomalies, including Interhemispheric Cyst with Hydrocephalus, Dandy-Walker Malformation, Neuronal Migration Disorder, Inferior Vermis Agenesis, Encephalocele, Interhemispheric Fissure Lipoma. The method of choice in establishing agenesis of the corpus callosum is the ultrasound examination.



## 5. PORTO-SYSTEMIC VENOUS SHUNTS

**Author:** Smerea Viorel

**Scientific advisor:** Suman Serghei, Professor, Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Portosystemic shunts are abnormal vessels that allow portal blood to enter the systemic circulation without passing through the liver. They can be extrahepatic, where the vascular abnormalities are outside the liver, or intrahepatic, where they are within the liver parenchyma.

**Aim of study.** To elucidate the current level of science on the impact of studying portosystemic shunts.

**Methods and materials.** A bibliographic study of scientific literature specialized at portosystemic venous shunts.

**Results.** The portal venous system is subject to various congenital and acquired disorders, the most important of which are portal venous obstruction/thrombosis and portal hypertension. Anatomical variants and congenital anomalies of the portal venous system are particularly important to identify in the context of considering liver transplantation or resection and interventional procedures such as transjugular intrahepatic portosystemic shunt, portal vein embolization, and hemodialysis.

**Conclusion.** A correct understanding of the anatomy of the portal venous system is essential for effective diagnosis, management and treatment planning of these disorders. Because of the liver's crucial role in metabolism, a liver shunt can cause serious health problems.

## 6. THE ANATOMICAL VARIABILITY OF THE LAST THREE PAIRS OF THE INTERCOSTAL ARTERIES



**Author:** Croitoru Dan; **Co-author:** Coşciug Stanislav

**Scientific advisor:** Vişnevschi Sergiu, Assistant Professor, Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The intercostal arteries are of vital significance in the vascularisation of the intercostal musculature, fascia and the ribs. The last three pairs are involved in the blood supply of the antero-lateral abdominal wall and may be considered during the surgical intervention in this region. These may also play a vital role in the neurosurgical approaches to the intervertebral disks because of the possibility of a dramatical protrusion of the disk during the surgical intervention.

**Aim of study.** To determine the particularities of the number, origin, trajectory and branching of the last three pairs of the intercostal arteries

**Methods and materials.** We have studied 20 sections of the Magnetic Resonance Imaging in contrast regime of the arterial window in order to identify the anatomical variability patterns. Overall there have been 14 female patients and 6 male patients. The statistically processed data has been acquired.

**Results.** The mean age of the patients in the study poll was  $58.55 \pm 13.24$  years. In the available literature reports the posterior intercostal arteries have branching patterns with the adjacent arterial systems. We have identified 14 cases that had collateral branches (70%) and 6 cases that did not have such branches (30%). The anatomical trajectory of the arteries is usually straight but in an advanced age they may become sinuous in some portions or in their whole trajectory. We have identified completely straight arteries in 2 cases (10%), partially straight and partially sinuous in 6 cases (30%) and completely sinuous in 12 cases (60%). Their length was not measured because in imagistic studies this is a relative limitation and it is already proven in numerous studies in different countries with different ethnic composition that there are no statistical significant factors which may influence it.

**Conclusion.** The last three intercostal arteries are of comparable anatomical variability with other countries. The most prevalent group is the one which has collateral branches and sinuous trajectory (particularly because of an advanced age in our study poll).

**Keywords.** Intercostal arteries, arterial variability, arterial branches.





## 7. VARIATION OF THE MASTOID SEGMENT OF THE FACIAL CANAL AND OF THE STYLOMASTOID FORAMEN

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**Introduction.** Taking into consideration that the ratio of the facial nerve iatrogenic injuries in primary mastoidectomy is 0.6%-3.7%, and a twice higher ratio of 4%-10% is reported for the revision surgery, the knowledge about variability of the mastoid segment of the facial canal and its exit orifice is of high clinical significance for the head and neck surgery.

**Aim of study.** The purpose of our study was to determine the variability and specific features of the mastoid segment of the facial canal and of the stylomastoid foramen.

**Methods and materials.** Our research was carried out at the Department of anatomy and clinical anatomy of *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova. Out of 82 temporal bones, 41 were from the right side and 41 were from the left one. The length of the mastoid segment of the facial canal, its exit angle, the transverse and longitudinal diameters of the stylomastoid foramen were taken. For the database storage an Excel 2019 sheath was used. For the statistical analysis of the obtained morphometric parameters the descriptive and inferential statistics methods were applied.

**Results.** Three variants of the mastoid segment exit angle were determined: sharp, right and obtuse angles. The exit angle of the mastoid segment on the right temporal bones had a mean value of  $112.9 \pm 23.61^\circ$  and on the left side it was  $113.1 \pm 19.76^\circ$ ,  $p=0.971$ . The mean length of the mastoid segment on the right temporal bones was  $15.7 \pm 3.66$  mm and on the left bones it was  $14.5 \pm 3.84$  mm,  $p=0.153$ . The transverse diameter of the stylomastoid foramen on the right specimens was  $2.9 \pm 0.80$  mm, and on the left ones it was  $2.4 \pm 0.60$  mm, with a statistically significant difference,  $p=0.012$ . The longitudinal diameter of the right stylomastoid foramens had a mean value of  $3.3 \pm 0.96$  mm, and of the left orifices it was  $2.7 \pm 0.81$  mm, with a statistically significant difference,  $p=0.007$ . Variable shapes of the stylomastoid foramen were established: oval, round, triangular, quadrangular, semilunar and irregular shapes.

**Conclusion.** Both the mastoid segment of the facial canal and the stylomastoid foramen are subjected to individual variability. Three variants were characteristic of the mastoid segment exit angle: sharp, right and obtuse ones. The exit angle of the mastoid segment of the facial canal was higher on the left side, but the length of the mastoid segment was higher on the right side. Both the transverse and the longitudinal diameters of the stylomastoid foramen were higher on the right side. The transverse diameter of the stylomastoid foramen, on both sides, had lower mean values compared to the mean values of its longitudinal diameter.

**Keywords.** Facial canal, mastoid segment, stylomastoid foramen, variability, morphometry

## 8. VARIATIONAL ASPECTS OF THE DEEP FEMORAL ARTERY



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**Introduction.** The deep femoral artery (DFA), also known as the deep artery of the thigh, classically, originates from the lateral semi-circumference of the femoral artery (FA), in the distal direction, at a distance of about 4 cm from the inguinal ligament. It is of huge interest both for the angiographic diagnostic procedures and for the vascular and endovascular surgeons, due to the role it has in the collateral circulation between the blood vessels in the pelvis and those ones in the popliteal-tibial area.

**Aim of study.** Studying the specialized references that describe the variational morphological peculiarities of the deep femoral artery.

**Methods and materials.** There have been studied 25 reference sources, 6 national and 19 international references. Aiming to achieve this goal, we have carried on a study, by examining and processing the information on this topic of study, from various sources.

**Results.** 22 sources provided the variants of origin of the deep femoral artery, as found with the frequency from 30 to 45%. In 80-85% of cases, the DFA originates from the FA. However, there are known variations of branching. In 48-60% of cases, the medial circumflex femoral artery (MCFA) and the lateral circumflex femoral artery (LCFA) originate from the DFA. In 25-34% of cases, the MCFA originates from the FA, while the LCFA originates from the DFA. In 9-12% of cases, the LCFA originates from the FA, and the MCFA originates from the DFA. There are also rare cases (1- 2%), when the DFA, MCFA and LCFA originate from the FA trifurcation. 20 reference sources have identified a range of anatomical variations of the DFA pathway, namely: in the majority of cases (from 40% to 55% of cases), the deep femoral artery goes in the posterolateral direction. It may also have the strictly posterior direction (from 20% to 40% of cases). It may also have the posteromedial pathway (from 5% to 14% of cases), or the strictly medial pathway (from 1.5% to 3.1% of cases). There are two extremely rare variations: DFA doubling, and DFA origin from the bifurcation of the external iliac artery, laterally to the femoral artery, with branching into the MCFA, LCFA, and two perforating arteries. Knowing the morphological variations of the deep femoral artery is essential for avoiding the arteriovenous femoral iatrogenic fistulas, which are caused by the femoral artery puncture.

**Conclusion.** Knowing the variations of origin and the pathway of the deep femoral artery and its branches, is very important for the successful results, both in the course of interventional and surgical procedures. Defining the vascular pattern before any and all invasive procedures will allow the surgeons to avoid iatrogenic injuries.



## **II. BIOCHEMISTRY SECTION**

*„Răspunsurile complete la multe întrebări ale medicinei nu le avem, dar un lucru este cert- aceste provocări vi le încredințăm vouă, tineretului nostru, care a demonstrat și va demonstra capacitatea sa intelectuală. Evoluția acestui congres științific confirmă participarea activă a tineretului. Iar profesorii noștri au datoria sfântă nu doar să studieze neconținut, ci și să-i învețe permanent la nivel contemporan și pe studenții de azi. Sperăm în viitorul vostru, fundamentul spiritual al acestui popor, care, după o muncă enormă, va proslăvi acest meleag.”*

*„Complete answers to many questions in medicine elude us, but one thing is certain- these challenges we entrust to you, our youth, who have demonstrated and will demonstrate their intellectual capacity. The evolution of this scientific forum confirms the active participation of the youth. And our teachers have the sacred duty not only to study incessantly but also to teach continuously at a contemporary level to today's students. We hope in your future, the spiritual foundation of this nation, which, after enormous effort, will glorify this land.”*

**Leonid Lîsîi,**

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## 1. BIOCHEMICAL ASPECTS OF HEART DISEASES IN PATIENTS WITH DIABETES MELLITUS.



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**Introduction.** The prevalence of diabetes mellitus is continuously increasing globally and is estimated to reach approx. 366 million by 2030. According to the latest research, the cardiovascular changes due to diabetes are based on metabolic, hormonal and genetic imbalances.

**Aim of study.** Elucidation of biochemical aspects of cardiovascular diseases induced by diabetes, in order to improve diagnosis and to develop effective treatment methods.

**Methods and materials.** To achieve the proposed goal, a bibliographic search was performed using 5 bibliographic sources, between the 2020-2023, including those of the Medical Scientific Library of USMF "*Nicolae Testemitanu*", data of the electronic libraries such as PubMed, Cambridge Journals Online, Elsevier, Medline, MedScape, Diabetes Care and Diabetologia.

**Results.** Diabetes Mellitus forms a hyperglycemic condition in patients, which leads to the increased secretion of interleukin 6 (IL-6), interleukin-1 $\beta$  (IL-1 $\beta$ ). This can induce cardiovascular problems like atherosclerosis and heart failure. The interleukin 6 (IL-6) has the role in the atherothrombosis formation in the coronary heart disease, heart failure. Interleukin 1 $\beta$  (IL-1 $\beta$ ) decreases the beta-adrenergic responsiveness of calcium channels and increases the activity of nitric oxide synthase (NOS), resulting in decreased myocardial contractility, increased myocardial hypertrophy and induces cardiomyocyte apoptosis. Interleukin-1beta (IL-1 $\beta$ ) can be detected in the endothelium and macrophages of the coronary arteries affected with atherosclerosis and coronary arteries from nonischemic cardiomyopathy hearts. Recently has been discovered a member of the interleukin family - interleukin 34 (IL-34). Its levels are high in coronary heart disease and diabetes. Interleukin 34 (IL-34) has pro-inflammatory actions, causing atherosclerosis and insulin resistance. Interleukin 6 (IL-6) and interleukin 1 $\beta$  (IL-1 $\beta$ ) stimulate the production of C- reactive protein. Sodium-glucose co-transporter-2 (SGLT2) inhibitors lower the interleukin levels which would lower the risk of cardiovascular outcomes and diabetes.

**Conclusion.** Type 2 diabetes patients are at high risk of cardiovascular diseases like atherosclerosis, myocardial infarction, heart failure due to the increased secretion of inflammatory cytokines like interleukin 6 (IL-6), interleukin 1 $\beta$  (IL-1 $\beta$ ). Scientific studies propose the implementation of regimes with SGLT2 inhibitors: canagliflozin, empagliflozin which are beneficial against the cardiovascular consequences of diabetes in humans.



## 2. BIOCHEMICAL ASPECTS OF MALABSORPTION SYNDROMES

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**Introduction.** Malabsorption affects millions of people worldwide. Prevalence of coeliac disease in the general population ranges from 0,5% to 2%, with an average of about 1%. At present over 100,000 people suffer from cystic fibrosis worldwide. Malabsorption can be caused by many different diseases and may lead to a wide spectrum of clinical signs, symptoms and biochemical findings including vitamin, mineral and macronutrient deficiency syndromes.

**Aim of study.** Malabsorption is a clinical term that refers to the impaired absorption of nutrients. It encompasses defects that occur during the digestion and absorption of food nutrients by, and infections of, the gastrointestinal tract.

**Methods and materials.** In the Pubmed and Google Scholar databases, we selected and analyzed 30 articles with embedded keywords: “Malabsorption syndromes”, “Coeliac Disease”, “Cystic Fibrosis”, etc.

**Results.** The absorption of nutrients occurs in three distinct stages: luminal, mucosal, and postabsorptive. Malabsorption syndromes can be classified depending on which of these three stages is affected. There are numerous causes of malabsorption, including lactose intolerance, inflammatory bowel diseases, cystic fibrosis, short bowel syndrome, and others. Therefore, it is important to thoroughly examine the family history. From a biochemical perspective, malabsorption syndromes can be classified based on which nutrients are not assimilated: proteins, fats, carbohydrates, or micronutrients. Malabsorption syndromes are manifested by both biochemical abnormalities (anemia, hypoalbuminemia, dyslipidemia, vitamin deficiencies, etc.) and a clinical triad, including chronic diarrhea, abdominal distension, and developmental and/or growth delay. Celiac disease should be considered a primary food-related condition with lifelong consequences for affected individuals. The specific role of HLA-DQA1 and HLA-DQB1 genes in presenting gluten peptides as antigens makes the MHC-HLA locus a crucial genetic factor in the development of celiac disease. Nutrition is closely linked to the disease outcome, and malnutrition in cystic fibrosis typically results in a chronic negative energy balance, leading to malabsorption due to pancreatic enzyme insufficiency.

**Conclusion.** Nutrient absorption can be disrupted by numerous pathophysiological conditions, including genetic disorders, such as those seen in celiac disease. Understanding the biochemical mechanisms of malabsorption syndromes is crucial for the diagnosis and management of these pathologies.

### 3. BIOCHEMICAL CHANGES OF THE VASCULAR ENDOTHELIUM IN DIABETIC PATHOLOGY



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**Introduction.** Diabetes mellitus (DM) is a multifactorial pathology that has become a worldwide problem due to its rapid spread and progression. Persistent hyperglycemia in DM induces disruption of vascular homeostasis by interfering with metabolic, hormonal and genetic imbalances. As a result of these disturbances, the functionality of the vascular endothelial cells changes, thus the amplification of proinflammatory and procoagulant processes, characteristic of diabetic pathology, takes place.

**Aim of study.** Elucidation of biochemical aspects in the pathogenesis of vascular changes caused by diabetes mellitus, which disrupt the quality of life. Detailed analysis of the molecular processes and understanding of the underlying mechanisms that contribute to the vascular dysfunction associated with DM.

**Methods and materials.** Analysis of published literature from the information resources of the Medical Scientific Library at *Nicolae Testemitanu* State University of Medicine and Pharmacy and articles from specialized medical scientific journals included in databases such as PubMed, Cambridge Journals Online, Elsevier, Diabetes Care, Medline and MedScape.

**Results.** In DM the vascular endothelium regulates the passage of macromolecules and circulating cells in the blood. This is a major target of oxidative stress, which leads to the activation of the polyol pathway, the acceleration of the formation of protein kinase C (PKC) isoforms and the intensification of the hexosamine pathway, which is due to the overproduction of superoxide anion at the level of the mitochondrial respiratory chain and promotes the formation of advanced glycation end products (AGEs). Glycated biological compounds, as well as collagen in the vascular endothelium and respiratory chain proteins in the mitochondria, undergo irreversible changes, lose their ability to act, which contributes to the installation of fibrotic and atrophic processes in the organs affected by the complications of diabetes and lead to the amplification of oxidative stress, which is closely related to the glycation process. Activation of PKC in the cells of the vascular wall leads to an increased expression of vascular endothelial growth factor that increases the permeability of the endothelial barrier and inhibits nitric oxide synthase, due to the direct effect of free radicals, which react with nitric oxide by inactivating it. Free radicals determine the activation of the hexosamine pathway that induces the procoagulant state attributed to diabetic pathology.

**Conclusion.** The structural changes in the vessels in diabetic patients are due to the alterations occurring as a result of oxidative stress and inflammation. Scientific studies propose the implementation of regimes with antioxidants: polyphenols, vitamins C and E, beneficial against the consequences of diabetes.



#### 4. DECODING AMD: EXPLORING LIPOFUSCIN ACCUMULATION AND METABOLOMICS INSIGHTS

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**Introduction.** Age-related macular degeneration (AMD) represents a multifactorial, degenerative pathology of the retina, with mechanisms that remain incompletely understood. Lipofuscin accumulation is believed to play a role in these mechanisms. AMD directly affects the visual analyzer, resulting in irreversible vision loss. Metabolomics plays a crucial role in unraveling the mechanisms associated with the development and progression of this pathology.

**Aim of study.** To elucidate the mechanism of action and the impact of lipofuscin (LF) accumulation on the progression of the disease and additionally, to identify the interrelationship between LF and alterations in the metabolic profile.

**Methods and materials.** The research is grounded in a comprehensive analysis of specialized literature sourced from databases including PubMed, NCBI, and Elsevier, spanning the last 5 years. The methodology involves a constructive critical examination, aligning with the designated keywords: lipofuscin, macular degeneration, and metabolomics.

**Results.** LF is acknowledged as a senescence-associated pigment, gradually accumulating in various tissues, notably in the retinal pigment epithelium (RPE). With phototoxic and cytotoxic potential, LF impacts homeostasis, induces oxidative stress accompanied by lipid peroxidation, and disrupts cholesterol metabolism. It was inferred the process by which antioxidants including carotenoids, vitamin E, resveratrol could prevent and provide protection against LF cytotoxicity and oxidative stress caused by A2E. Noteworthy is the investigation of *Bombyx mori*, a binding protein transporting zeaxanthin (ZEA) to the RPE, mitigating oxidative stress on photoreceptors. For the transport of ZEA and lutein (LUT) to the RPE, tween-40 (special micelles) was investigated, and for carotenoids: nanoemulsion liposomes and monoclonal antibodies. As LF fluorescence intensifies with age, indicating an increase in its concentration, ZEA has the role of reducing its lifetime, thus reducing the negative consequences. Another significant factor is JS-017, aiming to degrade A2E, suppressing pro-inflammatory and pro-apoptotic actions, along with NF- $\kappa$ B activation, thereby safeguarding the RPE.

**Conclusion.** Ongoing research seeks to discern whether the accumulation of lipofuscin (LF) is the primary cause of AMD or, alternatively, a consequence of these pathologies. New studies focus on the effect of chemiexcitation in identifying treatment strategies, as this process reduces the concentration of ocular LF. Consequently, it has been shown that an optimal level of carotenoids and retinoids is necessary to decrease the risk of AMD. Thus, currently studies are based on establishing targeted treatment strategies against different forms of AMD.



## 5. DISRUPTION OF THE IMMUNE RESPONSE IN PATIENTS WITH OBESITY DURING COVID-19



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**Introduction.** Obesity was one of the frequent comorbidities in hospitalized patients with SARS-CoV-2 infection. The recent studies of Covid-19 outcomes have noticed a correlation between obesity and more severe clinical evolution followed by worse outcomes. The disruption of the immune response was described as one of the multiple pathochemical mechanisms resulting in the development of a worse outcome.

**Aim of study.** Aim of study was to evaluate the severity of disrupted immune response as a possible prognostic factor in patients with Covid-19.

**Methods and materials.** The scientific articles (clinical trials and case reports), published between 2019 and 2023 in PubMed and Google Scholar databases, were analysed critically by using the key-words obesity, cytokines, Covid-19, immune response.

**Results.** The dysfunction of the immune system in severe SARS-CoV-2 is characterized by reduced production of interferons by innate immune cells in early stages followed by excessive production of cytokines by the adaptive immune system in the later ones. This dysfunction is exacerbated in obese COVID-19 patients, where the immune system fails to mount an effective antiviral response. SARS-CoV-2 employs NSP3, NSP16, and NSP1 to suppress the immune system. Through NSP3, it inhibits the phosphorylation, nuclear translocation and dimerization of the transcription factors IRF3 and IRF7, thus suppressing innate immunity. NSP16 inhibits mRNA splicing, reducing the recognition of viral RNA by helicase receptors. NSP1 prevents the formation of IFN $\beta$ , enhancing the degradation of IFN- $\beta$  mRNA. As a result, the production of IFN-induced genes (ISGs) is significantly reduced in obesity, leading to impaired immune responses.

**Conclusion.** The severe forms of COVID-19 were characterized by the dysfunction of the immune system. The early stages were followed by low production of interferons, that was essential for initiation of antiviral response, while in the later ones an excessive production of cytokines was identified, leading to an uncontrolled inflammatory response. It was shown that obesity exacerbated this dysfunction, resulting in more severe disease outcomes.



## 6. ESTROGEN THERAPY - METABOLIC AND CLINICAL CONSEQUENCES

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**Introduction.** Estrogen therapy has been a cornerstone in the treatment of various medical conditions, especially in menopausal management symptoms, preventing osteoporosis and addressing gynecological concerns. However, the administration of exogenous estrogen is not without its involvements, as the therapeutic benefits are accompanied by a spectrum of potential side effects. As the utilization of estrogen therapy becomes progressively widespread, a nuanced understanding of the associated risks is paramount. Among the risks, a significant focus has been established on its potential link to endometrial and breast cancers.

**Aim of study.** The aim of this review is to explore the intricate connection between estrogen therapy and the risks of developing endometrial and breast cancer.

**Methods and materials.** A comprehensive array of articles from PubMed, HINARI, NCBI, Google Scholar knowledge bases over the last ten years describing the quintessential role of estrogen in understanding the wide influence in oncogenesis and metabolic pathways. Usual used keywords: estrogen, breast cancer, endometrial cancer.

**Results.** The relationship between estrogen therapy and tumorigenesis is multi-faceted. Estrogen, while playing a fundamental role in mammary gland maturation, development, has been implicated in the growth of hormone receptor-positive breast cancers, highlighting the crucial contribution of estrogen receptors which are drivers of estrogen receptor positive breast cancer. However, when exposed to BRCA mutation or high levels of estrogens such as in the hormonal therapy, the proliferative effect of these steroids may cause cumulation of replication errors inducing to mutagenic and mitogenic consequences, triggering DNA damage in epithelial cells progression of breast cancer. Another target of estrogenic background is endometrial malignancy. Clinical evidence implies that combined hormone therapy, like estrogen and progestin, may decrease the risk of endometrial cancer in reference to estrogen therapy. This unbalance of progesterone insufficiency and estrogen predominance leads to amplification of estrogen receptors  $\alpha$  which promotes endometrial cell proliferation and increases the tissue hyperplasia, an obvious cancer condition.

**Conclusion.** By bringing into focus the intricate interplay between therapeutic benefits and drawbacks of estrogen therapy, this research seeks to unravel the intricacies of hormonal balance in the human body. The widely accepted viewpoint is that estrogen serves as an instigator for the advancement of cancerous cells, so the risk is additionally shaped by factors such as family history, genetic predisposition, the age of patient, duration of therapy and the medication doses.

## 7. EXPLORING THE ROLE OF N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE AS A DIAGNOSTIC BIOMARKER IN KAWASAKI DISEASE



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**Introduction.** Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is an acute febrile illness of unknown cause that stands out as a unique and challenging pediatric vasculitis, characterized by acute systemic inflammation and the potential for developing coronary artery complications. The most serious challenge is the development of coronary artery aneurysms, which are the predominant cause of morbidity and mortality among pediatric patients. Presently, the identification of KD relies on the manifestation of clinical features and lacks a distinct diagnostic biomarker.

**Aim of study.** Exploring the relationship between serum N-terminal pro-brain natriuretic peptide (NT-proBNP) blood concentrations and patients with acute and hyper-acute phases of KD.

**Methods and materials.** Were analyzed articles available on online medical platforms such as PubMed Databases, Medscape and other scientific documents provided on Google Scholar. The most relevant 20 articles were selected and investigated, including case studies, which were published between 2014 and 2023.

**Results.** The primary pathogenic occurrence in KD involves the activation of the innate immune system, leading to elevated secretion of interleukins (IL) 1, 4, 6, 10, and tumor necrosis factor (TNF). Given the significant evidence of myocardial engagement (often as myocarditis) in KD, new investigations have concentrated on exploring cardiac biomarkers, including serum NT-proBNP - a biomarker, as well as a prohormone, released from the heart's ventricles in response to enhanced pressure and volume. It reflects cardiac stress and its significantly elevated levels may indicate myocardial dysfunction in children and infants with KD in acute and hyper-acute ( $\leq 4$  days of fever, an insufficient duration for a conclusive diagnosis solely based on clinical criteria) phases of disease. In the acute phase of KD, NT-proBNP elevation primarily results from a combination of hemodynamic factors (myocardial stress due to pressure or volume overload and ventricular dysfunction) and non hemodynamic factors (myocardial inflammation, ischemia, and hypoxia). Higher NT-proBNP levels in the hyperacute phase are associated with an increased likelihood of coronary artery dilatation (CAD), which is a notable concern in KD. Furthermore, the lack of response to intravenous immunoglobulin (IVIG) therapy and the presence of coronary artery aneurysms (CAA) prove the elevated NT-proBNP levels, suggesting its prognostic utility.

**Conclusion.** NT-proBNP levels could serve as an alternative indicator for distinguishing Kawasaki Disease from other febrile and infectious conditions. Additionally, it may forecast the engagement of coronary arteries, enhancing diagnostic precision, especially in instances with incomplete diagnostic criteria.



## 8. FROM OXIDATIVE STRESS TO BONE HEALING: A BIOCHEMICAL INSIGHT INTO THE FRACTURE RECOVERY PROCESS

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**Introduction.** Within bone tissue, osteoclasts release oxidative stress (OS) compounds, vital for calcified tissue breakdown and bone healing after fractures. However, imbalances between oxidant compounds like reactive oxygen species (ROS) and antioxidant defenses, may result in bone loss and osteoporosis. Understanding the molecular intricacies of OS in bone tissue provides valuable insights into potential therapeutic approaches aimed at improving fracture recovery process and preserving overall bone health.

**Aim of study.** To explore the biochemical pathways involved in OS induced damage in bone tissue, impairing fracture healing and enhancing fracture risk.

**Methods and materials.** The groundwork of this scientific review is based upon a conscientious analysis of 20 publications from established databases like Science Direct, Springer Link, PubMed. All the publications were selected from a period spanning the last five years. Keywords used: oxidative stress, bone health, fracture healing.

**Results.** ROS, acting as signaling agents, can hinder osteogenic derivation, influencing the dynamic relationship between osteoblasts (OBs), responsible for synthesizing crucial organic and inorganic compounds (collagen, osteocalcin, osteopontin, hydroxyapatite) and osteoclasts (OCs) in bone tissue. Superoxide, as a member of the ROS family, has both physiological (redox signaling) and pathological (pro-apoptotic cascade, cellular necrosis) influence on bone tissue. Its reaction with nitric oxide (NO) produces peroxynitrite, which is highly reactive towards DNA and proteins. Given that OCs constitutively produce NO for their normal function, elevated superoxide levels directly affect the OB/OC ratio, thus affecting bone homeostasis. Impaired fracture healing due to OS can be reversed by means of specialized molecules like superoxide dismutase (SOD), glutathione peroxidase (GPx), vitamin C (ascorbic acid), vitamin E ( $\alpha$ -tocopherol) and carotenoids ( $\beta$ -carotene). The mitochondrial protein SIRT3, essential for OC and OB differentiation, proves noteworthy in the inflammatory and ischemic microenvironment during the initial stages of fracture healing, diminishing OS and favoring bone formation. Post-fracture damage to tissue generates a conspicuous amount of free radicals following the ischemia-reperfusion process, which emphasize the importance of SIRT3's OS decreasing properties, and suggest its relevance in mitigating the harmful effects of oxidative damage in the aftermath of a fracture.

**Conclusion.** Exploring the biochemical intricacies of OS in the context of bone healing offers valuable insights into the mechanisms underlying fracture recovery. Increased levels of plasma biomarkers of oxidant status, like malondialdehyde, marks the need for lifestyle/dietary changes and/or antioxidant supplementation, as to prevent fracture damage directly or indirectly (diseases like osteoporosis, diabetes mellitus, age-related hormonal modifications).



## 9. GLUTEN INTOLERANCE. CELIAC DISEASE.



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**Introduction.** Celiac disease (CD) is an immune-mediated inflammatory condition of the small intestine that occurs in genetically predisposed individuals when they are exposed to gluten (a plant-based protein component found in grains). The disease has a variable incidence, with a worldwide prevalence of approximately 1:100; Statistics have shown that 70% of patients reported with celiac disease are female. Distribution of population groups, reported that HLA DR3 Phenotype occurs in 70-90% of patients.

**Aim of study.** Celiac disease is an autoimmune disorder and an inflammatory disease that manifests itself upon ingestion of gluten in the upper small intestine and is characterized by the gradual deterioration of the intestinal mucosa. Biochemically, it highlights an immune reaction, which is mediated by certain cells of the immune system, which attack the cells of the small intestine.

**Methods and materials.** It has been scientifically proven that the prevalence of celiac disease in the majority of the population ranges from 0.5% to 1%. Medical science researchers have determined that the incidence is higher among people with autoimmune disorders. Patients with type 1 diabetes are prone to celiac disease, and in the last 20 years there has been a considerable increase in cases.

**Results.** Inflammation and nutrient malabsorption, in addition to diarrhea, distention and abdominal pain, lead to damage to many organs and systems such as: iron deficiency leading to anemia, vitamin deficiencies, osteoporosis, dermatitis herpetiformis, tooth enamel defects, chronic fatigue, joint pain, poor growth, delayed puberty, infertility or repeated miscarriages, and other autoimmune disorders. A number of neurological problems have also been associated with celiac disease; these include migraines, depression, attention deficit/hyperactivity disorder and epilepsy. The diagnosis of celiac disease is established: a) upon the histological finding of an increased number of intraepithelial T lymphocytes; of crypt hyperplasia; of the expansion of regenerative epithelial crypts until the total disappearance of villi; b) positive serological testing (IgA tissue transglutaminase, anti-deamidated gliadin-related peptides IgA and Ig G, IgA antibodies); c) by molecular genetic testing of HLA-DQA1 and HLA-DQB1 which can be determinant or of HLA-DQ2 and HLA-DQ8) which can be used to exclude celiac disease.

**Conclusion.** Celiac disease (CD) is a very common disorder but in most cases it starts silently. Many of the patients are identified through screening of at-risk groups or after the onset of symptoms of malabsorption, rarely for complications associated with the disease. The diagnosis of CD and its differential diagnosis is made from integrations between typical histological findings and clinical, serological and immunological features. The Corazza-Villanacci system is a useful method to assess mucosal damage and response to gluten-free diet in patient follow-up.

**Keywords.** Celiac disease, intestinal mucosa, gluten intolerance.



## 10. GLUTS GENETIC DEFECTS AS CAUSES OF DIABETES

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**Introduction.** Diabetes mellitus (DM) is a chronic disease marked by insulin secretion or action defects. The cause of diabetes can be genetic defects of glucose transporters – GLUT, the most characteristic being the GLUT2 defect, associated with Fanconi-Bickel syndrome (FBS). Until now approximately 144 cases of FBS with 70 different variants of the SLC2A2 gene have been reported.

**Aim of study.** The purpose of the study is to elucidate and describe the consequence GLUT dysfunction and the occurrence of diabetes.

**Methods and materials.** PubMed, Hinari, GoogleScholar. Published between 2018-2023. Keywords: „GLUT”, „Diabetes”.

**Results.** Deficiency or absence of GLUT-encoding genes has been intensively studied in mice, then making the tangent to deficits in humans. In humans, SLC2A2 gene defects are the cause of FBS. Those with this condition display a phenotype mirroring that of mice lacking the SLC2A2 gene. Mainly expressed in tissues that play important roles in glucose homeostasis: renal tubular cells, enterocytes, pancreatic  $\beta$ -cells, hepatocytes. Dysfunction and decreased GLUT2 expression lead to dysglycemia (fasting hypoglycemia, postprandial hyperglycemia, glucose intolerance), hepatomegaly, galactose intolerance. The cause of DM in these patients would be the GLUT2 defect in: 1) pancreas - insulin secretion deregulation; 2) liver - disturbances in glucose homeostasis, accumulation of fat and glycogen in the liver, problems in glucose synthesis.

**Conclusion.** DM is a chronic multifactorial disease that requires a vast study to identify the primordial cause of the disease. The primordial cause can be hidden in the human genetic code, and the treatment is closely related to it. Future GLUTs studies will be required for a better understanding of underlying molecular mechanisms of dysglycaemia in FBS and other GLUTs deficiencies.

## 11. HORMONAL DISTURBANCES IN THE POLYCYSTIC OVARY SYNDROME



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**Introduction.** Polycystic ovary syndrome (PCOS) is an endocrine pathology that affects women of reproductive age. Hormonal disturbances in the PCOS are the central cause of heterogenous clinical presentation involving infertility, metabolic disorders and ovarian dysfunction.

**Aim of study.** To identify and emphasize the most important hormonal disorders that have a pathogenetic impact in PCOS.

**Methods and materials.** Current articles from PubMed, ScienceDirect and Medscape databases were included and evaluated in the study, using keywords such as: polycystic ovary syndrome, androgens, insulin.

**Results.** The study has revealed that the compromised function of the hypothalamic-pituitary-ovarian axis leads to an increased pulsatile secretion of gonadotropin-releasing hormone (GnRh), favoring the synthesis of the luteinizing hormone (LH). Therefore, LH will influence an increased anabolism of androgens in the theca cells of the ovarian stroma, causing hyperandrogenism. Elevated levels of androgens can lead to the tissue insulin resistance, directly affecting insulin signaling mechanisms. Thereby, tissue insulin resistance can cause a compensatory state of hyperinsulinism which will intensify LH-induced androgen synthesis. On the other hand, it will inhibit the hepatic production of sex hormone-binding globulin, thus increasing bioavailability of free testosterone.

**Conclusion.** Hormonal disturbances in the polycystic ovary syndrome are responsible for various metabolic changes. The long-term persistence of these metabolic errors can provoke dyslipidemia, obesity, cardiovascular events and type 2 diabetes mellitus.



## 12. INTERPLAY OF GLUCOSE METABOLISM AND ITS INFLUENCE ON MYOPIA DEVELOPMENT

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**Introduction.** Available data suggests that by the year 2050, approximately half of the global population will experience nearsightedness, marking myopia as a genuine worldwide epidemic. To this day, the impact of nutrition on the progression of myopia has been lacking attention, but new researches are done in order to strengthen the idea, that high glycemic load carbohydrate diets, resulting in hyperglycemia and hyperinsulinemia, may potentially disrupt the proper development of the sclera and choroid, thus inducing lasting alterations in the progression of myopia during the critical period of childhood growth.

**Aim of study.** Elucidating the correlation between glucose metabolism, and its role in shaping the progression of myopia.

**Methods and materials.** The analysis encompassed 15 studies conducted between 2013 and 2023, exploring the correlation between Western dietary patterns, characterized by increased intake of high glycemic load foods, and the risk of developing myopia in various countries.

**Results.** Countries such as the United States, Australia, Sweden, Hungary, Switzerland, Iceland, France, Austria, Germany, Denmark, the Czech Republic, the Netherlands, Spain, Belgium, Finland, and New Zealand, collectively classified as the “Western diet countries”, have been noted to experience enhancing incidences of hyperglycemia, insulin resistance (IR), hyperinsulinemia, and type 2 diabetes (DM). These diseases are a cause of glucose metabolism malfunction, typically arising from the dysregulation of two crucial hormones in glucose homeostasis – insulin and glucagon. In type 2 DM, insulin secretion is defective and delayed, coupled with resistance to its action. This affects the removal of glucose from the bloodstream to cell membranes and hinders the glucose uptake in the liver. Proper insulin secretion is also of major importance due to the fact that it exerts control over glycolysis and gluconeogenesis, stimulating the former and reciprocally inhibiting the latter, by catalyzing the expression of phosphofructokinase, pyruvate kinase, and fructose 2,6-bisphosphate. Hyperglycaemia itself induces IR and beta-cell dysfunction, leading to glucotoxicity. Furthermore, the studies confirmed that myopia is more prevalent in diabetic patients compared to non-diabetic individuals, with ongoing debates among researchers regarding the influence of the resulting hyperinsulinemia from high glycaemic load carbohydrate diets on different growth factors resulting subsequently in scleral growth.

**Conclusion.** Even though the fundamental mechanism of refractive changes remains unclear, studies do indicate a connection between compromised glucose metabolic control resulting from the adoption of a Westernized lifestyle and the onset of myopia. These findings also serve as evidence that, in addition to genetic factors, myopia development can be mitigated in individuals through proper nutritional education and food choices.



### 13. KEY NON-RECEPTOR TYROSINE KINASES IN ADAPTIVE IMMUNITY



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**Introduction.** Non-receptor tyrosine kinases (NRTKs) are cytosolic enzymes, grouped together as a subclass of protein tyrosine kinases (TKs) due to their lack of an extracellular and transmembrane domain, unlike receptor tyrosine kinases (RTKs) – another sub-class of TKs. By means of protein phosphorylation NRTKs activate different signaling pathways, thus regulating a number of cellular functions: growth, proliferation, differentiation, adhesion, migration and apoptosis. Crucial is NRTKs involvement in the adaptive immune system by regulation of B and T cells activation and response.

**Aim of study.** This study aims to identify NRTKs that are specifically involved in the activation and regulation of adaptive immunity cells.

**Methods and materials.** A literature review has been performed using PubMed, Elsevier and Hinari databases. A number of 45 scientific articles related to the keywords have been identified, out of which only 37 met the inclusion criteria in the research topic.

**Results.** Non-receptor tyrosine kinases include 10 families, classified according to their structural and functional differences. Among these, several NRTKs from SYK (ZAP-70, SYK), TEC (ITK, TXK, BTK) and SRC (LCK, FYN, LYN) families have shown to play a critical role in adaptive immunity. In T cells, a signaling cascade is initiated when a T cell receptor (TRC) recognizes a foreign antigen associated with a major histocompatibility complex (MHC). This results in the activation of LCK and FYN, which phosphorylates the ITAM motifs present in the signal-transducing CD3 subunit of the TRC. The recruitment of ZAP-70 then takes place and a series of signaling events are initiated by phosphorylation of two adaptor proteins – LAT and SLP-76. These adaptors create a signaling complex by recruiting several important signaling molecules, including ITK, that activates phospholipase (PLC)  $\gamma$ 1. The subsequent activation of downstream signaling pathways leads to the activation of second messengers and an increase in intracellular  $Ca^{2+}$ . Transcriptional modifications are triggered following these events, leading to the production of interleukin-2 (IL-2) and T cell proliferation. ITK and TXK are also involved in T helper cell differentiation, with ITK being expressed in both Th1 and Th2 cells and TXK expression being limited to the Th2 cells only. Unlike T cells, B cells don't require an intermediate MHC for antigen recognition. Thus, after B cell receptor (BCR) binds to the antigen, ITAM domain is exposed and phosphorylated by the LYN kinase. SYK is then recruited and phosphorylates BLNK to form a multi molecular signaling complex with PLC- $\gamma$ 2 and BTK. This activates PIP2 and, similar to TCR signaling, leads to second messengers production and intracellular  $Ca^{2+}$  increase, the net result being B-cell proliferation and antibody production.

**Conclusion.** Non-receptor tyrosine kinases play a central role in B and T cells proliferation and regulation, thus knowledge of NRTKs effects and site of action opens new possibilities for addressing the immune disorders.



## 14. MECHANISMS OF ACTION AND METABOLIC EFFECTS OF ANTICOAGULANTS

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**Introduction.** Anticoagulant drugs antagonize coagulation and are used to prevent or prolong the clotting time. Nowadays physicians from different fields possess a broad panel of multiple anticoagulants to meet a patient's individual needs.

**Aim of study.** It was to analyze different types of anticoagulants and to mark the clinical importance of their different mechanisms of action and metabolism.

**Methods and materials.** This was an analytical literature review of scientific articles related to the keywords: anticoagulant drugs, oral anticoagulants, direct inhibitors, anticoagulant treatment. Through a comprehensive search on PubMed with the filters: clinical-trial, meta-analysis, in the last 5 years; 58 scientific articles were selected for the research topic.

**Results.** Scientific evidence has shown that anticoagulant therapy is currently based on four classes of agents: heparins, vitamin K-dependent antagonist (e.g., warfarin), direct thrombin inhibitors (dabigatran), and factor Xa inhibitors (rivaroxaban). Both heparins and oral anticoagulants (vitamin K antagonists) are efficacious antithrombotic drugs but their use has well-known limitations. They are not selective, acting on a broad range of substrates in the coagulation cascade. In addition, heparins are a heterogeneous mixture of different molecules purified from animal tissues and with variable antithrombotic activity. Oral anticoagulants showed adverse side effects in the form of tissue bruising, gastrointestinal bleeding, and intracranial hemorrhage whereas parental anticoagulants are having side effects in the form of thrombocytopenia and thromboembolism due to antibody-mediated platelet aggregation. Rivaroxaban competitively inhibits Factor Xa, and prevents the progression of the coagulation cascade through the final common pathway, inhibiting thrombin generation. Rivaroxaban is eliminated via both metabolic degradation and renal elimination as an unchanged drug, without modifications in the patient's homeostasis. Ximelagatran is the first oral direct synthetic thrombin inhibitor with favorable pharmacokinetics and pharmacodynamics; with rapid onset of action, fixed dosing, stable absorption, apparent low potential for medication interactions, and no requirement for monitoring of drug levels or dose adjustment. Its efficacy and safety versus the established treatment with vitamin K antagonists in the prevention of stroke in patients suffering from atrial fibrillation is being investigated.

**Conclusion.** The present review highlighted the clinical importance and the difference between the mechanisms of action of anticoagulant drugs. Through their inhibitory action at different levels of the coagulation cascade, anticoagulants determine various effects that can influence the therapeutic decision and require an individualized approach to each case.

## 15. METABOLIC PECULIARITIES OF IMMUNOTHERAPEUTIC MEDICINES (CHIMERIC ANTIGEN RECEPTOR T CELLS) USED IN CANCER TREATMENT (B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA)



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**Introduction.** In the dynamic realm of cancer therapeutics, many studies explore the metabolic nuances of Chimeric Antigen Receptor (CAR) T-cell therapy in treating B-cell acute lymphoblastic leukemia (B-ALL). Understanding these metabolic intricacies is pivotal for refining therapeutic strategies and improving patient outcomes. Advanced techniques and protocols guide this investigation-based review.

**Aim of study.** to explore the most recent dates about the metabolic intricacies in Chimeric Antigen Receptor (CAR) T-cell therapy for B-cell acute lymphoblastic leukemia (B-ALL), which are guiding treatment optimization and enhancing patient outcomes.

**Methods and materials.** This involved conducting an analytical literature review based on scientific articles using specific keywords: Chimeric Antigen Receptor (CAR) T-cell therapy and B-cell acute lymphoblastic leukemia (B-ALL). Through a comprehensive search on PubMed with the filters: clinical-trial, meta-analysis, in the last 5 years; 34 scientific articles were selected for the research topic.

**Results.** Scientific articles based on information unveiled significant metabolic alterations in Chimeric Antigen Receptor (CAR) T-cell therapy for B-cell acute lymphoblastic leukemia (B-ALL). CAR-T cells targeting CD-19, a key antigen expressed in B-cell malignancies- are the most commonly used combination to achieve the optimal therapeutic effect. There are distinct metabolic alterations induced by CAR-T cell therapy, revealing a pronounced shift towards glycolysis with concurrent suppression of oxidative phosphorylation. Notably, CD-28 and CD-3 coreceptor engagement played a crucial role in shaping the metabolic profile, influencing the magnitude of glycolytic flux and subsequent effector functions. Results of many studies highlight the intricate interplay between CD-19 targeting and coreceptor signaling in modulating CAR-T cell metabolism. Additionally, dynamic changes in amino acid metabolism and lipid biosynthesis took place, underscoring the multifaceted impact of immunotherapeutic interventions on cellular metabolic pathways. These findings provide valuable insights for optimizing CAR-T cell therapy efficacy and managing potential adverse effects.

**Conclusion.** The action of Chimeric antigen receptor (CAR) T-cell therapy for B-cell acute lymphoblastic leukemia (B-ALL) is based on complex mechanisms, including at the metabolic level. Deep knowledge of these modifications will allow optimization of therapeutic management and patient outcomes.



## 16. NONALCOHOLIC FATTY LIVER DISEASE PATHOGENIC MECHANISMS AND NON-INVASIVE DIAGNOSIS

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**Introduction.** Non-alcoholic fatty liver disease (NAFLD) affects a quarter of the world's population and is one of the most common liver diseases. It can progress to liver cirrhosis and hepatocellular carcinoma (HCC). Clinical scoring systems that can be used in general practice as initial screening tools may also be useful in diagnosing NAFLD.

**Aim of study.** To identify the pathogenic mechanisms of NAFLD and non-invasive diagnostic methods.

**Methods and materials.** Was conducted the analysis of the open access scientific publications from PubMed, Google Scholar, NCBI, ScienceDirect databases published between 2018-2023 using the keywords NAFLD, pathogenic mechanisms, and non-invasive diagnosis.

**Results.** NAFLD is considered to be the hepatic manifestation of metabolic syndrome, thus directly associated with insulin resistance, obesity, hypertension and dyslipidemia. NAFLD is often undiagnosed, and patients present to the doctor in late stages, when treatment options are limited. The gold standard for detecting steatosis/fibrosis is liver biopsy, but the method has limitations that include risks to the patient's life. Therefore, new non-invasive strategies are needed. Modern medicine presents a spectrum of informative non-invasive methods that allow timely diagnosis of NAFLD. Among such methods advanced imaging techniques to quantify steatosis (transient elastography and magnetic resonance imaging) and scores calculated from haematological indices and biochemical markers discriminating between different disease stages (fibrosis index-4 (FIB-4), NAFLD fibrosis score (NFS), BARD score, FibroTest, Steatotest, ActiTest, AshTest, NASH Test, HepatoScore, hepamet fibrosis score (HFS), APRI, Fibromax) may be mentioned.

**Conclusion.** Knowledge of the pathogenic mechanisms of development and of the non-invasive NAFLD diagnostic methods is essential for prevention of disease progression.. Early identification of high-risk patients by measuring a number of NAFLD-specific biomarkers is the main goal in preventing complications of hepatic steatosis. **Keywords:** hepatic steatosis, non-alcoholic fatty liver disease, pathogenic mechanisms, non-invasive diagnosis.



## 17. THE BIOCHEMICAL RELATIONSHIP BETWEEN STRESS AND AUTOIMMUNITY



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**Introduction.** Stress is a state of concern or psychological tension which appears because of a difficult situation. Stress is a normal response of our body that helps us survive all the challenges and threats of our day-to-day life, and increases our productivity and efficiency in our work and studies. However, we can talk about the positive effect of stress only if it's an occasional, small amount of stress. Being stressed daily has a contrary effect, with harmful consequences on mental and physical health. Stress has been associated with the majority of diseases that can cause death, like cardiovascular diseases, cancer, suicide, and even accidents. A lot of scientists consider that, nowadays, 70- 85% of all pathologies are caused by continuous and long-term stress. One of the most affected areas is immunity, leading to a lot of autoimmune diseases, like rheumatoid arthritis, diabetes, systemic lupus erythematosus, autoimmune thyroiditis.

**Aim of study.** To research the biochemical reactions between stress and autoimmune diseases, with possible identification of pathological pathways and with the possibility of preventing, or finding new mechanisms of treatment for these diseases.

**Methods and materials.** The presented work was created based on a review of literature exploring bibliographic sources, using articles and manuals published in databases: Google Scholar, PubMed, NCBI, and ScienceDirect.

**Conclusion.** Autoimmune diseases are debilitating pathologies that affect around 8 % of people worldwide, and that require a bigger amount of the state's budgets each year. Preventing them it's easier than treating them, taking into account the fact that the majority of them have no cure. So, by reducing the level of stress, by practicing psychotherapy, or finding other activities that aim to relax, and reduce the stress such as sports, yoga, reading, and walks in the open air we obtain lower levels of cytokines, IL-6, cortisol, and pro-inflammatory markers. At the same time, we reduce the probability of developing autoimmune diseases, and people who have healthy habits, and maintain just the positive effect of the stress, with the increase of productivity.



## 18. THE INFLUENCE OF TYPE 2 PREGESTATIONAL DIABETES MELLITUS ON THE FETUS

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**Introduction.** The prevalence of type 2 diabetes among women of reproductive age is increasing. According to the latest data from the International Diabetes Federation in 2019, one in six live births is affected by hyperglycemia during pregnancy, that represents a risk for the intrauterine development of the fetus, and despite significant advances in glycemic control of pregnancies with diabetes, adverse outcomes for the fetus are still very common.

**Aim of study.** To elucidate the biochemical mechanisms of influence of type 2 diabetes on the intrauterine development of the fetus with the aim of improving diagnosis, treatment and preventing the occurrence of adverse effects.

**Methods and materials.** To achieve the proposed goal, a bibliographic search was performed using 10 bibliographic sources, between the 2018-2023, including those of the Medical Scientific Library of USMF "*Nicolae Testemitanu*", data of the electronic libraries such as PubMed, MedScape, Medline, Diabetes Care and Diabetologia.

**Results.** Maternal hyperglycemia increases apoptosis in the embryo, which is specifically observed in neuroepithelial cells. An important role also has oxidative stress, which increases the BAX:BCL-2 ratio- indicator of apoptosis level in glioma cells, associated with the increase of cytochrome C in mitochondria and the activation of caspase 3 in embryonic cells. Increased glucose transfer from mother to the fetus induces fetal hyperglycemia, pancreatic  $\beta$ -cell hyperplasia, and consequently fetal hyperinsulinemia (FHI). Insulin influences glucose uptake and lipogenesis via the glucose transporter GLUT-4, expressed in fetal adipose tissue and induces fetal macrosomia. The placenta acts as a passive conduit for maternal glucose to the fetus, especially towards the end of gestation. Therefore, increased glucose transport from diabetic mothers, together with FHI, stimulates fetal triacylglycerol formation and deposition of excess fetal adipose tissue. FHI can delay lung development in the fetus of a diabetic mother. A physiological level of insulin plays a role as a stimulatory hormone in the synthesis of surfactant, but a high level of insulin can inhibit the lipid components of the surfactant: phosphatidylcholine (PC), phosphatidylglycerol (PG) and phosphatidylinositol (PI) and low level of surfactant protein expression. Thus, it decreases the ability of surfactant to reduce alveolar surface tension, increasing the risk of respiratory distress syndrome (RDS). Pregnant women usually have a pathological weight gain, associated with a high production of pro-inflammatory cytokines and adipokines - TNF- $\alpha$ , IL-1 $\beta$ , IL-6, responsible for insulin resistance.

**Conclusion.** Maintaining maternal glucose in optimal parameters is essential for the normal development of the fetus by reducing the risk of congenital malformations and preventing postpartum complications.

**Keywords.** Maternal hyperglycemia, diabetes, insulin resistance, fetal hyperinsulinemia.

## 19. THE INTERPLAY OF GROWTH HORMONE, INSULIN-LIKE GROWTH FACTORS, AND CANCER SUSCEPTIBILITY: A MEDICAL PERSPECTIVE



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**Introduction.** GH and IGF-I, known for promoting growth, are under scrutiny for their potential involvement in cancer progression. While we understand their normal effects, the disruption caused by these factors and their role in cancer initiation remain mostly unknown. Studies on transgenic mice and cancer cell lines indicate their contribution to tumor development.

**Aim of study.** To elucidate the intricate signaling pathways of growth hormone (GH) and insulin-like growth factors (IGFs) in cancer, providing foundational insights for targeted therapeutic interventions and advancing precision in cancer management.

**Methods and materials.** This scientific review is founded on a meticulous examination of 20 specialized articles retrieved from reputable databases such as: PubMed, Bioscientifica, and ScienceDirect over the last five years. Conducted with precision, it aligns with key words like: growth hormone, insulin-like growth factors, and cancer.

**Results.** GH and IGFs activate signaling pathways like Ras/MAPK and PI3K/Akt, fostering cell cycle progression and inhibiting apoptosis, which are critical in cancer development and progression. Abnormal activation of these pathways, often due to mutations in key elements like IGF-1R, can lead to uncontrolled cell division and oncogenesis. GH and IGFs also significantly contribute to angiogenesis, the formation of new blood vessels, crucial for tumor growth. They interact synergistically with factors like Vascular Endothelial Growth Factor (VEGF), amplifying angiogenesis and aiding in tissue repair and growth. In cancer, these hormones help tumor cells evade apoptosis and immune system detection, with IGFs exhibiting strong anti-apoptotic properties. Moreover, chronic hyperinsulinemia, a consequence of insulin resistance and metabolic disorders, characterized by elevated IGF-1 levels, is known to intensify the tumor-favorable environment in cancer. The tissue-specific effects of GH and IGFs vary across different cancer.

**Conclusion.** Ongoing research unravels the intricate role of GH and IGF-1 as a critical nexus in oncology, highlighting their significant impact on cell proliferation, survival, and apoptosis. Innovative multidisciplinary strategies like IGF-trap molecules and GH receptor inhibitors offer promising avenues in disrupting pivotal signaling pathways. Comprehensive knowledge of the intricate hormonal balance of cancer paves the way for innovative therapeutic strategies in the combat against the disease.



## 20. THE INVOLVEMENT OF micro-RNAs IN CARDIOVASCULAR PATHOLOGIES

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**Introduction.** Micro-RNAs are short molecules of ribonucleic acid with significant regulatory functions in controlling gene expression within eukaryotic cells. These small molecules play a crucial role in post-transcriptional regulation, influencing various cellular processes. Currently, circulating miRNAs are recognized as potential diagnostic biomarkers and emerging therapeutic targets for cardiovascular diseases. Their stability in body fluids and differential expression patterns in various cardiac conditions make them promising candidates for further research and clinical applications in the field of cardiology.

**Aim of study.** Understanding the involvement of miRNAs in cardiovascular disease development is crucial for enhancing diagnostic precision, predicting disease progression, and pinpointing effective therapeutic targets. This exploration aims to refine diagnosis, prognosis, and therapeutic strategies in the managing cardiovascular conditions.

**Methods and materials.** A comprehensive literature review has been performed, covering the past decade and incorporating information from 30 sources. These sources encompassed materials from the Scientific Medical Library of "*Nicolae Testemitanu*" State University of Medicine and Pharmacy. Additionally, electronic libraries, including PubMed, Elsevier, Cambridge Journals Online, Hinari, Medline and MedScape have been utilized to gather relevant data.

**Results.** Several studies have underscored the pivotal role of micro-RNAs in both diagnosing and treating cardiovascular diseases. Notably, elevated levels of miRNA-636, miRNA-380, and miRNA-17 have been observed in the plasma of individuals experiencing acute myocardial infarction (AMI). Additionally, miRNA-126, miRNA-37, and miR-221 show increased levels in heart failure patients. Furthermore, the prognostic efficacy of miRNA-182 surpasses that of natriuretic peptide and high-sensitivity C-reactive protein in heart failure (HF). Other studies have shown that MiR-499 had a more precise and significantly higher predictive value than the most reliable biomarkers for AMI: c troponin I (cTnI) and creatinkinase MB (CK-MB). In mouse models, intramyocardial injection of vesicles containing miRNA-99 has demonstrated a preventive effect on hypoxia-induced apoptosis and promoted autophagy. This intervention has resulted in improved left ventricular function and increased survival during four weeks after AMI.

**Conclusion.** Presently, miRNAs have the potential to be employed for diagnostic and therapeutic purposes in various cardiovascular diseases. They exert their influence on specific cellular pathways or processes through structures like liposomes, vesicles, or viral vectors designed for intracellular miRNA delivery.



## 21. THE ROLE OF GUT MICROBIOTA METABOLITES IN ATHEROSCLEROSIS



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**Introduction.** Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide. Changes in gut microbiota metabolites (GMM) is linked to the development of CVD, which includes atherosclerosis, hypertension, and heart failure. Some GMM, such as trimethylamine-N-oxide (TMAO), bile acids (BA), short-chain fatty acids (SCFA), coprostanol and others influence the atherosclerosis.

**Aim of study.** To research the biochemical pathways of GMM involved in triggering atherosclerosis, thus proving the possibility to use them as predictive markers in cardiovascular disease diagnosis and as treatment targets.

**Methods and materials.** Research, study and analysis of numerous articles from PubMed, NCBI, HINARI, Google Scholar databases over the last ten years.

**Results.** TMAO has been correlated with an increased risk of atherosclerotic cardiovascular disease. Following ingestion of animal products rich in phosphatidylcholine, carnitine and choline, gut microbiota (GM) can use them as a carbon source. GM enzyme trimethylamine (TMN) lyases cleave C-N bond of these nutrients releasing TMA waste product, which is further processed into TMAO by the liver enzyme flavin-dependent monooxygenase 3. TMAO activates NF- $\kappa$ B in endothelial cells and leads to increased expression of vascular cell adhesion molecule-1 (VCAM-1), trigger factor for atherosclerosis. TMAO enhances macrophage migration and adhesion due to VCAM-1, thus forming foam cells in plaque that contain cholesterol. Unbalanced GM, could lead to reduced deconjugation of primary bile acids to secondary bile acids, which can increase primary bile acids such as chenodeoxycholic acid, suppress enzyme cholesterol 7- $\alpha$ -hydroxylase, then downregulate bile acid production from cholesterol and so its concentration is elevated. SCFAs can lower serum lipid levels by blocking cholesterol synthesis and redirect them to the liver. SCFAs are a microbial-derived metabolites that are mostly formed by Bacteroidetes phylum fermentation of complex carbohydrates. SCFA-producing bacteria can be reduced in certain CVD, dysbiosis of patients with hypertension determined by atherosclerosis. Besides this, species of gut microbiota, such as *Eubacterium coprostanoligenes*, *Bacteroides dorei*, *Lactobacillus* sp. possess the ability to convert absorbable cholesterol to coprostanol, a reduced non-absorbable sterol, which is excreted in feces.

**Conclusion.** As previously mentioned, there is overwhelming evidence that GMM influences CVD-relevant phenotypes, such as atherosclerosis. Therefore the state of GM must be taken into account during atherosclerosis prevention, diagnosis and treatment.



## 22. THE ROLE OF LEPTIN IN THE PATHOGENESIS OF METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE

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**Introduction.** Metabolic dysfunction-associated fatty liver disease (MAFLD) has become one of the leading causes of end-stage liver disease. Its pathogenesis is not fully understood, but leptin may contribute to the development and progression of this disease, by multiple pathogenic pathways. Leptin, a polypeptide primarily synthesized by adipocytes, is mainly responsible for maintaining energy homeostasis. Circulating leptin levels reflect primarily body energy stores and secondarily acute changes in energy intake.

**Aim of study.** To elucidate the role of leptin in the pathogenesis of MAFLD.

**Methods and materials.** There have been relevant articles related to leptin, adipose tissue, and metabolic dysfunction-associated fatty liver disease, published between 01.01.2020-01.11.2023, on search engines PubMed and ScienceDirect.

**Results.** In the beginning, leptin was described as an anti-obesity hormone, but the studies revealed that leptin has pleiotropic effects. It is involved in body weight control, glucose metabolism, immune function, and metabolic programming. In a healthy state, leptin has anti-steatotic effects, preventing lipids storage in the liver and promoting their mobilization. Moreover, leptin improves insulin sensitivity, and suppresses hepatic glucose production and lipogenesis. The leptin level is directly proportional to the amount of adipocytes. Even though most of the MAFLD patients have an increased body mass index and high leptin level, it promotes lipotoxicity, insulin resistance, and up-regulation of proinflammatory cytokines. One reason could be the development of leptin resistance that provides a critical link between adipose tissue, liver, insulin resistance, and inflammation. In this way, hyperleptinemia and leptin resistance contribute to worsening hepatic steatosis and promote the progression to steatohepatitis and liver fibrosis.

**Conclusion.** Leptin represents a key milestone in the pathogenesis of MAFLD, which is considered the hepatic manifestation of the metabolic syndrome. Leptin level is positively associated with the severity of MAFLD and could be used as an independent predictor of the presence or development of this disease.

**Keywords.** Leptin, adipose tissue, fatty liver disease.

## 23. THE ROLE OF JAK-INHIBITORS IN THE TREATMENT OF RHEUMATOID ARTHRITIS



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**Introduction.** Rheumatoid arthritis is a systemic chronic autoimmune inflammatory disease characterized by persistent destructive synovitis with extra-articular manifestations. Despite the recent development and recommended use of inhibitors of TNF and IL-6, as well as the B cell depletion of CD20 cells as remedies for RA, a large number of patients remain unresponsive and intolerable to these medications. JAK-inhibitors are the newest drugs with a targeted mechanism of action and promising clinical results.

**Aim of study.** To elucidate the role of JAK-inhibitors as the long-term method and to evaluate the possible complications associated with this type of biological DMARD in order to identify clinically effective treatment for rheumatoid arthritis.

**Methods and materials.** The scientific articles ranging from 2000-2022 published in PubMed, NCBI, BioMed Central databases, describing the nature and role JAK-inhibitors, the biochemical mechanisms and physiological effects were explored using key phrases “Janus-kinase receptors”, “JAK-inhibitors”, “rheumatoid arthritis”, “monotherapy”.

**Results.** According to EULAR 2019 guidelines, JAK-inhibitors represents the 2nd line medication recommended in refractory to MTX monotherapy, moderate or high disease activity. Tofacitinib, an inhibitor of JAK1/JAK3, have shown response rates that were significantly higher compared to MTX monotherapy. The Tofacitinib + MTX combination was noninferior, establishing the same results as the standard adalimumab + MTX combination cure. Applying the modified van der Heijde Total Sharp Score, the monotherapy with Tofacitinib overcame MTX monotherapy in limiting the progression damage. The blockage of IL-6 by targeting JAK-STAT3 induced by Tofacitinib has diminished the pain within 24h. The published data show that frequent side effects of JAK-inhibitors were the infections of upper/lower respiratory and urinary tracts, cytopenia being caused by JAK-inhibitors that act through JAK-2 pathway.

**Conclusion.** The JAK-inhibitors have shown the same efficiency and safety profile as other types of bDMARDs. Oral administration, as well as early relief of pain prove JAK-inhibitors as promising treatment option increasingly used for proper medication of rheumatoid arthritis.



## 24. UNLOCKING THE SHIELD: EXAMINING RETINAL PROTECTION VIA MACULAR CAROTENOIDS' ANTIOXIDANT CAPACITY

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**Introduction.** The human retina, crucial for vision, is highly susceptible to oxidative damage due to its exposure to light and high metabolic activity. Three macular xanthophylls (MXs) – zeaxanthin (Z), lutein (L), and meso-zeaxanthin (MZ) – accumulate in the macula and play a pivotal role in the antioxidant defense system within the human retina. They mitigate oxidative damage, thereby preventing or slowing the progression of retinal diseases such as age-related macular degeneration, a leading cause of irreversible vision loss.

**Aim of study.** To explore the role of macular carotenoids in protecting the retina by examining their antioxidant functions and to analyze their physical and chemical actions as antioxidants, elucidating their specific contribution, considering the four photoprotective mechanisms of MXs.

**Methods and materials.** The study comprehensively analyzed 30 scientific articles published in the last decade out of a selection of 73. The following databases were used: PubMed, ScienceDirect, and NCBI to ensure a reliable groundwork for interpreting results. Articles lacking in relevance were ousted.

**Results.** The distinctive chemical structures of macular carotenoids define their properties. Various roles of MXs in providing photoprotection were outlined, encompassing physical and chemical antioxidant actions: blue-light filtration by absorbing 40–90% of incident short-wavelength, reactive oxygen species (ROS) interception, chain-breaking action, and quenching of excited triplet state of photosensitizers and singlet oxygen. While chemical quenching deactivates only a small fraction of singlet oxygen because it utilizes MXs and disrupts their original structure, the efficiency of MXs in physically quenching singlet oxygen is notably higher. The selective distribution of Z at the foveal center indicates its superior antioxidant capacity over L, with a ratio of Z/L at 2.4/1, compared to 1/2 in the periphery. This difference is attributed to the increased exposure to intense light and elevated metabolic activity in the central region. However, the combined administration of antioxidants proves to be more effective in preventing oxidative stress (OS) than their separate use.

**Conclusion.** MXs exhibit a dual nature of antioxidant properties, chemical and physical, that contribute to their effectiveness in safeguarding against oxidative damage. Maintaining the structural integrity of these compounds enhances protection. Given the vulnerability of the retina to ROS due to its structure and location, as well as the impact of aging on OS, MXs are emerging as promising agents both in the prevention and treatment of various retinal degenerative diseases. Thus, understanding their antioxidant capacities becomes imperative in outlining strategies to maintain retinal health via appropriate dietary intake and supplementation.



## 25. UNRAVELING THE MOLECULAR SIGNALING PATHWAYS IN GLIAL TUMORS WITH METHYLATED MGMT PROMOTERS



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**Introduction.** Most gliomas are typically assessed using imaging methods. A recent advancement in this regard involves the integration of biomarkers in conjunction with imaging techniques, such as 18F-FDG-PET-based radiomics for evaluating the methylation status of the MGMT promoter and relaxation-compensated multipool CEST MRI for assessing the mutation status of the IDH gene. The MGMT gene is situated on the 10q26 chromosome band. Its promoter lacks the TATA and CAT boxes, similar to other housekeeping genes. MGMT status can be determined through either a biopsy or by examining the DNA present in circulating extracellular vesicles (EVs) in the bloodstream. Methylation-specific PCR (MSP) is the preferred method for identifying DNA polymorphisms in the MGMT promoter.

**Aim of study.** To elucidate the biochemical mechanisms underlying chemotherapy susceptibility in patients with MGMT promoter methylation.

**Methods and materials.** After entering the keywords 'biochemical pathways in MGMT methylated glioma' into the PubMed database were retrieved a total of 1,255 results. Following a thorough review of the initial 100 sources, 37 of them were deemed relevant and considered for further analysis.

**Results.** O6-methylguanine-DNA methyltransferase (MGMT), often referred to as the, plays a pivotal role in repairing O6-guanine lesions in gliomas. Chemotherapeutic agents like temozolomide (TMZ), temozolomide/lomustine (TMZ/CCNU), bevacizumab/irinotecan (BEV/IRI), and enzastaurin induce cytotoxic lesions on O6-guanine, N7-guanine, and N3-adenine. Methylation of the MGMT promoter plays a crucial role in increasing susceptibility to the aforementioned chemotherapeutics in glioma treatment. An exception to this principle is observed in gliosarcomas, gray zone tumours (comprising alternating methylated/unmethylated cells) and among the patients in specific geographic regions, such as Spain. Notably, the methylation of the MGMT promoter and its expression are not influenced by a person's race. The explanation for population-based independence of MGMT promoter methylation status lies in the polymorphism of other housekeeping genes (XAF1, AEBP1, MTHFR, IFT25, HMGA2) that protect the glioma stem cells from apoptosis.

**Conclusion.** The MGMT promoter methylation status serves as a relative prognostic marker, as it does not apply universally to the more complex forms of gliomas. The typical glioma types have a linear correlation of survival in means of the number of methylations in the promoter region of the MGMT gene.

**Keywords.** O6-methylguanine-DNA-methyltransferase, gliomas, marker



## 26. VITAMIN D METABOLISM IN HEPATORENAL SYNDROME

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**Introduction.** Hepatorenal syndrome (HRS) is a consequence of liver cirrhosis, which is the final stage of chronic liver disease with irreversible damage and the existence of regenerating nodules. Renal function is disturbed in HRS, as evidenced by decreased renal flow, decreased glomerular filtration rate (GFR), ascites, and a rise in The blood creatinine level. All of these are well-known characteristics of HRS, however vitamin D3 dysmetabolism is also present in HRS.

**Aim of study.** To elucidate the biochemical pathway of vitamin D metabolism in HRS patients, establish the biochemical changes in the metabolism of vit. D3 of the body in both physiological and pathological conditions, to improve the diagnosis and to develop the effective treatment methods.

**Methods and materials.** To achieve the proposed goal, it has been constructed through a synthesis of literature published from 2018 to 2023 using 10 bibliographic sources, including those of the Medical Scientific Library of USMF "*Nicolae Testemitanu*", data of the electronic libraries such as PubMed, Medline, Medscape, Hinari and Biomed Central.

**Results.** The primary organs involved in the metabolism of vitamin D3 are the liver and kidney. In HRS, both organs lose their ability to metabolize the vitamin D3. It is not only the cause of renal damage but also results from hepato synthetic insufficiency of vitamin D2 (25(OH)D) and vitamin D binding protein (VDBP). Reduced levels of liver 25-hydroxylase enzymes, namely cytochrome P27A CYP27A (found in mitochondria) and cytochrome P2D25 (CYP2D25) (found in microsomes), have been reported to lower the bioavailability of circulating 25(OH)D. Additionally, decreased levels of renal enzyme 1 $\alpha$ -hydroxylase (CYP27B1) in renal tubules have been connected to the production of calcitriol (1,25(OH)2D3) that is closely associated to VDBP and vit.D2. Since the body uses vitamin D3 to regulate calcium homeostasis, deficiency in both vitamin D3 and VDBP limits the amount of calcium absorbed in the intestines. In response, the parathyroid hormone (PTH) activates the osteoclast in the bone to release stored calcium, which can occas

**Conclusion.** It has been observed that a deficiency in vitamin D3 manifests itself in cases of HRS. The observed phenomenon causes disruptions across several physiological systems, including the musculoskeletal, immune, endocrine, calcium, phosphorus regulatory, and nervous systems. In HRS may be used vitamin D supplementation but it doesn't help the patient very much, liver transplantation is the ultimate treatment option in HRS.

## **III. DERMATOVENEROLOGY SECTION**



*„Un medic este apreciat atunci când știe a trata pacientul, a trata sufletul celui în suferință și a trata colegii cu respect. Acestea sunt posibile doar când îți cunoști, vorbești și scrii profesia. Aici încercați să obțineți aceasta apreciere!”*

*"A doctor is appreciated when they know how to treat the patient, treat the soul of the one suffering, and treat colleagues with respect. These are only possible when you know, speak, and write about the profession. Here you try to achieve this appreciation!"*

**Mircea Bețiu,**

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## 1. BASAL CELL CARCINOMA, CLINICAL ASPECTS

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**Introduction.** Basal cell carcinoma (BCC) is a non-melanocytic skin cancer that originates from the basal cells of the epidermis. This condition is characterized by a continuously increasing incidence, attributed to the aging process of the population and extensive exposure to sunlight radiation. Predominantly located on the facial area, BCC can cause significant morbidity and disfigurement, highlighting its impact on the quality of life for affected patients.

**Aim of study.** Determining the specific clinical signs that characterize BCC.

**Methods and materials.** To identify relevant articles, databases such as NCBI, PubMed, and Medscape were utilized.

**Results.** Clinically, BCC presents with various morphologies. Cutaneous lesions in BCC can appear in different forms, such as nodules, plaques, or ulcers, affecting the skin surface. The color of BCC lesions can vary from pale pink to dark red. The edges of BCC-induced lesions can be pearly or translucent. BCC may cause mild bleeding or ulcers. Ulcers can form crusts and exhibit a dragging appearance. BCC tends to develop more frequently in sun-exposed areas, such as the face, ears, neck, and scalp. Generally, BCC develops slowly and rarely spreads to other parts of the body. Typically, BCC is not associated with intense pain. Patients often notice a change in skin texture or appearance rather than intense physical discomfort. Exposure to UV radiation is the primary risk factor for the development of basal cell carcinoma.

**Conclusion.** Specific features are characterized by an 85% occurrence of tumors on the face, head, and neck. Other characteristic features of BCC tumors include waxy papules with a central depression and a pearly appearance. Subsequent erosion or ulcers, often central and pigmented, persist with bleeding, especially when traumatized. Represented by surface telangiectasias and slow growth: 0.5 cm in 1-2 years.



## 2. BULLOUS PEMPHIGOID, CLINICAL ASPECTS AND TREATMENT



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**Introduction.** Bullous pemphigoid is a chronic, potentially fatal autoimmune skin disease that results in generalized pruritic bullous eruptions in older patients. Local and systemic glucocorticosteroid drugs are prescribed as initial therapy. Most patients require long-term maintenance therapy with immunosuppressive drugs.

**Aim of study.** Evaluation the standards for providing specialized medical care to patients with bullous pemphigoid with drugs that combine the optimal effectiveness-safety ratio.

**Methods and materials.** Systematic syntheses, meta-analyses, scientific articles, manuals, guidelines, clinical protocols published in the country and abroad in the last 10 years in the following databases were used as data sources: UpToDate, HINARI.

**Results.** Topical corticosteroids such as clobetasol cream 0.05% should be used for localized disease, and the prescribed dose of systemic drugs may be reduced. Patients with generalized disease often require systemic prednisone 60–80 mg orally once a day, tapered over several weeks to a maintenance dose of  $\leq 10$ –20 mg/day. Most patients go into remission within 2–10 months, but further treatment may be required for several years before complete recovery. For bullous pemphigoid, the anti-inflammatory activity of certain medications, such as combination therapy with tetracycline or minocycline and nicotinamide, is sometimes effective. Other treatment options include monotherapy with dapsone, sulfapyridine, or erythromycin. Intravenous immunoglobulins are sometimes used. For patients with generalized or treatment-resistant disease, and in some cases to reduce the dose of corticosteroids in chronic cases and reduce the side effects of the latter, immunosuppressants such as methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil and cyclosporine can be prescribed. Biological drugs that can be used are rituximab and omalizumab.

**Conclusion.** To avoid or minimize the use of systemic corticosteroids, patients are prescribed high-potency topical corticosteroids whenever possible. To reduce the dose of corticosteroids, therapy with anti-inflammatory, immunosuppressive and biological drugs can be used.



### 3. HERPES ZOSTER IN PATIENTS WITH HIV/AIDS. EPIDEMIOLOGICAL, CLINICAL AND TREATMENT FEATURES

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**Introduction.** Herpes Zoster represents the phenotype, conditioned by the reactivation of the Varicella zoster virus from its latent phase. It manifests itself as viral ganglioneuritis with damage to the intervertebral ganglia, ganglia of the cranial nerves, skin, posterior and anterior horns of the gray matter. Herpes zoster is more common and more severe in HIV-infected patients because cellular immunity is reduced.

**Aim of study.** Assessment of the clinical features, epidemiology and treatment of Herpes Zoster in people with diagnosed HIV/AIDS, hospitalized in the Dermatovenerology and Communicable Diseases Hospital, in the Republic of Moldova, during the 2018-2023 period.

**Methods and materials.** Data from the observation sheets of 143 patients, with diagnosed HIV/AIDS, hospitalized in the Dermatovenerology and Communicable Diseases Hospital in Chişinău, Republic of Moldova, were investigated according to the National Clinical Protocol. The following aspects were analyzed: signs of Herpes Zoster in patients with HIV/AIDS which includes the presence of vesicular eruptions in the intercostal region, in the cervical region, in the back region or post-zoster neuralgia. The data in the study was collected using laboratory examinations and clinical-anamnestic data as investigative methods.

**Results.** Among the investigated batch of patients, 50.3% (72) were men, 49.7% (71) - women, the average age being 43 years and 2 months. Post-zoster neuralgia was diagnosed in (107) 73.4% of the studied batch. Of those hospitalized with Herpes Zoster 26.6% (38) were in the active form, of which 57.9% (22) manifested vesicular eruptions in the intercostal region, 23.7% (9) manifested rashes in the back region and 18.4% (7) manifested rashes in the cervical region. The diagnosis of HIV was based on the following laboratory tests: anti-HIV antibodies, HIV DNA test and viral culture. More informative is the HIV DNA test (PCR). The diagnosis of Herpes Zoster is based on laboratory tests: VZV DNA test (PCR) and VZV viral culture.

**Conclusion.** HIV/AIDS remains a major public health issue worldwide. The evolution of HIV infection is highly variable, thus it has a large number of potential complications. One such complication which is investigated in this study is Herpes Zoster. Following the study of the characteristics associated with Herpes Zoster in patients with HIV/AIDS, hospitalized in the Republic of Moldova some conclusions regarding which phenotype is more prevalent. The data collected in this study once again indicate the importance of timely detection of specific Herpes Zoster symptoms, in order to prevent irreversible consequences.

**Keywords.** Post-zoster neuralgia, Herpes Zoster, HIV.

#### 4. FREQUENCY AND CHARACTERISTICS OF COMMON CUTANEOUS VESICULOBULLOUS DISORDERS IN THE REPUBLIC OF MOLDOVA



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**Scientific advisor:** Betiu Mircea, MD, PhD, Associate Professor, Head of Department of Dermatovenerology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The vesiculobullous pattern represents a large group of predominantly immune-related disorders, morphologically characterized by blistering eruptions localized within or below the epidermis. In this study, we will focus on the most commonly studied diseases of this type including pemphigus vulgaris, bullous pemphigoid, and dermatitis herpetiformis.

**Aim of study.** The main objective of this study is to examine the occurrence of the mentioned disease, the age group that is mainly affected, and the gender predominance in the Republic of Moldova. This updated research is crucial for effective resource allocation, gaining a deeper understanding of the significance of these autoimmune disorders, and identifying patterns and risk factors associated with these conditions.

**Methods and materials.** A retrospective observational study was conducted to assess the frequency of these disorders with data derived from patient registries at the Dermatological and Communicable Diseases Hospital in Chisinau, Republic of Moldova, during the 2019-2022 period.

**Results.** During the above-mentioned period, the Dermatological and Communicable Diseases Hospital in Chisinau, Republic of Moldova identified and registered 87 patients diagnosed with the noted diseases. Among these, 14 cases were attributed to dermatitis, 50 cases to pemphigus vulgaris, and 25 cases to bullous pemphigoid. The study revealed a higher occurrence of blistering diseases among women compared to men. Additionally, it was observed that the majority of patients affected by these disorders were over the age of 55. Among the patients studied, a significant proportion also presented with comorbid conditions such as hypertension, diabetes mellitus, and various forms of hepatitis.

**Conclusion.** Based on the institutional statistical analysis conducted in this study, it is evident that a detailed evaluation of vesiculobullous dermatological disorders is of utmost importance. This research not only enhances the provision of healthcare services, but also contributes to the development and implementation of preventive strategies, ultimately improving the well-being of individuals affected by blistering diseases. The proven results of this study have significant implications for accurate diagnosis, optimal management, and improved patient outcomes in the challenging field of bullous autoimmune dermatoses.



## 5. NEUROSYPHILIS CASE REPORT

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**Introduction.** Neurosyphilis is relatively rare in last decades, due to the epidemiological measures in force. Because of the variety of clinical manifestations, from mild behavioral disturbances to paralysis and death, neurosyphilis can be a diagnostic challenge.

**Case presentation.** A 42-year-old man, arrives at the hospital with suspected cerebro-vascular accident, which is not confirmed. The patient found with positive RPR, HIV negative, is referred to the Dermatology and Communicable Diseases Hospital. The patient was without lesions on the skin and mucous membranes, difficult to assess the moment of primary infection. From obvious manifestations - cognitive disorders, disorientation in time and space, passive position. The MoCA cognitive test was 9 points. The diagnosis was established based on CSF analysis - CSF VDRL positive titer 1:8; TPHA passive hemagglutination positive 4+, Westernblot IgG positive. On CT examination - punctate atheromatous deposits at the level of bilateral carotid siphons; no intracranial pathological foci were found. Treatment with high-dose penicillin was performed, but the cognitive symptoms did not change during and after the treatment.

**Discussion.** As presented in this case, cognitive decline was not significantly improved after treatment, but the neurological reevaluation of the patient at least 6 and 12 months after treatment is interesting.

**Conclusion.** Cognitive decline and personality disorders must be taken into consideration for the diagnosis of central nervous system infections, especially neurosyphilis. There are not enough data on the degree of reversibility of the neurological changes, related to the duration of the syphilitic infection.

**Keywords.** Neurosyphilis, cognitive disorders.



## 6. PSYCHO-EMOTIONAL STATE BEFORE AND AFTER THE INJECTABLE PROCEDURE



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**Introduction.** Persons who would like a change of the exterior, including those who are often afraid to start the aesthetic intervention for reasons when they want to stop the procedure, will look worse or are afraid of the pain caused by the intervention. The idea of beauty is as old as human culture and is self-expression. Injectable procedures as an aesthetic treatment are all about improving a person's beauty with minimal pain and no downtime.

**Aim of study.** To analyze personality type, and kind of fear before aesthetic intervention and satisfaction after cosmetic procedures.

**Methods and materials.** The cross-sectional study consisted of examination and questionnaires which include Ten-Item Personality Inventory (TIPI), Rozenberg self-esteem scale (SES), Fear Questionnaire (FQ), Questionnaire of cosmetic procedures, and Facial Line Treatment Satisfaction Questionnaire (FTSQ) by Likert Scale-7 and performance of injectable aesthetic procedures.

**Results.** Subjects over 18 years of age were included in the research, so 75 individuals were apportionment as needing cosmetic procedures. They answered the questions in the inventory. By TIPI self-disciplined -53,3%, extravert - 14,7, careless - 1,3, conventional - 30,7% cases. Rozenberg SES: self-esteem low - 37,3, medium - 34,7, high- 28,0 % cases, FQ slightly disturbing fear was 73,3%, definitely disturbing fear - 24,0% and very disturbing fear - 2,7% cases, Questionnaire of cosmetic procedures: the fear was high in 8,0%, moderate - 18,7 and low- 61,3%, no fear -12,0% cases. Performed procedures: lip augmentation - 68,0%, filling nasolabial folds 5,3% and its combination 26,7% cases. Analyzing the results according to Facial Line Treatment Satisfaction Questionnaire by Likert Scale we found 21.4% had side effects (local hyperemia minimal oedema), no sign of the procedure- 45.3% and lack of downtime in 33.3% cases.

**Conclusion.** Satisfaction after aesthetic procedures according to Likert Scale was divided in 3 domains: good and very good satisfaction - 94.7%, dissatisfaction - 1.3%, average - 4.0% subjects. Patients were unsure to stay in this aesthetic office were 8,0%, disagree expressed only 1.3% and agree - 90,7% subjects.



## **IV. ENDOCRINOLOGY SECTION**

***„Congresul MedEspera reprezintă o oportunitate pentru tinerii cercetători de a-și promova realizările științifice, de a-și dezvolta cunoștințele și abilitățile practice în domeniul medicinei și de a stabili relații de prietenie și de colaborare cu semenii lor din întreaga lume. Prin dedicarea voastră, perseverența și excelența în domeniul medical, deschideți noi orizonturi și aduceți contribuții semnificative care schimbă paradigmele medicale. Aceste lucrări reflectă angajamentul vostru pentru inovație și pentru îmbunătățirea continuă a practicii medicale. Sperăm ca descoperirile prezentate aici să inspire și să conducă la progrese remarcabile în medicina modernă.”***

***„The MedEspera Congress represents an opportunity for young researchers to promote their scientific achievements, to develop their knowledge and practical skills in the field of medicine, and to establish friendships and collaborations with their peers from around the world. Through your dedication, perseverance, and excellence in the medical field, you are opening new horizons and making significant contributions that change medical paradigms. These works reflect your commitment to innovation and continuous improvement in medical practice. We hope that the discoveries presented here will inspire and lead to remarkable progress in modern medicine.”***

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## 1. A CASE OF SUSPECTED LIPODYSTROPHY IN AN INSULIN-RESISTANT PATIENT



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**Introduction.** Lipodystrophy syndrome, a rare disease associated with leptin deficiency and characterized by disproportionate fat loss, is linked to metabolic disorders like dyslipidemia and severe insulin resistance. It is often accompanied by liver steatosis and can be familial or acquired. Diagnosis is built mainly on clinical findings and confirmed by genetic analysis, but it can be tricky sometimes as the extent of symptoms depends on the level of lipodystrophy.

**Case statement.** A 55-year-old female, known with type 2 diabetes mellitus (DM2), presents to the endocrinology department in November 2021 with complaints of extreme hunger, increased preprandial blood glucose of 12-15 mmol/l, postprandial glucose - 20-30 mmol/l, and high blood pressure of 140/70 mmHg. From anamnesis, she has been on insulin therapy since the onset of the disease in 2012 and has lost 20 kg of body weight mainly from subcutaneous fat in the upper and lower extremities. Besides DM2 she suffers from hepatitis B. Family history reveals that the patient's twin sister has the same constellation of hyperglycemia and hyperlipidemia, also her younger sister passed away at age 26 due to cirrhosis of unknown etiology. Her blood lipid profile shows abnormal triglyceride levels up to 86.39 mmol/l ( $N < 2.3$  mmol/l). The ApoB gene mutation was suspected and the test was positive. Insulin doses were up-titrated, but despite administering 160 units of insulin, normal blood glucose levels were not achieved. During 2021-2023 she was hospitalized multiple times in the endocrinology department due to elevated blood sugars, hepatology – due to worsening liver function tests, and surgery department – due to episodes of acute pancreatitis. Glycemic control was finally achieved using a basal-bolus regimen, including U-300 insulin in combination with sodium-glucose cotransporter-2 inhibitors.

**Discussions.** Irregular distribution of body fat, family history, and extreme insulin resistance raised the suspicion of a lipodystrophy syndrome. Familial hyperlipidemia was another presumptive diagnosis, but positive gene mutation of ApoB does not correlate with the unusually increased triglyceride levels. Genetic analysis would confirm the suspected diagnosis based on the clinical picture.

**Conclusion.** Lipodystrophy is an uncommon syndrome, but this might be an underestimation, as many cases remain unrecognized due to the phenotypic variability of this syndrome. The affected storing capacity and endocrine function of adipocytes result in insulin resistance and ectopic fat accumulation with severe metabolic complications. Raised awareness amongst clinicians can lead to early suspicion and diagnosis of the syndrome and as a result – better management of comorbidities.

**Keywords.** Dyslipidemia, Insulin resistance, Lipodystrophy syndrome, triglycerides, Type 2 Diabetes mellitus.



## 2. A CASE STUDY OF CARDIOVASCULAR DISORDERS AND ITS CONSEQUENCES IN A PATIENT WITH DIABETES MELLITUS TYPE 2 WITH METABOLIC DYSLIPIDEMIA.

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**Introduction.** The major aim of this case study is to analyse and understand the complicated relationship between cardiovascular disease, in a patient diagnosed with diabetes mellitus type 2 with a mixed complication stage along with dyslipidemia. Aim of Study: This study emphasis on the relationship between metabolic dyslipidemia and type 2 diabetes mellitus is one of the primary insights that may be achieved in order to comprehend complications within the cardiovascular system.

**Case statement.** A 77 year-old male patient presented with angina and discomfort. A complex medical history of poor compensated chronic stages of diabetes mellitus type 2 and dyslipidemia was noted, which also affected the cardiovascular system. The negative consequences of cardiovascular system such as: atrial fibrillation, major septal right bundle branch block, signs of LV and RV hypertrophy, and ischemic repolarization changes in the anterior region in the patient. Studying this patient's condition deserved a thorough analysis of physical examinations and paraclinical investigations, as well as the patient's diagnostic trajectory.

**Discussions.** This case study report describes a 77-year-old male patient with a complex medical history. Clinical documentation used in the study includes hospital medical records, diagnostic investigation reports such as blood panels, ECGs, Echocardiography. The patient's admission to the cardiology department the vital signs and further investigations and diagnostic tests were performed. Results: The patient's baseline physical characteristics were as follows: height: 176 cm; weight: 98 kg; body mass index (BMI): 31.6 kg/m<sup>2</sup>. His vital signs were as follows: blood pressure: 110/70 mmHg; body temperature: 36.6 (C); pulse: 120 beats/min; respiratory rate: 20 breaths/min; and SpO<sub>2</sub>: 92%. Further investigations found a combination of poor compensated diabetes mellitus type 2, and dyslipidemia (cholesterol = 287 mg/dL). A three periodic glycemic profile of a day revealed 07:00– 7.8 mmol/l, 13:00– 7.9 mmol/l, 17:00, 17:00– 10.8 mmol/l. The electrocardiogram shows atrial fibrillation, major septal right bundle branch block, signs of LV and RV hypertrophy, and ischemic repolarization changes in the anterior region.

**Conclusion.** Despite the overall condition of the patient, there were difficulties that remained to be addressed in managing complications related to cardiovascular complications. The complexity of this case is due to the chronic conditions of the patient, such as dyslipidemia associated with diabetes mellitus, which may also result in cardiovascular complications. This study emphasizes the need and the necessity for having a multidisciplinary approach in resolving cases such as this due to their complexity.



### 3. AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 2: A CASE REPORT



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**Introduction.** Autoimmune polyglandular syndromes are classified into two major subtypes, each characterized by involvement of specific endocrine glands. The autoimmune polyglandular syndrome type 2 is defined by the presence of at least two of the following endocrinopathies: Addison's disease, type 1 diabetes mellitus and autoimmune thyroiditis. Other autoimmune diseases belonging to the syndrome are: primary hypogonadism, myasthenia gravis, celiac disease, pernicious anemia, alopecia, vitiligo. The prevalence of APS-2 is estimated to be 1 : 20.000 in the general population.

**Case statement.** This study focuses on a complex case of Autoimmune Polyglandular Syndrome Type 2 (APS-2) in a 54-year-old female, characterized by: chronic autoimmune thyroiditis with hypothyroidism; followed by classic clinical findings for primary adrenocortical insufficiency which led to the diagnosis of Addison disease, and secondary amenorrhea at the age of 39, likely due to autoimmune primary ovarian insufficiency (POI). Hormone replacement therapy was initiated. Subsequently symptoms of hyperglycemia occurred in the context of excessive administration of glucocorticoids and steroid diabetes was diagnosed. C peptide value was within the normal reference values. Metformin was initiated, but glycemic control progressively worsened which questioned diagnosis. Elevated glutamic acid decarboxylase (GAD) antibodies >1000 were determined and the diagnosis of type 1 diabetes was established.

**Discussions.** This is a clinical study presenting a challenging case of autoimmune polyglandular syndrome type 2 involving 4 endocrinopathies in a 54 years old woman. The interplay between the thyroid, ovarian, and pancreatic dysfunctions underscores the need for an integrated diagnosis and treatment approach. The development of type 1 diabetes mellitus and Addison disease in a patient with Hashimoto thyroiditis typifies the unpredictable nature of autoimmune disorders and the challenge in achieving optimal endocrine balance. Occurrence of secondary amenorrhea in a woman below the age of 40 should raise awareness of autoimmune POI, which may occur as part of type 2 APS. The patient's response to treatment, particularly the stabilization of glycemic levels, highlights the effectiveness of personalized management strategies. The study emphasizes the progressive nature of APS-2 as well as the diagnostic challenges which illustrate the condition's multifaceted nature and the critical role of personalized approach in diagnosis and management.

**Conclusion.** The study highlights the rapidly progressive nature of untreated APS-2 and the critical role of personalized treatment plans, including hormone replacement and glycemic control.



#### 4. BIOETHICAL ASPECTS OF THE REHABILITATION OF PATIENTS WITH TYPE 2 DIABETES IN CONDITIONS OF ANTI-PANDEMIC RESTRICTIONS.

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**Introduction.** Rehabilitation is essential for many health conditions such as acute stroke, cardiac events and endocrine diseases and others. It is estimated that due to the SARS COV-2 pandemic, an estimated range of 1.3–2.2 million people in Europe had to interrupt their rehabilitation treatments. Shortly after the start of the pandemic, there were reports of an increase in new-onset diabetes presentations. Having diabetes was a risk factor for worse COVID-19, but also having COVID-19 was a risk factor for newly diagnosed diabetes and hyperglycemic emergencies. An essential support in rehabilitation in covid is that of bioethics.

**Aim of study.** Evaluation of the specificity of rehabilitation in patients with type 2 diabetes during the period of anti-pandemic restrictions through the lens of bioethical benchmarks.

**Methods and materials.** Data from the scientific literature were studied, identified from the databases PubMed, Cochrane, Scopus, international clinical protocols, about 50 sources.

**Results.** According to studies, it has been shown that during the COVID-19 pandemic, rehabilitation services and outpatient visits were affected, practically suspended, general healthcare services were reduced, face-to-face consultations were restricted, virtual consultations were switched to and some aspects of the consultation such as blood tests were omitted. A study of 25 million patients in the UK reported a significant reduction in type 2 diabetes diagnoses during the pandemic period. A recent report from the National Health Services (NHS), UK, World Health Organization (WHO) outlined the ethical obligations of healthcare providers during the pandemic in three distinct categories: moral, professional, legal. Guiding principles were emphasized to guide the conduct of ethics during the Covid-19 period: social and clinical value, favorable risk-benefit ratio, independent review, informed consent and respect for patients. Rehabilitation should be performed in a self-supervised manner via telemedicine. The most valuable bioethical benchmarks were the principles of information, autonomy, therapeutic integrity, vulnerabilities and the doctor-patient relationship. In some cases, it may be wiser to delay admission to rehabilitation until patients are no longer at risk of spreading COVID-19 to uninfected people, but poor blood glucose control is associated with serious complications, including mortality, and improving the control of risk factors is a priority.

**Conclusion.** Anti-pandemic restrictions have imposed new conditions on the rehabilitation act. The pandemic has highlighted the importance of guidance according to bioethical principles.

**Keywords.** Bioethics, rehabilitation, COVID-19, pandemic, anti-pandemic restrictions

## 5. CLINICAL MANIFESTATIONS AND COMPLICATIONS OF ACROMEGALY



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**Introduction.** Acromegaly is a rare disease that requires a specific approach in evaluating clinical symptoms and complications.

**Aim of study.** Evaluation of clinical manifestations, onset and complications of acromegaly for management tactics.

**Methods and materials.** Retrospective study based on medical charts of acromegaly patients hospitalized during the period 2018-2023 at the "Endocrinology" department, IMSP Republican Clinical Hospital "Timofei Mosneaga".

**Results.** The study included 28 patients: 20 women (71.4%) and 8 men (28.6%). Primary complaints included: facial changes (28.5%), headaches (25%), increased shoe size (21.4%), enlargement of extremities (17.8%), amenorrhea and galactorrhea (7.1%). The appearance of the first symptoms across all patients was on average at the age of 39.6 years, including 46.3 years in women and 25.5 years for men. The onset of acromegaly was due to the pituitary adenoma in all cases, of which: macroadenoma (60.7%), microadenoma (14.3%), unspecified (25%). Later, the most frequent symptoms detected during the disease were: headache (64.3%), visual disturbances (60.7%), facies acromegalica (57.1%), leg enlargement (53.6%), arthralgias (50%), increased shoe size (42.9%), hand enlargement (42.9%), weakness (39.3%), nose enlargement (35.7%), prognathism (28.6%), macroglossia (25%), pain in the spine (25%), xerostomia (21.4%), emotional lability (21.4%), vertigo (21.4%), prominent zygomatic/supraorbital arches (21.4%), hypertrophied tongue (17.9%), edema (17.9%), myalgia (17.9%), sleep disorders (17.9%), nocturnal snoring (17.9%). The detected complications were: cardiomyopathy (67.9%); arterial hypertension (57.1%); diseases of the thyroid and parathyroid glands (42.8%); type II diabetes (35.7%); sensory disorders (28.6%); diseases of the joints (28.6%); hyperlipidemia (25%); secondary hypogonadism (21.4%); nephrolithiasis (17.9%); benign formations (25%), specifically: prostate hyperplasia (7.1%), uterine myoma (7.1%), MEN-1 syndrome (3.6%), osteoma (3.6%), angiolioma (3.6%).

**Conclusion.** Acromegaly occurs 2.5 times more often in women compared to men. The results for the primary complaints correspond to the current literature, except for amenorrhoea and galactorrhea. In most cases, macroadenoma was detected. The most frequent symptoms detected during the disease were associated with local tumor effects, hormonal disorders and changes in metabolism. The major complications of acromegaly are the following: cardiomyopathy (67.9%); arterial hypertension (57.1%); diseases of the thyroid and parathyroid glands (42.8%); type II diabetes (35.7%).



## 6. DIETARY HABITS OF PATIENTS WITH ISCHEMIC HEART DISEASE

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**Introduction.** Ischemic heart disease continues to be the leading cause of mortality, morbidity and high hospitalization rates in both high-income and developing countries. According to data from the World Health Organization, almost 18 million people die from cardiovascular disease (CVD) every year, the mortality rate is 32.7% and it is the most common cause of death in developing countries. Unhealthy diet leads to CVD and its progression. Diet changes in patients with chronic and acute coronary syndromes (ACS) can reduce the mortality and cardiovascular events.

**Aim of study.** The aim of the study is to examine the relation between dietary habits and acute coronary syndrome.

**Methods and materials.** Retrospective study of 88 patients with acute coronary syndrome hospitalized during the period September 2023- november 2023 in Cardiac Catheterization Department, IMSP Institute of Cardiology. The dietary habits of patients with ACS were analyzed using a questionnaire of 60 questions including nutrition score (CONUT) that represents poor nutritional status and has been identified as an indicator of adverse outcomes. The patients were classified into: normal (0–1), mild (2–4), moderate–high (5–8), and marked high (9–12).

**Results.** The average age of the patients was  $65.61 \pm 8.4$  years, 68.2% of them are men. The average body mass index was  $29.27 \pm 3.86$ . Dyslipidemia (LDL > 2.6 mmol/l) was detected in 66 patients (75%) with an average  $3.39 + 1.14$  mmol /l. CONUT scores were mild in 78 patients (88.6%) and moderate-high in 10 patients (11.3%). Rare consumption of fish (once a week) was mentioned in 76 patients (86.36%) and frequent consumption of red meat (> 3 times/week) in 66 patients (75%).

**Conclusion.** Acute coronary syndrome is more susceptible in men over the age of 50 years. Weight gain, dyslipidemia, frequent red meat consumption and rare fish consumption increase the risk for acute coronary syndrome. In all patients with ACS it was appreciated an increased CONUT score.



## 7. FUNDOPLICATION-INDUCED HYPERINSULINEMIC HYPOGLYCEMIA



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**Introduction.** Hypoglycemia is often diagnosed in diabetic patients; however, this diagnosis is far rarer in non-diabetic patients. Hypoglycemia in non-diabetic persons is polyetiological. Patients often require an extensive history and array of investigations due to similar clinical presentations with insulinomas. Frequent hypoglycemic episodes in non-diabetic patients with a history of gastric surgery should raise concern for Late dumping syndrome (LDS).

**Case presentation.** A 52-year-old woman was admitted to Republican Clinical Hospital in September 2023 with complaints of tremors, hyperhidrosis, palpitations, headache, foggy vision, fatigue, and low tolerance to exertion. She attributes her symptoms to hypoglycemia. Further workup confirms episodes of low blood glucose (1.3 mmol/l). She states these episodes have been ongoing for the last 5 years. Her medical history highlights the presence of an adrenal tumor and a Nissen fundoplication in 2018. The patient mentions that the hypoglycemic episodes appear 1-1.5 hours after the intake of food. Available imaging of the abdomen reveals a unilateral adrenal mass and no signs of tumor formation in/around the pancreas. A 72-hour fasting test was conducted and no hypoglycemia was registered. Bloodwork revealed normal C-peptide and insulin levels. Follow-up of the adrenal tumor included metanephrine levels, aldosterone/renin ratio assessment, and low-dose dexamethasone test. Results demonstrate a non-secretory adrenal tumor. The absence of hypoglycemia during the 72-hour fast, coupled with normal insulin and C-peptide levels, excluded an insulinoma, and late dumping syndrome (LDS) was suspected given a history of gastric surgery and postprandial hypoglycemia. Adjustments of the patient's diet subsequently resolved the episodes of hypoglycemia.

**Discussions.** The work-up of a non-diabetic patient with episodic hypoglycemia is complex given the multifactorial etiologies. Things like alcohol or drug administration, liver, renal or primary adrenal failure, neoplasia, insulin/insulin receptor antibodies, insulinomas, and bariatric surgery could lead to hypoglycemia. Evaluation of the patient excluded endogenous hyperinsulinemia and ruled out most causes of hypoglycemia, apart from LDS – a possible adverse effect of the patient's gastric surgery.

**Conclusion.** This case represents the challenges of diagnosing hypoglycemia in non-diabetic patients. LDS can occur after gastric surgery. Patients experience episodes of postprandial hypoglycemia. A clinician's awareness of the adverse effects of gastric surgery and patient education on proper diet following surgery may help prevent LDS.

**Keywords.** Hypoglycemia, gastric surgery, late dumping syndrome



## 8. INCIDENCE, RISK FACTORS, AND COMPLICATIONS OF CARDIOVASCULAR SYSTEM IN PATIENT WITH GRAVES DISEASE

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**Introduction.** Graves' disease, a common autoimmune illness characterized by a rise in thyroid hormone production, has been widely researched in terms of its effects on the thyroid gland. However, a new study emphasizes the necessity of understanding the complex link between Graves' illness and cardiovascular health. While thyroid problems are the most common symptom of this disorder, there has been increasing recognition that the impact extends beyond the endocrine system.

**Aim of study.** Literature review of PubMed citations of patients with GD from 2009 to 2019 was included in the research and Temporal Dynamics of Atrial Fibrillation in Graves' Disease: A Retrospective Analysis (2009–2019) and other related articles

**Methods and materials.** Literature review of PubMed citation, patients with GD from 2009 to 2019 were included in the research. And Temporal Dynamics of Atrial Fibrillation in Graves' Disease: A Retrospective Analysis (2009–2019).

**Results.** The review of the publications and article shows that Heart failure occurred in 74 out of 1371 GD patients, representing 5.4% of the total. Further breakdown: 31 (2.3%) had heart failure with reduced ejection fraction (HFrEF), and 43 (3.1%) had heart failure with preserved ejection fraction (HFpEF). Atrial fibrillation (AF) and thyroid-stimulating hormone receptor antibody (TRAb) levels were identified as independent risk variables for HFrEF. Hazard Ratio (HR) for AF: 10.5 (3.0-37.3),  $p < 0.001$ . HR for TRAb level: 1.05 (1.01-1.09) per unit,  $p = 0.007$ . These findings suggest distinct risk factors and outcomes for HFrEF and HFpEF in GD patients. AF and TRAb levels were specifically associated with HFrEF, while factors such as COPD, aging, visible hyperthyroidism, higher BMI, and elevated blood pressure were linked to HFpEF. Both types of HF were associated with an increased risk of cardiovascular illness, but only HFrEF was linked to a higher risk of all-cause death. The overview of the report of an article state identified atrial fibrillation (AF) in 139 Graves' disease (GD) patients from 2009 to 2019, with 23.0% representing late-onset AF and half obtaining euthyroid. Early AF risk factors include age, overt hyperthyroidism, and male sex. Late AF is connected with aging, chronic obstructive pulmonary disease, and heart failure. Even after correcting for age, gender, and pre-existing AF, AF in GD was connected to increased mortality, acute coronary events, and cardiac hospitalizations. The findings underscore the necessity of cautious treatment and risk assessment in GD patients with AF.

**Conclusion.** Graves' disease (GD) patients face a 5.4% incidence of heart failure, with distinct risks for heart failure subtypes. Atrial fibrillation (AF) and thyroid-stimulating hormone receptor antibody (TRAb) levels are notable risk factors, particularly for heart failure with reduced ejection fraction (HFrEF). AF in GD is associated with heightened mortality and cardiovascular events, emphasizing the need for precise management strategies.

## 9. OBESITY: PARTICULAR COMPLICATIONS IN PREGNANT WOMEN



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**Introduction.** Obesity is a nosological entity determined by the body's psychosomatic imbalance, resulting in energy excess and pathological expansion of adipose tissue causing severe complications and increased overall mortality.

**Aim of study.** Studying obesity and complications in pregnant women

**Methods and materials.** Analysis of scientific publications by international search engines such as PubMed, ScienceDirect, UpToDate.

**Results.** Obesity causes pregnancy-related complications such as gestational hypertension, preeclampsia, gestational diabetes, prematurity. Morbidity through hemorrhage, thrombosis, embolism, sepsis, shock, anesthetic complications, uterine rupture is directly proportional to BMI. Fetal exposure to increased levels of glucose, insulin, lipids and persistent proinflammatory cytokines in the obese results in altered fetal metabolic programming and fetal macrosomia. The hormonal imbalance of obese women and the endometrial inflammation associated with polycystic ovary syndrome cause poor endometrial receptivity and increase the miscarriage rate by 20% to 40%.

**Conclusion.** Obesity is correlated with a clear increased risk of developing complications in pregnant women.

**Keywords.** Obesity, Pregnancy, Complications.



## 10. RECURRENT HYPOGLYCEMIA IN PATIENTS WITH DIABETES AND LIVER CIRRHOSIS – A REAL THERAPEUTIC CHALLENGE

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**Introduction.** Diabetes is a global health problem, currently about 540 million adults suffer from diabetes, according to data published by the International Diabetes Federation. Approximately 20-60% of patients with cirrhosis have diabetes, 60-80% may have impaired glucose tolerance, and 100% of patients exhibit insulin resistance. One of the most worrying consequences of diabetes is hypoglycaemia.

**Case statement.** Case presentation. A 49-year-old man was urgently admitted in an extremely serious condition with the following symptoms: drowsiness, lethargy, dizziness, severe hypoglycemia - glucose level 2.6 mmol/l. Concomitant pathologies: diagnosed with Type 2 Diabetes for 3 years; Toxic liver cirrhosis, decompensated Child-Pugh C. Ambulatory he administered long acting Insulin – Lantus 25 Un, s/c, in the evening, without blood sugar control. At the objective clinical examination – dry, icteric, cold skin; passive position; in the lungs - vesicular murmur; RR -19 breaths/min, SpO<sub>2</sub> – 94%, heart sounds, diminished, TA – 90/60 mmHg, heart frequency 102 beats/min. Abdomen - enlarged in size, the liver +4 cm under the costal rebord. Glasgow Scale - 12 points. Paraclinical investigations at admission detected – blood glucose level - 2,8 mmol/l, severe cytolytic syndrome, moderate cholestatic syndrome and HbA<sub>1C</sub> 10,9%, C-Peptid – 2,2 ng/ml. Despite high doses of bolus glucose (>100 g I/V), the hypoglycaemia persisted and the patient was transferred to intensive care unit for appropriate treatment. During hospitalization in the intensive care unit, the patient had several recurrent hypoglycemic episodes.**Discussions.** The management of patients with cirrhosis of the liver and diabetes is a real challenge in the context of the major risk of hypoglycemia in this category of patients. The incidence of hypoglycaemia in patients with severe liver disease is up to 56%. The patients with type 2 diabetes and cirrhosis have a 2.7 times higher risk of hypoglycaemia than those without cirrhosis. The dietary recommendations should ensure glycaemic control and avoid worsening sarcopenia and malnutrition. The caloric intake according to nutritional requirements in patients with cirrhosis should be 35-40 kcal/kg/day, and the daily protein requirement of 1.2 g/kg in the absence of malnutrition or 1.5 g/kg in case of malnutrition. Processed foods, fructose-rich drinks, alcohol consumption should not be included in the diet, respectively, are contraindicated. In patients at risk of hypoglycaemia, such antidiabetics are preferred: metformin, DPP-4 inhibitors; GLP-1 receptor agonists and SGLT-2 inhibitors. Insulin therapy is recommended for patients with decompensated cirrhosis, stage Child-Pugh C. Insulin analogues are preferable because they provide more satisfactory glycaemic control and are associated with a lower risk of hypoglycaemia. The particularity of this case represents the risk of severe, recurrent hypoglycaemia in patients with cirrhosis and diabetes.

**Conclusion.** The treatment of type 2 diabetes mellitus in patients with cirrhosis is challenging due to increased hypoglycemia risk, altered pharmacokinetics of oral antidiabetics, reduced hepatic insulin clearance, and, on the other hand, frequent blood glucose self-monitoring is essential in this category of patients for the prevention of severe hypoglycemic episodes.



## 11. ROLE OF MINERALOCORTICOID RECEPTOR PATHWAY IN THE PATHOGENESIS OF DIABETIC RETINOPATHY



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**Introduction.** Diabetic retinopathy (DR) represents a major cause of irreversible blindness among the working-age population. Aldosterone has an important role in the pathogenesis of DR, through vascular regulation, oxidative stress, inflammation and angiogenesis (neovascularization). Thus, activation of the mineralocorticoid receptor pathway plays multiple roles in the pathogenesis of diabetic retinopathy and understanding these mechanisms offers possibilities for the treatment of DR.

**Aim of study.** The aim of study is to review recent articles (published during 2017-2023) that addressed the role of mineralocorticoid receptor pathway in the pathogenesis of DR.

**Methods and materials.** Articles from PubMed, Google scholar database were selected and analyzed using keywords: "mineralocorticoid receptor pathway in diabetic retinopathy", "aldosterone in diabetic retinopathy", "angiogenesis".

**Results.** It has been estimated that the activation of mineralocorticoid receptor pathway (MRP) induces blood pressure changes that is mediated by activation of renin-angiotensin-aldosterone system (RAAS) and has an important pathogenetic part in DR. Activation of RAAS can change the blood flow in the ciliary body, iris and retina, can also modify intraocular pressure by modulating the production and excretion of aqueous humor, it participates in the development of macular edema. Aldosterone promotes inflammatory response by inducing the production of pro-inflammatory factors such as interleukin (IL)-1 $\beta$ , IL-6, CCL5, TNF- $\alpha$  and neovascularization in DR, Müller cells express high levels of mineralocorticoid receptors and induce production of VEGF. It also enhances the expression of the epithelial Na<sup>+</sup> channel ENaC  $\alpha$ , the K<sup>+</sup> channel Kir4.1 and the water channel AQP4 and promotes delocalization of Kir4.1 and AQP4 towards the outer limiting membrane, contributing to the accumulation of fluid in retina. However, spironolactone (an MR and aldosterone inhibitor) were shown to effectively reduce retinal angiopathy and inflammation, as well as prevent retinal neovascularization by reducing VEGF levels and inflammatory factors. In another study intraocular delivery of spironolactone has decreased the early and late pathogenic features of retinopathy in diabetic rats, such as retinal inflammation, vascular leakage, and retinal edema, through the upregulation of genes encoding proteins known to intervene in vascular permeability such as Hey1, Vldlr, Pten, Slc7a1, Tjp1, Dlg1, and Sesn2, but hasn't decreased VEGF. Spironolactone also has normalized the distribution of ion and water channels in macroglial cells.

**Conclusion.** MRP has an important pathogenetic role in DR by: 1. Activation of RAAS, modification of blood pressure, systemic and local effects in retina 2. Inducing the production of pro-inflammatory factors 3. Retinal neovascularization and modification in ion channels. Thus, an increased understanding of the role of these mechanisms in the pathogenesis of DR, will give us possibilities for treatment with MR inhibitors, which show positive effect in preclinical studies.



## 12. THE CONNECTION BETWEEN THE TREATMENT OF HYPOTHYROIDISM WITH LEVOTHYROXINE AND ITS EFFECTS ON THE CARDIOVASCULAR SYSTEM

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**Introduction.** Hypothyroidism is a common clinical condition. Thyroid hormones have multiple effects on the function of the cardiovascular system.

**Aim of study.** Literature analysis to determine the relationship between treatment with Levothyroxine and its effects on the function of the cardiovascular system.

**Methods and materials.** A bibliographic study of the specialized scientific literature was analyzed, searching for the necessary information on platforms such as: PubMed and Aha Journals.

**Results.** Levothyroxine treatment has been shown to have beneficial effects on the lipid profile, reducing total cholesterol, LDL and triglycerides, improving blood pressure, diastolic dysfunction, heart rate and heart rate variability during exercise. It has also been shown that the progression of atherosclerosis is delayed in patients under treatment. In a study of women with hypothyroidism, after 18 months of treatment, it was observed that it led to normalization of systolic and diastolic blood pressure and total and LDL cholesterol, as well as a decrease in carotid intimal thickness. Although there are no randomized clinical trials evaluating long-term cardiovascular outcomes and mortality in levothyroxine-treated patients, one study of levothyroxine-treated patients demonstrated that those with elevated TSH had a higher risk of cardiovascular events despite the administration of the drug, resulting in adverse effects.

**Conclusion.** Thyroid hormones play a significant role in the regulation of cardiac, vascular and metabolic physiology. The pathological changes of hypothyroidism on the cardiovascular system are varied, and treatment can reverse some, if not all, of the effects. There is evidence to suggest that treatment of mild dysfunctions may improve cardiovascular outcomes; however, randomized controlled clinical trials in this area are lacking and warranted. It is important to note that TSH levels can be higher in the elderly.

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***V. FAMILY MEDICINE  
SECTION***





## 1. AUTISM SPECTRUM DISORDER - A COMPREHENSIVE LITERARY REVIEW

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**Introduction.** Autism spectrum disorder (ASD) can be identified from other neurodevelopmental disorders by its distinctive combination of symptoms: difficulties in social interaction and communication, repetitive, stereotyped, and restricted behavior. According to the data provided by the World Health Organization, the worldwide prevalence of ASD is 1:100, while as per Centers for Disease Control and Prevention (CDC), in the USA (2020) 1 in 36 children were diagnosed with autism, in comparison with 2000 when the ratio was 1:150.

**Aim of study.** To elucidate the main key findings within the literature on autism spectrum disorder.

**Methods and materials.** To accomplish the proposed goal, research was performed on scientific and medical databases as HINARI, PubMed, Elsevier. Using the following keywords: “autism spectrum disorder”, “etiology”, “prevalence”, “early prevention” – 14 articles were selected.

**Results.** 1 to 2 percent of the overall population is diagnosed with autism, more commonly in men than in women (ratio 4:1). In ASD “spectrum” emphasizes the broad array of symptoms, the severity and which degree these symptoms manifest in each individual. The complexity of this disease can be explained by its heterogeneous origins. Several family studies have demonstrated that ASD is a highly heritable disorder, with heritability estimates ranging from 40% to 90%, underscoring the influence of genetic factors. Nevertheless, genetic alterations have been detected in only 20-30% of cases. This prompted an exploration of the impact of environmental factors, including drugs, maternal and paternal age, and neonatal hypoxia. These studies revealed that up to 40-50% of the variation in autism susceptibility could be attributed to these variables, and still not all cases of autism can be explained. Hence, an increasing number of studies are centered on exploring the interplay between genetics and the environment, or more precisely, how our surroundings and behavior impact the functioning of our genes—commonly referred to as epigenetics. These factors engage with each other in the prenatal and postnatal period, altering the development of the central nervous system and determining the appearance of the autistic phenotype. The diagnosis can be confirmed by the age of 2, prompting international recommendations to begin screening at 18 months.

**Conclusion.** Since the discovery of ASD, numerous studies have significantly advanced our understanding of the condition, revealing its multifactorial nature. Autism is a lifelong developmental disease for which there is no cure. Therefore, early intervention and diagnosis play a crucial role in influencing the quality of life for individuals with ASD.



## 2. CLINICAL CHARACTERISTIC OF ADULTS HOSPITALIZED WITH COVID-19 IN THE REPUBLIC OF MOLDOVA



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**Introduction.** The global impact of the unprecedented COVID-19 pandemic has prompted an urgent need to comprehensively understand the clinical characteristics of affected individuals for effective healthcare management. This study, focusing on the analysis of COVID-19's impact on adult patients and clinical outcomes, synthesizes contemporary international research. It provides a succinct overview of the disease's spread, infection rates, transmission pathways, and crucial factors such as age, gender, severity, and diverse disease progression.

**Aim of study.** The aim of the study is to investigate the epidemiological, clinical characteristics and disease progression of COVID-19 in adult patients treated in public healthcare institutions, with the purpose of identifying the infection's risk impact on health status.

**Methods and materials.** This retrospective cohort study analyzed 7441 adult patients included in the "Electronic Registry of Covid-19 Patients" treated in 7 medical institutions in Chisinau, Moldova, from March 1, 2020, to June 30, 2021. Subjects were selected based on clinical confirmation through SARS-CoV-2 RNA tests.

**Results.** Out of 7,441 adults with Covid-19, women constitute 65.42%, while men make up 34.57%. Predominantly urban (77.01%) and employed (54.44%) patients. 41.19% were hospitalized through inter-hospital transfers. 30.07% had close contact with an infected person in the last 14 days. Average age was 52.83 years, with prevalence in the 50-59 and 60-69 age groups. Moderate disease form was predominant (66.15%). Treatment was supportive, with antibiotics in 91.64%. Average hospitalization duration varied. 88.36% were discharged, and 7.92% succumbed. Persistent symptoms post-discharge included fatigue, headache, and behavioral changes. Comorbidities like diabetes and heart diseases increased the risk of death. Male/female ratio in death cases was 1.1 (310/280).

**Conclusion.** This study reveals a significant impact of COVID-19 on adult patients, with distinct epidemiological and clinical patterns. The predominance of moderate cases and the influence of comorbidities on disease severity underscore the complexity of managing COVID-19. Understanding these aspects is vital for optimizing healthcare strategies and resource allocation.



### 3. CLINICAL CHARACTERISTICS OF CHILDREN HOSPITALIZED WITH COVID 19 IN THE REPUBLIC OF MOLDOVA

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**Introduction.** The World Health Organization named 2019 the year of global emergency. The disease that left its mark on humanity caused by the SARS-CoV-2 virus was called COVID-19. In the Republic of Moldova, 5.1% of the population infected with SARS-CoV-2 are children, this number is double as compared with other countries. The importance of knowing the clinical characteristics, epidemiological, and laboratory features, has colossal meaning in establishing a diagnosis and treatment.

**Aim of study.** The study aims to evaluate pediatric patients with SARS-CoV-2 who were hospitalized in 7 Public Medical-Sanitary Institutions in the Republic of Moldova. This study helped us to determine clinical-epidemiological dynamics of positive cases which had an immense impact on children's health.

**Methods and materials.** We made a retrospective cohort study which included 724 pediatric patients with COVID-19, aged 1-18, treated in 7 MIPH of Chişinău municipality in the Republic of Moldova. The research was carried out from March 1, 2020, until June 30, 2021, based on a standardized form. Patients who tested positive by RT-PCR test are registered in the server of SUMPh „*Nicolae Testemitanu*” named "Electronic register of evidence patients with COVID-19".

**Results.** After carrying out the study was determined that 51.66% of patients were girls and 48.34% were boys, the predominance of the female sex does not represent a diagnostic criterion. A total of 724 patients, we determined that children aged 0-1 years constitute 15.06%, 2-5 years - 24.59%, 6-10 years -22.93%, 11-15 years - 24.45%, 16-18 years -12.98%. Most of the patients included in this study predominated from the urban region 69.89% because accessibility to medical services is bigger, and the rural region constituted 30.11%. Most of the infected children show clinical signs of a fever higher than 38°C -35.52% (249 patients), 37-38 °C - 51.07% (358 children), asthenia 45.22% (317 children), headache with a weight of 24.54% (172 children), other clinical manifestations such as drowsiness, rashes, arthralgias, myalgias, vertigo, and ageusia are much less common. Most patients had moderate forms of disease 83.29%, severe forms 8.56% of children, mild forms 8.15%.

**Conclusion.** The source of infection with SARS-CoV-2 remains unexplained in every 4th case of COVID-19 disease in children, which contributes to the uncontrolled spread of the infection. Children mainly acquire SARS-CoV-2 infection from their family members, but they seem to experience a less severe form of the disease than adults. The prognosis is favorable and recovery occurs 1 - 2 weeks after the onset of the disease. In most cases hospitalized children develop moderate clinical forms of COVID-19. The mean age of children with severe form is lower compared to those with moderate or mild form, the gender of patients does not influence the course of the disease. The evolution of pediatric COVID-19 infection is favorable, discharge from MIPHS is done in most cases in the absence of clinical manifestations, children being considered cured by the specialist doctor.

#### 4. PERSONALIZED MEDICINE AND CARDIOVASCULAR DISEASES



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**Introduction.** There was a remarkable growth in scientific publication on personalized medicine within the past few years in the field of cardiovascular disease. In the era of personalized/precision medicine the combination of genetic information with other biomarkers may add additional benefits for preventive and therapeutic strategies in individuals.

**Aim of study.** The objective of this research was to analyze the perspectives of personalized medicine implementation in cardiovascular pathologies.

**Methods and materials.** For this study were reviewed articles in English published in the time frame 2018-2023 from the PubMed and Google Scholar databases. The keywords used: “Personalized medicine” OR “Precision medicine” AND ”Cardiovascular” OR “Cardiology”

**Results.** The personalized approach can be largely implemented in cardiovascular diseases (CVD), starting from the prevention (risk stratification, genetic susceptibility), specific investigation through structural and functional testing, and not the least – genome based clinical/treatment decisions. Many studies reported the genetic predisposition and possible evaluation of CVD risk in myocardial infarction, atrial fibrillation, congestive heart failure, cardiomyopathies, hypertension, dyslipidaemia etc. The use of clinical genomic markers have a very good perspective in treatment decision making in cardiology: beta blockers, warfarin, angiotensin blockers, fenofibrate, ezetimibe, etc. New technologies such as high-resolution CT coronary imaging, high-resolution 2-D echocardiography, wearable devices, and other technologies are used to personalize care and to improve the efficacy as well as the safety of the treatment of patients with CVD.

**Conclusion.** Personalized approach based on genetic testing has clinical implications in terms of diagnosis, family screening, guiding therapies and management strategies, and providing personalized prognosis in different CVD.



## 5. STRATEGIES AND APPROACHES ADOPTED BY COMMUNITY NURSES FROM THE REPUBLIC OF MOLDOVA IN PROMOTING A HEALTHY LIFESTYLE

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**Introduction.** Community nurses play a vital role in promoting the health and well-being of the population, particularly in adopting and maintaining a healthy lifestyle. In the Republic of Moldova, these medical professionals are actively engaged in educating and guiding communities toward the adoption of healthy practices and behaviors. However, there is an increased need to better understand the strategies that community nurses use to promote healthy lifestyles among their local populations. In this context, the present study aims to analyze and highlight these strategies and approaches, providing relevant and detailed information about the methods and tools used by these professionals to influence the health behaviors and practices of their communities.

**Aim of study.** Identification and evaluation of strategies, methods, and specific approaches used by community nurses in the Republic of Moldova to promote a healthy lifestyle among their communities.

**Methods and materials.** The research was conducted in 2022 and involved a sample of 27 community nurses. A closed-ended questionnaire was used for data collection, distributed both online and in person to ensure adequate representation of the geographic and age diversity of participants. It was distributed both electronically through online platforms and in physical form to ensure broad and diverse data coverage.

**Results.** The results reveal the distribution of participants according to the region: 18.5% of nurses from the northern region, 55.6% from the central region, and 25.9% from the southern region. Regarding age categories, 3.7% of nurses were in the 18-25 age group, 29.6% in the 26-45 age group, 55.6% in the 46-63 age group, and 11.1% were over 64 years old. The predominant activities for promoting a healthy lifestyle were the following: 100% mentioned educational programs about healthy eating and physical exercise, working with schools to promote a healthy lifestyle in children and adolescents, assistance to quit smoking and drinking alcohol and promoting personal and environmental hygiene. In addition, 77.8% mentioned encouraging relaxation techniques such as meditation and yoga, and 81.5% mentioned organizing adventure or sports trips for the community. Regarding the topics covered, all nurses, 100%, highlighted the importance of healthy eating and balanced nutrition, physical activity, and exercise for physical health, as well as managing stress and promoting mental well-being. However, only 3.7% mentioned giving up habits harmful to health, and no nurse mentioned the integration of alternative healing methods or complementary practices.

**Conclusion.** The study demonstrated a significant commitment of community nurses to health promotion. Their extensive efforts in education and promoting a healthy lifestyle in the communities are evident. However, there is an obvious need to pay more attention to giving up harmful habits and exploring alternative healing methods in their health promotion activities.



## ***VI. GENETICS SECTION***



***„Trebuie să fim recunoscători părinților pentru că ne-au binecuvântat cu seturi de gene care ne permit să înaintăm ferm prin viață.”***

***„We must be grateful to our parents for blessing us with sets of genes that enable us to navigate through life firmly.”***

***Cemortan Igor,***  
*MD, PhD, Associate Professor,*  
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## 1. ADENO-ASSOCIATED VIRUS (AAV) - BASED GENE THERAPIES FOR RETINAL DISEASES

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**Introduction.** Retinal degeneration and macular dystrophies are the leading causes of visual acuity loss and blindness in middle-aged people worldwide. Existing treatment, although considered effective, often does not lead to a complete recovery of the patient, which leads to the need to find new alternatives. It has been proven that genetic factors play an important role in the development of retinal degeneration. Consequently, gene therapy has always been of great interest to scientists as a very promising field of study.

**Aim of study.** The adeno-associated virus has become the vector of choice for retinal diseases. This virus is very compact, has a high tropism to the retina and a relatively low immune response. The increased interest of the scientific community in this area led to the fact that in 2017 the FDA approved a gene therapy for Leber congenital amaurosis caused by the RPE65 mutation.

**Methods and materials.** Hu ML, Edwards TL, O'Hare F, Hickey DG, Wang JH, Liu Z, Ayton LN. Gene therapy for inherited retinal diseases: progress and possibilities. *Clin Exp Optom.* 2021 May;104(4):444-454. doi: 10.1080/08164622.2021.1880863. Epub 2021 Mar 2. PMID: 33689657. Bucher K, Rodríguez-Bocanegra E, Dauletbekov D, Fischer MD. Immune responses to retinal gene therapy using adeno-associated viral vectors - Implications for treatment success and safety. *Prog Retin Eye Res.* 2021 Jul;83:100915. doi: 10.1016/j.preteyeres.2020.100915. Epub 2020 Oct 15. PMID: 33069860. Botto C, Rucli M, Tekinsoy MD, Pulman J, Sahel JA, Dalkara D. Early and late stage gene therapy interventions for inherited retinal degenerations. *Prog Retin Eye Res.* 2022 Jan;86:100975. doi: 10.1016/j.preteyeres.2021.100975. Epub 2021 May 29. PMID: 34058340. Ku CA, Pennesi ME. The new landscape of retinal gene therapy. *Am J Med Genet C Semin Med Genet.* 2020 Sep;184(3):846-859. doi: 10.1002/ajmg.c.31842. Epub 2020 Sep 5. PMID: 32888388. Ail D, Malki H, Zin EA, Dalkara D. Adeno-Associated Virus (AAV) - Based Gene Therapies for Retinal Diseases: Where are We? *Appl Clin Genet.* 2023 May 30;16:111-130. doi: 10.2147/TACG.S383453. PMID: 37274131; PMCID: PMC10239239. Castro BFM, Steel JC, Layton CJ. AAV-Based Strategies for Treatment of Retinal and Choroidal Vascular Diseases: Advances in Age-Related Macular Degeneration and Diabetic Retinopathy Therapies. *BioDrugs.* 2023 Oct 25. doi: 10.1007/s40259-023-00629-y. Epub ahead of print. PMID: 37878215.

**Results.** Despite all the advantages, there are still many obstacles to the effective use of AAV for a wider range of retinal diseases. For example, the small size of AAV particles is also a disadvantage, since the viral capsid has a limited capacity. In addition, although the immune response is considered relatively low, various complications often occur that prevent the full delivery of AAV to the target organ.

**Conclusion.** Gene editing and gene replacement techniques have become a real breakthrough in the treatment of inherited retinal diseases. However, this treatment is effective if it is applied at an early stage of the disease, before the degeneration of photoreceptors. In addition, taking into account the fact that the use of AAV still causes an immune response, it is important to distinguish between an acceptable immune response and a destructive one, which exacerbates the course of the disease and prevents effective treatment.

## 2. CYSTIC FIBROSIS: CURRENT THERAPEUTIC TARGETS BASED ON SYMPTOMS OCCURRED DUE TO SPECIFIC CFRT GENE MUTATIONS



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**Introduction.** Cystic fibrosis (henceforth CF) is autosomal recessive disease involving mucus and sweat producing cells affecting multiple organs with lungs most severely affected leading to death in 90% of patients . A mutation in Cystic fibrosis trans-membrane conductance regulator (henceforth CFTR) gene changes a protein (a regulated chloride channel), which regulate the activity of other chloride and sodium channels at the cell surface epithelium. This mutation and some others, have attracted much attention in recent years due to significant advances in the pharmacological targeting. However, increasing evidence points to the reduced efficacy of single treatments, thus reinforcing the need to combine several therapeutic strategies to effectively target the multiple basic defect(s). Also mechanistic subdivisions of some of the major classes of mutations can be a good support in order to improve the success of drug-selection strategies.

**Aim of study.** Study about cystic fibrosis manifestation based on classes of CFRT mutations, and get acknowledged about currently approved drugs and exploration of future clinical development pipeline therapeutics for cystic fibrosis, and possible limitations in their use.

**Methods and materials.** Extensive literature search using individual and a combination of key words related to cystic fibrosis therapeutics.

**Results.** Cystic fibrosis is an autosomal recessive disorder results from mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The gene was identified in 1989, but more than 20 years later, the regulatory mechanisms controlling its complex expression are still not fully understood. Over the years, scientists have used several different ways of grouping these mutations into different classes. The most recent classification system groups mutations by the problems that they cause in the production of the CFTR protein: Protein production mutations (Class 1); Protein processing mutations (Class 2); Gating mutations (Class 3); Conduction mutations (Class 4); Insufficient protein mutations (Class 5) For many of the identified mutations, the disease liability is unknown, but efforts are under way to assess their functional consequence and clinical severity. Respiratory system and GIT are primarily involved but eventually multiple organs are affected leading to life threatening complications. Management requires drug therapy, extensive physiotherapy and nutritional support. Previously, the focus was on symptomatic improvement and complication prevention but recently the protein rectifiers are being studied which are claimed to correct underlying structural and functional abnormalities.

**Conclusion.** The ultimate goal of therotyping is to achieve optimal correction of a specific mutant defect by selecting the most efficacious CFTR modulator(s), including correctors(s), potentiator(s), and/or read-through drugs, or a combination of these drugs. Based on accumulating observations, however, mechanistic subdivisions of some of the major classes of mutations (classes I, II, and III) may be necessary to further improve the success of drug-selection strategies.



### 3. GENETIC ASPECTS OF MIGRAINE.

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**Introduction.** Migraine is a common neurological disorder which affects 15–20% of the population and usually begins at puberty, but has the greatest impact on people aged 35 to 45 years. Migraines present a severe headache with associated symptoms of nausea, vomiting, photo and phonophobia. The pain can localize on one side of the head. It can be aggravated by physical activity. There are migraines without aura (MO) and migraine with aura (MA) which include many other subtypes.

**Aim of study.** To investigate the molecular and genetic mechanisms of migraine and their impact on the quality of human life.

**Methods and materials.** From a variety of articles from PubMed, NCBI databases, Medlineplus.gov, Americanmigrainefoundation.org we selected and analyzed 25 sources describing the genetic manifestations of migraine in more detail

**Results.** Familial hemiplegic migraine (FHM) is the only known autosomal dominant subtype of migraine with aura. There are mutations in the calcium-channel gene *CACNA1A* which is present on chromosome 19p13. Four missense mutations were detected in the conserved regions of this gene. This gene usually encodes the pore-forming  $\alpha 1$  subunit of the neuronal voltage-gated Cav2.1 channel. The different migraine phenotypes are associated with deletion of the *CACNA1A* gene. Another involved in increasing the risk of migraines is *MTHFR* gene which is localized on chromosome 1p36.2 and encodes the enzyme methylenetetrahydrofolate reductase, normally involved in the metabolism of vitamin B9 (folic acid). The *MTHFR* enzyme catalyses the reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate which is needed for the conversion of homocysteine to methionine. The C677T mutation of the *MTHFR* gene is quite widespread. For example, it occurs in 35-55% of representatives of the European (Caucasian) race. Missense mutations in this gene lead to protein deficiency or defective protein synthesis. This will lead to an increased level of homocysteine in plasma and a decrease in the amount of methionine. The clinical consequences of elevated plasma homocysteine levels include damage to endothelial cells, spontaneous activation of trigeminal nerve cells, and changes in blood coagulation properties. It is believed that spontaneous activation of trigeminal nerve cells, leading to inflammation of the meninges and blockage of cerebral vessels, is the cause of migraine-related pain. Thus, homocysteine dysfunction can clearly increase the patient's propensity to develop migraines. In this case, the patient is forced to be motionless, since any exposure to light or noise makes the headache unbearable

**Conclusion.** Migraine is a complex brain disorder that occurs when homeostasis is lost, which leads to activation of the trigeminal vascular system and a cascade of events, the manifestation of which depends on mutations in the *MTHFR* and *CACNA1A* genes.

**Keywords.** Migraine, genetics, brain disorder, mutations.



#### 4. GENETIC ASPECTS OF THROMBOPHILIA IN PREGNANCY



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**Introduction.** Thrombophilia represents a condition that increases blood coagulability and the risk of clots. Physiological changes during pregnancy, such as excess fibrinogen synthesis and increased concentration of coagulation factors in the third trimester of pregnancy, can lead to thrombotic phenomena. The thrombophilia impact is intensified in pregnant women with specific variations in the genes responsible for coagulation.

**Aim of study.** Evaluation of the genetic aspects of thrombophilia in obstetric complications.

**Methods and materials.** A literature review was done, the search motors being PubMed, Google Scholar, ScienceDirect. Out of the 250 articles submitted, 89 met the research criteria.

**Results.** An important number of genetic variations with thrombophilia potential in pregnant women have been reported and correlated with: premature birth, intrauterine death of the fetus, premature detachment of the placenta, eclampsia, etc. There have been two groups of hereditary thrombophilia described: through hypomorphic mutations, for example antithrombin III deficiency, protein C and S deficiency; through hypermorphic mutations - factor V Leiden mutation, G20210A mutation in the prothrombin gene. Also, the involvement of the PAI-1 gene and more recently the MTHFR gene has been proven. The most common mutations (heterozygous F5 gene mutation G1691A and prothrombin gene mutation G20210A) are associated with a moderate to low risk of developing thrombophilia, while the rarest types like homozygous F5 and F2 gene mutations, antithrombin III, protein C or protein S deficiency, have a more considerable and higher risk.

**Conclusion.** Up to day the causes of pregnancy complications were attributed to various pathologies, infections or considered an incidence. Today, though, the evaluation of genetic aspects is required, as it can influence the evolution of the pregnancy too.



## 5. GENETIC FACTORS RESPONSIBLE FOR OVARIAN RESERVE

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**Introduction.** The number of primordial follicles at birth, their quality, and the rate of germ cell depletion are the factors that define reproductive lifespan in women. In some women, oocyte depletion occurs during the fetal stages of oogenesis, leaving them with a relatively small reserve until puberty. In others, there is an accelerated loss of oocytes after the reserve of primordial follicles is established. In addition, oocyte shedding is accelerated with age and is linked to deterioration of oocyte quality.

**Aim of study.** The evaluation of the genes that control different stages of follicle development that can open new approaches in the treatment of infertility.

**Methods and materials.** The study is based on the analysis of bibliographic sources published on PubMed, NCBI, ResearchGate and Medline, in the period 2013-2023.

**Results.** Ovarian reserve is influenced by a series of physiological, environmental, hormonal, iatrogenic and genetic factors. Recently, genetic defects have been directly associated with a significant reduction in ovarian reserve at different ontogenetic stages. A key role is attributed to the genes FMR1, EIF4ENIF1, BRCA1/2, H19, HMGB2, ADR- $\alpha$ 1, 2, ADR- $\beta$ 2, NR5A1, ATG7, ATG9A, KHDRBS1, FIGLA, 22q11.2, SPO11, HFM1, GDF9, TP53 ce are involved in a cascade of regulatory processes that direct granulosa cell proliferation, steroidogenesis, cumulus expansion and apoptosis, stimulating follicle maturation and survival. Multiple oocyte-specific transcription factors, including FIGLA, NOBOX, LHX8, SOHLH1, and SOHLH2 control follicular development. Thus, in cases of infertility, it is recommended to carry out a genetic screening to assess the extent and management possibilities of existing defects on female fertility. Assessment of ovarian reserve has become a standard parameter in infertility evaluation as well as treatment.

**Conclusion.** Existing data show an abundant amount of research on the genetic and epigenetic profiles that can influence the formation and consistency of the ovarian reserve. Identification of genetic predisposition to early depletion of ovarian reserve may be beneficial in family planning.

## 6. GENETIC VARIANTS OF COMT GENE EXPRESSION AND INFLUENCE ON PAIN PERCEPTION.



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**Introduction.** Catechol-O-methyltransferase (COMT) is a pivotal enzyme responsible for deactivating biologically active catechols, including crucial neurotransmitters such as dopamine, norepinephrine, and adrenaline. These neurotransmitters significantly influence pain modulation, and variations in the gene encoding the COMT enzyme directly impact pain sensitivity.

**Aim of study.** This study aims to comprehensively explore the genetic variants within the COMT gene and their consequential effects on pain perception.

**Methods and materials.** Conducting a thorough literature review, this study utilized PubMed and ScienceDirect databases to investigate key terms like "genetic variants of the COMT enzyme", "COMT enzyme", "COMT gene", "genetic variants of COMT and pain", and "polymorphism of the catechol-o-aminotransferase gene". 147 sources were found, from which we selected 15.

**Results.** Existing literature analysis reveals various types of COMT gene polymorphisms, with the most extensively studied being the single nucleotide type Rs4680 (Val158Met). This polymorphism substitutes valine for methionine at the 158 locus, leading to a significant reduction (three to four-fold) in COMT enzyme activity. Consequently, genotypes Val/Val, Val/Met, and Met/Met correspond to high, intermediate, and low levels of COMT enzyme activity. Lower COMT enzyme activity intensifies dopaminergic system activation, impacting the metabolism of catecholamines. Enhanced dopaminergic neurotransmission results in reduced enkephalin peptides, consequently heightening mu-opioid receptor regulation. Individuals with the Met/Met genotype exhibit increased regional density of mu-opioid receptors in the brain, correlated with heightened sensory and affective pain ratings.

**Conclusion.** This literature review highlights how distinct expressions of the COMT gene influence pain perception. Understanding these mechanisms aids in comprehending the development of various pain disorders, offering potential ways for refining pain management strategies in human populations.



## 7. INDICATIONS AND LIMITS OF GENE THERAPY

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**Introduction.** Gene therapies represent advanced medical tools that aim to fix or improve genes by correcting mutations or making modifications at a specific site. While there are several successful protocols, it remains a complex field, with many techniques requiring enhancements. Applicability of techniques are limited due to their innovative nature, risks and ethical concerns.

**Aim of study.** Analysis and synthesis of information on Gene Therapies, highlighting indications and limitations in modern medicine.

**Methods and materials.** The study was based on a systematic review of publications over the last decade on selected topics using Google Academic, PubMed and Scopus electronic databases, combining keywords related to gene therapy, indications, limits of gene therapy. A total of 343 articles were retrieved, 42 of which met the inclusion criteria.

**Results.** Genetic modification involves the transfer of DNA, but can also include oligonucleotides or RNA-based therapies. A relatively new technique is CRISPR-Cas9, a system adapted from the natural defense mechanisms of bacteria and archaea and enable highly precise molecular modifications. The approach of gene therapy is broad and has the potential to treat diseases caused by recessive genetic disorders, acquired conditions, and certain viral infections such as AIDS. Recombinant DNA technology, a commonly used technique, introduces the gene of interest into a vector, but risks include the presence of viral genetic material and the potential for oncogenic transformation. Limits, particularly in cancer treatment, arise from recurrences and neutralizing antibodies, impacting therapy effectiveness. The prevalence of neutralizing antibodies against certain subtypes of the virus reaches up to 70% in the general population, reducing the therapy's effectiveness and limiting the categories of patients who can participate in studies. Similarly, high costs limit access to treatments, for example, gene therapy for hemophilia B, Hemgenix, has become the most expensive therapy in the world, priced at 3.5 million dollars. Not least, ethical dilemmas raise numerous questions to be resolved, such as impact of germline genetic modifications and the possibility of creating "designer babies," as well as genetic diversity, informed consent and equitable access for all.

**Conclusion.** Gene therapies represent an alternative to conventional treatments. The design of new experimental vectors and the specificity of delivery systems can lead to the expansion of techniques in clinical applications. Similarly, it is necessary to understand the scientific and technological challenges, ethical concerns and public opinion to manage the challenges that could hinder the further development of the field.



## 8. MOLECULAR ASPECTS OF AMINOGLYCOSIDE OTOTOXICITY



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**Introduction.** Aminoglycosides are a class of antibiotics widely used in pediatric clinical practice due to their effectiveness against gram-negative bacterial infections. Despite this, they are known to have cochleotoxicity and vestibulotoxicity, which can occur as tinnitus and/or sensorineural hearing loss or vertigo, nausea, nystagmus, ataxia.

**Aim of study.** A wide range of 2% to 57% of the neonates treated with aminoglycosides develop bilateral profound hearing loss in a dose-dependent manner, aminoglycoside type, genetic constitution of the patient and the physiology of the renal system.

**Methods and materials.** Utilizing the repositories of Medline, PubMed, Google Scholar, a comprehensive review of the literature was made to find actual and relatable papers on "aminoglycoside ototoxicity".

**Results.** The mechanism of aminoglycoside-induced ototoxicity is complex and involves changes in the outer hair cells, perilymph and neural pathways. Firstly, the drugs entering the cells disrupt ionic homeostasis, whereas inside the cell they inhibit voltage gated K<sup>+</sup> channels, causing a prolonged depolarization and apoptosis. Secondly, due to bacterial lysis with releasing proapoptotic factors and oxidative enzymes inside the cells are generated reactive oxygen species with endoplasmatic reticulum stress and mitochondrial Ca<sup>2+</sup> influx. Aminoglycosides are also ribotoxic, by binding to cytosolic Rna and blocking protein synthesis. Moreover, in the perilymph aminoglycosides block the postsynaptic nicotinic-like cholinergic receptors interrupting the olivocochlear reflex. In addition, there are risk factors for developing aminoglycoside-induced hearing loss: prematurity, renal impairment, local inflammation, poor nutritional state, circadian time of daily administration, co-medication with cisplatin, noise exposure, prolonged therapy regimens, severe inflammatory response syndrome, and genetic susceptibility. Septic conditions lead to systemic accumulation of lipopolysaccharides and activation of toll-like receptor 4 which upregulate cochlear expression of aminoglycoside-permanent channels. Mutations in the mitochondrial 12S rRNA MT-RNR1 gene: 1555A>G, 1494C>T, m.1095T>C result in higher affinity of aminoglycosides to outer hair cells and influence codon interaction, compromise mitochondrial protein synthesis and reduce by 30% mitochondrial ATP synthesis. 100% of the patients carrying named mutations develop moderate to profound, bilateral, irreversible, one dose-dependent hearing loss.

**Conclusion.** Aminoglycosides ototoxicity remains a high-priority challenge. By studying the molecular basis, we can gain a better understanding of how it happens and what factors increase the risk. Since no therapy is currently available to reverse the ototoxic damage, the focus is on developing targeted otoprotective drugs and setting up a genetic testing policy in families with acquired deafness history.



## 9. MOLECULAR-GENETIC AND ENVIRONMENTAL MECHANISMS OF MYOPIA

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**Introduction.** Myopia is a multifactorial pathology that causes the decrease or loss of vision, in most cases the elongation of the longitudinal axis of the eyeball is involved. From an etiological point of view, numerous factors are involved in the appearance and development of myopia: genetic, constitutional, environmental, lifestyle, external factors. Pathogenetically, different molecules are involved that participate in the formation of structures that ensure the normal anatomy and proper functioning of the organ of vision.

**Aim of study.** Myopia is an important global public health and socioeconomic problem. According to a number of more than 100 studies on the prevalence of myopia, in 2020 there were 28% of registered cases of myopia globally and 4% of cases of high myopia. These numbers continue to grow annually, including the cases of myopia detected at a young age, and definitive treatments for this pathology do not exist, even surgical interventions have different recurrence rates.

**Methods and materials.** This work was created based on the review of specialized literature, using books and articles published in electronic sources recognized by the international medical community, such as: NCBI, PubMed, GeneCards, OMIM.

**Results.** According to studies, there are more than 200 genes involved in the occurrence and development of myopia. In some cases, the pathology appears isolated, in other cases it has a syndromic component. For example, the PAX-6 protein, encoded by the homonymous gene, is a regulator of gene transcription and is indispensable for the development of neural tissues, especially of the eye, and mutations in this gene are involved in the development of non-syndromic myopia, according to some studies. At the same time, in recent years, the topic of epigenetic changes is brought up more and more frequently. These can be significantly influenced by environmental factors, are time-dependent and have tissue specificity, all of which complicate the study of epigenetic characteristics, since myopia often appears in childhood and adolescence and it is practically impossible to obtain eye tissues at these ages.

**Conclusion.** Myopia is a pathology known for a long time and by many people, but most often it does not have a single and concrete cause. If in the case of syndromic myopia, it can be assumed antenatally due to the detection of certain syndromes during genetic testing, then in the case of epigenetic changes, determined by environmental factors and lifestyle, it cannot be precociously predicted. However, in the case of an emmetropic child in childhood and early adolescence and without myopic parents, reducing the time spent on activities that require close visual work, including the use of gadgets, as well as increasing the duration of outdoor activities, could be the first and simplest advice to delay the onset of myopia as much as possible and to minimize the risk of its rapid worsening and its complications in case of detection.

## 10. RPOB S450L MUTATION AND TRANSMISSION FEATURES OF MDR MYCOBACTERIUM TUBERCULOSIS STRAINS IN THE REPUBLIC OF MOLDOVA



**Author:** Chesov Elena

**Scientific advisor:** Crudu Valeriu, MD, PhD

**Introduction.** The Republic of Moldova (RM) faces a significant challenge with a high prevalence of multidrug-resistant tuberculosis (MDR-TB).

**Aim of study.** This study aims to explore the potential impact of rpoB S450L mutations on the phylogenetic features of MDR Mycobacterium tuberculosis strains in RM.

**Methods and materials.** We randomly selected MTB isolates from the biobank of the National Reference Tuberculosis Laboratory in RM, covering the period 2013-2018. After extracting MTB DNA, whole-genome sequencing (WGS) was performed. On the sequencing data a phylogenetic tree for the studied strains was generated, with consequent assessment of the impact of rpoB gene mutations on tree distribution.

**Results.** All 288 strains included in the study had at least one resistant mutation in the rpoB gene. Clustering rate in the sequenced strains was (51,7%). It was higher in lineage 4 (L4) than in lineage 2 (L2) strains (63% for L4 vs 36.3% for L2,  $p < 0,001$ ). In our study, 86.4% of MDR MTB strains exhibited the S450L mutation in the rpoB gene, with a frequency of 43% in lineage L2 and 57% in L4. Strains harboring the rpoB S450L mutation had a higher clustering rate (55,8% vs 25.6%,  $p=0.0005$ ). As well, among L4 strains with rpoB S450L mutations clustering rate was higher than in those without it (66% vs 31.8%,  $p=0.0016$ ). However, the difference in clustering rate in L2 strains with and without rpoB S450L was statistically insignificant (39.2% vs 17.6%,  $p=0.1068$ ). Compensatory mutations were found in 93.2% of strains with mutations in rpoB S450L, of which 83.9% were in the rpoC gene and 9.2% in the rpoB gene, whereas strains without the S450L mutation had a lower rate (38,4%) of compensatory mutation, of which in the rpoC (5.1%) and rpoB gene (33.3%).

**Conclusion.** The rpoB S450L mutation appears linked to the evolution of resistance and transmission dynamics of distinct MTB lineages in the Republic of Moldova.



## 11. TELOMERE AND TELOMERASE FUNCTION: SAFEGUARDING CHROMOSOMAL ENDS AND THEIR IMPLICATIONS IN AGING AND CANCER DEVELOPMENT

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**Introduction.** Telomeres, the protective caps at the ends of linear chromosomes, play a crucial role in maintaining genomic stability and integrity. As cells undergo repeated divisions, telomeres progressively shorten, eventually leading to cellular senescence or apoptosis.

**Aim of study.** The fundamental aspects of telomere function, its significance in safeguarding chromosomal ends, and the implications of telomere dynamics in the processes of aging and cancer development.

**Methods and materials:** 26 articles from PubMed and ScienceDirect. The keywords employed in this analysis included "telomeres," "aging," and "cancer".

**Results:** Telomeres present at the ends of the q and p arms of chromosomes consist of repetitive TTAGGG sequences. Their function is to prevent the fusion of non-homologous chromatids, chromosomal degradation, recombination and protecting genetic information. Telomere length becomes a "biomarker" in the aging process and the onset of various diseases, such as cancer development. The aging process leads to telomere shortening, and chromosomes lose their capabilities and stability. This results in numerous chromosomal rearrangements that can lead to apoptosis or replicative senescence. The telomere shortening process is dependent on the replication direction of linear molecules guided by DNA polymerase. DNA synthesis initiation requires an RNA primer, leading to DNA losses with each somatic cell division, causing telomeres to decrease in size. The gradual reduction in telomere length during replication cycles is associated with the activation of pRB and p53 pathways to genomic instability and replicative senescence. Telomerase, a ribonucleoprotein enzyme, counteracts telomere shortening by adding repetitive DNA sequences to chromosomal ends. Telomerase activity is regulated, with implications in both aging and cancer. Investigations into telomerase regulation and telomere length include cloning RNA components, telomerase-associated proteins, and antisense experiments demonstrating progressive telomere shortening in the absence of telomerase. Additionally, the identification of telomere-binding proteins suggests a regulatory role through negative feedback signals. Therapeutic regulation of telomerase activity holds promise in cancer therapy, as telomere shortening and maintenance are identified as crucial events in tumor formation. Cancer cells often achieve immortality through telomerase activation or alternative lengthening of telomeres mechanisms, allowing uncontrolled proliferation.

**Conclusion.** The role of telomeres and the telomerase offers the possibility to slow down the aging process, preserve cellular immunity, and to prevent tumors, thus opening up potential therapeutic directions. Continuous research in this field is necessary to unlock the full potential of these molecular entities in shaping the cellular life trajectory and preservation.



## 12. UNMASKING THE TECHNOLOGICAL INNOVATIONS: INSIGHTS THROUGH THE ENCODE PROJECT



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**Introduction.** The Encode (Encyclopaedia of DNA Elements) Project, launched over a decade ago has played a significant role in the research world by aiding in the elucidation of the intricate human genome and its fundamental components. The Encode Project provides accessibility to the blueprint of human life by decoding DNA. Encode has used a wide range of cutting-edge technologies, including complex computational studies and powerful sequencing methods, to shed light on the regulatory roles and functional significance of previously undiscovered areas of the genome.

**Aim of study.** This paper examines the innovations in technology that enabled this project, from the ability of ChIP-seq to elucidate protein-DNA interactions to the three-dimensional insights gained by Hi-C and 3C approaches. It highlights the project's noteworthy accomplishments, exposing regulatory elements and offering a glimpse into the future directions of genomics, predictive modeling, and personalized medicine.

**Methods and materials.** The research is based on bibliographic sources that were analyzed using PubMed, Google Scholar, Science Direct and other web sources, published within the period of 2013-2023.

**Results.** Through this review it was understood that, the ENCODE project's interdisciplinary approach harnesses a multitude of technological innovations. Using high-throughput sequencing methods including as ChIP-seq, RNA-seq, and ATAC-seq, scientists have tracked the dynamics of chromatin accessibility, transcription factor binding, and gene expression with exceptional resolution and accuracy. Innovative CRISPR-based methods made it possible to precisely modify genetic regions, leading to a better comprehension of their functional significance. Significant progress has been made in our understanding of the human genome because to the ENCODE Project, which annotated functional portions previously believed to be junk DNA or non-functional DNA. Via integrative analysis of many genomic datasets, it was found that about 80% of the genome contains components that are biochemically active and involved in regulatory processes. Advanced techniques like ChIP-seq have made it feasible to study protein-DNA interactions across many cell types by revealing intricate regulatory networks. These investigations identified transcription factor binding sites and described histone alterations associated with gene regulation. It demonstrated the intricate arrangement of regulatory components, offering insight into the synchronization of gene expression and cellular function. Furthermore, the project's use of Methyl-seq to explore epigenetics and the important findings from proteomic analyses have deepened our understanding of the intricate regulatory networks governing our genetic inheritance.

**Conclusion.** The ENCODE Project is an expression to human resourcefulness and technological mastery. Through a symphony of cutting-edge methods and relentless scientific research, this massive project has illuminated so far obscured pathways inside our genetic landscape. Future possibilities seem promising for single-cell resolutions, predictive modeling, and multi-omics integrations, as the project advances and the scientific community makes use of these technologies. Ongoing cooperation and free access to data will contribute to our growing understanding of disease mechanisms and the development of tailored therapy.



## **VII. HISTOLOGY SECTION**

***„Scopul final al histologiei este de a înțelege organizarea spațială a țesuturilor și organelor. Doar așa ajungi să deduci funcția și patologia. Fiecare vede în microscop exact atât cât cunoaște.”***

***"The ultimate goal of histology is to understand the spatial organization of tissues and organs. Only through this can one deduce function and pathology. Each person sees under the microscope exactly what they know."***

***Lilian Șaptefrăți,***

*MD, PhD, Professor,*

*Head of Department of Histology, Cytology and Embryology,  
Nicolae Testemitanu State University of Medicine and Pharmacy,  
Chisinau, Republic of Moldova.*

## 1. CHORIO-VILLOUS MESENCHYMAL STROMAL DYSPLASIA IN THE COURSE OF PREGNANCIES



**Author:** Grosu Eugenia

**Scientific advisor:** David Valeriu, MD, PhD, Associate professor, Department of Histology, Cytology and Embryology, Nicolae Testemițanu State University of Medicine and Pharmacy, Chișinău, Republic of Moldova

**Introduction.** Mesenchymal stromal dysplasia is a developmental anomaly of the placenta that is characterized microscopically by dilated stem villi with a myxoid or hydropic appearance, cisterna lacunae, and lack of trophoblastic proliferation in association with thick-walled blood vessels. The listed changes in structure lead to abnormalities in function of placenta and frequently associates with complications during pregnancies such as: intrauterine growth restriction, perinatal death, premature birth; emphasizing the crucial significance of detecting it early.

**Aim of study.** This study aimed to examine the multidisciplinary approach in the diagnosis of placental mesenchymal dysplasia, while addressing the possible etiopathogenetical mechanisms suspected in its origin.

**Methods and materials.** The study was conducted based on retrospective reviews, various scientific data, and specialized articles obtained through search engines such as PubMed, Google Scholar, Embase.

**Results.** Focusing on the most recent articles, the etiopathogenetical foundation is based on the androgenetic biparental mosaicism and chimera formation, depicted as failed replication of maternal genome after fertilization or as a result of dispermy phenomena. Molecular differences can be determined by genetically testing chorionic villous samplings. Beside genetic findings, integrating early ultrasound monitoring, clinical and laboratory screening, and morphological examination allows for improved surveillance of gestation, leading to better outcomes for pregnancies resulting in a normal delivery of the fetus.

**Conclusion.** Placental mesenchymal dysplasia is a condition that may have detrimental effects on fetal health but does not exclude a normal delivery. Therefore, providing necessary diagnostic efforts can aid in resolving complex clinical cases.



## 2. EPITHELIAL TISSUE AS A COMPONENT OF THE IMMUNE SYSTEM

**Author:** Pila Gheorghe

**Scientific advisor:** Fulga Veaceslav, Associate Professor, Department of Histology, Cytology and Embryology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Epithelial tissue is an essential component of the human body, not only for its basic functions such as protection, secretion and absorption, but also for its significant contribution to the immune system. This tissue covers the body's external surface, airways, digestive tract, and many other internal surfaces, forming a primary barrier against pathogens. Although, at first glance, the epithelial tissue may seem more like a passive protector, it has an active role in the body's immune response.

**Aim of study.** The purpose of the study is to explore and highlight the role of epithelial tissue within the immune system, the interactions of epithelial tissue with immune cells, the mechanisms by which epithelial tissue contributes to the detection and neutralization of pathogens, and how it may be involved in abnormal immune reactions, such as allergies or autoimmune diseases.

**Methods and materials.** Analysis of specialized literature from the electronic database PubMed, for the terms "Immune role", "Epithelial tissue".

**Results.** Following the analysis of the literature, it was found that epithelial cells play an active role in the detection and recognition of pathogens. They express different receptors and immunosensors that allow them to identify bacteria, viruses and other potential threats. This early recognition is due to intercellular communication in the epithelial tissue. By means of these mechanisms epithelial cells communicate with neighbouring immune cells to coordinate local immune responses. This communication can have a significant impact on the evolution of inflammatory processes and immunity.

**Conclusion.** This literature review provides a comprehensive insight into the importance of epithelial tissue in the immune system and highlights the need for future research to further unravel the complexity of these interactions. Deeper understanding of these interactions could lead to the development of more effective therapies and treatments for a diverse range of immune and inflammatory conditions.



### 3. HISTOGENESIS AND SPECIFIC MORPHOLOGICAL ASPECTS OF THE PHOTORECEPTORS



**Author:** Iusiumbeli Maria

**Scientific advisor:** Globa Tatiana, MD, PhD, Assistant Professor, Department of Histology, Cytology and Embryology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** People rely on visual cues to navigate the world around them. Vision begins with the detection of light by photoreceptors of the retina - the light sensitive cells of the eye. Photoreceptor types are defined by morphology, gene expression, light sensitivity and function.

**Aim of study.** The goal of this study was to elucidate the regulatory mechanisms of the process of retina histogenesis while highlighting the distinctive morphological attributes of photoreceptors that contribute to their optimal functionality.

**Methods and materials.** A bibliographic study of scientific literature specialized at histogenesis and morphological analysis of photoreceptors.

**Results.** In concordance to the total human photoreceptor population, the rod photoreceptors outnumber cones by 20:1 with average estimated cell numbers of 92 million rods and 4,6 million cones in the adult human retina. This striking difference reflects the visual specialization of these cell types. Rods are extremely sensitive to light, with the ability to produce a response to a single photon of light. On the other hand, cone photoreceptors are adapted for greater spatial resolution and visual acuity. Their shorter outer segments contain continuous open discs formed by invaginations of the ciliary plasma membrane. In addition, the cones do not become saturated at higher light levels and have a more linear circuitry, especially for central vision, where a one-to-one relationship is observed from ganglion cells to bipolar cells to cone cells.

**Conclusion.** This study reveals a complex network of regulatory mechanisms that are required during retinal development to ensure the correct spatial distribution and optimal function of photoreceptors.



#### 4. HPV STATUS AND ASSOCIATED PRECURSOR LESION IN VULVAR SQUAMOUS CELL CARCINOMA

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**Introduction.** There are distinctive precursor lesions related to vulvar squamous cell carcinoma (VSCC) that are associated with high-risk human papillomavirus (HPV) type 16,18 specifically vulvar intraepithelial neoplasia (VIN) and those with vulvar dermatoses not associated with HPV such as lichen sclerosus (LS). Risk factors are cigarette smoking, immunodeficiency, poor hygiene, lichen plan (LP).

**Aim of study.** Vulvar cancer is highly relevant in the context of being the most common invasive malignant tumor that affects the vulva epithelium and the fifth most common type of cancer among women.

**Methods and materials.** This literature review was based on exploring scientific articles from PubMed, Research Gate, Medscape to identify studies examining histologically verified and HPV-tested vulvar cancer.

**Results.** HPV-associated VSCC arise from high-grade squamous intraepithelial lesions, also referred to as vulvar intraepithelial neoplasia of usual type (HSIL/uVIN) in 30% of cases. HPV-independent VSCC derives from a premalignant lesion as differentiated vulvar intraepithelial neoplasia (dVIN) and is associated with chronic inflammatory dermatoses in 70% of cases. HPV-independent VSCC are well differentiated and highly keratinized and arise on an autoimmune background of T-lymphocyte-mediated inflammatory disorder among patients at 60-80 years old. In younger women age 30-40, the tumor has a warty or basaloid pattern. HSIL has a relatively low risk of progression to VSCC. The prognosis is worse in patients with VSCC associated with dVIN than in patients with uVIN.

**Conclusion.** HPV status is a risk factor for VSCC, which is correlated with the survival rate. HPV-negative VSCC have a worse survival rate than HPV-positive VSCC. The role of HPV as a potential biomarker for early cancer diagnosis and predictor of prognosis and cancer treatment is significant.

## 5. MICROSCOPIC AND ULTRASTRUCTURAL CHARACTERISTICS OF KERATINOCYTES



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**Introduction.** Keratinocytes are the principal epidermal cells, constituting the outermost layer of the skin - the external and largest organ of the human body. Epidermal keratinocytes are highly specialized epithelial cells that are designed to perform a very specific function: separating the organism from its environment, but not only.

**Aim of study.** The study aims was to describe microscopic and ultrastructural characteristics of keratinocytes and identification of keratinocytes specific markers.

**Methods and materials.** A bibliographic study of scientific literature specialized at microscopic and ultrastructural characteristics of keratinocytes and keratinocyte-specific markers

**Results.** Epidermal keratinocytes are differentiated progressively through the layers, from the basal, spiny and granular to the stratum corneum. Depending on their function and state of differentiation, they have different structural characteristics, sometimes more complex than those of the simple epithelial cells that make up the digestive tract and exocrine glands. Basal keratinocytes attach to the basement membrane with hemidesmosomes and have keratins such as KRT5 and KRT14. Suprabasal keratinocytes begin to produce KRT1 and KRT10 and are attached to the neighboring keratinocytes via desmosomes. Granular layer cells with keratohyalin granules express KRT2 and are attached to neighboring cells mostly by tight junctions. The advances in the understanding of skin development have provided information on new molecular markers such as filaggrin (Flg) (granular and cornified layer marker) and loricrin (Lor) (cornified layer marker), which are differentiation markers and play an important role in the barrier function of the skin.

**Conclusion.** The understanding of the molecular events underlying differentiation of the keratinocytes has advanced greatly in recent years. Progress has also been made in the understanding of the gene expressed regulations of human keratinocytes and, as well, in the elucidating of their structure and function.



## 6. MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL FEATURES IN THE DIFFERENTIAL DIAGNOSIS OF HYDATIFORM MOLE

**Author:** Rusnac Ioana Maria

**Scientific advisor:** David Valeriu, MD, PhD, Associate professor, Department of Histology, Cytology and Embryology, *Nicolae Testemițanu* State University of Medicine and Pharmacy, Chișinău, Republic of Moldova

**Introduction.** Hydatidiform mole is a pathological pregnancy that belongs to the gestational trophoblastic diseases group. During histomorphological lesion examination, differentiating between molar and non-molar lesions can be challenging due to morphological masking leading to imprecise results.

**Aim of study.** The aim of this study is to evaluate the morphological and immunohistochemical features in the differential diagnosis of hydatidiform mole.

**Methods and materials.** During this study information from databases such as PubMed, Scopus, Google Scholar, academic social networks such as ResearchGate and medical books published by: Elsevier, Springer, etc. has been utilized.

**Results.** Hydatidiform mole is a pathological pregnancy with a varying degree of trophoblast proliferation classified as part of molar pregnancies in the gestational trophoblastic disease group, which morphologically and cytogenetically can be either partial (with the predominance of genetic material from the father) or complete (only paternal genetic material is present). Complete hydatidiform mole's chorionic villi are enlarged with marked generalized hydrops, with often present cistern formation, with marked circumferential trophoblast hyperplasia, with marked trophoblast atypia at the implantation site and lack of fetal vessels and RBCs. Meanwhile, in partial hydatidiform mole are present 2 populations of villi – one with enlarged villi with scalloped and irregular contours and one with small fibrotic villi, frequent cistern formation, minimal trophoblast atypia, and the presence of fetal vessels and RBCs. Immunohistochemically, the genetic product of CDKN1C - p57 is applied, which will lack expression in CHM, and will be expressed in PHM.

**Conclusion.** The differential diagnosis of hydatidiform mole offers the possibility of establishing an accurate diagnosis and preventing medical errors.



## 7. MORPHOLOGICAL FEATURES OF THE UMBILICAL ARTERY IN NORMAL PREGNANCY AND PREECLAMPSIA



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**Introduction.** The vascular component of the umbilical cord is represented by two umbilical arteries and one corresponding vein. The characteristic structure of the umbilical arteries makes them highly vulnerable to any structural deviations. Therefore, the morphological state of these vessels is considered a crucial indicator of fetal status. Preeclampsia is a systemic vascular condition that typically manifests after the 20th week of gestation.

**Aim of study.** This study aimed to identify the distinct characteristics of the umbilical artery in normal pregnancies and preeclampsia, with an understanding of the pathological mechanisms involved in preeclampsia.

**Methods and materials.** The study was conducted based on retrospective reviews, various scientific data, and specialized articles obtained through search engines such as PubMed, Google Scholar, ScienceDirect, and IBN.

**Results.** The umbilical artery is a medium-sized muscular artery characterized by an irregularly contoured lumen and walls composed of two distinct layers: intima and media. The intima is the innermost layer of the vessel, much thicker compared to the umbilical vein. It is composed of endothelium and a reduced subendothelial space. Small-sized smooth muscle cells arranged perpendicularly to the endothelial basement membrane were also identified. The media layer contains bundles of smooth muscle cells arranged in two distinct layers. In conditions of preeclampsia, systemic endothelial dysfunction is observed, manifested by increased vascular permeability and fluid accumulation between smooth muscle cells of the media with the expansion of intercellular spaces. The arterial wall significantly increases in size, approximately by 20%, due to interstitial edema plus an increase in the intima and media layers, caused by the migration of smooth muscle cells toward the endothelium. These changes contribute to the narrowing of the arterial lumen.

**Conclusion.** The umbilical artery in pregnancies complicated by preeclampsia exhibits significant morphological changes. These alterations impact the supply of blood and nutrients to the fetus, resulting in hypoxia and impaired growth.



## 8. ROLE OF FIBROBLASTS AND OTHER NON-FIBROBLASTIC STROMAL CELLS IN SUSTAINING THE THYROID GLAND STRUCTURE

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**Introduction.** The thyroid gland is one of the most important endocrine organs that is responsible for producing hormones that regulate metabolism, growth, and development. Giving the primordial function of thyroid gland to secrete thyroid hormones, the majority of studies are oriented toward parenchima, the stroma being left in the shadow. In order for the parenchima to exert its function, it needs the stroma with its cells to support it, role of fibroblasts being undeniable. Stroma of the thyroid gland is still a mystery, that requires research and studies.

**Aim of study.** The study aims was to describe fibroblasts and other non-fibroblastic stromal structures role that sustain the structure of the thyroid gland.

**Methods and materials.** For this review were used articles and scientific publications from medical sites PubMed, Google Scholar, Medscape.

**Results.** Fibroblasts are connective tissue cells that secrete extracellular matrix components, which form a scaffold that supports the various cell types within the gland, including thyroid follicular cells responsible for hormone synthesis. Fibroblasts contribute to the maintenance of tissue architecture within the thyroid gland. Stromal cells, such as fibroblasts, mast cells and macrophages, participate in the regulation of angiogenesis by secreting growth factors and interacting with endothelial cells. Stromal cells help modulate the local immune environment, influencing the balance between tolerance and immune response to prevent autoimmune reactions. In addition, fibroblasts and other non-fibroblastic stromal cells play a role in facilitating regenerative process by providing the necessary support for cell proliferation and tissue remodeling.

**Conclusion.** Fibroblast functions extend beyond structural support to include regulatory roles in angiogenesis, immune modulation, extracellular matrix remodeling, and support for tissue regeneration. The collaboration between fibroblasts and other stromal cell types within the thyroid gland is essential for maintaining its structure and function. Key words. thyroid gland, stroma, fibroblasts, stromal cells.

## 9. THE HISTOLOGICAL MIRACLE OF THE CIRCULATORY SYSTEM



**Author:** Ustroj Liudmila

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**Introduction.** The cardiovascular or circulatory system is designed to ensure the survival of all cells in the body at all times and does this by maintaining the immediate chemical environment of each cell in the body at a composition suitable for that cell's normal function.

**Aim of study.** This study aims to describe the histological peculiarities of the circulatory system.

**Methods and materials.** A bibliographic study of scientific literature specialized at histological special features of circulatory systems.

**Results.** The human cardiovascular system is the product of hundreds of thousands of years of evolution. Throughout its long history, the cardiovascular system has been shaped and reshaped by developing adaptations to the haemodynamic challenges it faced at each step. The analysis of cardiovascular evolution provides a fascinating opportunity to identify the potential weaknesses of our cardiovascular system, to better understand the pathophysiology of disease and to formulate treatment alternatives. Our cardiovascular system is the result of the above-mentioned evolutionary process, and it reenacts this evolutionary history during embryogenesis. The fully developed 4-chambered human heart develops from the successive stages of the single peristaltic tube, the 2-chambered fish heart with a spongy ventricular cavity, the 3-chambered fish heart with a spongy ventricular cavity, more compact amphibian heart, and the three-and-a-half-chambered the three-and-a-half-chamber reptilian heart with a partially divided ventricle. Six pairs of pharyngeal arteries develop and either regress or metamorphose into mature vascular structures as predicted by evolutionary history. The microcirculation deserves special attention, because through the walls of these vessels oxygen is exchanged, among other substances. In addition, arterioles, also known as 'resistance' vessels, are the main site of blood flow control. Thus, the blood vessels of the microcirculation play important roles in both the convective (arterioles) and diffusive (capillaries) transport of oxygen. These blood vessels are classified as arterioles, capillaries and venules and range in diameter from about 100-200  $\mu\text{m}$  for the largest arterioles and venules to about 5  $\mu\text{m}$  for capillaries. In terms of their structure, all these vessels possess an inner layer of endothelial cells.

**Conclusion.** Every biological system we encounter is so detailed and rational that, far from being created by chance, the slightest deviation would clearly disrupt its functioning.



## 10. THE IMPACT OF COVID-19 DISEASE ON PLATELETS AND COAGULATION

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**Introduction.** Platelets are formed elements of blood that play an important role in blood clotting. As the main mediator of thrombus formation, platelets have become one of the key aspects in the study of SARS-CoV-2. COVID-19 is primarily a respiratory disease. However, critically ill patients may develop systemic symptoms, including coagulopathy. COVID-19 is associated with disseminated intravascular coagulation (DIC), sepsis-induced coagulopathy (SIC), local microthrombi, venous thromboembolism (VTE), arterial thrombotic complications and thrombotic inflammation, as well as other bleeding disorders.

**Aim of study.** To explore the possible mechanisms of platelets implications in coagulopathy disorders associated with COVID-19.

**Methods and materials.** We selected and analyzed 30 articles in the PubMed and Google Scholar databases based on the following keywords: COVID-19, coagulopathy, platelets in COVID-19.

**Results.** Based on the information, approximately 20%-50% of hospitalized patients with COVID-19 have hematologic abnormalities in coagulation tests (elevated D-dimer, prolonged PT, thrombocytopenia, and/or low fibrinogen levels). There are several mechanisms of interaction between platelets and the SARS-CoV-2 virus, the main of which is a dysfunctional and excessive immune response, often referred to as a cytokine storm. Elevated levels of proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- $\alpha$ ) are associated with coagulopathy. Inflammation can activate the coagulation cascade, increasing the formation of thrombin and fibrin, promoting clot formation. Other possible mechanisms include endothelial dysfunction, when the SARS-CoV-2 virus enters cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed on the surface of endothelial cells lining blood vessels where the virus enters and spreads replicated, this leads to endothelial dysfunction, which contributes to the procoagulant state and also promotes blood clot formation.

**Conclusion.** This review underscores the critical importance of comprehending the potential mechanisms of coagulation system involvement in SARS-CoV-2 infection, for the early detection of bleeding disorders and the avoidance of factors that contribute to progression of the disease.



## 11. THE MOLECULAR PROFILE OF THYROID CARCINOMAS



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**Introduction.** Thyroid cancer is the most common endocrine malignancy, accounting for the seventh most common cancer in women. Thyroid nodules are potentially malignant. The determination of any mutation such as TERT, BRAF, PAX8/PPAR $\gamma$ , RAS in a thyroid nodule provides a strong indication for malignancy.

**Aim of the study.** Studying the molecular profile for thyroid carcinomas

**Methods and materials.** An online database search of relevant published articles using the Cochrane Database of Systematic Reviews, PubMed, Embase and Google was performed via Google search.

**Results.** The specificity of the BRAF V600E PTC is 100%, but the sensitivity is 30%. BRAF mutations were found in 74% of PTC and 7.7% of FTC. RAS mutations are the primary changes in follicular adenomas up to 67%. The pAX/PPAR $\gamma$  fusion rearrangement has an inactivating effect on the PPAR $\gamma$  tumor suppressor gene and is found in 30–60% of FTC and 38% of the follicular variant of papillary thyroid cancer. TERTp mutations, more specifically C228T and C250T, account for 5–25% of PTC and 35% of FTC.

**Conclusion.** Molecular testing of thyroid nodules and thyroid cancer has improved the diagnostic accuracy of indeterminate thyroid nodules and provides useful information regarding tumor prognosis. Future development of predictive models that will combine genetic data with clinical and cytological findings will enable accurate preoperative risk assessment, precisely guiding individualized treatment options.

**Keywords.** Follicular thyroid cancer (FTC); molecular diagnosis; papillary thyroid cancer (PTC).



## 12. THE ROLE OF VEGF IN PSORIASIS

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**Scientific advisor:** Saptefrati Lilian, MD, PhD, Associate Professor, Department of Histology, Cytology and Embryology, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Psoriasis is a chronic inflammatory disease, which affects skin and joints. Psoriasis is also commonly associated with a increased capillary permeability, and excess VEGF production . As angiogenesis is one of the key features of psoriasis, various studies focus on the identification of pro-angiogenic mediators in psoriatic skin.

**Aim of the study.** Studying the role of VEGF in psoriasis

**Materials and methods.** An online database search of relevant published articles using the Cochrane Database of Systematic Reviews, PubMed, Embase and Google was performed via Google search.

**Results.** Histopathological markers of skin in psoriasis include: the infiltration of multiple immune cells, keratinocyte hyperplasia, activated mast cells, and accentuated vascularity in the dermis. Psoriasis is also commonly associated with a increased capillary permeability, and excess VEGF production. VEGF-A is highly expressed in the lesional skin of patients with psoriasis compared to non-lesional skin and healthy skin. In addition, the plasma levels of VEGF-A are higher in patients with psoriasis than in healthy individuals and levels correlate with disease severity. VEGF-A is mainly produced by activated keratinocytes in the skin of patients with psoriasis. Smaller amounts of VEGF-A are produced by fibroblasts and mast cells.

**Conclusion.** The VEGF-A receptors, VEGFR-1 and VEGFR-2 are expressed on blood endothelial cells. VEGFR-1 is also expressed on epidermal keratinocytes in healthy skin and in the skin of patients with psoriasis.

**Keywords.** Psoriasis skin, VEGF-1 receptors, VEGF-2 receptors.

### 13. TROP-2 EXPRESSION IN PAPILLARY THYROID CARCINOMAS



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**Introduction.** Papillary thyroid carcinoma (PTC) represents the most common primary malignant thyroid lesion. As the diagnosis of PTC could be challenging in some cases and borderline nuclear features could be seen in some benign lesions, trophoblast cell surface antigen-2 (Trop-2) is proposed to help make the correct diagnosis. Trophoblast cell surface antigen-2 (Trop-2) is a glycoprotein that was first described as a membrane marker of trophoblast cells and was associated with regenerative abilities.

**Aim of study.** Evaluating of Trop-2 expression in papillary thyroid carcinomas

**Methods and materials.** We studied the data of the scientific medical literature, identified by the Google Search search engine, from the databases: PubMed, Cochrane, Scopus, international clinical guidelines, NCCN, and ESMO.

**Results.** Trop -2 has been reported to be overexpressed in various human carcinomas and is suggested to be a prognostic marker. Our findings in data of a distinct membranous staining pattern of TROP-2 in 90% of papillary thyroid carcinomas on expression on tissue microarray sections and none of the benign thyroid lesions suggested the potential diagnostic utility of TROP-2 in the classification of thyroid neoplasms. The immunohistochemistry results in different experiments further showed that the positive expression rate of TROP2 protein in PTC was ~70%, while the positive expression rate of TROP2 protein in adjacent tissues was ~35%. TROP-2 showed ~90% sensitivity ~98% specificity~ 95% and ~93% accuracy.

**Conclusion.** TROP2 was found to be highly expressed in PTC and promoted the proliferation, invasion and migration of PTC. TROP-2 shows high specificity and better accuracy than other markers.

**Keywords.** Papillary thyroid cancer (PTC), Trop-2, lesion.

## **VIII. INTERNAL MEDICINE SECTION**

***„Educația și sănătatea sunt 2 piloni fundamentali pe care se bazează o societate prosperă. Vă doresc succes în misiunea nobilă care ați ales-o. “***

***„Education and health are 2 fundamental pillars on which a prosperous society is based. I wish you success in your chosen noble mission.”***

***Sergiu Matcovschi,***

*Professor, MD, PhD,*

*Clinical Synthesis Discipline, Department of Internal Medicine,*

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***„Medicina internă este o ecuație provocătoare. Medicul internist conjugă empatia, cunoștințele adunate și decizia de diagnostic, îngrijind suferința cu curaj, smerenie și înțelepciune.”***

***„Internal medicine is a challenging equation. The internist combines empathy, accumulated knowledge, and diagnostic decision-making, caring for suffering with courage, humility, and wisdom.”***

***Minodora Mazur,***

*Discipline of Internal Medicine-Semiology,*

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# CARDIOLOGY SECTION



*„Cardiologia deschide ușa către dansul intricate al ritmului inimii, unde fiecare bătaie răsună ca o simfonie a echilibrului subtil dintre vigoare și vulnerabilitate, inspirând mințile curioase să dezlege misterele sale. În călătoria educației medicale, studenții pătrund în adâncurile palpitate ale cardiologiei, unde fiecare descoperire devine o mărturie a căutării neobosite pentru înțelegerea sacralității sănătății și a rezilienței spiritului uman.”*

*„The realm of cardiology unveils the intricate dance of the heart's rhythm, where each beat echoes the symphony of life's delicate balance between vigor and vulnerability, inspiring inquisitive minds to unravel its mysteries. In the journey of medical education, students delve into the pulsating depths of cardiology, where every discovery becomes a testament to the relentless pursuit of understanding the sanctity of health and the resilience of the human spirit.”*

**Marcel Abraș,**

*MD, PhD, Associate Professor,*

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## 1. A COMPARATIVE STUDY ON THE OPTIMAL SHUNT TYPES FOR SURGICAL MANAGEMENT OF TOF

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**Introduction.** Tetralogy of Fallot (TOF) is a congenital cardiac anomaly with intricate structural aberrations. Surgical approaches for TOF range from immediate repair to staged methodology. Blalock et al. pioneered the Blalock-Taussig shunt, which reduced cyanosis in patients with pulmonary stenosis or atresia. Modifications led to the emergence of the modified Blalock-Taussig shunt (mBTS), which uses a Gore-Tex tube. Contemporary formulations like the Waterston shunt and Potts shunt establish connections between the ascending aorta and the main/right pulmonary artery.

**Aim of study.** The study compares various shunts and their techniques to determine the superior option and explain the rationales behind their differences.

**Methods and materials.** The study focused on articles from 2000-2023. The study excluded non-English language literature, meta-analysis, systematic reviews, and abstracts. The search was filtered with articles based on the keywords “Tetralogy of Fallot,” “Surgical treatment of tetralogy of Fallot,” “Shunts in TOF,” etc. from PUBMED, Embase and Google scholar.

**Results.** This systematic review of 11 studies on shunt interventions in pediatric Tetralogy of Fallot patients undergoing palliative or staged repair revealed distinct outcomes for each type. The Modified Blalock-Taussig (BT) Shunt was the most prominent, with 10 studies focusing on it (90.9%). It was found to be favorable for symptomatic Tetralogy of Fallot (TOF) patients with hypercyanotic spells, ductal dependent pulmonary circulation, and weight <4 kg. However, it was deemed ineligible for TOF/PA with patent ductus arteriosus and TOF with severe right ventricular outflow tract obstruction (RVOTO) due to documented post-procedure deaths. The study highlighted advantages such as avoidance of circulatory arrest, low mortality, low morbidity, and a low incidence of reoperation after complete repair when management strategies catering to patient size, systemic arterial saturation, and anatomy were adopted. However, complications such as over circulation, shunt thrombosis, seroma, and pseudoaneurysm were noted.

**Conclusion.** The primary choice for shunt interventions in pediatric Tetralogy of Fallot patients was the Modified Blalock-Taussig Shunt, demonstrating positive outcomes. However, the Classic BT Shunt and central shunt showed less significance, with the Modified BT Shunt showing suitability but associated complications, and the Classic BT Shunt offering personalized management benefits.

## 2. ADHERENCE TO TREATMENT OF PATIENTS WITH HYPERTENSION



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**Introduction.** Hypertension (HTN) has a high incidence, in Europe one in three people are diagnosed with high blood pressure. Among the determinants of hypertension, as well as cardiovascular risk factors, others such as socioeconomic status, education level, income and occupation are also being investigated.

**Aim of study.** Evaluation of the socio-economic status of patients with arterial hypertension from urban and rural areas and assessment of treatment compliance.

**Methods and materials.** In accordance with the proposed aim and objectives, we created a study group of 70 HTN questioned patients, average age  $62.25 \pm 8.8$  years, from the Institute of Cardiology, hospitalized between 2021 -2022 using Hill-Bone scale.

**Results.** The results obtained revealed a similar compliance in the 3 areas evaluated: reducing sodium intake, keeping doctor's appointments and taking medication. There were 32 (40%) patients in the non-compliant category, including 9 (11.25%) women and 23 (28.75%) men. Patients from the rural area have incomes lower than 10,600 lei in 77.12% versus the urban region only in 68.56%,  $p < 0.05$ . Appreciation of the level of education through higher education scores in the urban area 40%, compared to the rural area 34.27%, when they are not influenced by the employee status,  $p > 0.05$ .

**Conclusion.** The assessment of the socioeconomic status in patients with arterial hypertension was mainly influenced by the average level of education 61.4%, the status of employee in 62.85% and low income in 72.8%. People with high incomes and with high levels of education are more aware of their own health and therefore have a significantly reduced prevalence of HTN. Differences in the relationship between educational groups and the prevalence of hypertension may be explained by significantly poorer health care by education level and income. In addition, people with lower levels of education have less information and poorer therapy.



### 3. ANEMIA IN CARDIORENAL SYNDROME

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**Introduction.** Cardio-renal syndrome is frequently complicated with anemia leading to reciprocal and progressive cardiac and/or renal damage. The interaction between HF, IR and anemia forms a triad, called anemic cardio-renal syndrome (CARS), a complex disease that is accompanied with adverse reactions, increased risk of hospitalization, mortality and decreased quality of life.

**Aim of study.** Studying the role of anemia in patients with cardiorenal syndrome based on the current literature.

**Methods and materials.** A systematic review of the literature was performed using the Medline, PubMed, Scopus and Web of Science databases to identify relevant articles referring to "anemia", "heart failure" and "chronic kidney disease".

**Results.** The obtained results will provide additional opportunities to improve the treatment of anemia. The concept of installing anemia in SCR is also described and perfected. The particularities of the incidence of anemia in HF and of iron deficiency in HF correlated with LVEF will be reported. New therapeutic options may improve the survival rate of SCR patients and/or mitigate disease progression.

**Conclusion.** Management of ACS requires a multidisciplinary approach that takes into account functional and absolute iron status, cardiac/renal disease classification, and prognostic indicators for clinical worsening. The results of such clinical trials will help in the design of therapeutic strategies for the management of anemia following cardio-renal pathologies.

**Keywords.** Anemia, heart failure, cardiorenal syndrome.

#### 4. CANCER-ASSOCIATED THROMBOSIS



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**Introduction.** Cancer-associated thrombosis is one of the leading causes of morbidity and mortality in cancer patients. It occurs frequently in patients with clinically active malignancy, however, there is a subgroup of patients in whom thrombosis may be the first manifestation of cancer. Because the diagnosis of malignancies can be challenging in pulmonary embolism, some laboratory tests might suggest a neoplastic process.

**Case statement.** A 48-year-old male was referred to the Cardiology Institute with suspicion of infective endocarditis. Without any known chronic disease, he went to the hospital after a long driving trip (about 48 h). The patient was directed to Cardiology Institute with thromboembolic disease: deep vein thrombosis of the right lower limb, pulmonary embolism, pneumonia-infarction and ischemic thalamic stroke. At admission to the hospital, he presented lumbar, thoracic, interscapular and subscapular pains, marked general weakness and diffuse headache. Infective endocarditis was excluded by blood culture and echocardiography. The patient, being on anticoagulant treatment (antivitamin K medication), complains of intensification of chest pain and CK-MB values increase up to 462 U/L (reference values: 0-24 U/L) and thrombocytopenia occurs. Later, CK-MB reaches values of 1530 U/L and severe thrombocytopenia ( $21 \times 10^9/L$ ). EKG without ischemic changes, the troponin values were within the reference values. Thoracic and abdominal CT shows mediastinal, abdominal lymphadenopathy and vertebral metastases. The histopathological examination of the supraclavicular lymph nodes: lymph nodes with squamous malignant tumor metastases (of uncertain origin), cellular pleomorphism, frequent atypical mitoses, lympho-vascular invasion. The diagnosis of lung and abdominal carcinomatosis with bone metastases of unknown primary origin was confirmed.

**Discussions.** We aimed to present that in some cases thromboembolic disease can hide a neoplastic process. Numerous reports have appeared that deal with the presence of CK-MB or CK elevations in a variety of malignancies in the absence of obvious cardiac injury. This case indicates that our patient's thrombosis with his severe complications did originate from cancer.

**Conclusion.** Patients with malignancy have often an increased risk of thrombosis, both venous and arterial. Although the association between cancer and thrombosis has been appreciated for over 150 years, the mechanisms of cancer-associated thrombosis, like cancer itself, are multifactorial and incompletely understood. Cancer type, stage, tumor-derived factors, and genetics all affect the risk of cancer-associated thrombosis.



## 5. CARDIAC ABSCESS, FATAL COMPLICATION IN INFECTIVE ENDOCARDITIS, CLINICAL CASE

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**Introduction.** The incidence of infective endocarditis (IE) is 3-10 per 100.000 people/year, the disease causing a high mortality rate (30%) in 1 month. The incidence of cardiac abscesses among patients with IE is between 30-40%, and the aortic valve (AoV), the interventricular septum, and the mitral valve (MV) are the most affected cardiac structures.

**Case statement.** The 82 y.o. man was hospitalized by emergency in the V-th Department of the Institute of Cardiology with complaints: dyspnea during minimal physical activity, fatigue, fever, sweating. Objective data: pallor of the teguments, moderate peripheral edema, decreased basal vesicular murmur, arrhythmic heart sounds, mitral diastolic and aortic systolic murmur, HB - 81 b/min, BP - 100/60 mmHg. Paraclinical: Hb 138 g/l, erythrocytes  $4.48 \times 10^{12}$ , leukocytes  $7.4 \times 10^9$ , prothrombin 68%, CRP 48 U/L. EcoCG: EF- 45%. Old vegetations on the aortic valve. Moderate stenosis of AoV, regurgitation of MV III deg., AoV - II deg., TrV - IV deg. Severe pulmonary hypertension. Suspected myocardial abscess in right atrium (RA) and fistula between the right coronary sinus and RA. Chest X-ray: Hydrothorax in the left sinus and subdiaphragmatic. Enlarged transverse diameter of the heart. The treatment with triple antimicrobial and antifungal therapy, cardiac glycosides, anticoagulants and diuretics was initiated and the team discussed the emergency of the surgical treatment.

**Discussions.** In this case, due to the unstable condition of this patient, the doctors decided to postpone the surgical intervention until the additional investigations are made. This led to the significant worsening of the patient's condition and the decompensation of the cardiac pathology.

**Conclusion.** Infective Endocarditis complicated with cardiac abscess requires prompt eradication of the infection by emergency cardiac surgery, to save the patient and minimize the chance of other complications developing.



## 6. CARDIORENAL SYNDROME



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**Introduction.** Cardiorenal syndrome (CRS) is a condition characterized by the complex bidirectional relationship between the heart and kidneys, leading to acute or chronic dysfunction of these organs. The relationship between cardiorenal connectors and hemodynamic and non-hemodynamic factors is essential to understanding this syndrome. The clinical importance of these interactions relates to the observed changes in hemodynamic factors, neurohormonal markers, and inflammatory processes. It is a complex disease that is associated with adverse reactions, increased risk of hospitalization, mortality and decreased quality of life.

**Aim of study.** Study of cardiorenal syndrome based on contemporary literature.

**Methods and materials.** A systematic review of the literature was performed using the Medline, PubMed, Scopus and Web of Science databases to identify relevant articles referring to "cardiorenal syndrome", "heart failure" and "chronic kidney disease".

**Results.** This review focuses on the classification and subcategories of the cardiorenal syndrome, the clinical significance of biomarkers in the diagnosis of CRS, and the identification of mechanisms underlying its development and progression. In the end, the review summarizes the available therapeutic options that can improve the survival of patients with CRS and/or mitigate the progression of the disease.

**Conclusion.** Cardiorenal syndrome must be managed appropriately to efficiently reduce mortality and morbidity rates, requiring a strategic, multidisciplinary, multidimensional, and systematic approach. Managing CRS provides valuable perspectives for researchers, healthcare professionals, and decision-makers involved in the complex management and treatment of this condition.

**Keywords.** Cardiorenal syndrome, heart failure, chronic kidney disease.



## 7. CHALLENGING CLINICAL CASE

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**Introduction.** Atrial septal defect is a congenital disease characterized by the presence of communication between the right and left atria, leading to abnormal blood movement at the heart level. This defect occurs in 1 out of 1,500 newborns. There are several complications that can occur in the postoperative period, one of which we will talk about in this case.

**Case statement.** In this work we present the case of an 18-year-old girl with a congenital atrial septal defect. An operation was performed in 2019 in order to eliminate the defect and perform a plastic repair of the tricuspid valve. In the postoperative period a complication such as a complete AV block was detected. To fix this complication during a preventive procedure a VVI Endurity type pacemaker (St. Jude/Abbott) was implanted. During the routine examination the patient underwent echocardiography which established that the ejection fraction was 30%. It was decided to implant a CRTD Solara (Medtronic) pacemaker on 11/20/2023.

**Discussions.** During installation of the CRT-D pacemaker we encountered difficulties such as cannulation of the coronary sinus. We tried to fix this problem by using Guide wire floppy, but as its strength was not enough, we resorted to using Guide grand slam, because it is denser in its properties. As a result, coronary sinus cannulation was successfully performed, as well as the installation of atrial and ventricular leads.

**Conclusion.** CRT-D remains the gold standard treatment for dilative CMP and this medical case is proof of that.

## 8. COMPREHENSIVE EVALUATION OF PATIENT WITH HEART FAILURE DUE TO ISCHEMIC HEART DISEASE



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**Introduction.** Heart failure is one of the critical and challenging conditions in the medical field, which is a leading cause of mortality and morbidity. It's a widespread notable issue in public health. Ischemic heart disease can lead to heart failure. This clinical case study aims to provide information about the evolution of the disease and effectiveness of the adjusted treatment.

**Case statement.** Case presentation. A 64-year-old male patient was admitted to the Institute of Cardiology with complaints of severe chest pain, dyspnea with slight limitation of physical activity, orthopnea, and severe headache. His condition worsened for about one week. He has a long history of dyslipidemia and hypertension with peak blood pressure of 230/120 mmHg. Moderate edema of the legs was noted during physical examination, and lung auscultation revealed the presence of rales. On paraclinical examination, blood test shows elevated level of NT-proBNP which is 600ng/ml and increased level of troponin. ECG shows the presence of an inferior myocardial infarction with ST elevation in leads II, III and AVF and echocardiography shows a preserved ejection fraction along with mild mitral regurgitation. Acute coronary syndrome was established, and he underwent right coronary artery stenting. This patient's diagnosis is Heart failure due to ischemic heart disease, NYHA class III. After discharge, he was advised to continue treatment with dapagliflozin, angiotensin II receptor blockers, beta-blockers and mineralocorticoid receptor antagonists, dual antiplatelets, and a statin. After 12 weeks of follow-up, the patient's condition was improved and stable

**Discussions.** In the presented case, the cause of heart failure with preserved EF is due to ischemic heart disease. The comprehensive approach to this patient involves ongoing medication follow-up and regular monitoring.

**Conclusion.** Certain risk factors are the main cause of acute coronary syndrome and heart failure, so to prevent this, we need to maintain an appropriate lifestyle modification, dietary control and adjusted medical treatment so that we can improve the quality of life of the patient and reduce hospitalizations.



## 9. CRITICAL DECISIONS IN CORONARY INTERVENTIONS: BYPASS VS. STENT - A DETAILED ANALYSIS

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**Introduction.** In the context of cardiovascular interventions, coronary artery bypass grafting (CABG) and coronary stenting represent distinct approaches to address coronary artery disease and the choice between them represents a pivotal decision that significantly impacts patient outcomes. CABG involves the surgical rerouting of blood flow around blocked coronary arteries using grafts, typically harvested from the patient's own vessels. On the other hand, coronary stenting is a percutaneous procedure where a stent, a small metal mesh tube, is inserted to prop open narrowed arteries, restoring blood flow.

**Aim of study.** The research was conducted on Web of Science using the keywords "coronary stent," "CABG," "coronary bypass" and "percutaneous coronary intervention."

**Methods and materials.** Scientific papers were selected based on inclusion criteria, which involved patient groups treated with both CABG and coronary stent, hospitalization period, in-hospital mortality, bleeding events, stroke, postoperative delirium, the well-being of patients and procedure effectiveness. Articles mentioning patients with major comorbidities, NSTEMI, angina pectoris and any other cardiac surgical intervention ongoing during the same period of hospitalization were excluded. Risk of bias was not assessed, and PRISMA criteria were used for data synthesis. Out of the total of 16 articles found, 6 studies with 5 between 2005 and 2007, and the sixth conducted in 2018 were selected.

**Results.** The cohort comprised 12038 patients, with 2215 treated using CABG and 9823 through percutaneous coronary intervention. The patient group treated with CABG had a hospitalization period of 13.04+- 9.26 days, while the group treated with PCI had a hospitalization period of 5.71 +- 7.60 days. In the CABG-treated patient group, 52 out of 2215 (2.34%) patients died, while in the PCI-treated group, 251 out of 9823 (2.55%) patients succumbed. In the CABG-treated group of 2,215 patients, 30 experienced a stroke (1.35%), compared to 45 strokes among the 9,823 patients treated with stents (0.45%).

**Conclusion.** In conclusion, the comparative analysis of Coronary Artery Bypass Grafting (CABG) and Percutaneous Coronary Intervention (PCI) suggests nuanced considerations. Both interventions demonstrate similar mortality rates. The decision between these procedures should be meticulously tailored to individual patient characteristics, considering factors like lesion complexity, and long-term outcomes. A comprehensive evaluation, weighing the advantages and disadvantages of CABG versus PCI, remains crucial in optimizing cardiovascular care."

## 10. DEEP VENOUS THROMBOSIS COMPLICATED WITH ACUTE PULMONARY EMBOLISM, A CASE OF A PATIENT WITH PROVEN THROMBOPHILIA



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**Introduction.** Pulmonary thromboembolism is the clinical condition that is the consequence of thrombus embolic obstruction of the pulmonary arteries or its branches, representing a major cardiovascular emergency. Venous thromboembolism (VTE) presents clinically as deep vein thrombosis (DVT) or pulmonary embolism (PE). According to the literature, pulmonary embolism ranks third among acute cardiovascular syndromes, after myocardial infarction and stroke.

**Case statement.** We present the case of a patient hospitalized with complaints of marked dyspnea at rest, acrocyanosis, fatigue. Hemodynamically detected sinus tachycardia (FCC 102 c/min) decreased oxygen saturation (SaO<sub>2</sub> 85%), BP 130/80 mmHg. High risk was determined when assessing the WELLS score. Laboratory analyzes determined D-Dimers >8.27 mg/l. At echocardiography (echo-cg), dilation of the right parts of the heart is found. In the cavity of the right atrium, hypermobile inhomogeneous formations of large sizes were visualized, with a protrusion in the right ventricle. Venous doppler evaluation detected thrombosis of the popliteal vein on the right. PESI prediction score – intermediate risk. Angio CT reported thrombi in both pulmonary arteries with dimensions of 3.4 cm on the right and 2.0 cm on the left respectively. The evolution of the disease with the presence of thrombi with different localization suggested the determination of genetic polymorphisms where the presence of mutations in the genes responsible for hereditary thrombophilia was confirmed. Treatment with fondaparinux and oral anticoagulant was instituted, with target INR values maintained at 2-3. After the establishment of the diagnosis and the institution of effective treatment, the improvement of the clinical condition was noted, the complete resorption of thrombi from the heart and the lower limb. Echo-CG revealed the return to normal of the right sides of the heart. Complete resolution of thrombi in the pulmonary arteries was demonstrated at CT angio after five months.

**Discussions.** PE is a serious manifestation of VTE with a 90-day mortality rate of approximately 15-20%. One of the common causes of VTE is thrombophilia, which can be of three types: hereditary, acquired, and mixed. Several hereditary mutations/polymorphisms affecting genes encoding factors involved in hemostasis are described. In the patient presented with VTE, we determined four genetic mutations: F2/Prothrombin (coagulation factor II), FGB/Fibrinogen (coagulation factor I), ITGA2-O2/integrin (platelet receptor for collagen), PAI-1/Serpin (tissue plasminogen activator antagonist).

**Conclusion.** Considering the case of the patient in whom venous thrombosis with various localization was demonstrated, we suspected a thrombophilia, later demonstrated by genetic polymorphism analysis and genetic mutations were diagnosed. Consequently, the decision was made for long-term treatment with oral anticoagulants.





## 11. DRUG-DRUG INTERACTIONS AMONG HYPERTENSIVE PATIENTS

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**Introduction.** Hypertension has increased prevalence and concurrent comorbidities, because these patients are treated with a complex therapeutic regimen comprising multiple different drugs. A drug interaction is a reaction between two (or more) drugs or between a drug and a portion of food, beverage, or supplement and can cause an unwanted reaction.

**Aim of study.** It was to assess the utilization pattern of antihypertensive and comorbidities drugs and their interaction in hypertensive patients.

**Methods and materials.** 62 patients from the Institute of Cardiology were questioned based on the questionnaire consisting of 68 questions and drug interactions were checked through a drug interaction checker.

**Results.** Among the 62 patients with the average age  $65 \pm 8.8$  years the average number of cardiological medications was 7. Scientific evidence has shown that 70.9% of prescriptions were identified as having at least one drug-drug interaction. Also, the study showed that in 65% of cases among the surveyed patients, clopidogrel is prescribed with pantoprazole, which represents a medium-level interaction. As well, the study noted that 45% of patients administer drugs without a doctor's prescription, which increases the risk of developing interactions with drugs prescribed by a cardiologist. The average Charlson index in patients present in the study was 5.5, which represented a valid predictor of morbidity in patients and demonstrated the association of drugs prescribed by another specialist. The average number of drugs associated with a pathology other than cardiac is 3 drugs and represents a risk factor for the development of interactions other than those known to the cardiologist. Likewise, the study showed that in 21% of prescriptions the spironolactone + valsartan combination was present, which represented a serious interaction that increases the level of potassium in the blood. Concomitant use of angiotensin II receptor blockers (ARBs) and potassium-sparing diuretics may increase the risk of hyperkalemia. Inhibition of angiotensin II results in decreased aldosterone secretion, which can lead to increases in serum potassium that may be additive with that induced by potassium-sparing diuretics.

**Conclusion.** This study identified the potential drug-drug interaction and documented interactions in hypertensive patients. Although, potential drug-drug interactions, though common in this study comprised mainly of minor and moderate types. Notwithstanding, physicians need to be reminded of the potential interactions.

## 12. EFFICACY OF INTERVENTIONAL TREATMENT IN AORTIC STENOSIS PATIENTS WITH INTERMEDIATE AND HIGH RISK



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**Introduction.** Valvular heart disease is a leading cause of cardiovascular morbidity and mortality worldwide. It is a condition that reduces blood flow through the aortic orifice due to incomplete opening of the aortic valve during systole, with the most common causes being calcific (degenerative), bicuspid aortic valve, and rheumatic.

**Aim of study.** Stratification of surgical risk and studying the paraclinical characteristics and complications in patients with aortic valve stenosis to assess the quality of life of post-procedural patients.

**Methods and materials.** The study included 90 patients with aortic valve stenosis, post-TAVI, selected between 2019 and 2023 from the Institute of Cardiology. The patient cohort was divided into: high-risk patients (EuroSCORE II  $\geq 8$ ) (n=8), intermediate-risk patients (EuroSCORE II = 4-8) (n=32), and low-risk patients (EuroSCORE II  $\leq 4$ ) (n=50). Our aim was to assess echocardiographic data and post-procedural complications for intermediate and high-risk patients.

**Results.** The mean age of the patients in the study was  $77.1 \pm 4.3$  years, with known presence of two or more comorbidities: hypertension (n=84), obesity (n=40), diabetes mellitus (n=32), atrial fibrillation (n=26), and dyslipidemia (n=39). The mean pre-procedural values of maximum pressure gradient and mean pressure gradient were 88.32 mmHg and 54.80 mmHg, respectively, with a mean velocity across the aortic valve of 4.69 m/s. After TAVI procedure, there was a significant decrease in mean pressure gradient, with the mean value being 12.26 mmHg for intermediate-risk patients and 12.085 for high-risk patients. We observed a decrease in transaortic velocity and a non-significant increase in ejection fraction. Post-procedural heart failure showed a significant decrease, manifested by NYHA class II (n=71) and only III (n=19). Among the possible complications post-TAVI, in the high-risk patient group, mild regurgitations (n=5), moderate regurgitation (n=2); valve embolization (n=1), severe bleeding (n=1), AV block gr. I (n=1), AV block gr. III (n=1), atrial arrhythmias (n=1), vascular complications (n=1), permanent pacemaker (n=1) were developed. In the intermediate-risk patient group, noted complications were: mild aortic regurgitations (n=16), moderate aortic regurgitation (n=2); severe bleeding (n=1), AV block gr. I (n=1), AV block gr. III (n=1), left bundle branch block (n=1), bradyarrhythmias (n=1), atrial arrhythmias (n=1), ventricular arrhythmias (n=1), vascular complications (n=1), permanent pacemaker (n=2), and procedure-related death (n=2).

**Conclusion.** Current research evidence has highlighted the improvement in hemodynamics in both the intermediate and high-risk patient groups, as evidenced by Gpmed, systolic, and diastolic function of the left ventricle, suggesting a favorable long-term prognosis for this category of patients. These findings underline the benefits of TAVI intervention and support its use aiming to improve the quality of life of patients with aortic valve stenosis.



### 13. HEART RATE (ARRHYTHMIAS) IN OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME

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**Introduction.** Normal sleep provides an advantageous physiological recovery period for the cardiovascular system (CVS). During non-rapid eye movement sleep (80%), sympathetic activity decreases and parasympathetic activity increases, resulting in a decrease in blood pressure (BP) and heart rate (HR). The study aims to determine the pathophysiological mechanisms of obstructive sleep apnea/hypopnea syndrome (OSAHS) that generate heart rate modifications and even arrhythmias.

**Aim of study.** OSAHS induces a cyclic variation in FCC with bradycardia during the episode of sleep apnea, followed by tachycardia caused by post-apneic hyperventilation, which presents an underestimated clinical problem with detrimental consequences.

**Methods and materials.** Performing literature review search from 2010-2023 using Google Scholar, PubMed and Medline databases using the keywords: “obstructive sleep apnea”, “sinoatrial node dysfunction”, “brady-tachy syndrome”.

**Results.** The pathophysiology of OSAHS is characterized by recurrent episodes of partial or complete collapse of the upper airways during sleep, with a reduction in airflow or its complete cessation. Inspiratory efforts at the beginning of obstructive apnea will generate negative intrathoracic pressure, which will cause an increase in the vagal tone. At the same time, due to the decrease in HR and the stroke volume of the left ventricle, cardiac output and systemic arterial pressure will decrease, respectively. The reduction of adequate alveolar ventilation leads to the development of hypoxemia and hypercapnia, which in turn will trigger respiratory arousal (post-apneic hyperventilation will occur) and autonomic arousal (the sympathetic tone will increase), which will cause the triggering of tachycardia and the increase of BP values. These changes in the cardiac autonomic nervous system activity during OSAHS cause hemodynamically and electrophysiologically increased susceptibility to developing sinus node dysfunction, complete AV block, or atrial fibrillation.

**Conclusion.** High-quality sleep is essential in maintaining cardiovascular health, providing a period of physiological recovery in which sympathetic activity decreases and parasympathetic activity increases, contributing to the optimal regulation of blood pressure and FCC. Pathophysiological mechanisms of OSAHS, characterized by repeated upper airway collapse and negative intrathoracic pressure, initially cause an increase in vagal tone. However, reduced alveolar ventilation develops hypoxia and hypercapnia, triggering autonomic and respiratory awakening by enhancing sympathetic tone. These changes in the autonomic activity of the cardiac nervous system in OSAHS predispose to the development of sinus node dysfunction, complete AV block, or atrial fibrillation.

## 14. IMPACT OF CLIMATE CHANGE ON CARDIOVASCULAR OUTCOMES



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**Introduction** Cardiovascular disease (CVD) remains a leading cause of global morbidity and mortality, through an interplay between climate change and the prevalence, progression, and prevention of CVD. In late years, a growing number of research articles have explored the various dimensions of this kinship, shedding light on the temperature-related effects over which climate change impacts cardiovascular health.

**Aim of study.** The aim of this study is to research the impact of rising temperatures on CVD, exploring the specific mechanisms through which heat stress and prolonged heat waves contribute to increased risks and occurrences of cardiovascular events. By elucidating the thermal influences on CVD, this review aims to inform the state of affairs and the alert for doctors who fight with established cardiovascular diseases, but also for their prevention.

**Methods and materials.** The results include in detail selecting and inspecting a collection of the newer sources from electronic databases as PubMed, NCBI, HINARI and AHA/ASA Journals.

**Results.** Our study notes compelling evidence that a 1°C increase in temperature increases the rate of cardiovascular events and increases CVD mortality by 4.15%. Analysis of these studies also demonstrated a correlation between each 1°C increase in temperature with the frequency of hospital admissions related to cardiovascular damage. It highlights the alarming impact of climate change, marked by the increase in global average temperature over the past decade, on CVD. The increase in extreme heat events, exemplified by the 2003 Central European heat wave that caused more than 70,000 deaths, highlights the immediate consequences of high temperatures. At the same time, there is an increased risk of myocardial infarction (MI) observed at temperatures >18°C, affecting especially people with type 2 diabetes or hypertension. In addition, the study emphasizes the effects of sweating, increased pulse, vasodilatation, impaired coagulation are just some of the consequences that lead to increased blood pressure, increased systemic inflammation and the risk of cardiovascular events.

**Conclusion.** Need for action on awareness of climate change, global warming and its effects on cardiovascular health. Concrete instructions for doctors, patients and their relatives through the educational method "train to train" for the management of patients with established cardiovascular diseases and/or for their prevention.





## 15. INFECTIVE ENDOCARDITIS CAUSED BY STAPHYLOCOCCUS AUREUS

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**Scientific advisor:** Tinica Grigore, Bacusca Alberto

**Introduction.** Infective endocarditis (IE) is an infection of the endothelium of the heart that can occur in 1-6% of patients. The clinical presentation may present as an acute, subacute, or chronic condition reflecting the variable causative microorganisms, the most prevalent cause being *Staphylococcus aureus* (~26.6%).

**Case statement.** A 59-year-old male patient, presented to the hospital with an altered general condition: afebrile, pain in the right hypochondrium, severe lumbago on mobilization and paresthesias of the lower limbs with an onset of approximately 4 weeks. During the transthoracic and transesophageal echocardiography, a hyperechoic formation on the atrial face of the posterior mitral valve is revealed, causing a severe mitral regurgitation, with septic embolization: L5-S1 spondylodiscitis with left foraminal inflammation with a small left paravertebral abscess (2.52/4.3/1.26 cm) at the hepatic and splenic level. The presence of two major criteria (two positive blood cultures with *S.aureus*, echocardiographically documented vegetation) and one minor (embolic phenomena) established the diagnosis of infective endocarditis, requiring surgical intervention. After the debridement of the infected tissue, the medical team opted for the mitral valve prosthesis using a patch of bovine pericardium.

**Discussions.** In our case, the late diagnosis, the patient's age, his medical history: type 2 diabetes, viral hepatitis C, as well as post-infective endocarditis complications made medical treatment difficult, decreasing the patient's life expectancy.

**Conclusion.** Infective endocarditis is associated with significant morbidity and mortality despite improvements in diagnosis and microbiological techniques. It is imperative to establish an early diagnosis and a prompt surgical intervention is necessary.



## 16. INFECTIVE ENDOCARDITIS IN A HAEMODIALYSIS PATIENT: A CHALLENGING CLINICAL CASE



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**Introduction.** Although haemodialysis is an irreplaceable treatment in the end-stage chronic kidney disease, it represents an important risk factor for haematogenous infections. Infective endocarditis is a rare and severe complication, accounting for 2 to 6% of haemodialysis patients.

**Case statement.** We present a case of a 61 year-old female patient, admitted to the hospital with a 4-week vesperal fever up to 39°C, anasarca and dyspnea. The list of previous comorbidities included: chronic glomerulonephritis from the age of 17, haemodialysis due to end-stage kidney disease (for the last 8 months), secondary arterial hypertension, secondary anemia, chronic viral hepatitis C and chronic atrial fibrillation. The presence of clinical data (decreased vesicular murmur on both lung bases, decreased sound I on apex and on tricuspid valve point, arrhythmic heart sounds, heart rate 110 bpm, blood pressure 125/45 mmHg) and laboratory systemic inflammatory response syndrome imposed the diagnostic work-up of an infection (pneumonia, urinary tract infections, endocarditis), malignancy, autoimmune disease. The chest X-ray showed the presence of Kerley lines, a small bilateral effusion and cardiomegaly. Repeated hemoculture, uroculture and oncological markers were negative and the pharyngeal swab revealed a high titer of *Streptococcus viridans*. The echocardiography performed on day 3 revealed: vegetation on the mitral valve (12x8mm) and on the aortic valve (9,6x7mm), dilation of all heart chambers; degree III-IV regurgitation on aortic, mitral and tricuspid valve, degree II-III regurgitation on pulmonary valve; ejection fraction of the left ventricle 52%, severe pulmonary hypertension. Under the treatment with vancomycin and gentamicin, the patient attended clinical stability and the decrease of vegetations' size on repeated echocardiography. The patient underwent a successful cardiac surgery for mitral and aortic valve replacement.

**Discussions.** In this multiple-problem patient, similar to other published studies, the valves affected by endocarditis were those aortic and mitral. A 2023 ESC Endocarditis Guidelines "clinical stability" strategy was applied to this patient, resulting in a good surgical outcome, regardless of high preoperative risk.

**Conclusion.** This clinical case demonstrates the difficulties in the diagnosis and treatment of endocarditis, in a multiple-problem haemodialysed patient.



## 17. INTERVENTIONAL TREATMENT IN ELDERLY PATIENTS WITH SEVERE AORTIC VALVE STENOSIS AND CORONARY ARTERY DISEASE.

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**Introduction.** Aortic stenosis (AS) is a valvular heart disease commonly found in the elderly patients and frequently is associated with coronary artery disease (CAD), sharing multiple risk factors and common pathophysiological mechanisms, such as age, smoking, hypertension, and hyperlipidemia. The prevalence of CAD in patients with severe AS is between 15% and 80% and the impact of coronary involvement on postprocedural outcomes is controversial and incompletely studied.

**Aim of study.** This study aims to compare clinical and hemodynamic outcomes, as well as the rate of major adverse cardiovascular and cerebrovascular events (MACCE) in patients undergoing TAVI with PCI (patients with AS and CAD) versus isolated TAVI (patients with AS).

**Methods and materials.** A retrospective study was performed that included 41 patients older than 70 years with a diagnosis of severe aortic valve stenosis and CAD. Patients were divided into two groups: 32 patients without significant coronary lesions and 9 patients with significant multivessel lesions and Syntax Score <22. In these patients, we aimed to assess the valvular pressure gradient, and aortic valve peak velocity, pre-procedural, post-procedural, 30 days and 1 year post-TAVI. To assess the postprocedural results, the rate of major adverse cardiovascular events (MACCE) is recorded, represented by: cardiovascular mortality, cerebrovascular accident, acute myocardial infarction or myocardial revascularization, readmission due to heart failure.

**Results.** After analyzing the data, it was determined that in group I the proportion of men was 21.87%, compared to 22.2% in group no. II, and the average age was  $78.15 \pm 4.61$  vs  $75.66 \pm 5.02$ ,  $p < 0,09$ . The mean values of the maximum transaortic pressure gradient were  $93.11 \text{ mmHg} \pm 21.55$  in group 1 and  $103.07 \text{ mmHg} \pm 20.19$ , respectively,  $p < 0,156$ ; the mean transaortic pressure gradient  $57.52 \text{ mmHg} \pm 15.25$  vs  $63.98 \pm 15.0$ ,  $p < 0,156$ , and the mean value of the peak velocity through the aortic valve was  $4.78 \text{ m/s} \pm 0.56$  in group I and  $5.05 \text{ m/s} \pm 0.54$  in the second group,  $p < 0,142$ . After the procedure, the average pressure gradient decreased impressively, the average value being  $12.59 \pm 5.62 \text{ mmHg}$  vs  $14.78 \pm 8.73 \text{ mmHg}$ ,  $p < 0.338$ . The peak velocity of the jet through the aortic valve is  $2.36 \pm 0.50 \text{ m/s}$  vs  $2.53 \pm 0.83 \text{ m/s}$ ,  $p < 0.361$ . In this study, one case of death associated with the procedure, which represents 3.12%, and 2 cases of stroke, which constituted 6.25%, were documented in group I. At the same time, in both groups 2 cases of readmission due to heart failure were reported.

**Conclusion.** In patients with severe AS and complex CAD, TAVI + PCI was not associated with a higher rate of MACCE after a 12-month follow-up compared with patients with severe AS without CAD and approached by TAVI, probably due to the small study group and short follow-up period. Performing PCI before TAVI in patients with a Syntax score <22 appears to be safe, with no differences in echocardiographic parameters or MACCE compared to the group of patients without coronary lesions. **Keywords.** Aortic stenosis, transcatheter aortic valve implantation, coronary artery disease.

## 18. MULTIVASCULAR ATHEROSCLEROSIS IN CASE OF CORONARY ARTERIES BYPASS GRAFTING



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**Scientific advisor:** Nekrošius Rokas

**Introduction.** Atherotic vascular disease is the leading cause of death and disability in Lithuania. Coronary, carotid and leg arteries are the most often affected vessels. Multiple disease locations increase the risk of cardiovascular events as well as mortality compared with patients having multiple risk factors only. Peripheral arterial disease patients being those with the highest cardiovascular mortality rate. This case report presents a relatively young man who was diagnosed with excessive atherosclerosis of coronary, carotid and peripheral arteries.

**Case statement.** A 61 year old male patient was admitted to Kaunas Clinics Cardiology department because of stable angina pectoris. The patient had a previous history of intermittent claudication, arterial hypertension, deep vein thrombosis, pneumonia, COVID-19 and smoking. An ultrasonography showed lowered left ventricle ejection fraction. Coronary angiography revealed multiple stenoses in the coronary arteries requiring coronary artery bypass surgery. Bilateral lower limb angiography revealed complete occlusion of the left iliac and right inguinal arteries. Ultrasonography of the neck showed total occlusion of both internal carotid arteries with very good extra/intra collaterals through ophthalmic arteries. Both vertebral arteries were compensatory dilated without stenosis. A decision was made to perform coronary artery bypass surgery with postponing of lower limb revascularisation. During the first postoperative day an urgent right endarterectomy and arterioplasty of the right femoral artery due to acute right lower limb was performed. After the surgery reperfusion syndrome was observed in the right calf and urgent reconstructive surgery using axillofemoral shunt was done. The surgery was successful, however, the patient's condition deteriorated. The postoperative course was complicated by cardiogenic shock, renal failure, metabolic disorders, and ischaemia of lower limbs. The patient died of multiorgan dysfunction syndrome 4 days after the initial cardiac revascularization surgery.

**Discussions.** Severe atherosclerotic vascular disease has been identified as an independent risk factor for high postoperative mortality in patients undergoing coronary artery bypass surgery. Moreover, life expectancy is substantially reduced in patients with more than one atherothrombotic event and peripheral arterial disease.

**Conclusion.** This case report highlights a case of outspread atherosclerosis and coronary artery bypass surgery which resulted in a fatal outcome.



## 19. MUSIC THERAPY INTERVENTION ON CARDIAC PARAMETERS IN HYPERTENSIVE PATIENTS: MYTH OR REALITY

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**Introduction.** Music therapy is an aged medical practice. Since ancient times it has been used by Socrates to relieve mental and physical suffering. In contemporary medicine, melotherapy gained momentum in the 20th century, with the appearance of the first specialized institutions in the field of music therapy.

**Aim of study.** Music therapy is a medical practice that is gaining wider use, while more and more studies are appearing that demonstrate its effectiveness in various medical fields such as general medicine, surgery, intensive care, pediatrics, pulmonology, cardiology, oncology, and pain management.

**Methods and materials.** We analyzed PubMed and Cochrane database from last 10 years. The following combinations of keywords were used: "music therapy", "music therapy, hypertension" and "music therapy, blood pressure". The articles were divided into categories by keywords and by the year of publication.

**Results.** On the PubMed platform, 4767 articles containing the keyword "music therapy" were found, and on the Cochrane platform 36 articles, all published during the last 10 years. The number of articles published on PubMed was twice as high in 2023 compared to 2013, and those published on the Cochrane platform were 4 times more in 2023 compared to 2013. The highest number of articles per year, containing the keyword "music therapy", was 756 in 2021, on the Pubmed platform, and 7 in 2020 on the Cochrane platform. On Elsevier's Scopus platform, 1902 books containing the keyword "music therapy" are published, 14 having it as an element of the title. Only 1087 books have been published in the last 10 years, and 41 are planned to be published in 2024.

**Conclusion.** Interest in the subject of music therapy is continuously growing, and its practice in the field of cardiology is promising, but continued, high-quality research is needed to confirm the veracity of the effectiveness of music therapy in the complementary treatment of hypertension.



## 20. NOSOCOMIAL INFECTIVE ENDOCARDITIS IN THE BACKGROUND OF HYPERTROPHIC CARDIOMYOPATHY. CLINICAL CASE



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**Introduction.** Infective endocarditis (IE) is a severe pathology, non-responsive to treatment with a lethal end in 20-25%. Risk factors of IE are subdivided in 3 categories: predisposing cardiac pathologies, morbid circumstances and comorbidities. Among predisposing cardiac pathologies for IE are: congenital cardiopathies (10,3%), rheumatic valvulopathies (46.3%), valvular prostheses (30.3%), degenerative cardiopathies (3%), IE in the history (8.8%) and hypertrophic cardiomyopathy in 2.2%.

**Case statement.** Man, 66 y.o. was admitted to the Institute of Cardiology in November 2023, a little over 6 months after heart surgery with complaints: dyspnoea in moderate physical exertion, fever (up to 39°C), abundant nocturnal sweating, fatigue, and decreased tolerance to physical exertion. Objective data: diminished basal murmurs on the right, arrhythmic heart sounds, protodiastolic sound in the projection of the prosthesis, FCC 68b/min, BP 100/70mmHg. Objective data: toxic anemia (HB 118g/l x 10<sup>9</sup>), leukocytosis (L 22.5g/l x 10<sup>12</sup>), increased ESR (46mm/h), increased CRP (48mg), glycemia (7.80 mmol/l), increased INR (2.48), low prothrombin because of oral anticoagulants administration (27.7%) and creatininemia 120µmol/l. Hemoculture with *Mycoplasma pneumoniae* detection. EcoCG: mobile linear vegetations (2-3mm) in AoV prosthesis, aortal paraprosthetic regurgitation of 2-nd degree, regurgitation on MV 2-nd degree and on TrV 2-nd degree. EKG: paroxistic atrial fibrillation, tachisitic, postoperative sechele in anterior region of the LV. Treatment: tachysistolic, paroxysmal atrial fibrillation, postoperative sequelae in the anterior region of LV. Treatment: Vancomycin 2g/day, Gentamicin 240mg/day, Levofloxacin 1g/day, antifungals, anticoagulants, statins, β-blockers and diuretics.

**Discussions.** This case represents clinical interest because this is a case of nosocomial IE, with *Mycoplasma pneumoniae* involvement that is used only in cases with detection of this microorganism.

**Conclusion.** Patient known with obstructive hypertrophic cardiomyopathy, develops over 6 months after partial septal myoectomy with aortic valve replacement with biological prosthesis and aorto-caronary bypass, nosocomial IE. The pathology was established early, solved conservatively by adequate treatment, which caused a favorable prognosis.





## 21. PREVALENCE OF POAF FOLLOWING CARDIAC SURGERY AND COMPARATIVE STUDY ON THE PREFERRED TREATMENT MODALITIES

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**Introduction.** Postoperative atrial fibrillation (POAF) is a common arrhythmia after cardiac surgery, with an incidence ranging from 10-65%. It is more common in older patients and non-cardiac surgery patients. POAF usually develops between day 2 and 4, with the maximum incidence on day 2. Risk factors include age, hypertension, obesity, diabetes, inflammation, and longer pump and cross clamp times. Stroke is the most significant clinical outcome, and female gender is a risk factor for cardiovascular disease.

**Aim of study.** This literature review is investigating the prevalence outcome and management of POAF following cardiac surgery.

**Methods and materials.** The study included articles published in English, cohort studies, randomized controlled trials and management in cardiac surgery for POAF. Search was conducted filtering articles based on the keywords "Postoperative Atrial Fibrillation," "POAF following cardiac surgery," "POAF management," etc. on databases (PubMed, Google Scholar, Embase, Cochrane...etc.).

**Results.** The review analyzed 1849 studies, excluding duplicates, ineligible records, and 1338 records. After evaluating 396 studies, 40 were included, with 346 deemed eligible. The study found apixaban and edoxaban are more effective than rivaroxaban in treating POAF. POAF was linked to increased risk of death in men but not in women. The AF recurrence rate was higher in cardiac surgery patients (CS) compared to non-cardiac surgery patients (NCS). In long-term follow-up, CVA was more common in patients with POAF after CS compared to NCS. Atrial fibrillation occurred in a higher percentage of patients in the landiolol group compared to the control group. Most patients with POAF had a history of hypertension and diabetes mellitus, with male predominance. Vitamin D treatment reduced the risk of POAF development by 0.24 times. Atrial fibrillation developed after CABG in 156 patients, with patients with POAF generally older and more often presenting comorbidities. New-onset POAF was independently related to the presence and number of fQRS in patients undergoing CABG surgery.

**Conclusion.** The different aspects of POAF facilitate an all-inclusive approach for factors such as gender disparity, surgical methods, anticoagulant choice, etc. The gathered outcomes from these studies deliver helpful data for clinicians, focusing on the need for individual risk management and treatment methods to decrease the effect of POAF on patients.

## 22. SECONDARY PREVENTION OF SUDDEN CARDIAC DEATH IN PATIENT WITH ISCHEMIC HEART DISEASE



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**Introduction.** Sudden cardiac death (SCD) is the cause of about ½ of all cardiovascular deaths, while up to 50% is the first manifestation of heart disease. The annual incidence of SCD increases with age, so in the eighth decade of life it reaches 200 cases per 100.000 population.

**Case statement.** A 68 years old man known with heart disease for about 25 years, when he suffered acute myocardial infarction, simultaneously suffers from hypertension, atrial fibrillation receiving irregular treatment. The general condition worsened 6 years ago, when he developed a syncope, being resuscitated by the application of the precordial blow, which was repeated during hospitalization on 25.09.17. On the ECG, there was sustained ventricular tachycardia, suppressed by electric cardioversion. The patient was examined at the Institute of Cardiology by echocardiography: dilation of the heart chambers, moderate hypertrophy of the LV myocardium, severe of the IVS, hypokinesia and akinesia of the basal and middle segment, posterior and lateral walls of the LV, FE LV -36%; on the ECG: tahi-bradi form of atrial fibrillation; on coronarography: absence of stenotic lesions on the coronary arteries. Drug treatment with rivaroxaban, aspirin, bisoprolol, amiodarone, lisinopril, rosuvastatin, spironolactone and furosemide was initiated. On 04/10/17 was implanted with a cardiac defibrillator (ICD) Iforia3 VR-T type VVI Biotronik. After discharge from the hospital, the patient's condition stabilized, notable that 6 electrical discharges of the ICD were recorded only in the first year after implantation. Over 6 years the patient is in good condition and continues the drug treatment for chronic heart failure; on ECG: stimulated rhythm with HR 70 b/min; ECoCG parameters show improvement.

**Discussions.** The case demonstrate the role of device therapy, additional to optimal drug therapy with angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta-blockers, and mineralocorticoid receptor antagonist to prevent SCD and improve condition of patients with ischemic heart disease.

**Conclusion.** Sudden cardiac death (SCD) occurs unexpectedly and is usually the result of ventricular arrhythmia in patients with structural heart disease. Implantable cardioverter defibrillator (ICD), with biventricular stimulation, has been shown to be protective for ischemic heart disease and heart failure patients with a reduced ejection fraction of <35% (HFrEF).



## 23. STUDY OF RISK FACTORS IN PATIENTS WITH AORTIC STENOSIS

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**Introduction.** Aortic valve stenosis is commonly considered a degenerative disorder with no recommended preventive intervention. With increased life expectancy and aging of the population, aortic stenosis is now one of the most common valvular heart diseases. Early recognition and management of aortic stenosis are of paramount importance because untreated symptomatic severe disease is universally fatal.

**Aim of study.** It is generally accepted that aortic valve stenosis is a degenerative illness for which there is no suggested course of treatment. Populations getting older and greater longevity have made aortic stenosis one of the world's most widespread valvular cardiac conditions. Since untreated symptomatic severe illness is always life-threatening, early identification and therapy of aortic stenosis are critical.

**Methods and materials.** The following online databases were included in the search strategy, limiting results to a range of 2021-2023 years, retaining a total of 110 articles as the primary studies of the study selection process. As the basic search engine used IEEE Xplore, ScienceDirect and PubMed as the free version of MEDLINE, is highly authoritative. For a more effective study of the articles, the keywords used in the research were: aortic valve stenosis, risk factors, lipid profile, blood cholesterol.

**Results.** The results of the research emphasize that risk factors predominate in people depending on their age, gender, lifestyle, status in society, and their income. Several studies have also indicated infrequency of exercise and individual education levels as determining factors of aortic stenosis. Another study revealed that significant predictors of aortic stenosis, particularly around the age of 55 (women and men), include maternal smoking during pregnancy, childhood neurological functions and trait conscientiousness.

**Conclusion.** Aortic stenosis is common and expected to increase in prevalence with the aging population. In addition to aging, clinical risk factors for the development of AS include hypertension, hyperlipidemia, diabetes and lifelong exposure to high LDL-cholesterol suggesting that LDL-lowering treatment may be effective in its prevention. The collected findings are promising, but additional research is required to increase understanding of this disease. Moreover, this study briefly examined the most influential factors that cause or worsen aortic stenosis.

## 24. THE CARDIOTOXICITY OF LOCAL ANESTHETICS



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**Introduction.** Local anesthetic toxicity is, occasionally, the cause of severe cardiovascular complications. The long-acting local anesthetics as bupivacaine, levobupivacaine and ropivacaine have their toxicity mostly attributed to high plasma concentrations. The aim of this review is to single out the mechanisms of local anesthetic induced cardiotoxicity and treatment using lipid emulsion.

**Aim of study.** Long-lasting local anesthetic utilization is bounded by possible arrhythmias and contractile depression, potentially leading to cardiac arrest. One of the main mechanisms of anesthetic-induced cardiac depression is thought to be blocked  $Ca^{2+}$ -channels in myocardial tissue.

**Methods and materials.** The analysis of a range of publications from PubMed and NihGov databases, selected according to the keywords: „cardiotoxicity”, „anesthesia”, „cardiolipin”, „bupivacaine”.

**Results.** In vivo studies have revealed bupivacaine to be a negative inotropic agent that causes significant decreases in blood pressure and heart rate through alterations in electrical excitability of the heart, dilatation of blood vessels and inhibition of the firing rate of the sinoatrial node. In vitro studies illustrated that bupivacaine more severely dysregulated calcium dynamics than ropivacaine. Calcium supplementation improved tissue contractility and restored normal beating rhythm for bupivacaine-treated tissues. Calcium channel blocker nifedipine coadministration with bupivacaine, but not ropivacaine, exacerbated cardiotoxicity, supporting the role of calcium flux in differentiating toxicity.

**Conclusion.** Although many anesthetics can cause cardiotoxicity, bupivacaine demonstrates a higher toxicity risk, adversely altering cardiomyocyte calcium dynamics in a functional human-derived tissue model. The same effect was not observed with ropivacaine, where toxicity risk is lower. Current cardiotoxicity treatments are restricted to cardiopulmonary support and intravenous lipid emulsion administration. Fatty acids would increase the flux of acylcarnitines into the mitochondrial matrix of cardiomyocytes and re-enable oxygen–energy coupling in cardiac tissue.



## **25. THE CORRECT EARLY DIAGNOSIS ESTABLISHED BY THE MULTIDISCIPLINARY TEAM IS THE KEY TO SUCCESS IN THE TREATMENT OF THE POST-MYOCARDIAL INFARCTION PATIENT, COMPLICATED WITH RENAL INFARCTION AND PNEUMONIA-INFARCTION**

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**Introduction.** According to the ESC guideline for the management of Acute Coronary Syndrome (ACS) it meets a spectrum of conditions, from symptoms and signs, with or without 12-lead ECG changes and with or without positive troponins. ACS is the cause of death in 1.9 million male patients and 2.2 million female patients annually.

**Case statement.** In the given article I present the clinical case of a 66-year-old male patient, diagnosed in an outpatient setting with arrhythmia and aggravated pectoral angina. The given case was studied through the lens of the ACS guideline of the ESC (2023), articles on the subject of ACS, AMI, renal infarction and infarction-pneumonia.

**Discussions.** From the patient's laboratory analyses: complete blood count – thrombocytopenia ( $142-167 \times 10^9/l$ ), blood biochemistry – no changes, Troponins – negative (0.07 ng/ml). On ECG: tachysystolic atrial fibrillation-flutter and signs of left bundle branch block of His fascicle. On echocardiography: mild dilatation of the left atrium, right atrium, hypertrophy of the left ventricular myocardium, multiple regions with akinesia and dyskinesia and apical parietal thrombus with dimensions of 28x18 mm, fixed, ejection fraction – 45%. The patient's clinic is complicated by discomfort and dull pain in the right meso-hypogastrium. Computed tomography of the internal organs shows signs of renal infarction, thrombosis of the hepatic veins and inferior vena cava, infarction-pneumonia on the right. At coronary angiography, subocclusive LAD stenosis was detected, at renal arteriography - no pathological changes.

**Conclusion.** Due to early established multidisciplinary diagnosis, high-performance investigative methods and effective targeted therapy, the patient was treated and discharged with improvement and curative ambulatory measures.



## 26. THE MEDICAL REHABILITATION PROGRAM IMPROVES THE QUALITY OF LIFE OF PATIENTS WITH AMI



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**Introduction.** The incidence of acute myocardial infarction (AMI) is continuously increasing. In 2019, mortality from cardiovascular diseases reached 9 million people each year in Europe. Cardiovascular diseases are the main cause of death in the Republic of Moldova, representing 58.5% of total mortality. In 2019 more than 21,500 people died in the Republic of Moldova due to diseases of the circulatory system.

**Aim of study.** Analysis of the cardiovascular rehabilitation process in hospitalized patients with acute myocardial infarction using physical therapy.

**Methods and materials.** The study group of 60 AMI patients with an average age of  $63.3 \pm 13$  years, hospitalized during the period of 2021-2022 in the Institute of Cardiology, using the method of the "6 minutes test", performed before the rehabilitation and repeated after 7 days of daily implementation of the rehabilitation program.

**Results.** According to the results, the average value of the distance walked by the patients before following the rehabilitation program was 391.66 m. This value was between the minimum limits of 250 m and the maximum 600 m. The average value of FCC at the beginning of the test was 69.63 beats/minute, and at the end were recorded - 78.86 beats/minute. Over 7 days of rehabilitation the average value of the distance was 416.66 m. This value was between the minimum limits of 250 m and the maximum 600 m. The average value of the FCC at the beginning of the test was 69.26 beats/minute, and at the end increased average values were recorded - 82.1 beats/minute.

**Conclusion.** Performing physical exercises has a beneficial effect on the functional state of patients because, this program an increase in the average distance covered over 7 days of rehabilitation was highlighted.



## 27. THE SIGNIFICANT IMPACT OF ARTIFICIAL INTELLIGENCE IN TAVI

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**Introduction.** Currently, TAVI represents a benchmark in the treatment of patients with severe aortic stenosis, becoming a durable and preferred option compared to the traditional SAVR method. The success of TAVI significantly relies on the careful evaluation of the patient before, during, and after the procedure. A new paradigm in the assessment of patients for TAVI has emerged with the introduction of AI, providing more flexible, adaptable, and potentially more accurate approaches for risk estimation and patient selection in the context of the TAVI procedure.

**Aim of study.** Through the analysis of existing studies and literature, we aim to highlight the ways in which AI can enhance various aspects of the TAVI procedure, from diagnosis and planning to image analysis and complication management. Understanding how AI can contribute to the planning and execution of the TAVI procedure can optimize the patient selection process, reduce complications, and improve post-procedural outcomes for patients.

**Methods and materials.** This is a synthesis of newest medical articles and national protocols published during the years 2021-2024, found by the search engines Google Scholar, HINARI, and NCBI.

**Results.** Decision algorithms contribute to establishing a personalized patient profile, determining the relative benefits of TAVI compared to other treatment options. A study cohort of 151 patients shows that simulation algorithms can provide a virtual preview of the procedure with 100% sensitivity, allowing the medical team to prepare efficiently for the intervention. This contributes to optimizing the size and positioning of the valve or blood vessels course, based on imagistic analysis, and assessing relevant anatomical details, automatically with 100% precision in 2 min compared to the 10 min required for manual measuring. This visualizing opportunity can lead to a decrease in post-procedural complications, such as paravalvular regurgitation, with a 76% positive prediction and 100% negative prediction. Already knowing the probability of readmission, with a high probability, predicted by AI in the study of a 917 patient cohort, and the patient's postoperative mortality, validated in a study of 10,000 patients, where the accuracy reached 80% of cases, physicians can more easily guide the clinical future of the patient in the right direction. The AI feedback can contribute to the continuous improvement of the procedure and treatment, based on accumulated clinical experience.

**Conclusion.** Integrating this technology into TAVI practice, brings significant benefits in improving efficiency, accuracy, and clinical outcomes. A current worrisome trend is data privacy of patients because of the need for large and high-quality datasets and the development of precise, reliable, and interpretable artificial intelligence algorithms.

**Keywords.** Artificial Intelligence (AI), TAVI, TAVR, Machine Learning.

## HEMATOLOGY SECTION



***„În numele comunității universitare, vă salut cu drag în cadrul ediției a 10-a MedEspera care reprezintă continuarea frumoasei tradiții de colaborare internațională. Prezența studentului cu o comunicare la o conferință îi oferă posibilitatea nu numai să-și găsească locul personal printre colegii care îmbrățișează aceeași specialitate, dar și să determine nivelul universității în întregime în comparație cu alte centre de pregătire a specialiștilor în domeniul medicinei. Sunt convinsă, că această colaborare va contribui la promovarea spiritului participativ și stimularea inițiativelor tinerilor. Rămânem în speranța că prin eforturile noastre conjugate și prin colaborarea deja inițiată, vom reuși să obținem excelența științifică încununată cu rezultatele de impact așteptat.”***

***„On behalf of the university community, I warmly welcome you to the 10th edition of MedEspera, which represents the continuation of the beautiful tradition of international collaboration. The presence of the student with a communication at a conference gives him the opportunity not only to find his personal place among colleagues who embrace the same specialty, but also to determine the level of the university as a whole in comparison with other centers for training specialists in the field of medicine. I am convinced that this collaboration will contribute to the promotion of the participatory spirit and the stimulation of young people's initiatives. We remain hopeful that through our joint efforts and through the already initiated collaboration, we will succeed in achieving scientific excellence crowned with the expected impact results.”***

**Sanda Buruiană,**

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## 1. CLINICAL AND HEMATOLOGICAL FEATURES AND DIAGNOSTIC OPTIONS IN EXTRANODAL AGGRESSIVE NON-HODGKIN'S LYMPHOMAS

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**Introduction.** Lymphomas can be simply defined as malignant neoplasms of lymphocytes and their precursor cells. Common sites of extranodal manifestations are the gastrointestinal tract, especially the ventricle, pharynx, thyroid gland and skin. In the head and neck region, the most common site is Waldeyer's ring.

**Aim of study.** To identify and evaluate the clinical-evolutionary, hematological features and diagnostic options in aggressive extranodal non-Hodgkin's lymphomas.

**Methods and materials.** We studied the ambulatory cards and medical records of 80 patients with morphologically confirmed diagnoses of non-Hodgkin's lymphoma, who had at least one extranodal presentation.

**Results.** Among studied patients, all had at least one extranodal involvement, in 43% of cases the nasopharynx was affected, 38% the liver, 25% the spleen, 14% the spinal cord. Most patients spend 4 months -1 year to establish a concrete diagnosis. Sometimes this was due to the patient's own fault, postponing the visit to the doctor until the last moment or atypical symptoms making the diagnosis more difficult to establish. The presence of B symptoms was recorded in 42% of patients, and 76% had stage IV at diagnosis. The anemic syndrome was present in 14% of cases, with specific changes in the differential blood count. The final diagnosis was proved on the basis of morphology and immunohistochemical examination of the biopsied lymph nodes or tissue. The immunohistochemistry panel used was: CD20, CD3, CD5, CD10, CD45, BCL2, BCL6, Ki-67, IRF4/MUM1, and MYC which confirmed the diagnosis of lymphoma with the specification of the immunohistochemical type. Complete staging and monitoring of the disease evolution was possible due to high-precision MRI, CT PET-CT investigations. Patients received treatment courses of RCHOP, RCOP, BR with 80% of cases achieving clinic-morphological remission.

**Conclusion.** A surgically excised tissue with immunohistochemical examination is widely accepted as the gold standard for lymphoma diagnosis based on current international guidelines. It should be evaluated by immunocytochemistry, flow cytometry (if received unfixed), FISH studies, DNA and RNA extraction for molecular diagnosis.

## 2. EPIDEMIOLOGICAL AND CLINICAL ASPECTS OF INDOLENT EXTRANODAL NON-HODGKIN'S LYMPHOMA IN THE REPUBLIC OF MOLDOVA



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**Introduction.** Non-Hodgkin's lymphoma (NHL)-lymphoproliferative tumors that are histologically and biologically heterogeneous. The most common subtypes of indolent NHL being follicular lymphoma (FL), marginal zone lymphoma (MZL), and small lymphocytic lymphoma (SLL).

**Aim of study.** To highlight the clinical-epidemiological characteristics of indolent extranodal NHL.

**Methods and materials.** The study included 42 patients (men-17, women-25) with a mean age of 59.8 years, with extranodal onset of indolent NHL, treated in the Hematology Department of the Oncological Institute. The study is based on the analysis of data (age, gender, living environment, primary site of involvement) from outpatient medical records based on a questionnaire.

**Results.** A distinctive gender distribution emerges, with uniformity until the age of 60, with higher frequency in women (66%) and urban residency (60%). Notably, FL emerges as the predominant histological form (69%), with MZL following closely (24%). The spleen is the leading onset (73.8%), followed by the stomach (14.2%). The spleen as the primary site reveals SLL in 83.8% of cases, with an average onset age of 59 years, predominantly affecting females in advanced stage IV (93.5%). The stomach predominantly develops extranodal MZL of mucosa-associated lymphoid tissue MALT (66.6%), with an average onset age of 56.3 years, predominantly affecting males, stages II and IV.

**Conclusion.** Indolent extranodal NHL tends to occur more often at females, 51-70 years old. Living in urban areas is associated with an increased prevalence of the condition. The gastrointestinal system most often develops extranodal lymphoma with the predominant involvement of the spleen, followed by the stomach.





### 3. IMMUNOHISTOCHEMICAL PARTICULARITIES AS PROGNOSTIC FACTORS IN DIFFUSE LARGE B-CELL NON-HODGKIN LYMPHOMA

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**Introduction.** Diffuse Large B-Cell Lymphoma (DLBCL), the most common type of Non-Hodgkin Lymphoma (NHL) globally, is classified into two distinct biological categories based on the gene expression profile (GEP): the germinal center B-cell (GCB) subtype and the activated B-cell (ABC) or non-GCB subtype.

**Aim of study.** Identification of Immunohistochemical Particularities as Prognostic Factors in Diffuse Large B-Cell Non-Hodgkin Lymphoma.

**Methods and materials.** Data from medical scientific literature were examined, identified through Google Search and databases such as PubMed, Cochrane, Scopus, along with international clinical guidelines from NCCN and ESMO.

**Results.** Studies have indicated that determining the cell of origin phenotype in DLBCL using gene expression profile (GEP) is significant for establishing the prognosis. Tumors with the GCB phenotype showed a better clinical course compared to those with the ABC/non-GCB phenotype. The classification into GCB and non-GCB subtypes, using the Hans algorithm, suggests a correlation between the expression of CD10 and BCL6 genes in DLBCL GCB and MUM1 in DLBCL non-GCB. In a study led by Patrascu A-M and his team (2017) on a sample of 601 patients, subjects with GCB type DLBCL exhibited a higher overall survival rate and progression-free survival compared to those with non-GCB DLBCL, although the prognosis may vary depending on the specific markers expressed within the same subtype. Studies using fluorescent in situ hybridization (FISH) reported that 7% to 10% of DLBCL cases harbored genetic translocations MYC, BCL2, and/or BCL6 and were termed “double-hit” lymphoma (DHL) or triple-hit lymphoma. More than 90% of patients with DHL present high-risk clinical features, such as leukocytosis, central nervous system (CNS) involvement, lactate dehydrogenase values three times above the upper limit, and an advanced disease stage. The presence of MYC rearrangements in combination with BCL2 and/or BCL6 has been described as a distinct entity with prognostic significance, presenting a poor long-term prognosis, refractoriness to therapy, and an increased risk of relapse.

**Conclusion.** Research and studies emphasize the importance of evaluating the expression of MYC, BCL2, and BCL6 genetic rearrangements, through IHC and FISH, in patients recently diagnosed with DLBCL, for a more accurate assessment of disease progression, prognosis, and progression-free survival.

**Keywords.** Large B-Cell Non-Hodgkin Lymphoma, Immunohistochemistry, BCL-2, BCL-6, MYC

#### 4. THE IMPACT OF COVID-19 ON PATIENTS WITH NON-HODGKIN LYMPHOMA



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**Introduction.** Patients diagnosed with coronavirus 2019 (COVID-19) disease during hematological malignancies have been described as having a poor outcome, with only a few reports specifically addressing patients with lymphoma. Various studies are available on the impact and mortality rates of COVID-19 in hematological malignancies, reporting mortality rates between 33% and 52%, however, specific studies for lymphoma subtypes are very limited.

**Aim of study.** Studying the influence of COVID-19 infection on patients with non-Hodgkin's lymphomas.

**Methods and materials.** We studied medical scientific literature data, identified by Google Search, from medical databases PubMed, Cochrane, Scopus, international clinical guidelines, WHO, NCCN, ESMO.

**Results.** Among the genetic variants that confer increased susceptibility to SARS-CoV-2 infection those that express angiotensin-converting enzyme (ACE) receptors are key factors in the cross-linking of SARS-CoV-2 cell membranes, and HLA-DRB1 alleles were more frequently observed in symptomatic patients with COVID-19. The infection with SARS-CoV-2 with very severe respiratory symptoms may be a potential risk factor for diffuse large B-cell lymphoma. According to Visco et colab. (2022) there were no differences in survival of patients on active anti-lymphoma treatment ( $\leq 6$  months) compared to all others. Passamonti F. et al. colab. (2020) and the European Hematology Association reported results from 132 centers in 32 countries, revealing that COVID-19 was the main cause of death in 173 patients (14.6%) of hematological malignancy studied patients. Bonuomo V (2021) described in his study that the persistence of positive PCR for SARS-CoV-2 after week 6 was significantly associated with mortality. The available evidence suggests that in patients with mature B-cell NHL, bendamustine and anti-CD20 were generally associated with worse COVID-19 outcomes, while tyrosine kinase inhibitors had either a neutral or protective effect.

**Conclusion.** It is imperative to understand the COVID-19-related outcomes of lymphoma patients so that the medical management of lymphoma may be optimized.



## 5. TREATMENT OF ACUTE NON-LYMPHOBLASTIC LEUKEMIAS

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**Introduction.** Acute myeloid leukemias (AML) are a group of hematological malignancies with primary involvement of the bone marrow (BM). These disorders of hematopoietic system develop due to genetic changes in blood cell precursors that lead to the overproduction of neoplastic clonal myeloid blast cells. It is the most common group of leukemias among the adult population and account for 80% of all cases. Ongoing research and clinical trials continue to explore new therapies and management approaches for AML, including targeted therapies, immunotherapies and personalized medicine strategies based on a patient's genetic mutations.

**Aim of study.** Identification of clinical and laboratory features, evaluation of the effectiveness of different treatment methods of AML.

**Methods and materials.** We present the results of retrospective and prospective analysis of medical records of patients with AML, diagnosed and treated at the Institute of Oncology between 2016-2023. The type of leukemia was identified according to the WHO classification of hematological malignancies and FAB classification of acute leukemias. Our study enrolled 50 adult patients.

**Results.** All of the studied patients presented with anemic syndrome, 87.3% - with hemorrhagic syndrome, 52.1% - with proliferative syndrome and 66.19% - with infectious complications. According to the complete blood count parameters, 97% of the patients had low hemoglobin and erythrocyte levels, 66.17% - leukocytosis, in 19.71% - leukopenia and all patients had changes in the leukocyte formula. Blast cells in the peripheral blood were found in 67% of cases. The BM aspiration revealed more than 20% blasts at diagnosis in 95.7% of cases. According to the FAB classification, M3 and M4 predominated - 22.55% and 35.2% respectively. Induction and consolidation treatments were carried out according to 2+5, 3+7 regimes, low doses of Cytarabine and ATRA. Maintenance treatment was performed with 2+5, 5+Mercaptopurin, 5+Cyclophosphamide and Cytarabin+Mercaptopurin. The chemotherapy treatment was associated with complications: pancytopenia - 73%, infectious complications - 23%, ATRA syndrome - 4%. The mortality rate among studied patients was 57.7%. The most frequent causes of death in our study were multiple organs dysfunction syndrome and hemorrhagic stroke.

**Conclusion.** AML are oncological diseases with progressive evolution and unfavourable prognosis. Early diagnosis and adequate treatment initiation will contribute to the increase of survival. In spite of advances of treatment and increased life expectancy, AML may still be considered a challenging disease for management, especially in old patients.

**Keywords.** AML, treatment, complications.

## 6. TREATMENT OF GENERALIZED NODAL NON-HODGKIN'S LYMPHOMAS



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**Introduction.** Non-Hodgkin's lymphomas (NHL) comprise a diverse group of malignant lymphoid tumors, with multiple distinct histological and immunohistochemical subtypes. Understanding and differentiating these subtypes is crucial for effective diagnosis and treatment. NHL survival rates have improved recently due to the advances in treatment strategies and options. The past decade has seen remarkable progress with the addition of new therapeutic modalities such as antibody-targeted therapy, bispecific antibody therapy, epigenetic modulator therapy, CAR-T cell therapy, and conventional chemotherapy.

**Aim of study.** Identification and evaluation of treatment options for generalized nodal non-Hodgkin lymphomas in the Republic of Moldova.

**Methods and materials.** The ambulatory files and medical records of 84 patients with a morphologically confirmed diagnosis of generalized nodular non-Hodgkin's Lymphoma were studied, in terms of performed treatment and remission rates. The staging was realized according to the criteria of Lugano Classification of Malignant Lymphomas. The patients' follow-up was performed at the comprehensive cancer center, and related to the hospitalized and outpatient care. The mainly used antineoplastic regimens were those combined with anti-CD20 monoclonal antibodies Rituximab (R-CHOP, R-COP, BR) and conventional chemotherapy (CHOP and CHOEP).

**Results.** The patients included in the study were aged over 40 to 78 years, with the incidence rate of 37% at the age of 60-70. All patients were hospitalized with several locations of the enlarged lymph nodes, and 68% - with B symptoms (sweating, weight loss). According to the WHO classification, diffuse large B cell lymphoma represented 57% of cases, prolymphocytic lymphoma – 13 % of cases. Marginal zone lymphoma, lymphocytic, lymphoblastic and other unspecified lymphomas were revealed at diagnosis in smaller percentages. All types of lymphoma were confirmed by morphological and immunohistochemical examination, 95% of them being CD20+. The administered combined immunochemotherapy treatment showed complete remission rates in 70% of cases. A complete remission rate of 13% was achieved under the combined chemotherapy with radiotherapy. Post-chemotherapy complications were: pancytopenia (39%), mucositis, stomatitis (89%), respiratory infections (53%), nausea and vomiting (85%).

**Conclusion.** The majority of patients achieved complete remission under the combined treatment with chemotherapy and Rituximab. The international studies have demonstrated that maintenance therapy with anti-CD20 antibodies (Rituximab) prolongs remission and survival rates.





## 7. TREATMENT OF HODGKIN'S LYMPHOMA IN ADVANCED STAGES

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**Introduction.** Hodgkin's lymphoma is a relatively frequent neoplasm of the lymphatic system representing one of the most common types of cancer in young adults. Hodgkin's lymphoma is an aggressive, clinico-pathologically heterogenous group of lymphomas arising from the germinal center B cells. The last decades have seen significant progress in the management of patients with Hodgkin Lymphoma; it is now curable in at least 80% of patients. The therapeutic approach to each patient depends on clinical prognostic factors, comorbidities, and toxicity profile. Therefore, finding ways to reduce treatment-related morbidity and mortality is now a major goal of scientific research and clinical trials.

**Aim of study.** Studying the treatment options in the advanced stages of Hodgkin's lymphoma.

**Methods and materials.** We studied the medical records of patients diagnosed and treated in the Oncological Institute with the confirmed diagnosis of Hodgkin's lymphoma in the advanced stages.

**Results.** According to the results of the performed study, women comprised 62% of all cases with Hodgkin's lymphoma. The predominant age group was 40-50 years with a rate of 36%, followed by the age group of 50-60 years (23% of cases). The time elapsed from the first symptoms to a confirmed diagnosis of Hodgkin's lymphoma was 2-4 months in 43% of cases. There were 6% of cases diagnosed within one year after the appearance of the first symptoms. According to the histopathological results, most of the lymphoma cases were attributed to nodular sclerosis type (87%). The main symptoms were: an increase in the size of peripheral lymph nodes (100% of cases), cough and breath shortness (78% of cases with mediastinal involvement). The stage of the disease at diagnosis was IIIB in 68% of the patients. The patients were treated with combined chemotherapy according to the schemes: ABVD and BEACOPP. Complete remissions were obtained in 35% of cases, partial remissions - in 38% of cases. Treatment failure or relapse were registered in 27% of cases. 62% of patients obtained partial or complete remissions after 8 courses of combined chemotherapy. The following post-chemotherapy complications were recorded: agranulocytosis in 78% of cases, toxic liver disease in 42% of cases and gastrointestinal disturbances in 98% of cases.

**Conclusion.** The patients with Hodgkin's lymphoma are treated in Moldova and abroad with combined chemotherapy schemes such as BEACOPP and ABVD. Radiotherapy is performed in cases with residual tumor masses and in bulky diseases. Current treatment options allow to achieve the complete and partial remission rate of 73% in the advanced stages of Hodgkin lymphoma.



# **GASTROENTEROLOGY SECTION**



***„Calea omului de știință e tumultuoasă, începătorii fiind supuși unui curent copleșitor de informație, iar identificarea studiilor veritabile constituie o adevărată provocare. În postura de cercetător, îndemn să vă păstrați verticalitatea și să filtrați fluxul de informație, precum o face „laboratorul central” al organismului, ficatul. Și fie ca funcționalitatea perfectă a tractului digestiv să vă ofere energia necesară în începuturile voastre științifice!”***

***"The path of a scientist is tumultuous, with beginners subjected to an overwhelming stream of information, and identifying genuine studies posing a real challenge. In the role of a researcher, I urge you to maintain your integrity and filter the flow of information, much like the 'central laboratory' of the body, the liver. And may the perfect functionality of the digestive tract provide you with the energy you need in your scientific beginnings!"***

***Eugen Tcaciuc,***

*MD, PhD, Professor,*

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## 1. APPLICABILITY OF THE CLDQ IN THE MONITORING OF PATIENTS WITH DELTA VIRAL LIVER CIRRHOSIS

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**Introduction.** The clinical burden of delta viral cirrhosis is significant in terms of health, quality of life, and economic impact on patients and society. The Chronic Liver Disease Questionnaire (CLDQ) is an instrument that is specifically created to evaluate the health-related quality of life in individuals with chronic liver disease, but it has not been evaluated in patients with HDV.

**Aim of study.** To evaluate the applicability of CLDQ in Moldavian individuals with delta viral liver cirrhosis.

**Methods and materials.** We conducted a prospective study of adult patients with delta viral liver cirrhosis seen in a tertiary center Department of Gastroenterology & Hepatology, SCR “Timofei Mosneaga” who completed the CLDQ questionnaires. A comprehensive clinical and neuropsychological assessment was performed on all patients.

**Results.** The CLDQ was performed in 42 patients (59.5% females, median age 55 years) on discharge. Severity of delta viral cirrhosis was divided into compensated cirrhosis (21.4%), and decompensated cirrhosis (78.6%). The CLDQ was interpreted according to six domains, all being impaired variables according to 1-7 scale, ranging from “all of the time” to “none of the time”. For a good understanding it was decided to present the results as severe impairment for 1-3 answers according to scale, 4 –moderate and 5-7 slight. The domains affected mostly were systemic symptoms- 47%, worry 42%, abdominal symptoms 40%, emotional health- 39% with severe impairment. The fatigue domain was present in a mild form in 42% patients. Most of the patients found the CLDQ clear and easy to complete. The CLDQ-HDV showed a gradient between patients with compensated/ decompensated cirrhosis. Future investigations among participants with HDV require assessing the responsiveness of the CLDQ to medical therapies and disease progression, being in process an electronic form too.

**Conclusion.** The CLDQ is a brief questionnaire, easily understood, and acceptable to patients with delta liver cirrhosis, being linked to the severity of liver disease with a role in differentiating it.

## 2. CLINICAL "ODYSSEY" IN WILSON'S DISEASE PATIENTS FROM THE REPUBLIC OF MOLDOVA



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**Introduction.** Wilson's disease (WD) presents high clinical heterogeneity, independent of age and sex. In our country, it is the first study that analyzes the phenotype of patients with this genetic disorder.

**Aim of study.** The study aims to evaluate the clinical features of patients with WD in the Republic of Moldova.

**Methods and materials.** A retrospective and prospective study was performed on 170 people suspected of WD, between 2006 and 2023. The modified Leipzig Scoring System was used to specify the diagnosis; a score  $\geq 4$  points establishes the diagnosis of WD. All patients were genetically tested by the Sanger sequencing method. Statistical analysis was performed using EpiInfo.

**Results.** Out of 170 people, 50 patients had a score of  $\geq 4$  points. The mean age was 23 years  $\pm$  9.3 (range 5-46 years), and the median was 24.5 years. 23% of pts are  $<18$  years old. The female/male ratio is 1:1.5. The average duration of the period of the diagnosis was 25.7 months (range 1-96 months). All persons were of Caucasian origin. No consanguineous relationships have been described. Hepatic onset was associated in 43.9%, in both sexes equally, while neurological onset was associated in 56.09%, predominating in men (73.09%). Patients with hepatic presentation are diagnosed at younger ages (17.67 years  $\pm$  9.07), while those with neuro-psychiatric type are diagnosed at older ages (27.39 years  $\pm$  7.81) and with longer diagnosis delays. After examination, liver disease was diagnosed in 52.17% of those with neurological onset; and in those with hepatic onset, neurological lesions were detected in 16.7%. In 58.82%, the liver phenotype was represented by liver cirrhosis (decompensated – 70%). The most frequent neurological manifestations were postural instability – 43.47%, pseudo-bulbar syndrome (dysphagia, dysarthria) - 35%, and tremors of the limbs - 30%. The psychiatric presentation includes depression - 47%, sleep disturbance - 25%, and mood changes - 17%. The Kayser-Fleischer ring was identified in 32%, of which 75% was associated with neurological lesions. Splenomegaly was identified in 58.54%, of which 79.17% were associated with hepatomegaly. One patient underwent a liver transplant due to acute liver failure. Genetic testing was performed in 92%, and most of them were compound heterozygotes. The most common mutation was p.H1069Q (69.57%).

**Conclusion.** Our study observed that hepatic presentation was diagnosed at younger ages, while neuropsychiatric manifestations were identified at older ages and with longer diagnostic delays. Also, the late establishment of the diagnosis was associated with various complications and irreversible organic damage.



### 3. EXTERNAL VALIDATION OF A NEW PROGNOSTIC SCORE FOR MORTALITY IN THE FIRST 3 MONTHS OF PATIENTS ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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**Introduction.** Viral liver cirrhosis is one of the most serious problems for the population due to its global spread, increased morbidity and mortality, and the high degree of disability caused by its rapid progression.

**Aim of study.** To determine the survival of recipients on the liver transplant waiting list, several prognostic scores were proposed to predict the survival rate in patients with liver cirrhosis of viral etiology within 3 months of listing.

**Methods and materials.** The cross-sectional clinical cohort study included 265 patients with viral liver cirrhosis aged 18-65 years on the waiting list for liver transplantation between 2013 and 2022, to whom 10 prognostic scores were applied.

**Results.** Prognostic mortality at 3 months after listing for liver transplantation for the 10 scores the largest area under the ROC curve was observed for the MELD 3.0 score was 0.790 (0.694-0.885) the p-value being less than 0.005 which means that the model is good for application in clinical practice and is statistically significant, being a score that excludes the discrepancy between male and female gender, thus ensuring a better distribution of liver transplants.

**Conclusion.** The MELD 3.0 score can in fact be used to enroll patients on the waiting list for liver transplantation in the national program as a score for the future, being a useful prognostic predictor of both short-term and long-term survival.

#### 4. HYPERFERRITINEMIA IN LIVER DISEASES - DIAGNOSIS AND CONTROVERSIES



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**Introduction.** Ferritin is a protein that plays a crucial role in iron storage and regulation within the body. It is found primarily within cells, particularly in the liver, spleen, bone marrow, and other tissues that store and utilize iron. Ferritin serves as a means of storing excess iron in a safe form. Hyperferritinemia is a phenomenon characterized by elevated levels of ferritin, a vital iron-regulating protein, that gained substantial attention in the realm of healthcare. Ferritin, traditionally recognized for its role against iron deficiency, plays a dual role as both a storage depot and a gatekeeper for this essential mineral.

**Aim of study.** The aim of study was to evaluate the causes and diagnostic implications of hyperferritinemia in liver diseases.

**Methods and materials.** A comprehensive literature search using PubMed, Clinical Review, and Google Scholar, targeting articles, meta-analyses, and references from relevant articles and textbooks published between 2010 and 2013 as well as 2017 and 2023. The data is collected at multiple time points to help readers understand when each set of data was collected.

**Results.** Non-Alcoholic Fatty Liver Disease is one of the most common causes of liver diseases. In some cases of this cause, hyperferritinemia can occur without iron overload, leading to debate about the role of iron in the disease. Elevated ferritin levels may reflect liver inflammation rather than iron overload in these cases which is highly controversial.

**Conclusion.** It is becoming evident that ferritin has numerous functions beyond its traditional role as an intracellular iron storage protein. There are still many unknown aspects of ferritin biology, and ongoing debates in the scientific community indicate the need for further experiments. Determining the underlying causes of hyperferritinemia can often be accomplished through assessments.

**Keywords.** Hyperferritinemia, ferritin, liver diseases, iron overloads





## 5. LABORATORY MARKERS IN THE DIAGNOSIS OF HEREDITARY GLUTEN INTOLERANCE

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**Introduction.** Gluten intolerance (celiac disease) is a genetic autoimmune disease with a prevalence of approximately 1% of the population in which the consumption of gluten-containing foods causes damage to the small intestine.

**Aim of study.** The purpose of this study was to review the literature in order to outline the laboratory diagnostic algorithm for hereditary gluten intolerance and to establish the frequency of the alleles of the HLA-DQA1 and HLA-DQB1 genes in the population of Moldova.

**Methods and materials.** A bibliographic study of the scientific literature in Pubmed and Google Scholar databases, and also the analysis of the medical records of the patients tested in a private laboratory accredited according to ISO 15189 in the Republic of Moldova.

**Results.** After finishing this study, we predict that we will have described the diagnostic algorithm for celiac disease, with a description of each step and the role of each laboratory marker in determining the susceptibility for hereditary gluten intolerance. Another result that we will obtain from this study will be the frequency of the alleles of the HLA-DQA1 and HLA-DQB1 genes in the population of the Republic of Moldova, as well as their correlation with other specific laboratory indices in the diagnosis of celiac disease.

**Conclusion.** The diagnosis of hereditary gluten intolerance generally involves a combination of methods, such as: genealogical analysis, serological investigations for the detection of antibodies specific to celiac disease, biopsies and genetic testing to determine the presence or absence of DQ2/DQ8 heterodimers. A correct diagnosis and adequate management can significantly improve the quality of life for people with celiac disease.

## 6. PORTAL HYPERTENSION: DIAGNOSIS AND TREATMENT MANAGEMENT



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**Introduction.** Portal hypertension is responsible for the more severe and even lethal complications of chronic liver disease and cirrhosis.

**Aim of study.** Evaluation of the effect of ozone therapy on the state of circulation of hepatic venous flow.

**Methods and Materials.** 44 patients were examined with chronic hepatitis C – 28 men (64%), 16 women (36%) aged from 45 to 62. The diagnosis was confirmed by clinical, biochemical, imagistic and morphopathological investigations (Knodell-Desmet/Fibroscan). Hemodynamics parameters were studied by Doppler color.

**Results.** Depending on the treatment, all patients were divided into 2 lots. The 1 lot included 26 patients who concurrently with the complex therapy administered ozone therapy. The 2 lot included 18 patients treated without ozone therapy. The control group was made up of 10 healthy volunteers. All patients with chronic viral hepatitis C had a significant veridical increase in the diameter of the portal (Dvp) and lienalis vein (Dvs), rise of congestion index (CI) and the decrease of the linear velocity of blood flow in the portal vein - maximum systolic velocity of blood flow (Vmax) and the end diastolic velocity of the blood circuit (Vmin). Indicators of blood volume velocity (Qvp) in the portal vein in both groups did not differ. Simultaneous blood volume (Qvl) in the lienalis vein in patients with chronic viral hepatitis C was significantly higher than in the control group. At the end of the treatment course, the indices of venous blood circulation of the liver were repeatedly evaluated in two lots. As a result, it was found that in group 1 a dynamic of hepatic venous blood flow was estimated positive: Dvp  $11.3 \pm 0.44$  mm, Dvs  $7.2 \pm 0.44$  mm, CI  $0.041 \pm 0.008$ , Vmax  $19.4 \pm 0.8$  cm/s, Vmin  $13.8 \pm 0.8$  cm/s, in comparison with the group 2: Dvp  $12.6 \pm 0.65$  mm, Dvs  $10.0 \pm 0.45$  mm, CI  $0.077 \pm 0.007$ , Vmax  $19.8 \pm 0.8$  cm/s, Vmin  $14.0 \pm 0.9$  cm/s.

**Conclusion.** Inclusion of ozone therapy in the complex treatment allows more obvious compensation of flow irregularities in liver blood.

**Keywords.** Hepatitis C, portal hypertension, ozone therapy.



## 7. THE INFLUENCE OF OBESITY ON THE QUALITY OF LIFE IN PATIENTS WITH GASTRO-ESOPHAGEAL REFLUX DISEASE

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**Introduction.** Obesity or exaggerated growth of adipose tissue according to body mass index (BMI) has shown an increase in the prevalence of gastroesophageal reflux disease (GERD), which significantly affects the quality of life in patients suffering from GERD. The lowest prevalence of GERD was 6.64% for people with a BMI of 18.5, while the highest prevalence of GERD was seen in those with a BMI  $\geq 30.0$  and is 22.63%.

**Aim of study.** To determine the mechanisms by which obesity influences the development and progression of GERD symptoms and patients' quality of life.

**Methods and materials.** The study was carried out by researching the articles that were published in the period 2020-2023, using the PubMed, NCIB, Medscape, Mendeley databases, using the keywords: "GERD", "obesity", "quality of life", "relationship", "treatment", also analysis of 100 SF-36 questionnaires.

**Results.** Previous research has indicated that high BMI is a risk factor for the development and severity of GERD symptoms. The mechanisms by which obesity is involved in the development of GERD are: increased intragastric pressure, decreased lower esophageal sphincter pressure, and increased frequency of transient relaxation of the lower esophageal sphincter, which results in acid reflux. Significantly poorer scores on all 8 SF-36 scales, physical function and well-being, and emotional well-being in patients with obesity and GERD compared to the general population have been reported in the scientific literature. Thus, an individualized diet, especially a Mediterranean one, weight loss and targeted treatment for GERD results in the patient's quality of life outcome.

**Conclusion.** Only a few mechanisms by which obesity causes and/or influences the severity of GERD symptoms are described, all further studies are needed to determine the exact mechanism and establish new therapeutic approaches culminating in improving the quality of life of patients with obesity and GERD.

# **PNEUMOLOGY AND ALLERGOLOGY SECTION**



*„Cei chemați și cu iubire de oameni îmbrățișează truda învățării permanente, depășind nedreptățile și ispitele cotidianului, vor atinge cunoașterea, măiestria și înțelepciunea, necesare pentru a ajuta providența întru salvarea de vieți omenești - clipe de sublimă fericire.”*

*"Those called and embraced by love for humanity embrace the toil of lifelong learning, surpassing the injustices and temptations of daily life. They will attain the knowledge, mastery, and wisdom necessary to aid providence in the salvation of human lives - moments of sublime happiness."*

**Victor Botnaru,**  
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## 1. "CANCER NEVER TAKES A BREAK — A NEW REALITY, THE SAME RELENTLESS ADVERSARY"

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**Introduction.** Lung cancer presents a significant global health challenge, posing a pervasive threat to individuals worldwide. It stands as a major concern, often linked to severe prognoses and a substantial impact on quality of life.

**Case statement.** A 76-year-old man living in an urban environment, non-smoker, and HIV-negative, presented with the onset of the disease approximately 7 days ago. He exhibited toxicoinfectious syndrome symptoms, including subfebrility up to 37.7 degrees, chills, and sweats. Bronchial syndrome manifested with a persistent dry cough and dyspnea rated as mMRC III, while an asthenovegetative syndrome was marked by general weakness. The patient has a medical history significant for a right kidney tumor in 2003 and lung cancer, leading to a lower right lobectomy in 2021. Despite symptomatic treatment, there was no clinical improvement. Biologically, a pronounced inflammatory syndrome was evident. Chest X-ray imaging revealed asymmetrical lung fields, with the right lung showing decreased volume, no exclusion of lower lobe atelectasis, and pleurisy on the right at the anterior arch of the sixth rib, accentuating the lung pattern. Fiberbronchoscopy results indicated biopsy fragments predominantly constituted of blood and fibrin with occasional neutrophils and benign respiratory epithelium fragments. Discohesive cells with hyperchromatic nuclei, featuring an increased nucleus-to-cytoplasm ratio, were occasionally observed. An obstructive tumor lesion was identified at the level of the right intermediate bronchus.

**Discussions.** The reactivation of the tumor process can pose a challenge in cancer management, demanding special attention in treatment and monitoring strategies for patients.

**Conclusion.** As a standard surgical procedure for lung cancer, lobectomy has proven effective in removing tumors and treating the disease in its early stages. It is crucial to emphasize that individual responses may vary, and each patient undergoes a unique postoperative experience. Efficient management and optimization of outcomes after lobectomy in lung cancer require close monitoring and collaboration with the medical team.



## 2. CHALLENGES AND OPPORTUNITIES OF THE ARTIFICIAL INTELLIGENCE IN RESPIRATORY MEDICINE



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**Introduction.** Artificial Intelligence is a mechanism capable of actively perceiving the surrounding environment, taking initiatives to maximize the chances of successfully achieving its objectives. Additionally, it can interpret and analyze data in a way that simulates and reproduces human cognitive processes, such as learning, reasoning, and analysis. Scientific papers increasingly address its applicability in medicine, aiming for more precise diagnostics and avoiding the influence of human factor. An increasing number of respiratory pathologies pose a challenge for clinicians due to their heterogeneity. AI could serve as assistance in establishing a more coherent diagnosis by interpreting functional respiratory tests and imagistics methods.

**Aim of study.** The aim of the study is to identify and describe scientific papers that demonstrate the applicability of AI in pneumology and to acknowledge the need for its implementation in the healthcare system.

**Methods and materials.** Literature review of the PubMed, GoogleScholar electronic database, 11 articles for the terms „ Artificial intelligence in respiratory disease ” and the American Thoracic Society (ATS)/European Respiratory Society (ERS) original research article.

**Results.** The research of AI in respiratory medicine focuses primarily on pulmonary function tests (PFTs), the diagnosis and management of conditions like acute respiratory distress syndrome (ARDS), idiopathic pulmonary fibrosis, COPD and other obstructive lung diseases. AI-based software can precisely measure spirometry data quality, comparable to expert over-readers, potentially offering immediate feedback and consistent results, which could benefit clinical trials. The ATS/ERS guidelines served as the gold standard benchmark for interpreting PFT patterns. The study compares the accuracy and consistency of pulmonologists' interpretations of PFTs with those of an AI-based software developed from a large dataset of patient cases. 120 pulmonologists evaluated 50 cases each, resulting in 6000 interpretations, while the AI software analyzed the same data. The investigation revealed that pulmonologists' interpretations matched guidelines in 74.4% of cases, with moderate interrater agreement ( $\kappa=0.67$ ). However, correct diagnoses were made in only 44.6% of cases, with significant variability among raters ( $\kappa=0.35$ ). In contrast, the AI software matched PFT patterns perfectly and provided correct diagnoses in 82% of cases, significantly outperforming pulmonologists and highlighting the potential for AI-based software to provide more accurate results.

**Conclusion.** In conclusion, the research underscores the significant potential of AI in revolutionizing respiratory medicine, with a particular focus on PFTs. AI offers the capability to meticulously assess data, providing immediate feedback and consistent results, suggesting its viability as a decision support tool in clinical practice.

**Keywords.** AI, respiratory medicine, PFTs.



### 3. CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND DEPRESSION

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**Introduction.** Chronic obstructive pulmonary disease encompasses various complications and comorbidities such as respiratory failure, cardiovascular disease, the development of lung cancer, osteoporosis, metabolic syndrome, diabetes and mental health issues, including a propensity towards depression. Individuals with chronic obstructive pulmonary disease often experience depression due to the significant impact of the disease on their quality of life, daily activities, and overall health.

**Aim of study.** This study aims to investigate and assess the quality of life of patients with chronic obstructive pulmonary disease associated with depression and anxiety, to provide information for more effective management of these comorbidities and to improve the quality of life of patients with chronic obstructive pulmonary disease.

**Methods and materials.** This involved conducting an analytical literature review of scientific articles associated with specific keywords. Initially, 40 articles were selected, but only 29 met the inclusion criteria for the research topic.

**Results.** Approximately 40% of study participants were identified as smokers, with an average annual cigarette consumption of 34.3 packs. Overall, the modified Medical Research Council Dyspnea Scale (mMRC) had a mean value of 2.86, and the mean Chronic Obstructive Pulmonary Disease (COPD) assessment test score was 21.75. Study participants experienced an average of 1.93 COPD exacerbations per year. For symptoms of anxiety and depression, the mean scores among COPD subjects were 10.65% and 9.93%, respectively. No significant differences were found between smokers and ex-smokers in anxiety, depression or panic attack scores. Bivariate correlation analysis revealed associations between anxiety, depression, panic attacks and disease severity as well as poor quality of life in COPD patients, regardless of their current tobacco use status.

**Conclusion.** Study results indicate that participants with chronic obstructive pulmonary disease (COPD) show a significant association between anxiety, depression, panic attacks and disease severity, also highlighting a low quality of life, with no significant differences in symptomatology between smokers and former smokers in this population.

#### 4. CONSEQUENCES OF PULMONARY HYPERTENSION AND RIGHT-SIDED HEART FAILURE



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**Introduction.** Pulmonary hypertension (PH) is common in several pathologies and maintains high levels of morbidity and mortality. In PH the main consequence is right heart failure, which leads to complex clinical syndrome affecting several organ systems. The systemic nature of PH and right heart failure is often neglected or underestimated, which ultimately has a negative effect on the patient's condition.

**Aim of study.** Review the literature targeting the analysis of the correlation between pulmonary hypertension and right heart failure.

**Methods and materials.** Multivariate study based on a review of the literature over the past 5 years regarding the effects of pulmonary hypertension and right heart failure on different systems and their mutual impact on disease progression.

**Results.** While the systemic nature of PH and right heart failure is often neglected or underestimated, pulmonary hypertension affects up to one percent of the global population and occurs at an incidence of up to 10% in people over 65 years of age, leading to a poor prognosis for the patient. Thus both systemic venous congestion caused by right ventricular dysfunction and impaired peripheral perfusion caused by right heart/left heart interaction and decreased systemic flow contribute to multiple organ system damage and inter-organ interaction, which can lead to a systemic inflammatory state.

**Conclusion.** It should be pointed out that a greater part of available evidence on secondary organ damage (especially liver and kidney damage) is mainly related to left heart failure, whereas the consequences of isolated right heart failure caused by PH are understudied.



## 5. DIAGNOSTIC ACCURACY OF XPERT ULTRA FOR MICROBIOLOGICAL CONFIRMATION OF PULMONARY TUBERCULOSIS IN PATIENTS WITH PAUCIBACILLARY DISEASE

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**Introduction.** Worldwide, up to one-third of pulmonary tuberculosis patients are missed for microbiological confirmation. Assessment of specimens obtained during bronchoscopy is one of the well-recognized methods that can increase the rate of microbiological confirmation in pulmonary tuberculosis. The data on the diagnostic accuracy of Xpert MTB Ultra, a real-time PCR-based diagnostic tool, in bronchial aspirate specimens is very limited.

**Aim of study.** In the presented study, we have evaluated the performance of Xpert MTB Ultra in bronchial aspirate samples in patients with negative smear microscopy and Xpert MTB Ultra in freely expectorated sputum.

**Methods and materials.** We retrospectively reviewed microbiological and basic clinical characteristics of all patients who were consulted for suspected pulmonary tuberculosis at the Institute of Phthtisiopneumology in Moldova during 2022 and had both negative smear and Xpert Ultra results in sputum samples and in whom bronchial aspirate was obtained by bronchoscopy with further microbiological examination by Xpert MTB Ultra and culture for *M. tuberculosis*.

**Results.** 393 cases with a complete dataset have been analyzed, of which 80 have been diagnosed with pulmonary tuberculosis. Positive culture for *M. tuberculosis* was obtained in 2.5%, smear microscopy was positive in 1.8% (13 cases), and Xpert Ultra in 4.2% (30 cases) of bronchial aspirate samples. The sensitivity and specificity of Xpert Ultra in bronchial aspirate, using culture as a reference standard, were correspondingly 80.0% (95% CI, 37.5% – 99.0%) and 98.7% (95% CI, 97.0% - 99.4%). Additional microbiological confirmation of pulmonary tuberculosis was obtained in 11.2% (9/80) of the patients diagnosed with pulmonary TB.

**Conclusion.** Xpert MTB Ultra has good diagnostic accuracy in bronchial aspirate samples. That could improve the rate of microbiological confirmation and potentially reduce the time to treatment initiation in patients with pulmonary tuberculosis.

## 6. HEREDITARY ANGIOEDEMA WITH C1INHIBITOR DEFICIENCY



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**Introduction.** Hereditary angioedema (HAE) is a rare autosomal dominant disease with deficiency or/and dysfunction of C1 inhibitor, caused by mutations in the C1-INH gene. HAE is characterized by potentially life-threatening episodes of subcutaneous and/or submucosal edema without urticaria, prevalence 1:50,000 individuals. The primary mediator of swelling in HAE is bradykinin. The symptoms vary in severity, location, and duration, but the organs involved include the upper airways, skin, and gastrointestinal tract.

**Case statement.** A 19 y.o. man was admitted in the ICU with severe dyspnoea, bronchospasm, oedema of face and extremities, acute respiratory failure. Patient was diagnosed in 2018 with hereditary angioedema with C1Inh deficiency. Symptoms of severe angioedema (upper and lower limbs lasting for 2-3 days, abdominal attacks, nausea and vomiting, facial edema associated with difficult swallowing) started at age 2 years. The patient has frequent episodes of angioedema every month (predominantly limbs, face) caused by various triggers: stress, low/high temperatures, trauma and other factors. Sometimes marginal erythema may be present as a prodromal symptom. Investigations: C1 inhibitor 0,0411 g/l (N 0,21-0,4), C1 inhibitor function 0,0411% (N 70-130%), C3 0,86 g/l (N 0.9-1.8), C4 0.08 (N 0.1-0.4), d-Dimers 8,24 (0-0.55 mg FEU/l), qualitative troponin positive, CK-MB 96 (N 0 - 25 U/L ), CRP 26 (0-5 mg/l). EKG, Echocardiography were normal. Treatment of choice: A plasma-derived C1 Esterase Inhibitor, fresh frozen plasma and tracheal intubation in severe cases (laryngeal angioedema). Patient was discharged on the 10th day with improvement of general condition with recommendation on management and prevention of further HAE attacks.

**Discussions.** Because the disease is very rare, it is not uncommon for patients to remain undiagnosed for many years. Diagnostic delays impact the accuracy of management. Treatment is different from histamine-associated angioedema, antihistamines, corticosteroids, and epinephrine have no effect. Acute treatment of HAE can include IV infusions of C1-INH, receptor antagonists, and kallikrein inhibitors. Short- and long-term prophylaxis can also be administered to patients with HAE.

**Conclusion.** In patients with early onset of repetitive angioedema episodes, not responding to antihistamines, corticosteroids therapy the diagnosis of HAE should be considered.





## 7. HYPEREOSINOPHILIC SYNDROME - DIAGNOSTIC CHALLENGES IN ALLERGIC PATIENTS

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**Introduction.** Eosinophilia is a common laboratory manifestation associated with multiple diseases (allergic, parasitic, infectious or oncological diseases). Eosinophilia is an increase in the absolute values of eosinophils in peripheral blood, bone marrow or other tissues above normal limits (350-500 cells/ $\mu$ l). The severity of eosinophilia is classified as mild (500-1500/ $\mu$ l), moderate (1500-5000/ $\mu$ l) or severe (>5000/ $\mu$ l).

**Case statement.** We present the clinical case of a 32-year-old female, with severe hypereosinophilia (5000-9000/ $\mu$ l) persistent for 2 years, with reversible bronchoconstrictive syndrome, manifestations of chronic urticaria. Diagnosed with moderate persistent uncontrolled allergic asthma and chronic urticaria. Multiple food allergies (cow's milk protein, egg, latex, raspberry), latex-food syndrome. Total IgE values range from 1000-3200 IU/ml. Parasitic invasion assessment confirmed the presence of *Ascaris lumbricoides* and *Toxocara canis*. Serum hypereosinophilia (36-57%) in the last 2 years was mainly attributed to allergic diseases, the presence of symptoms on exposure and elevated specific IgE values to multiple food and inhalant allergens (cow's milk casein and lactalbumin, ovomucoid and ovalbumin, serum albumin, latex, banana, kiwi, pollens, mites). Eosinophilic bronchoalveolar lavage (69% eosinophils) and persistent elevated serum values (>5000/ $\mu$ l) required differential diagnosis with eosinophilic myeloproliferative syndrome, chronic eosinophilic leukemia was confirmed by bone marrow aspiration.

**Discussions.** Increased serum eosinophil values >1500 cells/ $\mu$ l for more than 6 consecutive months require consideration of hypereosinophilic syndrome (HES), which is characterized by a heterogeneous group of rare disorders characterized by significant blood eosinophilia (>1500/ $\mu$ l) without an underlying cause and with important clinical features caused by eosinophilic infiltration of tissues and organs.

**Conclusion.** Patients with hypereosinophilia most commonly present with allergic or parasitic diseases. An eosinophil count in the blood >1500/ $\mu$ l or higher that lasts over time should require a differential diagnosis with myeloproliferative malignant diseases.

## 8. IMPACT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON QUALITY OF LIFE



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**Introduction.** Chronic Obstructive Pulmonary Disease (COPD) is the leading cause of morbidity and mortality worldwide. According to the World Health Organization, globally, COPD is the third leading cause of death, accounting for 6% of total deaths in 2019, with over 80% occurring in low- and middle-income countries. In the Republic of Moldova, in 2022, 433 individuals lost their lives due to COPD, compared to 489 deaths in 2021 and 506 deaths in 2020.

**Aim of study.** Highlighting the impact of obstructive pulmonary diseases on quality of life.

**Methods and materials.** This review represents an analysis of actual information about the impact of chronic obstructive disease on quality of life from online biomedical sources, found with the research motors PubMed, Google Scholar and NCBI sites.

**Results.** The literature data suggests that individuals experiencing symptoms of COPD in the early morning and during the night are prone to have a lower health-related quality of life compared to those without these symptoms. In a study, overall health status was assessed using the CAT test, which was found to be significantly lower among patients exhibiting at least one COPD symptom compared to those without COPD symptoms. Physical activity is consistently influenced by the clinical and functional determinants of COPD, limiting patients' capacities in performing daily activities and exercises. Specific activities such as dressing, getting out of bed and climbing stairs are most severely affected, prompting some patients to require assistance, making them feel like a burden to others. Consequently, COPD patients reduce physical activity in the early stages of the disease to avoid symptoms. Over 70% of COPD patients experience sleep disorders, including difficulties falling asleep, maintaining sleep, and frequent nocturnal awakenings, caused by ventilation disorders, gas exchange issues, and the presence of nocturnal respiratory symptoms.

**Conclusion.** COPD symptoms are associated with a significant decline in quality of life, overall health, and prognosis for affected individuals. Regular symptom assessment should be conducted using patient-oriented questionnaires, and healthcare professionals should integrate symptoms into treatment plans, as effective symptom management throughout the day is crucial for improving quality of life. Physical, psychological, and social support should be provided from the onset of the disease, adopting a holistic approach throughout the entire treatment process. It is essential that this holistic support be offered without delay, avoiding waiting until the disease reaches a severe stage, and its burden becomes debilitating.



## 9. IMPACT OF NEW CLASSIFICATION OF COPD ON ASSESSMENT OF SEVERITY

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**Introduction.** Chronic obstructive pulmonary disease is a respiratory disease caused by abnormalities of the airways, alveoli, accompanied by chronic respiratory symptoms (dyspnea, cough, expectoration), characterized by a persistent, progressive and irreversible evolution resulting in the consequent impairment of the quality of life. It is one of the main causes of death worldwide, early diagnosis and adequate treatment being essential in slowing down the progression of the disease. The GOLD classification helps considerably in the management of COPD by evaluating its severity based on symptoms, exacerbation history and lung function.

**Aim of study.** In recent years, there has been a significant evolution in the understanding and management of chronic obstructive pulmonary disease, recently a new classification of COPD has been introduced, which aims to provide a more comprehensive perspective on the assessment of the severity of this disease.

**Methods and materials.** Data collected for this study was obtained from the Global Initiative for Chronic Obstructive Pulmonary Disease database and articles published in PubMed. The data were studied to understand the strategy aimed at the new classification of COPD in order to better determine the definition of exacerbations and their severity.

**Results.** Through this study, I have found that the new classification of COPD tends to introduce into practice a new process of more accurate assessment of patients diagnosed with COPD to establish an accurate level of severity for the purpose of a more individualized approach to treatment. Considering the instability of the targeted results of EPOC as a result of the modest resources of the primary medical care globally, the new classification proposes the use of some clinical variables (dyspnea intensity, using VSA from 0 to 10, RR, HR, SaO<sub>2</sub>, in the available places it is also proposed the level of C-reactive protein in the blood, blood gasometry) that are easy to specify and are useful for determining the severity of EPOC. This approach helps to monitor the disease more efficiently and to personalize the treatment.

**Conclusion.** The new classification of COPD represents an important strategy towards the consolidation of a new evaluation system for patients with COPD. Produces significant changes in disease monitoring, the more detailed approach helps to more accurately establish disease stage, severity level and individualize treatment resulting in more effective disease management.

## 10. POST-COVID-19 SEQUELAE



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**Introduction.** COVID-19 is a pandemic infection caused by the novel severe acute respiratory syndrome coronavirus-2, affecting millions of people worldwide and having devastating consequences on health systems, the economy, and human lives. While a significant portion of the infected population has fully recovered, others continue to experience persistent symptoms after overcoming the disease, termed post-COVID-19 sequelae or post-COVID-19 syndrome.

**Aim of study.** The aim of this research is to comprehensively investigate the long-term consequences, or sequelae, following COVID-19. The focus is on gaining insights into the impact of the virus on various physiological systems, exploring potential variations in outcomes, and contributing to a more nuanced understanding of post-COVID-19 health implications.

**Methods and materials.** In this literature review, I utilized the PubMed database to search for key terms such as "post-Covid consequences," "post-Covid-19 syndrome," and "post-Covid-19 complications." I identified over 4000 results, with all articles ranging from 2020 to 2023.

**Results.** According to existing literature, the analysis of the late consequences of COVID-19 reveals a broad range of implications in various systems and organs. Among them, pulmonary sequelae include: 1. Pulmonary Fibrosis - Studies have documented the progression of pulmonary fibrosis in patients recovered from COVID-19, with changes in lung tissue that can persist and cause chronic respiratory difficulties. 2. Post-COVID Dyspnea Syndrome - Dyspnea, including the sensation of suffocation, may remain a recurrent issue after recovery. 3. Permanent Pulmonary Lesions - In severe cases, COVID-19 can cause irreversible lung lesions, impacting pulmonary capacity.

**Conclusion.** This literature review illustrates the complexity and diversity of the late consequences of COVID-19, emphasizing the need for ongoing research and personalized care for patients with persistent symptoms. Current data suggest that COVID-19 can leave a significant and varied impact on long-term health, justifying the necessity of an interdisciplinary approach for the management and treatment of these patients.



## 11. PULMONARY TUBERCULOSIS WITH CHRONIC EVOLUTION – CLINICAL ASPECTS

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**Introduction.** Evaluating the clinical features of TB in patients with chronic pulmonary processes and the effectiveness of the administered treatment

**Aim of study.** Pulmonary tuberculosis (TB) is a public health problem, being an infectious disease that depends on the "health" of society and the presence of social factors. Patients with chronic pulmonary TB are the main sources of spread of *Mycobacterium tuberculosis* infection.

**Methods and materials.** A number of 87 medical records of patients with the presence of the chronic process criteria of pulmonary TB, admitted in IMSP SCMF during 2021-2022, were analyzed. The particularities of the course of the disease and the effectiveness of the treatment were studied.

**Results.** The study included 67(77%) men and 21 women (33%). Patients aged 45-65 years predominated - 62 (71.3%) cases. Social factors were found in most cases - 82 (94.3%) cases. Among the established clinical forms were: fibrocavitary TB-26(30%), disseminated TB-28(32.2%), caseous pneumonia-33(37.8%) cases. According to the type of case, "New Case" predominated-57 (65.5%), cases of "Retreatment" - 30 (35.5%). Complications developed in all patients (100%) included in the study, the most frequently noted being Chronic Pulmonary Cord-67(78%) and Cardiopulmonary Insufficiency-76(88%). The forms of resistant TB were in 75 (86.2%) cases. "Death" caused by TB was recorded in 2021-7 (8.1%) and in 2022-2 (2.3%) cases. Adverse reactions of the treatment developed in ½ of the patients, requiring the modification of the therapeutic scheme and the use of individualized regimens. 39 (44.8%) patients had "therapeutic success".

**Conclusion.** Pulmonary TB with chronic evolution develops frequently in men in the presence of social factors. The rate of new TB cases is high, indicating late detection of the disease. Drug resistance and adverse reactions to treatment are significant for therapeutic success.



## 12. PULMONARY TUBERCULOSIS WITH PNEUMONIA-LIKE ONSET IN POST-PANDEMIC ERA: CASE SERIES



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**Introduction.** Outbreak of pulmonary tuberculosis (TB) in post-COVID-19 era represents a real medical and social problem. It remains a diagnostic challenge due to a variety of respiratory (pneumonia, malignancy etc.) and extrapulmonary clinical "masks". This complexity often results in a delayed initiation of an appropriate therapy, thereby heightening the risk of *Mycobacterium tuberculosis* transmission.

**Case statement.** We present three clinical cases of difficult-to-diagnose tuberculosis, with an acute pneumonia-like onset, physical signs of lung consolidation, HIV-negative and lack of response to antibacterial treatment. *M.tuberculosis* infection was confirmed by PCR examination (GeneXpert MTB) of sputum/pleural fluid. Clinical case 1: a 39-year-old male, known with type 1 decompensated diabetes mellitus, admitted with fever up to 39°C, left-sided chest pain, chills, muco-purulent sputum in small quantities. Chest CT revealed bilateral polysegmentary consolidations and minimal left-sided pleural effusion. Pleural fluid examination found 35-40 WBCs per visual field, of them polymorphonuclears 92% and lymphocytes 8%. Clinical case 2, patient, 87 years old, with sequelae of stroke, global heart failure, admitted with mixed dyspnea on minimal physical exertion, cough with muco-purulent sputum, fever up to 38.3°C, postural instability. The Chest X-ray revealed right-sided pleural effusion.

**Discussions.** In line with our cases, published studies indicate that pseudopneumonic manifestations associated with tuberculosis are more prevalent than other atypical presentations. Diagnosing these manifestations is further complicated by the presence of concomitant diseases such as lymphoma, heart failure etc.

**Conclusion.** Maintaining vigilance for potential mycobacterial infections and adopting a multidisciplinary approach for patients with multiple comorbidities remain the fundamental pillars in establishing the diagnosis of tuberculosis in the post-pandemic era.



### 13. RISK FACTORS FOR PULMONARY TUBERCULOSIS DEFINED ACCORDING TO THE DRUG-RESISTANCE PROFILE

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**Introduction.** Tuberculosis (TB) represents a major health problem, listed among 30 countries with the highest burden of the drug-resistant tuberculosis (MDR-TB) and its prevalence is correlated with the risk factors such as socioeconomic conditions, healthcare infrastructure, and public health measures. The MDR-TB is caused by Mycobacterium resistant to isoniazid and rifampicin. The most effective anti-TB treatment for drug susceptible TB is standardized, consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol. Lack of the direct observed treatment (DOT) leads to acquisition of the MDR-TB, which reduces the treatment effectiveness and increases the risk for low treatment outcomes, complications and death.

**Aim of study.** The guidelines and treatment recommendations are updated regularly, and the new drugs are proposed. Therefore, the risk factors for MDR-TB should be continuously monitored. The aim of the study was the assessment of risk factors (RF) for pulmonary TB defined according to the results of the drug-susceptibility tests (DST).

**Methods and materials.** It was realised a prospective case-control study which included 97 patients with pulmonary TB registered in R Moldova during 2022. Including criteria were adult age, TB with pulmonary localization and signed informed consent. The patients were distributed in the 1st group (1st SG) in which were enrolled 30 patients with DST showing MDR-TB, in the 2nd group (2nd G) – 56 with drug-susceptible TB and 3rd group (3rd G) – 11 which acquired (ac.) MDR-TB during the anti-TB treatment.

**Results.** Distributing patients by sex was established that the male sex was a low RF for MDR-TB OR=1,35 (CI 95%: 1,09-1, 51), medium RF for ac. MDR-TB, OR=1,4 (CI 95%: 1,22-2,67), urban residence – medium RF for MDR-TB OR=1,8 (CI 95%: 1,51-1,99), and rural residence-high risk factor for ac. MDR-TB, OR=2,5 (CI 95%: 1,92-3.13). The average age in 1st SG was 42.4 y., in the 2nd G=38.2 and 3rd G=49.1. Economically disadvantaged state was a neutral peculiarity for MDR-TB, OR=1,09 (CI 95%: 0.87-3.1) and high RF for ac. MDR-TB OR=4.41 (CI 95%: 2.76-5.81). Tobacco smoking was neutral for MDR-TB OR=1,18(CI 95%: 0,98-3.1) and high RF for ac. MDR-TB OR=5.01 (CI 95%: 3.32-6.92), alcohol abuse was high RF for developing drug-susceptible TB OR=4.21 (95%CI:1.41-12.54) and neutral for ac. MDR-TB 1,01 (CI 95%: 8.01-2.3) and comorbid state was a high RF for ac. MDR-TB OR=8,91 (95%CI: 6.8-14.19), HIV-Infection was a high RF for drug-susceptible TB OR=3,9 (95%CI: 2.6-5.1). Economic migration and recent returning from abroad was a high RF

**Conclusion.** The study demonstrated that high risk on developing of the drug-susceptible TB was caused by the alcohol abuse, HIV-infection and economic migration, but for ac. MDR-TB the economically-disadvantaged state, rural residence, tobacco-smoking, and commodities.

**Keywords.** Tuberculosis, risk factors, drug resistance

## 14. SARCOIDOSIS AND TUBERCULOSIS- A DIAGNOSTIC AND MANAGEMENT CHALLENGE



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**Introduction.** The intricate relationship between sarcoidosis and tuberculosis has been a subject of considerable debate among clinicians and researchers as both diseases exhibit clear clinical parallels that make differential diagnosis extremely difficult especially in nations where tuberculosis is highly prevalent. Given that immunosuppression, a treatment of sarcoidosis, is not desired in tuberculosis patients, this has significant consequences for treatment choices.

**Case statement.** This case report presents a complex medical history of a 71 year old female patient, previously diagnosed with pulmonary tuberculosis (TB) in 2012 and treated with specific DOTS therapy, experienced a relapse in 2013, leading to disseminated pulmonary TB. Despite initial improvement, subsequent exacerbations occurred, with symptoms including dry cough, dyspnea, chest discomfort, vertigo, periodic headache, general weakness, and weight loss.

**Discussions.** Detailed medical history reveals a progression of symptoms since 2017, prompting further investigation. Chest CT scans demonstrated negative dynamics compared to previous years, suggesting a potential recurrence of infiltrative pulmonary TB or progression of pulmonary sarcoidosis with advanced fibrosis.

**Conclusion.** This case underscores the challenges in managing recurrent pulmonary conditions and highlights the need for a multidisciplinary approach in the diagnosis and treatment of complex cases.



## 15. THE DIAGNOSTIC CHALLENGE IN A PATIENT WITH METACHRONOUS MALIGNANCIES

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**Introduction.** Metachronous malignancies are a rare entity in clinical practice. This case report reveals interconnection between a malignant adrenal tumor diagnosed 6 years ago and a rare central bronchial carcinoid tumor that developed later. This case also illustrates the differential diagnosis with the pathology of fungal etiology.

**Case statement.** A 64-year-old woman, never a smoker, with a history of malignant adrenal tumor diagnosed in 2017, presented with complaints of dry cough, chest discomfort and fatigue. Despite previous treatments with minimal improvement, suspicion of malignancy led to referral to the Oncology Institute. Bronchoscopy revealed a complete bronchial obstruction of the upper lobar bronchus. Pathological examination of the biopsy specimen showed fragments of necrotic masses, with positive Grocott staining revealing *Aspergillus* hyphae. Being suspected of pulmonary aspergillosis the patient was referred to the tertiary level pulmonology clinic for diagnosis and treatment. A repeated biopsy from the bronchial mass obstructing the bronchus identified a carcinoid tumor in the upper lobe of the right lung, while the contrast chest CT showed evidence of pulmonary metastasis on the contralateral lung.

**Discussions.** Metachronous malignant tumors are a rare phenomenon, with an incidence ranging between 1.33% and 5.8%. Moreover, carcinoid tumors are rare malignancies of the neuroendocrine system which account for 2% of all lung cancer cases. The present case illustrates the unique coexistence of these rare medical entities.

**Conclusion.** This case report demonstrates the need for a comprehensive approach to patients with a history of malignant tumors in view of the possibility of metachronous cancers.

## 16. THE ROLE OF SYSTEMATIC SCREENING IN THE DETECTION OF PULMONARY TUBERCULOSIS IN DIABETIC PATIENTS



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**Introduction.** The burden of diabetes mellitus (DM) is increasing globally. The association between DM and tuberculosis (TB) is the next challenge for TB control worldwide. DM and TB represent a mutually disadvantageous disease association. The risk of TB disease is twofold to threefold as common in diabetics as in non-diabetics. Prevention, screening and treatment of both diseases together is more effective.

**Aim of study.** Studying the role of systematic screening for pulmonary TB detection in diabetics patients.

**Methods and materials.** In the study were included 68 patients with association of DM and pulmonary TB, new cases, admitted in the Municipal Clinical Phthisiopneumology Hospital, Chisinau, in 2022. The patients were divided into 2 groups: the study group – 30 patients, identified by systematic screening or active case finding (ACF), the control group – 38 patients, detected by passive case finding (PCF) by examination of symptomatic persons. Analysis methods: comparison, synthesis, Fisher's exact test.

**Results.** Men predominated in the both groups, the M/F ratio among patients detected by ACF was 1.5:1 and by PCF – 4.4:1, ( $p < 0.05$ ). The most of the study patients were over 55 years old. Almost half (13 (43%) cases) of the patients from study group had no identified contact with TB patient, in the control group the TB contact was identified in 36 (94,7%) of cases, ( $p < 0.05$ ). In diabetics identified with TB by PCF the predominance of bilateral pulmonary TB (31 (81.6%) cases), in the phase of destruction (29 (76%) cases), with dissemination (13 (34%) cases) was established. Comparison with patients diagnosed by ACF it was established lower rate of bilateral lung damage (14 (46.7%) case), ( $p < 0.05$ ), with destruction (17 (56,7%) cases), ( $p < 0.05$ ) and dissemination – 8 (26.7%) cases. The rate of TB diagnosis confirmed by microbiological or molecular-biological tests was higher in the control group, 26 (68.4%) patients, compared with study group, 10 (33%) patients, ( $p < 0.05$ ). TB treatment success rate in diabetics identified by ACF was higher, 24 (80%) cases compared with diabetics detected by PCF, 22 (57.9%) cases, ( $p < 0.05$ ).

**Conclusion.** The role of systematic screening for identification of pulmonary tuberculosis in patients with diabetes mellitus is obvious. The positive impact of systematic screening on the treatment success rate is explained by prompt detection of pulmonary tuberculosis in diabetics in the early stages with unilateral damage of the lung parenchyma without the destruction and dissemination.

**Keywords.** Tuberculosis, diabetes mellitus, systematic screening, symptomatic screening.





## 17. TWO ENDS OF THERAPEUTIC RESPONSE SPECTRUM IN THE CLINICAL EVOLUTION OF EOSINOPHILIC PNEUMONITIS.

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**Introduction.** Eosinophilic pneumonia (EP) is a rare disorder encompassing a heterogeneous presentation. The two primary types of EP are acute eosinophilic pneumonia (AEP) and chronic eosinophilic pneumonia (CEP), both characterized by significant eosinophil accumulation in lung tissues and/or bronchoalveolar lavage (BAL) fluid

**Case statement.** We present a series of clinical cases illustrating diverse therapeutic outcomes in Eosinophilic Pneumonia. Case no 1. A 57 y.o. female, reported progressive dyspnea, cough, and fatigue. Her rest saturation was 90%, with rapid desaturation at 76% at moderate physical exercise. Chest imaging showed bilateral ground glass opacities, and pulmonary consolidation areas, with predominant basal distribution, accompanied by a mild hilar lymphadenopathy up to 12mm. Her lung function presented a severe restrictive disorder, with an FVC at 36.9% and significantly decreased DLCO at 19%. Bronchoalveolar lavage (BAL) showed 23% eosinophils. Corticosteroid therapy (Tab. Prednisolone 60 mg) led to significant clinical improvement, with substantial radiological regression. There was an improvement in lung function, but only with a 10% increase in all parameters after 1 month of treatment. Case no 2. A 64 y.o. female, previously known with allergic asthma for more than 30 years, has experienced an episode of Eosinophilic Pneumonitis 6 years ago, with a rapid improvement to corticosteroids. Her exposure history revealed a contact with her pet dog, and some herbal formulation that she has been taking lately. She presented dyspnea, back pain, and fatigue. Radiological findings indicated bilateral lung lesions, with pulmonary consolidation areas suggesting the reversed halo sign. She had a restrictive ventilator abnormality with FVC at 41.5%, FEV1 at 48%, and severely decreased DLCO at 20.2%. Her CBC was consistent with peripheral eosinophilia. During hospitalization she received corticosteroid therapy with Dexamethasone 12 mg, resulting in significant clinical improvement within 8 days and complete radiological resolution of bilateral bronchlobular lesions.

**Discussions.** Eosinophilic pneumonia (EP) is characterized by eosinophilic infiltration into the lungs, often accompanied by peripheral blood eosinophilia. This categorization excludes conditions, such as allergic asthma, where airway and peripheral eosinophilias are present without parenchymal infiltration and radiographic changes. The cause can be quite diverse, the most common being parasitic invasions, drug allergies, smoking and Churg Straus syndrome. The response to corticosteroid therapy unveils distinct trajectories in the evolution of eosinophilic pneumonia, exemplified by the contrasting outcomes in these two cases.

**Conclusion.** Eosinophilic pneumonia should be suspected in any case with peripheral pulmonary consolidation and can occur on a background of asthma. The pulmonary lesions combined with peripheral eosinophilia and more important eosinophilia in the BAL can lead to a clear cut diagnosis of EP. Corticosteroids are the mainstay of the treatment and usually induces dramatic improvement.

**18. WHEAT-DEPENDENT EXERCISE-INDUCED ANAPHYLAXIS****Author:** Cebotari Iuliana**Scientific advisor:** Toma Cristina, PhD, MD, Associate Professor, Pneumology and Allergology Discipline, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a rare food allergy that can lead to severe anaphylactic reactions. The reactions usually occur 1–4 hours after consuming wheat, followed by physical activity. The omega-5 gliadin protein is responsible for WDEIA.

**Case statement.** The patient is a 25-year-old man who has experienced recurrent wheals localized on the chest, abdomen, back, limbs, along with auricular, head, and neck pruritus for the last five years, after the consumption of specific food (pizza, burgers), observed especially if after-meal physical activity was performed. If the ingredients are separately consumed, the clinical manifestations do not present themselves. When there is no after-meal physical activity involved, the wheals are present, but in a smaller number. The patient administers non-sedating H1-antihistamines (cetirizine) at the first manifestations of urticaria. In cases of more severe episodes, the patient seeks emergency care, where intravenous fluids are administered (the patient cannot specify the names of the medications). In addition, the patient has been suffering from clear rhinorrhea, and paroxysms of sneezing in the early spring-summer season. The patient underwent laboratory tests, including the ALEX (ELISA-based in-vitro multiplex allergy) test, which revealed a positive analysis for Tri a 19 omega-5-gliadin (wheat major allergen). Other positive allergens: Cyn d 1 (scutch grass), Lol p 1 (ryegrass), Phl p 1 (timothy grass). Other laboratory tests included high total IgE levels, a normal complete blood count, normal thyroid hormones, and anti-thyroid antibodies, and low DAO (diamine oxidase) levels. The patient was diagnosed with wheat-dependent exercise-induced anaphylaxis (WDEIA) and allergic rhinitis. The recommendations include maintaining a wheat-free diet indefinitely, carrying an epinephrine auto-injector, having corticosteroid and non-sedating H1-antihistamine tablets on hand, and implementing measures for the control of seasonal rhinitis manifestations, such as intranasal corticosteroids.

**Discussions.** WDEIA is a rare form of anaphylaxis, and its manifestations can range from chronic urticaria to more severe reactions, including anaphylaxis. Treatment for wheat-dependent exercise-induced anaphylaxis involves a wheat-free diet and using adrenaline in cases of severe allergic reactions.

**Conclusion.** Testing for specific IgE (sIgE) to omega-5-gliadin should be considered in patients with exercise-induced anaphylaxis. WDEIA should be included in the differential diagnosis when evaluating patients with symptoms resembling exercise-induced anaphylaxis.

**Keywords.** Wheat allergy; omega-5-gliadin; exercise-induced anaphylaxis.

A large, light blue abstract graphic that resembles a stylized bird in flight or a wave, positioned vertically in the center of the page. It has a long, curved body and several pointed, feather-like or tail-like shapes extending from it.

# ***RHEUMATOLOGY SECTION***

## 1. CLINICAL AND SEROLOGICAL EXPRESSIONS OF SLE AMONG PATIENTS FROM REPUBLIC OF MOLDOVA AND INDIA



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**Introduction.** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that may affect all systems and presents with a broad spectrum of immune abnormalities. The skin is the second organ in terms of frequency of damage and may precede classical systemic manifestations. The correlation between systemic manifestations and immunological profile is known, but the interaction between antibodies and skin disorders is a discussed and dependent on genetic and racial attribution.

**Aim of study.** The present study aims to evaluate skin lesions and their correlation with systemic manifestations and serological profile in SLE in patients from the Republic of Moldova and India.

**Methods and materials.** A total of 40 patients diagnosed with SLE were recruited, who meet the criteria of the International Clinics for Collaboration with Systemic Lupus (SLICC) (2012), which are registered in the Department of Rheumatology of the Republican Clinical Hospital "Timofei Mosneaga". Demographic details, assessment of skin lesions and systemic examination and serological profile tests were noted. The epidemiological study of patients in India was used as a reference (Systemic Lupus Erythematosus in India: A Clinico-Serological Correlation, Rachita Mathur, Kirti Deo, Aishwarya Raheja)

**Results.** Common specific lesions were malar rash (90% in Republic of Moldova and 77.5% in India,  $p < 0.05$ ), photosensitivity (77.5% vs 70%,  $p < 0.05$ ) and generalized maculopapular rash (22.5% vs 20%,  $p > 0.05$ ). Nonspecific lesions were alopecia without scars (40% vs 60%,  $p < 0.05$ ), oral ulcers (20% vs 45%,  $p < 0.05$ ) and vasculitis (40% vs 12.5%,  $p < 0.01$ ). Arthritis (72.5% vs 77.5%,  $p > 0.05$ ) and nephritis (30% vs 30%,  $p > 0.05$ ) were common systemic findings. According to the results of serological analyzes, all patients had antinuclear antibodies (ANA) and anti-dsDNA), anti-Smith (52.5% vs 70%,  $p < 0.01$ ) and anti-RO/SSA (60% vs 47.5%) antibodies in serum.

**Conclusion.** Following the study, we found that in patients with SLE in the Republic of Moldova, skin rashes are determined more frequently, compared to patients from India, but without difference in generalized maculopapular rashes. Such changes as alopecia and oral ulcers were found significantly less frequently compared to patients from India, with the exception of vasculitis. No differences were determined in arthritis and nephritis, with an equal weight in the presence of specific antibodies (ANA and anti-dsDNA), but more frequently in anti-RO/SSA in serum.



## 2. COMORBIDITIES IN GOUT

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**Introduction.** Gout is a member of the microcrystalline arthritis group characterized by musculoskeletal involvement and is also associated with a high incidence of comorbidities. Serum urate concentrations in patients with gout vary with age, risk factors and gender. Gout increases the incidence of obesity, chronic kidney disease, hypertension, type 2 diabetes, dyslipidemia, heart disease and peripheral arterial disease. Comorbidities should be considered in gout, as they may contribute to worsening the prognosis of patients with gout and complicate its treatment. Comorbidities also interfere with the use of urate-lowering drugs to treat gout.

**Aim of study.** Assessment of comorbidities and the course of the diseases of gout.

**Methods and materials.** A retrospective study was performed, analyzing 100 medical records of patients diagnosed with gout (according to EULAR and American College of Rheumatology (ACR) 2015 criteria), hospitalized in Nephrology, Rheumatology and Arthrology Department of the Timofei Mosneaga Republican Clinical Hospital during 2017-2023. Patients were investigated clinically, laboratory and instrumentally.

**Results.** There were included 100 patients in the study: males 50 (50%), females 50 (50%). The age of patients between 41 and 78 years, average age  $59,5 \pm 1$  years. According to disease progression: acute gout was detected in 16 patients (16%), chronic gout in 84 patients (84%). According to comorbid pathologies, the following pathologies were determined in the studied group, among which hypertension in 74 patients (74%), ischemic heart disease in 61 patients (61%), chronic tubulointerstitial nephropathy in 53 patients (53%) and/or nephrolithiasis in 33 patients (33%), dyslipidemias in 49 patients (49%); obesity in 46 patients (46%), hepatic steatosis (with USG signs) in 38 patients (38%), type 2 diabetes in 18 patients (18%). After the distribution of the nosological units in the category of comorbid pathologies in the examined patients according to sex, the statistically significant difference is observed after two pathologies: obesity which is present in women 29 (58%) more frequently than in men 17 (34%), but the presence of nephrolithiasis more often observed in men – 44%, and in women – 22%. Outpatient treatment administered by patients: allopurinol 47 patients (47%), anti-inflammatory- nonsteroidal 91 patients (91%), colchicine 14 patients (14%), glucocorticosteroid 39 patients (39%), febuxostat 36 patients (36%), acetylsalicylic acid 32 patients (32%), diuretics 15 patients (15%).

**Conclusion.** In gout, comorbidities play an important role in the development of complications associated with premature death of the patient. For the timely treatment of these patients, a comprehensive examination and proper selection of treatment, taking into account risk factors, is necessary.



### 3. DIAGNOSIS AND TREATMENT: INSIGHTS ON A CLINICAL CASE OF VISCERAL SARCOIDOSIS



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**Introduction.** Sarcoidosis is a systemic disease involving formation of granulomas that can affect the lungs, skin or lymph nodes, and less commonly the eyes, heart, liver and brain, though any organ can be affected. The illness's etiology is unclear and 50% of the patients are asymptomatic. Its annual incidence is 1-15 per 100.000 depending on the region. Although sarcoidosis in most cases has a benign evolution, the important part of the disease is represented by the fact that sometimes it can present negative evolution with the appearance of multiple organ failure and death.

**Case statement.** A 55 years old North African female patient showed up for investigation at the end of September 2023 for progressive deterioration of general state. She was complaining of asthenia, weight loss (>10 kg in 3 months), dyspnea during effort, intense headache and visual disturbance with sensitivity to light and painful eye. Further clinical examinations reveal painful red eye and mucocutaneous pallor. The initial examination tried to exclude as the cause of the current state both the antecedents of hypertension and iatrogenic hypothyroidism after thyroidectomy, the patient being known to have these disorders. The results show well-controlled blood pressure and effective hormone replacement with levothyroxine 125 mcg. intense and purple thickening of the abdominal scar from her C-section. The biological assessment found an important inflammatory syndrome with increased erythrocyte sedimentation rate at 100 mm/h, hyper alpha1-, beta2- and gamma-globulinemia. In addition to hypercalcemia at 144mg/l, she presented normal calciuria 105 mg/l, low parathyroid hormone < 0.4 pg/ml, high alkaline phosphatase 584 IU/L and high gamma-GT level 106 IU/L, normal blood count. Disturbed renal function with minimal renal insufficiency, urea 0.54 g/l, Creatinine 11.49 mg/l (normal range : 4.7-11 mg/l) (GFR/MDRD 49 ml/min). There was no intradermal reaction to tuberculin. The thoraco-abdominal-pelvic CT scan shows a bilateral diffuse interstitial lung disease with pulmonary fibrosis, predominantly in the hilar and peribronchial areas associated with multiple hilar lymphadenopathies and heterogeneous micro- and macrocalcifications in the mediastinal tissue. Also, an important splenomegaly was discovered with pseudo-nodular rearrangement of the liver and abdominopelvic lymphadenopathies and calcified mesenteric nodules (the adenopathies were of eggshell aspect the most voluminous was : lower right paratracheal 17x26 mm, subcranial 21x26 mm, subaortic (aortopulmonary window) 19x21 mm and 16x27 mm). The cardiac ultrasound revealed cardiomegaly, left ventricular hypertrophy but preserved ejection fraction and no filling anomalies. The ECG showed left bundle branch block. The ophthalmologic results specify ocular hypertonia in the right eye at 34 mmHg, right pseudophakia and left eye cataract. Based on the clinical and paraclinical results the diagnosis of sarcoidosis was made with the following visceral involvement: Pulmonary lesions (stage III), cutaneous lesions (thickening of the abdominal scar). Splenomegaly. Ocular hypertonia. Pseudonodular liver. Multiple cervical, thoracic, abdominal and pelvic lymphadenopathies. Left ventricular hypertrophy and conduction disorders. The patient was put on corticosteroid therapy at a rate of 60 mg of prednisolone (treatment started on 11/11/2023). After 4 weeks of treatment the patient presented favorable clinical and biological evolution: improvement of the general condition, normalized ESR, improvement of the renal function, normal serum calcium level of 88 mg/l. A radiological evaluation will be done after 6 months of treatment.

**Discussions.** The diagnosis of sarcoidosis in this case was made following different criteria as the inflammatory syndrome, the hypercalcemia and the tuberculin/anergy skin test in addition to the CT scan (pulmonary involvement of stage 3) that confirmed the diagnosis and excluded the other probabilities of pathologies as tuberculosis (due to non-caseating granulomatous inflammation) or lymphoma (due to the favorable response to corticoids).

**Conclusion.** Sarcoidosis still poses diagnostic and therapeutic challenges because the disease often produces few signs and symptoms in its early stages. When symptoms do occur, they may mimic those of other disorders. Further research may be crucial to understand the mechanisms of this enigmatic disease, and for discovering an affordable, minimal invasive biomarker for early diagnosis.



#### 4. EPIDEMIOLOGY AND CLINIC-PARACLINIC FEATURES OF OSTEOPOROSIS IN MEN

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**Introduction.** Osteoporosis is the disease of bone tissue and it is not limited to postmenopausal women. In recent decades, increasing attention has been paid to osteoporosis in older men. It has been established that men suffer from osteoporotic fractures about 10 years later than women, but life expectancy increases faster in men than in women. Although the prevalence of osteoporosis is greater in women, mortality after fracture is higher among men.

**Aim of study.** Osteoporosis, traditionally perceived as a predominantly female affliction, has long overshadowed its impact on the male population. While it is well-established that women are susceptible to bone fragility and fractures as they age, the prevalence and consequences of osteoporosis in men have been underappreciated and, consequently, understudied.

**Methods and materials.** A systematic review on the published literature was conducted which focused on osteoporosis in men. It is recommended to evaluate calcium, phosphorus, alkaline phosphatase, and serum protein levels, as well as liver, kidney, thyroid, adrenal, and pituitary function tests. As well as determining the level of total testosterone, estrone, estradiol and sex hormone-binding globulin, PTH, 25-hydroxyvitamin D and osteocalcin. It is an important calculation of the FRAX index. Performing DXA to determine the BMD and degree of osteoporosis. Bone biopsy to rule out occult forms of osteomalacia, acquired osteogenesis imperfecta, mastocytosis and malignancy.

**Results.** After 50-year-old, one in three osteoporotic fractures occurs in men, and the morbidity and mortality associated with fractures is even greater than in women. In 50% of men with osteoporosis, an underlying cause can be identified and it is in the secondary osteoporosis. In the absence of an identifiable etiology, male osteoporosis is referred to as "idiopathic osteoporosis" in men aged 30 to 70 years and "age-related osteoporosis" in older men. As in women, the presence of estrogen, not testosterone, is the most important sex steroid regulating male skeletal status. Diagnostic and treatment recommendations are still largely based on bone mineral density (BMD), with osteoporosis defined as a T-score of 2.5 standard deviations below the values for young people. To this day guidelines for the diagnostic evaluation of male osteoporosis are not as well validated as in postmenopausal osteoporosis.

**Conclusion.** Osteoporosis in men is an increasingly important health problem: after the age of 50, one in three osteoporotic fractures occurs in men, therefore the morbidity and mortality associated with fractures are higher than in women. Men have larger bones than women, which makes bone density appear higher on DXA, and the standard deviation of DXA is different from that of women. Age-related osteoporosis is due to decreased levels of sex steroids, changes in growth hormone-like growth factor axis 1. In men with low BMD, 50% have an underlying cause, most often glucocorticoid excess, hypogonadism, or alcohol abuse. But if DXA and FRAX are both used, a large proportion of older men will be candidates for osteoporosis treatment.

## 5. EXPRESSION OF THE INFLAMMATORY SYNDROME MANIFESTATIONS IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS



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**Introduction.** Rheumatoid arthritis (RA), a systemic autoimmune disease that is predominantly affecting synovial joints through a progressive destructive process, is classified into 2 subgroups - seronegative (SNRA) and seropositive (SPRA) - which is important for predicting disease progression and response to treatment.

**Aim of study.** To study the status of RA inflammatory activity according to seropositivity (rheumatoid factor and anti-CCP antibodies).

**Methods and materials.** 38 patients with RA were included in the study, who were diagnosed according to American College of Rheumatology ACR/EULAR 2010 criteria: group 1 (24 patients) - seropositive (RF+ and/or ACCP+) and group 2 (14 patients) – seronegative (RF- and ACCP-). Clinical data, the degree of expression of the inflammatory syndrome by DAS28 score and Ritchie Articular index were studied.

**Results.** Seronegative patients were older than seropositive patients ( $55.8 \pm 12.1$  years vs  $50.7 \pm 10.9$  years,  $p=0.04$ ), which is possibly determined by the onset of the disease at an older age, while the gender distribution did not show any statistical difference ( $p=0.091$ ). The number of swollen joints showed a statistically significant higher value in the SPRA group compared to the SNRA group (median 17 vs 8,  $p<0.001$ ), a finding confirmed by the DAS28-CRP score ( $3.9 \pm 0.6$  vs  $3.4 \pm 0.4$ ,  $p=0.03$ ). However, it is required to mention comparable statistical values for the number of painful joints (median 19 vs 20,  $p>0.091$ ) and physician-determined VAS ( $49.1 \pm 2.33$  vs  $48.9 \pm 3.12$ ,  $p=0.006$ ), which emphasizes the marked inflammatory entity of rheumatoid arthritis regardless of serum profile. But, following on from the objective, we were interested in extending the study of nonspecific markers of inflammation between groups, so that we obtained some unexpected results. Therefore, comparing mean values of CRP and VSH we determined that they were significantly higher among patients in the SNRA group compared to SPRA (CRP(SNRA)  $52.5 \pm 6.9$  vs CRP(SPRA)  $41.25 \pm 7.2$ ,  $p<0.05$ ; ESR(SNRA)  $56 \pm 12.8$  vs. ESR(SPRA)  $43 \pm 15.0$ ,  $p<0.05$ ).

**Conclusion.** The seronegative variant of rheumatoid arthritis is characterized by a marked magnitude of the systemic inflammatory process expressed by elevated CRP and ESR, but with statistically significant lower values of DAS28, which is due to the lower contribution of the number of swollen joints value to the overall score, compared to seropositive rheumatoid arthritis.



## 6. KIDNEY DAMAGE IN GOUT PATIENTS

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**Introduction.** In patients who have suffered from gouty arthritis for many years, renal cone disease is very common. After arthritis, the most common clinical manifestation of hyperuricemia is renal interest.

**Aim of study.** Study the clinical and paraclinical aspects of renal lesions in gout for early diagnosis of these lesions, followed by initiation of early treatment to prevent the development of comorbid diseases.

**Methods and materials.** It has been used the information resources of the Medical Scientific Library of the *Nicolae Testemitanu* State University of Medicine and Pharmacy, as well as the publications from the specialized journals in PubMed, Medline, MedScape, Google Scholar, Wikipedia.

**Results.** The only marker currently recognized as highly specific and sensitive for ischemic injury in the proximal renal tubules is KIM-1. This is a transmembrane protein with immunoglobulin and mucin domains, first described in 1998. In intact renal tissue it is found in small amounts, but after ischemia its level in regenerating proximal tubules is significantly increased. As experimental studies have shown, increased KIM-1 levels are associated with ischemic effect on the kidney and are not always accompanied by an increase in blood urea nitrogen and creatinine, indicating a high diagnostic value of KIM-1 as an early diagnostic marker of proximal tubule damage and has therefore been studied in recent years as a marker of renal damage in CKD of various etiologies. Studies in patients with non-diabetic proteinuric nephropathy have been performed and have shown that KIM-1 is significantly increased in patients with proteinuria compared to controls and has a direct correlation with urine protein levels - it decreases in response to ACE inhibitor treatment, but even when the target urine protein level (1 g/l) is reached, KIM-1 does not reach normal values, confirming continued deterioration of the renal tubular apparatus and, if increased against a background of decreased left ventricular function, is considered a predictor of all-cause mortality and repeated hospitalizations for heart failure. Based on the findings of Jungbauer CG et al, it has been suggested that tubular lesions in CKD may be present in patients with normal renal function. Despite the high sensitivity, specificity and prognostic value of KIM-1 in the diagnosis of tubular renal lesions in CKD of various etiologies, this protein has not been studied in patients with gout.

**Conclusion.** The assessment of early kidney damage in patients with gout will improve the prognosis of kidney damage, at the same time we will contribute to decrease sudden complications and disability of patients, so they will remain fit for work.



## 7. NEUROLOGICAL IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS



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**Scientific advisor:** Groppa Liliana, PhD, Professor, Discipline of Rheumatology and Nephrology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** SLE is a multifactorial autoimmune disease of unknown etiology, which is characterized by a diverse multisystemic effect that appears as the result of certain imperfect immunoregulatory processes.

**Aim of study.** Identifying the main neurological manifestations in patients with SLE.

**Methods and materials.** In order to identify suggestive articles, databases such as PubMed, Google Scholar, HINARY, Medscape and Scopus were studied and analyzed according to the keywords „SLE”, „neurological manifestations”.

**Results.** Neurological impairment is widespread among patients with SLE, both central nervous system (CNS) and peripheral nervous system (PNS) being affected. Among the main manifestations of SLE patients, the following are established: persistent headache, psychoses, paresthesia, anxiety disorders, depression, various forms of neuropathies such as sensorimotor neuropathy, cranial neuropathy, polyneuropathies. The most eloquent neurological manifestation in patients with SLE proved to be cognitive impairment. The mechanism that reflects the essence of cognitive deficiency is not entirely uncovered, but one cause would be the effect mediated by the autoantibodies. Cognitive changes in patients with SLE can be temporary and their substrate is poorly defined. Currently, both corticosteroids and NMDA-receptors have not been proved to be effective in improving cognitive function in SLE.

**Conclusions.** The identification and evaluation of neurological manifestations in SLE patients requires increased and continuous clinical monitoring. It is essential to pay attention to the triggering factors of the disease, in order to manage forward treatment strategies.





## 8. PARTICULAR FEATURES OF RHEUMATOID ARTHRITIS ONSET IN THE ELDERLY

**Author:** Curilov Maria

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**Introduction.** Rheumatoid arthritis (RA) is a chronic inflammatory disease that can occur at any age, but it can manifest differently in different decades of age. Obvious and significant manifestations of RA occur in those aged  $\geq 65$  years. The literature confirms the presence of more severe onset in patients in the eRA (elderly-RA) group compared to patients in the aRA (adult-RA) group.

**Aim of study.** To assess the clinical-paraclinical characteristics and joint functional status in elderly patients with RA.

**Methods and materials.** This study included 52 patients diagnosed with RA according to the 2010 ACR/EULAR criteria from 2019-2023. According to the age of disease onset, patients were divided into 2 groups- aRA (<55 years) and eRA (>55 years), also clinical-paraclinical data and radiological expression (by Sharp score) were compared.

**Results.** Female patients predominated in both groups- aRA (67.2%) and eRA (70.1%), with no statistically significant difference ( $p=0.23$ ). aRA group was specified a longer disease duration but shorter duration of pre-diagnostic symptoms compared to eRA ( $39 \pm 1.0$  months vs  $34 \pm 3.0$ ,  $p < 0.01$  and  $18 \pm 1.0$  months vs  $25 \pm 2.0$  months,  $p=0.002$ , correspondingly). Extra-articular manifestations were more common in patients with eRA, possibly due to correlation with longer duration of pre-diagnostic sympathetic symptoms ( $r=0.89$ ,  $p < 0.01$ ), especially the presence of rheumatoid nodules ( $45.1\%$  vs  $20.2\%$ ,  $p=0.011$ ) and weight loss (by  $7.0 \pm 0.5$  kg in 6 months), ( $83.1\%$  vs  $33.7\%$ ,  $p < 0.001$ ). Analyzing the radiological results (according to Sharp score), more patients showed erosions were characteristic in the eRA group ( $48.7\%$ ) than in the aRA group ( $33.3\%$ ,  $p < 0.01$ ). In the eRA group predominantly erosions were determined in the lower limbs compared to the eRA group where they were in the upper limbs. Disease activity according to the DAS28 score (PCR) was similar between the two groups of patients and did not show any statistically significant differences ( $p > 0.05$ ).

**Conclusion.** In the elderly, a longer duration of symptoms was determined before the diagnosis was established, which therefore also determines the presence of extra-articular manifestations. Compared to adults, more patients with bone erosions were found in the elderly and predominantly in the lower limbs.

## 9. PREVALENCE OF ANXIOUS DEPRESSIVE SYNDROME IN HOSPITALIZED IN INFLAMMATORY ARTHRITIS



**Author:** Manoharan Ajitha Ancy

**Scientific advisor:** Cazac Victor Ion

**Introduction.** Inflammatory arthritis is a chronic disorder that affects the joints. Inflammatory arthritis includes Rheumatoid arthritis, reactive arthritis, JIA, ankylosing spondylitis, etc. there have been studies that show that inflammation plays a role in the pathogenesis of psychiatric diseases.

**Aim of study.** The conduct a literature review of the prevalence of anxious-depressive syndrome in hospitalized patients with inflammatory arthritis

**Methods and materials.** I conducted a literature search in CDC Symptoms of Anxiety and Depression Among Adults with Arthritis — United States, 2015–2017, American college of rheumatology anxiety and depression among US adults with arthritis: prevalence and correlates, PubMed, journal of clinical rheumatology and immunology. This review includes full text articles published in English that reported on patients with anxious-depressive syndrome with inflammatory arthritis

**Results.** Anxiety and depression are fairly common in inflammatory arthritis; close to one-third of arthritis patients are estimated to have anxious-depressive syndromes. The studies are carried out utilizing screening measures such as the Hospital Anxiety and Depression Screening (HADS) and the Depression Anxiety Stress Scale (DASS), as well as the Multidimensional Health Assessment Questionnaire (MDHAQ). Depression and anxiety are more frequent in females and are generally multifactorial. According to the papers, proinflammatory variables such as IL-6 and TNF-  $\alpha$  are higher in inflammatory arthritis, supporting the inflammatory theory. The age-standardized prevalences of anxiety and depressive symptoms in individuals with arthritis were 22.5% and 12.1%, respectively, compared to 10.7% and 4.7% in persons without arthritis. Anxiety outnumbered depression (31% against 18%).

**Conclusion.** The high prevalence of symptoms of depression and anxiety is observed in arthritic patients compared to the general population. It is observed that inflammation can induce anxiety and depression. Screening of anxious-depressive syndromes are necessary and essential for the better-quality living of those with arthritis.



## 10. THE BONE IN THE ELDERLY

**Author:** Trofimov Cristian; **Co-author:** Mazur-Nicorici Lucia, Stratulat Silvia

**Scientific advisor:** Mazur Minodora, MD, PhD, Professor, Discipline of Internal Medicine-Semiology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova; Silvia Stratulat, MD, PhD, Associate Professor, Head of Department of Biochemistry and Clinical Biochemistry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova; Mazur-Nicorici Lucia, MD, PhD, Professor, Discipline of Cardiology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

**Introduction.** Bone remodeling is a complex phenomenon regulated by bone cells and enzymes implicated in bone metabolism.

**Aim of study.** The aim of the study was to describe the processes involved in bone remodeling during aging.

**Methods and materials.** We conducted an electronic literature search from 01.12.2020 to 01.12.2023 in PUBMED, Clarivate, Google Scholar, Science Citation Index and fulfilled the predefined requirements. Publications were included if they addressed in the title the keywords: remodeling, osteoporosis, bone turnover and telopeptides. Study quality was assessed using the study validation score developed by the investigators.

**Results.** A total of 99 publications were analyzed, of which 20 were studies, 25- articles and 26 abstracts, at the same time 28 were eliminated. Out of 71 only 56 met all the criteria for inclusion in the study. Evidence suggests that some proteins are critical to the functioning of bone cells, including osteoblasts, osteocytes, and osteoclasts in the onset of osteoporosis - a loss of bone density among aging adults, but it's not part of the natural aging process. It is possible to prevent, delay or reduce bone loss. RANKL has been shown to regulate osteoclast activation both in normal and pathologic bone remodeling, characterized by increased bone turnover. Metalloproteinases and their inhibitors also regulate the resorption. Biochemical markers specific for bone formation include bone-specific phosphatase, osteocalcin, and type I procollagen N-terminal propeptide. Specific markers of bone resorption include pyridinoline cross links N-telopeptides, and C-telopeptides in urine and in serum.

**Conclusion.** It has been established that the aging process significantly decreases collagen content and affects matrix remodeling enzymes which correlates with reduced bone fracture resistance. Telopeptides should be evaluated for early diagnosis of osteoporosis.

## 11. THE CLINICAL VALUE OF ENTHESITIS IN THE EARLY DIAGNOSIS OF PSORIATIC ARTHRITIS



**Author:** Melnic Nicolae

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**Introduction.** Joint diseases are one of the most common chronic diseases of society, and one of the most common is psoriatic arthritis (PsA), which is differentiated by a high incidence of enthesitis.

**Aim of study.** Appreciation of ligamentous and muscular damage through enthesopathy in patients with psoriatic arthritis.

**Methods and materials.** The study included 50 patients diagnosed with PsA (according to CASPAR criteria): group 1 – duration of disease <2 years (n = 24), group 2 – >2 years (n = 26); age 18-65 (51.0±3.4) years. For the evaluation of enthesitis MASES score (Maastricht Ankylosing Spondylitis Enthesitis Score) was applied.

**Results.** Following the study, it was established that the frequency of the anatomical and clinical features of the joint syndrome was different in patients with early PsA and those with late PsA, in early PsA, unlike the late one, the oligoarticular variant was attested (41.7% and 15.3%, respectively), and less often – the spondyloarticular variant (8.3% and 19.2%), the polyarticular variant (33.3% and 38.4%), and the distal one (16.7% and 15.3%), was found with the same frequency in both cases, while the osteolytic variant was observed only in the late stage of PsA (1.15%). Enthesities, by the MASES method, were determined with approximately the same frequency both in the early PsA group and in the group of patients with late PsA, in 10 (41.6%) and 11 (45.8%) patients, respectively (p>0.05). The mean values of MASES were higher in the late PsA group than in the early PsA 4.03±0.8 and 2.6±0.5 (p = 0.0032). In patients with early PsA, MASES was associated with the number of painful joints (r = 0.31 p = 0.03), the number of swollen joints (r = 0.29 p = 0.04), the BASDAI score (r = 0.34 p = 0.02) and BASFI (r = 0.39 p = 0.02), as well as the index score DAS28 (r = 0.31 p = 0.03). In patients with a longer evolution of the disease, the correlation of the MASES index only with the BASFI index was verified (r = 0.35 p = 0.02). The objectification of enthesitis was performed by musculoskeletal USG, the average value of the GUESS score in the late PsA group was 3.6 ± 0.3 compared to early 2.43 ± 0.2 (p = 0.02).

**Conclusion.** The early stage of PsA is characterized by a marked heterogeneity of its manifestations with the particularities of the joint syndrome and damage to the tendons and ligaments – oligoarticular and polyarticular variants of the joint syndrome are more frequently attested. Enthesitis is a characteristic manifestation of early PsA, it was found in 40% of patients, and the ultrasonographic examination of the calcaneal region confirmed it more frequently than the clinical data (69% and 31%).





## 12. TREAT- TO- TARGET STRATEGY IN THE TREATMENT OF RHEUMATOID ARTHRITIS

**Author:** Sufichae Simona

**Scientific advisor:** Deseatnicova Elena, MD, PhD, Associate Professor, Discipline of Rheumatology and Nephrology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Rheumatoid arthritis (RA) is a chronic autoimmune condition characterized by progressive joint inflammation and structural damage that frequently results in severe disability.

**Aim of study.** The "Treat-to-Target" (T2T) strategy is a paradigm in the management of RA, with an emphasis on how well it works to improve clinical outcomes and how to apply it practically.

**Methods and materials.** The data were collected from literature searches of Pubmed, Embase and Cochrane Library for studies published up to October 2023. The search strategy was composed of both controlled vocabulary such as Medical Subject Headings and keywords. The total number of 51 literature sources was analyzed.

**Results.** According to our literature review, the target strategy is used to acquire data on the results of RA patients treated with a T2T approach, including disease activity measures, radiographic progression, functional status, and patient-reported outcomes. This strategy has a positive influence on both the prevention of long-term joint damage and the achievement of low disease activity or sustained remission. The main objective of T2T strategy is achievement of sustained remission by DAS28 and radiological data. Implementation of new therapeutic agents, such as biologic and targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs) help reach T2T objectives. Some authors report difficulties of incorporating T2T into standard clinical practice. According to the results of our review, the comprehension of T2T as a flexible and patient-focused method of managing RA can substantially contribute to better prognosis and outcome of the patients with RA. Healthcare providers are strongly advised to optimize their treatment strategies, ultimately improving the long-term outcomes and quality of life for individuals with rheumatoid arthritis. The data from our review show this by clarifying the clinical benefits and addressing implementation challenges.

**Conclusion.** Treat-to-Target (T2T) strategy is changing the landscape of management of rheumatoid arthritis (RA). The summary of available data highlights the effectiveness of T2T in enhancing clinical outcomes, with a focus on maintaining remission or low disease activity, halting radiographic progression, and improving overall patient well-being. The examination of T2T's practical application exposed the complexities and difficulties involved in incorporating this dynamic approach into standard clinical practice. Although the advantages are obvious, obstacles like patient preferences, resource limitations, and the practicality of frequent monitoring call for thoughtful analysis and well-thought-out solutions in order to ensure successful adoption.

**Keywords.** "Rheumatoid arthritis" "Treat-to-target strategy", "disease activity", "outcome"



## ***IX. INFECTIOUS DISEASE SECTION***



***„Infecțiologia modernă atestă o evoluție în ascensiune de noi provocări. Bolile infecțioase nu au hotare, sunt multidisciplinare, au evoluție, uneori, imprevizibilă, atât clinic, cât și epidemiologic. Îndemn tinerii mediciști în aprofundarea cunoștințelor, cercetărilor științifice și exersărilor practice în patologia infecțioasă. Lucru în echipă! Succese!***

***"Modern infectious diseases attest to a rising evolution of new challenges. Infectious diseases know no borders, they are multidisciplinary, and their evolution is sometimes unpredictable, both clinically and epidemiologically. I encourage young medical professionals to deepen their knowledge, scientific research, and practical exercises in infectious pathology. Teamwork is key! Success!"***

***Gheorghe Plăcintă,***

*MD, PhD, Associate Professor,*

*Dean of Faculty Medicine No. 1,*

*Head of Department of Infectious Diseases,*

*Nicolae Testemitanu State University of Medicine and Pharmacy,*

*Chisinau, Republic of Moldova.*



## 1. ADENOVIRAL INFECTION IN CHILDREN: CASE REPORT

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**Scientific advisor:** Alexeev Tatiana, MD, PhD, Associate Professor, Department of Infectious Diseases, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

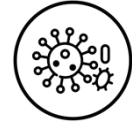
**Introduction.** Adenoviruses cause acute respiratory infections, clinically characterized by symptoms such as fever, intoxication, and a range of extra respiratory signs, including conjunctivitis, lymphadenopathy, diarrhea, and rarely hepatitis. During October-November 2021, multiple countries reported cases of severe acute hepatitis of unknown etiology (SAHUA) not caused by hepatitis A–E viruses.

**Case statement.** Patient N., 10-year-old, with a referral diagnosis of Acute Respiratory Infection (ARI) with Abdominal Syndrome, acute hepatitis of unknown etiology. Symptoms included fever (39.2°C), nasal obstruction, seromucous rhinorrhea, nasal snoring, headache, and repeated vomiting. Objective findings: Pale skin, shadows under the eyes. Anterior cervical lymph nodes (1.0 x 1.5 cm), mobile, non-painful. Pharyngeal isthmus hyperemic, palatine tonsils hypertrophied (grade II), without deposits. Liver +1.0 cm. No contact with individuals with liver disease or injury, and toxic factors have been excluded. The referral diagnosis was contradicted by laboratory results: Leukocytosis, lymphopenia, neutrophilia. Blood biochemistry: Hypertransaminasemia (ALT=386.6 U/L; AST=354.7 U/L), CRP=18.14 mmol/L. Viral hepatitis markers: HBsAg - negative, Anti-HBc total - negative, Anti-HBc IgM - negative, Anti-HCV total - negative, HEV IgM, IgG - negative. Other markers: EBV VCA IgM - negative, EBV EA IgG - negative. CMV IgM, IgG - negative. Autoimmune antibodies: ANCA MPO, ANCA PR3, Anti AMA-2, Anti ANA, Anti LKM-1 - within normal limits - autoimmune hepatitis was excluded. PCR analysis (Nasopharyngeal swab) for Adenovirus - positive. Thus, the final diagnosis is Adenoviral infection with rhinopharyngitis. Adenoviral hepatitis. The patient received symptomatic treatment, including fever control, intravenous rehydration, and hepatoprotective therapy, resulting in a favorable outcome.

**Discussions.** Recent literature states that 65% of adenoviral hepatitis cases occur in children. As of June 17, 2022, the WHO, CDC, and ECDC reported 991 cases in 35 countries. Among these, 50 children required liver transplants and 28 died. The WHO advises laboratory tests to rule out hepatitis viruses A-E in these probable adenoviral hepatitis cases.

**Conclusion.** Adenoviruses can lead to different infections, sometimes prompting unnecessary antibiotic use. In this case, the patient had a favorable recovery and was discharged after 7 days in satisfactory condition. Globally, testing for Adenovirus is recommended in reported cases of SAHUA. Identifying Adenovirus as a cause can significantly enhance care and, in some cases, save lives.

## 2. CLINICAL FEATURES OF EPSTEIN-BARR VIRUS INFECTION IN CHILDREN AGED 0-3 YEARS



**Author:** Vlad Vasile

**Scientific advisor:** Birca Ludmila, Associate Professor, Department of Infectious Diseases, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Epstein-Barr virus (EBV), or human herpesvirus 4, is a gammaherpesvirus that infects more than 95% of the world's population, most commonly manifesting itself through acute infectious mononucleosis, frequently found in adolescents and young adults. EBV manifests itself through a dual-life cycle, either lifelong latency in circulating memory B lymphocytes or lytic replication in epithelial cells. Classic triad include sore throat, fever, and lymphadenopathy, but the symptoms may vary in children depending on their age.

**Aim of study.** This review aims to describe the clinical features of Epstein-Barr virus in infants and children under the age of 3.

**Methods and materials.** In order to create this review, we used articles that were published between 2020-2023 from sources like ScholarGoogle, NihGov, NCBI, and PubMed. We also used keywords like: "Epstein-Barr virus", "EBV infection in infants", "clinical characteristics", "children", "infants".

**Results.** By the age of 5, 50 % of the population is already infected with EBV, its prevalence rising in regions with a shakier socioeconomic status. Children under 3 years old infected with EBV might either be asymptomatic or display atypical symptoms that are no different than mild respiratory viral infections. Unlike in older children with classic signs of mononucleosis syndrome, EBV debuts in 50% of cases with rhinitis and cough. The symptoms might be accompanied by dyspnea, eyelid edema, facial puffiness, polyadenopathy. In some cases it might be associated with a symmetric erythematous maculopapular rash and plaques that may persist for 15-50 days (Gianotti-Crosti syndrome). Pseudomembranous tonsillitis appears early in the first 3 days after the onset, possibly resulting from viral-bacterial associations. A fever that is up to 39-40 C and lasts around 2 weeks might also be the only clinical manifestation, being a common cause of hospitalization in young children. It is also important to note that because of its B lymphotropic nature, the reduced clinical manifestations might be explained by the immaturity of the immune system, but also the presence of transplacental immunity. Serological tests are rarely positive and in much lower titers. The evolution of the disease is favorable for complete healing, but the reactivation of the infection during life is not excluded.

**Conclusion.** Primary infection with EBV in children displays different symptoms according to the age of the affected, the classic triad being mostly determined in older children with mild to severe forms, while younger children manifest atypical infections. They are in most cases asymptomatic or suffer from mild forms that might involve some typical signs, but are usually similar to a cold. The prognosis is also favorable.



### 3. MENINGOCOCCAL INFECTION: CLINICAL-EVOLUTIONARY PARTICULARITIES

**Author:** Caramalac Cristina

**Scientific advisor:** Cojuhari Lilia, Associate Professor, Department of Infectious Diseases, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Meningococcal infection is an acute infectious disease caused by meningococcus, occurring with a variety of clinical manifestations - from asymptomatic carriage and nasopharyngitis to generalized forms (purulent meningitis, meningococcal meningitis and meningococemia with damage to various organs and systems). The incidence of endemic meningococcal disease ranges from 1 to 5 per 100,000 in developed countries, and from 10 to 25 per 100,000 in developing countries, with an increase in the number of cases in winter and spring, in temperate climates.

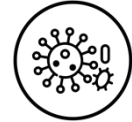
**Aim of study.** To report the clinical data of meningococcal infection from Republic of Moldova, from June 2018 through April 2022.

**Methods and materials.** The study is based on the analysis of the medical records of 21 children, of which 11 (52%) are male and 10 (48%) are female aged from 4 months to 11 years old, admitted to the Toma Ciorbă CHID during 2018- 2022. The diagnosis was confirmed by the following clinical and paraclinical methods: clinical signs, anamnestic data, bacteriological and bacterioscopic investigations.

**Results.** Of the total number of patients meningococemia occurred in 21 cases (100%), meningococcal meningitis in 19 cases (90,5%) and 18 patients (85,7%) had both. The most common manifestations were fever (100%) and hemorrhagic rash (stellate, dotted) (100%), followed by meningeal signs (66,6%) along with hyperemic oropharynx (66,6%), vomiting (61,9%), harsh breathing (23,8), hemorrhagic rash with necrosis (23,8), diarrhea (19%), headache (19%), hypertrophied tonsils (19%) , injected conjunctiva (9,5%), photophobia (9,5), enanthema (9,5), paresis-paralysis (4,7%) and in the fulminant form - coma (4,7%). Consequences of meningococemia that were found: infectious-toxic shock in 76,9 % of cases, cerebral edema in 23,8%, disseminated intravascular coagulation syndrome (DIC) in 9,5%, pulmonary edema in 4,7%, postoperative necrosis 4,7%, toxic nephropathy 4,7%. Another type of meningococcal infection, less common, meningococcal arthritis occurred in 5 cases (23,8%) of experimental / studied patients. From the study group, one case associated with DIC, acute respiratory failure, pulmonary edema, toxic nephropathy and systemic inflammatory response syndrome resulted in death.

**Conclusion.** Among the two most common forms of meningococcal infection: meningitis and meningococemia, the second one was the most prevalent in the Republic of Moldova, with corresponding complications.

#### 4. TREAT- TO- TARGET STRATEGY IN THE TREATMENT OF RHEUMATOID ARTHRITIS



**Author:** Sufichaev Simona

**Scientific advisor:** Deseatnicova Elena, MD, PhD, Associate Professor, Discipline of Rheumatology and Nephrology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Rheumatoid arthritis (RA) is a chronic autoimmune condition characterized by progressive joint inflammation and structural damage that frequently results in severe disability.

**Aim of study.** The "Treat-to-Target" (T2T) strategy is a paradigm in the management of RA, with an emphasis on how well it works to improve clinical outcomes and how to apply it practically.

**Methods and materials.** The data were collected from literature searches of Pubmed, Embase and Cochrane Library for studies published up to October 2023. The search strategy was composed of both controlled vocabulary such as Medical Subject Headings and keywords. The total number of 51 literature sources was analyzed.

**Results.** According to our literature review, the target strategy is used to acquire data on the results of RA patients treated with a T2T approach, including disease activity measures, radiographic progression, functional status, and patient-reported outcomes. This strategy has a positive influence on both the prevention of long-term joint damage and the achievement of low disease activity or sustained remission. The main objective of T2T strategy is achievement of sustained remission by DAS28 and radiological data. Implementation of new therapeutic agents, such as biologic and targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs) help reach T2T objectives. Some authors report difficulties of incorporating T2T into standard clinical practice. According to the results of our review, the comprehension of T2T as a flexible and patient-focused method of managing RA can substantially contribute to better prognosis and outcome of the patients with RA. Healthcare providers are strongly advised to optimize their treatment strategies, ultimately improving the long-term outcomes and quality of life for individuals with rheumatoid arthritis. The data from our review show this by clarifying the clinical benefits and addressing implementation challenges.

**Conclusion.** Treat-to-Target (T2T) strategy is changing the landscape of management of rheumatoid arthritis (RA). The summary of available data highlights the effectiveness of T2T in enhancing clinical outcomes, with a focus on maintaining remission or low disease activity, halting radiographic progression, and improving overall patient well-being. The examination of T2T's practical application exposed the complexities and difficulties involved in incorporating this dynamic approach into standard clinical practice. Although the advantages are obvious, obstacles like patient preferences, resource limitations, and the practicality of frequent monitoring call for thoughtful analysis and well-thought-out solutions in order to ensure successful adoption.

**Keywords.** "Rheumatoid arthritis" "Treat-to-target strategy", "disease activity", "outcome".



A large, light blue abstract graphic that resembles a stylized bird in flight or a wave. It starts with a sharp point at the top left and curves downwards and to the right, ending in a wide, sweeping tail at the bottom right.

***X. NEUROLOGY AND  
NEUROSURGERY SECTION***

## 1. ACUTE VIRAL INFECTION AS A TRIGGER FOR DSNMG: A CASE REPORT



**Author:** Stafi Vlada; **Co-author:** Stavila Iulia, Tofan Lucian

**Scientific advisor:** Manole Elena, MD, PhD, Associate Professor, Neurology Department No.2, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Categorical evidence shows that patients with Acute Respiratory Viral Infections have a higher risk of concurrently developing autoimmune diseases, reflecting phenotypic heterogeneity in MG. The association between Double Seronegative Myasthenia Gravis and Interstitial Pneumonia has been rarely reported in the Republic of Moldova. The present case aims to report the coexistence of dSNMG and ARVI confirmed in patient.

**Case presentation.** Patient F, 58 years old, presented symptoms of ARVI, including sore throat, general weakness, headache for 10 days. On the 10th day, she developed general weakness, numbness throughout the body, with emphasis on the left hand, speech disturbances and diplopia. She sought medical attention at the Neuroemergency department for investigation. On clinical examination, the patient scored GCS=15p., bilateral external ophthalmoplegia, hemihypoesthesia on the L, Romberg sign(+), palatal veil deviated to the L, dysphagia, dysphonia, dysarthria, without signs of oral automatism. CSF analysis showed the Pandi test(+). Presumptive diagnosis: Myasthenic crisis. Within 2 days, the patient's condition worsened, adding respiratory disorders and sialorrhea, and transferred to the ICU. Initiation of treatment with Prednisolone 5mg with a daily dose increase up to 11 tab. and Calimin 60 mg tab.—initially ½ twice a day, then 1 tab. twice a day—was decided. Chest CT showed bilateral interstitial pneumonia, involuted thymus, and ground-glass opacities in S3-S5 on the R and S4-S5 on the L. The Prozerin test led to a slight regression of eyelid ptosis. On the 4th day of hospitalization, she was intubated and connected to assisted ventilation, with variable oxygen levels. On the 5th day from onset, antibodies were collected, and the result was: Anti-AChR antibodies (<0.07), Anti-MuSK antibodies (<0.01). On the 6th day, plasmapheresis was initiated, followed by immunoglobulin treatment with positive reaction, to which the patient responded positively. She was extubated after 13 days, transitioning to an oxygen mask with FiO<sub>2</sub> ~30%.

**Discussions.** This report describes the case of a woman who initially presented ARVI signs, and eventually diagnosed with dSNMG for both AChR and MuSK antibodies. The disease evolved negatively which caused the transfer to ICU. This case suggests that acute viral infections should be qualified as a trigger for aggressive dSNMG.

**Conclusion.** The case highlights the complexity of the relationship between ARVI and MG, emphasizing the importance of careful monitoring and management. These observations align with reports of other infections inducing autoimmune disorders, as well as the growing evidence of other neurological conditions with presumed autoimmune mechanisms following the onset of ARVI.

**Keywords.** dSNMG, ARVI.



## 2. ANOSMIA – A NEUROLOGICAL COMPLICATION IN COVID-19.

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**Introduction.** Anosmia is a partial or complete loss of smell. It has gained great attention during COVID-19 pandemic, as many infected individuals have reported distorted sense of smell. Anosmia is a condition that can result from various causes, including viral infections, head injuries, or other neurological disorders.

**Aim of study.** A New strain of coronavirus - SARS-CoV-2 emerged in 2019 and led to a global pandemic of respiratory infection named COVID-19. It demonstrated some unique features including rapid transmission of a wide range of respiratory and neurological symptoms. Among these, anosmia, commonly accompanied by dysgeusia, emerged as one of the most common neurological symptoms, sometimes even presenting as the only symptom and significantly impacting the quality of patients' life.

**Methods and materials.** Systematic literature review of the latest published articles was conducted using platforms such as PubMed, Google Scholar and Cochrane focusing on olfactory and taste dysfunction induced by SARS-CoV-2 using the keywords SARS-CoV-2, COVID-19, anosmia, dysgeusia, TMPRSS2, ACE2. Possible pathophysiologic mechanisms, symptomatology, and treatment were analyzed and summarized

**Results.** The most supported theory for pathogenesis of anosmia is viral infection and damage of sustentacular supporting cells and/or inflammatory damage to olfactory mucosa. This leads to disturbed odorant processing and signal transmission. Additionally, comparison of anosmia in other respiratory viruses like influenza, revealed no common pathophysiology with COVID-19 induced anosmia. Although SARS-CoV-2 was found in the CNS, the route of spread and contamination is still under research and possible ways that are suggested are hematogenous spread and direct spread through cribriform plate and olfactory pathways. Most patients recover within 2 weeks. In cases of prolonged anosmia, therapy options include smell training, corticosteroids, and psychological support.

**Conclusion.** COVID-19 induced smell disorder is likely a result of unique damage to supporting olfactory cells and local inflammation. While most patients recover fully within 2 weeks, there is a need for more research to conclude why patients experience prolonged anosmia and how to treat it.

### 3. APPLICATION OF VIRTUAL REALITY (VR) IN THE PLANNING AND SIMULATION OF URGENT NEUROSURGICAL INTERVENTIONS.



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**Introduction.** Emergency neurosurgery is required for acute cerebrovascular disorders, intracranial and spinal cord traumas, and pre-cerebral artery occlusion/stenosis. It requires immediate and accurate management. Virtual reality (VR) is a technology that creates immersive and three-dimensional worlds. It is increasingly being used for surgical planning and training. The uses of this technology encompass anatomic modeling, computer-generated graphics, visualization, haptic feedback, and physical simulation. These advancements have the potential to greatly transform surgical education and preparation.

**Aim of study.** This study seeks to clarify the function of virtual reality in the planning and simulation of urgent neurosurgical operations, emphasizing its advantages in improving surgical readiness.

**Methods and materials.** A systematic literature review was conducted across major databases, including Hinari, PubMed, and NCBI. A search using keywords such as "neurosurgical planning," "neurosurgical simulation," "three-dimensional reconstruction," and "virtual reality" resulted in finding 294 studies that were related to the topic. This research investigated the application of virtual reality (VR) in the fields of surgical planning and simulation.

**Results.** The integration of virtual reality (VR) technology in the field of neurosurgery has demonstrated a significant enhancement in the understanding of intricate anatomical structures and the spatial perception abilities of inexperienced neurosurgeons. Virtual reality (VR) technology allows the surgical team to plan surgeries in advance, helping them to spot probable difficulties and choose the most effective surgical methods. This improves the overall results of the surgery.

**Conclusion.** Virtual reality is at the forefront of surgical innovation, as it enhances the comprehension of patient-specific anatomy during surgical planning. It provides a comprehensive educational experience in medical anatomy and allows neurosurgeons to participate in safe and practical training. Moreover, virtual reality (VR) plays a crucial role in neuronavigation systems by enhancing surgical visualization, leading to enhanced accuracy and effectiveness. The implementation of this technology in neurosurgery not only enhances the level of patient care but also guarantees safer and more precise surgical procedures.



#### 4. ARTIFICIAL INTELLIGENCE INVOLVEMENT IN NEUROSURGERY

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**Introduction.** The incorporation of Artificial Intelligence (AI) in medicine involves the application of sophisticated machine learning algorithms to examine vast datasets, encompassing medical and genetic patient data. This enables the development of customized treatment strategies, with the goal of improving health results and patient satisfaction.

**Aim of study.** This review seeks to examine the influence of artificial intelligence (AI) in the field of neurosurgery, including its involvement in both active and passive procedures throughout the entire range of preoperative, intra-operative, and postoperative healthcare. Additionally, it analyzes the impact of AI on several aspects of neurosurgery, such as diagnostics, clinical decision-making, surgical techniques, prognostics, data collecting, and research.

**Methods and materials.** An exhaustive literature review was conducted using major databases such as PubMed and NCBI. The search, targeting the terms "artificial intelligence" and "neurosurgery," produced 213 pertinent research out of a total of 2360 conducted in the last five years. These studies focused on the implementation of artificial intelligence algorithms in several areas of neurosurgical care and the process of making decisions.

**Results.** The application of artificial intelligence (AI) in the field of neurosurgery expands the limits of what is possible and observable, providing substantial advantages to both medical professionals and individuals receiving treatment. It enhances the ability of neurosurgeons, improving the provision of both interventional and non-interventional care. The contribution of AI in enhancing diagnostic precision, prognostic forecasting, and surgical efficiency is significant. Furthermore, the utilization of AI-assisted robotic systems in surgery serves to reduce the influence of human error, thereby highlighting the growing significance of AI as technology advances.

**Conclusion.** The integration of artificial intelligence into healthcare signifies a fundamental change in the field of neurosurgery. It promotes collaboration among physicians and researchers to create novel diagnostic and treatment tools and approaches. The wide-ranging uses of artificial intelligence (AI) in the area of neurosurgery, namely in improving the precision of diagnoses and predicting outcomes, are set to have a profound impact on the future of the discipline. Upcoming doctors must prioritize staying updated on these innovations and incorporating them to improve patient outcomes and rethink neurosurgical practices.



## 5. AWARENESS OF STROKE– DEGREE OF PATIENTS CONCERN REGARDING THIS CONDITION



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**Introduction.** One in four people will suffer a stroke in their lifetime, so stroke can affect all of us. The person who develops a stroke needs ultra-fast access to the medical facility able to provide him specialized medical assistance. Thus, knowing the onset signs and symptoms is crucial in the management of this pathology.

**Aim of study.** Evaluation of the degree of information and awareness about stroke among patients admitted in the neurological departments of IMSP SCM "Sfânta Treime".

**Methods and materials.** For data collection, a transversal questionnaire was elaborated, which includes the set of questions with multiple choice options, which allowed it to be easily completed by the patients.

**Results.** During the period from March 20 to May 20, 2023, a total of 105 responses were collected. Of which 15 were invalidated, due to incomplete answers. According to the obtained results, 25% of respondents believe that stroke affects the heart and cannot be treated. 13% of them believe that at the critical moment it is necessary to call relatives for help. Only 34% recognized limitation of movements on one side of the body as a sign of stroke, and only 27% aware about speech disturbances. 36% have sought for the emergency assistance and only 17% know that stroke can be treated.

**Conclusion.** The research study shows that people often do not recognize the key signs of a stroke and do not immediately seek emergency medical attention. Because the therapeutic window for a stroke is very narrow, most do not reach the hospital in time and are not eligible for revascularization treatment.



## 6. CEREBRAL VENOUS THROMBOSIS AFTER TOTAL KNEE ARTHROPLASTY: CLINICAL CASE REPORT

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**Introduction.** Cerebral venous thrombosis (CVT) represents a rare subtype of stroke involving cerebral veins and sinuses, characterized by challenging diagnosis due to its atypical clinical presentations and low occurrence. Emphasis on thrombosis prophylaxis post-prosthesis surgery is essential due to increased risk in these patients.

**Case statement.** This case study focuses on a 66-year-old female who developed CVT following total knee arthroplasty, a scenario that heightens thrombosis risk. We detail her clinical progression, diagnostic imaging, and laboratory results, alongside a comparative analysis of similar cases in existing literature. The case underscores the importance of preemptive measures against venous thrombosis in postoperative care. The patient, presenting with altered consciousness, convergent strabismus, and left-sided hemiparesis, was admitted three days post-surgery of total knee replacement. Initial CT findings showed a significant cerebellar lesion, with subsequent CTA confirming right transverse sinus thrombosis. Emergency EVD placement and prompt anticoagulant therapy was administered, leading to her discharge with minimal residual impairments after 36 days of comprehensive treatment.

**Discussions.** CVT diagnosis demands high clinical suspicion and an integrated approach between clinical and radiological teams due to its diverse manifestations and rarity. This case particularly highlights the importance of vigilant thrombosis prophylaxis in post-prosthesis surgery patients, a demographic with elevated risk.

**Conclusion.** CVT is an uncommon yet critical condition that manifests diversely, necessitating a multidisciplinary approach for timely diagnosis and management. The presented case illustrates the importance of thrombosis prophylaxis in postoperative care, particularly following prosthesis surgery. Adhering to established treatment protocols and preventive measures significantly improves outcomes, as evidenced in this patient's recovery.

## 7. CLINICAL AND NEUROPHYSIOLOGICAL FEATURES OF SHOULDER PAIN



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**Introduction.** Shoulder pain is a common and incapacitating ailment that affects a wide range of people globally. A variety of etiologies, including structural traumas, inflammatory processes, and neurological dysregulations, can cause shoulder discomfort, which is a complex issue. Comprehending the many clinical manifestations of this condition is essential for precise diagnosis and focused care.

**Aim of study.** The goal of the research is to highlight the phenotypic, genotypic, neurologic, and pathophysiological aspects of the painful shoulder by looking at the various variables that lead to the beginning and progression of pain in the dolor shoulder area.

**Methods and materials.** For the purpose of the study there was used literature from relevant sources found in PubMed, ScienceDirect such as NihGov. With the usage of keywords such as “shoulder pain”, “hemiplegic shoulder”, “brachial plexus neuropathy”, “diabetic shoulder”.

**Results.** After examining the relevant sources there are two sorts of etiopathological phenotypes: traumatic ones caused by traumas such as fractures or sprains, and non-traumatic ones caused by inflammatory (rheumatoid arthritis), degenerative (osteoarthritis), or neurological (impingement syndrome) diseases. Genetic propensity to disorders such as tendinopathies, where particular genetic variations may impact the predisposition to tendon injury in the shoulder, resulting in tendinitis or tendinosis, is determined by genotypic phenotypes. The pathophysiological phenotypes are inflammatory, produced by an inflammatory reaction of the tissues, as in bursitis or tendinitis, and degenerative, induced by the gradual wear and tear of the joint, as in osteoarthritis. Understanding these pathophysiological phenotypes is crucial for differentiating between shoulder pain in rheumatic patients, diabetic patients, and climacteric individuals. Neurological disorders are brought on by compressions of the nerves, as in the case of impingement syndrome, disc herniation, or brachial plexus suffering from a variety of conditions ranging from neoplastic, neoplastic, and oncological ones to infectious disorders of any other etiology, such as pulmonary infectious pathology or the infectious thyroid gland disease (subacute post-infectious thyroiditis), which causes the lymph nodes in the affected area to enlarge, as well as the dolor shoulder phenomenon in the absence of osteotentine pathology.

**Conclusion.** In conclusion, understanding the clinical and neurophysiological aspects of shoulder pain is crucial for effective diagnosis and management. Comprehensive evaluation and targeted interventions can enhance patient outcomes and quality of life.



## 8. DEPRESSION AFTER CEREBRAL VASCULAR ACCIDENT: FREQUENCY, RISK FACTORS AND IMPACT ON QUALITY OF LIFE

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**Introduction.** Post-stroke depression is one of the most common complications, affecting about one third from the survivors after a stroke. In combination with cognitive aggravation, post-stroke depression slows down the rehabilitation of patients, the activation of their social and everyday functioning, contributes to increasing disability, which worsens the quality of patients' lives.

**Aim of study.** The aim of this thesis is to make a comparative analysis of depression after stroke, according to sex and age, the part of the injury and the severity of the neurological deficit.

**Methods and materials.** The study was carried out on a group of 30 patients in the post-stroke period. In total, the examination of one patient lasted 10 days, where in the acute post - stroke period the patients were monitored according to a specialized program, considering their general stare and physical ability to complete questionnaires with the help of an examiner. On the basis of the following scales (Zung, Ranking, HAD) the onset of depression, its exacerbation and the evolution was determined too.

**Results.** Studies have shown that in most cases, patients after a stroke show mild and moderate levels of depression. The post-clinical analysis shows that a stroke negatively affects the functional and the psychological aspect of the patients, which subsequently leads to impairments in adapting to everyday life.

**Conclusion.** Post-stroke depression is a commune and underdiagnosed problem, which negatively affects the lives of patients. Risk factors or post-stroke depression must be monitored and stopped to prevent the psychological complications. We can make a conclusion that depression after stroke appears in older patients, in female patients, in patients who have a stroke in the left hemisphere and big disability score.

## 9. EPILEPSY ASSOCIATED WITH CEREBRAL TOXOPLASMOSIS

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**Introduction.** Parasitic infections of the central nervous system (CNS) are an acquired cause of epileptic seizures and epilepsy in countries with low and medium economic incomes, including the Republic of Moldova. Cerebral toxoplasmosis is caused by the intracellular protozoan parasite, *Toxoplasma gondii*, which forms brain cysts, especially in immunocompromised patients. Parasite proliferation and microglia produce a modulation in the expression of pro-inflammatory genes, with the establishment of chronic latent infection. The latest studies show that toxoplasmosis-induced structural damage in the brain parenchyma and recurrent inflammation interfere with GABAergic signaling, which is mainly responsible for the occurrence of epileptic seizures, using it as a carbon source for parasite metabolism and facilitating parasite dissemination.

**Aim of study.** Evaluation of neurological manifestations, seizure semiology, electrophysiological and neuroimaging changes in epilepsy caused by cerebral toxoplasmosis, and the neurobiological mechanisms involved in epileptogenesis.

**Methods and materials.** The study included 11 patients with cerebral toxoplasmosis and epileptic seizures. The diagnosis was established based on the clinical manifestations, serological tests analysis, electrophysiological (EEG) and neuroimaging examination.

**Results.** In the study 8 patients were HIV positive, stage C3 and 1 patient suffered from congenital toxoplasmosis. Typical seizure semiology showed focal onset: clonic 54.2%, tonic, cognitive and focal to bilateral tonic-clonic. EEG abnormalities was found in 39.2 % as focal slowing and focal epileptiform discharges. All patients performed neuroimaging, which identified cystic lesions in affected areas of CNS: frontal and temporal lobes, basal ganglia, thalami, periventricular regions and cerebellar white matter.

**Conclusion.** Toxoplasmosis is a frequent opportunistic infection in immunocompromised patients, a late complication of HIV infection and usually occurs in patients with CD4-T-cell counts below 200/mm<sup>3</sup>. The clinical manifestations and epileptic seizures caused by cerebral toxoplasmosis are polymorphic and depends on the number and location of the cysts, and also on the host's immune response.

**Keywords.** Cerebral toxoplasmosis, cysts, epilepsy.





## 10. FLUCTUATIONS IN BETA FREQUENCY DURING THE TRANSITION TO INTERICTAL AND ICTAL STATES IN PATIENTS WITH MYOCLONIC SEIZURES

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**Introduction.** Juvenile myoclonic epilepsy (JME) is the most common syndrome among idiopathic generalized epilepsies manifested by generalized myoclonic and tonic-clonic seizures and spike-slow-wave (SSW) discharges on electroencephalography (EEG). Currently, the pathophysiological concepts addressing the generation of SSW in the JME are still incomplete.

**Aim of study.** We aimed to determine the temporal and spatial organization of functional networks and their dynamic properties.

**Methods and materials.** 40 patients with JME were included in the study. Using high-density EEG (HD-EEG) and 3T MRI epilepsy protocol in patients with JME, we investigated the organization and dynamic properties of brain network modules (communities) during the transition from the resting state to the interictal and ictal state.

**Results.** The average age of the patients included in the study was  $25.4 \pm 7.6$  years, 25 women. Several modules comprising specific cortical and subcortical regions were identified depending on the analyzed time periods of the HD-EEG recordings. In particular, regions of the frontal and parietal lobes were more frequently involved in the time periods preceding the onset of interictal or ictal discharges and the basal ganglia during ictal discharges.

**Conclusion.** Fluctuations in beta frequency could initiate a trigger phenomenon in functional segregation that is further supported by increased clustering coefficient. The timing of observed changes in brain connectivity could serve as markers in the development of innovative, targeted, brain state-dependent therapies.

**Keywords.** Juvenile myoclonic epilepsy, neural networks.

## 11. IMAGISTIC METHODS IN SUPRATENTORIAL CEREBRAL TUMORS PROLONG THE SURVIVAL AMONG ADULT PATIENTS



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**Introduction.** Supratentorial cerebral tumors are life-threatening conditions and may lead to a variable survivability among adult patients. It was proven that the complexity of the imagistic methods along with neuronavigation is improving the survival among these patients. The size of the tumor as well as the dimension of its extension margins is not a statistically significant factor for the survival of the patients. Other factors as genetic predisposition to chemotherapy, extensive combinations of drug therapy, composite drug delivery systems, thermotherapy and radiotherapy are also of interest for prolonging the survival among these patients but the addition of imagistic studies to the mandatory investigations is of special interest for a supportive second or maybe third opinion of the same neurosurgeon along with his colleagues although the main factor for each neurosurgical clinical case is the neurosurgeon's skill.

**Aim of study.** To determine if an improvement in the imagistic investigations assessment is useful in supratentorial cerebral tumors clinical management.

**Methods and materials.** We have revised the patients that had supratentorial cerebral tumors and were admitted to the Emergency Hospital from Chisinau, Republic of Moldova. The time interval for inpatienting them was 01.01.2022-08.12.2023 and there were 63 patients. Overall there were 26 (41.27%) males and 37 (58.73%) females. Gender was not a significant factor for predicting survivability. The number of inpatient days was  $11.56 \pm 4.24$  days for the alive group and  $8.5 \pm 3.33$  days for the deceased group.

**Results.** In the study poll 12/63 (19.05%) patients had died at that time of data collection and 51/63 were still alive (80.95%). In the first group there were 11 patients who had undergone  $\leq 2$  imagistic investigations and 1 that had undergone 4 of them while in the second group there were 50 patients that had undergone  $\geq 1$  imagistic investigations and 1 of them had undergone 0. The patients that were deceased during the data collection had undergone surgical interventions only in 4 (33.33%) cases with an average number of imagistic investigations of  $1.75 \pm 0.375$  and the alive group had 37 (72.5%) surgical interventions with an average number of imagistic investigations of  $2.40 \pm 0.82$ . The before-mentioned raises many questions regarding the secondary factors that lead to this difference. Age was not a significant factor of survivability in the patients but had slightly increased values in the non-survival group ( $54.66 \pm 11.22$  years compared to  $52.05 \pm 12.52$  years).

**Conclusion.** An increased number of imagistic investigations is prolonging the survival time of the patients with supratentorial cerebral tumors because it enhances the surgical intervention quality and makes the neurosurgeon more focused on the tumor extension without regard to the resection margins.

**Keywords.** Supratentorial cerebral tumor, imagistic investigation, neuronavigation



## 12. MICROSURGICAL TACTICS OF IV VENTRICLE INFILTRATIVE EPENDYMOMAS

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**Introduction.** Indicators of survival without recurrence at 5 years in intracranial ependymomas range within 23-50%, with an overall survival of 40-60%.

**Case statement.** Patient B., 6 y.o., presents to the ED with periodic headache, vomiting and seizures, with a history of being sick for 6 months. The disease started with vomiting and unsteady gait. Two weeks before admission to the INN "Diomid Gherman", the boy developed tonic convulsions with loss of consciousness and repeated vomiting. Neurological status: Awake but drowsy. Symmetrical pupils. Pupillary reaction preserved. Convergence absent. Mild central paresis of the VII nerve. Somatosensory deficit is absent. Tendinous and periosteal reflexes accentuated on the left, slight clonus of the soles bilaterally. Positive Romberg test. Coordination tests are disrupted. Fundoscopic examination revealed congestion of the optic nerves with hemorrhage. CT scan in the region of the cerebellar vermis and IV ventricle revealed the presence of a tumor with irregular contour. Third ventricle and lateral ventricles are moderately dilated. Surgical treatment: Removal of the tumor of the IV ventricle. Incision of soft tissues on the midline in the occipito-cervical region. Osteoplastic trepanation of the occipital bone. The arch of the first cervical vertebra is resected. Incision in "Y,, of the dura mater. When examining the IV ventricle through the Magendie foramen, the tumor is detected. At a depth of 1 cm, the gray and soft tumor is determined. The tumor occupies the entire cavity of the IV ventricle, extending into both lateral apertures and into the "calamus scriptorius" region and infiltrating in the inferior wall. The tumor is richly vascularized. Total removal was carried out. Haemostasis. The layered closure of the wound. Biopsy revealed anaplastic ependymoma. CT control revealed the absence of residual tumor.

**Discussions.** During surgery, the region of lateral apertures of the IV ventricle is obligatorily revised to exclude extraventricular expansion of the tumor through the Lushka foramen, into the lateral cisterna of the pons and on its ventral surface.

**Conclusion.** Microsurgical removal of infiltrative growth ependymoma should be performed up to the microscopic level of determination of brain substance, which must form all walls of the operative defect.

### 13. MINIMALLY INVASIVE TREATMENT OF PITUITARY ADENOMAS



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**Introduction.** Pituitary adenomas (PAs) are among the most common tumors of the central nervous system, frequently diagnosed in the third and fourth decades of life. Despite their benign classification, PAs can result in significant morbidity and mortality due to excessive hormonal secretion, hypopituitarism, or mass effect. Minimally invasive approaches have become the gold standard in PAs surgery, offering expedited clinical outcomes and facilitating a quicker return to daily activities for patients.

**Aim of study.** This study aims to critically evaluate the role of minimally invasive surgery in the treatment of pituitary adenomas, emphasizing patient outcomes and recovery..

**Methods and materials.** This article synthesizes data from international peer-reviewed publications and authoritative online resources. A thorough review of recent literature, including systematic reviews and meta-analyses, was conducted to gather the latest evidence in this field.

**Results.** Pituitary adenomas are predominantly benign, and a comprehensive analysis of imaging and laboratory results guides the treatment pathway. The treatment for confirmed PAs is determined based on tumor size, clinical presentation, and whether the adenoma is functioning or non-functioning. The primary treatments are medication, surgery, and radiation therapy. Medication and radiation are typically reserved for specific cases or as adjuncts, with surgery remaining the preferred approach. Surgical goals include alleviating the tumor's mass effect while preserving hormonal function. Transsphenoidal surgery (TSS), either via a microsurgical or endoscopic approach, is the most common minimally invasive technique. The transcranial approach is limited to large, invasive tumors not amenable to TSS. Minimally invasive access is well-received by patients, leading to better postoperative outcomes and psychological recovery. Perioperative complications and endocrine imbalances are less frequent with TSS compared to traditional approaches, leading to shorter hospital stays and faster resumption of daily activities.

**Conclusion.** Minimally invasive treatment of pituitary adenomas, particularly transsphenoidal surgery, demonstrates superior outcomes compared to traditional surgical methods, with reduced hospitalization and enhanced patient compliance with follow-up treatments. For optimal results, TSS should be performed by experienced neurosurgeons in coordination with a multidisciplinary medical team.

**Keywords.** Pituitary adenomas, treatment, transsphenoidal surgery.





## 14. POST-TRAUMATIC STRESS DISORDER AND ITS INFLUENCE ON DIFFERENT BRAIN STRUCTURES

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**Introduction.** Post-Traumatic Stress Disorder (PTSD) is a mental health condition that can develop after experiencing or witnessing a traumatic event. Trauma varies widely and can include combat, sexual assault, accidents, or any life-threatening situation. Individuals with PTSD face challenges in coping with traumatic experiences, often triggered by factors unique to each person. Triggers can cause symptoms like anxiety, panic attacks, nightmares, or flashbacks, transporting individuals back to the traumatic moment. It was supposed that there are some parts of the brain affected by PTSD, like- Hippocampus, amygdala and prefrontal cortex.

**Aim of study.** Our purpose was to study through meta-analysis the neuroanatomy of the brain in patients with Post-Traumatic-Stress-Disorder.

**Methods and materials.** We started our investigation on specialized medical platforms, such as: National Library of Medicine, Research Gate, Science Direct; and identified above 10 articles which described the changes of different brain structures according to mental health conditions characterized in this abstract (PTSD). We've chosen key discoveries spanning a diverse array of PTSD literature to explore how psychological trauma influences neurobiological systems, especially neuroanatomic systems.

**Results.** The hippocampus plays a significant role in the development and manifestation of Post-Traumatic Stress Disorder (PTSD). We have discovered such changes as: reduced volume (early studies utilizing magnetic resonance imaging (MRI) revealed reduced hippocampal volumes in both Vietnam Veterans diagnosed with PTSD and individuals experiencing abuse-related PTSD when compared to control groups), impaired functioning, hypersensitivity to cortisol (N-acetyl aspartate- a marker of neuronal integrity was correlated with cortisol levels). Changes in amygdala function, particularly hyperactivity, contribute to exaggerated fear responses in PTSD. Disruptions in inhibitory control from the prefrontal cortex may intensify amygdala hyperactivity. The prefrontal cortex is essential for processing and contextualizing emotional memories, emphasizing the intricate neural aspects of PTSD. In PTSD, there may be difficulties in the way traumatic memories are processed, leading to their persistence and intrusive nature.

**Conclusion.** In summary, understanding the affected structures of the brain in people with PTSD is essential for advancing our knowledge of the disorder, improving treatment outcomes, reducing stigma, and developing more effective and personalized interventions.



## 15. RISK FACTORS OF ISCHEMIC STROKE IN PREGNANCY



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**Introduction.** Ischemic stroke during pregnancy is relatively rare, but when it occurs, the greatest risk is in the postpartum period, which requires immediate recognition and evaluation for acute management to prevent potential neurological sequelae.

**Aim of study.** This study aimed to analyze the etiology, epidemiology, risk factors of ischemic stroke associated with pregnancy, treatment and prevention methods.

**Methods and materials.** The information was selected based on the articles found in the online resource (PUBMED, NHLBI, HINARI etc.) using the key words: “risk factors”, “pregnancy”, “stroke”.

**Results.** The incidence of stroke in pregnant women is 30 in 100.000, but this rate is approximately 3 times higher than stroke in young adults overall. There are a wide variety of underlying causes and risk factors, some that are common to both pregnant and non-pregnant women, and others that are unique to pregnancy. The main risk factors for ischemic stroke associated with pregnancy are: preeclampsia, eclampsia, gestational hypertension and migraine. According to the study from Maryland and Washington, preeclampsia and eclampsia were identified in women with stroke in 47% of cases. Other risk factors may be cardioembolism, postpartum angiopathy and postpartum cardiomyopathy, posterior reversible encephalopathy, hypercoagulability, diabetes mellitus and advanced maternal age, and smoking. Treatment of stroke during pregnancy is based on current recommendations for nonpregnant patients with stroke, assuming that the benefits of these treatments likely outweigh the risks. These decisions should be made with appropriate stroke and endovascular specialists, as well as obstetricians/gynecologists.

**Conclusion.** The risk of ischemic stroke increased with the number of risk factors, having an increased incidence of 22.6% but also a mortality rate of 2.7%. Surveillance and counseling of pregnant women, especially those with multiple risk factors, is crucial for preventing pregnancy-related ischemic stroke.



## 16. ROLE OF NEUROFILAMENT LIGHT CHAIN IN NEUROLOGICAL DISEASE

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**Introduction.** Neurofilament light chain (NF-L) is a cytoplasmic protein highly expressed in large-caliber myelinated axons. The degree of axonal damage in a variety of neurological disorders, including inflammatory, neurodegenerative, traumatic, and cerebrovascular diseases are proportionally correlated with increased levels of NF-L in cerebrospinal fluid (CSF) and blood.

**Aim of study.** To evaluate the role of NF-L as a diagnostic biomarker, monitoring therapy, and prognostic biomarker for neurological disorders.

**Methods and materials.** There were analyzed articles from PubMed and ScienceDirect databases from the last 5 years, from 2018 to 2023, that mentioned such words as “Neurofilament light chain”, and “Neurological disease”.

**Results.** Firstly, we analyzed the literature about NL-F levels in elderly persons. NL-F levels are correlated to the age of elderly persons. Differences between sexes aren't found. Comorbidities also present a major role in correlation with NF-L ranges; the ranges were increased in patients with neurological disorders, cardiovascular diseases, and a history of fracture, compared with people who didn't report these comorbidities. Literature analysis showed a higher level of NF-L in neurocognitive disorders. Various studies have previously explored the role of the biomarker in the diagnostic process, monitoring, and prognosis of dementia: Alzheimer's dementia, motor neuron disease, Parkinsonian syndrome, cerebral small-vessel disease, and psychiatric disorders. It is a biomarker of axonal injury in neurological diseases and has a substantial correlation with cognitive decline. It was studied that biomarker is elevated in metachromatic leukodystrophy, a lethal metabolic disease. Another study uses NF-L not only for diagnosis, also, for studying effectiveness across disease-modifying therapies in Multiple Sclerosis and for prognostic of disease.

**Conclusion.** Biomarker NL-F can be one of the early diagnostic biomarkers in cognitive decline, in neurological disorders. Also, it can be used to evaluate treatment therapy and may be as a prognostic biomarker.

## 17. STRESS AND NEURONAL CELL DEATH: PATHOGENETIC MECHANISMS, MANAGEMENT AND TREATMENT



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**Introduction.** The nervous system is the most complex organ in the human body, as structurally – consisting of billions of neurons, as functionally – being responsible for cognition, behavior, and conscience. Therefore, the tiniest modification of nervous system homeostasis can alter its welfare. Psychological and physical stress are the most common causes of neuronal milieu dyshomeostasis, beside aging. Neuroglia, including astrocytes and microglia, is the most important factor in coping with neuronal stress and inflammation, being crucial in events like neuron growth and death.

**Aim of study.** As the speed and consistency of our everyday life are steadily increasing, psychological stress is becoming a normal part of it. The nervous system is sensible to stress, providing several clinical conditions related to apoptosis and brain atrophy. Our aim was to emphasize the mechanisms of stress-induced neuronal death and the methods of prevention and treatment.

**Methods and materials.** The current literature review is based on several scientific and medical articles found on PubMed, Google Scholar, Medscape, Elsevier, ResearchGate, Frontiers and medical books.

**Results.** Severe and prolonged stress, as well as chronic mild stress induce the hyperactivation of hypothalamus-pituitary-adrenal axis, with the consequent release of corticosterone, that collaborates with amine neurotransmitters and proinflammatory cytokines to induce neuronal senescence and cell death by apoptosis. Other means of neuronal damage initiated by chronic stress are the decrease of dopamine and serotonin levels, excitotoxicity, microgliosis, astroglia and oxidative stress. All of these are pathological protective reactions directed by endocrine, immune and nervous systems. Paraclinical examinations as PET imaging of TREM1 or caspase-3 activity assay can help setting the diagnosis. Antidepressant drugs, like desipramine, were shown to increase neuronal survival and genesis and to prevent brain tissue atrophy. Adjusting one's daily regimen, physical activity and diet can prevent neuronal apoptosis. Therapy targeting apoptotic genes, proteins and pro-inflammatory cytokines was proven effective.

**Conclusion.** The modifications seen in stress-affected human brains are similar to those in individuals suffering from neurodegenerative diseases, depression and old age. Synaptic loss and cell senescence lead to severe cognitive decline. Stress-induced damage to the nervous system is focused mainly on the dentate hippocampal gyrus and prefrontal cortex, preventing normal neurogenesis and inducing cell apoptosis. The prophylaxis and treatment of the condition are possible and require further research.



## 18. STROKE IN ASSOCIATION WITH IN VITRO FERTILIZATION

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**Introduction.** The incidence of stroke in pregnancy is increasing. In vitro fertilization (IVF) now accounts for 4.5% of all live births in Europe. A prospective cohort study showed an increased risk of cardiovascular disease after failed IVF. A meta-analysis involving women who received fertility treatment revealed an elevated risk of stroke or transient ischemic attack in pregnancy.

**Aim of study.** The study aims to analyze IVF, as a potential risk factor for stroke development, and type of stroke -ischemic, hemorrhagic, or cerebral venous thrombosis.

**Methods and materials.** The incidence of stroke in pregnancy is increasing. In vitro fertilization (IVF) now accounts for 4.5% of all live births in Europe. A prospective cohort study showed an increased risk of cardiovascular disease after failed IVF. A meta-analysis involving women who received fertility treatment revealed an elevated risk of stroke or transient ischemic attack in pregnancy.

**Results.** The incidence of thrombotic events after FIV has been reported to gain 0-2%. A lot of studies showed an increased risk of developing stroke in patients who were treated for infertility. A lot of cases showed a correlation between FIV and ischemic stroke. A study from Rutgers University showed that the risk of hemorrhagic stroke hospitalization was bigger compared to ischemic stroke hospitalization in women who were treated with fertility therapy. Another study found a correlation between FIV and hypertension after delivery. A Canadian study showed a higher prevalence of hyperlipidemia, hypertension and diabetes among women who received FIV compared to the control group. Sweden study found only correlation between hypertension after delivery and FIV. There are described some clinical cases that correlate FIV and cerebral venous thrombosis. Ovarian hyperstimulation syndrome can be due to thromboembolic disease. Suspected mechanisms could be: 1. increased risk factors as vascular complication after FIV- placental disease (preeclampsia), kidney disease and metabolic troubles (gestational diabetes); 2. physiologic prothrombotic state in pregnancy; 3. patients may already have disorders that could be associated with stroke risk factors (antiphospholipidic syndrome).

**Conclusion.** IVF can increase the risk of stroke. The risk for developing thrombosis during IFV is low, but it is higher compared to the general population. Correlation between type of stroke and IVF needs more clinical studies.

**Keywords.** In vitro fertilization (IVF), stroke.

## 19. STROKE IN PREGNANCY AND POSTPARTUM



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**Introduction.** Stroke is a medical emergency that requires urgent care and treatment. As everyone, regardless of age, gender or health, can experience this condition, pregnant women can have it as well. In addition to major changes in their bodies during the pregnancy and the first weeks after birth, the health complications during that period may raise the risks of having a stroke.

**Aim of study.** The aim is to list and clear up the epidemiology, risk factors and other characteristics of the stroke in pregnancy and postpartum, as well as the methods of treatment.

**Methods and materials.** The information was selected and based on the articles found in online resources (NCIB, NIH, NHLBI etc.) using the following keywords: “pregnancy”, “stroke”, “risk factors”, “treatment”.

**Results.** The incidence of stroke in pregnant women is 30 in 100.000, about three times more than among non-pregnant ones. However, the risk of stroke in women with common pregnancy-related issues such as preeclampsia, can be up to six times higher. In addition to the percentage of maternal mortality caused by stroke, which is 7,4% (and it can be underestimated), pregnant women may face a possibility of having disabilities, thus dealing with difficulties in selfcare, childcare, personal and professional life. According to studies from Canada, the number of cases of maternal stroke between 2003 and 2016 became more frequent by 60%. The period with the highest risk of stroke in the last month of the pregnancy and the first six weeks puerperium. Besides the common risk factors that are present in the general public, there are conditions that occur during the pregnancy and are prone to causing stroke: preeclampsia, gestational diabetes, paradoxical cardioembolism, carotid artery dissection, coagulopathies and others. One of the major issues in this topic is the lack of trials in pregnant women and balancing the maternal and fetal health in investigating and treating stroke. Providing treatment to pregnant women who are at high risk of stroke is a challenge for doctors as some of the drugs (ACE inhibitors, statins, warfarin etc.), that are crucial for the general public, have a negative impact on the fetal development.

**Conclusion.** Stroke in pregnancy and postpartum became a more approached and a more discussed topic in recent years. Dealing with a pregnant woman, especially one with health conditions that may put her life at risk, requires a rigorous supervision, treatment, and collaboration between multiple specialists from different fields in order to keep her safe from further complications.





## 20. TELENEUROLOGY A 21ST CENTURY CHALLENGE IN MONITORING CHRONIC NEUROLOGICAL CONDITIONS

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**Introduction.** Chronic neurological conditions, spanning neurodegenerative to autoimmune disorders, manifest prolonged and complex symptoms post-brain injuries. These challenges affect social interactions, career performance, daily activities, and healthcare access. In the field of telemedicine, remote monitoring thrives, facilitated by affordable devices like smartphones and wearables, representing a noteworthy advancement in accessible and efficient healthcare

**Aim of study.** The study aims to explore the role of remote monitoring within telemedicine, taking into account the distinct characteristics of individual disorders and the potential benefits provided by tele-neurology.

**Methods and materials.** The article relies on global publication data and online resources, referencing pertinent literature from databases such as Neurology.org, PubMed, Medline, and ScienceDirect, using specific keywords like "tele-neurology," "stroke," "epilepsy," "telemedicine," and "long-term neurological conditions."

**Results.** Examining telemedicine's current role in common neurological conditions from both clinician and patient viewpoints reveals potential in telephone interviews to replace face-to-face assessments for cognitive measurement scales. Wearable devices and mobile apps offer fresh insights into Huntington's disease features and clinical progression, particularly in cognition, upper body motor function, stability, and gait. Multiple Sclerosis remote monitoring incorporates a dedicated symptom tracker page for comparing symptom severity and observing trends. Disability measurement in multiple sclerosis via the Expanded Disability Status Scale may occur through telephone interviews or videoconference links. Telestroke, driven partly by the urgency of thrombolytic treatments, denotes the use of telemedicine in stroke management.

**Conclusion.** Teleneurology, including teleconsultation, teleconferencing, and tele-education, has transitioned from yesterday's innovations to today's standard practice, firmly establishing itself as an integral part of neurological care for clinicians and patients, and its presence is enduring.

## 21. THE CLINICAL AND IMMUNOLOGICAL FEATURES OF MYASTHENIA GRAVIS WITH ANTI-MUSK ANTIBODIES.



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**Introduction.** Myasthenia gravis is an autoimmune disorder of the neuromuscular junction, caused by autoantibodies synthesized against AChR, MuSK or LRP4. There is also a seronegative form, where antibodies are not detected. The disease is more prevalent in women, especially after the age of 40, but it tends to have a milder course in women compared to men. The mortality rate usually does not exceed 5-9%. Frequently, the disease begins with ocular manifestations such as ptosis and diplopia, only occasionally initiating with bulbar symptoms. However, the primary symptom remains muscle weakness, which is detected in the majority of patients.

**Case statement.** A 30-year-old female patient presented with the following complaints: muscle weakness in the hands, speech and swallowing disturbances. She has considered herself ill since 2014, following childbirth. She was consulted by a neurologist in 2015 and 2016. In 2018, a CT scan of the mediastinum revealed a persistent thymus, leading to the following diagnosis: Myasthenia gravis, with a relapse characterized by pronounced muscular fatigability, accentuated in the muscles of mastication and nasopharynx and mild oculomotor disorders. The patient was prescribed pyridostigmine 60 mg three times a day and in 2019, she underwent thymectomy. The patient's neurological status includes diminished convergence, slightly reduced pharyngeal reflex and reduced muscle strength in the orbital muscles. A prozerin test was conducted and the patient's condition improved, indicating a positive response. The diagnosis: Myasthenia gravis, generalized form, subcompensated, post-thymectomy state in 2019.

**Discussions.** In this case, the patient followed the doctor's instructions, undergoing treatment with prozerin. The patient responded positively to the treatment, but despite the exacerbation of myasthenia gravis, her condition deteriorated, indicating the unpredictable course of the disease.

**Conclusion.** The presented case emphasizes the imperative of ongoing investigation into myasthenia gravis and the need to elucidate treatment methods to prevent exacerbations and control the unpredictable evolution of the disease. Additionally, a personalized approach and careful monitoring of myasthenia gravis patients are necessary to adapt treatment based on the disease's progression. It is evident that the correct diagnosis of the disease's form is essential for establishing an appropriate treatment plan, underscoring the importance of research and therapeutic developments in this field.



## 22. THE CONSEQUENCES OF CRANIOCEREBRAL INJURIES CAUSED BY ELECTRIC SCOOTERS.

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**Introduction.** The burgeoning popularity of electric scooters (ES) has been paralleled by a rise in associated craniocerebral injuries (CCIs). As these modern, portable vehicles gain widespread use in numerous developed countries, their convenience is offset by the escalating incidence of traumatic injuries. This literature review scrutinizes the aftermath of CCIs sustained in ES-related accidents, delving into the implications these injuries have on patient health and recuperation.

**Aim of study.** This study aims to methodically evaluate the severity and characteristics of head injuries incurred in ES-related incidents. It seeks to identify risk factors, immediate and long-term ramifications of these injuries, and the role of medical intervention in the healing process.

**Methods and materials.** A comprehensive review was conducted using 30 scholarly articles sourced from open-access databases including Google Scholar, WHO websites, Medline (PubMed), and Scopus. Selection was based on relevance to keywords such as craniocerebral trauma, electric scooter, e-scooter, dislocation, traffic accident, fracture, and traumatic brain injury.

**Results.** The analysis indicates a substantial proportion of individuals suffering moderate to severe CCIs, characterized by skull fractures, cerebral hemorrhages, and diffuse axonal injuries. Factors influencing the severity of ES accidents, including age, velocity, and usage of safety gear, were found to have a significant correlation with the extent of the trauma.

**Conclusion.** Electric scooter-related falls resulting in cranio-cerebral trauma present considerable health implications, underscoring the need for enhanced preventive strategies and the promotion of safety equipment. This review accentuates the necessity of preventive measures and safety education for ES users to mitigate the risk of such injuries and foster a safer riding environment.

## 23. THE ROLE OF COGNITIVE FACTORS AND RESPIRATORY DYSFUNCTION IN CHRONIC PAIN



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**Introduction.** In the last two decades the thorough study of cognition and breathing in the context of chronic pain have found a crucial role in the adaptation of new therapies for the management of CP ( chronic pain). The cognitive-evaluative variables ( such as the presence of catastrophic thoughts or the role of self-efficacy expectations) and respiratory ( hyperventilation syndrome) negatively influence the dynamics of patients with chronic pain, being predictors of the persistence of the pain syndrome, as a result leading to the impairment of both physical health and and psychic.

**Aim of study.** Study and analysis of modern scientific publications to identify the role of the cognitive component and respiratory dysfunction in the clinical manifestations of chronic pain.

**Methods and materials.** In order to achieve the proposed goal, a narrative synthesis of the publications and articles in the Google Scholar databases was carried out, which in the last 5 years have investigated the peculiarities of cognitive and respiratory functioning in patients with chronic pain and, last but not least, how by manipulating them can obtain lasting therapeutic results.

**Results.** Studies show that there is a relationship between cognition, breathing and pain. In the context of the cognitive component (for example attention) it would have been proven that the distraction from pain is accompanied by a decrease in the activity of ascending nociceptive pathways and systems, therefore the shift of attention from the current focus to another adapts the subject's behavior in the event of sudden onset of a potentially dangerous stimulus ( painful stimulus). In the context of the respiratory component (pathological respiratory pattern) such as hyperventilation, which results from the excitation of the limbic system, causes hypocapnia with the development of hypoxia. At the level of the CNS (central nervous system), hypoxia activates the components of the limbic system. It follows that hyperventilation leads to neuronal hyperexcitability, and this plays a key role in the generation of pain by altering somatosensory information.

**Conclusion.** Chronic pain still remains a major health problem that needs to be eradicated or cured not only by managing the pain phenomenon, but also by applying new management therapies such as: attention manipulation, which results in the voluntary control of attention because susceptibility to painful stimuli is so great that attention is involuntarily drawn to them. Another type of therapy would be breathing techniques that could help improve chronic pain management.



## 24. THE ROLE OF PREDICTIVE FACTORS OF HEMORRHAGIC TRANSFORMATION IN PATIENTS WITH ISCHEMIC STROKE UNDERGOING INTRAVENOUS THROMBOLYSIS

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**Introduction.** Intravenous thrombolysis (IT) is the standard intervention for patients with ischemic stroke that demonstrates a significant rate of reduction in mortality and disability. Hemorrhagic transformation (HT) after IT is the most common and life-threatening complication and can manifest itself from small hemorrhagic petechiae to massive hematomas.

**Aim of study.** The purpose of the review is to identify the role of predictive factors of HT on the character of the complication from harmless to devastating.

**Methods and materials.** This review includes clinical articles from the last 5 years from the Google Scholar, NCBI and PubMed databases.

**Results.** A multitude of factors influence the occurrence as well as the negative character of HT. A blood glucose  $> 8.32$  mmol/l triples the risk of HT, and a value at admission  $> 11.11$  mmol/l and an HbA1c  $> 6.5\%$  increase the risk of symptomatic HT. Fibrinogen  $< 1.5$  g/l shows a severe impact on HT and hematoma evolution. An initial NIHSS score  $< 10$  has been reported to produce  $< 3\%$  of HT, an NIHSS  $> 20$  - a risk  $> 5\%$  and it increases by 1.35 times for every 1 point over. Revascularization time delay of more than 180 minutes was associated with eventual HT. Male gender increases the risk 2.7 times, while blood pressure values  $> 180$  mmHg - 2.4 times and 1.03 times for every 1 mmHg above the limit. Values above the norm of ALT with every 1 U/l increases the risk of HT by 1.05 times.

**Conclusion.** Knowing and correcting the risk factors allows not only the primary prevention of stroke, but also increases the stroke success rate of IT and reduce HT risk. The patient's awareness of the risk factors can improve the primary prophylaxis of HT.



## 25. THE ROLE OF VIRTUAL AND AUGMENTED REALITY IN NEUROSCIENCE



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**Introduction.** Virtual (VR) and augmented reality (AR) are new tools that are already being successfully used in neurorehabilitation and therapy. But these technologies are still perceived by some experts with skepticism.

**Aim of study.** Description of VR and AR technologies and introduction to the possibility of their use in neurology and neurosurgery.

**Methods and materials.** For this review, publications were selected from various resources, such as PubMed, Neurology.org, Google Scholar. The searches were based on keywords: “neurorehabilitation”, “virtual reality”, “post-stroke”, “virtual environments”.

**Results.** Research from several sources has shown that virtual and augmented reality are successfully used in many areas of medicine, particularly in neuroscience. Virtual and augmented reality have contributed to neurorehabilitation, especially in post-stroke patients. VR affects the psychological state of patients, increasing motivation and task specificity. An example is Gait-triggered mixed reality, which aims to rehabilitate the lower extremities. Another example is the Rehabilitation Gaming System for aphasia, which focuses on training for lexical disorders. VR and AR have also contributed to the treatment of acute pain by distracting the patient's attention. Thus, a combination of psychological and pharmacological methods of pain relief improves the comfort and well-being of patients. Virtual reality facilitates medical procedures for patients with various injuries, especially in pediatrics, and reduces pain during physical therapy. Moreover, unlike painkillers, VR has no side effects, risks of overdose, or addiction.

**Conclusion.** Virtual and augmented reality open up new opportunities for neurology and neurosurgery and can be successfully used in the training and practice of doctors, neurorehabilitation, pain management, and the improvement of psychological comfort for patients



## 26. TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION EFFICACY IN DRUG RESISTANT EPILEPSY TREATMENT

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**Introduction.** Transcutaneous auricular vagus stimulation (taVNS) modulates the locus coeruleus-norepinephrine (LC-NE) network through impulses delivered to the external ear via A $\beta$  fibers using frequencies mostly between 10-30 Hz which could desynchronize ictal rhythms and prevent seizure onset. taVNS might be a viable therapeutic adjunctive option in drug resistant epilepsy, with no response to 2 different medications (25% of all cases).

**Aim of study.** Assessment of taVNS's impact on neural oscillations via modulation of seizure-free period duration, seizure frequency, P3 event-related potential amplitude, tonic pupil size, salivary cortisol levels, and evaluate potential side effects.

**Methods and materials.** Clinical trials, prospective studies, and meta-analyses published between 2018 and 2024, using PubMed and ILAE databases with 267 references in total.

**Results.** Across 3 studies the results at 8, 16 and 24 weeks, displayed average seizure frequency reduction of 36.2%, 49.1%, and 55.6%, compared to the baseline. On average 24% of the participants were reported to be seizure free compared to the control group. In a different study, interictal EEG at 44 weeks displayed a reduction of abnormal findings during wakefulness. LC-NE modulation research reveals heterogeneous outcomes, as taVNS does not induce changes in P3 amplitude and pupil size diameter ( $p = 0.3-0.4$ ), yet a mitigated decrease in salivary cortisol was observed ( $p=0.4$ ). Across 10 studies adverse effects amounted to 10%, most prevalent being headache, skin irritation and ear pain (8.9%, 7.1%, 4.6%).

**Conclusion.** Research reveals an improved quality of life and seizure control in patients undergoing taVNS. The physiological markers did not seem to be modulated by taVNS, however hormonal responses that would indicate LC-NE network activation were attested. Gaining further insights into optimal adjustment of taVNS parameters which would impede ictal rhythm synchronization without adverse effects is crucial for enhancing effectiveness on a case-by-case basis. This is particularly significant for individuals with drug-resistant epilepsy, as it expands the range of available adjunctive therapeutic options.

**Keywords.** Drug resistant epilepsy, transcutaneous auricular vagus nerve stimulation, network.

# **XI. OBSTETRICS AND GYNECOLOGY SECTION**



*„Ajuns la acest prag semnificativ al vieții, răsfoind filă cu filă arhiva anilor trecuți, mai găsesc întrebări, la care urmează a fi găsite și formulate răspunsuri. Sunt încrezător și mă bucur că aceste răspunsuri vor fi date de către Dumneavoastră, dragi tineri colegi! Știința continuă să evolueze, viața rămâne a fi extrem de interesantă. Să ridicăm în continuare prestigiul medicinei la cotele cele mai înalte ale creației umane.”*

*„Having reached this significant threshold of life, leafing through the archive of the past years, I find more questions, to which it is necessary to find and formulate answers. I am confident and glad that these answers will be given by you, dear young colleagues! Science continues to evolve; life remains extremely interesting. Let us continue to raise the prestige of medicine to the highest heights of human creation.”*

**Gheorghe Paladi,**

*Professor, MD, PhD, Academician,*

*Order of the Republic Moldova,*

*Obstetrics and Gynecology Department,*

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## 1. A COMPREHENSIVE APPROACH TO IMPROVING MANAGEMENT IN POSTPARTUM HEMORRHAGE

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**Introduction.** Postpartum hemorrhage (PPH) is a leading cause of maternal mortality and morbidity, which needs a vigilant approach for early qualified diagnosis and timely multidisciplinary management. Pregnant women at high risk for PPH require proper antenatal assessment. In cases of planned cesarean section (C-section), it is recommended a high level qualified surgical team to manage the clinical situation.

**Aim of study.** This research is aimed to analyze the evolution of PPH  $\geq 1000$  ml at the patients admitted in a tertiary perinatal center.

**Methods and materials.** A descriptive study was performed by assessing 78 cases with PPH. Medical history, clinical and paraclinical signs, and management algorithms were assessed.

**Results.** Patient age ranged from 21 to 30 years, majority being multiparous (71.2%). They had a high level of miscarriages and stillbirths (41.5%). Previous C-section was observed in 34.7% of cases. The blood loss were estimated between 1000-1499 ml in 45 cases (57.7%); 1500-2499 ml in 26 cases (33.3%), and HPP $\geq 2500$  ml in 7 cases (9.0%). The hemorrhage volume was measured by visual method, hemostatic materials and clots weighing. The diagnosis was established based on the 4T's rule. Placental pathology (51.7%) and deep laceration of birth canal (22.8%) were the main causes, especially in massive hemorrhages. The clinical management was perform according to Transfusion and volume resuscitation management for Massive Obstetric Hemorrhage Guideline. The correction of coagulation factors deficiency and anemia were important steps in PPH $>1500$  ml cases. Compression sutures (B-Lynch) were performed in 8 cases (6.8%), and 37 cases (31.4%) underwent hysterectomy for hemostasis. Re-laparotomy was required in all PPH  $\geq 2500$  ml cases. All patients developed moderate or severe anemia in postpartum period, and 33 cases (42.3%) with PPH $>1500$  ml were complicated with hemorrhagic shock. Multiple organ dysfunction syndrome (MODS) occurred in 7 cases (9.0%), hepatic and acute renal dysfunction being the main injuries. Disseminated intravascular coagulation (DIC) was noted in 9 cases (11.5%) in post-partum period, systemic inflammatory response syndrome (SIRS) complicated 22 cases (28.2%), immune and nutritional deficiencies (hypoalbuminemia, absolute lymphopenia  $<500$ ) determined in 14 cases (18.0%).

**Conclusion.** Placental pathology and deep laceration of the birth canal remain main causes of PPH. Timely and comprehensive correction of coagulation factors deficiencies and anemia, decrease the risk of MODS in postpartum period. PPH can lead to the post-partum complications, requiring an appropriate and individualized management, and a comprehensive approach.

## 2. ASSESSMENT OF THE CASES OF POSTPARTUM HEMORRHAGE IN MULTIPAROUS WOMEN



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**Introduction.** Postpartum hemorrhage (PPH) is one of the leading obstetric complications, affecting 5-15% births. Being a major factor in maternal mortality and morbidity, PPH causes about 25% of maternal deaths worldwide.

**Aim of study.** The aim of the study was to assess the cases of PPH in multiparous women, admitted to the Tertiary Perinatal Center.

**Methods and materials.** The retrospective study was performed by assessing 81 clinical cases of PPH in multiparous women. Total blood loss in labor or C-section was performed by using graduated vessels, and all the sterile material used was weighted. For continuous variables, the mean values and standard deviation of the mean were calculated; the median (Me) as well as the interquartile range (Q1;Q3) in the case of a distribution of characteristics that differs from the normal.

**Results.** The average age of women was  $31.6 \pm 5.5$  years (Me 32 (28;35.5)), varying in the limits of 20-42 years. The majority of participants delivered for the second time - 38 cases (46.9% (95% CI 33.3-59.9)), however, 30 women (37.0% (95% CI 25.9-48.2)) gave birth for the third time, and 13 women (16.1% (95% CI 8.5-27.4)) had 4th – 9th delivery. In 41 cases (50.6% (95% CI 40.7-61.7)) a c-section was performed. The mean blood loss in vaginal delivery was  $850 \pm 308$  (Me 800 (600;1050)) mL, varying in the limits of 500– 1600 mL. Compared to the mean blood loss in C-section –  $1752 \pm 1093$  (Me 1500 (1100;1850)) mL, varying in the limits of 1000 – 5250 mL. In the structure of PPH there were assessed 26 cases (32.1% (95% CI 20.9-47.0)) of the placental defect or placenta adherens, 15 cases (18.5% (95% CI 10.3-30.5)) of lacerations of the birth canal, 11 cases (13.6% (95% CI 7.4-23.4)) of uterine atonia, and 2 cases (2.5% (95% CI 0-7.3)) of uterine rupture. Hence, in 46 women (56.8% (95% CI 44.6-69.1)) it was applied conservative management of the cases. However, in 20 cases (24.6% (95% CI 15.0-38.1)) an operative management was applied, from which 7 cases (8.6% (95% CI 3.7-14.7)) hemostatic sutures were applied. In 13 cases (16.0% (95% CI 8.5-27.4)) hysterectomy was performed, from which 9 cases (69.2% (95% CI 31.6-100)) subtotal hysterectomy without annexes was the elective method for definitive hemostasis.

**Conclusion.** PPH is a major obstetric complication, which occurs more frequently in multiparous women, in association with placental pathology and birth canal trauma, explained by overextension of the uterus and coagulation disorders, requiring extensive surgical management.





### 3. AUXILIARY DIAGNOSTIC METHODS FOR HYDATIDIFORM MOLE: A CONCISE REVIEW

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**Introduction.** Hydatidiform moles (HMs) are premalignant conditions within gestational trophoblastic disease (GTD). Early diagnosis is crucial due to the risk of malignant transformation, with neoplasia risks for complete hydatidiform mole (CHM) at 15-20% and for partial hydatidiform mole (PHM) at 0.5-1%.

**Aim of study.** This research aims to evaluate advanced diagnostic methods in hydatidiform mole patients to prevent recurrences and gestational trophoblastic neoplasia.

**Methods and materials.** A bibliographic study was conducted using articles from databases (NCBI, PubMed, Nature, Medscape, MDPI) published between 2013-2023. Key terms included gestational trophoblastic disease, hydatidiform mole, complete and partial hydatidiform mole, genotyping, immunohistochemistry p57.

**Results.** Routine microscopic evaluation, even by experienced pathologists, misclassified 20% of cases. Morphological assessment limitations and overlap with other entities necessitate an algorithmic approach, combining p57 immunohistochemistry and molecular genotyping. P57, a paternal imprinted gene product, is absent in CHMs and early forms due to lacking maternal genetic contribution. In contrast, PHM and nonmolar pregnancies exhibit diffuse p57 expression. However, it cannot distinguish PHM from nonmolar pregnancies, necessitating genotyping. STR genotyping excels in distinguishing CHM, PHM, and nonmolar pregnancies by discerning androgenetic diploidy, diandric triploidy, and biparental diploidy. Other techniques (karyotyping, DNA ploidy analysis, FISH) fail to distinguish maternal from paternal contributions.

**Conclusion.** Auxiliary methods enhance hydatidiform mole diagnosis, yet challenges persist. P57 immunohistochemistry struggles to differentiate PHM from nonmolar pregnancies. Molecular genotyping faces difficulties in mosaic conceptions and rare trisomies, potentially leading to misclassification. Further research is needed to refine these techniques and overcome current limitations.

#### 4. CASE REPORT OF A PERFORATED INTRAUTERINE DEVICE INTO SIGMOID COLON



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**Introduction.** Intrauterine devices (IUD) have become one of the most popular birth control methods worldwide. Uterine perforation is an uncommon complication of IUD, with an incidence 1: 1,000 insertions. Perforation may be complete, with the device totally in the abdominal cavity, or partial, with the device to varying degrees within the uterine wall. Two mechanisms of uterine perforation exist: immediate traumatic perforation, and later “secondary” perforation caused by gradual erosion through the myometrium. The European Active Surveillance Study for IUD study confirmed a subset of patients with asymptomatic IUD perforations, leading to their late presentation and management (months or years after insertion). Perforated intrauterine devices can generally be removed successfully at laparoscopy.

**Case statement.** A 39-year-old patient was admitted for scheduled laparoscopic surgery for an incorrectly placed IUD in 2014. She had no symptoms. Pelvic USG revealed a 50% invasion of the myometrium by the IUD. Intraoperator: thick adherent flanges between the sigmoid colon, omentum and fundic uterine region. Adhesiolysis was performed and revealed the device that has protruded into the peritoneal cavity but was still fixed in the myometrium, attached with one horizontal branch to the omentum and the other one was in the intestinal lumen. The IUD was removed, the intestinal defect was sutured. Her recovery thereafter was uneventful.

**Discussions.** Is necessary to raise awareness of the consequences of uterine perforation by IUDs. Although it is a potentially serious complication of intrauterine contraceptive use, it is uncommon and it can often be asymptomatic.

**Conclusion.** While being an uncommon phenomenon, uterine perforation with an IUD is an important risk that must be explained to patients, prevented if possible by taking all steps to insert devices safely, and diagnosed and managed appropriately.



## 5. DIAGNOSIS OF FETAL GROWTH RESTRICTION

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**Introduction.** The prevalence of intrauterine fetal growth restriction continues to rise with an increased risk of perinatal mortality and morbidity. Accurate recognition of Intrauterine Growth Restriction (IUGR) holds significant importance since it allows for targeted management.

**Aim of study.** The purpose of the study is to highlight warning criteria in diagnosing IUGR and to achieve an early diagnosis for appropriate management.

**Methods and materials.** There were used international databases: PubMed, sciencedirect, Medscape, and have been analyzed publications from the past 10 years.

**Results.** Detecting IUGR during pregnancy is crucial for reducing mortality and morbidity risks. It typically starts with clinical suspicion, examining for a than expected uterine size, abdominal palpation, and measuring the symphyseal-fundal distance. Doppler velocimetry plays a significant role in distinguishing between a fetus that is SGA (small for gestational age) yet healthy and one with true IUGR. Monitoring pregnancies affected by fetal growth restriction (FGR) using umbilical artery (UA) Doppler has demonstrated a reduction in mortality rates and decreased instances of antepartum admissions, labor induction, and Caesarean deliveries. The fetal biophysical profile (BPP) encompasses various measurements, including amniotic fluid volume, fetal tone, movements, breathing, and fetal heart rate monitoring (NST), each parameter receiving a maximum of two points for a total of ten points when within normal limits. Additionally, multiple biomarkers have been studied for screening and diagnosing FGR, such as PAPP-A, hCG, PlGF, and sFlt-1. Gaccioli et al. summarized the predictive accuracy of maternal circulating biomarkers for FGR, encompassing early onset biomarkers, angiogenic factors, hormonal factors, endothelial stress markers, and cytokines. Combining Doppler assessments with angiogenic factors has shown potential in enhancing the prediction of FGR.

**Conclusion.** It's essential to assess high-risk factors for FGR in every pregnancy. Precise diagnosis involves utilizing serial growth charts, DFMC (symphysis-fundal height measurement), CTG (fetal heart rate monitoring), and Doppler studies of various arteries like uterine, umbilical, middle cerebral, CPR (cerebroplacental ratio), and ductus venosus blood flow. These tests aid in distinguishing between healthy SGA babies and those with pathological FGR, offering valuable insights into prognosis.

**Keywords.** Ultrasonography; IUGR; Cerebroplacental ratio; Placental insufficiency

## 6. CONDUCT OF PATIENTS WITH CERVICAL PATHOLOGY



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**Introduction.** The cervix, essential in female reproduction, raises significant concerns regarding precancerous conditions with a significant global and local impact. In the Republic of Moldova, 600-700 women per year are diagnosed with precancerous conditions, and 300-350 with cervical cancer. In the European Union, there are 52,000 cases per year, with 27,000 deaths. Globally, cervical cancer is the fourth most common cancer in women, with 342,000 deaths and 604,000 cases per year.

**Aim of study.** To thoroughly investigate precancerous conditions of the cervix, focusing on identifying risk factors, diagnostic methods, and treatment options.

**Methods and materials.** The study included the analysis of a representative sample of women, assessing menstrual history, history of STIs, postcoital bleeding, parity, steroid use, and attitudes towards cervical cancer screening. All significant data were extracted from the analysis of available literature in open sources such as PubMed, Medscape, Mayo Clinic, and MedlinePlus, using key terms: precancerous conditions of cervical cancer, HPV, and cervical dysplasia.

**Results.** The prevalence of lesions affected 27.4% of participants, with an average age of 35-36 years. Strong knowledge (63.4%) and a positive attitude (67.6%) were highlighted. Risk factors include irregular menstrual history, sexually transmitted infections (STIs), postcoital bleeding, high parity, and steroid use. HPV 16 and 18 were identified as significant risk factors. Sexual behavior, smoking, dietary habits, and immunosuppression are involved in HPV infection, with an incidence of 7% at 20-25 years and less than 2% over 30 years. An unfavorable attitude towards screening contributes to increased risk.

**Conclusion.** The prevalence of precancerous cervical lesions is significant (27.4%). Risk factors emphasize the complexity of the issue. Reproductive health management requires a comprehensive approach. Educating women for early detection and preventing progression to advanced stages is essential. Women's strong conviction plays a crucial role in the fight against precancerous cervical lesions and cervical cancer.



## 7. DIAGNOSTIC CHALLENGES IN UNUSUAL GYNECOLOGICAL SYNCHRONOUS TUMOR: A PATHOLOGIST'S PERSPECTIVE

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**Introduction.** Ovarian carcinosarcoma (OCS) is an uncommon high-risk malignant biphasic neoplasm consisting of morphologically high-grade carcinomatous and sarcomatous tissue elements. OCS has an incidence of 2.5% (4 cases reported since 2013) operated in our gynecological unit. The prediction of the biological behavior of OCS is unfavorable, due to the absence of markers for early diagnosis, high recurrence and mortality.

**Case statement.** A 59-year-old patient without significant history was admitted in the Obstetrics and Gynecology, Cuza Vodă Hospital, Iași, Romania. The pelvic MRI revealed two ovarian and one uterine mass. A total hysterectomy with bilateral adnexectomy, pelvic lymphadenectomy and omentectomy was performed. Ovarian and uterine specimens were examined using hematoxylin–eosin and immunohistochemistry staining to confirm the carcinomatous and sarcomatous components in the ovarian mass.

**Discussions.** Upon microscopic examination, OCS was confirmed by poorly differentiated carcinomatous tissue morphology, with areas of squamous differentiation, associated with mesenchymal component, as undifferentiated sarcoma next to areas with heterologous rhabdomyoblastic differentiation. After the surgery, the patient was referred to the Oncology Clinic, Iasi, Romania, for the postoperative oncological treatment. Three months after chemotherapy the pelvic CT detected two more pelvic tumoral masses, which had infiltrated the recto-sigmoid wall. The immunohistochemical analysis turned out to be AE1/AE3 positive for the carcinomatous tumor cells, while P63 immunoexpression confirmed squamous differentiation and desmin supported the mesenchymal component origin. Also, endometrial samples revealed a low grade endometrial endometrioid adenocarcinoma (G2) with intraepithelial endometrial neoplasia.

**Conclusion.** OCS has a wide range of morphological activity with high potential of recurrence or metastasis. Providing additional data, the present case report contributes to expanding knowledge of these aggressive neoplasms. A multidisciplinary approach including clinical surgical findings, histopathological features and treatment options are required for final diagnosis. Also, molecular studies are important to reveal a clonal relationship between these two synchronous malignant cell populations.

**Keywords.** Biphasic neoplasm, endometrial adenocarcinoma, rhabdomyoblastic differentiation, immunohistochemistry



## 8. ENDOCRINE CHANGES AND MENSTRUAL DYSFUNCTIONS IN ADOLESCENT GIRLS WITH OBESITY



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**Introduction.** In recent decades, there has been a significant increase in the obesity rate among adolescent girls. According to the specialized literature, obesity induces hormonal changes that have consequences on sexual development during puberty and menstrual function. Among the most common endocrine changes are thyroid dysfunction, hyperprolactinemia, and insulin resistance.

**Aim of study.** To determine endocrine disorders and menstrual cycle dysfunctions in adolescent girls with obesity.

**Methods and materials.** The current research is a non-experimental, descriptive study. The overall research sample consisted of 150 adolescent girls with obesity. The research was conducted based on the medical records of inpatients at the Institute of Mother and Child, during 2018-2023.

**Results.** The average age of the study participants was  $14.87 \pm 1.78$  years. The impact of obesity on menstrual function and the occurrence of hormonal imbalances is well known in the medical literature. In our study, 7 patients (4.67%) were overweight, 132 patients (88%) were diagnosed with grade I obesity, 8 patients (5.34%) with grade II obesity, and 3 patients (2%) with morbid obesity. The majority of the adolescent girls in the study were diagnosed with Polycystic Ovary Syndrome 35 (23.3%), with 22 (62.8%) of them presenting hyperandrogenism, manifested by elevated serum levels of testosterone, and 14 (40%) of them also showing clinical hyperandrogenism - hirsutism and acne. Oligomenorrhea affected 23 patients (15.3%), and secondary amenorrhea had affected 21 patients (14%), representing menstrual dysfunctions observed in the study participants with PCOS and obesity. Other hormonal imbalances were hyperprolactinemia in 12 patients (27.27%), hypoestrogenemia in 9 patients (20.45%), and hypothyroidism in 19 patients (43.18%). In 10 patients (52.63%), hypothyroidism was associated with hyperprolactinemia. The mechanism of menstrual dysfunction in the studied adolescents can be explained by the effects of thyroid function, hyperandrogenemia, and hyperprolactinemia on gonadotropic hormones, resulting in anovulation and prolonged menstrual cycles for over 45 days.

**Conclusion.** Obesity in adolescent girls is associated with a series of hormonal disorders and menstrual cycle dysfunctions, including hyperandrogenemia, hypothyroidism, hyperprolactinemia, oligomenorrhea, and secondary amenorrhea. Understanding these associations can be crucial for developing management strategies and appropriate interventions in treating reproductive health issues in these patients.



## 9. ETIOLOGY, PATHOGENESIS, DIAGNOSIS AND TREATMENT OF OVARIAN CANCER

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**Introduction.** The 5th most common cause of death among women is caused by ovarian cancer. According to the American Cancer Society, the risk of being diagnosed with ovarian cancer throughout life for women is 1 in 78. In the US, it is expected to be detected in 2023, 19,710 new cases of ovarian cancer and about 13,270 deaths from ovarian cancer.

**Aim of study.** To study and analyze the current articles on etiology, pathogenesis, diagnosis and treatment of ovarian cancer.

**Methods and materials.** This abstract was done by exploring and analyzing medical publications from PubMed, Medscape, NCBI, MEDLINE.

**Results.** Ovarian cancer is detected at an early stage only in 20-25%. Most often it is diagnosed in postmenopausal women. The primary risk factor is a family history of ovarian or breast cancer. First-line investigations include detection of CA-125 marker in blood and transvaginal ultrasonography. In addition, abdominal and pelvic CT, PET scanning and MRI of the pelvic region can be used to visualize the extension of the tumor. Currently, ovarian cancer treatment consists of combining surgery with chemotherapy. According to the latest data, laparoscopic surgery is preferred, as it is less invasive and has a faster recovery than debulking operations. Tumor progression and tumor recurrence occurs more frequently in advanced stages.

**Conclusion.** Currently, ovarian cancer remains one of the most common causes of lethality in women, the main cause being the lack of effective strategies for early detection of ovarian cancer. The latest studies show that median survival for stage 1 ovarian cancer is between 70% and 90%, and for stage 4 it is less than 6%.

## 10. GESTATIONAL DIABETES MELLITUS AND MACROSOMIA: MUNICIPAL CLINICAL HOSPITAL "GHEORGHE PALADI" EXPERIENCE



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**Introduction.** Gestational diabetes mellitus (GDM) is a metabolic complication during pregnancy. It is defined by the development of glucose intolerance, primarily diagnosed in pregnancy. According to literature between 15-45% of newborns of mothers with GDM are macrosomic. Fetal macrosomia (FM) is a term used for newborns with birth weight  $\geq 4000$  g.

**Aim of study.** To reveal the correlation between GDM and macrosomia, to discuss the diagnosis of macrosomia and therapeutic options.

**Methods and materials.** The retrospective study was conducted in the Obstetrics Department no.1 of Municipal Clinical Hospital "Gheorghe Paladi" during 2021 and 83 patients were selected. Evaluated parameters were: epidemiological data, type of GDM, maternal obesity, the birth weight of the newborns, gestational age, Apgar score, type of baby delivery.

**Results.** Mothers without GDM – 70 (84,33%), mothers with GDM – 13 (15,66%) with mean age 30,7 years. Among patients with GDM – 11 (84,61%) were with compensated form of GDM and 2 (15,38%) with decompensated form of GDM. Maternal obesity was attested in 16 (19,27%) cases, among them 5 (31,25%) delivered macrosomic newborn, 3 (18,75%) have maternal obesity associated with GDM and macrosomia and 1 (6,25%) – maternal obesity, GDM and normal weight newborn. Mothers without GDM and normal birth weight newborn – 62 (74,69%), mothers with GDM and macrosomic fetus – 9 (10,84%), mothers without GDM, but with macrosomic fetus – 8 (9,63%), mothers with GDM and normal birth weight newborn – 4 (4,81%). Newborns with birth weight  $<4000$  g – 66 (79,51%), newborns with birth weight  $>4000$  g – 17 (20,48%). The average birth weight of the newborns – 3932 g. The Apgar score rates were between 0/0 – 9/9. The most common rate of the Apgar score was 8/9 (30,12%), followed by 8/8 (26,5%), 9/9 (22,89%), 7/8 (10,84), 6/7 (4,81%), 5/6 and 0/0 (1,20% each of them). The macrosomia was established in 14 cases (82%) using ultrasound. Predictive values used to estimate fetal weight were biparietal diameter, head and abdomen circumferences, femur length. GDM was primarily diagnosed at 4 nulliparous (30,76%) and 2 multiparous (15,38%). Vaginal delivery was elected in 58 cases (69,87%) and C-section 25 times (30,12%). The most frequent indications for C-section are scarred uterus, placental detachment, diabetic fetopathy, fitopelvic disproportion, dynamic distocia.

**Conclusion.** Fetal macrosomia is a common complication among GDM patients. The correct management of glucose abnormality in the pregnancy will contribute to avoiding complications and will decrease the ratio of macrosomia.



## 11. HEMORRHAGE IN THE 3 STAGE OF LABOR AND POSTPARTUM. MOTHERS HEALTH.

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**Introduction.** Postpartum hemorrhage (PPH) is a major reason for maternal complications and deaths worldwide. The overall prevalence of PPH worldwide is estimated to be 6-11% of births with substantial variation across regions. It occurs due to issues in one of four fundamental processes, with uterine atony being the most prevalent. PPH is defined as blood loss exceeding 500 mL following vaginal birth and 1000 mL following cesarean. PPH is frequent and may happen in patients with no identified risk factors.

**Aim of study.** The study aims to investigate hemorrhage during the third stage of labor and postpartum, focusing on its impact on maternal health.

**Methods and materials.** For the study, available online medical platforms such as PubMed Databases, The Global Library of Women's Medicine, Scopus and other scientific libraries were analyzed. Were selected and analyzed 40 articles including case studies and reviews, published in the last 10 years.

**Results.** The most common etiology of PPH is uterine atony which occurs in about 80% of cases. Atony may be related to overdilatation of the uterus, infection, placental abnormalities or bladder distention. There are also clinical factors associated with uterine atony such as polyhydramnios, multiple gestation and prolonged labor, may lead to a higher index of suspicion. Other causes of PPH include retained placenta or clots, lacerations, uterine rupture or inversion, and inherited or acquired coagulation abnormalities.

**Conclusion.** In conclusion, the study highlights the substantial impact of hemorrhage during the third stage of labor and postpartum on maternal health. Addressing this issue is crucial for improving outcomes and necessitates ongoing research and effective intervention measures.



## 12. HOW TO BETTER LEARN HYPERTENSIVE DISORDERS OF PREGNANCY THROUGH SIMULATION IN REPUBLIC OF MOLDOVA



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**Introduction.** The incidence of hypertensive disorders of pregnancy (HDP) has been reported up to 5-9%, with a significant rate of subsequent preeclampsia (15%), eclampsia (2%), and a high rate of maternal /fetal mortality (up to 35%). In the last 3 years, 1019 cases of preeclampsia were assessed in the Republic of Moldova (RM), accounting for 11.7% of all admissions to the obstetric and gynecological intensive care unit. Hence, simulations were deemed necessary to obtain important information and practical skills in emergency obstetrics.

**Aim of study.** To assess the significance of simulation in enhancing understanding and practical skills in HDP.

**Methods and materials.** A total of 78 participants, consisting of 41 doctors (52.6%) and 37 nurses (47.4%), were surveyed during simulation training for obstetric emergencies at the Tertiary Perinatal Center in Chisinau, RM.

**Results.** During the simulation, 3 scenarios were presented. Pregnancy-induced hypertensive states were defined by: Systolic blood pressure (SBP)  $\geq 140$  mmHg and diastolic blood pressure (DBP)  $\geq 90$  mmHg (2 assessments, 4h interval) or DBP  $\geq 110$  mmHg (single assessment) at  $\geq 20$  weeks of pregnancy. Preeclampsia presented: SBP  $\geq 160$  mmHg and DBP  $\geq 110$  mmHg, also target organ signs. Eclampsia was identified by the appearance of convulsions. The objective examination was performed. The diagnosis was established based on the patient's history, BP, pulse, Fetal heart rate, US exams, and Doppler velocimetry on the uterine, umbilical, and middle cerebral arteries of the fetus and the ductus venous. The laboratory data were used. During the medical emergency simulation, the management of HDP included: MgSO<sub>4</sub> and antihypertensive therapy, as well as the way of delivery (mainly by C-section). All of the above mentioned were necessary to prevent possible complications, such as *abruptio placenta*, bleeding, fetal distress, prematurity, thrombotic complications, and fetal /maternal death. Almost all participants (96.2%) emphasized the importance of simulation in the learning of emergency obstetric conditions, specifically in cases of HDP.

**Conclusion.** HDP and preeclampsia are often associated with several complications, the mandatory treatment being the urgent termination of pregnancy (often by C-section). The simulation is a powerful tool in training doctors and nurses to handle HDP, and is a practical way to translate knowledge into real-life scenarios.

**Keywords.** Hypertensive disorders of pregnancy, preeclampsia, simulation.





### 13. IMMUNOLOGICAL PECULIARITIES AND THE SPECIFICS OF THE USE OF THERAPEUTIC OZONE IN WOMEN WITH THE RISK OF INFERTILITY

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**Introduction.** A quite specific problem regarding sexual and reproductive health that nowadays' society is facing is represented by infertility amongst young women. This condition can be caused by a myriad of pathologies, most noticeable of them being tubal occlusion, endometritis, vaginitis and ischemia of the ovaries leading to oocyte loss and damage towards the female reproductive organs, which eventually could lead to worse outcomes regarding fecundity rate. An adjuvant method could be the usage of therapeutical ozone. In small therapeutic doses ozone possesses the ability to dampen the chronic inflammatory response.

**Aim of study.** Ozone therapy may be proposed as a complementary method for fertility treatments incorporated in pre-conceiving preparation.

**Methods and materials.** To achieve the objective, the initial search of the specialized scientific literature, identified by the search engine Google Scholar and from the databases PubMed, NihGov was performed. The publications were selected according to the following keywords: „female reproductive health”, „fertility”, „ozone therapy”, „inflammation”. After processing the information in the databases, we selected all publications in English starting with January 2019.

**Results.** Following the conditions mentioned beforehand, a poor prognosis regarding female fertility might be concluded, yet the usage of therapeutic ozone might combat post pathological sequelae, thus reducing the infertility rate. The following mechanisms were proposed as ozone's effects on female reproductive organs: anti-inflammatory, bactericidal, fungicidal and virucidal, antioxidant effect, etc. In proximal obstruction, ozone has the potency to dissolve the mucus plug due to its oxidative properties yet preserving the healthy mucosal lineage of the salpinx. In distal tubule blockage that is caused mostly by bacterial infections, ozone can exert its bactericidal effects and reduce the bacterial titer, reduce inflammation by stimulation of IL-4, IL-10, IL-13, reducing IL-6, TNF-alpha and IF-gamma, reducing the oedema and facilitate the regenerative process of the salpinx. Regarding endometriosis and vaginitis, treatment and convalescence may be difficult. Ozone therapy might be used as a direct virucidal factor. In a 2019 study, 100 percent of infections with mycoplasmosis and chlamydiosis were eradicated. 13 out of 30 instances of ureaplasmosis and nineteen out of 21 cases of gardnerellosis were successfully treated. Out of 7 patients, 5 were cured of their CMV infection and herpes simplex. After three months of receiving ozone therapy in its entirety, eight out of fifty infertile women became pregnant.

**Conclusion.** Gynecological diseases have a paramount influence on reducing fertility rate in young females, thus a methodical treatment and prophylaxis approach should be undertaken. The use of therapeutical ozone may facilitate the recovery process and improve the chances of experiencing potential pregnancy, because of its vasodilator, antioxidant and anti-inflammatory actions.

## 14. INFECTIOUS COMPLICATIONS AFTER CAESAREAN DELIVERY



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**Introduction.** Cesarean delivery, also known as a C-section, is characterized by the delivery of a fetus through surgical incisions performed on both the abdominal wall (laparotomy) and the uterine wall (hysterotomy). Cesarean birth is crucial in some cases, but for most low-risk pregnancies, it poses a higher risk of morbidity and mortality compared to vaginal birth. Infections are a common complication following cesarean delivery. Puerperal infection refers to an infection in the genital tract, occurring during any stage of labor and extending up to the 42nd day postpartum, marked by two or more of these symptoms: incision pain, fever, purulent lochia, chills, and uterine subinvolution.

**Aim of study.** Analysis of aspects of etiology, diagnosis, treatment and impact of puerperal infections.

**Methods and materials.** Data from relevant articles from databases such as: NCBI, PubMed, Medscape, Oxford Academic were analyzed.

**Results.** The global caesarean section rate, as reported by the World Health Organization, is on the rise and now represents more than 1 in 5 (21%) of all births. In the Republic of Moldova, over the past decade, the incidence of cesarean section procedures has risen from 14.3% in 2010 to 19.7% in 2020. Despite its benefits, a caesarean section can be complicated by serious issues. The incidence of short-term complications following cesarean delivery includes: ileus (10-20%), endometritis (6-11%), wound complications (1-2%), massive hemorrhages (2-4%), surgical injuries (0.2-0.5%), and thromboembolism (240 per 100,000 births). Pre-existing maternal conditions such as malnutrition, diabetes, obesity, severe anemia, bacterial vaginosis, and group B streptococcal infections, along with factors like prolonged rupture of membranes, multiple vaginal examinations, manual placental removal, as well as cesarean section, were identified as significant contributors to puerperal infection. Successful management of puerperal and postpartum infections post-caesarean section necessitates a multidisciplinary approach that involves antimicrobial therapy, wound care, and abscess drainage

**Conclusion.** Accurate identification of risk factors and appropriate determination of indications for a caesarean section are pivotal for effective patient management in the postpartum period and for lowering the incidence of infectious complications



## 15. IS MENSTRUAL BLOOD A POSSIBLE SUSTAINABLE SOURCE OF STEM CELLS FOR REGENERATIVE MEDICINE?

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**Introduction.** Cells with mesenchymal stem cell properties have been discovered in menstrual blood and called menstrual blood-derived stem cells (MenSCs). They have been attracting more and more attention since their discovery in 2007 due to properties found such as: a greater proliferation and differentiation potential, painless collection process and lack of complex ethical concerns, thus making them a perspective tool in further clinical practice.

**Aim of study.** The objective of this study was to evaluate the latest advances in menstrual blood-derived stem cells (MenSCs) research and their application potential. Highlighting the main aspects in the stages of obtaining stem cells in the laboratory

**Methods and materials.** This study is a review of the literature, based on the synthesis of clinical studies published in the period 2007-2022, 40 scientific sources were researched. This article includes publications identified through Google Search Engines, PubMed Databases, etc. The information has been systematized, highlighting the most important aspects of the detection and use of menstrual blood-derived stem cells (MenSCs).

**Results.** The human endometrium is a dynamically remodeling tissue that undergoes monthly cycles of growth, differentiation and elimination approximately 400 times until menopause. Compared to stem cells from bone marrow and adipose tissues, MenSCs originate from body secretions and obtaining them is non-invasive to the body, easy to collect, and there are no ethical concerns. There is therefore a growing interest in the functions of MenSCs and their potential application in regenerative medicine.

**Conclusion.** In recent years, researchers have gained more interest in MenSCs due to their advantages. Menstrual blood collection and processing protocols need to be evaluated and refined and adapted to the conditions of the Tissue Engineering and Cell Culture laboratory.

## 16. ISOLATED FALLOPIAN TUBE TORSION ASSOCIATED WITH PREGNANCY: A CASE REPORT



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**Introduction.** Isolated fallopian tube torsion (IFTT) is a rare gynecologic emergency that requires a high index of suspicion and immediate surgical intervention. IFTT associated with pregnancy is a rare condition in the population. The etiologies of torsion of the fallopian tube are unknown. It is frequently misdiagnosed as acute appendicitis or ovarian torsion owing to the lack of specific symptoms or signs. Early diagnosis is essential to consideration of conservative management. Laparotomy and laparoscopy are important tools in the diagnosis and prognosis of isolated torsion of a fallopian tube, and can help to preserve the fertility of these patients.

**Case statement.** A 32-year-old secundipara was hospitalized at the Chisinau Municipal Hospital “Gh. Paladi” at 7 weeks of gestation with complaints of lower abdominal pain for 2 days. This pain was situated in the right lower abdomen. Vomiting and nausea were associated with the pain. The patient's vital signs were stable, and she was afebrile. Abdominal examination revealed a painful and soft abdomen. The uterus enlarged in volume, corresponding to the period of gestation. An ultrasonography showed a monofetal pregnancy, corresponding to the 7 weeks. An anechoic mass was observed in the right lower abdomen and free fluid in the abdominal cavity. A diagnosis of the right ovarian cyst was considered, and diagnostic laparoscopy was decided upon. The findings were as follows: free fluid in the abdominal cavity in volume 200 ml, isolated 360° torsion of the right fallopian tube had occurred at the proximal end of the isthmus, and part of the right tube from the isthmus to the fimbriae showed slightly cyanotic, without signs of necrosis. A detorsion of the right fallopian tube was performed. The patient was discharged on the seventh postoperative day in good condition.

**Discussions.** The incidence of fallopian tube torsion was 1/1.5 million women. Isolated twisted fallopian tube in pregnancy are very rare, with only 12% of cases being identified during pregnancy. Because the patient had a history of good health, the cause of tubal torsion may have been gravid uterus, hemodynamic abnormalities, or sudden body position changes. Other reports describe presentations with similar features to our patient such as lower abdominal/pelvic pain that radiates to the flank, nausea, vomiting. If, during exploratory laparoscopy, isolated fallopian tube torsion is confirmed, the surgeon should opt for conservative management or perform salpingectomy according to macroscopic characteristics, possibility of detorsion and signs of revascularization.

**Conclusion.** Fallopian tube torsion has nonspecific signs and symptoms that overlap with other gynecologic pathologies. Our case demonstrates the presence and absence of the various findings suggestive of tubal torsion. Early diagnosis and trying conservative management in this group of patients are essential.





## 17. LIPID PROFILE VARIATIONS DURING PREGNANCY

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**Introduction.** Variations in the maternal lipid profile during pregnancy are an absolutely normal phenomenon, this contributes to good fetal intrauterine development. Hyperlipidemia is appreciated more frequently starting with the 2nd trimester of pregnancy. Also, analyzing the variations of the lipid profile we can relate certain situations during pregnancy such as: gestational diabetes, intrauterine growth restriction, preeclampsia, and other pathological conditions.

**Aim of study.** The purpose of the study was to determine the variation of the maternal lipid profile, which includes total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TGs) during pregnancy.

**Methods and materials.** This is a prospective study with the participation of 50 pregnant women, in which the lipid profile variations were analyzed in each trimester of pregnancy.

**Results.** Following the tests performed on the women included in the study, we received the following data: for the first trimester of pregnancy, the average value of total cholesterol (TC) was  $4,36 \pm 0,51$  mmol/L, for triglycerides (TGs)  $1,18 \pm 0,29$  mmol/L, low-density lipoprotein (LDL)  $2,38 \pm 0,63$  mmol/L, and for high-density lipoprotein (HDL) the value was  $1,7 \pm 0,45$  mmol/L. The concentrations for the 2nd trimester of pregnancy came as follows: TC  $4,72 \pm 0,39$  mmol/L, TGs  $1,32 \pm 0,17$  mmol/L, LDL  $2,63 \pm 0,47$  mmol/L, and the level of HDL was  $1,83 \pm 0,35$  mmol/L. Towards the end of pregnancy, in most of the women included in the study, an increase in the level of TC  $5,65 \pm 0,43$  mmol/L, TGs  $1,7 \pm 0,27$  mmol/L, and LDL  $3,4 \pm 0,62$  mmol/L was reported, at the same time a significant decrease in HDL  $1,45 \pm 0,47$  mmol/L was detected. Respectively, during the entire pregnancy, an increase in serum concentrations of TC, LDL and TGs was detected, while the amounts of HDL increased from the 1st to the 2nd trimester with a slight decrease in the 3rd trimester.

**Conclusion.** Although, certain norms for the variation of the maternal lipid profile during pregnancy are not established. When there is a noticeable increase starting with the first trimester of pregnancy, above the normal value established for non-pregnant women in the concentration of total cholesterol, triglycerides, and low-density lipoprotein, most often these pregnancies are complicated with intrauterine growth restriction and gestational hypertension, and in case of consistently lower high-density lipoprotein level with gestational diabetes.

**Keywords.** Lipid profile; Pregnancy.



## 18. MANAGEMENT OF POSTPARTUM HEMORRHAGE



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**Introduction.** Postpartum hemorrhage (PPH) is defined as a blood loss from the genital tract of  $\geq 500$  mL associated with vaginal delivery or greater than 1000 mL following cesarean section, which requires emergency hysterectomy in severe cases. PH is classified as Primary if bleeding occurs within the first 24 h following delivery of the fetus. Secondary PPH occurs between 24 h and 12 weeks post-delivery. According to WHO, each year about 14 million women experience postpartum hemorrhage resulting in about 70.000 maternal deaths globally

**Aim of study.** Review of the risk factors and management of hemorrhage after delivery.

**Methods and materials.** Current review is based on articles published in the online databases as FIGO, PubMed, Medscape, mdpi.com, ScienceDirect using the Key words: “ postpartum hemorrhage”, “maternal morbidity”, “bleeding after childbirth”, “retained placenta” .

**Results.** This birth complication affects 2–4% of vaginal and 6% of cesarean deliveries. Common causes include uterine atony, retained placenta, trauma and coagulopathy. Therefore, women experiencing postpartum hemorrhage are vulnerable to hemorrhagic shock, blood transfusion, infertility secondary to hysterectomy. The effective management of PPH requires prompt recognition. Uterine atony causes 70-80% of PPH. Atony is suspected first and requires immediate medical intervention including: uterine massage, uterotonics (misoprostol, oxytocin, methylergometrin), Bakri ballon, tranexamic acid, intravenous fluids, B-lynch suture. To prevent PPH, a uterotonic drug is administered during the 3rd stage of labor in all births. Retained placental tissue is a cause which occurs in 1–3% of deliveries and increases the incidence of PPH by 3.5 times. Genital tract trauma accounts for 15% of cases. Over 85% of women who have a vaginal delivery will sustain perineal trauma. Performing examination of the genital tract is necessary to identify any trauma to the cervix, vagina or perineum to prevent significant blood loss. Coagulation disorders, both inherited and acquired, are reported in approximately 1% of PPH. Identification and correction of any coagulopathy could improve the outcome.

**Conclusion.** Postpartum hemorrhage affects 1% to 10% of pregnancies. Taking the above information into consideration, identification of risk factors antenatally, suitable management of the 3rd stage of labor, appropriate patient monitoring and hemostatic interventions based on protocols are important, because the postpartum hemorrhage is the direct cause of mortality, accounting for 27.1% of maternal deaths worldwide.



## 19. MANAGEMENT OF UTERINE FIBROIDS AND ITS COMPLICATIONS DURING PREGNANCY

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**Introduction.** Uterine fibroids are a very common finding in women of reproductive age. The major complication of myomas in pregnancy is recurrent pain, however, miscarriage is the main threat. The negative impact of fibroids on the course of pregnancy may also result in uterine bleeding, preterm labor, placenta abruption, cesarean delivery, higher incidence of maternal-fetal incommunicability, an incorrect position of the fetus and its deformities.

**Aim of study.** Studying the evolution of uterine fibroids in pregnancy to highlight the most common complications. Analyzing the screening, diagnosis, and treatment criteria to reveal their effect on maternal and neonatal outcomes.

**Methods and materials.** A systematic review of the literature was performed, using the databases PubMed, Google Scholar, Hinari, and NCBI, to identify relevant articles, concerning "uterine fibroids", "pregnancy", and "complications". This review represents an analysis of actual information on the publication from the last 5 years.

**Results.** Several studies have shown that women with uterine fibroids have a higher risk of imminent premature labor, premature rupture of the amniotic membranes, insufficient contraction forces, and hypotonic hemorrhage. Most authors point out that uterine fibroids favor primary or secondary insufficiency of the birth activity. The complicated evolution of pregnancy and birth determines the high frequency of surgical interventions and obstetric procedures in pregnant women with uterine fibroids. Among the indications for cesarean section, uterine fibroids constitute about 0.4 - 0.8%. If the fibroids are small, birth can occur naturally, but if the fibroids are large and have a topography that affects the mechanism of birth, then a cesarean section is required. At the same time, cesarean section in the presence of uterine myoma can be completed by expanding the volume of the intervention (myomectomy, hysterectomy).

**Conclusion.** Analyzing the selected publications, we concluded that observational studies have shown that uterine fibroids in pregnancy may be associated with complications affecting the course of pregnancy and labor. So, pregnancy must be cautiously monitored in the antenatal period, through regular follow-up.

## 20. MEDICAL AND SOCIAL PATTERNS OF PELVIC INFLAMMATORY DISEASE IN THE REPUBLIC OF MOLDOVA



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**Introduction.** Pelvic inflammatory disease (PID) represents a significant medical and social problem. It encompasses conditions such as endometritis, salpingitis, hydrosalpinx, pyosalpinx, and tubo-ovarian abscess. The etiology is often polymicrobial, caused by *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in about 40% of cases. PID frequently presents with urinary and gastrointestinal clinical signs, raising a diagnostic dilemma that often requires confirmation through various imaging investigations, including US exam, computed tomography, magnetic resonance imaging, hysterosalpingography, and laparoscopy.

**Aim of study.** To analyze the medical and social determinants, and the diagnostic imaging characteristics of PID.

**Methods and materials.** A number of 644 PID clinical cases, admitted at the Septic Gynecology Unit, Tertiary Perinatal Center, were assessed. The social and medical characteristics, as well as the diagnostic tools were evaluated in establishing and confirming PID.

**Results.** Age of the patients ranged from 18 to 52 years, with an average age of  $27.4 \pm 0.3$  years. The initiation of sexual activity under the age of 17 was noted in 68.9% of cases, often associated with multiple partners and unprotected sexual intercourse (58.4%). Approximately 23.6% of patients reported inadequate intimate hygiene. A failure to seek medical attention upon symptom onset was reported by 59.2% of women. Regrettably, 129 patients (20.0%) reported to have an intrauterine device for more than ten years. A history of medical intrauterine interventions and/or clinical procedures in the pelvic cavity were reported by 11.0% of participants. Late hospitalization occurred in 71.9% of cases. The imaging methods used for diagnosis in all cases showed a 95% sensitivity, 89% specificity and 93% diagnostic accuracy. Signs of salpingitis (such as thickened fallopian tubes  $>5\text{cm}$  – the "cogwheel sign," incomplete septa, and peritubal inflammatory fluid) were determined. Hydrosalpinx was characterized by echogenic walls with fine visibility, incomplete septa and the persistence of intraluminal structures – the "pearls on a string" sign. Pyosalpinx was identified by echogenic fluid content with pronounced shadowing, thickened walls and hydroaeric levels. Tubal obstruction was presented as a hitch to the contrast material flow through the fallopian tubes. Oophoritis was indicated by enlarged ovaries with a polycystic appearance.

**Conclusion.** PID is characterized by distinctive medical and social patterns. The imaging exams allow us to appreciate the location and spreading of PID in the pelvic cavity, acting as an important tool in the decision-making process.

**Keywords.** Pelvic inflammatory disease, salpingitis, hydrosalpinx, pyosalpinx, US exam.



## 21. METHODS OF TERM LABOR INDUCTION FOR WOMEN WITH A PREVIOUS CAESAREAN SECTION

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**Introduction.** The term pertains to diverse methodologies employed for the initiation of parturition in gravid individuals who have previously had a cesarean section(c-sec) and have reached the full term gestational period. The objective is frequently the facilitation of a vaginal birth subsequent to a prior cesarean (VBAC). Women with a c-sec history may elect to pursue a VBAC for next pregnancy, the instigation of labor becomes imperative to commence the parturient process. In case of induction for VBAC, there is a risk of uterine rupture, marked by the tearing of the scar tissue from the last c-sec during contractions.

**Aim of study.** This research aims to explore and evaluate different methods used to start labor in pregnant individuals who have had a c-sec and are at full term pregnancy. The focus of this review is to describe techniques that may be applied with no or minimal sequelae for both mother and fetus.

**Methods and materials.** In leading this literature review, I used 16 articles from PubMed, ScienceDirect database to explore crucial terms like "VBAC", " Labor induction in women with prior c-sec," "Outcomes in VBAC induction".

**Results.** Exploring the literature reveals rich insights into diverse labor induction methods and their respective effects on both maternal and fetal outcomes. 1. In comparing vaginal PGE2 to intravenous oxytocin in a trial with 42 women, there were no vast differences in terms of c-sec risk (RR 0.67, 95% CI 0.22 to 2.03, low-quality evidence) or serious neonatal and maternal morbidity or death (RR 3.00, 95% CI 0.13 to 69.70, evidence graded low). Notably, no clear distinctions were observed for reported secondary outcomes. 2. In a trial involving 38 women, a comparison between vaginal misoprostol and intravenous oxytocin was prematurely halted due to a uterine rupture in one woman who received misoprostol (RR 3.67, 95% CI 0.16 to 84.66) and uterine dehiscence in another. Unfortunately, no additional outcomes, including GRADE outcomes, were reported in the trial. 3. In a trial involving 200 women, comparing vaginal PGE2 pessary to vaginal PGE2 tablet showed no significant disparity in c-sec rates (RR 1.09, 95% CI 0.74 to 1.60, very low-quality evidence) and other reported secondary outcomes.

**Conclusion.** This review on VBAC labor induction methods prioritizes safety for both mother and fetus. While trials offer insights into induction agents, data gaps, particularly in critical outcomes like achieving vaginal delivery within 24 hours and assessing uterine hyperstimulation, underscore the need for more research and standardized reporting to advance evidence-based practices.



## 22. OVARIAN FUNCTION IN WOMEN OF REPRODUCTIVE AGE AFTER HYSTERECTOMY



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**Introduction.** As a core reproductive organ, the ovary has two distinct functions, producing mature oocytes for fertilization and secreting sex hormones to sustain the normal activities of multiple organs.

**Aim of study.** Ovarian function after hysterectomy has been a focus of research by various authors over many years. However, the nature of changes in the hormonal profile, their chronological sequence, the issue of prognosis and possible preventive measures remain contradictory and fragmentary. This lack of clarity prompted the initiation of this research. The aim of this study was to analyze the function of the ovaries after hysterectomy due to benign gynecological causes in women of reproductive and premenopausal age.

**Methods and materials.** The current study is based on a prospective analysis of 25 cases involving hysterectomy without ovariectomy in women of reproductive and premenopausal age. The control group comprised 25 healthy women of similar age to the research group. To assess the ovarian function, the serum level of follicle-stimulating hormone (FSH), estradiol (E2) and anti-Mullerian hormone (AMH) were measured preoperatively, on the 10-12th postoperative day, and at 6 and 12 months postoperatively.

**Results.** Although the initial preoperative level of AMH in the research group ( $1.63 \pm 3.36$  ng/ml) was higher compared to the control group ( $0.69 \pm 0.52$  ng/ml) hysterectomy had a negative impact on ovarian function, resulting in a noticeable decrease in AMH level at 6 and 12 months postoperatively ( $0.39 \pm 0.22$  and  $0.33 \pm 0.32$  ng/ml, respectively). The serum level of E2 has an insignificant decreasing trend in the research group (from  $137.49 \pm 60.91$  pg/ml preoperatively, to  $124.48 \pm 9.99$  pg/ml on the 10-12th postoperative day, and respectively  $119.35 \pm 21.66$  pg/ml at 6 months and  $133.46 \pm 50.12$  at 12 months postoperatively). However, it recorded a non-significantly lower level compared to the control group ( $139.90 \pm 38.17$  pg/ml). The preoperative serum FSH level in women undergoing hysterectomy was  $14.09 \pm 11.46$  IU/l, representing higher values compared to the control group ( $8.62 \pm 3.49$  IU/l). Postoperatively, on the 10th-12th day, serum FSH level was  $12.03 \pm 13.75$  IU/l, at 6 months the highest level was  $18.61 \pm 15.26$  IU/l, and at 12 months postoperatively, it was  $12.72 \pm 8.92$  IU/l.

**Conclusion.** This study aimed to investigate the impact of hysterectomy on ovarian function. The results indicate a significant decrease in ovarian reserve within the first year after the intervention. Counseling, coupled with appropriate hormonal support emerges as a potential strategy to enhance the quality of life of these patients.





## 23. PERINATAL OUTCOMES IN PREGNANCY WITH GESTATIONAL DIABETES

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**Introduction.** Gestational diabetes mellitus (GDM) traditionally refers to abnormal glucose tolerance with onset or first recognition during pregnancy. The increasing obesity rate is leading to an increase in gestational diabetes mellitus (GDM) and perinatal complications. Global GDM rates have increased due to the obesity epidemic, highlighting the need for comprehensive research on its implications for perinatal health.

**Aim of study.** This, therefore, purposes to assess the perinatal outcomes and most specifically the gestational diabetes effects. The assessment will explore the incidence rates for macrosomia, neonatal care needs, and the impact of improved outcomes through strategies related to glycemic control.

**Methods and materials.** To these substantiations, databases were screened in Google Scholar and PubMed according to the standards and recommended rules of the American Diabetes Association, with an eye on the publication of the last ten years.

**Results.** The study found a significant link between gestational diabetes and increased macrosomia risk in pregnancy, indicating that neonates require more care. Strict glycemic control reduces risks, making it a key factor in GDM treatment.

**Conclusion.** In fact, gestational diabetes significantly influences perinatal outcomes with increasing risks of macrosomia, which requires neonatal care at an advanced level. This, therefore, increases the importance of uniform glycemic management guidelines in GDM-affected pregnancies to optimize perinatal health. Further research should, therefore, aim at polishing exact glycemic targets and concurrently explore innovative means of managing it in order to improve outcomes for both the mother and offspring.

## 24. POSTPARTUM SPONTANEOUS HEMOPERITONEUM AND ENDOMETRIOSIS – CASE REPORT



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**Introduction.** Spontaneous hemoperitoneum in pregnancy (SHiP) is characterized by unprovoked intraperitoneal bleeding with an incidence rate of 1:10000 pregnancies. Endometriosis represents one of the main risk factors and it is associated with 55.9% cases of SHiP.

**Case statement.** A 37-year-old primipara was admitted for spontaneous labor at 40+4 weeks of gestation. She had a normal pregnancy with no history of endometriosis. The complications occurred in the second period of labor, manifested with acute fetal distress, therefore a rapid vacuum extraction was performed and a boy was born with an Apgar score of 8/8 points. About 10 h after the delivery, the patient complained of abdominal distension, she became tachycardic and hypotensive, the hemoglobin value dropped to 91 g/l. During transabdominal sonography it was noticed free peritoneal fluid. The patient was taken to OR for a laparotomy, intraoperative was detected with a hemoperitoneum of  $\approx 1700$  ml. The endometrial tissue was on the posterior surface of the uterus with active venous bleeding. The local area had a blue to purple discoloration measuring 2 cm  $\times$  1 cm. Hysterectomy was performed. Total blood loss was  $\approx 3500$  ml. Histopathology of the bleeding site was consistent with endometriosis, characterized by decidualization of the lesion and glandular structures. The patient was discharged on the 16th postoperative day without complications.

**Discussions.** Brosens et al. in 2009 reviewed all cases of SHiP described since 1987, during the study he noticed that SHiP was associated with endometriosis in  $> 50\%$  of cases. However, one-third of the endometriosis-associated SHiP cases had no history of endometriosis. In the latest review of 59 cases in 2017, the maternal death rate was 1.7%. Current hypothesis suggested that decidualization, chronic inflammation, and preexisting adhesion of endometriosis play a role in SHiP development. Physical efforts were reported as the triggering factor of SHiP, such as pushing during labor and the use of vacuum extraction. Due to the difficulty of diagnosis and the frequent presentation of unstable maternal hemodynamic conditions, surgical intervention is unavoidable in most SHiP cases. The main choice of surgical approach is laparotomy. Common bleeding sites in SHiP include the serosa of the posterior wall of the uterus, the broad ligaments, or the uterosacral ligaments.

**Conclusion.** SHiP is a rare but dramatic cause of maternal mortality and morbidity. The pelvic endometriosis may play an important role in the pathogenesis of SHiP. Management requires a multidisciplinary approach with early surgical intervention and fluid optimisation for appropriate intravascular volume replacement.



## 25. PRENATAL DIAGNOSIS OF FETAL FACIAL ABNORMALITIES IN THE FIRST TRIMESTER OF PREGNANCY

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**Introduction.** The fetal face is a complex anatomical structure due to its embryological elaborate development and represents an important key for fetal conditions and syndromes. Changes in the embryological development may lead from simple appearance deformities to serious conditions that may be very dangerous for the fetus' life.

**Aim of study.** Since three-dimensional (3D) and four-dimensional (4D) ultrasonography (US) started being used, remarkable progress has been made in the prenatal diagnosis of fetal facial anomalies, developing a new area named sonoembryology.

**Methods and materials.** We performed a search in the PubMed literature, regarding the ultrasonographic diagnostic tools for prenatal diagnosis of fetal face anomalies in the first trimester of pregnancy. The terms that we seek were: “two-dimensional ultrasonography”, “three-dimensional ultrasonography”, “four-dimensional ultrasonography”, “fetal face” and “anomalies”. We made a comparative essay between the ultrasonographic devices but also the Magnetic Resonance Imaging (MRI) tool that are used for the assessment of the fetal face conditions.

**Results.** The use of 3DUS and 4DUS is clearly superior to 2DUS for the first trimester evaluation of the fetal face structures and facial movements. MRI helps the assessment of fetal palate, cerebral structures and micrognathia. The diagnosis of fetal face malformations and various syndromes have become possible since the first trimester due to 3DUS and 4DUS but their treatment is still controversial.

**Conclusion.** Three-dimensional ultrasonography and four-dimensional ultrasonography allows the prenatal diagnosis of fetal cranial-facial anomalies. Moreover, it represents an important tool in the assessment of fetal neurobehaviour.

**Keywords.** Three-dimensional ultrasonography, four-dimensional ultrasonography, fetal facial anomalies, fetal neurobehavior.

## 26. PROFILE OF WOMEN WITH PREGNANCY ACHIEVED THROUGH IN VITRO FERTILIZATION



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**Introduction.** Pregnancy obtained through In Vitro Fertilization (IVF) has increased to 3-5% of all births worldwide. This is due to increasing infertility in couples as well as the development of fertilization techniques, which have become more affordable. Although major progress is being made in this area, the service remains quite expensive and the success of the procedure does not depend solely on medical technology.

**Aim of study.** Analysis of the profile of the women who obtained the pregnancy through the in vitro fertilization procedure.

**Methods and materials.** A retrospective study was conducted in which the profiles of 100 women with pregnancies achieved through IVF were analyzed.

**Results.** The mean age of the patients included in the study was  $33.1 \pm 4$  years. Most frequently they were from urban environment - 86%, had higher education - 67%. Primary infertility with a mean period of  $6.5 \pm 3$  years was the main cause for accessing IVF services - 69%. The participants in the study did not have a major health problem, in 86% of cases infertility was the only reason for seeking medical services. Prior to the IVF procedure, patients had multiple investigations: laparoscopies - 43% cases, hysteroscopies - 14%, tubal patency tests - 44%. The most common cause of infertility was tubal impermeability - 70% and post-intervention tubal lack - 8% cases.

**Conclusion.** Women with infertility who achieved pregnancy through IVF are those aged after 30. Fallopian tube damage remains one of the main causes of infertility, and the long period of infertility is indicative of the effort involved in achieving pregnancy.



## 27. SIMULATION AS AN EFFICIENT TRAINING TOOL IN OBSTETRIC EMERGENCIES

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**Introduction.** Despite the era of high-tech medicine, high quality obstetric management requires a good collaboration between multidisciplinary professionals based on the improvement and acquisition of knowledge and practical skills. Simulation is a great method of transposing clinical cases in practice, as it allows the acquisition of knowledge through communication and error management.

**Aim of study.** The Aim of the study was to assess the efficiency of simulation and its impact on multidisciplinary teamwork in obstetric emergency service providers training

**Methods and materials.** 196 people were part of an obstetric emergencies simulation training program. The program was based on the "at the patient's bedside" principle and included 18 courses that lasted 3 days each within the Simulation Center. 78 people were surveyed, of which 41 doctors (52.6%) and 37 nurses (47.4%). The teams included specialists that were subjected to five scenarios. The cognitive learning model was based on factual articulation and conceptual articulation. To assess the degree of satisfaction, the participants completed an anonymous survey, which included 43 questions.

**Results.** Participants highlighted a general interest in simulation training in 76 cases (97.4%). Despite the initial reservations in 37 trainees (47.3%), at the end of the training all the surveyees described it as "a positive experience, which must be repeated at least once a year". The simulation consisted of briefing, simulation, and debriefing. The trainees were monitored by video and audio. Structured and constructive feedback was provided while encouraging assertive and non-judging communication. The mutual emotional support was emphasized in 74 cases (94.9%), in particular the importance of communication. During each scenario the team developed the standard management, being able to perform it repeatedly afterwards to strengthen their skills and reinforce the quality of the communication process. All participants specified that the proposed scenarios were well adapted and have greatly facilitated the learning process. According to 76 people (97.4%), there was an improvement in team dynamics, but the majority expressed the need for a leader (75 cases – 96.2%). 77 participants (98.7%) conveyed the importance of simulation as a training process and 75 people (96.15%) underlined its positive impact in dealing with obstetric emergencies. Simulation was proven to be an essential training specialists tool. Moreover, in 68 cases (87.2%), participants believe that the acquired skills will improve the workplace yield.

**Conclusion.** Simulation training led to better obstetric emergencies management through teamwork and correct decision making. It implemented the acquired theoretical knowledge through practical and communication skills development. The importance of communication while working in a multidisciplinary team was determined, with repeated simulation training serving as a model for continuing education.



## 28. THE IMPACT OF OBESITY ON PREGNANT WOMEN AND FETUS



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**Introduction.** Obesity is a condition characterised by excess of body fat and low body mass (BMI  $\geq 30$ ). Statistics show that more than 50% of obese and overweight people in Europe are overweight, 26.5% of women of reproductive age are overweight, about 40.4% are obese and about 10% are morbidly obese.

**Aim of study.** Review of data on the management and complications of maternal and fetal obesity in pregnancy.

**Methods and materials.** All relevant information was obtained from literature review from the open access databases as Cambridge Journals Online, PubMed, Medscape, ScienceDirect, using the Key words: “gestational obesity”, “obesity in pregnancy”, “gestational diabetes”, “gestational hypertension”.

**Results.** Pregnant women with BMI  $>30$  kg/m<sup>2</sup> can suffer from a variety of complications, including: gestational diabetes 3-4.6 times more often than patients with BMI  $< 30$  kg/m<sup>2</sup>, increases the risk twice of developing gestational hypertension, 2-4 times the risk of developing pre-eclampsia and 4 times the risk of developing venous thromboembolism. Maternal obesity is associated with the risk of congenital malformations to the fetus, such as heart defects, neural tube defects (1.7 times), urinary tract and renal anomalies and increased risk of delivering infants with macrosomia (37%). Also, the risk of stillbirth increases 2.1 times. Some studies show that 11-20% of stillbirths were a consequence of maternal obesity. BMI  $> 30$  kg/m<sup>2</sup> without other additional factors is not an indication for caesarean section. Also, the risk of infection is 2.4 times higher in caesarean section than patients with BMI  $< 30$  kg/m<sup>2</sup>.

**Conclusion.** We note that obesity among women of reproductive age is encountered quite often (up to 44%), knowing the risks and consequences of obesity on pregnant women and fetus we can say that these patients require more attention during pregnancy, labor and postpartum period.



## 29. THE INFLUENCE OF PREGNANCY ON THE EVOLUTION OF UTERINE MYOMA

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**Scientific advisor:** Marian-Pavlenco Angela, MD, PhD, Associate Professor, Obstetrics, Gynaecology and Human Reproduction Discipline, Obstetrics and Gynaecology Department, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Uterine myoma is a benign, hormone-dependent tumor that occurs more frequently in women aged 25-45. It comprises 30-35% of all gynecological diseases with a correlation between pregnancy and uterine myoma.

**Case statement.** The 27-year-old patient was admitted on 11.12.2023 to the Aseptic Gynecology department with complaints of pain in the hypogastric region, bloody vaginal discharge. She noticed a rapid increase of the abdomen over a month. Ultrasound revealed 6 weeks of pregnancy, a giant myomatous nodule type 3-5 FIGO on the postero-lateral uterine wall. During the gynecological examination, the uterus increased up to 16-17 weeks of gestation due to myomatous nodules. Considering the data of the gynecological examination, USG, patient's symptoms, manual vacuum aspiration was performed. Two days later, the patient developed a fever of 38.0°C. Despite antibiotic and anti-inflammatory treatment, there was no improvement. On 18.12.2023 she was hospitalized with the diagnosis of endometritis after abortion by vacuum aspiration. Giant myomatous nodule type 3-5 FIGO. Anemia grade II. Ultrasound revealed a giant uterine myoma with hemorrhagic degenerative changes, with a compressive effect on the uterine cavity, urinary bladder and intestinal loops.

**Discussions.** Surgical treatment was decided and a conservative myomectomy was performed. Intraoperatively, a 16-17 weeks gestation uterus was visualized with a 11x12x13 cm myomatous nodule type 3 FIGO showing signs of ischemia. The nodule was enucleated without entering the cavity and the wound was sutured in 3 layers. The specimen was sent for histopathological examination.

**Conclusion.** Uterine myoma are more frequently detected during pregnancy due to increased ultrasound usage and maternal age. Pregnancy influences the evolution of myomatous nodule through the reorganization of uterine hemodynamics, leading to their size increase. One of the severe complications can be necrosis of the nodule.

### 30. THE PECULIARITIES OF THE PSYCHOLOGICAL PROFILE IN THE PERINATAL PERIOD IN PREGNANT ADOLESCENTS



**Author:** Valache Mădălina; **Co-authors:** Budianu Cătălina, Leșco Dorina

**Scientific advisor:** Iliadi-Tulbure Corina, MD, Associate Professor, Obstetrics and Gynecology Department, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova; Jubîrcă Svetlana, PhD

**Introduction.** The mental health of pregnant women has long been a focus of reproductive health. Pregnant adolescents, being an important link, are at greater risk of developing reproductive health problems. To be able to support the health and well-being of pregnant adolescents it is essential to have a comprehensive understanding of the mental health issues they face during pregnancy.

**Aim of study.** The overall birth rate among adolescents has declined over the past two decades - from 56 births/1000 to 43.9/1000 - but this decline has been slower in low- and middle-income countries. In an analysis of Demographic and Health Survey data from 30 low- and middle-income countries, the proportion of all new-borns with adolescent mothers varied between countries with an average of 18% for young people under the age of 20.

**Methods and materials.** The study was carried out in the Level III Perinatal Centre, IMSP Institute of Mother and Child, where 261 patients were evaluated, divided into two groups: group no. 1 with age 13 - 18 years 11 months 29 days - 126 (48.3%) of patients and group no. 2 comprising adult pregnant women aged 19 - 25 years - 135 (51.7%) of patients. The Symptom Checklist - 90 (SCL-90) questionnaire was used to analyze the peculiarities of psychological status. This is a widely applied self-report instrument to assess a wide range of mental disorders, through the following symptoms: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. It also includes three global indices of psychological distress: Global Severity Index, Distress Index for Positive Symptoms, and Total Positive Symptoms. Analysis of the data obtained was performed using Microsoft Office Excel and EpiInfo 7.1 software.

**Results.** A statistically significant higher frequency in the intensity of psychological symptoms was identified in pregnant adolescents. Thus, in pregnant adolescents, a somatization index of 0.83, a level of interpersonal sensitivity index of 0.86, a depression index of 0.78, an anxiety index of 0.76, a phobic anxiety index of 0.68, a level of paranoid ideation index of 0.77 and a level of psychoticism index of 0.55, compared to the level of the same indices in adult pregnant women: 0.71, 0.64, 0.63, 0.56, 0.48, 0.55, 0.33, these data having a statistical significance  $p < 0.05/0.01$ . Prenatal Depression (PD) occurred in 94 (55.95%) cases in the adolescent group, compared to 74 (54.8%) cases in the adult pregnant group. The severity of psychological impairment in pregnant adolescents who suffered from PD is manifested by elevation of the indices: obsessive-compulsive  $p < 0.004$ ; anxiety  $p < 0.02$ ; oscillatory  $p < 0.04$ ; phobic anxiety  $p < 0.04$ ; paranoid ideation  $p < 0.006$ ; psychoticism  $p < 0.01$ . In pregnant women aged 19-25 years with PD, elevated indices were identified: anxiety  $p < 0.002$ ; phobic anxiety  $p < 0.009$  and psychoticism  $p < 0.005$ . Postpartum, the study shows that the severity of psychological symptoms increases in both groups investigated, but the more significant increase prevails in the group of pregnant teenagers.

**Conclusion.** The psychological profile during pregnancy is affected in both adult and adolescent women, the former being much more vulnerable during the perinatal period, which directly influences the bearing of the psychological consequences of pregnancy.



### 31. THE PRINCIPLES OF THE "FAST TRACK" PROGRAM IN OBSTETRICAL EMERGENCIES

**Author:** Vasilachi Cristian

**Scientific advisor:** Friptu Valentin, MD, PhD, Professor, Head of Obstetrics, Gynaecology and Human Reproduction Discipline, Obstetrics and Gynaecology Department, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

**Introduction.** Currently, the trend of contemporary surgery is to ensure a perioperative result of an increased quality, with the reduction of the stressful impact of the surgical act on the internal homeostasis of the human body. In Urgent Obstetrics, this element is very important, given the fact that it involves a pregnant patient, whose birth requires a quick solution, while ensuring, at the same time, high-performance results. It is exactly at this stage, when the ERAS (Enhanced Recovery After Surgery) programs steps in, especially "Fast Track" protocols. Given the specificity of these programs (they can be applied mainly in scheduled interventions), it is desired to determine those principles and manipulations, provided by them, which can also be useful during urgent interventions. The purpose of this study is to evaluate the procedures of the ERAS programs that can be applied in urgent obstetric situations, which would have a significantly better effect on the body of both the mother and the fetus; the conditions in which they can be applied and their efficiency, in order to ensure perioperative results of an increased quality.

**Aim of study.** As for now, there exist different ERAS Society guidelines for perioperative care in obstetrics, regarding interventional delivery, that provide best practice recommendations in each phase of medical care, but almost all of them are implementing practice principles that could be used only in scheduled interventions. In the meantime – the efficiency and applicability of those are questionable regarding fast birth delivery, via cesarean surgical intervention. Thus it is extremely important to create a „focused” pathway process for urgent ERAS Cesarean Delivery, starting from „decision to operate” (up to 30 min before skin incision) – to hospital discharge, and therefore postpartum monitoring.

**Methods and materials.** There was made a literature review, including recent studies made between 2017 - 2023, regarding the applicability of prophylaxis and treatment options, used in programmed cesarean delivery, that could be used in emergency surgical - birth solutions. Titles and abstracts were analyzed to identify potentially relevant articles. Meta Analysis, systematic reviews, randomized controlled studies, nonrandomized controlled studies, reviews, and case series were considered for each individual topic.

**Results.** Guidelines for perioperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations, that were demonstrated as grade A : Antibacterial prophylaxis is mandatory less than an hour before skin-incision Use of body-warm solutions and increased operating room temperature results in better post-operative recuperation Special cesarean delivery surgical techniques do not improve the final outcome, in comparison with the traditional ones Perioperative fluid management should be done using the 2 : 1 coefficient, regarding the overall blood loss Regardless of the fetal status – immediate neonatal resuscitation team is mandatory Use of analgesic potentiators is essential, in order to reduce the need of morphine derivated drugs Early patient mobilization (4h after cesarean delivery) results in faster recuperation of self-care and child-care activities

**Conclusion.** We are looking to detect optimized perioperative conduct methods, to elaborate a guideline, in order to improve the surgical result of obstetrical patients, increase the efficiency of the medical act, reduce its costs and enhance the trust level of citizens towards the local health system.



## 32. THE ROLE OF ENDOMETRIAL BIOPSY IN THE DIAGNOSIS OF ENDOMETRIAL HYPERPLASIA



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**Introduction.** Endometrial hyperplasia (EH) is a pathological process of the uterine mucosa characterized by gland proliferation and an increase in the gland-stromal ratio, which develops as a result of excessive estrogenic stimulation with a relative deficiency of the counterbalancing effects of progesterone. The actuality of the problem is due to the increasing prevalence of endometrial cancer, the precursor of which is endometrial hyperplastic processes. There are 2 types of EH: EH without atypia (usually not neoplastic) and EH with atypia (neoplastic, also referred to as endometrial intraepithelial neoplasia). EH is manifested by abnormal uterine bleeding in the form of heavy or intermenstrual bleeding with or without a regular menstrual cycle. The diagnosis of EH requires morphologic verification. Endometrial biopsy can be obtained by: Uterine dilation and curettage; Hysteroscopy; Pipelle biopsy; Histological examination post hysterectomy. According to the American College of Obstetrics and Gynecology (ACOG) hysteroscopy is considered the gold standard, it allows a clear visualization of the uterine cavity and focal lesions, which can be biopsied.

**Aim of study.** The purpose of this study was to analyze the results of histopathological examination of endometrial tissue obtained by endometrial biopsy in people with suspected endometrial hyperplasia.

**Methods and materials.** Our clinical research represents a retrospective study based on 433 case histories analysis of patients with suspected EH, who underwent the endometrial biopsy obtained by dilatation and curettage procedure, admitted in the Department of Gynecology of the Gheorghe Paladi Municipal Hospital during the 2022 year.

**Results.** As a result of the study, it was found that EH without atypia was identified in 42% cases, and it is the most frequent endometrial pathology in any age group, endometrial polyp was diagnosed in 30% cases. EH with atypia was identified in 13% cases, in women over the age of 50. In 15% cases, pathomorphological diagnosis was not made due to insufficient material in the scrape. The prevalence increases with age: from around 1% for those aged <25 years to >41,57% in those aged 45 years or over.

**Conclusion.** Thus, our study confirmed the high significance of diagnostic endometrial biopsies for determining the causes of abnormal uterine bleeding and diagnosing EH. Even though dilatation and curettage is considered the traditional method of diagnosis for EH, it should be replaced by techniques, with superior diagnostic accuracy.





### 33. TINY SEEDS, MIGHTY STRUGGLES: PREGNANCY EVOLUTION IN INTRAUTERINE GROWTH RESTRICTION

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**Scientific advisor:** Iliadi-Tulbure Corina, MD, Associate Professor, Obstetrics and Gynecology Department, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Intrauterine Growth Restriction (IUGR) represents a very serious yet often silent threat to fetal and neonatal welfare, manifesting as a rate of fetal growth below the expected norm for a given infant. IUGR arises from a myriad of factors, encompassing maternal, placental, fetal and genetic influences. When talking about the antenatal aspects of IUGR, there is an imperative need for effective management strategies and preventive interventions to soften its potential long-term health consequences.

**Aim of study.** Assessment of the evolution of pregnancy, birth and perinatal outcomes in 294 pregnant women diagnosed with IUGR.

**Methods and materials.** The study was performed in the Tertiary Perinatal Center, Chisinau, Republic of Moldova (RM), over the last 3 years. We used clinical methods (assessment of uterine fundal height, hemodynamic parameters, auscultation of the fetal heart rate) and paraclinical methods (US exam, Doppler velocimetry on the uterine, umbilical, middle cerebral arteries of the fetus and/or the ductus venosus, coagulation tests, etc.).

**Results.** The incidence of IUGR remains well nigh unchanged in RM in the last 5 years (apr. 6.0%). The average age of the patients was  $27 \pm 6.9$  years, the most troublesome cases being appreciated in women under 18 years old and over 42 years old, relating IUGR in previous pregnancies, as well as reproductive losses, severe preeclampsia and TORCH infections in the mother. The diagnosis was mainly settled at multiparous (173 cases – 58,8 % cases), with various somatic conditions. The diagnosis was established in 100% cases by US exams. There were determined several maternal, fetal and placental risk factors. The associated maternal diseases were identified in 196 cases (66,6 %), such as: chronic hypertension, cardiovascular disease, diabetes mellitus, chronic pyelonephritis etc. There were also determined several cases of fetal diseases (91 cases – 30,9 %) and placental induced diseases (134 cases – 45,5 %). Pregnancies diagnosed with IUGR were complicated by: fetal hypoxia (69 cases – 23,4 %), severe preeclampsia (41 cases – 13,9 %), which integrates in the majority of the cases (103 cases – 35 %), indications to handling those clinical cases by C-section. Women delivered vaginally in 191 cases (64,9 %); in all cases, an epidural analgesia was performed. In 162 cases (55,1 %) pregnancies were finished at term and 132 cases (44,8 %) – prematurely. The perinatal mortality was determined in 10 cases, all pregnancies being managed between 26-30 weeks of gestation.

**Conclusion.** IUGR is a major-league problem, often associated with a number of complications, the basic treatment being the emergent termination of pregnancy, more often by C-section. According to these, it is necessary to address pregnant women to specialists to double-check the diagnosis and get a back-up plan about the management of pregnancy and delivery.

### 34. UNDERSTANDING THE IMPACT OF COVID-19 ON PREGNANCY: A COMPREHENSIVE STUDY



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**Scientific advisor:** Popusoi Olga, MD, Associate Professor, Obstetrics, Gynaecology and Human Reproduction Discipline, Obstetrics and Gynaecology Department, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The COVID-19 pandemic has raised concerns about its potential impact on pregnant individuals. This study aims to fill the existing knowledge gap by investigating how COVID-19 affects pregnancy. With the virus continuing to pose a global health threat, understanding its implications for expectant mothers is crucial.

**Aim of study.** Our study seeks to assess the risks and outcomes of COVID-19 in pregnant women. We aim to identify specific challenges, determine high-risk factors, and contribute to the growing body of knowledge guiding healthcare practices during the pandemic.

**Methods and materials.** We conducted a retrospective analysis of medical records from pregnant individuals with confirmed COVID-19 cases. The study included data from multiple healthcare facilities, covering diverse demographics. Statistical analyses, including logistic regression, were employed to assess the association between COVID-19 and pregnancy outcomes.

**Results.** Our findings indicate an increased risk of complications, including preterm birth and gestational diabetes, among pregnant individuals with COVID-19. The severity of maternal infection correlated with adverse neonatal outcomes. Additionally, our study highlights the importance of vaccination in mitigating these risks.

**Conclusion.** In conclusion, our study underscores the significance of understanding how COVID-19 impacts pregnancy. The increased risk of complications emphasizes the need for vigilant prenatal care and emphasizes the importance of vaccination for pregnant individuals. This research contributes valuable insights to the evolving understanding of managing pregnancy during the ongoing pandemic.



### **35. UNINTENDED PREGNANCY DESPITE IUD, COMPLICATED WITH HUGE FIBROID AND SCARRED UTERUS, A RARE CASE REPORT**

**Author:** Marin Dimitris; **Co-author:** Ciobanu Victoria, Henegariu Irina, Furău Cristian, Furău Gheorghe

**Scientific advisor:** Furau Cristian George, PhD, Professor, Department of Biology and Life Sciences, *Vasile Goldiș* Western University, Arad

**Introduction.** Unintended pregnancy rates remain high as a percentage in adolescents, socioeconomic groups and women that are already closed to the familiar planning. Thus, the variety of contraception methods are increasing (oral contraception, intrauterine devices etc.) in order to decrease the number of unintended pregnancies. Contraception methods are so accessible in women upper than 40 years old such as IUD's, in order to avoid an unintended pregnancy and venous thromboembolization (VTE) but what happens when fibroids appear. The aim of this study is to demonstrate that the correct treatment remains a provocation and a difficult decision for the physician, accompanied with the patient's history, wishes and health status of each patient.

**Case statement.** We describe the case of a 42 years old patient, who had an unintended pregnancy, after a placement of IUD 8 years ago and accidentally discovered a fibroid at a routine check-up. The patient is a smoker and also had hypertension and obesity first grade. After rigorous counseling of the patient, description of the risks if pregnancy evolves, the patient undergone under a general anesthesia a subtotal hysterectomy with bilateral adnexectomy in order to remove the Uterus (gestational sack, huge fibroid and IUD), all undergone under histopathologic examination

**Discussions.** Even if the pregnancy was wished for, it will be difficult for the patient and baby to survive, due to the huge size of fibroma, the placement of the pregnancy, comorbidities and the malposition of IUD without strings accompanied with scarred uterus.

**Conclusion.** There are various outcomes but all of them always depend on the primary diagnosis of pre-existing pregnancy pathologies, the desire to have and develop a healthy pregnancy and the obstetrical history of the patient. Also, the literature showed cases with pregnancies and IUD or pregnancies with leiomyoma outcomes but not with all those three in the same case, plus scarred uterus due to previous Cesarean section.

### 36. VAGINAL CONES WITH VIBRATING BALL INSIDE IN PELVIC FLOOR DYSFUNCTION



**Author:** Federico Villani; **Co-authors:** Damiano Rigano, Elisabetta Moratti, Bruno Minopoli, Alessandra Guglielmino, Oana Todut, Victoria Ciobanu, Roxana Furau, Cristian Furau.

**Scientific advisor:** Furau Cristian George, PhD, Professor, Department of Biology and Life Sciences, Vasile Goldiș Western University, Arad

**Introduction.** These are the first results of an ongoing multicentrum observative trial to determine the effectiveness of vaginal cones (VC) in pelvic floor (PF) training. Because of a high economic burden of urine incontinence in Europe, we chose VC as a good cost-effective method for the training of PF muscles in women, to manage urinary incontinence and/or sexual dysfunctions. This methodology allows freedom and empowerment to women, thanks to the autonomous use of the device without any additional costs for the National Health System.

**Aim of study.** Validating the effective use of VC in PF training.

**Methods and materials.** We carried out a test based on a newly developed type of VC with a vibrating ball inside with 37 women (25-78 years old), who signed a consent form and trained PF muscles with a set of 3 VC after explanation of exercises. They were classified according to individual scores by a Pubo-coccygeus muscle test (strength, endurance, fatigability) and Quality of Life questionnaire, at the beginning and after 3 months.

**Results.** Out of 37 women involved, 10 dropped out due to lack of commitment. Out of the 27 women left, 7 with urgency, 11 with effort, 3 with mixed problems, 24 reported a clear improvement of the pathologies, 88% successful. All 16 women with sexual dysfunctions reported a gain of sexual pleasure.

**Conclusion.** You may notice a complete training leads to an improvement of pathologies related to the weakness of the PF. The verifiable limit to the treatment is the arbitrary level of commitment. Further studies are necessary. Autor's conclusion: It is evident that PFMT is the first line treatment for urinary incontinence, but it is also a prevention method recommended to all women after pregnancy and/or menopause. This rise of awareness is addressed mainly to gynecologists, midwives and family doctors, since it is them who are mainly in contact with the patient, to prescribe the pelvic floor muscle training with the help of purposely designed devices, like VC, at the patient's expenses, to use at home and autonomously





### 37. WHAT DO STUDENTS KNOW ABOUT SEXUALLY TRANSMITTED DISEASES AND METHODS OF CONTRACEPTION? A SURVEY STUDY ABOUT KNOWLEDGE AND SEXUAL RISK BEHAVIOURS AMONG UNIVERSITY STUDENTS

**Author:** Denisa-Amalia Jurca

**Scientific advisor:** Furau Cristian George, PhD, Professor, Department of Biology and Life Sciences, Vasile Goldiș Western University, Arad

**Introduction.** Sexual life is of considerable importance, particularly in youngsters, not only because of its Sexual life is extremely important, especially for young people, not just because it affects intellectual development but also because of potential health effects. STIs are among the most prevalent diseases in the world, and unwanted pregnancies and sexually transmitted diseases (STDs) rank among the most serious issues globally. Every day around the world, more than 1 million STIs are acquired and every year there are around 500 million new infections, most commonly syphilis, chlamydia, trichomoniasis and gonorrhoea (WHO,2014). Sexual behaviour is the key determinant of STI transmission all over the world. ( Fenton, 2004). Adolescents and young adults are at higher risk for such behaviour, frequently as a result of their immature decision making. Additionally, these sexual risk behaviour patterns may persist into adulthood (Epstein et al., 2014).

**Aim of study.** This study aims to investigate the level of knowledge, perception, sexual risk behaviours and attitudes about sexual matters, among university students. Furthermore, to improve strategies for family planning and sexual health education among youths.

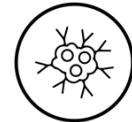
**Methods and materials.** The study was conducted with an online survey questionnaire. The link was shared with students attending different universities. The questionnaire was divided into 3 parts: the first part includes general information; the second includes questions related to sexual matters; the third aims to assess students' knowledge. The statistical analysis was conducted using SPSS software.

**Results.** The total number of participants was 564. The majority were Romanians, female, Orthodox, 21-25 years old, Caucasian, single and studying at a biomedical university. The most knowledgeable students about sexual matters were Serbians studying in a biomedical faculty. The most commonly used source of information was the Internet-TV (76.80%) while the most commonly used contraceptive method was the condom. Most students never received sexual health education (51.06%), and among those who received it, the majority were Serbians. Regarding FP, the majority would like to have their first child at 26-29 years. Students who were less engaged in sexual risk behaviors were females, Muslims black/African-American with few sexual partners. Students who used the EC pill multiple times were mainly Romanian.

**Conclusion.** Students who received sexual education were more knowledgeable about sexual matters. Sociodemographic and cultural factors are all aspects that influence sexual risk behaviours. Improvement of students' knowledge, perceptions, and attitudes towards these topics is still needed.

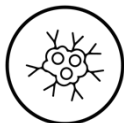


## XII. ONCOLOGY SECTION



### *Evoluția practico-științifică a oncologiei*

*Patologiile oncologice apar odată cu apariția animalelor și speciei umane. Dezvoltarea oncologiei poate fi divizată în câteva perioade-epoci. Perioada preistorică – tumori osteogene la mamuți. Antichitate– 3000 de ani Î.Cr. tumori mamare la mumii (vezi papyrusul Egiptean descoperit de Edwin Smith), Hipocrate (450-375 Î. Cr.) termenul karkinos, Galenus sec. II e.n. cancrum – latină. Au trecut secole până s-a ajuns la concepțiile contemporane ale etiopatogenezei, diagnosticului, tratamentului și profilaxiei tumorilor maligne. Sec. 18 Antonie van Leeuwenhoek inventează microscopul și Marcello Malpighi pune bazele investigațiilor histologice. Sec. 19 Rudolf Virchow 1862 prezintă ipoteza concepțiilor contemporane ale histogenezei tumorilor maligne. Un salt enorm în studierea dezvoltării, diagnosticului și tratamentului de cancer are loc odată cu descoperirea razelor X de către Rontgen în 1895 și a radiației de către soții Curie în 1898 odată cu aceasta apare tratamentul radioterapic. Pe lângă marile școli de oncologie americane, franceze, germane, engleze, exsovietice și japoneze se afirmă și se consolidează Școala Românească (Amza Jianu, Șt. Nicolau, D. Gerota, I. Andreoiu, etc.). Fondatorul școlii oncologice autohtone basarabene este Ipatii Sorocean. Au contribuit la dezvoltarea oncologiei frații Coșciug, frații Gladun, frații Ghidirim, Țâbârnă, prof. Țurcan, Bideac, Corcimaru, soții Sofroni, Jovmir, Bulat, Cernat, I. Iacomlev, A. Cernii, N. Belen, Hohelidze și alții. La ora actuală există o gamă largă de metode de tratament: Chirurgical (radical, paliativ); terapeutic (neoadjuvant și adjuvant); Chimioterapică (neo și adjuvantă); Hormonoterapică, imunoterapică (interferon, interleukine, anticorpi monoclonali etc.); Laseroterapică, terapia moleculară țintită și altele. Tratamentul complex este asigurat de o echipă multi-disciplinară (oncolog, chirurg, Radioterapeut, chimioterapeut, ATI și alții).*



## ***The practical scientific evolution of oncology***

***Oncological pathologies have been present since the appearance of animals and the human species. The development of oncology can be divided into several periods or epochs. The prehistoric period saw osteogenic tumors in mammoths. In antiquity, around 3000 years BC, there were reports of mammary tumors in mummies (as seen in the Egyptian papyrus discovered by Edwin Smith). Hippocrates (450-375 BC) introduced the term "karkinos", and Galen in the 2nd century AD used the term "cancrum" in Latin. It took centuries to reach contemporary concepts of the etiopathogenesis, diagnosis, treatment, and prevention of malignant tumors. In the 18th century, Antonie van Leeuwenhoek invented the microscope, and Marcello Malpighi laid the foundations for histological investigations. In the 19th century, Rudolf Virchow (1862) presented hypotheses on the contemporary concepts of the histogenesis of malignant tumors. A significant leap in the study of cancer development, diagnosis, and treatment occurred with the discovery of X-rays by Röntgen in 1895 and of radiation by the Curies in 1898, which led to the development of radiotherapy. In addition to major oncology schools in America, France, Germany, England, the former Soviet Union, and Japan, the Romanian School (including figures like Amza Jianu, Șt. Nicolau, D. Gerota, I. Andreoiu, etc.) made its mark. The founder of the oncological school in Bessarabia was Ipatii Sorocean. Contributions to oncology came from the Coșciug brothers, the Gladun brothers, the Ghidirim brothers, Țâbârnă, Prof. Țurcan, Bideac, Corcimaru, the Sofroni spouses, Jovmir, Bulat, Cernat, I. Iacomlev, A. Cernîi, N. Belen, Hohelidze, and others. At present, there is a wide range of treatment methods available: surgical (radical, palliative), therapeutic (neoadjuvant and adjuvant), chemotherapeutic (neo and adjuvant), hormone therapy, immunotherapy (interferon, interleukins, monoclonal antibodies, etc.), laser therapy, targeted molecular therapy, and others. Comprehensive treatment is ensured by a multidisciplinary team including oncologists, surgeons, radiation therapists, chemotherapists, ICU staff, and others.***

***Nicolae Ghidirim,***

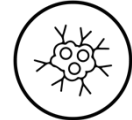
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## 1. ANOMALOUS 12MM MELANOMA



**Author:** Tomuț Alexandru-Nicușor

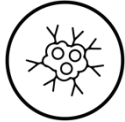
**Scientific advisor:** Sabău Adrian-Horațiu Asist univ. drd., Pathology department, Country Hospital of Targu Mures, University of Medicine, Pharmacy, Science and Technology “George Emil Palade” of Târgu Mureș, Romania

**Introduction.** Despite its relatively low frequency, melanoma is considered the most hazardous form of skin cancer. It manifests as a developmental atypia of melanocytes, cells derived from the neural crest. Frequent sites of melanomas are on the trunk in males and the lower limbs in females. They often present as asymmetrical lesions on the skin surface that can infiltrate the underlying tissue. Factors influencing melanoma development include skin immunity, genetic predisposition, environmental elements (UV radiation), and lifestyle variables. Misdiagnosis or underdiagnosis of melanoma can occur, potentially leading to delayed treatment and severe complications.

**Case statement.** We report a case of an 86-year-old man admitted to the Surgery Department for a dorsal cutaneous tumor. After surgical excision, a round-ellipsoidal cutaneous flap with 8mm of subcutaneous tissue was admitted. Macroscopic examination revealed a brown nodular proliferation with a gray, irregular, and imprecisely delimited surrounding area. The histological examination revealed an ulcerating epithelioid nodular melanoma infiltrating the hypoderm with a substantial thickness of 12mm. The tumor presented an increased mitotic index of 69 mitoses/10HPF, brisk tumor-infiltrating lymphocytes (TILs), both horizontal and vertical proliferation, and a pagetoid migration pattern. Immunohistochemistry revealed a high proliferation index of Ki67 in 60-70% of the tumoral cell population, along with intense positivity for anti-S100, SOX10, Melan A, and HMB45 antibodies.

**Discussions.** Histological and immunohistochemical investigations were crucial in reaching the final diagnosis of an ulcerated epithelioid nodular melanoma. The Breslow index, measuring the maximum thickness of the tumor, was determined to be 12 mm. The tumor was classified as Clark V stage, indicating infiltration into the hypoderm, and assigned a pT4bNxMx stage. The comprehensive analysis of histological features, immunohistochemical markers, and genetic testing contributes to a more accurate diagnosis and aids in developing an appropriate management plan for the patient.

**Conclusion.** Atypical cases of melanoma, although sporadic, play a crucial role in advancing our understanding of this pathology. In cases such as the one described, where the conventional outlines are exceeded, reporting becomes essential.



## 2. BONE SCINTIGRAPHY - THE CONER STONE IN TREATMENT MANAGEMENT FOR OSTEOPHILIC NEOPLASMS

**Author:** Gorea Diana Valentina; **Co-author:** Asavei Letitia

**Scientific advisor:** Ionescu Teodor Marian, University of Medicine and Pharmacy, Iasi, Romania

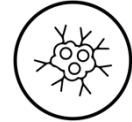
**Introduction.** Bone scintigraphy is a nuclear medicine imaging investigation that studies the biodistribution of a radiotracer at the skeletal level. It is considered to be a very sensitive technique due to the fact that it can detect and diagnose the presence of bone metastasis especially in case of osteophilic neoplasms, thus proving to be invaluable in staging. Reevaluations throw bone scintigraphy can also be helpful in treatment management, mainly because it can compare acquired images at different time intervals and determine if the treatment the patient is undergoing is efficient or not.

**Case statement.** We present the case of a 67 years old male patient that presented to the Nuclear Medicine Laboratory of “Sf. Spiridon” hospital, with the referral diagnosis of prostate neoplasm (Gleason score = 7). This was the patient’s second bone scintigraphy. He underwent hormone therapy in the time between the two bone scintigraphy. The delay between the bone scans was approximately one year. PSA levels decreased during the treatment, however the patient was still complaining of increased generalized bone pain which led him to undergo a second bone scintigraphy. The patient underwent bone scintigraphy with a Siemens Dual-Head Gamma Camera equipped with a low energy, high resolution collimator. We acquired whole body images at 2 and a half hours after the i.v. administration of  $^{99m}\text{Tc}$  – HDP (dose = 9,86MBq/kg). By comparing the previous image with the current one, it was concluded that the patient’s treatment was working and that some of the previous uptake sites on the skeleton have diminished or even disappeared.

**Discussions.** Bone scintigraphy is indicated especially in patient’s suspected or diagnosed with osteophilic neoplasms such as breast, prostate, lung, kidney and thyroid. This type of investigation has proven to be most effective in detecting and diagnosing the presence of metastatic dissemination at the skeleton level and by offering vital information for staggging purposes. Nevertheless, the influence on the treatment management should not be underestimated, as it can accurately determine the effectiveness of certain therapies compared to others.

**Conclusion.** Bone scintigraphy has proven to be invaluable in detecting and diagnosing the presence of bone metastasis. Nevertheless, the importance of bone scintigraphy in treatment management should not be overlooked as it can offer a more accurate evaluation of the treatment efficiency, especially in osteophilic neoplasms.

### 3. COMBINED ADMINISTRATION OF DOCETAXEL AND APIGENIN INHIBITS BREAST CANCER CELL SURVIVAL AND MIGRATION



**Author:** Nizamudeen Fathima

**Scientific advisor:** Suat Erdogan , Riza Serttas -Department of Molecular Biology, Trakya University, School of Medicine, Edirne, Türkiye

**Introduction.** Breast cancer, an urgent global health issue, necessitates innovative therapeutic approaches. This study focuses on HER2-positive breast cancer characterized by overexpression of the HER2 gene. Apigenin, a natural flavonoid, has been reported to potentially act as a chemosensitizer in certain types of cancer. However, its role in the treatment of HER2-positive breast cancer remains unknown.

**Aim of study.** The aim of the study was to determine the potential synergistic anti-proliferative and anti-migratory effects of docetaxel, a commonly used chemotherapeutic agent, and apigenin on the progression of SKBR3 breast cancer cells.

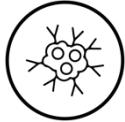
**Methods and materials.** SKBR3 cells were treated with various concentrations of docetaxel, apigenin, and their combinations. Cell viability, apoptosis and migration were assessed using the MTT test, imaging techniques, Hoechst staining and wound healing assays, respectively.

**Results.** Over a 72-hour incubation, apigenin demonstrates significant, dose-dependent inhibition of SKBR3 breast cancer cells. Co-administration of 12.5  $\mu\text{M}$  apigenin and 3 nM docetaxel notably amplifies cell death induction compared to individual treatments ( $p < 0.01$ ). The mechanism of cell death was identified to be apoptosis. Furthermore, the combined treatment strategies exhibit more effective inhibition of cell migration compared to docetaxel alone ( $p < 0.05$ ).

**Conclusion.** Cancer cells can spread to different tissues, forming secondary tumor foci. Cells in these tissues being resistant to treatment can increase the risk of death. Therefore, preventing metastasis through treatments is desirable. Our study demonstrates that the combination treatment of apigenin increases cell death and significantly suppresses migration, potentially reducing the risk of metastasis compared to single docetaxel application. The observed synergistic effects of docetaxel and apigenin offer a promising avenue for clinical research, presenting potential therapeutic strategies for HER2-positive breast cancer.

**Keywords.** Apigenin, Docetaxel, HER2 positive, Breast cancer, Cell Migration





#### 4. EPIDEMIOLOGICAL FEATURES OF KAPOSI'S SARCOMA WITH CUTANEOUS INVOLVEMENT IN THE ONCOLOGICAL INSTITUTE OF THE REPUBLIC OF MOLDOVA OVER THE YEARS 2018-2023.

**Author:** Stascoveac Iadviga

**Scientific advisor:** Şveţ Veronica, PhD, Assistant Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** According to GLOBOCAN 2020 database incidence is 34270 and mortality 15086 for both sexes and all ages. The most affected population is Africa, 73%, followed by European countries 8,8%. This disease becomes even more difficult due to concomitant pathologies such as HIV/AIDS, syphilis, autoimmune diseases, heart, kidney, liver and other diseases, with a high rate of addressability and repeated exacerbations. The interest in epidemiological features of Kaposi's Sarcoma is based on the fact that it's less studied.

**Aim of study.** To analyze Kaposi's Sarcoma among the population of the Republic of Moldova based on sex, age, residence distribution, cutaneous affected areas and occurrence of comorbidities.

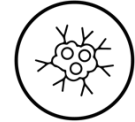
**Methods and materials.** The study was carried out on 27 medical records of patients diagnosed with Kaposi's Sarcoma, registered within Moldovan Oncology Institute database, skin cancers, melanoma and locomotor system department, over the years 2018-2023.

**Results.** Based of 27 reported cases, 8 cases (29,60%) are among women and 19 cases (70,40%) among men. The male to female ratio is approximately 2:1 (19 cases versus 8 cases). 26 patients (96,30%) are under the age of 40. Patients aged 40-50 account 3 (11,11%), aged 50-60 only 2 (7,41%), aged 60-70 are 12 (44,44%), aged 70-80 account 6 (22,22%), aged 80-90 are 3 (11,11%) and a single case of a 24 year old patient (3,70%). Residents of rural area are 11 patients (40,74%), while residents of urban area 16 (59,26%). 15 patients have cutaneous lesions localized on the lower extremities (55,56%), 3 patients have it on the upper extremities (11,11%), 3 patients have it on multiple areas (11,11%), and 6 patients have another localization as nose, trunk and other types of Kaposi's sarcoma. 1 patient (3,70%) out of 27 has AIDS. 12 patients (44,44%) have heart disease. 10 patients (37,04%) have kidney disease. 4 patients (14,82%) have liver disease. In 2020, 1 patient came for another surgical procedure due to worse health state. In 2022 and 2023, 1 patient came to repeat local excision.

**Conclusion.** Increased SK incidence is among men and especially of urban residence which probably can be associated with biological factors, lifestyle and environmental factors. The most common affected sites are lower extremities. Heart diseases are usually associated with Kaposi's Sarcoma and the proper explanation could be the patient's age. The number of repeated surgical procedures has increased since 2020 and it can be linked to the period of infection with SARS-COV-2.

**Keywords.** Kaposi sarcoma, cutaneous lesions, epidemiology, comorbidity.

## 5. ETIOLOGY AND DIAGNOSTIC PARTICULARS OF BENIGN OVARIAN TUMORS



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**Scientific advisor:** Rotaru Tudor, MD, PhD, Associate Professor, Department of Oncology, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

**Introduction.** According to the official data, the most widespread diseases of the reproductive system, at women of reproductive age, are ovarian tumors. The research results address the etiology and diagnosis of benign ovarian tumors.

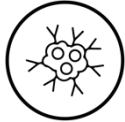
**Aim of study:** Evaluation of etiology and diagnostic particulars of benign ovarian tumors.

**Materials and methods.** The research results are based on the retrospective study of anamnestic, clinical data and the results of paraclinical examinations, taken from the examination sheets of 70 patients, hospitalized in the Gynecology department of Oncologic Institute during 2018-2022.

**Results.** Benign ovarian tumors in 42.85% of cases are found in the 51-60 age group, in rural patients (57.14%), with unilateral localization (85.71%), accompanied by obesity (60.00 %), multiple leiomyomas of the uterine body (34.28%), irregular menstrual cycle (95.71%), represented in 25.71% cases by polymenorrhea. Incidence of reduced morphological variants: papillary serous cystadenoma - 37.14%, mucinous cystadenoma - 22.85%, cystadenofibroma - 11.42%, teratoma thecoma - 17.14%, hemorrhagic luteal cyst, dermoid cyst, fibroma and endometrioid cystadenoma in 2.85% respectively. The level of oncological markers CA125 (0 – 0.35 U/ml) was assessed in 5.71% of cases. Instrumental examination performed by abdominal ultrasonography and lung x-ray (100%), computed tomography (68.57%), nuclear magnetic resonance (NMR) (32.85%), laparoscopy (14.28%), videocolonoscopy (VCS) (2.85%), cystoscopy (1.42%), rectoromanoscopy (RRS) (4.28%).

**Conclusion.** Benign ovarian tumors are mainly found in patients aged 51-60 years, from rural areas, suffering from obesity, multiple uterine leiomyoma and irregular menstrual cycle, represented, in particular, by papillary serous cystadenoma and mucinous cystadenoma. The methods of instrumental and laboratory examinations correspond to the provisions of the national clinical protocols.

**Keywords.** Serous ovarian cyst, benign ovarian tumors, incidence.



## 6. ETIOPATHOGENETIC FRONTIERS OF TROPHOBLASTIC NEOPLASMS: A COMPREHENSIVE REVIEW

**Author:** Zingan Mihaela

**Scientific advisor:** Sofroni Dumitru, PhD, Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova; Vîrlan Mariana, MD, Assistant Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Trophoblastic neoplasms, a heterogeneous group of gestational trophoblastic diseases, present intricate challenges in deciphering their etiological and pathogenetic underpinnings. While these rare gestational disorders arise from abnormal proliferation of trophoblastic cells, the precise factors initiating and sustaining this aberrant growth remain elusive.

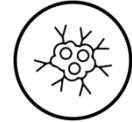
**Aim of study.** Considering a high incidence (2.02 out of 1000 pregnancies) of trophoblastic neoplasms amongst women of reproductive age, this constitutes a pressing social problem. By studying the origins and intricacies of this pathology, we could contribute to the understanding and prevention of it. Previous studies have hinted at genetic mutations, hormonal imbalances, and environmental influences as potential contributors to the development of trophoblastic neoplasms. However, a comprehensive understanding of these etiologic factors is paramount for advancing diagnostic precision and therapeutic interventions.

**Methods and materials.** A systematic literature review was conducted, encompassing studies from databases such as PubMed, Elsevier, and Scopus as well as prominent oncology journals like JCO, JNCI and JGOHR. Emphasis was placed on molecular analyses, genetic studies, and epidemiological investigations to compile a comprehensive overview of the current state of knowledge on the subject.

**Results.** The etiopathogenesis of trophoblastic neoplasms is multifactorial, involving genetic, epigenetic, and environmental factors. Aberrations in genomic imprinting, particularly in genes associated with trophoblast development, contribute to the dysregulated growth observed in these neoplasms. The genetic factors include the transcription of Factor p63 and Y-Chromosomal Complements. Additionally, disruptions in signaling pathways, such as the transforming growth factor-beta (TGF- $\beta$ ) pathway, play a pivotal role in the pathogenesis. Environmental influences, including nutritional (folic acid deficiency) and hormonal factors (elevated levels of hCG and prolactin), further modulate the risk and progression of trophoblastic neoplasms.

**Conclusion.** This comprehensive review consolidates current knowledge on the etiologic aspects of trophoblastic neoplasms. Genetic, molecular, and environmental factors collectively shape the landscape of these gestational disorders, providing potential targets for future research and therapeutic interventions. Understanding the intricate interplay of these factors holds promise for refining diagnostic approaches and developing targeted therapies, ultimately improving patient outcomes. As we unravel the complexities of trophoblastic neoplasms, this synthesis serves as a foundation for further exploration into the intricacies of their etiopathogenesis.

**7. HISTOLOGICAL AND IMMUNOHISTOCHEMICAL PARTICULARITY OF PECTORALIS GLAND CANCER. RETROSPECTIVE STUDY IN ONCOLOGY INSTITUTE FROM MOLDOVA (2017-2022)**



**Author:** Ameena Jasmin Rahman Nareekode Paramba Mujeeb Rahman

**Scientific advisor:** Şveţ Veronica, PhD, Assistant Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Pectoral Gland cancer in men is rare and occurs in 0.5-1% of all breast cancers. The risk factors are various, but the most common are the genetic mutation of BRCA2, familial history, and hormone disbalance. Most frequently in the past, pectoral gland cancer was detected in stages 3 and 4, more aggressive histological and immunohistochemical forms, so that makes the subject more interesting to study.

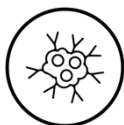
**Aim of study.** Studying histological and immunohistochemistry particularity of the pectoralis gland cancer.

**Methods and materials.** Studying the retrospective analysis of primary documentation, SIMU program of 40 patients with histological and immunohistochemistry of pectoralis cancer at IMSP Institute Oncology from 2017 – 2022 in the Republic of Moldova

**Results.** In the study, 40 hospitalized patients from 2017 – 2022, were around the age of 41 – 80 years, the high incidence of pectoral gland cancer was between the ages 61 – 70 years with 22 cases (55%), and the low incidence is between 41 – 50 years with 3 cases (7.5%). The central part of the gland is most affected with 25 cases (62.5%), and the inferolateral quadrant with the least cases of 1 (2.5%). The most affected are the right gland with 23 cases (57.5%) and the left gland with 17 cases (42.5%). The diagnosis is confirmed by cytology with 28 cases (70%), cytology & histology with 3 cases (7.5%), histology with immunohistochemistry of 4 cases (10%) and 5 cases (12.5%) are not confirmed. Histology was done in 7 cases and 7 out 4 cases are confirmed by immunohistochemistry. Invasive Ductal Carcinoma was seen in 5 cases (71.42%) and 1 case (14.28%) of cancer of Paget's disease of the nipple. Immunohistochemistry confirms the histology of two types. 3 cases (75%) of Luminal subtype B and 1 case (25%) of Luminal subtype A. Stage 3B has the highest number of cases of 12 (30%) and Stage 1 and Stage 3C have the least cases of 1 (2.5%) respectively, 4 cases (10%) are not staged accordingly.

**Conclusion.** The histological forms and immunohistochemistry of pectoral gland cancer are the diagnoses confirming characteristics in the assessment for the evolution of the malignant process.





## 8. MALE BREAST CANCER: EPIDEMIOLOGY AND RISK FACTORS

**Author:** Saini Jai

**Scientific advisor:** Bacalim Lilia, MD, Associate Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Although the prevalence of breast cancer is significantly lower in men than in women, understanding the unique epidemiology and associated risk factors of breast cancer is of paramount importance. This study examines recent data on breast cancer cases among Moldovan men over the past five years and aims to elucidate breast cancer patterns and potential causes of the disease.

**Aim of study.** The study aims to analyze the epidemiology of male breast cancer in Moldova over the last five years, specifying risk factors.

**Methods and materials.** A comprehensive study was carried out to analyze the cases of male breast cancer reported in Moldova from 2019 to 2023. The data for this study were collected from national cancer registries, hospital records, and databases of the Institute of Oncology in Moldova. By examining the clinical characteristics and risk factor profiles, we aimed to gain a complete understanding of this disease.

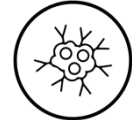
**Results.** The study revealed in the last five years (2019 – 2023), a total of 4636 cases of breast cancer were reported out of which 86 were in males accounting for 1.85%, highlighting the lower number compared to female breast cancer. During this period the number of male breast cancer as per each year as follow-up 2019 – 14 cases, with age range 35-39y/o (1),40-44y/o (1),45-49y/o (1),50-54(1),55-59y/o (2), 60-64y/o (2), 65-69y/o (2), 70-74 y/o. (2),75-79(1),85+y/o (1), 2020- 18 cases, with age range 40-44y/o (1) ,45-49y/o (2) ,50-54(4), 60-64y/o (1), 65-69y/o (4), 70-74 y/o. (5), 80-84y/o (1), 2021 – 21 cases with age range 30-34y/o (1), 35-39y/o (2) ,40-44y/o (2) ,50-54(1) ,55-59y/o (2), 60-64y/o (3), 65-69y/o (4), 70-74 y/o. (4),80-84y/o (1),85+y/o (1), 2022 – 20 cases, with age range 30-34y/o (1),40-44y/o (1), 60-64y/o (6), 65-69y/o (4), 70-74 y/o. (3),75-79(2),80-84y/o (1),85+y/o (1) 2023 – 13 cases. The average age at diagnosis was 60 years, with noteworthy distribution observed across different age groups. Several significant risk factors influence the development of male breast cancer. These include advancing age, hormonal imbalance, exposure to radiation, and having a family history of breast cancer. In particular, the occurrence of male breast cancer can be associated with mutations in high- or low-penetrance genes. However, the most crucial risk factor for the development of male breast cancer is a mutation in the BRCA2 gene.

**Conclusion.** The study identified the lower prevalence of male breast cancer compared to female breast cancer over the past five years with an average age of 60 years, with the most crucial risk being a mutation in the BRCA2 gene.

**Keywords.** Epidemiology, Male breast cancer, Moldova, BRCA1, BRCA2, Risk factors.



## 9. MALIGNANT TUMORS IN CHILDREN: EPIDEMIOLOGICAL AND EVOLUTIONARY ASPECTS



**Author:** Rusu Maria

**Scientific advisor:** Bacalim Lilia, MD, Associate Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

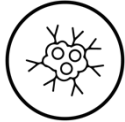
**Introduction.** The spectrum of malignant tumors in children differs significantly from that of adults. Whereas adult tumors are the result of cell differentiation from a mature tissue histologically, pediatric tumors originate from certain anomalies of embryogenesis, as well as immature.

**Aim of study.** To study the epidemiological and evolutionary aspects of malignant tumors in children compared to malignant tumors in adults.

**Methods and materials.** The study is based on a review of the national and specialized literature internationally (ESMO, SIOF, Google Scholar, NCCN). The literature review was conducted in the period of 2013-2023.

**Results.** Pediatric tumors are rare, they represent approximately 0.5-1% of the total number of cancers. Every year, worldwide, around 400,000 children aged between 0-19 are diagnosed with cancer, this disease being considered the main cause of non-accidental death in children and adolescents in developed countries and in an increasing number in increasing numbers of developing countries. In the Republic of Moldova (RM), according to National Cancer Registry data (2023), the incidence of malignant tumors in children decreased from 13.5‰ in 2021 to 11.2‰ in 2022. Children aged between 5-14 years, with a slight predominance among boys compared to girls (11.4‰ vs. 11.0‰). The most common neoplasms in children are those affecting the hematopoietic system - leukemias or lymphomas (about 50%), as well as CNS, embryonic tumors (retino-, nephro- or neuroblastoma). Tumors in children usually have a shorter latency period, grow faster, are more aggressive, but usually respond better to treatment than in adults. Also, in the case of pediatric patients, there is great variability regarding the type of cancer and its prognosis. The survival rate worldwide, as well as in the Republic of Moldova, has increased considerably in the last 30 years, from about 20% (in 1975) to over 70% (in 2023). However, malignant tumors in children remain the most common cause of death in the 5-9 age group and second in the 10-19 age group.

**Conclusion.** Despite the high incidence and the evolutionary peculiarities of malignant tumors in children, the prognosis of the disease is considered better in pediatric oncology than in adults, thus about 70-80% of children are long-term survivors, if the disease is diagnosed in time and treated correctly.



## 10. NAVIGATING THE CHALLENGES OF SHORT BOWEL SYNDROME

**Author:** Cucu Alexandra-Gabriela

**Scientific advisor:** Dimofte Mihail-Gabriel, PhD, Professor, The 2nd Surgical Oncology Department of Regional Institute of Oncology, “Gr. T. Popa” University of Medicine and Pharmacy, Iași; Iacob Ștefan, MD, Associate Professor, the 2nd Surgical Oncology Department of the Regional Institute of Oncology, “Gr. T. Popa” University of Medicine and Pharmacy, Iași

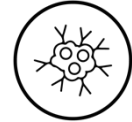
**Introduction.** Short bowel syndrome (SBS) is a rare condition characterized by malabsorption of macronutrients, micronutrients, electrolytes, and water following extensive resection or loss of a significant portion of the small bowel. Managing SBS poses significant challenges, necessitating a multidisciplinary approach. When patients fail to return to an oral diet despite medical therapy, long-term parenteral nutrition becomes essential, accompanied by potential risks such as gallstones, oxalate kidney stones, or steatohepatitis associated with parenteral nutrition.

**Case statement.** A 44-year-old patient with a history of right colon neoplasm, right colectomy, and enterectomy due to accidental ingestion of a dental prosthesis, presented with recurrent sub-occlusive episodes. These episodes were unresponsive to conservative measures for sub-occlusive syndrome attributed to abdominal adhesions, leading to surgical intervention. Intraoperatively, complex abdominal adhesions and numerous fistulas were discovered, necessitating extensive short bowel resection. Subsequently, anastomotic fistulas occurred, leading to a slow postoperative course with prolonged paralytic ileus. The patient eventually developed an enterocutaneous fistula, externalizing approximately 4000 mL daily for 3 weeks. Conservative management involved parenteral nutrition, targeted antibiotic therapy, GLP-2 analogue and opioid medication to control fistula flow. Despite these efforts, increased fistula output necessitated surgical reintervention, resulting in the creation of an enterostoma, ultimately leading to the development of SBS. The patient faced challenges during hospitalization, including severe nutritional deficits, cachexia, complex nutritional deficits, and pancytopenia, which were managed with granulocyte stimulating factors and repeated transfusions. Although the patient initially responded transiently, he ultimately succumbed to cardiac arrest that was refractory to resuscitation maneuvers.

**Discussion.** The ideal treatment for this patient would have been a small bowel transplant; however, the oncologic history precluded this option. Small bowel transplant guidelines recommend a progression-free disease interval of 2-5 years, which our patient did not meet, being less than 2 years from diagnosis.

**Conclusion.** This case highlights the development of short bowel syndrome following multiple surgical interventions for abdominal adhesions, anastomotic leaks, and enterocutaneous fistulas. Managing SBS is intricate, with poor outcomes and high costs if not approached judiciously.

## 11. ROLE OF NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED GASTRIC CANCER



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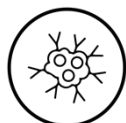
**Introduction.** Locally advanced gastric cancer (LAGC) remains a very aggressive condition, being the 5th most common malignant tumor worldwide and the 4th leading cause of death, surgical intervention remaining as the main treatment option. However, almost a third of gastric cancers are unresectable and have poor survival, newly neoadjuvant chemotherapy has attracted increasing attention due to the elimination of micro-metastases and substantial reduction of tumor mass, thus leading to an increase in the rate of R0 resection and better survival.

**Aim of study.** Evaluation of the efficacy of neoadjuvant chemotherapy (nCT) in the treatment of locally advanced gastric cancer (LAGC) and analysis of future perspectives in different cancer stages.

**Methods and materials.** A meta-analysis of randomized controlled trials (RCT) of neoadjuvant chemotherapy (nCT) followed by surgery vs monotherapy surgery for patients with stage II and greater locally advanced gastric cancer (LAGC) was performed using the data sources PubMed, Cochrane Central Register of Controlled Trials, MEDLINE up to 10 years old. The following criteria were included: overall survival, clinical and pathological response rate (according to RECIST and tumor regression score), R0 resection rate, quality of life and adverse events. Subsequently, relevant articles were reviewed to identify other potentially eligible studies.

**Results.** The main chemotherapy regimens (FLOT, ECF/ECX, CAPOX, FOLFOX, FC) used in locally advanced gastric cancer (LAGC) were highlighted. The radical surgical act was often insufficient or inapplicable for some stages of cancer. Following meta-analysis, patients who underwent neoadjuvant chemotherapy (nCT) followed by surgery demonstrated better overall survival, R0 resection rate, 5-year survival rate, quality of life and adverse effects compared to patients who performed the surgical treatment in monotherapy.

**Conclusion.** Individualized treatment based on chemotherapy (nCT) in locally advanced gastric cancer (LAGC) treatment programs have been shown greater effectiveness in achieving more favorable disease management and an increase in long-term patient survival.



## 12. STUDY OF THE CHEMOTHERAPY TREATMENT OF PATIENTS WITH MALIGNANT MELANOMA WITH DISTANT METASTASES DURING THE YEARS 2018-2022 WITHIN THE IMSPIO OF THE REPUBLIC OF MOLDOVA

**Author:** Miaun Cătălin-Cătălina

**Scientific advisor:** Şveţ Veronica, PhD, Assistant Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Malignant melanoma is one of the most aggressive malignant tumors in the world, and the incidence and mortality increase annually due to the multitude of risk factors and insufficient information among the population. The treatment of malignant melanoma is based on the combined and complex one, depending on the stage of the tumor, the clinical form, the general condition and the comorbidities of the patient. Because it is a very aggressive and progressive pathology, multiple metastases can be detected during the treatment, which make this disease even more difficult and, unfortunately, an unfavorable evolution.

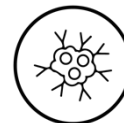
**Aim of study.** Study of the chemotherapy treatment of patients with malignant melanoma with distant metastases during the years 2018-2022 within the IMSPIO of the Republic of Moldova

**Methods and materials.** The study included a total of 85 patients with malignant melanoma who underwent chemotherapy treatment from the Chemotherapy I, II and III department of the IMSP Oncological Institute from 2018-2022.

**Results.** From the total number of 85 patients studied - 48 (56.4%) were diagnosed with the progression of the tumor process, of which the most with metastases in the regional lymph nodes 38 (79.1%), followed by lung and pleural metastases 12 (25%), liver metastases 9 (18.7%), skin metastases 4 (8.3%), brain metastases 4 (8.3%). The ratio of women to men is 41 (85%) men and 7 (14.5%) women, the majority of whom are between the ages of 55-60. Most of the patients included in the study 77 (90.5%) followed the CVD polychemotherapy treatment scheme - 5 (5.8%), 4 (8.3%) after the CVDI scheme, 3 (3.5%) after the TP scheme. In 34 (40%) patients, metastases were diagnosed and removed at the stage of surgical treatment, these are the regional lymph nodes, and another 14 (16.4%) cases of metastases appeared during immunotherapy or chemotherapy treatment, and in 3 (6.25%) cases the surgical treatment was initially palliative due to the presence of distant metastases.

**Conclusion.** More and more studies are focused on the chemo/immunotherapy treatment of malignant melanoma and metastases, however, they retain their aggressiveness depending on the stage of the tumor. Research abroad shows us new possibilities, results and higher effectiveness of treatments compared to the Republic of Moldova, with various treatment schemes and more informative molecular genetic diagnosis.

### 13. SURGICAL TREATMENT OF CUTANEOUS MALIGNANT MELANOMA



**Author:** Pușcaș Nina

**Scientific advisor:** Mereuță Ion, MD, PhD, Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Cutaneous malignant melanoma (MMC) represents a current problem of clinical oncology, the cause being its biological particularities, aggressive evolution and early metastasis. The actuality is determined by the increase in the incidence of MMC in all countries. In some regions of the globe, a doubling of the incidence of melanoma has been recorded over the course of a decade. The incidence of MMC in EU countries is 10 cases/100 thousand annually. MMC is registered more frequently at an advanced age (the morbidity per 100,000 population up to the age of 30 is 0.3, and after 70 years it is 10.7/100,000. Studies have shown that MM prevails between the ages of 30-50. In the treatment of primary tumors, in the early stages, surgical intervention is of great importance; in case of early diagnosis, 90% of patients can be treated by excision. Tactics and technique of surgical intervention, volume, continuity of tissue incision in the region of the primary tumor and in the area of the regional lymph nodes is treated differently in the specialized literature. Currently, electroexcision of the primary tumor and cryodestruction, laser therapy, hyperthermotherapy, radiotherapy are considered the optimal method.

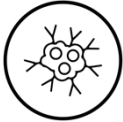
**Aim of study.** Study of surgical treatment methods of MMC.

**Methods and materials.** 227 patient files from the Cancer Registry of patients with malignant cutaneous melanoma were studied – 206 (90.7%) and 21 (9.3%) in CMP "Sancos", women – 105 (46.2%), men - 122 (53.8%), age between 21-80 years.

**Results.** The surgical treatment carried out in the Clinic of the Oncological Institute and Private CM "Sancos" was performed by the electroexcision method - 98 (43.2%), excision - 28 (12.3%), electroexcision+lymphodenectomy - 46 (20.3%), electroexcision according to the method of establishing the limits of the primary tumor excision – 46 (20.3%), vacuum-electroexcision – 5 (2.2%), cryosurgery+single-moment electroexcision – 4 (1.7%).

**Conclusion.** Cutaneous malignant melanoma more frequently affects men - 53.8%, residents of the rural sector - 60.8%, the superficial form is mainly detected - 47.6% and epithelioid - 38.7%, the treatment is carried out surgically by the electroexcision method – 43.2%.





## 14. THE ESSENCE OF THE BIOPSYCHOSOCIAL MODEL IN MEDICAL REHABILITATION

**Author:** Ojovan Vitalina

**Scientific advisor:** Mereuță Ion, MD, PhD, Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The biopsychosocial model is an approach that establishes the existence of multiple factors that influence a person's development and well-being in the context of a disease, disorder, or disability. There are three types of factors: biological (genetics, anatomy, biochemical disorders, endocrine, etc.), psychological (thinking, emotions, behavior) and social (socio-economic factors, factors of the social microenvironment, cultural factors). Rehabilitation includes various aspects and methods and aims at both mental and physical health, the integrity of the body.

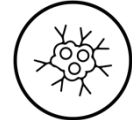
**Aim of study.** Highlighting the biopsychosocial aspects within the complex medical rehabilitation actions in order to make the therapy more efficient and increase the quality of life.

**Methods and materials.** In this literature review were analyzed publications from PubMed, NCBI, Hinari, Elseiver, etc., using the terms «rehabilitation» and «biopsychosocial».

**Results.** The analysis of scientific sources published highlights the important role of the biopsychosocial model in the medical rehabilitation process. Highlighting the biopsychosocial context represents an advance in understanding health in general, because before it, the prevailing model was the medical or biological model (a traditional model, where only biological factors matter). Biopsychosocial factors affect the patient's subjective experience, clinical outcomes, and effective treatment throughout the rehabilitation process or the course of an illness. Essential emphases in the rehabilitation process according to a biopsychosocial model initially consist in a thorough assessment of the general state of health of the body and the psycho-emotional and social components, then in the monitoring and optimization of treatment, psychological counseling and a complex of medical education. Through special medical, psychological and educational actions, the negative impact of the disease on physical and psycho-emotional development can be reduced and and improve a person's abilities to integrate into the family or social environment.

**Conclusion.** 1. The biopsychosocial model is based on understanding the dynamic nature of the various factors that affect the patient's condition and the final results of rehabilitation. 2. The doctor must be aware of the correlation of all the factors that influence the person's state of health. 3. The effective application of the biopsychosocial model, within the complex rehabilitation processes, offers effective possibilities for improving the quality of life.

## 15. THE OCCURRENCE OF VENOUS THROMBOEMBOLISM AT PATIENTS UNDERGOING NEOADJUVANT CHEMOTHERAPY



**Author:** Rotaru Dan

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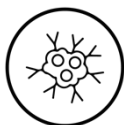
**Introduction.** Venous thromboembolism (VTE) is a common complication in cancer patients receiving adjuvant treatment, but its prevalence during neoadjuvant chemo-radiotherapy remains uncertain.

**Aim of study.** This systematic review was conducted to evaluate the frequency of venous thromboembolism (VTE) at patients with cancer who are undergoing neoadjuvant treatment.

**Methods and materials.** The review included 22 cohort studies with 6977 cancer patients, exploring MEDLINE, SCOPUS, EMBASE, PubMed, HINARI. The findings from the literature search were supplemented by reviewing the conference proceedings of the American Society of Clinical Oncology (2014-2020) and the International Society of Thrombosis and Haemostasis (2013-2018). The majority of cohorts focused on gastrointestinal cancer (78%).

**Results.** The analysis comprised twenty-two observational studies involving 6977 patients with cancer. Nineteen studies employed a retrospective design. Gastrointestinal cancer was the primary focus of twelve cohorts, constituting over two-thirds of the total study population (n = 5442, 78%). Among 6977 patients, 490 were diagnosed with at least one episode of venous thromboembolism (VTE) during neoadjuvant treatment, yielding a consolidated VTE incidence of 7% with no substantial between-study heterogeneity. The observed heterogeneity remained unexplained by the site of cancer or specific study design characteristics. Pulmonary embolism emerged as the predominant form of VTE, ranging from 20% to 92% across ten cohorts, with symptoms apparent in 24% to 98% of patients in twelve cohorts. Noteworthy is the observation that the highest VTE rates were found in individuals with bladder (11.4%) or esophageal (9.2%) cancer.

**Conclusion.** In summary, the analysis of 22 observational studies involving 6977 cancer patients revealed a consolidated venous thromboembolism (VTE) incidence of 7% during neoadjuvant treatment. Despite a focus on gastrointestinal cancer in 12 cohorts, there was no significant heterogeneity explained by cancer site or study design characteristics. Pulmonary embolism emerged as the predominant form of VTE, showing variability across cohorts. Notably, individuals with bladder (11.4%) or esophageal (9.2%) cancer exhibited the highest VTE rates. These findings emphasize the need for heightened awareness of VTE risk in specific cancer types during neoadjuvant treatment.



## 16. THE ROLE OF 3D-PRINTING TECHNOLOGIES IN ONCOLOGY - A COMPREHENSIVE STUDY AMONG MEDICAL STUDENTS

**Author:** Valic Eugeniu; **Co-author:** Valic Vladimir

**Scientific advisor:** Mereuță Ion, MD, PhD, Professor, Department of Oncology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The 3D-printing technologies (3D-PT) are considered as a game-changing way of manufacturing a variety of objects and products with a computer-guided precision. They are used nowadays in various domains, especially in the oncology field. With the development of new diagnostic and treatment methods in oncology, 3D-PT have proved their role in different areas of cancer management, being an innovative way of modeling and creating personalized applicators, prostheses and interactive 3D-printed models of patients' tumors for both educational and treatment purposes.

**Aim of study.** Assessment of the level of knowledge and attitudes among medical students who have already completed an oncology module about the role of 3D-printing technologies (3D-PT) in oncology and their implementation in the studying process.

**Methods and materials.** A descriptive cross-sectional study was conducted in the period of May 2023- September 2023 with the participation of 158 students, including 140 students of the Vth year from Medicine nr.1 faculty of *Nicolae Testemitanu* SUMPh who have already completed Oncology module during the year of study 2022-2023 and 18 students from 12 countries (Azerbaijan, Bulgaria, Croatia, Georgia, Germany, Latvia, Northern Macedonia, Pakistan, Poland, România, Turkey and Ukraine)- participants of ESO-ESSO-ESTRO-SIOPE Multidisciplinary Course in Oncology for Medical Students 2023 in Poznan, Poland, who have already completed Oncology module as of September 2023. The respondents were invited to fill in an online questionnaire to collect data about their knowledge and attitudes related to the role of 3D-printing technologies in oncology.

**Results.** Of the total number of participants (N=158), 119 were female (75,3%) and 39 were male (24,7%), median age- 24,5 years. The majority of the students (147 students, 93%) have heard about 3D-PT, 103 of them (65,2%) appreciated their knowledge about them as low and 48 (30,4%) as moderate. Only 29 students (18%) used a 3D-printed object. 110 students (70% of respondents) considered the use of 3D-PT in oncology as highly necessary. The possible management of cancer types with 3D-PT were bone (34,2%), breast (26,6%) and lung (17%) cancers. Of the possible directions for the implementation of 3D-PT in oncology, 22,1% responded for diagnosis, 25,3% preoperative management, 29,7% postoperative management, 36,7% educational, and 34,8% research. A majority of 98% considered the possibility of exposing the data from imaging investigations in the 3D-printed version as highly necessary and necessary. Moreover, 82% stated that 3D-PT would have a high impact in improving the quality of studies with the introduction of them in the studying process at the Oncology module.

**Conclusion.** The majority of the students who responded considered that 3D-PT would have an important role in the improvement of the studying process at Oncology module as well as a potential role in the development of personalized treatment of cancer patients.

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# ***XIII. OPHTHALMOLOGY SECTION***





## 1. DRY EYE SYNDROME AMONG YOUNG PEOPLE: IMPLICATIONS, RISK FACTORS AND PERSPECTIVES

**Author:** Vlas Daria

**Scientific advisor:** Iacobitchii Maria, Assistant Professor, Department of Ophthalmology-Optometry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

**Introduction.** Dry eye syndrome (DES) has become a major problem among young people, being associated with prolonged exposure to digital screens and psychological stress. Increased prevalence and impact on eye health have prompted more research to identify risk factors and effective management strategies (Aberame, A., 2019; Aljammaz, H. 2023; Hyon, J. Y., 2019; Supiyaphun, C. 2021; Talens-Estarells, C. 2022; Tripathi, A., 2022).

**Aim of study.** This research analyzed the prevalence, risk factors, and impact of the COVID-19 pandemic on young adults, in order to find out new directions for prevention and management of this disease.

**Methods and materials.** A research of recent literature and 22 clinical trials from medical databases such as: PubMed, ScienceDirect, Google Scholar between 2019-2023 has been made to identify relevant studies on DES in youth. Data about prevalence, risk factors and management strategies has been included in study.

**Results.** The studies showed a significant prevalence of DES among young people, especially in women. Also, those who used contact lenses (20,3%) and those who were exposed to digital screens for a long time (62%) were affected by DES (Aćimović, L. 2022). The increased level of stress is a significant risk factor contributing to DES development. The COVID-19 pandemic has contributed to the exacerbation of symptoms, creating a great need of preventive and therapeutic interventions.

**Conclusion.** DES has become a major problem among young people, and risk factors such as screen exposure, history of contact lens use and psychological stress have been identified. Preventive approaches, adjustment of screen parameters and new developing therapies represent promising directions for the management and treatment of this condition. The study covers the essential aspects of dry eye syndrome among young people, highlighting the necessity to pay more attention to eye health in this vulnerable population.



## 2. EVOLUTIONARY METHODS TO IDENTIFY THE OCULAR LYMPHATIC 1,61 1,61 SYSTEM



**Author:** Ciorba Nadejda

**Scientific advisor:** Cusnir Valeriu, MD, PhD, Professor, Department of Ophthalmology-Optometry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Compared to blood vessels, lymphatics can be identified much harder in the human body, especially at the eye level. Lymphatics very often present an irregular, collapsed structure, which creates difficulty in their histological visualization. For a long time, lymphatics were identified based on histological criteria: absence of erythrocytes in the lumen, discontinuous basement membrane. However, these criteria aren't sufficient. The analysis of specialized literature provides information regarding new methods of detecting lymphatic vessels at the level of each structure of the eyeball. These include- the detection of immunomarkers: podoplanin, LYVE-1, PROX-1, VEGFR-3. These immunomarkers confirm the development of lymphatic vessels and lymphangiogenesis.

**Aim of study.** Studying the presence of lymphatic vessels at the level of specific structures of the eyeball: cornea, conjunctiva, uveal tract, retina, eye appendages.

**Methods and materials.** This is an analytical study based on scientific articles published on PubMed, MedlinePlus, ScienceDirect, NCBI, with information published in the last 5 years.

**Results:** Under normal conditions, the cornea is an avascular structure. Corneal lymphatic vessels can be induced only by inflammatory, infectious, traumatic, chemical or toxic processes. Likewise, lymphangiogenesis was induced in laboratory conditions by causing chemical burns, applied sutures, implantation of inflammatory cells on the corneal surface. The de novo developed lymphatics were marked by detecting immunomarkers specific to lymphatic vessels at the corneal level: LYVE-1 and CD-31. The conjunctiva, under normal conditions, is endowed with both blood and lymphatic vessels. Immunohistochemical studies found immunomarkers in the stroma of the ciliary body: podoplanin and LYVE-1. Retina, as well as the eyelids, lacrimal glands, extraocular muscles, optic nerve sheath was confirmed to be provided with LYVE-1 and PROX-1 cells. However, the role of these cells in lymphangiogenesis remains to be confirmed.

**Conclusion.** Performant studies can confirm the presence of specific immunomarkers at the eye level, which represents an evolution compared to the histological criteria used in the past. To certainly prove that these markers are present it is necessary to perform multiple immunohistochemical tests, finding at least two of them. Their presence is also a criteria that proves the development of new lymphatic vessels (lymphangiogenesis) in pathological conditions.



### 3. GENETICALLY DETERMINED PIGMENTARY RETINOPATHY (PR) IN SYSTEMIC DISEASES

**Author:** Moldavskaia Zlata

**Scientific advisor:** Corduneanu Angela, MD, PhD, Associate Professor, Department of Ophthalmology-Optometry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The term "pigmentary retinopathy" broadly refers to a widespread alteration of the retina and pigment epithelium preventing normal vision. The condition is clinically diverse and can be inherited in various ways. It can be associated with different genetic syndromes and can be indicative of systemic disease

**Aim of study.** To analyze the relationship between pigmentary retinopathy and systemic diseases, shedding light on the underlying genetic factors contributing to this condition.

**Methods and materials.** Databases - PubMed, Scopus, and Web of Science - selected articles according to the keywords. Out of 280 articles only 42 of these studies met our strict inclusion criteria and were included in our analysis

**Results.** Pigmentary retinopathy can have different symptoms and severity levels among individuals. Genetic polymorphism has been extensively studied and has revealed genes and variations that increase the risk of developing the condition. Some hereditary pigmentary retinopathies are part of syndromes that involve multiple organ systems. They can be inherited in different modes of genetic transmission, including through autosomal recessive, autosomal dominant, X-linked recessive, digenic, or mitochondrial transmission.

**Conclusion.** Understanding the genetic basis of pigmentary retinopathy and its relation to systemic diseases, is crucial for accurate diagnosis and predicting the visual prognosis.

#### 4. HETEROCHROMIA: CAUSES, RISK FACTORS, TREATMENT



**Author:** Aramă Crina

**Scientific advisor:** Dumbraveanu Lilia, MD, PhD, Associate Professor, Department of Ophthalmology-Optometry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** According to the National Center for Biotechnology Information, approximately 1% of the global population is diagnosed with heterochromia. Iris heterochromia is the uneven pigmentation of the iris, either unilateral, central, or sectoral. As a benign mutation, congenital heterochromia occurs in both humans and animals and is genetically determined by Horner's syndrome, Waardenburg syndrome, and Sturge-Weber syndrome. Acquired heterochromia is less commonly observed compared to congenital heterochromia and can result from various factors, including diseases, injuries, or medical treatment with prostaglandins (latanoprost).

**Aim of study.** Identification and study of causes, risk factors, and a recent innovative treatment method: iris iridoplasty.

**Methods and materials.** I have analyzed scientifically verified documents from websites such as: PubMed, NCBI, American Academy of Ophthalmology, using keywords like heterochromia, congenital, ophthalmology, visual acuity, iris heterochromia, photoablative cosmetic iridoplasty, and eye color change.

**Results.** According to literature data, nearly 50% of the U.S. population has brown eyes, and this color predominates in regions with a warm climate. People with blue eyes lack melanin in the stroma, causing light to scatter upon contact with the eyes. The most uncommon color is green, representing only 2% of the population. Heterochromia is more common in women than in men, based on a study conducted several decades ago in Austria. The treatment of heterochromia is still under study. In the past, treatments included the use of contact lenses, intraocular lenses, and autopigmentation. However, these invasive techniques led to frequent and severe complications such as glaucoma, uveitis, endothelial damage, and reduced visual acuity. Consequently, there is currently no efficient and safe long-term technique. Four types of equipment were tested, and ultimately, it was concluded that the best results are provided by the Nd: Yag Crystal Q-switched laser.

**Conclusion.** Congenital heterochromia should not scare anyone, as research from the American Academy of Ophthalmology, in most cases, congenital heterochromia does not affect visual acuity (VA). However, there are cases of acquired heterochromia where VA may be compromised. Additionally, I want to highlight the effectiveness, safety, reliability, and results of photoablative cosmetic iridoplasty (PCI) using the Nd: Yag Crystal Q-switched laser-the success rate of this treatment is 95%.



## 5. IMPACT OF OXIDATIVE STRESS ON LENS PROTEINS

**Author:** Marciuc Vlada

**Scientific advisor:** Pavlovschi Ecaterina, Assistant Professor, Department of Biochemistry and Clinical Biochemistry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The impact of oxidative stress (OS) on lens proteins is a crucial aspect of ocular health, as the lens plays an essential role in visual function. The intricate interplay between oxidative stressors and lens proteins, shed a light on its potential implications for eye health and contribute to our understanding of age-related ocular conditions (ex. cataract).

**Aim of study.** To illustrate and convey the effects of oxidative stress on lens proteins, as well as its role in the formation of cataracts.

**Methods and materials.** 20 articles, selected from PubMed databases and published in the last two decades, were analyzed. The keywords employed in this analysis included “oxidative stress”, “cataract”, “lens proteins”.

**Results.** The eye is particularly susceptible to OS due to its continuous exposure to light and the high metabolic activity of various structures. The lens of the eye seems to be a unique organ that is shielded from OS through the regulation of oxygen tension. Lens transparency is maintained by lens proteins, primarily composed of  $\alpha$ A and  $\alpha$ B-crystallin, accounting for approximately 40-50% of the total. While all these proteins contribute to the lens's structure and refraction,  $\alpha$ -crystallin specifically prevents protein aggregation. Oxidation of this molecule leads to the loss of its chaperone functions, playing a crucial role in the development of cataracts. Mitochondrial respiration plays a key role in preserving diminished oxygen partial pressure in the lens, with cortical fiber cells's outermost layers, containing mitochondria that consume nearly 90% of incoming oxygen. The fundamental mechanism, evolved over evolution, maintains low oxygen concentrations within the lens, supported by the resistance to oxidation in both lipid components and cytoplasmic proteins. Disruption of this mechanism can lead to elevated oxygen levels and the onset of cataracts. The structural damage to the crystalline lens and its role in cataract formation result from free radicals, including reactive oxygen species like superoxide anion radical ( $\cdot O_2^-$ ),  $H_2O_2$ , and hydroxyl free radical (OH). OS occurs when pro-oxidants surpass antioxidant levels. A research demonstrate that a treatment of human lens epithelial cells with 17  $\beta$ -estradiol has been shown to protect against oxidative stress by preserving mitochondria and increasing Manganese Superoxide Dismutase (MnSOD) activity - an enzyme that plays a crucial role in antioxidant defense within cells. MnSOD regulates OS in lens epithelial cells through both up- and down-regulation of the enzyme.

**Conclusion.** The primary step in cataract development and lens protection is the maintenance of a low oxygen partial pressure at the lens surface. Recent global research emphasizes the significant role of oxidative stress in the increasing prevalence of cataracts worldwide, highlighting the importance of the lens's antioxidant defenses in preserving transparency.

## 6. MODERN APPROACHES TO GLAUCOMA SURGICAL TREATMENT



**Author:** Omer Levy

**Scientific advisor:** Iacubitchii Maria, Assistant Professor, Department of Ophthalmology-Optometry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Primary open-angle glaucoma, the leading cause of irreversible blindness globally, affects over 3% of people over 40 and is expected to exceed 111 million cases by 2040. Traditional management methods include pharmacological interventions and surgical techniques like laser therapy and trabeculectomy. Researchers are exploring alternative surgical methods like ab-interno procedures and microinvasive glaucoma surgery to reduce intraocular pressure and promote recovery. This literature review aims to study the various treatment methods in POAG to establish their functionality and clinical significance.

**Aim of study.** Studying the variety of methods of treatment in open angle glaucoma in order to establish the functionality and clinical significance.

**Methods and materials.** The study analyzed literature on MIGS from 50 abstracts and articles using the PubMed database, optimizing search using Medical Subject Headings terms and free-text keywords, including randomized controlled trials and case series.

**Results.** MIGS is a potential treatment for glaucoma, targeting different pathways for aqueous humour drainage. It offers improved safety features and shorter recovery times. It is often recommended for mild to moderate glaucoma due to its smaller effect on IOP reduction. However, its efficacy in advanced cases or patients with lower target IOP may be limited. Further research is needed to assess long-term consequences and comparative effectiveness across different MIGS methods. The cost-effectiveness of MIGS compared to traditional glaucoma operations remains uncertain.

**Conclusions.** The study demonstrates that minimally invasive glaucoma surgery can significantly improve the quality of life and overall well-being of individuals. The majority of MIGS techniques are efficient and faster in restoring visual function compared to fistulating surgeries. The ab interno technique also has minimal complications, no antimetabolite usage, and preserves conjunctival integrity, making it suitable for combined cataract surgery.





## 7. TREATMENT AND REHABILITATION OF CHILDREN WITH CONGENITAL, UVEAL AND TRAUMATIC CATARACTS

**Author:** Lopotencu Francesca

**Scientific advisor:** Ivanov Gheorghe, MD, PhD, Associate Professor, Department of Ophthalmology-Optometry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

**Introduction.** Cataract among children is one of the major causes of preventable childhood blindness, affecting approximately 200,000 children worldwide, with an estimated prevalence ranging from 3 to 6 per 10,000 new-borns. Early diagnosis and treatment are crucial to prevent the development of irreversible amblyopia and strabismus.

**Aim of study.** Appreciation of treatment methods and rehabilitation of children with congenital, uveal and traumatic cataracts.

**Methods and materials.** Clinical research was based on the evaluation of 35 medical records. The aspects investigated were: children's gender, age, living environment, diagnosis, associated pathologies, heredo-collateral antecedents, morphological type of cataract, associated ocular diseases, visual acuity, treatment, complications, postoperative rehabilitation (binocular vision).

**Results.** Thirty-five children participated in the study, of which 29 children were diagnosed with congenital cataract, 4 with uveal cataract and 2 children with post-traumatic cataract. Most of them were males with a 2:1 ratio. The majority of study subjects were infants ( $n = 12$ ) and children aged 2 to 12 years ( $n = 23$ ). Posterior polar cataract reported 51.4% was the most common morphological form. Nystagmus in 28.5%, convergent strabismus in 14.2% and divergent strabismus in 5.7%, amblyopia in 14.2%, microcornea in 5.7% and microphthalmia in 6.60% were found as associated eye features. The method of choice in the treatment of congenital cataract has been surgery. In 80% cases, ECE (extracapsular cataract extraction) was performed by phacoaspiration with IOL (intraocular lens) implant. The IOL models used for surgery were: Acrysof IQ - SN60WF; Acrysof Multipiece - MA60BM; Acrysof IQ Toric - SN60T3; Acrysof IQ Panoptix - TFNT00; Bi-Flex POB-MA - 877PAY. Among post-traumatic children, anterior chamber placement and removal of lens masses was performed. Intraoperative complications were detected among 20% of children and postoperative complications at 57.14% of children, including: corneal edema 17.14%, macular edema 2.85%, iritis 2.85%, exudative reaction in anterior chamber 5.71%, secondary incipient peripheral cataract 54.28%, posterior capsule fibrosis 11.42%, corneal dystrophy 5.71%. The most common intraoperative complication was vitreous body herniation in the anterior chamber. Secondary incipient peripheral cataract was the most popular postoperative complication, solved by laser capsulotomy. The use of video computerized self-training in postoperative period contributed to the restoration of binocular vision and correction of obscurative amblyopia.

**Conclusion.** As demonstrated in our study, CMV infection is the most common cause of congenital pediatric cataract. Other causes being herpes simplex virus infection, congenital TB or Down's syndrome associated. Recent advances in surgical techniques, more predictable IOL power calculation, IOLs composition and design, early postoperative use of contact lenses for optical rehabilitation have contributed to improved outcomes after pediatric cataract surgery.

## **XIV. OTORHINOLARINGOLOGY SECTION**



*„Cercetarea este un pilon fundamental al progresului și inovației în lumea științifică și academică. Implicarea studenților în activități științifice nu este doar o oportunitate, ci și o necesitate în formarea lor ca viitori profesioniști și lideri în diverse domenii. Studenții au posibilitatea de a-și dezvolta abilitățile practice și de a aplica cunoștințele teoretice într-un mediu real. Această experiență nu doar consolidează înțelegerea lor asupra subiectelor studiate, ci îi pregătește pentru a deveni profesioniști competenți în cariera lor viitoare. Implicarea în cercetare îi ajută pe studenți să-și dezvolte gândirea critică, abilitățile de analiză și sinteză, capacitatea de rezolvare a problemelor și abilitățile de comunicare. Mai mult decât atât, activitățile de cercetare oferă studenților oportunitatea de a contribui la progresul științific și de a aduce inovație în domeniile lor de interes.*

*Fiți curajoși, fiți pasionați și angajați-vă în această călătorie extraordinară către cunoaștere și inovație. Vă urez mult succes și satisfacție în călătoria voastră în lumea cercetării!”*



***"Research is a fundamental pillar of progress and innovation in the scientific and academic world. Involvement of students in scientific activities is not just an opportunity but also a necessity in shaping them as future professionals and leaders in various fields. Students have the opportunity to develop their practical skills and apply theoretical knowledge in a real-world setting. This experience not only consolidates their understanding of the subjects studied but also prepares them to become competent professionals in their future careers. Involvement in research helps students to develop critical thinking, analytical, and problem-solving skills, as well as communication abilities. Furthermore, research activities provide students with the opportunity to contribute to scientific progress and bring innovation to their areas of interest.***

***Be brave, be passionate, and engage in this extraordinary journey towards knowledge and innovation. I wish you much success and satisfaction in your journey in the world of research!"***



***Ion Ababii,***

*Professor, MD, PhD, Academician,*

*Department of Otorhinolaryngology,*

*Nicolae Testemitanu State University of Medicine and Pharmacy,*

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## 1. BENIGN TUMORS OF THE VOCAL CORDS. GENERAL NOTIONS. EPIDEMIOLOGY, ETIOPATHOGENESIS AND TREATMENT.



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**Introduction.** Benign vocal lesions are non-malignant growths of abnormal tissue on the vocal cords. The common benign lesions of vocal cord are singer's nodule, polyps, papilloma, polypoid degeneration (Reinke's edema) and cysts. Others are sulcus vocalis, mucosal bridge, intracordal cysts, vocal cord varices and anterior webs. Several factors can be responsible for the development of the benign vocal lesions such as vocal abuse, overuse or misuse of voice, chronic infections of upper airway, allergy, smoking and gastroesophageal reflux. Frequent coughing and throat clearing also contribute to the mucosal irritation which worsens the voice. Excessive mechanical trauma and stress in the mid membranous area of the vocal cord leads to wound formation. Subsequently remodeling of the superficial layer of the lamina propria and, to a lesser extent, epithelium results in the formation of vocal cord nodules, polyps, and cysts. Several studies have demonstrated that the pathologic changes in vocal cord polyps, nodules, and cysts occur within the superficial layer of the lamina propria

**Aim of study.** The etiological relationship between smoking and vocal fold polyps has been widely studied. Some authors consider smoking as the primary factor for the development of vocal fold polyps, mainly when associated with vocal abuse.

**Methods and materials.** The present study is a review article based on a bibliographic search using platforms, databases and search engines, without restrictions on means of publication, methodological quality or language. Articles on benign vocal cord tumors related to the study object published in the last 5 years were included.

**Results.** Vocal trauma, especially in women and children, is a strong risk factor for vocal cord nodules and cysts. Gastroesophageal reflux is a suggested risk factor for Reinke's edema and contact granuloma. Smoking and alcohol consumption are the risk factors that predominate in the male gender causing especially polyps and Reinke's edema. Identifying risk factors is an important step in therapy planning.

**Conclusion.** The voice is the main actor in our daily life. It allows us the main means of communication between people. Approximately 30% of the population has dysphonia at some point in their lives. Since dysphonia is only a symptom and not a diagnosis, each case of dysphonia must be carefully examined to determine the causes. Also, early diagnosis of benign tumor processes is very important for treatment and restoration of the voice as quickly as possible.



## 2. CELL THERAPY IN CHRONIC RHINOSINUSITIS IN CHILDREN

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**Introduction.** Chronic Rhinosinusitis is one of the most common chronic diseases worldwide, having an incidence between 1%-12% Globally and an incidence of 10.9% in Europe. CRS (Chronic Rhinosinusitis) is an underestimated disease, this condition leads to a significant impact on the quality of life of the patients it affects, furthermore, CRS has an unquestionable impact on a societal level with increasing economic losses attributed to this disease.

**Aim of study.** This literature review aims to find and discuss evidence that relates to the complex treatment of CRS with Cell Therapy, putting in the spotlight the molecular, morphological, and structural nuances that stand at the base of understanding CRS and its treatment with Cell Therapy.

**Methods and materials.** For the elaboration of this literature review, scientific evidence about the efficacy of Cell Therapy in CRS was collected from sources such as ScienceDirect, PubMed, The International Journal of Cell Differentiation and Proliferation, and The Moldovan Medical Journal.

**Results.** In a study conducted on 19 pediatric patients with CRS and 116 healthy children, statistically significant differences were found. CRS patients have shown higher levels of IG E ( $9.2 \pm 0.27$  vs  $57.9 \pm 22.79$ ) and CD4/CD8 thus showing an allergic and inflammatory implication. ASL-O was also significantly higher in patients suffering from CRS in contrast to the healthy control group ( $11.5 \pm 2.08$  vs  $178 \pm 96.5$ ). In addition, a statistically significant decrease of T-lymphocyte activity was reported in ill individuals in comparison to healthy individuals. Furthermore, an increase of B-lymphocyte activity was noted with the increase in IG A levels. Treatment using cell therapy was administered, the study group was treated and assessed over a period of one year. During this period clinically significant improvements were noted, a decrease in nasal resistance, and an increase in total volume indices were found in all children treated with autologous mononuclear cells. Another In Vivo study has shown the role of mesenchymal stem cells in the treatment of CRS. 70 subjects were studied, of which 32 were the control group and 32 where exposed to *Aspergillus fumigatus*, 12 of those exposed to *Aspergillus fumigatus* underwent treatment with mesenchymal stem cells (MSC). Subjects treated with MSC daily evolution were monitored, which showed great improvement in contrast with the group that did not undergo MSC treatment. Histological lesions were minimal, and most of the sinuses and nasal mucosa were found to be normal. Furthermore, Patients that underwent Cell therapy have shown lesser resistance to antibiotics.

**Conclusion.** The aforementioned results have shown evidence that Cell Therapy is effective in the complex treatment of CRS.



### 3. CHRONIC SUPPURATIVE OTITIS MEDIA COMPLICATED WITH FACIAL PARESIS



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**Scientific advisor:** Vetricean Sergiu, MD, PhD, Professor, Department of Otorhinolaryngology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** Chronic otitis media (COM) is a recurrent infection affecting the middle ear and/or mastoid air cells, often accompanied by a perforated tympanic membrane (TM). Additionally, COM may progress to a condition known as cholesteatoma, characterized by the presence of a skin cyst situated behind the eardrum. As the cholesteatoma enlarges over time, it damages the fragile middle ear bones. Both chronic otitis media and cholesteatoma have the potential to extend into the inner ear, resulting in enduring complications such as hearing loss, vertigo, and facial paralysis. If the infection spreads further to the brain, it can lead to severe health issues.

**Case statement.** We present the case of a 29-year-old patient, who had facial paresis consulting a neurologist and that took the medical treatment and did physiotherapeutic procedures with no success, with the general mood going worse, associating left facial hemiparesis. Since childhood he has suffered from hypoacusis on the left ear. Based on clinical exam the patient is diagnosed with chronic suppurative otitis media, for treatment being decided to perform enlarged petromastoidian evidation with facial nerve decompression.

**Discussions.** Under local anesthesia and sedo-analgesia, in aseptic conditions, there was performed retroauricular incision with taking off the soft tissues and highlighting the Spine of Henle and the mastoid region, the mastoid was milled, in the attack triangle we visualize the external cortex, the first pneumatic cells. In the projection of the antrum there are highlighted masses of cholesteatoma, upon removal of the cholesteatomatous content and the posterior wall of the external auditory canal, the portion of the facial nerve is highlighted in the tympanic region, the nerve being exposed, it was edematous, it was decompressed with the help of curette, there was scooped fallopian tube to the region digastrica, along the entire route of the edematous nerve. There was also identified the presence of cholesteatoma with dissemination in the lateral semicircular canal with its destruction and the posterior semicircular canal. The surgery was finished with an open wound. Dressings were performed daily, after 10 days the wound was sutured and meatoplasty was performed.

**Conclusions.** The case emphasizes the seriousness of chronic suppurative otitis media (COM) progressing to cholesteatoma, leading to significant complications, and also demonstrates the importance of early diagnosis and proper treatment that could avoid facial paresis and other complications.



#### 4. COCHLEAR IMPLANTATION IN DEAF-MUTE ADULT WITH PARTIAL OPTIC NERVE ATROPHY

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**Introduction.** Congenital deafness together with that acquired at a young age represent important pathological conditions, with an incidence of about 1-3 cases per 1000 live births, being diagnosed relatively late has negative effects on the development of spoken language. Cochlear implant is the most effective method of restoration of auditory function at patients with severe neurosensory deafness. It is an electronic device that converts sound information into electrical impulses and directly stimulates the auditory nerve.

**Case statement.** Patient C., 26 years old, has double impairment of both hearing and vision - diagnosed with "Bilateral sensorineural deafness severe - profound form. Partial optic nerve atrophy". The patient was considered to be sick since early childhood, after suffering a perinatal cranio-cerebral trauma. As a result of severe hearing and vision impairments, the child presented retardation in neuropsychic development. Thus, in order to improve the patient's quality of life, it was established the necessity of carrying out the cochlear device implantation intervention at the level of the right ear. The preoperative preparation of the patient included clinical and paraclinical examination of organ systems. ORL local status: bilateral otoscopy – wide external auditory canal, tympanic membrane gray, absent perforation; rhinoscopic - nasal mucosa pink-pale, nasal septum located on the midline, nasal turbinates normotrophic; oropharyngoscopic - pink and moist oral mucosa, wet and clean tongue, normotrophic palatine tonsils.

**Discussions.** During the years the presence of visual impairment together with the prelingual sensorineural deafness had have serious repercussions on the development of verbal language and neuro-cognitive evolution of the patient, affecting the quality of his life in all spheres, realizing interpersonal and social interaction through the tactile sense provided by the mother's hands.

**Conclusion.** However, cochlear implant in adult patients diagnosed with prelingual sensorineural deafness cannot fully recover auditory-verbal development. At the currently examined patient who also presents a decrease in visual acuity – the intervention resulted in an improvement of the quality of the life, giving him possibility of spatial orientation and interaction with society not only through tactile perception but also through auditory perception.

## 5. COMPLICATION OF RHINOPLASTY



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**Introduction.** Rhinoplasty is one of the most frequent plastic surgeries in the maxillofacial region, the purpose of which is to change the shape and size of the nose, eliminate curvature, align the nasal septum, correct nasal defects, both congenital and acquired, as well as to improve the functions of the nose. However, like any other surgery, rhinoplasty involves risks and complications, so every practicing surgeon must have a thorough understanding of the anatomy of the nose and the surgical manipulations involved to reduce risks and avoid complications. Central to the evaluation and planning of surgery is a thorough anamnesis, physical examination, preoperative consultation with allied specialists, and a discussion of all risks, possible complications, and alternative treatments directly with the patient.

**Aim of study.** Assessment of likely immediate and delayed complications of rhinoplasty.

**Methods and materials.** The evidence base is built on the analysis of scientific articles from Google Scholar, PubMed, ResearchGate, Elsevier, using keywords such as "rhinoplasty," "rhinoplasty complications," "immediate complications," and "delayed complications" for the period from 2013 to 2023, totaling 55 scientific articles.

**Results.** According to the results of analyzing scientific articles, most authors note that complications of rhinoplasty can be both immediate and delayed. The most frequent immediate complications are nasal bleeding (hematoma), which occurs in 0.2-3% of cases. The second place is occupied by infections at the surgical site (cellulitis or abscess) - up to 1.5%, out of which venous thromboembolism - 0.1%, the third place - divergence of edges/sutures - 0-5%. The delayed complications may be the following: septal perforation - 1-5%, changes in breathing or taste - less than 1%, postoperative scars - 0-1.5%, and skin discoloration. The reoperation itself after the detection of complications is noted separately, as repeated traumatization of the operated area increases the possible risks of new complications by 5-15% according to different sources. According to many authors, even additional operations in other areas of the body (nose - complication rate of 0.58%, nose + face - 1.04%, nose + body - 0.84%, nose + chest + face + body - 7.14%, etc.) increase the likelihood of complications, including on the rhinoplasty performed.

**Conclusion.** The result of rhinoplasty is difficult to predict, but by conducting comprehensive work in the form of preoperative preparation (careful collection of anamnesis, photo documentation, physical examination), knowledge of likely complications and methods of their elimination, as well as constant contact with the patient and a discussion of alternatives, will reduce the likelihood of risks and objectively assess the results of treatment.



## 6. DISTANT COMPLICATIONS OF CHRONIC TONSILLITIS.

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**Introduction.** Chronic tonsillitis is a persistent inflammation of the palatine tonsils, often marked by recurrent acute episodes of tonsils inflammation, known as angina. While the condition primarily affects the throat, the consequences of chronic tonsillitis extend beyond the immediate site of infection, leading to distant complications, such as arthritis, glomerulonephritis or other related conditions.

**Aim of study.** This review aims to highlight the incidence of the most commonly encountered distant chronic complication that may arise in this infection.

**Methods and materials.** We have analyzed the medical records of those patients who were hospitalized in the IMSP Institute of the Mother and Child Clinic „Emilian Cotaga,, between 2021-2023, focusing on individuals diagnosed with chronic tonsillitis.

**Results.** In the selection process, we identified patients who developed complications. This detailed approach has allowed us to highlight factors such as gender distribution, the impact of the living environment of the condition, and the type of complications encountered. One thousand eighty-nine (1089) patients were collected during this period, 717 (65.8%) of them were with uncomplicated tonsillitis, 372 (34.2%) with complication, female – 243 (65.3%) and boys – 129 (34.7%), urban – 539 (49.5%), rural – 550 (50.5%) . The complications observed in this study varied, with reactive arthritis – 187 (50.2%) being the most prevalent, followed by rheumatic fever – 123 (33.1%) and poststreptococcal glomerulonephritis – 62 (16.7%).

**Conclusion.** Our study on chronic tonsillitis aimed to illuminate the incidence of its most prevalent distant complications. The timely identification of distant complications associated with chronic tonsillitis in children and the implementation of a tonsillectomy are essential measures that can prevent serious consequences such as disability. At the same time, they can significantly contribute to improving the quality of their life.

## 7. EMPTY NOSE SYNDROME



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**Introduction.** Empty nose syndrome (ENS) is considered primarily an iatrogenic pathology, secondary to surgical treatment on the middle and lower nasal cornet. The frequency of ENS is not known exactly, several studies have reported an occurrence rate of 8%-22% in patients who have undergone turbinate reduction.

**Aim of study.** To review current knowledge of pathophysiological mechanisms and clinical manifestations in relation to empty nose syndrome (ENT).

**Methods and materials.** A literature review of articles published on PubMed, Elsevier, Medline. To identify the relevant articles, the following keywords were used: "empty nose syndrome", "nasal obstruction", "turbinate reduction".

**Results.** Empty nose syndrome (ENS) remains a controversial topic in contemporary rhinology, despite an initial description almost 30 years ago. Although total turbine excision is the most common cause of ENS, smaller procedures (e.g., submucosal cauterization, submucosal resection, and, laser therapy and cryosurgery) for reducing turbinates can also cause problems if performed in an excessively aggressive manner. With a reduced surface area of the mucosa and no turbulent physiological airflow in patients with empty nose syndrome, the nasal mucosa cannot perform its main functions of air conditioning and cleansing generating a string of symptoms (paradoxical perception of nasal obstruction, despite normal nasal permeability, nasal crusting, dryness, nasal discharge, facial pain, sleep disorders, mental concentration disorders and suffocation). Standardized questionnaires SNOT-25 and ENS6Q are useful in diagnosing and evaluating subsequent treatment. A score of 11 out of 30 or greater on the ENS6Q has a specificity of more than 95% and a sensitivity or more than 85% for ENS. Pathology management includes mucosal humidification, irrigation and emollients. Surgical therapy should be reserved for refractory cases and may involve reconstruction of the cornetae, most commonly using implantable biomaterials.

**Conclusion.** Empty nose syndrome is a complex pathology. Recognition of empty nose syndrome is necessary in order to reduce the risk of ENS by aggressive turbinate surgery (total turbinate resection) which can lead to the development of the mentioned syndrome, except cases of tumor excision.





## 8. ETIOLOGICAL, DIAGNOSTIC AND TREATMENT ASPECTS OF CHRONIC LARYNGITIS.

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**Introduction.** Inflammatory processes affecting the upper respiratory tract can simultaneously exert a significant influence on the larynx and the surrounding mucosal surfaces. Inflammation in the larynx can be the direct result of exposure to irritants, toxins and antigens, but it can also be due to the involvement of mechanical and infectious factors. It can also occur as a consequence of a person's behavioral tendencies. Laryngitis is an inflammation caused by factors such as overuse, irritation or prolonged infection of the larynx. This manifests itself at the level of the laryngeal mucosa through edema, congestion, infiltration and proliferation of the epithelium, causing a chronic non-specific and non-tumoral alteration of it. Chronic inflammatory and degenerative processes, resulting from local irritant factors, contribute to damage to the laryngeal epithelium and can lead to the development of dysplasia and hyperplasia, including cancer. Chronic laryngitis, which manifests itself through voice disturbances and inability to talk, especially in cases of professionals that utilize mostly their speech, is also a social problem. A laryngitis that persists for more than 3 weeks is considered to be chronic laryngitis.

**Aim of study.** The aim of the paper is to review the etiological, diagnostic and treatment aspects of chronic laryngitis in the context of contemporary technical-scientific development.

**Methods and materials.** Specialized literature was used, while processing the information through the narrative synthesis method. Information was collected from the web field, namely publications from "pubmed", "reasearch4life" and other platforms, as well as national clinical protocols, national and international guidelines for the "ENT" field, manuals, articles, etc. all of these materials being published within 5-10 years from the date of access.

**Results.** There are numerous forms of chronic laryngitis, but all of them fall into these two big entities, namely: specific and non-specific laryngitis. In this study, all aspects of chronic laryngitis are addressed, from forms, symptoms to diagnosis and treatment.

**Conclusion.** We can say with confidence that chronic laryngitis is a complex pathology that requires a multidisciplinary approach, especially when discussing the specific types of laryngitis. Contemporary investigative methods currently available to specialists are essential, valuable and indispensable when it comes to diagnosing this pathology. The diagnosis and treatment of chronic laryngitis must begin as early as possible to avoid its transformation into cancerous forms, since chronic laryngitis itself is a precancerous stage.

## 9. OTOMYCOSIS: SYMPTOMS, CAUSES AND TREATMENT



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**Introduction.** Otomycosis is an isolated fungal infection of the external acoustic meatus. The causative strains that form biofilm inside the ear canal are mostly *Aspergillus* and *Candida*. Fungal external otitis has a worldwide distribution ranging from 9% to 30%.

**Aim of study.** This comprehensive review aims to create awareness about otomycosis and its management.

**Methods and materials.** This review is based on articles that were published during the last 5 years from the databases: PubMed, Medscape, NCBI, NIH. The keywords used are ‘otomycosis’, ‘fungal infections of external auditory canal’, ‘antifungal treatment of otomycosis’.

**Results.** Various predisposing factors may increase susceptibility of developing otomycosis, including heat, humidity, a history of ear surgical procedures, bacterial infections, immunosuppressive diseases, poor personal hygiene, etc. Fungal ear infection is usually unilateral with patients complaining of severe itching, aural discharge, otalgia, ear fullness, hearing loss and tinnitus. Examination of the ear canal is usually done through otoscopy and biomicroscopy, while confirmation is obtained through mycological exams. Treatment selection including the choice of antimycotics and method of application, should be based on specific fungal causative agents. Antifungal should be advised after antifungal sensitivity test. Suction evacuation and proper cleaning is the first step of treatment and dryness of the ear should be maintained. Topical therapy with antifungal or other antimicrobial agents is also necessary. Overall antifungals from the azoles class such as clotrimazole, fluconazole, ketoconazole and miconazole are more effective, followed by nystatin.

**Conclusion.** Otomycosis presents as a challenging disease for its long-term treatment and follow up, yet its recurrence rate remains high. Empirical therapy of treatment should be avoided and should maintain proper self-hygiene to avoid complications.



## 10. RHINOPNEUMOMETRY

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**Introduction.** Rhinopneumometry is an objective method of investigating nasal function, which allows to evaluate the capacity of the nasal passages and to determine possible nasal breathing disorders. This method is widely used in otorhinolaryngology to diagnose various diseases of the nose and adjacent areas.

**Aim of study.** To carry out measurements of air pressure and airflow velocity with subsequent computer processing of the obtained data in adults and children under the influence of various factors.

**Methods and materials.** In order to recognize the necessary publications were used databases such as PubMed, Medscape, Oxford Academic, using keywords: "Rhinopneumometry", "nasal breathing assessment", "nasal respiratory function"

**Results.** Rhinopneumometry allows to determine the presence and degree of respiratory function disorders, such as nasal obstruction, increased airway resistance and other pathologies, which allows to correctly diagnose and classify diseases, as well as to choose the most effective method of treatment. Subsequently, it can be used to evaluate the effectiveness of treatment of respiratory diseases and determine how successful the treatment is and what adjustments are necessary. Not unimportant for monitoring chronic respiratory diseases, regular measurements of airflow volume and velocity can help monitor disease progression and treatment efficacy.

**Conclusion.** Rhinopneumometry, in the modern understanding, is a combination of scientific and technological progress in the diagnosis, treatment and monitoring of respiratory diseases, as well as to assess physical activity. Respiratory function is the main one, and its violation affects the functional state of other organs and systems.

## 11. UNILATERAL SENSORINEURAL DEAFNESS CONTEMPORARY ASPECTS OF ETIOPATHOGENESIS, DIAGNOSIS AND TREATMENT.



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**Introduction.** Unilateral sensorineural hearing loss (SNHL) affects people of any age, can present as an acute or progressive process, and can range from mild to profound. Although the vast majority of cases have an unknown cause, known causes of unilateral SNHL must be excluded, including neoplasms, stroke, demyelinating and autoimmune diseases, infections, trauma, perilymphatic fistula and Meniere's disease.

**Aim of study.** The given study needs to be studied because many children with unilateral deafness are still not identified and diagnosed in time and need special attention to be evaluated, diagnosed, and treated for a better quality of life.

**Methods and materials.** The clinical observation sheets of the patients in the Republican Center of Audiology, Hearing Prosthetics and Pedagogical Rehabilitation served as study materials. 245 patients with unilateral deafness were selected. The age of the patients varied between 5 months and 17 years.

**Results.** Following the study of the 1211 files of patients with different types of hearing impairment, the patients with the diagnosis of confirmed unilateral sensorineural deafness were selected, being 245 (20.25%) in number. The male gender predominates in the study group 173(70.61%) of patients, female gender-72 (29.39%) patients. The causes of deafness following the selection of children are: 11 (4.5%) posttraumatic, 6 (2.44%) postinfectious, 3 (1.22%) acoustic trauma, 2 (0.81%) genetic malformation and the rest of unknown causes. In the nosological structure of deafness, the neurosensory type prevails in 1011 cases (90%), followed by mixed transmission types in 54 cases (5%). Of the 54 cases of mixed type deafness, 46 were congenital (4%), and 4 acquired (1%). Analyzing the information regarding the place of residence, it can be observed that the majority of children with unilateral sensorineural deafness come from the urban environment, more precisely from the municipality of Chisinau, followed by the districts of Ungheni, Cahul, Hîncești. The explanation would be the higher population density and more accessible medical services, especially audiological.

**Conclusion.** Hearing is one of the six senses that is the basis of communication, speech development and cognitive abilities of the child, contributing to the formation of the child as a personality. Hearing impairment in children, regardless of the etiology, leaves its mark not only on the quality of life, but also on the possibility of inclusion in society.

A large, light blue abstract graphic consisting of several curved, overlapping shapes that resemble a stylized bird in flight or a flowing ribbon, positioned vertically in the center of the page.

***XV. PATHOLOGY  
SECTION***



## 1. AN IN-DEPTH INVESTIGATION OF SYNCHRONOUS MULTIPLE PRIMARY TUMOURS (MULTICENTRIC AND BIVALENT) IN THE PANCREAS AND COLON.



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**Introduction.** Multiple primary synchronous malignancy refers to the development of multiple cancerous growths in one or more organs, which are identified within a timeframe of 2-6 months (according to SEER-IARC/IARC). The diagnostic criteria suggested by Warren and Gates hold significant importance.

**Case statement.** The intricate macroscopic surgical specimen from a 56-year-old patient was analyzed. The pancreatoduodenal complex includes a tumour located at the pancreatic head, measuring 4 cm with a star-like shape. The tumour has infiltrated the muscular layer of the duodenal wall, peripancreatic adipose tissue, and extends up to 2 mm from the surgical resection margin. The second tumour in the ascending colon exhibits an ulcerative-infiltrative appearance, it is 9 cm in size. The third tumour in the sigmoid colon displays an ulcerative-infiltrative appearance, with a size of 2 cm. The histological examination shows the presence of several synchronous multicentric and bivalent primary tumours in the ascending and sigmoid colon, as well as the pancreas. A poorly differentiated ductal adenocarcinoma in the pancreas. In the ascending colon, there is a mucinous adenocarcinoma with signet ring cells. In the sigmoid colon, there is a submucosal adenocarcinoma, moderately differentiated. From a clinical perspective, the patient exhibits symptoms of overall debility, body weight loss and jaundice.

**Discussions.** The prevalence of diagnosing multiple main tumours has markedly risen from the early studies, ranging from 2.4% to 17% in the past two decades.

**Conclusion.** The existence of several primary tumours, whether occurring simultaneously or at different times, highlights the intricate and diverse nature of cancer presentations. The management of multiple tumours presents diagnostic and therapeutic problems that necessitate a personalised and multidisciplinary approach.

**Keywords.** Synchronous, tumours.



## 2. CORONARY PERFUSION: REGULATION AND MECHANISMS OF DISORDERS

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**Introduction.** Coronary perfusion is a complex phenomenon ensuring the myocardial supply with oxygen and nutrients which is dependent on 2 major factors, such as myocardial compliance and feasibility of coronary arteries adequately to response on natural vasoconstricting and vasorelaxant agents. The coronary perfusion impairment could be either acute or chronic leading to development respectively of acute coronary syndrome (ACS) and chronic ischemic disease.

**Aim of study.** To reveal the main tools of coronary perfusion regulation and the key pathogenic mechanisms of coronary dysfunction.

**Methods and materials.** Was analyzed a material reflected in 20 recent articles found in Google.

**Results.** The crucial tool of coronary perfusion control is based on coronary Gregg phenomenon which embraces the capacity of coronary arteries to dilate on action of vasorelaxant factors mediated by endothelium, such as acetylcholine, bradykinin, adenosine, and prostacyclin. The main endothelium derived mediators are nitric oxide (NO), hydrogen sulfide, carbon oxide and endothelial hyperpolarizing factor which also confine the coronary constricting effect of norepinephrine, endothelin-1 and angiotensin II. Likewise, Vanhoutte coronary phenomenon providing coronary dilation due to hyperpolarization by epoxyeicosatrienoic acid (derivate of arachidonic acid) is also an important tool of coronary perfusion regulation. Moreover, it has a significant benefit in comparison with the Gregg phenomenon inasmuch does not depend on endothelium feasibility. Myocardium compliance or diastolic rigidity is tightly linked to its lusitropic function and quality of remodeling. Coronary atherosclerosis is considered as the main cause of coronary dysfunction, mainly based on endothelium dependent coronary reactivity impairment. When an atherosclerotic plaque obstructs an epicardial coronary artery more than 75% ACS develops and the worst clinical entity being acute myocardial infarction. Chronic coronary disease in the majority of cases is the result of decreased production of NO and negative coronary artery remodeling especially of subendocardial arterioles. Likewise, myocardial hypertrophy and increased fibrosis of extracellular matrix are significant pathogenic factors contributing to coronary perfusion diminution.

**Conclusion.** Endothelium dependent coronary perfusion is the physiological axis of normal hearts. Its disorder in association with coronary artery remodeling and myocardium diastolic rigidity represent main factors of coronary dysfunction. Meanwhile, the Vanhoutte coronary phenomenon dependent on hyperpolarization becomes a compensatory mechanism.

### 3. HEMOSTASIS DISORDERS IN CARDIOVASCULAR PATHOLOGIES AND CIRCULATORY MARKERS



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**Introduction.** Hemostasis as an important compartment of general homeostasis plays a crucial role in regulation of blood fluidity and vascular wall defect closing and recovery. However, hemostasis disorders accompanied with prothrombotic activity boosting lead to a risk of thrombus formation.

**Aim of study.** To reveal the main mechanisms of hemostasis disorders in diverse cardiovascular pathologies, and proper circulating markers.

**Methods and materials.** Was analyzed a material reflected in 22 recent articles found in Google.

**Results.** Conceptually hemostasis consists of 3 systems: pro-coagulant, anticoagulant and fibrinolytic. Installed prothrombotic statement is a result of primary hemostasis triggering by platelets followed by secondary hemostasis activation due to increased ratio of pro/anticoagulant involvement. White thrombus is characteristic for artery bed leading to a risk of acute myocardial infarction and stroke, but red thrombus is formed in veins being a trigger of deep vein thrombosis and pulmonary thromboembolism. Common for them is endothelial injury due to atherosclerosis, dyslipidemia, inflammation, oxidative stress. Likewise, antiphospholipid syndrome (eg, systemic lupus), decreased activity of anticoagulant and fibrinolytic systems, and pro-coagulant boosting are involved. The pathogenesis of arterial thrombus embraces a special mechanism linked to von Willebrand factor (vWF) released by damaged endotheliocytes which being a pentamer can open its sites for platelet receptors and collagen subendothelial fibers only in a rapid and turbulent blood flow inherent to arteries. For hemostasis disorders assessment are used indices reflecting these 3 systems of hemostasis. Thus, for pro-coagulant activation it's characteristic increased plasma level of vWF, fibrinogen, prothrombin, factor V, anti-phospholipid autoantibodies and monomers of fibrin (the last marker underlines the intensity of fibrinogen depolymerization under the action of thrombin). Anticoagulant decline is represented by decrease of antithrombin III, thrombomodulin, protein C and its cofactor protein S. The anticoagulant property of protein C is linked to endothelium expression of its specific receptors (family of annexins) which might be inhibited by anti-phospholipid autoantibodies. Fibrinolytic incompetence is assayed by diminution of plasmin level.

**Conclusion.** The main tool of hemostasis disorders induced circulatory dyshomeostasis is based on pro-thrombotic setting and the used markers are referring to activation of the coagulant system as well diminution of anticoagulant and fibrinolytic systems.



#### 4. IRON METABOLISM ASPECTS: MALABSORPTION, TRANSPORT AND STORAGE RELATED DISEASES

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**Introduction.** Iron Deficiency Anemia (IDA), the main Iron deficiency-based disorder, is one of the leading global health problems, affecting 22,8% (2019) of the population, the most exposed groups being rapidly growing children and premenopausal women. However, due to the variety of causes of iron deficiency, more groups have begun developing IDA. This fact provokes huge interest for medical researchers and clinicians upon diagnosis and treatment.

**Aim of study.** To identify the damage within metabolism mechanisms in iron deficiency and its systemic manifestations upon organ systems involved in the supply, transport and storage of iron.

**Methods and materials.** Systemic review of articles regarding the iron metabolism, transport and storage, and the manifestations of the disorders, provided by PubMed dated 2011-2019 and data provided by ScienceDirect dated 2014-2020. At the end of the selection process, 17 sources have been selected using keywords including „Malabsorption. Anemia. Deficiency. Transferrin. Metabolism.”, to be used in the literature review.

**Results.** The physiological iron circuit presents the uptake of iron from transferrin by erythroblasts development, the incorporation of iron into the heme, red blood cell (RBC) production, RBC survival, and RBC senescence in the spleen through transferring with the recycling of iron to the bone marrow. Diet is necessary to compensate for the amount of iron normally lost daily via the sloughing off of intestinal mucosal cells and menstrual blood loss in people with female reproductive systems of reproductive age. Various damage alongside the circuit (e.g. weak bioavailability, antacid treatment or elevated gastric pH, competition with other metals (e.g., copper, lead), loss or dysfunction of absorptive enterocytes, bowel resection, defects of intrinsic enterocyte, abundant blood loss etc.) including genetic disorders (e.g. Sickle cell anemia, . Hypotransferrinemia, etc.) and dietary insufficiency, can occur causing deficiency. The before-mentioned are able to cause bone-marrow, liver, spleen and intestine disorders, joined by complex clinical manifestations.

**Conclusion.** Iron deficiency associated disorders can present various etiological causes which require careful observation of the iron metabolism and its every step. Disorders caused by lack of uptake, malabsorption or other dysregulations manifest through systemic affections which can get more complicated if neglected.

## 5. MORPHOPATHOLOGY SIGNIFICANCE IN DETECTION AND DIFFERENTIAL DIAGNOSIS OF GASTRITIS.



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**Introduction.** The term Gastritis in morphopathology is used to describe the inflammation of gastric mucosa. Ordinarily gastritis is associated with *Helicobacter Pylori* which is positive in 85 % of patients, other cases of gastritis can be alcohol injury, unhealthy food. Definite diagnosis of gastritis is a correlation between endoscopy, laboratory and pathology report. It is essential to make a preventive diagnostic in time because an atrophic gastritis with intestinal metaplasia is a precancerous condition and can be turned into adenocarcinoma of the stomach within fifteen months.

**Aim of study.** Application of morphological, histochemical and clinical criteria in the correct diagnosis of gastritis.

**Methods and materials.** Were examined endoscopic biopsies from different anatomical parts of the stomach, later special histochemical reactions were used to detect *Helicobacter Pylori*. All final reports were described according to the international gastritis evaluation protocols.

**Results.** The examination of gastric biopsies highlighted the need for the correlation of the morphopathologist with the endoscopist in order to take more biopsy fragments according to the Sydney protocol. After the histological and histochemical study of the biopsy material, it was observed that in most cases of atrophic gastritis associated with *helicobacter pylori*, complete or incomplete metaplasia is present, which falls into the category of precancerous conditions. This speaks about the need to diagnose atrophic gastritis as early as possible with an appropriate treatment.

**Conclusion.** In conclusion we can establish that a correct diagnosis is a close multidisciplinary correlation between the morphopathologist, the endoscopist and the clinical data, and in this context, it would be good to implement Tumor board in every hospital, which will help to establish a correct diagnosis and the appropriate subsequent treatment of the patient.





## 6. PATHOGENESIS OF SEXUAL DYSFUNCTION

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**Introduction.** This text discusses the prevalence and impact of sexual dysfunction, including issues like erectile dysfunction, orgasmic disorders, delayed ejaculation, premature ejaculation, and sexual pain disorders.

**Aim of study.** The findings highlight the widespread nature of these problems, emphasizing their impact on mood, interpersonal relationships, and overall quality of life in both men and women.

**Methods and materials.** This comprehensive literature review explores the global prevalence of erectile dysfunction (ED) and various sexual dysfunctions, providing insights into their epidemiology, impact on quality of life, and physiological aspects. The references cited cover a wide range of studies and sources, contributing to a thorough understanding of the addressed problems in male and female sexual health.

**Results.** This text provides insights into the diverse causes of sexual dysfunctions, emphasizing factors such as alcohol intake, neurogenic disorders, psychological issues, relationship problems, medications, stress, and cocaine use. It delves into the classifications of erectile dysfunction, including neurogenic origins, and explores the influence of hormones like testosterone on sexual function. Additionally, it discusses hypogonadism, hyperprolactinemia, and vascular factors as contributors to sexual dysfunction. The complexity of veno-occlusive dysfunction and its role in vasculogenic impotence is also outlined.

**Conclusion.** 1. Female sexual disorders are classified into: hypoactive sexual desire disorder, sexual aversion disorder, sexual arousal disorder, orgasmic disorders, sexual pain disorders. 2. Male sexual dysfunction (MSD) is associated with a wide range of physical and psychological conditions. 3. Erectile dysfunction is the most common studied aspect of MSD. 4. Multiple regulatory systems are involved in normal erectile function. 5. Disruption of psychological, neurological, hormonal, vascular, and cavernosal factors, individually, or in combination, can induce erectile dysfunction (ED). 6. The neurogenic, vascular, and cavernosal factors was reviewed, while psychological and hormonal factors contributing to ED

## 7. THE IMPACT OF THE 3 ENDOTHELIUM DERIVED GASSES (H<sub>2</sub>S, NO, CO) ON VASCULAR ENDOTHELIUM HOMEOSTASIS



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**Introduction.** Vascular endothelium fulfills a lot of functions having a decisive role in the control of circulatory and general homeostasis. Among the endothelium derived factors three gasses occupy a special position being tightly connected to the intrinsic system orchestrating vascular homeostasis.

**Aim of study.** To assess the role of nitric oxide (NO), hydrogen sulfide (H<sub>2</sub>S) and carbon monoxide (CO) in the regulation of native endothelial functions.

**Methods and materials.** It has been selected and analyzed 30 recent articles from Google discussed this approach.

**Results.** NO is synthesized from L-arginine under the action of endothelial nitric oxide synthase (NOS3). Its main role consists in vascular muscular media relaxation due to formation of cGMP in smooth myocytes. Thus, NO provides the vasorelaxant effect of acetylcholine, bradykinin, adenosine and also mediates the impact of hemodynamic stress in order to equilibrate the blood flowing in systole and diastole. NO decreases the expression of pro-inflammatory cytokines, and this effect is connected to antioxidant system boosting. Likewise, NO reduces the oxLDL passing in neointima and expression of MCP-1 (monocyte chemoattractant protein) resulting in atherosclerosis mitigation. Another important effect of NO is blunting of smooth myocytes hypertrophy and their migration when secretory phenotype appears. Endothelial H<sub>2</sub>S is produced from L-cysteine and also has a vasorelaxant effect provided by 2 mechanisms: hyperpolarization and decreased expression of phosphodiesterase. In addition to antiplatelet and antithrombotic effects H<sub>2</sub>S stimulates angiogenesis, reduces smooth vascular myocyte proliferation and damaging impact of hyperglycemia, hyperhomocysteinemia and hypercholesterolemia. Remarkably, NO augments the H<sub>2</sub>S production due stimulation of L-cysteine uptake, and the decrease of their circulating level is occurring in patients with arterial hypertension and diverse kinds of endothelial injury. Endothelial CO is generated by two heme-oxygenase enzymes and demonstrates many similar effects to NO and H<sub>2</sub>S. CO independently dilates small arteries, but also interplays with NO in the process of vascular relaxation, because of increased expression of NOS3. CO stimulates angiogenesis, confines inflammatory response due to nuclear factor expression inhibition and vascular cell apoptosis due to mitochondrial cytochrome c leakage reduction.

**Conclusion.** NO, H<sub>2</sub>S and CO have many common beneficial effects regarding the native endothelial homeostasis, such as: vasodilatation, antioxidant, anti-inflammatory, antiplatelet, antithrombotic, antiproliferation, anti-remodeling.



## 8. THE MORPHOPATHOLOGICAL ASPECT OF METABOLIC-ASSOCIATED FATTY LIVER DISEASE.

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**Introduction.** Being proposed in 2020, the novel terminology for Metabolic-Associated Fatty Liver Disease (MAFLD) involves the strong association of fatty liver disease with metabolic factors rather than NAFLD, the term used to describe fatty liver conditions in the absence of significant alcohol consumption. The terminology transition involves the optimization of the wide spectrum of individuals with hepatic steatosis and their inclusion in a subphenotype that would comprise those with metabolic risk factors such as obesity, metabolic risk abnormalities and diabetes 2 mellitus. The accurate diagnosis of MAFLD necessitates a comprehensive and multidisciplinary approach, since one of the most relevant aspects in the diagnostic process is the histopathological examination in conjunction with clinical, laboratory and imaging assessments.

**Aim of study.** The purpose of the study involves recognition of distinctive histopathological criteria understanding different aspects of the disease, its mechanisms, risk factors and associations, diagnostic accuracy, treatment efficacy and overall impact on health.

**Methods and materials.** The research was carried out by reviewing a range of research studies and scientific literature from the PubMed database over the last years. An extensive investigation in English was performed on several articles related to the keywords: MAFLD, metabolic, morphopathology.

**Results.** Following the analysis of the reference literature it was found that for establishing the diagnosis of MAFLD an important link is the presence of overweight, type 2 diabetes mellitus or dysregulated metabolic factors. These criteria in association with steatosis contributes to the progression of the disease as well as the generation of extrahepatic complications. The histopathological analysis reveals the presence of lipid infiltrate in hepatocytes which, in association with oxidative stress, causes the subsequent appearance of high inflammatory activity and cirrhosis. The conclusive factor remains the significantly increased risk for fibrosis, cardiovascular associated diseases and gut dysbiosis.

**Conclusion.** Although the new classification presents many nuances and imperfections, histopathologically it is assumed that the specific triad for MAFLD "steatosis-inflammation-fibrosis" includes a favorable pharmacological scenario. The diversity of cardiovascular complications and other metabolic comorbidities helps to clearly delimit the pathogens, presenting an essential advantage to the new nomenclature. Unfortunately, being a relatively recently introduced term, it requires time for additional research as well as multidisciplinary involvement.

## 9. THE PATHOPHYSIOLOGY OF IRON DEFICIENCY IN THE BODY, ENDANGERMENT OF THE ABSORPTION, TRANSPORT AND STORAGE OF THE CATION. THE MAIN MECHANISMS.



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**Introduction.** Iron plays an important role in a multitude of physiological processes, such as the transport of oxygen from the lungs to the tissues, the release of molecular oxygen from organic compounds, favors the exchange of electrons in the redox process as well as the regulation of gene expression. Iron deficiency is manifested by the depletion of iron in the body, especially the reserves in macrophages and hepatocytes. Iron homeostasis is regulated by the hormone hepcidin, which controls the entry of iron into the plasma. By binding to its receptor (FPN), this hormone induces its degradation. Due to the increased expression of FPN on macrophages and enterocytes, the inhibition of hepcidin, which occurs in iron deficiency, increases the uptake and release of iron from macrophages. The scientific value of this work lies in its topicality, as 27% of the world's population suffers from liver-deficiency anemia, the most affected people being among young and pregnant women, children and adolescents.

**Aim of study.** Identifying the mechanisms that endanger iron absorption, transport and storage.

**Methods and materials.** The literature review from the PubMed and Google Scholar scientific databases was used in the research. The selected sources are from the period 2017-2022. The selection of sources was made using the key words: hepcidin, iron deficiency, anemia, iron absorption.

**Results.** The pathophysiological mechanisms of iron deficiency are mainly due to unbalanced nutrition. Normally, in the adult body, the amount of iron is estimated to be between 4 and 5g, it being unevenly distributed, the largest amount of iron being present in the blood cells (hemoglobin). Since the human body absorbs iron with difficulty, about 1-2 mg per day, the individual's daily intake should be about 10-15 mg. We get our iron intake from various foods such as legumes, meat, vegetables and fruits. Iron absorption is strongly influenced by different dietary factors. Inhibitors of iron absorption being calcium, phytates (substances obtained by combining phytic acid with various minerals), oxalic acid and polyphenols. At the same time, we also have substances that facilitate the absorption of iron, such as ascorbic acid and some proteins.

**Conclusion.** There are 3 mechanisms responsible for iron deficiency in the body. The first is systemic regulation that occurs with the help of the hormone hepcidin. The second system is cellular regulation that is controlled by IRPs. The third system is iron-restricted erythropoiesis that occurs as a compensatory mechanism to maintain stores of iron in the body, which also becomes the source of anemia.





## 10. THE ROLE OF CARDIAC FIBROSIS IN DIASTOLIC HEART DYSFUNCTION

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**Introduction.** Cardiac diastolic dysfunction (DD) represents globally one of the main causes for congestive cardiac failure, occurring in 1/3 of reported cases. DD is most commonly a consequence of systemic arterial hypertension and ischemic cardiomyopathy. Histopathologic studies of hearts affected by DD have determined excessive deposits of extracellular collagen and the reconstruction of the heart architecture, known as cardiac fibrosis. The remodeling of the extracellular matrix decreases the filling rate, compliance, and diastolic suction of the heart, therefore altering cardiac function. Current discoveries suggest therapeutic potential for reversing cardiac damage.

**Aim of study.** Emphasizing the pathophysiological and functional alterations of the fibrotic myocardium in the cardiac cycle and identifying therapeutic methods for countermanding cardiac damage.

**Methods and materials.** Systemic analysis of up to date articles about cardiac fibrosis and diastolic dysfunction via PubMed, Google Scholar, Medscape. 14 articles (2004-2020) were chosen as the main sources.

**Results.** The particular attribute in which cardiac fibrosis exerts modifications is the negative pressure created by the ventricle during diastole, leading to a rapid ventricular filling time, in which the collagen fibers act as an elastic system that stores energy with each contraction, consequently releasing it along with elongating the ventricle wall. From a pathophysiological outlook, the key point is the loss of energy during the distortion of the perimysial collagen, caused by the friction of internal molecules, a phenomenon called viscoelasticity. Therefore, the energy loss yields in passive stiffness and noncompliance of the ventricle wall, decreasing the diastolic suction and thus the preload of the heart. The aggregate of energy loss is directly relative to the rate between type I collagen fibers, and type III, with the latter decreasing as the fibrosis progresses. An additional factor that contributes to passive stiffness is the capacity of contraction by the fibrous tissue, independent of that of the muscle fibers, a process accomplished by the myofibroblasts. Excessive collagen synthesis has been demonstrated to be stimulated by the renin-angiotensin-aldosterone system, therefore angiotensin converting enzyme inhibitors, along with the activation of metalloproteinases may allow for reversing cardiac damage.

**Conclusion.** Cardiac fibrosis and associated diseases can manifest in various pathogenetic ways, therefore understanding the mechanisms of diastolic dysfunction allow for a better management of affected patients.



## 11. THE ROLE OF GENETIC ASPECTS IN PATHOPHYSIOLOGY OF CUSHING SYNDROME



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**Introduction.** Cushing's syndrome is considered a rare disease with an incidence of 0.2– 0.5 million population per year, with an average age of 41 years at diagnosis and 1–2 cases per 100,000 population per year. As known, at the base of syndrome stay hypercortisolism, that can be primary, secondary and tertiary. The most frequent cause of syndrome is pituitary adenoma, being 85%. But less encountered and well known is the genetic aspect, being 5% of causes.

**Aim of study.** To identify the role of genetic factors involved in pathophysiology of Cushing syndrome, as defects in PDE (phosphodiesterase), gene encoding the catalytic subunit of PKA (PRKACA) and ubiquitin-specific peptidase 8 (USP8).

**Methods and materials.** A synthesis of the literature published between 2020-2023 was performed using databases such as PubMed, Google Scholar, and ScienceDirect. It has been analyzed and 30 relevant articles and literature reviews published in the last decade, were reviewed to compile a comprehensive approach in pathophysiology of Cushing syndrome.

**Results.** As known the secretion of cortisol is dependent on the functioning of the hypothalamic-pituitary-adrenal axis, mediated by the hormones such as CRH and ACTH, feedback mechanism and on the different regulatory enzymes. The ACTH acts on the MCR2 receptors on the adrenal gland, which interact with specific associated proteins, activates adenylate cyclase (AC) and form cAMP that releases the C subunit from its inactivating regulatory form of PKA (PRKACA), thus activating PKA that phosphorylates different intracellular targets genes and transcription factor, responsible for synthesis of cortisol. Genetic defects of PRKAR1A gene lead to increased free catalytic subunits and protein kinase A activity. The mechanism that counteracts the action of PKA is the specific enzyme phosphodiesterase (PDE) which is responsible for the degradation of the intracellular cAMP, such decreasing activity of PKA. Genetic defects of PDE lead to permanent activation of PKA, leading to oversecretion of cortisol. New gene variant identified in the pathogenesis of Cushing's syndrome, as ubiquitin-specific peptidase 8 (USP8) gene, is responsible for recycling to the plasma membrane of epidermal growth factor receptor (EGFR) founded on pituitary corticotroph cells. The mutation of USP8 results in increased deubiquitination of EGFR that activates a mitogen activated protein kinase (MAPK)-dependent pathway which stimulates the expression of the ACTH secretion and in turn cortisol secretion.

**Conclusion.** Studying the literature, it has been found that a big role in pathogenesis of Cushing syndrome also has genetic factors, such as defects in PRKAR1A gene, defects in PDE gene expression, and more new research identifies another cause as mutation in USP8 gene. All of these gene defects are responsible for the development of hypercortisolism ACTH dependent and independent and are promising targets in a therapeutic perspective for Cushing's syndrome patients.



## 12. THE ROLE OF NO AND H<sub>2</sub>S IN CIRCULATORY HOMEOSTASIS REGULATION AND DYSFUNCTION

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**Introduction.** Modern concept corroborates vascular endothelium as a crucial pillar regarding the control of a lot of vascular derived functions in circulatory homeostasis, such as: basal vascular tone and blood pressure, anti-platelet, anti-thrombotic, anti-apoptotic, anti-growing, anti-proliferative activity etc. Nitric oxide (NO) and hydrogen sulfide (H<sub>2</sub>S) are considered as important factors in this range of events, because their deficiency is associated with tangible disorders of circulatory homeostasis.

**Aim of study.** Unraveling the role of NO and H<sub>2</sub>S in circulatory homeostasis regulation and dysfunction.

**Methods and materials.** Was analyzed a material reflected in 20 recent articles found in Google.

**Results.** NO is a gas produced by endotheliocytes from L-arginine under the action of neuroendocrine factors and hemodynamic stress. One of its main functions is vascular dilation due to cGMP formation in the smooth vascular cells. Likewise, NO inhibits expression of proinflammatory cytokines, blunts oxidative stress, decreases platelet adhesion, and mitigates vascular remodeling. H<sub>2</sub>S is also a gas produced by endotheliocytes from cysteine. It decreases vascular tone due to phosphodiesterase inhibition, upregulates antioxidant enzymes and decreases oxygen radical production, inhibits smooth vascular cell hypertrophy and proliferation, prevents platelet aggregation, has anti-atherogenic effect because decreases the level of homocysteine and LDL-cholesterol. Such serious diseases as arterial hypertension, stroke, and acute myocardial infarction are associated with reduced amounts of NO and H<sub>2</sub>S. A common pathogenic factor of NO and H<sub>2</sub>S lack is endothelium injury due to atherosclerosis, systemic inflammation, diabetes.

**Conclusion.** Both NO and H<sub>2</sub>S, as endothelium derived factors, demonstrate a large palette of beneficial functions concerning the circulatory homeostasis regulation, and their penury due to endothelial damage is viewed as an important trigger and tool of serious cardiovascular maladies, such as arterial hypertension, stroke and acute myocardial infarction.

### 13. TRANSTHYRETIN CARDIAC AMYLOIDOSIS AND BONE SCINTIGRAPHY: STATE OF THE ART DETECTION IN RARE DISEASES



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**Introduction.** Transthyretin cardiac amyloidosis (ATTR-ca) is a rare protein deposition disease characterized by the accumulation of amyloid in the myocardium altering its function. Diagnosing it has proven to be a challenge even for the most experienced physician mainly because the symptoms that these patients present are common in more than one disease. Until this day, the gold standard method for diagnosing ATTR is endomyocardial biopsy. However, due to the risk that it presents and the fact that it is widely unavailable, a correlation between clinical and paraclinical investigations is recommended in such cases.

**Case statement.** We present the case of an 82 years old female patient, suspect of cardiac amyloidosis based upon electrocardiography and ultrasonography criteria. The patient was sent to the nuclear medicine laboratory of “Sf. Spiridon” County Emergency Hospital and underwent bone scintigraphy with a Siemens Dual-Head Gamma Camera equipped with a low energy, high resolution collimator. We acquired whole body images (early at 10 minutes and delayed at 2 hours) followed by static and SPECT centered on the thorax, 2 hours after the i.v. administration of  $^{99m}\text{Tc}$  – HDP (dose = 9,86MBq/kg). The bone scan revealed high radiopharmaceutical uptake in the myocardium, suggestive for ATTR cardiac amyloidosis. As a result, the patient was referred to undergo genetic testing in order to determine the ATTR subtype involved (wild type - ATTRwt or mutated - ATTRm).

**Discussions.** Diagnosing ATTR-ca has always represented a problem for the practicing physician. Endomyocardial biopsy is not widely available and presents certain risks. Therefore, a correlation between the existing techniques (biomarker, electrocardiography, ultrasonography) may represent the alternative solution. Nevertheless, these investigations are also limited, due to the fact that they are able to determine the presence of a possible cardiac amyloidosis, but are unable to determine the subtype involved. As a result, more complex investigations are required. Bone scintigraphy has demonstrated a unique ability for detecting and differentiating ATTR-ca from other forms of cardiac amyloidosis that affect the myocardium. The disadvantage in this case is the inability of bone scintigraphy to detect the ATTR subtype involved, therefore additional tests being required (genetic testing). Nevertheless, bone scintigraphy should always be taken into consideration if cardiac amyloidosis is suspected.

**Conclusion.** If endomyocardial biopsy is not an option and the patient is suspected for cardiac amyloidosis, then bone scintigraphy represents a viable alternative for detecting and differentiating ATTR cardiac amyloidosis. Therefore, this investigation should be considered as a must in the diagnostic algorithm for patients suspected of cardiac amyloidosis.



## ***XVI. PEDIATRY SECTION***

***„Dragi colegi, stimați studenți și rezidenți, vă doresc să deveniți adevărați profesionali, cu mare atenție față de micii pacienți și familiile lor, să aveți mereu parte de tot ce-i mai bun și frumos!”***

***„Dear colleagues, esteemed students, and residents, I wish for you to become true professionals, with great care for the little patients and their families, to always experience the best and most beautiful things in life!”***

***Ninel Revenco,***

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## 1. A CASE REPORT OF SINGLE VENTRICLE - PECULIARITIES OF EVOLUTION IN A 8-MONTH-OLD CHILD



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**Introduction.** Single ventricle is a type of malformation when the heart has both normally developed atria, but they open into a single ventricular chamber. The disease has a multifactorial nature in which both genetic and teratogenic factors during pregnancy are involved. This is a rare type of congenital heart defects (CHD): it accounts for no more than 2.5% of all, the overall incidence does not exceed 13 cases per 100,000 live newborns. Gender and ethnic differences in morbidity have not been established. The disease refers to critical congenital malformations, manifests soon after birth and is associated with a high risk of mortality. This explains its great importance in practical cardiology which requires improvement of medical care for such patients.

**Case presentation.** We present a case of a child born on 19.04.2023 from 4th pregnancy, 3rd delivery at 40-41 weeks of gestation (3rd pregnancy ended-up with spontaneous abortion at early stage). The body weight at birth was 2445 g and body length 49 cm. Apgar score was 7/8 points. The pregnancy was marked by oligohydramnios, severe gestosis in the first trimester and maternal smoking. Mother was not taking folic acid as recommended. Congenital heart disease in the fetus was diagnosed at 38 weeks of gestational age. After birth was confirmed the diagnosis of “Double inlet left ventricle associated with transposition of great vessels and pulmonary stenosis”. This type of univentricular atrioventricular connection accounts for two-thirds of cases. Although L-transposition of the great arteries (L-TGA) occurs more frequently, in our case was confirmed the D-transposition of the great arteries (D-TGA). During the first 5 months of life the child developed two episodes of pneumonia manifested clinically with peripheral cyanosis, fatigue, tachypnea and chest retractions, and poor weight gain. At the age of 7 months, he underwent pulmonary artery banding and bidirectional Glenn procedure. However, at the age of 8 months the child has severe malnutrition: weight 6,5 kg (<3 percentiles; <-2 z-scores), height 71 cm (50 percentiles) and weight-for-length ratio (<3 percentiles; <-3 z-scores). Unfortunately, the diseases progressed and at the age of 8 months and 12 days the child was hospitalized in an extremely severe condition with significant respiratory distress, severe malnutrition, unstable hemodynamic parameters and risk for sudden death.

**Discussions.** Although the child underwent surgical correction, the prognosis remains reserved due to additional risk factors, including malnutrition and generalized tissular hypoxia. In such cases supplemental oxygen may help alleviate hypoxemia, and acid-base or metabolic disturbances should have correctable factors mended.

**Conclusion.** The management of such complex types of congenital heart disease need a multidisciplinary approach with timely applied nutritional, metabolic and circulatory corrective measures.

**Keywords.** Complex congenital heart disease, single ventricle, pneumonia, malnutrition.





## 2. BURDEN OF BULLYING FOR MENTAL HEALTH STATE IN CHILDREN AND ADOLESCENTS

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**Introduction.** School bullying constitutes a complex and alarming societal issue that negatively impacts students worldwide. The term "bullying" refers to repeated behaviors of intimidation, aggression, or verbal and physical violence among students, resulting in an unequal power dynamic between the aggressor and the victim. This form of destructive behavior can have long-term consequences on the emotional and academic well-being of children and adolescents, adversely affecting the school atmosphere and creating an environment where learning becomes challenging and stressful. The incidence rate of bullying is on the rise, largely due to the indifference of adults, as some mature individuals persist in bullying behavior towards other adults and, especially, towards children.

**Aim of study.** Aim of study was to evaluate incidence rate of bullying among schoolers of 10-15 years old and to analyze their perception about its influence on their mental and physical well-being.

**Methods and materials.** I conducted a descriptive incidence study, which included a sample of 102 students from Chişinău. The research protocol was based on the method of surveying children and adolescents from various schools in the municipality of Chişinău. The study was conducted in January 2024 as part of a collaborative project between the Society of Pediatrics of the Republic of Moldova and school entities.

**Results.** In this survey, 5% of participants were 10 years old, 23.5% - 11 years old, 14.7% - 12 years old, 19.6% - 13 years old, 22.5% - 14 years old, and 14.7% - 15 years old. The gender distribution shows an approximately even split, with girls at 52.9% and boys at 47.1%. Most students (94.1%) are familiar with the concept of bullying. They understand physical abuse as a form of bullying (82.4%), followed by various forms of verbal abuse. Children most commonly perceive verbal bullying (51.5%) as the most prevalent, followed by social and online bullying, each at 17.2%. It's noteworthy that children perceive online bullying as equally serious as offline bullying (62.7%). Overall, the incidence rate of bullying is alarming among students, with 63.7% witnessing bullying acts, and 50.5% of students having been victims at least once. In the past year, 29.4% of children have been victims of bullying by multiple peers several times, 8.8% repeatedly, and 4.9% almost every day. Most children are likely to seek help from a family member (52.9%). Additionally, approximately 8% of children may not seek help, which could have repercussions on their mental health.

**Conclusion.** The study on the incidence rate of bullying among students aged 10 to 15 reveals a concerning social reality. The analysis of collected data highlights that a significant percentage of schoolers face various forms of bullying in their school environment. This finding emphasizes the need for a proactive approach to prevent and manage this phenomenon.

### 3. CARDIOVASCULAR DAMAGE IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS



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**Introduction.** Juvenile Systemic Lupus Erythematosus (jSLE) is a rare autoimmune disorder affecting multiple systems in children and adolescents causing unique challenges in diagnosis and management. Cardiovascular involvement, although rare, is a potentially life-threatening complication of jSLE, necessitating a thorough exploration of existing literature to understand the extent and implications of cardiovascular damage in this vulnerable population.

**Aim of study.** Kids are not to be treated as ‘little people’. While research has progressed in understanding the cardiovascular implications of adult-onset SLE, the scarcity of studies on cardiovascular damage in children with SLE is a concern due to significant differences in clinical features. This literature review aims to thoroughly examine the cardiovascular damage in children with Systemic Lupus Erythematosus. It seeks to analyze the prevalence and types of cardiovascular complications, identify risk factors and explore early diagnostic markers. The ultimate objective is to improve comprehension, guide future research and develop recommendations for the prevention and management of cardiovascular complications in jSLE.

**Methods and materials.** A systematic approach was employed to examine peer-reviewed articles and studies across databases such as PubMed, Google Scholar and Science Direct, prioritizing publications from the last decade. Keywords include “juvenile systemic lupus erythematosus” “children with sle” “cardiovascular damage in sle”

**Results.** The synthesis of the literature reveals that cardiovascular involvement in jSLE is primarily manifested as pericarditis, valvulopathies, and premature atherosclerosis. Non infective endocarditis and cardiac tamponade are rare. Vasculitis is predominantly cutaneous than visceral. Additionally, the review highlights the presence of increased disease activity, impact of traditional cardiovascular risk factors and immunological factors on the development and progression of cardiovascular damage in this pediatric population. Early disease onset and exposure to early corticosteroid treatment further burdens ease of life for children.

**Conclusion.** In conclusion, this literature review reveals the need for heightened awareness and comprehensive management of cardiovascular damage in children with SLE. The findings emphasize the multifactorial nature of cardiovascular damage in jSLE and the importance of early detection and age-appropriate interventions to improve outcomes and quality of life for children and adolescents with SLE.



#### 4. CONGENITAL HEART DISEASE LEFT -TO- RIGHT SHUNT

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**Introduction.** The congenital heart condition, known as cardiac septal defect, involves lesions in the atrial or ventricular septum, significantly impacting infant and child mortality. This malformation stems from disrupted developmental pathways responsible for heart structure, but the precise genetic, epigenetic, and environmental factors involved remain unclear. Approximately 8-12 of every 1000 live births experience congenital cardiac disease, necessitating around 10,000 surgical interventions annually in the United Kingdom. While these abnormalities often surface during pregnancy or early life, diagnoses may be delayed until later stages. Echocardiography, rapid, affordable, and adept at revealing structural abnormalities, stands as the preferred imaging modality for congenital heart issues.

**Aim of study.** To evaluate the clinical and paraclinical characteristics of CHD with left to right shunt in relation to defect type and specific characteristics.

**Methods and materials.** The observational study includes children with atrial septal defect (ASD) and ventricular septal defect (VSD). We randomly chosen 40 patients. 20 patients in a group of A with ASD and in a group B we have a 20 patient with VSD. Criteria of inclusion: preoperative period patient aged 0 to 18. Criteria of exclusion: those who undergone the surgical intervention. Keywords: congenital heart malformation, atrial septal defect, ventricular septal defect, left to right shunt

**Results.** Group A: Children aged  $3.8 \pm 0.6$  years, with ASD cases including ostium secundum 12 (60%), ostium primum 6 (30%), sinus venosus 2 (10%). Risk factors: alcohol usage (25%), Down syndrome (30%), maternal age over 35 (15%). Symptoms: dyspnea (20%), fatigue (35%), poor physical development (30%), respiratory infections (10%), chest retractions (5%). Only 7 (35%) experienced symptoms. Group B: Children aged  $1.1 \pm 0.2$  years, with VSD cases including membranous 10 (50%), muscular 6 (30%), infundibular 4 (20%). Risk factors: Down syndrome (45%), maternal age over 35 (35%). Symptoms: dyspnea (80%), fatigue (90%), poor physical development (65%), respiratory infections (65%), chest retractions (60%). 18 (90%) experienced symptoms. Comparison: Group B experienced pulmonary hypertension more frequently (90% vs. 25% in Group A;  $p < 0.01$ ).

**Conclusion.** Most ASD and VSD diagnoses occur in early childhood. ASD patients are often asymptomatic and identified during routine clinical exams, while VSD tends to manifest clinical signs earlier. ASD typically displays a more benign progression compared to VSD. Although the "ostium secundum" ASD type may close spontaneously, significant-sized ventricular defects can rapidly lead to complications, such as cardiac insufficiency and pulmonary hypertension.

## 5. CONGENITAL VASCULAR MALFORMATIONS OF THE AORTIC ARCH AS A RISK FACTOR FOR RECURRENT PNEUMONIA IN CHILDREN - CASE REPORT



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**Introduction.** Congenital heart disease (CHD) is one of the most common congenital structural disorders in childhood morbidity with a prevalence of 10 cases per 1000 live births, and is an important cause of childhood mortality. Aortic arch anomalies represent a less common group of CHD with an incidence of 0.003/1000 live births and account for about 1% of all CHD, which also include vascular rings with an estimated prevalence of about 1 in 10,000 live births.

**Case presentation.** Child A.S., male, born on 29.09.2020 at 41 weeks of gestation. The child is from the 2nd pregnancy, and is the 2nd child in the family. He was born with weight 3000 g (25-50 percentiles) and body length 52 cm (85 percentiles). At the age of 3 months, based on imaging data, the child was diagnosed with CHD with dextroposition of the aortic arch and descending thoracic aorta, and moderate focal narrowing of the left pulmonary artery lumen at the level of the pulmonary trunk bifurcation. Over the course of the disease, the child developed COVID-19 infection complicated by bilateral polysegmental pneumonia (in S6, S10 on the right and S6, S8, S9, S10 on the left), with severe evolution and atelectasis formation. At the age of 17 months the child's Angio-CT showed an aberrant right subclavian artery with incomplete vascular ring formation and signs of moderate pulmonary hypertension. By the age of 24 months, at which time surgical correction of the CHD was performed, the child had suffered five episodes of complicated pneumonia with progressive and persistent course, anemia (hemoglobin level reaching 90 g/l) and malnutrition - at the age of 24 months the child weighed 10 kg (5 percentiles, -1.67 z-scores). Despite the vascular ring excision and rudimentary aortic arch resection with tracheal release, the child develops congestive heart failure, NYHA functional class II.

**Discussions.** Symptomatology in vascular ring depends on the degree of compression of two mediastinal structures - trachea and esophagus, the severity of which correlates directly with the degree of compression. The most common symptoms include stridor, chronic cough, recurrent respiratory infections including pneumonia. The vessel that by its trajectory creates a vascular ring around the trachea and esophagus is the aberrant right subclavian artery, which usually arises just distal to the left subclavian artery and crosses the posterior part of the mediastinum on its way to the right upper extremity.

**Conclusion.** Knowing the characteristic signs for the association of vascular malformations with trachea stenosis is important for establishing the diagnosis at early stages of the disease and applying surgical methods of treatment, as well as providing an effective strategy for the prevention of recurrent pulmonary infections, which may in turn have a negative impact on the cardiac function in the child with congenital malformation of the heart and vessels.

**Keywords.** Aberrant subclavian artery, stenosis, vascular ring.



## 6. EMICIZUMAB IN PEDIATRIC HEMOPHILIA A: A CASE STUDY

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**Introduction.** The development of inhibitors that neutralize the function of clotting factor VIII is currently the most challenging complication associated with the hemophilia A treatment. Emicizumab is a humanized bispecific monoclonal antibody that is designed to substitute the hemostatic function of activated FVIII by bridging activated factor IX and factor X to activate FX, thereby facilitating the coagulation cascade and achieving hemostasis in patients with hemophilia A. Due to this mechanism of action, severe HA is changed into a mild form with an estimated FVIII activity of at least 9%.

**Case statement.** This study explores emicizumab intervention in a one-year-old with hemophilia A and inhibitors. Clinical records, labs, and imaging assessed bleeding severity. Emicizumab, following evaluation of history and titers, showed a reduction in bleeding frequency and severity. Improved clinical outcomes, joint health, and quality of life were observed. The study, addressing gaps in hemophilia A management in infants, emphasizes early diagnosis and personalized treatment.

**Discussions.** Emicizumab was licensed for bleeding prophylaxis in PWHIA with inhibitors and is thus the first approved non replacement therapy. Emicizumab prophylaxis resulted in a markedly reduced annual bleeding rate. After a loading phase of 4 weeks with a dose of 3 mg/kg body weight (BW) weekly, the maintenance therapy can be performed with 1.5 mg/kg BW weekly, 3 mg/kg every 2 weeks or 6 mg/kg BW every 4 weeks. Emicizumab is associated with beneficial effects on health-related quality of life and health status, and is generally well tolerated

**Conclusion.** Emicizumab's promising results highlight its potential in revolutionizing hemophilia A with inhibitors in infants, contributing to growing evidence supporting its efficacy in this challenging population



## 7. ETIOLOGY AND TREATMENT OF SUPRAVENTRICULAR ARRHYTHMIAS IN CHILDREN



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**Introduction.** The irregular heartbeats that take place above the ventricles are known as supraventricular arrhythmias. This study aims to investigate the causes as well as available treatments of supraventricular arrhythmias in pediatric patients.

**Aim of study.** Genetic factors and structural heart defects are two possible causes of these arrhythmias in children.

**Methods and materials.** A review of previous research, from 2020 till 2023 and case studies pertaining to pediatric supraventricular arrhythmias were conducted as part of the study.

**Results.** The study findings indicate that the etiology of supraventricular arrhythmias in children may be complex, involving factors such structural heart defects and genetic predispositions. Treatment options included medication with 70% success rate for single drug therapy, 90% success rate for catheter ablation, and, in certain circumstances, surgical intervention. These alternatives varied depending on the unique needs of each child.

**Conclusion.** In summary, a comprehensive strategy that takes individual circumstances into account is necessary for the etiology and treatment of supraventricular arrhythmias in children. In order to give all children individualized care and establish the best course of action, working together with pediatric cardiologists and other specialists is essential.



## 8. EVALUATION OF ADIPOSITY INDICES IN PEDIATRIC RHEUMATOLOGICAL DISORDERS

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**Introduction.** The Body Mass Index (BMI) is currently the most used indicator that assesses the nutritional status of children and adults, but it cannot fully reflect the difference between excess adipose tissue and that of muscle mass. The Tri-Ponderal Mass Index (TPI) is used as an alternative to calculate body weight recently, being successfully used to determine obesity, but also cardiovascular and metabolic risk factors. Data comparing BMI and TPI in the pediatric population with rheumatic pathology are currently not available.

**Aim of study.** To evaluate the effectiveness of the TPI, as well as to compare the usefulness of the TPI and BMI in assessing the growth and development of children.

**Methods and materials.** Our study included 881 children, hospitalized for a period of 2 years, in the Rheumatology section of the Mother and Child Institute, between December 1, 2021 and November 30, 2023. The value of the anthropometric indicators was calculated by age groups of children, as well as evaluated according to gender. The data were analyzed using the Microsoft Excel Office365 calculation program.

**Results.** Of the 881 children included in the study, 394 (44.72%) were boys and 487 (55.28%) were girls. The mean age of the children included in the study was  $10.73 \pm 4.54$  years (95% CI: 10.43; 11.03), with a ratio of girls/boys 1.23:1.0. The average values of the anthropometric indicators evaluated in the study were for BMI  $18.38 \pm 3.92$  (95% CI: 18.12; 18.64), and for TPI it was  $12.96 \pm 2.90$  (95% CI: 12.76; 13.15). Under the age of 3 years, 85 children were registered, of which 47 boys and 38 girls, between 4 and 10 years, 287 children (140 boys, 147 girls), and most of the children included in the study (57.78%) were older than 14 years (509 children: 207 boys, 302 girls). BMI in children up to 3 years was  $15.56 \pm 2.08$  (95% CI: 15.11; 16.01), and TPI included a value of  $17.15 \pm 3.65$  (95% CI: 16.36; 17.94). In children aged between 4 and 10 years, BMI included a value of  $16.49 \pm 3.67$  (95% CI: 16.06; 16.92), and TPI was  $12.89 \pm 2.76$  (95% CI: 12.57; 13.21). Most of the children included in the study obtained a value of  $19.92 \pm 3.54$  (95% CI: 1.1).

**Conclusion.** TPI represents an eloquent parameter of nutritional status and can be used to assess the growth and development of children, both in boys and girls. It can also be a predictive element of obesity and metabolic syndrome, as well as its associated factors. The TPI estimates body fat percentage more accurately than BMI in study children, and requires only one value for each gender, instead of the multiple complicated age- and gender-specific values required for BMI to be used especially in adolescents.

## 9. INTERVENTIONS FOR THE PREVENTION OF SMOKING AMONG CHILDREN AND ADOLESCENTS



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**Introduction.** Smoking is one of the most accepted habits among children and adolescents. Young people who use e-cigarettes or 'vaping' and other alternative forms of smoking have a wrong view of the risks they present.

**Aim of study.** Prevention of smoking among children and adolescents and the involvement of family doctors in this process.

**Methods and materials.** We conducted a descriptive incidence study, which included a group of 53 family doctors from Hâncești and Strășeni districts. The research protocol was based on the method of questioning family doctors during the organized workshops. The study took place during the month of December 2023 according to the collaboration project between the Pediatric Society of the Republic of Moldova and the American Academy of Pediatrics.

**Results.** The rate of e-cigarette use increases significantly as late adolescence is progressing. After the age of 14, the rate of e-cigarette use exceeds to 50%. The age at which children try other alternatives for smoking is another alarming aspect. According to the data, 2.38% and 3.17% of children mention the beginning of electronic smoking at the age of 8 and 9, respectively. By the age of 10, 7.94% of children have tried it and after the age of 11, more than 10%. Children most frequently tried electronic smoking at the age of 13 (26.19%). After the age of 14, the rate of initiation of alternative smoking among children decreases. The general data from the pretest reveal the knowledge of the medical public in relation to the variety of commercial products in the tobacco industry, thus 17% are informed about Snus, 28.3% know about Heated Products, 26.4% - about Patches. The potential problems of nicotine use known to the public are intoxication (92.5%) and dependence (98.1%), less withdrawal (39.6%) and abstinence (37.7%). Among the highly recommended clinical intervention methods, group counseling remains the most popular, personalized, individualized (62.3%). After the workshop, a substantial change in answers was noticed. From the total number of family doctors, 81.3% became familiar with Snus, 83.3% with Heated products, 72.9% with Patches. The potential problems of nicotine use known to the public became intoxication (97.9%), dependence (95.8%), resistance (68.8%), abstinence (56.3%), withdrawal (87.5%). Among the highly recommended clinical intervention methods, group counseling remains the most popular, personalized, individualized (91.7%).

**Conclusion.** Smoking is one of the most important problems among children and adolescents both in the Republic of Moldova and throughout the world. An important step is training and involving as many family doctors as possible in the process of detecting active and passive smokers.



## 10. OVERLAP SYNDROME

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**Introduction.** Overlap syndromes are inflammatory rheumatic conditions in which patients have clinical manifestations suggestive of multiple distinct immune diseases. The diseases most commonly involved in overlap syndromes include rheumatoid arthritis, lupus, scleroderma, and myositis.

**Case statement.** A 13-year-old patient presents with polyarthralgias and swelling in the lower and upper limbs (shoulder joints bilaterally, metacarpophalangeal joints bilaterally, radiocarpal joints bilaterally, proximal interphalangeal joints I-V bilaterally, knees bilaterally), morning stiffness > 1h, visual analogue scale of pain (VAS) 70 mm, fatigue, heliotrope rash, Gottron papules. The disease began with polyarthralgias in the upper and lower limbs, weight loss of 12 kg in 3 months, enthesitis in the Achilles tendon. Since the age of 9, she has been in the endocrinologist's records with diabetes type 1, the severe form, unbalanced. She is receiving insulin replacement therapy. From the paraclinical data performed: Screening ANA-positive; ANA profile: SS-A 61; Ro-52 100; Jo-1 103; CEN B 27; Anti-AMA, Anti-LKM, Anti-ASMA negative; S100 protein 0,05; CBC: Tr 550; VSH 35 mm/h; Biochemistry: ALAT 57,7; ASAT 74,4; Creatine kinase 1606; Creatine Kinase MB 99,5; LDH 551; Coagulogram: Fibrinogen 4,32; Immunology: RF >160 IU/ml; CRP 23,2. The clinical diagnosis was established: OVERLAP syndrome: Juvenile idiopathic arthritis, polyarticular form, seropositive (RF >160 IU/ml), high disease activity (JADAS10-27pt), joint erosions. Juvenile dermatomyositis with skin involvement (Gottron papules, mechanic's hands, heliotrope rash), muscle (muscle weakness, increased muscle breakdown enzymes), joint (inflammatory arthritis), autoimmune abnormalities (anti ANA positive, ANA profile: SS-A 61; Ro-52 100; Jo-1 103; CEN B 27). Type 1 diabetes, severe form, unbalanced. Autoimmune thyroiditis.

**Discussions.** Dermatomyositis is an idiopathic inflammatory myopathy with characteristic cutaneous findings that occur in children and adults. This systemic disorder most frequently affects the skin and muscles but may also affect the joints, the esophagus, the lungs and, less commonly, the heart. Examination for cutaneous dermatomyositis may reveal the following findings: characteristic, possibly pathognomonic cutaneous features: heliotrope rash, Gottron papules. Laboratory and other studies that may be helpful include the following: muscle enzyme levels (eg, creatine kinase, aldolase, aspartate aminotransferase, lactate dehydrogenase), myositis-specific antibodies, antinuclear antibody levels, pulmonary function studies with diffusion capacity, electrocardiography. Juvenile idiopathic arthritis (JIA) is chronic arthritis that affects approximately 1 in every 1,000 children. JIA affects children less than 16 years of age. It is not usually inherited. JIA may affect one or many joints. Children with JIA may also have silent eye inflammation, fevers, or rash. Systemic onset JIA may affect many joints and organs. Oligoarticular JIA occurs in half of all children with JIA. It affects fewer than five joints and occurs more often in girls. Polyarticular JIA affects five or more joints. Other forms of JIA include juvenile psoriatic arthritis and enthesitis-related arthritis.

**Conclusion.** Early diagnosis and early addressing to a specialist will prevent patients from radical laborious interventions and possible complications.

## 11. PARENTS' KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING INFANT FEEDING



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**Introduction.** Adequate nutrition in the first year of life is an essential condition for the healthy growth and development of a child. According to periodic studies in the field, there are variable but constant deficiencies related to the knowledge of the principles of rational feeding of infants, as well as wrong feeding attitudes or practices, which can negatively influence the growth, development and health of children

**Aim of study.** Research the knowledge, attitudes and practices of parents regarding the feeding of infants.

**Methods and materials.** We analyzed the data of the specialized scientific literature, identified with the Google Search search engine, from the databases: PubMed, Cochrane, Scopus, international clinical protocols

**Results.** According to the studies analyzed regarding parents' knowledge regarding infant feeding, not all parents have adequate knowledge regarding infant feeding. Although most mothers know that infants should be exclusively breastfed for 6 months, the rate of exclusive breastfeeding for the first 6 months was much lower (44%), according to Gülümser Şişko S et al. (2022). Some gaps and serious mistakes in parents' knowledge are also listed, such as the use of foods other than milk from the age of 4 months. ). The report from the research of Raymond Ade Adesanmi et al. (2022) showed that 88.3% of mothers are aware when to introduce complementary food, while only 1.6% did it earlier (between 1-4 months), which is lower compared to the reported percentage by the Centers for Disease Control and Prevention for the US (31.9%). Interestingly, although most mothers indicated that breastfeeding is healthy for their baby, they are unsure about the procedures related to expressing and storing breast milk. During the last years,

**Conclusion.** To improve practices, it would be important to strengthen information from healthcare professionals about infant feeding, to stop the spread of misconceptions and to provide correct information about appropriate infant feeding practices.





## 12. PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA IN CHILDREN

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**Introduction.** Supraventricular tachycardia is an abnormally rapid heartbeat. SVT is the most prevalent rhythm irregularity. According to estimates, it can happen to up to 1 in 250 otherwise healthy kids. Episodes are generally recurrent and have the capacity to damage one's life, but seldom being fatal. SVT affects 50% of children within the first 12 months, with highest incidence in neonates and adolescents. Over 90% of newborns spontaneously resolve by one year, with 15% of patients recovering spontaneously after one year.

**Aim of study.** The study evaluates the prevalence and rate of paroxysmal supraventricular tachycardia in children, identifies clinical and paraclinical features, and evaluates pharmacological and non-pharmacological treatment and diagnosis.

**Methods and materials.** This research has gained information from researches, books, and published scientific articles, such as the PubMed, UpToDate, WHO Guidelines and Medscape websites the last 10 years connected to supraventricular tachycardia in children.

**Results.** The results of the study according to bibliography reveals that most SVTs in children are reentrant rhythms. This includes atrioventricular reentrant tachycardia (AVRT, including Wolff-Parkinson-White [WPW] syndrome) and atrioventricular nodal reentrant tachycardia (AVNRT). A reentrant beat involves two independent channels for conduction with a unidirectional block in one of the two routes. signs of SVT may include pallor, fussiness, irritability, poor feeding, and/or cyanosis. Tachycardia symptoms may be slight, and can take months to manifest itself. Because of this, newborns often appear with symptoms of heart failure (e.g., tachypnea, tiredness with feeding, poor weight gain. The best method of diagnosis in SVT is the Holter monitoring, which provides a specific result.

**Conclusion.** Supraventricular tachycardia in children requires a long time to treat and can cause severe disorders.

### 13. PARTICULARITIES OF PRESENTATION, DIAGNOSIS AND TREATMENT OF INFECTIOUS MONONUCLEOSIS. CLINICAL CASE



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**Introduction.** Infectious mononucleosis is an acute condition characterized by sore throat, fever, fatigue, cervical lymphadenopathy, and atypical large peripheral blood lymphocytes also called Downey cells. Most common causative agent is Epstein–Barr virus (EBV), and occurs most commonly in children and adolescents. EBV is transmitted by saliva and has an incubation period of approximately 6 weeks. Infectious mononucleosis is medically important because of the severity, duration and its long-term consequences, especially in the development of certain malignancies and autoimmune conditions.

**Case statement.** Patient is a 7 year old male with a longstanding fever max. 40.1°C for about 10 days. The patient also experienced arthralgia during the peak of the fever at the level of the knee, shoulder, radiocarpal and metacarpophalangeal joints with myalgia. Initial management antibiotic therapy with Ceftriaxone 300 mg, administered at a dosage of 1/2 tablet twice daily and later was replaced with Amoxicillin-clavulanic acid, yet the patient's condition showed no improvement. The physical examination unveiled signs of inflammation, with a hyperemic posterior pharyngeal wall. Palpation revealed enlarged and mildly painful cervical lymph nodes, notably more prominent on the left side. Additionally, a subtle hepatomegaly was identified, with the liver edge situated 2.0 cm from the costal margin. Laboratory investigations revealed the presence of EBV specific IgG and IgM antibodies with that diagnosis of IM was made. The patient is advised to prioritize rest, avoid overexertion, and follow a balanced diet. Adherence to international quarantine regulations is recommended. The medical treatment plan included Folic acid, Vitamin D3+K2, and Ursodeoxycholic acid.

**Discussions.** This case report emphasizes the variable clinical presentations and age-dependent onset of infectious mononucleosis (IM). Beyond the typical symptoms, it underscores the potential for rarer complications such as lymphocytosis, impaired liver function, peritonsillar abscess, airway obstruction, and splenic rupture. The findings highlight the need for a nuanced clinical approach to promptly recognize and manage the diverse manifestations and potential complications associated with IM.

**Conclusion.** In conclusion, this case illustrates the varied clinical presentation and age-specific onset of infectious mononucleosis. The patient's management, involving antibiotics followed by a tailored treatment plan, underscores the need for individualized approaches. This report highlights the potential complications associated with IM, emphasizing the importance of timely recognition and intervention.



## 14. PSYCHOLOGICAL CONSEQUENCES OF CHILDHOOD OBESITY

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**Introduction.** Childhood obesity, once thought of as a sign of health, now raises concerns among parents, healthcare professionals, and society. Beyond its association with somatic consequences, it imposes significant negative psychosocial challenges, including depression, anxiety, and oppositional defiant disorder

**Aim of study.** This study explores the evolving dynamics of childhood obesity, revealing the intricate interplay with emerging mental health consequences beyond conventional health concerns.

**Methods and materials.** The literature synthesis covered 2018-2023, using Google Scholar, UpToDate, and ScienceDirect. Inclusion criteria focused on studies of children with obesity, excluding comorbidities, with key terms like "childhood obesity and psychological consequences."

**Results.** Numerous studies show a link between BMI and psychopathology, with common symptoms like depression, anxiety, binge eating, and attention deprivation disorders. Correlations between childhood obesity and depression, anxiety, and increased bullying, especially in girls, are established. Among the bibliographic sources found, depression frequency in adolescents ranged from 13% to 63%. No single cause has been identified, but chronic stress due to weight-related bullying may contribute. Some researchers suggest depression severity correlates with the child's waist circumference. About 45% of obese children and adolescents surveyed are dissatisfied with their figure, contributing to low self-esteem. Research says that parents' negative comments about their child's weight exacerbate self-esteem issues. Reviews highlight links with anxiety and behavioural disorders, projecting future increases tied to family and environmental, physical and relational bullying. As a result, obese children avoid physical activities, negatively impacting school performance. Research shows at least a third of girls and a quarter of boys refuse to participate in group activities due to weight related shame. The lasting impact of obesity significantly reduces the quality of life for obese children affecting physical, emotional, and social aspects. Duration of obesity is identified as a risk factor, emphasizing the need for active intervention.

**Conclusion.** Obesity, beyond its physical consequences, significantly affects the child's psychological state, leading to depression, anxiety, body shaming, and a diminished quality of life. Optimizing obesity treatment and preserving mental health require a multidisciplinary approach, including early screening for psychosocial factors and providing timely psychological support.

## 15. RETINAL VASCULATURE PECULIARITIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: INSIGHTS FROM OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY



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**Introduction.** Juvenile Idiopathic Arthritis (JIA) is a chronic autoimmune disorder that primarily affects children and adolescents, causing inflammation in the synovium of joints. While the musculoskeletal manifestations of JIA have been extensively studied, there is a growing recognition of the extra-articular involvement of various organ systems, including the eyes. Ocular complications in JIA, such as uveitis, are well-documented, but the impact of the disease on the retinal vasculature remains an area of evolving research.

**Aim of study.** Understanding the specific retinal vascular peculiarities in patients with JIA could provide valuable insights into the pathophysiology of ocular involvement in this autoimmune disorder and may have implications for early detection and management of ocular complications. This study aimed to evaluate the quantitative Foveal Avascular Zone (FAZ) and retino-choroidal vessel density (VD) using Optical Coherence Tomography Angiography in patients diagnosed with juvenile idiopathic arthritis.

**Methods and materials.** A prospective study involving 50 patients diagnosed with JIA and JIA-associated uveitis (JIA-U) was conducted. OCT-A imaging was employed to assess retinal vasculature, focusing on key parameters such as vessel density, FAZ characteristics, and other relevant metrics. Clinical data, including disease duration and ocular complications, were also collected.

**Results.** The study included 50 JIA patients (93 eyes) with a mean age of  $10.84 \pm 4.21$  years and a disease duration of  $44.36 \pm 36.81$  months, of which 32/50 (64%) were females. Thirteen (26%) patients had JIA-U (Group 1, 19 eyes), while 37 (74%) had JIA without uveitis (Group 2, 74 eyes). The mean foveal superficial and deep capillary plexuses (SCP/DCP) vascular density (VD) were  $14.6 \pm 4.7$  and  $28.93 \pm 6.29$  in the 6x6 scan, respectively, in patients with JIA-U; and  $16.5 \pm 3.8$  and  $30.53 \pm 2.98$  in the 6x6 scan, respectively, in patients with JIA without uveitis. The mean FAZ area in the 6x6 scans was  $0.33 \pm 0.17$  mm<sup>2</sup> in patients with JIA-U and  $0.28 \pm 0.08$  mm<sup>2</sup> in patients from the second group. The mean central macular thickness (CMT) for patients from Group 1 and 2 in the 6x6 scans was  $365.75 \pm 193.17$  μm and  $116.47 \pm 114.68$  μm, respectively. It is noteworthy that 7 eyes were excluded from the study due to consistently poor-quality OCT-A images or excessive artifacts and severe ocular complications, including band keratopathy, uveal cataract, vitreous body destruction, and cystoid macular edema.

**Conclusion.** This study provides insights into retinal vasculature peculiarities in JIA patients, highlighting differences in SCP/DCP VD, FAZ area, and CMT between those with and without uveitis. These findings contribute to a better understanding of the ocular implications of JIA and may aid in early detection and management of ocular complications in affected children.



## 16. THE TRANSCONDYLAR FRACTURES IN CHILDREN, PARTICULARITIES OF DIAGNOSIS AND TREATMENT.

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**Introduction.** Transcondylar fractures of the humerus are the most frequent fractures at the level of elbow facing children. These can be extremely difficult to manage and if the way if treatment is not correct, then complications such as joint stiffness could appear.

**Aim of study.** Appreciation of diagnostic features and treatment of transcondylar fractures in children.

**Methods and materials.** This study included 115 patients with ages varying between 3 years to 18 years old, 75 boys and 40 girls, who presented themselves to IMSP Mother and Child Institute from Chisinau, department of Orthopedics, Traumatology and Vertebrology between 2021 and 2022. All these children were subject to transcondylar fractures of the humerus.

**Results.** Patients have been categorized by gender: 40 girls (35%) and 75 boys (65%). In 63 of the children (55%) the upper side of the right member has been affected, while in 52 children (45%) has been affected the upper side of the left member. Considering the symptomatic point of view, the most common sign of all has been the significant pain (100%) to the affected member. Other clinical characteristics have been such as oedema (100%) and hematoma (85%). The diagnosis was given based on the clinical examination and radiological assessment of the affected member in two incidents (front and lateral). The I-III grade fractures (Lagrange-Rigault Classification) have had indication for orthopedic treatment (37%), while the IV-V grade fractures have had indication for surgery (63%). After the surgical interventions, they have undergone treatment with antibiotics, inflammatory, local treatment with aseptic dressings. The threads have been removed on day ten. The duration of 80% from the surgeries has been around 30-40 minutes. The plaster cast immobilization was kept 3 weeks, after which it was removed together with brooches. The recovery treatment after the removal of immobilization contained physical therapy and light massage.

**Conclusion.** Transcondylar fractures are predominant for masculine gender and mainly affected is the right upper member. Orthopedic treatment is recommended for I-III grades (Lagrange-Rigault Classification), while the surgery is compulsory in IV-V grades or in case of failure in orthopedic treatment. The cases with late diagnosis (over 3-5 days after the trauma) need surgical intervention to reconstruct the elbow joint.



## 17. TREATMENT OF CERVICAL CYSTIC LYMPHANGIOMA IN CHILDREN



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**Introduction.** Cervical cystic lymphangioma is a malformation of the lymphatic vessels predominantly located in the cervical, head or axillary area, but can affect any region. The location of lymphangioma in the cervical area is of increased interest due to the involvement of vital anatomical structures and the risk of obstructive syndrome. Since it is an infiltrative lesion involving vessels and nerves, complete resection cannot always be achieved surgically and requires alternative methods of treatment with a reduced risk of complications.

**Aim of study.** The aim of this study was to analyze the scientific material presenting the various methods applied in the treatment of cervical cystic lymphangioma in children.

**Methods and materials.** Articles published in PubMed and Google Scholar between 2018-2023 were analyzed. Using the key words cervical lymphangioma and children we selected the most relevant articles.

**Results.** The localization of cystic lymphangioma in the cervical area is most often manifested by the presence of a mass which, reaching large sizes, can cause airway obstruction, dysphagia and dysphonia. Treatment depends on the complexity of the lesion, the localization of the lymphangioma, the level of involvement of vital structures, the age of the patient and the presence of complications. The standard method is complete surgical resection in a single operation or sometimes multiple surgeries are required for complete resection. In particular, surgery is chosen if complications such as recurrent infection, bleeding in the cyst, airway compression, dysphagia or accelerated growth occur. In some cases, however, involvement of major vessels and nerves prevents complete resection, increasing the risk of recurrence of lymphangioma. Late postoperative complications such as lymphorrhea, lymphoedema, hematoma, superinfection may also occur. Currently there are various non-surgical methods of treatment such as sclerotherapy (OK-432, bleomycin, monoclonal antibodies, doxycycline), simple drainage, corticosteroids, radiotherapy, cryotherapy, laser excision, radiofrequency ablation, etc. New therapies include the use of sildenafil, propranolol, sirolimus.

**Conclusion.** Surgical treatment remains the preferable method for cervical localization of cystic lymphangioma as it allows complete removal and decreases the risk of recurrence. However, the use of new treatment methods allows us to successfully manage complex cases of lymphangioma with a reduced level of complications compared to surgery and is proposed by some specialists as first line treatment.



## 18. TRI PONDERAL INDEX AS A CRITERION FOR OBESITY IN CHILDREN

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**Introduction.** Childhood obesity, a global health concern linked to premature mortality, lacks a single accurate assessment method. Common anthropometric measures (weight, height, neck, abdomen, hip, arm circumferences, body fat percent, body mass index (BMI), etc.) fall short in accurately defining obesity in children. TPI (Tri Ponderal index), a unique measure utilizing the cube root of height, offers a more precise evaluation of body mass in the pediatric population compared to traditional BMI. This study conducts a comparative anthropometric analysis using TPI to identify significant differences between normal and obese children, highlighting TPI's potential as an improved indicator of weight status in this group.

**Aim of study.** To compare anthropometric parameters of children with normal weight and obesity according to TPI.

**Methods and materials.** 30 healthy and 30 obese children aged 10-15 (median age-12 $\pm$ 1.7 years) were included, with equal gender distribution in both groups. Anthropometric exams covered weight, height, arm, neck, and abdomen circumferences, total body fat assessment, abdomen to hip circumference, abdominal circumference-to-height indexes, BMI and TPI. Two groups were formed based on TPI: Normal group N (n=30) and Obese group O (n=30). All examinations were conducted on empty stomachs. Keywords: obesity, children, anthropometric methods, Triponderal index

**Results.** Heights ranged from 138 to 184 cm, averaging 157.5 $\pm$ 11.9 cm, with no significant intergroup differences. The obese group had a weight average of 64.6 $\pm$ 19.5 kg, significantly higher than the control group's 41.8 $\pm$ 9.7 kg ( $p<0.05$ ). Statistically significant differences were seen in medium waist (N=61 $\pm$ 5.9cm, O=82 $\pm$ 13.4cm,  $p<0.05$ ), hip (N=78.5 $\pm$ 7.8 cm, O=96.5 $\pm$ 11.5 cm,  $p<0.05$ ), neck (N=29 $\pm$ 2.5cm, O=32.5 $\pm$ 3.4cm,  $p<0.05$ ), and arm (N=21 $\pm$ 2.6cm, O=27.5 $\pm$ 3.9cm,  $p<0.05$ ) circumferences between normal weight and obese children. Total body fat % found using bioelectrical impedance analysis also differed between group N (16.4 $\pm$ 6.0%) and O (32.2 $\pm$ 5.2%,  $p<0.05$ ). Waist to hip ratio averaged 0.77 $\pm$ 0.1 in group N and 0.87 $\pm$ 0.1 in group O ( $p<0.05$ ). Waist circumference-to-height ratio varied from 0.33 to 0.64, averaging 0.38 $\pm$ 0.03 in group N and 0.53 $\pm$ 0.05 in group O ( $p<0.05$ ). A correlation analysis of the indicators was carried out and strong positive correlations were identified between TPI and weight ( $r=0,75$ ), waist ( $r=0,82$ ), hip ( $r=0,76$ ), arm circumference ( $r=0,79$ ), total body fat % ( $r=0,76$ ).

**Conclusion.** Significant differences were identified among other anthropometric indicators in children with normal weight and obesity according to TPI. Strong positive correlations between TPI and weight, waist, hip, arm circumferences, and total body fat % allows us to consider this indicator to determine weight status in children.

## ***XVII. PHARMACOLOGY SECTION***



- 1. Învață pentru a face fericiți oamenii cu suferință***
- 2. Cercetarea este în proces în spirală ce te provoacă la noi orizonturi***
- 3. Medicul tratează cu cunoștințe, suflet și cuvinte***

- 1. Learn to make suffering people happy.***
- 2. Research is a spiral process that challenges you to new horizons.***
- 3. The doctor treats with knowledge, soul, and words***

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## 1. ACUTE DRUG INTOXICATION - A MODERN LOOK AT OLD PROBLEM

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**Introduction.** Acute drug intoxication is a persistent and critical problem in the modern healthcare landscape. Study of the problem in recent years has marked an increase in the incidence of acute poisoning. Given the relatively high frequency of intoxication and the importance of early medical interventions, there is an essential need for the ability to diagnose acute drug intoxication promptly and accurately.

**Aim of study.** Examination and exploration of the nosological entity known as acute drug intoxication.

**Methods and materials.** The study included 100 clinical observation sheets of patients hospitalized in the Department of Toxicology during 2023 with a diagnosis of acute drug intoxication. Data collection included examination of: age, sex of patients, type of poisoning (accidental or suicidal), duration of hospitalization, toxic agent.

**Results.** The age of patients with acute poisoning ranged from 18 to 85 years, but the predominant age range was 18-39 years with 53%, followed by 40-59 years with 33% and third was the category above 60 years with 14%. The study showed that 71% of patients were female and only 29% male. The ratio of suicidal to accidental poisonings was 90% to 10%. Although living conditions have changed, the trend of maintaining this 2:1 ratio over the last 10 years requires further study of the issue. Hospitalization rates for auto-intoxication were 90.14% among women and 89.66% among men. The average hospitalization time is  $4.9 \pm 2.25$  days, depending on the dose of the intoxicating agent and the time interval before initiation of therapeutic measures. The study of drugs used for suicidal purposes found that psychotropic drugs ranked first – 51%, non-steroidal anti-inflammatory drugs ranked second with 15%, followed by antihypertensive with 8%.

**Conclusion.** Acute drug poisoning remains a major problem in society to the present day. This requires further study of the problem; work with the public on poisoning prevention, and stricter accounting of psychotropic drugs.

## 2. ADVANCING PARKINSON'S DISEASE MANAGEMENT: NOVEL STRATEGIES AND THERAPEUTIC INNOVATIONS



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**Introduction.** Parkinson's disease is a long-term neurodegenerative condition of the central nervous system that mainly affects the control of voluntary movements due to the gradual degeneration of dopaminergic neurons in the *substantia nigra* region of the brain. The treatment of Parkinson's disease has improved continuously, with a strong focus on developing innovative methods to effectively manage the complexities of this disorder for each patient.

**Aim of study.** To explore the most recent concepts of Parkinson's disease pharmacotherapy based on the pathophysiological mechanism at the central nervous system (CNS) level.

**Methods and materials.** The current review involved carefully selecting and examining a curated set of academic literature from electronic databases such as HINARI, PubMed, NCBI, and ScienceDirect.

**Results.** Parkinson's disease treatment still relies on Levodopa (LD) as the gold standard. Despite this, prolonged use of levodopa has been shown to result in motor complications, known as the "on-off phenomenon", in most patients. Peripheral metabolism of LD (plasma circulating level fluctuations) may lead to systemic effects, including cardiac arrhythmias, hypotension, and vomiting. Modern strategies have been formulated to synthesize LD and dopamine prodrugs (ester, amide, cyclic prodrugs, also chemical delivery systems, enzyme models), aiming to maintain LD's effectiveness while reducing side effects. Add-on oral therapies like dopamine agonists (DAAs), monoamine oxidase Type-B inhibitors (MAO-B Is), and COMT inhibitors (COMT-Is), along with amantadine ER and adenosine A2A receptor antagonists (AA2AA), were developed to improve life expectancy and enhance the long-term response to LD therapy. In recent years, researchers have studied iron chelators as neuroprotective agents. The dopaminergic neurons of the CNS contain a significant amount of neuromelanin (NM), a dense and insoluble pigment with a strong affinity for iron. The chelator's removal of iron will prevent the excessive formation of reactive oxygen species, which leads to neuroinflammation.

**Conclusion.** The diligent research and continuous improvement of drug treatment for Parkinson's disease lead to a major improvement in patients' quality of life. Recreating the enzyme model in prodrug synthesis can improve the pharmacokinetic and pharmacodynamic properties, resulting in a successful drug delivery system that specifically targets them to the *substantia nigra*. Recent studies also investigate the potential neuroprotective role of iron chelators in management of Parkinson's disease.

**Keywords.** Parkinson's disease, therapeutic management, levodopa.





### 3. COMBINATION OF BETA-BLOCKERS WITH ACE INHIBITORS IN THE TREATMENT OF HYPERTENSION IN PATIENTS WITH CARDIAC COMORBIDITIES

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**Introduction.** Approximately 1.28 billion people worldwide are estimated to have hypertension, and it can either promote or accompany other cardiac comorbidities. The combination of beta-blockers with angiotensin-converting enzyme inhibitors in the management of arterial hypertension in patients with various cardiac comorbidities brings benefits by reducing the influence of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS).

**Aim of study.** Determining the benefits of combining antihypertensive medications in patients with cardiac comorbidities.

**Methods and materials.** In a retrospective study, analyzing 24 patient records from the CMH "Arhanghel Mihail", the groups of antihypertensive medications were identified, along with their combination in patients with cardiac comorbidities.

**Results.** In terms of gender, we obtained that 70% were female and 30% male, with ages ranging from 55 to 82 years, average  $69.9 \pm 2.3$ . All patients upon admission presented elevated blood pressure values, as follows: 7 with a blood pressure of 180 mmHg, 12 - 190 mmHg, 3 with 200 mmHg, and 2 patients with 220 mmHg; as well as other cardiac comorbidities: 19 with angina pectoris (AP), 12 with heart failure (HF), 12 with atrial fibrillation, and 4 with supraventricular tachycardia. For the treatment of patients' conditions, ACEIs were used, including Ramipril 5mg in the evening for 1 patient, Ramipril in combination with a beta-blocker Bisoprolol 2.5 mg for 8 patients, Lisinopril 10 mg associated with Bisoprolol 2.5 mg for 13 patients, and Bisoprolol 2.5 mg for 2 patients. Only 2 patients experienced a hypertensive crisis on the 6th day of treatment, one receiving only a beta-blocker and one using the combination of ramipril with bisoprolol. After 10 days of treatment, the condition of the patients (24) at discharge improved, with BP values lowered to 140 mmHg (70.8%), 135 mmHg (16.6%), and 120 mmHg (12.5%), and no dyspnea or peripheral edema.

**Conclusion.** The combination of beta-blockers and ACEIs represents a promising therapeutic strategy in the treatment of arterial hypertension in patients with cardiac comorbidities. One blocks sympathetic influences, the other the RAAS—thus reducing cardiovascular risk and the consequences of the disease. Current data highlight the synergistic benefits of these two classes of medications. In addition to their antihypertensive actions, beta-blockers are used to manage arrhythmias, AP and HF, while ACE inhibitors ensure cardioprotection in patients with acute coronary syndromes and treat congestive heart failure.

#### 4. CONTEMPORARY APPROACHES TO THE TREATMENT OF FRONTOTEMPORAL DEMENTIA



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**Introduction.** Frontotemporal dementia or FTD relates to a group of diseases that are caused by neuronal degeneration. FTD is mainly of genetic etiology, due to mutations occurring in specific genes, and may be transmitted hereditarily. The most common mutations affect the MAPT, PGRN, C9orf72, VCP, TARDBP and FUS genes. Depending on which genes or regions of the brain are altered, patients diagnosed with FTD express different symptoms and variants of the same disease. The control of neuropsychiatric symptoms has been the only universal approach to managing FTD.

**Aim of study.** Our study aimed to review new pharmacological treatment options that are available for patients with different variations of FTD or that can potentially be implemented in the near future.

**Methods and materials.** This article is based on data analysis of several articles available on PubMed, PMC and Google Scholar, that have been published since 2015.

**Results.** Earlier case reports confirmed behavioral improvements after administering antidepressants (trazodone, fluvoxamine and citalopram), antiepileptics, atypical antipsychotics (quetiapine, risperidone), and even psychostimulants (methylphenidate and dextroamphetamine). However, some present a significant risk of adverse effects. More novel symptomatic approaches include agomelatine, a 5-HT<sub>2C</sub> receptor antagonist that elevates dopamine and noradrenaline levels and reduces apathy, and oxytocin, an important mediator of empathy and social behaviour. In addition, low doses of lithium could potentially ameliorate agitation and psychosis. Even though there are no definitive disease-specific approaches available yet, molecule-based therapies are being studied. Drug induced selective autophagy and tau acetylation and aggregation inhibitors can decrease tau levels in neurons, while tau-targeting antibodies have shown potential in increasing tau clearance. By resorting to sortilin receptor blockers and AAV-Grn vectors or by managing biological pathways using suberoylanilide hydroxamic acid and bafilomycin A1, higher levels of PRGN in the brain can be achieved. Metformin blocks PKR phosphorylation, which eventually lowers toxic RAN (repeat associated non-AUG) protein levels, caused by abnormal C9orf72 gene expansions. Moreover, antisense oligonucleotides (ASO), like WVE-004, could be used to promote the degradation of C9orf72 expanded mRNAs by binding the hexanucleotide expansion.

**Conclusion.** A lot of progress has been made regarding pharmacological treatment options for patients with FTD. Nevertheless, no pharmacological therapy is completely successful or approved, meaning a lot of work and research is yet to be done.



## 5. DAPAGLIFLOZIN AS AN SGLT2 INHIBITOR AND ITS EFFECT ON THE TREATMENT OF TYPE 2 DIABETES

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**Introduction.** Sodium-glucose cotransporter 2 (SGLT2) inhibitors represent a drug class commonly used in the management of type 2 diabetes.

**Aim of study.** Dapagliflozin demonstrated a significant decrease in the occurrence of cardiovascular (CV) death or hospitalization due to heart failure (HHF).

**Methods and materials.** Based on articles about SGLT2 inhibitors from the PubMed platform, we selected the fundamentals of this drug's actions on human metabolism, specifically in patients with type 2 diabetes.

**Results.** The studies consulted from various medical search platforms such as PubMed, Google Scholar, etc., highlight an emphasis on examining the impact of dapagliflozin on body weight. It was observed that this medication assists patients in reducing fat mass, contributing to as much as two-thirds of the overall weight loss, and demonstrates a smaller waist circumference compared to patients who were administered an add-on placebo. Dapagliflozin was orally administered to patients once daily.

**Conclusion.** Real-world studies provided evidence supporting the effectiveness of dapagliflozin in individuals with type 2 diabetes (T2D).

## 6. DRUGS OF CHOICE IN HYPERTENSIVE EMERGENCY ASSOCIATED WITH ACUTE AORTIC DISSECTION



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**Introduction.** Acute aortic dissection is a hypertensive emergency that requires an immediate reduction of blood pressure (BP) by administering intravenous drug therapy. Diligent control of BP is the most crucial in order to stop the progression of dissection and prevent target organ damage.

**Aim of study.** Aim of study was to select the antihypertensive drugs recommended by international guidelines for the management of this major emergency.

**Methods and materials.** The scientific papers in the PubMed database from the last 5 years with reference to the management of hypertensive emergencies, including acute aortic dissections, were selected and analyzed.

**Results.** Studies have shown that for the management of acute aortic dissection, it is recommended to use adequate analgesia, which includes morphine as it decreases sympathetic output as well. In the absence of aortic regurgitation, the most favored agent is a beta-blocker, such as esmolol, labetalol or metoprolol, targeting a heart rate of 60-80 beats/ min and a systolic blood pressure of 100-120 mm/Hg, because the effect of beta-blockers in lowering the heart rate and blood pressure, helps to reduce the aortic wall tension and limit the extent of dissection. In patients with contraindications to beta-blockers, diltiazem and verapamil- non dihydropyridine calcium channel blockers, angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB), should be considered. If the systolic blood pressure remains elevated, a combination of a vasodilator such as nitroprusside or nitroglycerine and  $\beta$ -blocker is preferred.

**Conclusion.** The drug of first choice has to be a short-acting i/v beta-blocker agent, (esmolol, labetalol, metoprolol) as it is able to reduce the force of left ventricular ejection, or combined with a vasodilator in severe hypertension. The use of  $\beta$ -blockers, ACEIs, or ARBs was associated with benefits in the long- term treatment of aortic dissection.



## 7. GENE THERAPY FOR ADENOSINE DEAMINASE SEVERE COMBINED IMMUNODEFICIENCY (ADA-SCID)

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**Introduction.** About 1 in 500,000 people are born with severe combined immunodeficiency (SCID). The adenosine deaminase variant is a fatal inborn error of purine metabolism. Accumulation of adenosine and deoxyadenosine leads to inhibition of DNA synthesis and repair, as well as abnormalities of thymocyte development, vital in an evolving immune system. Patients with ADA-SCID often die prematurely from infection. Currently, treatments include PEGylated enzyme therapy and allogenic stem cell transplantation from a matching HLA donor, however their success is variable. These treatments are also temporary, complicated, and carry a high risk of death. Gene therapy using a Lentiviral vector shows promising results for treatment of SCID.

**Aim of study.** Evaluating the current possibilities and post-treatment outcomes of implementing gene therapy for ADA-SCID.

**Methods and materials.** The study includes a specialized literature review of research/clinical trials published in PubMed, NIH, and the New England journal of medicine. Key words include “SCID” “Gene therapy”. Information contains results of studies done in Asia, Europe, and the United States evaluating efficacy, safety and long-standing outcomes of gene therapy for ADA-SCID with viral vectors.

**Results.** Comparing patients treated with PEGylated enzyme therapy and stem cell transplant, patients enrolled in clinical trials treated with Gene therapy (GT) demonstrated immune reconstitution, and event free survival. Treatment involves obtaining stem cells from the patient’s bone marrow. Once isolated the therapeutic genetic material is implemented into a lentiviral vector (LVV). The LVV can integrate the RNA into the nuclear DNA of the host target cells. The patients are given an injection of Busulfan to decrease their defective cells. The new cells are then transfused back to the patient, effectively coding for the deficient ADA gene leading to production of the enzyme. Results show decreased toxic metabolites and immune reconstitution. Although survival rates in patients treated with GT are 100%, clinical trials remain highly limited and commercial GT is not currently available.

**Conclusion.** Genetic therapy using Lentiviral vectors is an effective and safe treatment for patients with ADA-SCID. Long term outcomes show minimal complications and complete cure of the disease. The therapy remains limited due to resources and high costs.

**Keywords.** SCID, gene therapy, lentiviral vector.



## 8. MECHANISMS OF DRUG-INDUCED NEPHROTOXICITY



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**Introduction.** Drug-induced nephrotoxicity or drug-induced renal disease (DRID) is a common clinical problem. It has been reported that the incidence of drug-induced renal disease in adults can range from 14-26% to 66% and up to 16% in children. Research reports on drug-induced nephrotoxicity have increased significantly from 80 articles in the years 1930–1969 to over 5000 in the years 2010–2018. Understanding the risk factors, phenotypes through clinical presentation, development mechanisms, prevention and mitigation strategies of nephrotoxicity is essential due to the number of drugs used in medical practice and the possibilities for researching nephrotoxicity.

**Aim of study.** The aim of the study was to analyze and elucidate the molecular mechanisms of drug-induced nephrotoxicity.

**Methods and materials.** The study was analytical and focused on the selection of articles published between 2018 and 2023 in the PubMed and Google Scholar databases using the keywords nephrotoxicity and drug-induced nephrotoxicity.

**Results.** The following phenotypes of drug-induced nephrotoxicity were highlighted: acute kidney diseases; glomerular dysfunctions; tubular injuries; and nephrolithiasis. These phenotypes can be achieved through different mechanisms, such as: alteration of renal intraglomerular hemodynamics, direct and/or indirect tubular toxicity, development of inflammation and immune processes (glomerulonephritis and interstitial nephritis), glomerular damage, nephropathy caused by crystals, nephrotic syndrome, and thrombotic microangiopathy. The biochemical and molecular mechanisms of nephrotoxicity lead to cellular death through apoptosis, autophagy, and necrosis. The exact mechanism depends on the type of cells involved, the dose and duration of exposure, patient-dependent factors (sex, age, comorbidities, etc.). At the same time, the nephrotoxic action can be reflected on several types of cells, as well as it can develop against the background of hypertension, obesity, liver, lung, heart diseases, or the abuse of exogenous substances (alcohol, cigarette smoke, drugs, etc.).

**Conclusion.** Drug-induced nephrotoxicity represents a significant challenge in clinical practice and requires a complex and thorough approach to the prevention of kidney damage, the differentiation between the damaging action of the drugs and the kidney disease itself, the selection of appropriate specific and early biomarkers. Understanding these compartments and the mechanisms underlying drug-induced renal injury will enable an appropriate and rational treatment approach, early monitoring to address nephrotoxicity issues in the reversible stages of the processes.



## 9. MESENCHYMAL STEM CELL-DERIVED EXOSOMES AND THEIR ANTINEOPLASTIC POTENTIAL

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**Introduction.** Mesenchymal stem cells (MSC) are pluripotent cell types derived from mesenchyme able to differentiate and proliferate into a variety of tissues. Exosomes derived from MSC exhibit a round morphology (40-160 nm) beneficial in ferrying various materials like metabolites, proteins, lipids, and nucleic acids (DNA, mRNA, miRNA and ncRNA). Their function is believed to be involved in numerous physiological and pathological states. Exosomes can act as both therapeutic targets and biomarkers for certain diseases, however they may also possess positive and negative influences on cancer. Their efficacy and therapeutic potential are still developing and may provide significant benefit once fine-tuned.

**Aim of study.** Review of the application potential of mesenchymal stem cell-derived exosomes in cancer therapy.

**Methods and materials.** Methods include literature review of research/clinical trials published in PubMed and NIH. Keywords include “MSC-derived exosomes”, “cancer”, “stem cells”.

**Results.** Clinical and preclinical studies highlighted both beneficial and detrimental effects of MSC-derived exosomes on different types of neoplastic diseases. In patients with chronic myelogenous leukemia, exosomes loaded with tyrosine kinase inhibitors and proteasome inhibitors showed higher efficacy compared to traditional chemotherapy. Additionally, they employ positive modulatory effects in apoptosis related proteins, by delivering critical proteins and RNAs which decrease the avoidance of apoptosis in cancer cells. Simultaneously they promote entrance of cancer cells in the G0 phase evoking tumor dormancy. Further involvement of MSC-derived exosomes is important in immunoregulatory function on different immune cells, as T-, B-lymphocytes, and NK cells, by stimulating or inhibiting their function in the microenvironment of the cancer cells which is important in tumor destruction or tumor escape. Other effects of MSC-derived exosomes are their potential for tissue regeneration after radiotherapy, involving cellular proliferation, reducing the pathogenesis of fibrosis, suppressing inflammation and oxidative stress. Negative effects of exosome therapy may be attributed to their subsequent stimulatory effects of angiogenesis which may feed tumors and worsen the prognosis.

**Conclusion.** Preliminary research demonstrated that MSC-derived exosomes used as transporters for chemotherapeutic agents improve the treatment outcomes of some neoplastic diseases. Despite this, there are some specific negative effects of exosomes that limit their broad use and underscore the need for further research in this area.

## 10. NEW CONCEPTS OF TREATMENT OF CARPAL TUNNEL SYNDROME



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**Introduction.** Carpal tunnel syndrome is the most common form of focal peripheral compressive mononeuropathy of the median nerve accompanied by pain, paresthesia, weakness along the nerve's path and represents approximately 90% of all tunnel neuropathies. The prevalence rate is higher among women than among men.

**Aim of study.** The study of the specialized literature of the physiopathological and clinical interrelationships affecting the peripheral nervous system, but also the analysis of the pharmacotherapeutic treatment in carpal tunnel syndrome.

**Methods and materials.** A retrospective study was carried out on 61 patients, analyzing the drug treatment used for patients admitted to the NNI "Diomid Gherman" with carpal tunnel syndrome during the period 2021-2023, comparing the available pharmacological treatment in the Republic of Moldova with the current information from the specialized literature review, articles published in electronic sources recognized by the international medical society: ScienceDirect, PubMed, Google Scholar, from the last 10 years. The data from the patients' reports were analyzed statistically: Microsoft Excel, Epi Info -3.5, depending on: gender, age, treatment administered, etc.

**Results.** It was found that out of 61 patients, 19 patients were men (31.1%) and 42 patients were women (68.9%), aged between 31-82 years. Of the total number of patients, 83.6% benefited from NSAID treatment, 34.4% - vitamins and metabolic preparations, 13.1% - central antispasmodics, 11.5% - gastroprotectors and 26.2% were administered antibiotics. The preparations administered in the treatment scheme are found in the national clinical protocol and they only offered a temporary improvement of the symptoms, at the same time new preparations such as linalool, acetyl-L carnitine etc. were not found in the list of indications, thus all patients were subjected to the intervention surgical - decompression of the median nerve. The literature data currently proposes a new ultrasound-guided treatment method with the local injection of platelet-rich plasma into the carpal tunnel in a single dose of 1-3.5 ml, demonstrating a success rate of 76.9% compared to other conservative treatments in terms of regarding medium-term efficacy in relieving inflammation and pain, peripheral nerve regeneration.

**Conclusion.** Currently, new drugs (plasma rich in platelets, acetyl-L carnitine, etc.) are not used in the Republic of Moldova in the treatment of carpal tunnel syndrome, which have an increased effectiveness in the medium term in relieving inflammation, pain, regulating angiogenesis, neurogenesis, and regeneration of peripheral nerves. Surgical decompression of the median nerve remains the main treatment option in avoiding further complications and improving the quality of life of patients.



## 11. PARTICULARITIES OF THE ACTION OF THE INHIBITORS OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN MEN AND WOMEN

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**Scientific advisor:** Bacinschi Nicolae, PhD, Professor, Head of Department of Pharmacology and Clinical Pharmacology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

**Introduction.** The renin-angiotensin-aldosterone system (RAAS) plays a significant role in cardiovascular pathology, including arterial hypertension (HTA). It has been demonstrated that endogenous sex hormones interact with RAAS. Testosterone causes a vasoconstrictor effect, possibly by increasing angiotensinogen ARN messenger and plasma renin activity, and estrogens antagonize RAAS by decreasing plasma renin activity, angiotensin-converting enzyme expression, and angiotensin 1 receptor expression.

**Aim of study.** The purpose of this review was to elucidate the action particularities of RAAS inhibitors according to the sex of patients.

**Methods and materials.** Data from the PubMed database on the efficacy and safety of RAAS inhibitors in men and women were analyzed.

**Results.** The benefits of angiotensin-converting enzyme (ACE) inhibitors in women were reported to be reduced during treatment, while angiotensin receptor blockers (ARBs) decreased blood pressure more in women than in men. These discoveries can be associated to sex differences in the intrarenal components of RAAS. ACEI has been shown to produce a significantly greater decrease in blood pressure in men compared to women. This result could be due to the inhibition of bradykinin degradation by ACEI and its cumulation causes a vasodilating effect. Bradykinin may help increase the effectiveness of ACEI in men by releasing nitric oxide with reduction of oxidative stress. It has been estimated that men have higher levels of oxidative stress than women in HTA. In women the cardiovascular advantages of ARB over ACEI are stronger than in men due to the higher expression of angiotensin 2 receptors, especially in afferent and efferent arterioles, as well as a less excitable and more easily repressed renal sympathetic system in women. It has been shown that women may experience adverse reactions to antihypertensives more frequently than men. Thus, women had a higher incidence of adverse reactions to ACEI, thiazides, potassium-sparing diuretics. Adverse reactions to aldosterone antagonists have been reported more frequently in men, the most reported being hyperkalemia.

**Conclusion.** The particularities of RAAS in women and men may be responsible for the efficacy and harmlessness of RAAS inhibitors. The elucidation of the sex-determined aspects of the action of ACEI, ARB, aldosterone antagonists, and renin inhibitors will contribute to the development of new strategies in the rational selection of RAAS inhibitors in women and men.



## 12. PHARMACOLOGICAL APPROACH TO WERNICKE-KORSAKOFF SYNDROME



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**Introduction.** Wernicke-Korsakoff Syndrome (WKS) represents, in 16-38% of cases, a clinical triad of confusion, ataxia and nystagmus. Conceptualized as two distinct syndromes, 85% of survivors of the untreated acute phase of Wernicke encephalopathy (WE), caused by vitamin B1 (thiamine) deficiency, develop Korsakoff syndrome (KS) – with anterograde, retrograde amnesia, spatiotemporal disorientation, confabulation.

**Aim of study.** The aim of our study was elucidation of drug treatment in Wernicke-Korsakoff syndrome.

**Methods and materials.** This article is based on data collected from several articles available on Medscape, NCBI, PubMed, Google Scholar and that have been published since 2013.

**Results.** Since earlier conducted case reports showed that thiamine deficiency causes WKS, clearly its therapy would focus on the choice of dose, route and duration of vitamin B1 administration. However, the practical application of the treatment is more difficult, since 75-80% of cases of Wernicke encephalopathy, which occurs most of the time primary to KS, is misdiagnosed with other conditions, which makes 80% of cases of Wernicke encephalopathy end with the development of Korsakoff syndrome, 15-20% ending lethally. Thiamine treatment is urgent to prevent further neurological changes. Alcoholic patients with WE can be treated with 500 mg thiamine hydrochloride in 100 ml of 0.9% NaCl solution, by intravenous infusion for 30 min, repeated 2-3 times a day. If the patient doesn't respond after 2 days of treatment, it can be stopped. If a response is observed - the dose changes to 250 mg intramuscularly or intravenously daily for 3-5 days or until observed clinical improvement. Some studies recommend prolonging the course with oral doses of 300 mg thiamine daily for 1-2 weeks. In addition, it is recommended to take electrolytes (Mg and K), for the good absorption of vitamin B1 and functioning of enzymes. In non-alcoholic patients with WE, response is seen at doses of at least 100-200 mg intravenously of thiamine, followed by thiamine administered orally daily.

**Conclusion.** The direction of Wernicke-Korsakoff Syndrome treatment was pretty clear due its etiology - thiamine deficiency. However, the main obstacle in providing adequate treatment is the misdiagnosis of WE - a risk for KS development. To avoid the latter, timely administration of thiamine substitution therapy with daily doses of 500-1500 mg in alcoholic patients and minimum 200 mg in non-alcoholic patients, followed by oral doses of vitamin B1 and electrolytes until recovery, is the best solution.





### 13. PHARMACOLOGICAL MANAGEMENT OF PATENT DUCTUS ARTERIOSUS

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**Introduction.** The ductus arteriosus (DA) is located between the aortic arch and the pulmonary artery in the fetal circulation, and its closure is one of the most important changes required for the transition to extrauterine life. Persistent hemodynamically significant patent ductus arteriosus (hsPDA) is a common cause of morbidity and mortality affecting over 40% of preterm infants. Prolonged hsPDA disrupts systemic hemodynamics, causing pulmonary hemorrhage, bronchopulmonary dysplasia, neurological disorders, acute renal failure, septicemia.

**Aim of study.** The aim of the study was to review and analyze the pharmacological management of patent ductus arteriosus

**Methods and materials.** This article is based on data collected from several articles available on PubMed, NCBI and Google Scholar, Medscape that have been published since 2017.

**Results.** Currently, the most common drugs aimed at pharmacological closure of patent ductus arteriosus are cyclooxygenase (COX) inhibitors, especially indomethacin and ibuprofen. Analysis of formal studies in databases demonstrated the efficacy of indomethacin in the persistence of patent ductus arteriosus. During treatment there was a response in 13 out of 15 in the indomethacin group and in 3 out of 15 in the control group. Paracetamol was used in children unresponsive to indomethacin or ibuprofen, or in those in whom COX inhibitors were contraindicated, and the DA closure rate was observed to be greater than 90%. In a study conducted by the Turkish Society of Neonatology, it was compared with oral paracetamol and ibuprofen, and it was found that the rates of ductal closure were similar and no difference was found in what adverse effects were found. However, paracetamol is not the standard treatment option, studies need to be conducted to demonstrate its effectiveness and safety. Ibuprofen (intravenous or oral), compared with placebo, was significantly more effective in reducing the presence of patent ductus arteriosus (PDA) at 72 hours of treatment. The spontaneous PDA rate was 58% in the control group.

**Conclusion.** NSAID-induced PDA closure is considered to be 75-80% effective. NSAID therapy (indomethacin, ibuprofen), started in the first days after birth, leads to a decrease and even closure of the duct. After oral administration of the drug, closure of the PDA occurs in 18-20%, and after intravenous administration in 88-90% of cases. Indomethacin is used intravenously at a rate of 0.2 mg/kg/day for 2-3 days. Ibuprofen lysine IV and indomethacin are chemically different and inhibit COX-1 and COX-2 isoforms to different degrees. They were shown to be equally effective in closing PDA in preterm infants and significantly more effective than placebo. The need for rescue medical treatment was significantly reduced, as was the need for surgical closure of the PDA.

## 14. PHARMACOLOGICAL TREATMENT OF METABOLIC SYNDROME IN CHILDREN



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**Introduction.** The increasing prevalence of metabolic syndrome in children has become a major public health concern, in parallel with the global rise in childhood obesity. Metabolic syndrome, represented by a group of interlinked risk factors such as abdominal obesity, insulin resistance, dyslipidemia and hypertension, significantly increases the risk of developing cardiovascular disease and type 2 diabetes in adulthood. This alarming trend highlights the importance of researching and developing effective treatments to ensure a high quality of life.

**Aim of study.** This study aims to select, analyze and synthesize literature data on metabolic syndrome, present the latest evidence on treatment for major components of MetS in children and adolescents.

**Methods and materials.** A literature review was conducted using PubMed, Google Scholar, Mendeley search engines. Inclusion criteria included studies involving children and adolescents (aged 2-18 years) diagnosed with metabolic syndrome or its individual components. Extracted data were analyzed to identify commonalities and differences in treatment approaches.

**Results.** The first step in the treatment of metabolic syndrome (MetS) in children is lifestyle intervention, which includes changes in diet and exercise. This approach aims to improve insulin resistance, obesity, dyslipidemia, hypertension and non-alcoholic fatty liver disease (NAFLD). Pharmacologically there are drugs that are used for adults (Orlistat, Phentermine, Metformin), and subsequently tried in children with success, but still have many side effects. These are still under investigation and further studies are needed to assess their efficacy and safety. Another option is bariatric surgery such as gastric bypass or sleeve gastrectomy, but it is still controversial and requires careful consideration because of potential risks and long-term consequences.

**Conclusion.** A clear definition and treatment plan for MetS and its components in children and adolescents is currently not available. Pharmacological options show promise, further research is essential to establish their safety and long-term efficacy in the pediatric population.



## 15. THE ROLE OF ESTROGENS IN CARDIOVASCULAR DISEASE

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**Introduction.** Epidemiological studies have shown that 17beta-estradiol (E2) levels are inversely associated with cardiovascular disease (CVD) events in post-menopausal women. This indicates that estrogens have a possible implication in CVD pathogenesis, through their genomic and non-genomic mechanisms of action.

**Aim of study.** Highlighting the role of estrogens and estrogen receptors in cardiovascular disease pathophysiology.

**Methods and materials.** Publications from the last 5 years, from specialized journals of the PubMed databases, were selected and analyzed using the following keywords: estrogen, estrogen receptors, genomic and non-genomic mechanisms, cardiovascular disease.

**Results.** Estrogens, through their specific receptors (ER $\alpha$ , ER $\beta$  and GPR30s), displayed prominent effects on cardiovascular disease pathogenesis. Evidence suggests their role in the management of systemic and pulmonary arterial hypertension, protecting against atherogenesis, ischemia-reperfusion injury, and safeguarding against heart failure with either reduced or preserved ejection fraction (EF). The specific mechanisms of ER $\alpha$  include reducing sympathetic outflow and endothelial dysfunction, decreasing fibrosis and pulmonary vascular remodeling, preserving EF, and enhancing systolic function. ER $\beta$  performs by decreasing vasoconstriction, vascular resistance and hypertrophy, mitigating fibrosis and inflammation, reducing apoptosis and preserving mitochondrial integrity, promoting cardiac angiogenesis and normalizing hemodynamic parameters. GPR30s mechanisms of action encompass relaxation of vascular smooth muscle, influence on nitric oxide synthesis, calcium level regulation, modulating cholesterol levels, and minimizing both inflammation and reactive oxygen species production.

**Conclusion.** Estrogens displayed a possible involvement in managing cardiovascular disease, by reducing both the progression and severity of numerous cardiovascular pathologies through various genomic and non-genomic mechanisms of action. Elucidation of cardio protective mechanisms, determined by estrogens and estrogen receptors, will contribute to the development of effective therapeutic strategies for CVD treatment.

## 16. THE USE OF NEW INSULIN ANALOGS IN TYPE 1 DIABETES



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**Introduction.** Diabetes mellitus is a metabolic condition with diverse causes, marked by persistent high levels of blood sugar and disruptions in carbohydrate, protein, and fat metabolism. It arises from deficiencies in insulin secretion, its effectiveness, or a combination of both. Managing type 1 diabetes involves supplementing  $\beta$  cell functions to achieve normal blood glucose levels. New insulin analogs, like rapid-acting (aspart, lispro, glulisine) and long-acting basal analogs (glargine, detemir, degludec), have been formulated to allow for a closer replication of a normal insulin profile.

**Aim of study.** Updated information regarding the use of new insulin analogs in patients with Type 1 Diabetes were analyzed to demonstrate the impact of analog therapy on achieving normoglycemia without hypoglycemia and complications of diabetes mellitus.

**Methods and materials.** We have accessed information from pertinent literature available in books, guidelines or databases like PubMed, NCBI, and ScienceDirect. This was achieved by employing specific keywords such as „type 1 diabetes”, „insulin analogs”, „pharmacokinetic”, „pharmacodynamic”.

**Results.** Several research studies have indicated that individuals with diabetes who use insulin analogs express higher satisfaction with their insulin therapy compared to those utilizing regular human insulin products. In a 64-week prospective, multicenter, randomized, open-label, parallel-group study involving 423 patients with type 1 diabetes undergoing basal-bolus therapy, participants were randomly allocated to either human insulin or insulin aspart as their bolus insulin. Treatment satisfaction was evaluated using the WHO Diabetes Treatment Satisfaction Questionnaire. Scores related to perceived hyperglycemia were lower in the insulin aspart group, suggesting that individuals using aspart perceived elevated blood glucose levels to be less pronounced than those using human insulin ( $P=0.005$ ). The insulin aspart group also reported greater treatment flexibility compared to those using human insulin ( $P=0.022$ ). The recent target for insulin administration involves delivering 0.5 – 1.0 IU/kg/day or higher doses to restore metabolic balance. The total daily dose depends on factors such as age, body weight, diabetes duration and stage, pubertal stage, carbohydrate intake, local insulin administration, self-monitoring, HbA1c levels, daily routine, and the presence of acute complications like infections or sick days. New insulins, such as degludec, can be used alone or combined with insulin aspart for better glycemic control, reduced variability, and a lower incidence of hypoglycemia.

**Conclusion.** The availability of well-established rapid-acting and long-acting insulin analogs has empowered a greater number of individuals with type 1 diabetes mellitus to achieve improved glucose targets. This has been associated with reduced rates of hypoglycemia and an enhanced quality of life compared to what was achievable with short-acting and long-acting human insulin.





## 17. THE USE OF NOOTROPICS IN THE TREATMENT OF PERIPHERAL NEUROLOGICAL PATHOLOGIES

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**Introduction.** Peripheral neurological pathologies, about 10% out of all nosological entities, refer to a group of disorders that affect the peripheral nervous system and are associated with various symptoms such as muscle weakness, numbness and pain

**Aim of study.** Researching the nootropics used in the treatment of peripheral neurological pathologies and the most efficient drug association that will have the best outcome.

**Methods and materials.** A retrospective study was conducted on a sample of 35 hospitalized patients with various peripheral neuropathies at the CMH “Arhangel Mihail”. Demographic variables, as well as administered medications, were recorded.

**Results.** It was established that out of the 35 randomly analyzed cases, 19 belonged to females (54,2%) and 16(45,8%) to males, with ages ranging from 45-81 years, mean age  $67,34 \pm 1,7$ . The selected peripheral neurological pathologies from the records were distributed as follows: 27 - lumbosacral radiculopathy, 3 neuropathic pain syndrome on the right, 2 spondylosis with persistent bilateral lumboischialgia, 2 unspecified polyneuropathy with lower flaccid paraparesis, 1 facial neuropathy with paralysis of facial muscles on the right. The administered treatment was complex, but only nootropic drugs were selected. All the patients (100%) were administered solution of 20% piracetam - 5 ml, 0.5% vinpocetine - 2 ml, 25 mg cinnarizine, 2% pentoxifylline - 5 ml, once a day, used simultaneously as follows: cinnarizine + vinpocetine + piracetam (16 cases), pentoxifylline + piracetam + cinnarizine (13 cases), piracetam + vinpocetine (6 cases). The patients showed improvement upon discharge. It was recommended to continue the nootropic treatment for at least 1 month to achieve the desired pharmacological effect.

**Conclusion.** Recent studies selected from the scientific literature argue the use of nootropics through various mechanisms. Firstly, the development of the analgesic effect of piracetam in peripheral neuropathic pain is emphasized. Moreover, current research is investigating the anti-inflammatory effects of pentoxifylline. Acting as a phosphodiesterase inhibitor, pentoxifylline inhibits the secretion of TNF-alpha, significantly reducing pain in patients with lumbosacral radiculopathy. The anti-inflammatory effect of pentoxifylline in facial neuropathy has only been demonstrated when administered in combination with steroids and low molecular weight dextran. Similarly, vinpocetine is noted for inducing an anti-inflammatory effect. The results obtained so far are encouraging and support the use of nootropics in peripheral neurological pathologies.



## 18. THREE GENERATIONS OF B-BLOCKERS: CLASS DIFFERENCES AND CLINICAL APPLICABILITY



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**Introduction:** The evolution of beta-blockers remedies has greatly influenced the management of a large scale of disorders. Research divides all beta blockers into three generations: first-generation nonselective  $\beta$ -blockers (propranolol), second generation more cardioselective  $\beta$ -blockers (nebivolol), and third generation highly selective  $\beta$ -blockers with vasodilating action (labetalol).

**Aim of study.** The aim of the study was highlighting the main differences between different generations of beta blockers.

**Methods and materials.** Articles from PubMed, NCBI, Cochrane in the period 2018-2023 regarding  $\beta$ -blockers were analyzed.

**Results.** The common mechanism of all  $\beta$ -blockers is their affinity for binding to  $\beta$ -adrenoreceptors, which reduces sympathetic nervous system activity. The differential affinity of  $\beta$ -blockers for  $\beta_1$ - over  $\beta_2$ -receptors contributes to their specificity. Propranolol was the first clinically used  $\beta$ -blocker and reduced the heart contractile strength and its rate. It was found useful in patients suffering from hypertension, angina and post-myocardial infarction, but was not suitable for patients with diabetes or with specific lung pathologies. The discovery of practolol, a second-generation drug with selectivity for  $\beta_1$ -adrenoreceptors, presents less risk of side effects associated with  $\beta_2$ -receptor antagonism. As a result of an analysis, it was confirmed that in addition to generation-dependent effects, different beta blockers have their own individual properties inherent only to a specific drug, which allows choosing the drug for various clinical situations. There are beta blockers that have a negative metabolic effect and increase the risk of developing diabetes, and there are metabolically neutral drugs (carvedilol). The mechanism of the vasodilating effect is also different, in some it occurs due to internal sympathomimetic activity (carteolol), others due to blockade of alpha-adrenergic receptors (carvedilol), betaxolol dilates blood vessels due to blockade of calcium channels, drugs such as nebivolol, dilate blood vessels by increasing the synthesis of nitric oxide. The representatives of third generation  $\beta$ -blockers can reduce peripheral vascular resistance by a decrease in oxygen demands of the heart. This includes drugs such as labetalol, the first  $\beta$ -receptor antagonist with less potency than propranolol, and nebivolol, which differs completely from the molecular structure of propranolol. Also, studies established that some  $\beta$ -blockers ameliorate endothelial and cardiac dysfunction and can be used for hypertension during pregnancy.

**Conclusion.**  $\beta$ -blockers occupy a central place in the treatment of patients suffering from cardiovascular diseases. Currently, the indications are: arterial hypertension, stable angina, previous MI, CHF, tachyarrhythmia, glaucoma and pregnancy. As first-line drugs,  $\beta$ -blockers are not recommended for use in individuals with metabolic syndrome and a high risk of developing diabetes mellitus.



## 19. TIRZEPATIDE – NEW TREATMENT OPTION FOR PATIENT WITH TYPE 2 DIABETES

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**Introduction.** Type II diabetes is a global problem of the 21st century. The incidence of diabetes is increasing significantly and alarmingly over the years, thus according to WHO data the rate of diabetes has increased 8 times during the last 20 years. In the Republic of Moldova, over 131 thousand people suffer from diabetes, of which 9% - type I diabetes and 91% with type II diabetes (in 80% of cases they are overweight people, who through excessive consumption of animal fats have developed a resistance of cells to the action of insulin). According to scientific data, this number will increase in geometric progression and will reach up to 690 million people in the next 20 years. A new **first-in-class** drug for the treatment of type 2 diabetes is tirzepatide. Approved by the FDA in the USA, Europe, Canada and Australia in 2022.

**Aim of study.** To analyze the studies of tirzepatide's clinical efficacy in individuals with type II diabetes (T2DM).

**Methods and materials.** Were used scientific publications and articles from the PubMed, NCBI, Medscape databases published during 2015-2023.

**Results.** Data collected through a literature review, analysis of clinical trials SURPASS and SURMOUNT demonstrated the effectiveness of tirzepatide. Increased affinity for GIP receptors and less for GLP-1, tirzepatide produces a considerable reduction in hyperglycemia compared to a selective GLP-1 receptor agonist. Tirzepatide increases the levels of adiponectin, which constantly regulates glucose and lipid metabolism. Recent studies in 2021 demonstrated significant glycemic efficacy and obesity reduction with tirzepatide, and superiority over dulaglutide, semaglutide, degludec, and insulin glargine. It works as a dual GLP-1 agonist and GIP agonist, and leads to significantly improved glycemic control in type 2 diabetics and significant weight reduction. Tirzepatide's bioavailability is approximately 80%, plasma protein binding 99%, a half-life 5 days, after once-weekly dosing 2.5 mg subcutaneously. It is not available in oral form. Based on scientific data from side effects can be decreased appetite, acid reflux, sinus tachycardia, also may cause thyroid C-cell tumors.

**Conclusion.** In patients with type 2 diabetes mellitus, tirzepatide with its dual action on both GLP-1 and GIP receptors shows significant therapeutic promise. It is given between 2.5 to 15mg with 6 dose options. Although it has some side effects and contraindications for some patients (like a family history of medullary thyroid carcinoma) is outweighed by its outstanding effect on both decreasing blood glucose levels and losing weight. Additionally, it shows improvements in lipid profile, and cardiac and renal risks despite the limited data. Many studies suggest that tirzepatide, as part of individualized patient-centered care, may be a useful therapy for many people with type 2 diabetes.

## 20. TREATMENT OF CONVULSIVE SYNDROME IN PEDIATRIC PATIENTS



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**Introduction.** Convulsive syndrome represents paroxysmal cerebral crises, related to excessive and hypersynchronous activity of cortical and subcortical neurons. This condition is marked by uncontrolled muscle contractions, which may or may not be associated with neurovegetative, sensory, and psychological symptoms, as well as consciousness disorders. Convulsive Syndrome is a common condition among children, highlighting the importance of researching and developing effective treatments to ensure a high quality of life.

**Aim of study.** This study aims to select, analyze, and synthesize bibliographic data regarding convulsive syndrome, examining and determining the most commonly used medications in Moldova and their effectiveness.

**Methods and materials.** This article describes a retrospective study conducted on a group of 50 case histories analysis of patients suffering from Convulsive syndrome. This study took place in the Neurology and Psychiatric departments of the IMSP Municipal Clinical Hospital for Children “Valentin Ignatenco” during the 2023 year.

**Results.** In the majority of the patients, convulsions lasted less than 5 minutes. Due to the brief duration of the convulsions, there was often no need for emergent anticonvulsive medication. Instead, the primary approach to treatment for these patients was recovery and rehabilitation, focusing on managing the condition without immediate pharmacological intervention. In cases where a convulsive episode lasted more than 5 minutes, a different treatment approach was taken. Diazepam, a medication known for its effectiveness in controlling seizures, was commonly used. For these prolonged convulsive episodes, Diazepam was administered at a dose of 5 and 10 mg, the route of administration was intrarectal.

**Conclusion.** A tailored approach to treating convulsive syndrome in pediatric patients emphasizes the importance of evaluating the duration of convulsions to decide the most appropriate treatment strategy.



## 21. USE OF SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS IN HEART FAILURE

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**Introduction.** Heart failure syndrome has been designated as a major clinical and public health problem. Ischemic cardiopathy, arterial hypertension, cardiomyopathies, myocarditis, pericarditis valvulopathies, arrhythmias, toxic conditions and diabetes are considered the most common causes of heart failure (HF). Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, calcium channel blockers and beta adrenoblockers are recommended as first-line medications in the treatment of HF. Recent research has shown that sodium-glucose cotransporter 2 inhibitors (SGLT2-empagliflozin, dapagliflozin, and canagliflozin) have shown favorable effects in patients with HF.

**Aim of study.** The study's aim was to elucidate the mechanisms and effects of SGLT2 responsible for the efficacy in heart failure.

**Methods and materials.** A review was performed in the PubMed database of scientific articles reflecting the efficacy of SGLT2 inhibitors in HF by using the keywords "heart failure" and "sodium-glucose cotransporter 2 inhibitors".

**Results.** It has been suggested that SGLT2 inhibitors, simultaneously with the antihyperglycemic effect, may manifest cardioprotective and renoprotective effects in patients with HF, along with or without diabetes mellitus. These effects can be determined by: 1) inhibition of the glucose and sodium reabsorption with weight loss and a natriuresis, which reduces the volume of circulating blood, pre - and post-pregnancy; 2) blocking of the hydrogen and sodium reabsorption in the proximal tubules with the elimination of natrium and preservation of renal perfusion, as well as a decrease in cardiomyocytes and prevention of cardiomyocyte death; 3) annihilation of oxidative stress by direct action (SGLT2 and SGLT1 inhibition) and indirect (improvement of glycemic control); 4) improvement of vascular function by reducing activation and dysfunction of endothelial cells and direct vasodilation; 5) reduction of the sympathetic nervous system hyperactivity with the decrease of arterial stiffness, endothelial dysfunction and alteration of renal hydroelectrolytic balance; 6) modulation of the activity of the renin-angiotensin-aldosterone system.

**Conclusion.** SGLT2 inhibitors will show beneficial influences on the pathogenetic links of heart failure with the reduction of hospitalizations and mortality of patients with HF. Through the pleiotropic effects, SGLT2 inhibitors will contribute to advantageous hemodynamic and metabolic effects in patients with kidney and heart diseases, and diabetes.

**Keywords.** Heart failure, sodium-glucose cotransporter 2 inhibitors, dapagliflozin, empagliflozin.



## **XVIII. PHARMACY SECTION**



***„Dragi studenți, tineri medici, farmaciști!***

***Suntem extrem de fericiți să știm că voi sunteți cei care nu încetați niciodată să cercetați, să vă dezvoltați și să învățați. Universitatea noastră va sprijini întotdeauna tinerii pentru inițiativa și dedicarea lor. În acest an, Universitatea de Stat de Medicină și Farmacie "Nicolae Testemițanu" găzduiește a zecea ediție a Congresului Internațional MedEspera. Datorită vouă, suntem convingși că medicina și farmacia se dezvoltă întotdeauna. Aceasta este încă un motiv pentru care să luptăm pentru visurile noastre în beneficiul omenirii. Vă dorim tuturor succes și o experiență de neuitat în timpul Congresului.”***

***"Dear students, young doctors and pharmacists!***

***We are extremely happy to know that you are the ones who never stop researching, developing, and learning. Our university will always support the young generation for initiative and dedication. This year, the "Nicolae Testemitanu" State University of Medicine and Pharmacy is hosting the tenth edition of the MedEspera International Congress. Thanks to you, we are convinced that medicine and pharmacy is always developing. This is one more reason to fight for our dreams for the good of humanity. We wish you all, success and an unforgettable experience during the Congress.”***

***Nicolae Ciobanu,***

*MD, PhD, Associate Professor,*

*Dean of Faculty of Pharmacy,*

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## 1. ACTION OF BIOPHARMACEUTICAL FACTORS ON DRUG BIOAVAILABILITY

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**Introduction.** According to the Food and Drug Administration (FDA), bioavailability represents the amount of active substance released from a pharmaceutical form, absorbed into the bloodstream, and reaching the site of action, manifesting its therapeutic effect. Thus, bioavailability can be affected by a series of factors: biopharmaceutical and physiological factors, drug administration form, and interactions with other medicinal substances. Optimization of these factors is essential for improving drug bioavailability and preventing tragic events, such as the global impact generated by thalidomide.

**Aim of study.** Analysis of the main biopharmaceutical factors influencing drug bioavailability.

**Methods and materials.** It was evaluated 32 articles, using databases: PubMed, MEDLINE, The Thomson Corporation.

**Results.** It was established that the series of biopharmaceutical factors, such as chemical structure, solubility, pharmaceutical form, micronization, and isomerism, influence drug bioavailability both positively and negatively. Modification of the chemical structure: introduction some radicals (methylprednisolone (MP), obtained by attaching CH<sub>3</sub>-group in the C6 of prednisolone, showed that MP on average 4 times as effective as hydrocortisone); salt form (sodium benzylpenicillin has a higher water solubility than benzylpenicillin). Another significant factor influencing bioavailability is isomerism (the S(+) isomer of ofloxacin has an antibacterial action approximately 10 times greater than its R(-) form). The following factors are polymorphism (metastable polymorphic form of dicaine has 2-3 times greater anesthetic activity); micronization of powders (griseofulvin, acetylsalicylic acid, ibuprofen). However, in the case of acetylsalicylic acid, micronization can lead to aggregation, reducing the active surface and consequently its bioavailability, therefore micronization is carried out in the presence of axillary substance - polysorbate 80 (wetting agent).

**Conclusion.** Biopharmaceutical factors can influence drug bioavailability by changing the chemical structure, increasing solubility, obtaining a new pharmaceutical form, which leads to modifications in absorption and therapeutic efficacy of drugs.

## 2. ANTI-CANCER COMPOUNDS IN BRASSICA VEGETABLES



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**Introduction.** Cancer is the main cause of mortality and morbidity worldwide. According to the World Cancer Research Fund an estimated 40% of all human cancers are related to diet. Although a large variety of therapeutic approaches have been developed and translated into clinical protocols, the toxic side effects of cancer treatments negatively impact patients, allowing cancer to grow. Cabbage, broccoli, Brussels sprouts, and other members of the g. Brassica have been widely regarded as potentially cancer preventative. A lower risk of colorectal, cervical, and lung cancers was found to be associated with a high intake of cruciferous vegetables. What differentiates Brassicaceae from other plants is the presence of the secondary metabolites called glucosinolates, recognized for both their role in plant defense and human health.

**Aim of study.** This review aims to examine the roles of Brassicaceae vegetables and their important bioactive metabolites in prevention and treatment of different cancers.

**Methods and materials.** In order to fulfill the purpose of the study the scientific articles (about 60) from the last decade on Google scholar, Science Direct, PubMed databases were searched by following parameters: Brassicaceae nutrients, compounds, phytochemicals; Brassicaceae in health benefits, cancer prevention and treatment and other.

**Results.** The family Brassicaceae genus Brassica consists of the species Brassica oleracea (e.g., broccoli, cabbage, cauliflower, Brussels sprouts, kale, turnips, collards), which are the most frequently consumed vegetables worldwide. In the last couple of decades, growing scientific evidence has suggested that consumption of cruciferous vegetables has a preventive role against a variety of human diseases. It has been demonstrated that the chemopreventive potential of cruciferous vegetables is likely due to glucosinolates and their secondary metabolites (e.g., isothiocyanates (ITCs)). In vitro and in vivo studies have shown that ITCs are able to activate phase II detoxification enzymes (such as quinone reductase and glutathione S-transferase) as well as to disrupt tubulin polymerization, inducing cell cycle arrest and the activation of apoptosis in cancer cells. Additionally, since dietary ITCs are well absorbed and have good bioavailability, these compounds are promising candidates for anti-cancer therapies.

**Conclusion.** The family Brassicaceae signifies to be an outstanding source of health-promoting phytochemicals and nutrients that would pay beneficial dietary importance against certain types of diseases. Numerous epidemiological studies indicate that Brassica vegetables protect humans against cancer. Thus, Brassica metabolites are emerging as new weapons for anti-cancer therapeutics.



### 3. ANTIBACTERIAL ACTIVITY OF BASIL ESSENTIAL OIL

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**Introduction.** Basil essential oil has been demonstrated to possess various beneficial properties, including analgesic, anti-inflammatory, antibacterial, hepatoprotective, and immunomodulatory effects. The multifunctionality of Basil oil makes it an important candidate for incorporation into different dosage forms. The massive use of antibiotics has resulted in the emergence of resistant microorganisms, which is another problem affecting public health. *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella* spp, *Staphylococcus aureus*, *Shigella* spp., *Enterococcus* spp., *Escherichia coli* are the main bacteria that have developed this resistance. Plants and other natural resources can provide a wide range of complex and structurally different compounds.

**Aim of study.** To determine the antibacterial activity of basil oil.

**Methods and materials.** The antimicrobial activity of Basil essential oil was assessed against various indicator strains using the filter paper disc diffusion method. The in vitro testing of the samples was performed on ATCC strains from the collection of the Microbiology Laboratory of Saarland University on *Escherichia coli* (ATCC 25923) and *S. epidermidis* (ATCC 25922) strains. The strains were revived by overnight growth in Brain-Heart Infusion broth (Oxoid, CM1135) at 37°C and were diluted to an optical density of 0.5 McFarland standard ( $1.5 \times 10^8$  CFU/ml).

**Results.** The data obtained from the disc diffusion method, followed by measurement of MIC, indicate that *E. coli* and *S. epidermidis* showed lower values of MIC (1.25 mg/mL, respectively). Therefore, the Basil oil was shown to exhibit strong antimicrobial activity against all microorganisms tested, both Gram-positive and Gram-negative bacteria, even though Gram-positive strains seem to be more sensitive to it. Overall, the observed antimicrobial activity of Basil oil might be attributed to the high contents of linalool that possesses a stronger antimicrobial activity against Gram-positive bacteria than against Gram-negative bacteria.

**Conclusion.** Basil oil is a natural source that can be used in formulation of dosage forms with antibacterial activity.

#### 4. COMPARATIVE ANALYSIS OF THE NATIONAL AND INTERNATIONAL LEGISLATIVE FRAMEWORK REGARDING THE STORAGE OF MEDICINAL PRODUCTS FOR HUMAN USE



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**Introduction.** Globally, regulating and managing medicines is vital for public health. This presentation compares how the Republic of Moldova and the European Union handle the storage and preservation of medicines. It highlights similarities and differences in authorization procedures, pharmacovigilance, GMP, GDP standards and future collaboration prospects. The analysis offers insights into ensuring optimal quality and safety for users in both jurisdictions.

**Aim of study.** To carry out the comparative analysis of the national and international legislative frameworks regarding the preservation of medicines of human use from different points.

**Methods and materials.** There have been used relevant articles and directives related to the national legislative framework in the field of medicine storage, international legislative framework in the field of medicine storage, published between 01.01.2020-01.11.2024 on search engines PubMed and ScienceDirect.

**Results.** In the Republic of Moldova, Order of the Ministry of Health no. 28 of 16.01.2006 regarding the storage of medicines, parapharmaceutical products and medical articles sets strict requirements for the storage and preservation of medicines, including temperature conditions, humidity and safety standards. The Medicines and medical Devices Agency monitors and regulates this field. In the European Union, Directive 2001/83/EC regulates medical products for human use, setting strict standards for authorization, distribution, storage and preservation. The European Medicines Agency (EMA) is responsible for the evaluation and supervision of medicines in the EU. The comparative analysis reveals significant similarities between the two jurisdictions highlighting the emphasis on drug safety and efficacy. Storage and preservation requirements are similar, imposing strict conditions on factors such as temperature and humidity. Both sides have specialized agencies for drug oversight and regulation. In perspective, the EU promotes the harmonization of standards and procedures in member states, ensuring cohesion in the regulation of medicines. The Republic of Moldova as an aspirant to international standards, can adopt and adapt several European Provisions to improve its regulation in the field of medicines.

**Conclusion.** The comparative analysis of the legislative framework regarding the storage and preservation of medicines in the Republic of Moldova and the European Union highlights significant similarities in the approach to standards and procedures. With both jurisdictions focused on drug safety and efficacy, the Republic of Moldova, in its process of alignment with EU norms, has the opportunity to adopt and adapt to the EU to further improve its drug regulation.



## 5. DRUG INTERACTIONS AND ERRORS IN THE TREATMENT OF HYPERTENSION IN THE ELDERLY

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**Introduction.** Hypertension is a condition in which the systolic and diastolic pressures are increased above the permissible limit. According to the European Society of Hypertension, for people without diabetes, the values of 140mmHg systolic and 90mmHg diastolic are considered, and for those with diabetes, starting from 130 mmHg systolic and 80mmHg diastolic. Hypertension is treated in a complex way depending on the chronic pathologies of the patients, so medical errors and interactions are common.

**Aim of study.** To report clinical and pharmacological aspects of interactions and errors in the management of hypertension.

**Methods and materials.** A literature review of PubMed, NCBI, MeSH databases was conducted.

**Results.** The majority of patients with hypertension are elderly people with pain of various origins. They are usually given COX2 selective inhibitors to avoid affecting their acidity. Inhibited COX2 sharply decreases prostacyclin 2 levels leading to vasoconstriction of coronary vessels and increased risk of myocardial infarction. A common error is the combination of ACE+ potassium-sparing diuretic or ARBs + potassium-sparing diuretic, as a common cumulative adverse effect is hyperkalemia leading to arrhythmias and/or renal failure. Another drug interaction is the use of digoxin in patients using diuretics (furosemide, torasemide) in which low K levels lead to increased serum digoxin and toxicity, because the alkaloid binds with K from the Na/K ATP-asa pump, and conversely in hyperkalemia the effect of digoxin decreases.

**Conclusion.** The antihypertensive pharmacological groups possess significant interactions with other classes of drugs in the complex treatment of hypertension. Rational selection and correct use of monotherapy or combination therapy to improve the patient's quality of life.



## 6. EVALUATION OF PHENOLIC COMPOUNDS IN ETHANOLIC EXTRACT OF CICHORIUM INTYBUS L. BY HPLC METHOD



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**Introduction.** *Cichorium intybus* L (Chicory), of the Asteraceae family, is a perennial herbaceous plant with a long tradition of use and various pharmacological activity such as: antibacterial, anti-inflammatory, analgesic, sedative, antidiabetic, hepatoprotective and antitumor.

**Aim of study.** Determination of phenolic compounds in ethanolic extract of the aerial part of *Cichorium intybus* by the HPLC method with UV-VIS detection.

**Methods and materials.** The aerial part of Chicory was harvested during the flowering period from the collection of the Scientific Practical Center in the Field of Medicinal Plants of Nicolae Testemitanu State University of Medicine and Pharmacy. The dry extracts were concentrated using a rotary evaporator-Laborota 4011. The analysis was carried out on Shimadzu LC-20AD chromatograph with UV detector, under the following conditions: stationary phase: Zorbax Exlipse Plus C18; 2 mobile phases: solvent mixture: methanol: water (40:60) with gradient elution and orthophosphoric acid 0.5%: acetonitrile (80:20) with isocratic elution mode; detection at wavelengths of 280, 325 and 360 nm.

**Results.** Optimal separation of phenolic compounds was achieved in the solvent system of 0.5% orthophosphoric acid:acetonitrile (80:20) at a wavelength of 325 nm. The presence of hydroxycinnamic acids (cycoric, chlorogenic, caffeic, and ellagic), flavonoids (rutin, quercetin, luteolin, kaempferol, apigenin) and tannins (catechin and epicatechin) was found in the dry extract of *C. intybus*. The identification of the nominated compounds was carried out by comparing the retention times on the chromatogram of the extract with those on the chromatograms of the standard solutions.

**Conclusion.** The developed HPLC technique with UV-VIS detection can be used for the separation, identification and quantification of phenolic compounds in the ethanolic extract of *Cichorium intybus*.



## 7. HYSSOPUS OFFICINALIS L. THE SOURCE OF DIOSMIN AS THE THERAPEUTIC AGENT IN DIFFERENT DISEASES

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**Introduction.** The species *Hyssopus officinalis* L. is known over the years as a medicinal plant based on volatile oils. In the last 3 decades, scientific researchers have highlighted different classes of therapeutically valuable chemical compounds, in particular flavonoids, represented by different constituents, and the major interest is represented by diosmin.

**Aim of study.** This review aims to examine the roles of diosmin from flavonoids as an efficient therapeutic agent from *H. officinalis* L. species.

**Methods and materials.** In order to fulfill the purpose of the study, about 65 scientific articles were analyzed in the databases on the Google scholar, Science Direct, PubMed platforms on several criteria: the physico-chemical characteristics of diosmin, the method of obtaining it, the health benefits, the mechanisms of action.

**Results.** Oxidative stress has been reported as a driving factor in the development of various diseases, including myocardial ischemia, neuronal cell damage, hypoxia, diabetes, and cancer. Diosmin has several therapeutic properties due to its antioxidant activity. The hepato-protective potential of diosmin is prominently exerted by its anti-oxidant and anti-inflammatory activity. Many diseases, including arthritis, allergy, asthma, atherosclerosis, diabetes and cancer are the result of inflammation, characterized by inflammatory markers. Diosmin has demonstrated therapeutic effects on diabetes and its complications. It has also been found to improve lipid metabolism abnormalities associated with diabetes. Diosmin has also been noted to alleviate these markers in many studies due to its anti-inflammatory property. Recent studies have shown that diosmin exerts dose-dependent proapoptotic effects on various types of cancer, including breast, prostate, colon, oral bladder, and urinary. More recently, diosmin has demonstrated antimicrobial activity against a broad spectrum of pathogens with high antibiotic resistance. Diosmin (phlebotropic agent) is a veno-active drug administered orally for the treatment of chronic venous insufficiency.

**Conclusion.** In a series of recent scientific works, the therapeutic value of diosmin has been demonstrated, which plays a major critical role in the control of various metabolic processes, which lead to the development of various severe diseases. Thus, diosmin, from hyssop possesses antioxidant, anti-cancer, anti-diabetic and anti-bacterial properties and diosmin treatment looks promising in the treatment of different kinds of cancers, diabetes and diseases associated with oxidative stress and inflammation.

## 8. LIPOSOME BIOPHARMACEUTIC AND NANOPARTICLES IN HUMAN BODY



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**Introduction.** The use of nanotechnology in medicine, and more specifically in drug delivery, is rapidly spreading. Numerous substances are currently being researched for drug delivery and, in particular, cancer therapy.

**Aim of study.** This study aims to describe biopharmaceutical peculiarities of liposomes and nanoparticles in the human body.

**Methods and materials.** A bibliographic study of scientific literature specialized at biopharmaceutical peculiarities of liposomes and nanoparticles in the human body.

**Results.** Nanoscale drug design has been widely studied and is by far the most advanced technology in nanoparticle applications due to its potential advantages, such as the ability to modify properties like solubility, drug release profiles, diffusivity, bioavailability and immunogenicity. Nanomedicines have improved solubility due to the presence of both hydrophilic and hydrophobic environments. A number of well-known nanodrugs are already available on the market. Since 1995, 50 nanopharmaceuticals have received Food and Drug Administration (FDA) approval and are currently available for clinical use. Pharmaceutical sciences use nanoparticles to reduce the toxicity and side effects of drugs and, until recently, have not realized that the delivery systems themselves may impose risks to the patient.

**Conclusion.** The benefits of nanoparticles for modern medicine are numerous. Indeed, there are some cases where nanoparticles enable analyses and therapies that simply cannot be performed otherwise. However, nanoparticles also bring with them unique challenges for the environment and society, particularly in terms of toxicity.



## 9. PHYTOCHEMICAL ANALYSIS OF HYSSOPUS OFFICINALIS L. FROM REPUBLIC OF MOLDOVA

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**Introduction.** *H. officinalis* widely grows in southern Europe, Central Asia, Russia and Iran. This species is one of the important medicinal plants and is extensively cultivated in Spain, France and Italy. The aerial shoots of this plant are useful for the treatment of respiratory diseases, including asthma, bronchitis and coughs, as they contain chemicals such as terpenes, flavonoids, volatile oils, tannins and resin.

**Aim of study.** The determination of total polyphenols and hydroxycinnamic acids in dried extracts obtained from the aerial parts of three varieties (roseus, albus and cyanus form)

**Methods and materials.** The aerial parts of three genotypes of the *H. officinalis* L. were collected from the collection of the IGPhPP. The extracts were obtained with 70% ethanol by maceration with stirring. The total phenolic content in the dried extracts was quantified using the Folin-Ciocalteu method, while the total hydroxycinnamic acids were determined spectrophotometrically using the Arnow reagent.

**Results.** Spectrophotometric analysis determined the total content of polyphenols in dried extracts obtained from the aerial parts of three varieties of *H. officinalis* (roseus, albus and cyanus forms). The highest concentration of polyphenols (mg GA/g extract) was found in the dried extract from *Hyssopi herba* in the roseus form (37), followed by extracts obtained from the cyanus (32.88) and albus (24.65) forms. The total hydroxycinnamic acids, expressed as caffeic acid, ranged from 22.65% (roseus) to 15.52% (albus).

**Conclusion.** The chemical study of the analysed samples determined that the dry extract obtained from *Hyssopi herba*, especially *H. officinalis* in the roseus form, showed the highest content of phenolic compounds.

## 10. PROSPECTS FOR OBTAINING LIPOSOMES WITH STANDARDIZED PLANT EXTRACT



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**Introduction.** In recent years, scientists have shown an increasing interest in incorporating biologically active compounds extracted from plants into nanoparticle delivery systems. Examples of such delivery systems include liposomes, solid lipid nanoparticles, carbon nanotubes, graphene and many others. The need to develop an advanced phytocompound administration system is based on the fact that most biologically active compounds extracted from plants suffer from having low absorption and undergoing intensive metabolism which limits their efficacy and contributes to their lack of selectivity. Therefore, the incorporation of phytocompound into modern nanoparticle delivery systems would indeed increase their therapeutic efficiency and bioavailability.

**Aim of study.** Firstly, exploring different approaches for generating, analyzing and controlling liposomes reported in the literature, and secondly generating and evaluating liposomes with standardized polyphenolic extract content.

**Methods and materials.** For the literature review, open access scientific articles from databases such as PubMed and Scopus are collected (n=40 articles). With regard to the preparation of liposomes, dry artichoke extract standardized in chlorogenic acid is used, as a polymer, a mixture of Cholesterol: Lecithin: PEG-600 (0,3:1:1) is utilized. Samples are ultrasonicated and dried using a rotary evaporator (IKA VACSTAR). The resulting Liposomes are evaluated under electron microscope (VWR® Binocular Microscope) and their Zeta potential is determined (Malvern Zetasizer Nano ZS).

**Results.** Liposomes possess multiple advantages which allow for the availability of several phytocompounds on the nutraceuticals market. The highest percentage of liposomal phytoconstituents refers to those of phenolic nature with antioxidant properties. Thus, for the research, the standardized extract from artichoke leaves cultivated in the collection of the Practical Scientific Center in the Field of Medicinal Plants of *Nicolae Testemitanu* SUMPh was used. The liposomes were obtained by the classic method of preparation with the application of the thin film hydration technique, followed by ultrasound, using soy lecithin, PEG 600, cholesterol and methanol as solvent. The obtained phospholipid vesicles with average diameter of 550 nm were observed under the electron microscope, with electric potential of 0.8, determined by means of the dynamic light diffusion method.

**Conclusion.** The research results present important opportunities for capitalizing on natural extractive products through the development of new pharmaceutical forms to ensure the population with quality products and high bioavailability.





## 11. SOME ASPECTS OF OPTIMIZATION GERIATRIC PHARMACOTHERAPY

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**Introduction.** One of the main tasks of the modern health system is ensuring an adequate quality of life for the elderly, whose share in the world is constantly increasing. At the same time, the changes associated with the aging of the body require new approaches to improve pharmacotherapy, the use of specially selected medicinal preparations that would ensure an adequate therapeutic effect as well as their effective use.

**Aim of study.** Evaluation of pharmacokinetics peculiarities of medicinal preparations on elderly, as well as ways to optimize geriatric pharmacotherapy.

**Methods and materials.** Analytical-descriptive study of specialized literature using electronic databases such as Scopus, PubMed and EBSCO.

**Results.** As a result of the data from the specialized literature, it is known that changes in the function of organs and systems induced by the natural aging processes of the body can directly influence the pharmacokinetics of medicinal preparations and can increase the risk of adverse reactions. One of the factors influencing the pharmacokinetics of drugs in geriatric patients is the violation of the motor function of the gastrointestinal tract and a decrease in the secretion of digestive enzymes. This leads to slower absorption of oral medications used by the elderly. Adjusting the dose of drugs for the elderly takes into account the hydrophilic-lipophilic properties of the active substances. Due to the increase in the percentage of adipose tissue, the depletion of connective tissue, as well as the reduction of the amount of water in elderly people, the distribution of lipophilic drugs (tetracyclines, benzodiazepines, barbiturates, etc.) increases with age, which require a longer period of time to obtain the therapeutic concentration in the blood, thus prolonging their half-life. For example, for diazepam, a fat-soluble preparation, the volume of distribution in the elderly is 2 times greater, that is, the half-life of the drug in an elderly patient will be twice as long as in a middle-aged patient. These changes have been shown to directly affect drug absorption, metabolism, distribution and excretion and may in turn alter the patient's safety profile. The record of all changes in geriatric patients, the regular monitoring of the effectiveness of the use of drugs, the change of their dosage regimen can influence the optimization of pharmacotherapy and reduce the risk of the development of some unwanted reactions.

**Conclusion.** In recent years worldwide the proportion of the elderly population is growing rapidly, and age-related changes require the development of new medicinal preparations and delivery systems with adjustable doses, for the maximum benefit without adverse effects.

## 12. STUDY OF MEDICATIONS DESIGNED FOR URETHRAL ADMINISTRATION



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**Introduction.** Currently, worldwide, according to studies, approximately 60% of women and 20% of men declare a urinary problem throughout their lives, such as: urethritis, cystitis, prostatitis, etc. Thus, for a complex and effective treatment medicinal preparations with local and systemic actions are used.

**Aim of study.** The study of the magistral pharmaceutical forms, distinctly solutions, that are prescribed in various urological diseases.

**Methods and materials.** The scientific databases: Scopus and Pubmed served as materials, as well as the magistral prescriptions from the production department of the „Vasile Procopisin” University Pharmaceutical Center, regarding the assortment of urethral solutions (instillations) used in the local treatment of urological diseases.

**Results.** The instillation of medicinal solutions into urethra through a catheter, is one of the most recommended treatments by many urological associations. This method is characterized by lack of side effects, through which medicinal substances reach the place of action directly. The study of prescriptions from „Vasile Procopisin” University Pharmaceutical Center, prescribed by doctors from various health institutions from the Republic of Moldova, revealed that majority of prescribed urethral medicinal forms were solutions containing colloidal substances such as protargol and collargol, composed of silver oxide particles and protein, effective for fighting bacterial infections. Doctors also recommended instilling the urethra with sea buckthorn oil and a 3% solution of boric acid. Thus, the high proportion of medical prescriptions with liquid forms shows that, thanks to the direct action on the localization of infection and inflammation, the improvement of treatment could be reached.

**Conclusion.** The study of prescriptions designed for ureteral administration showed increased interest of doctors in magistral pharmaceutical forms prepared in pharmacies. After identifying the frequency of prescriptions, it was found that the liquid magistral forms are the most used in the treatment of urological conditions due to the local and beneficial action they exercise.



### 13. STUDY ON CLINICAL CASES OF ATOPIC DERMATITIS IN CHILDREN

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**Introduction.** Allergic contact dermatitis (ACD) was once considered a rarity in children, but recent estimates suggest that it affects 4.4 million children in the United States alone. Currently, there is no cure, but an increasing number of innovative and targeted therapies show promise in gaining control over the disease, even in patients with refractory conditions. This has prompted us to investigate clinical cases of ACD.

**Aim of study.** To evaluate clinical cases of atopic dermatitis in children.

**Methods and materials.** An analysis was conducted on 43 medical records of pediatric atopic dermatitis cases over a 2-year period in outpatient practice.

**Results.** Based on the SCORAD score, it was found that 7% of children exhibited a mild form of progression, 43% had a moderate form, and 50% showed severe progression. Many examined children also suffer from other associated allergic pathologies. Thus, out of the total number of allergic dermatitis patients, 24 children have bronchial asthma (9%) and allergic rhinitis (15%), aligning with existing literature. The most common manifestations observed in children were nonspecific dermatitis on the hands and feet (76%), dry skin (63%), itching (57%), facial erythema (44%), eczema (23%), etc. Current guidelines suggest that sedative antihistamines are favored over non-sedative antihistamines for alleviating allergic itching. We analyzed data from the National Ambulatory Medical Care Survey to compare antihistamine use between dermatologists and non-dermatologists. Overall, dermatologists are more inclined to prescribe sedative antihistamines than non-sedative ones compared to non-dermatologists. Patients under the age of 21 were also more likely to receive sedative antihistamines than non-sedative ones. These findings highlight differential prescribing practices for atopic dermatitis among physicians.

**Conclusion.** Providing appropriate antiallergic medication in conjunction with avoiding the detrimental effects of allergic factors will contribute to reducing the incidence of atopic dermatitis morbidity. Among first-generation antihistamines, the most commonly used are clemastine, chlorpheniramine, and cyproheptadine, which are preferably prescribed in acute forms of atopic dermatitis, while second and third-generation antihistamines are typically used in subacute and chronic forms.

**Keywords.** Atopic dermatitis, children, treatment.

## 14. THE PHARMACIST'S ROLE IN THE MANAGEMENT OF THE ELDERLY'S MEDICATION AT HOME



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**Introduction.** Pharmacists have a central role in ensuring the safety of medicines throughout the pharmaceutical care process. Providing advanced drug therapy management services in outpatient settings ensures the reduction of problems related to the medication of the elderly and improves their therapeutic compliance.

**Aim of study.** Evaluation of the elderly's perception of the problems encountered during the administration of medicines at home to highlight ways to involve the pharmacist in their prevention.

**Methods and materials.** The study method used in the research is the survey of elderly people who use drugs. 194 questionnaires were collected and validated which describe the difficulties of using medicines in the elderly.

**Results.** The answers given by the elderly indicate that only 15.97% of the respondents have problems related to the administration of medicines; 61,07% often ask the pharmacist about the correct way of administration, thus, only 14.94% indicated that they very rarely make the wrong way of administering the medicine. 44,84% of the respondents had cases of correct storage of the medicine in domestic conditions, even if 32.98% often asked about the correct way to store the requested medicine at home. In a quarter of the respondents occurred cases of polypharmacy (25.77%), adverse reactions (25.25%) and only 30.87% know how to report adverse reactions. 21, 64% of the respondents are rarely unable to use the medicines, and 27.83% do not understand/read its instructions.

**Conclusion.** Being the last in direct contact with the patient, the pharmacist during the act of dispensing the medicines through the appropriate counseling provided to the elderly patient would improve their drug administration and storage practices at home.



## 15. THE PHARMACIST'S ROLE IN THE THERAPEUTIC PARTNERSHIP RELATIONSHIP WITH THE ELDERLY PATIENT

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**Introduction.** The collaboration between the pharmacist and the elderly in the community pharmacy is being defined through a therapeutic partnership that ensures the quality of pharmaceutical care provided. This relationship is based on the comprehensive assessment of the specific needs of elderly patients, trust, and the pharmacist's communication skills, which as a whole ensures the improvement of the experience of the elderly related to medicines use in outpatient settings.

**Aim of study.** To describe the characteristics of the relationship between the elderly pharmacy visitor and the pharmacist from the perspective of the elderly to highlight the specifics of the pharmaceutical care provided in the community pharmacy.

**Methods and materials.** The tool used in this research is the sociological questionnaire, care consists of 10 written questions and refers to several aspects of the collaborative relationship between the pharmacist and the elderly established during the pharmaceutical act. The study was carried out for 6 months, the respondents being pharmacy visitors aged over 60 and who are drug users.

**Results.** A survey of 194 elderly respondents, showed a very good level of trust in the pharmacist as a specialist in the field of medicine (61,85%), and the elderly often addressed (45,3%) to the pharmacist when experiencing difficulties in using medicines. The level of information by the pharmacist after the last visit to the pharmacy is a very good one (55,15%). The respondents noted a good level of retention of the information provided by the pharmacist during counseling at the last visit to the pharmacy (51,54%) and that they always strictly followed the pharmacist's recommendations regarding the use of the requested medicines (53,6%). A less common practice in the elderly is the use of supplementary instructions or various medical accessories to facilitate the use of medicines, 58,76% indicated that they do not use them and the pharmacists do not inform them (74,74%) about their usefulness. The elderly use 5 drugs simultaneously (86,08%), antihypertensive drugs were listed most frequently. To benefit from pharmaceutical assistance appropriate to their needs, respondents support (93,81%) specialization and continuous training of the pharmacist in providing geriatric pharmaceutical services.

**Conclusion.** Pharmaceutical care oriented towards the satisfaction of needs related to the administration of medicines in the elderly at home contributes to improving their knowledge about medicines and is based on the partnership relationship formed between the pharmacist and the elderly.



## 16. THE ROLE OF POLYMERS IN THE DEVELOPMENT OF SOME ADHESIVE FORMS



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**Introduction.** Oropharyngeal preparations represent a modern trend in the technology of solid forms, which have been developed to overcome some disadvantages of other forms (complex manufacturing, variable stability). These pharmaceutical forms (bioadhesives) present solid, semi-solid or liquid preparations, containing one or more active substances, intended for administration in the oral cavity or pharynx, in order to obtain a local or systemic action.

**Aim of study.** Study of bioadhesive polymers and their role for the formulation of mucoadhesive oral tablets.

**Methods and materials.** Study of pharmaceutical and medical literature using electronic databases such as: Scopus, Pubmed and EBSCO.

**Results.** Mucoadhesive oral tablets that consist of monolithic matrices or multilayered matrices are part of the oropharyngeal forms. Currently, this type of tablets are prepared using efficient and modern technologies based on polymers, so they can contain large amounts of medicinal substances, which, depending on the way of incorporation, can be released throughout the oral cavity. Formulations with bioadhesive polymers are used to prolong the contact of pharmaceutical forms with the oral mucosa and to modify the release profile of medicinal substances. As mucoadhesive polymers for the preparation of oral mucoadhesive tablets, the following are often used: natural polymers (chitosan, sodium alginate); semi-synthetic polymers (sodium carboxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose); synthetic polymers (carbopols, polyvinylpyrrolidone). A mucoadhesive polymer must possess the following characteristics: be non-toxic and non-absorbable; to be non-irritating to the mucous membrane; to adhere quickly to wet epithelium; to present site specificity; to easily incorporate the medicinal substance and to yield it easily. Thus, oral bioadhesive tablets based on bioadhesive polymers ensure the release of the substance in a certain area for a longer time, with the aim of increasing bioavailability.

**Conclusion.** The development of systems for the release of medicinal substances in the oral cavity could be a solution to the access of substances in the systemic circulation. The quantity of the released and absorbed substance is directly correlated to the nature and type of the polymer present in the bioadhesive tablets.



## 17. THE USE OF MAGNESIUM SALTS IN THE THERAPY OF ARTERIAL HYPERTENSION

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**Introduction.** Annually, more than 10 million lives are lost due to high blood pressure (HT). A low magnesium content in drinking water leads to increased risk of developing cardiovascular disease (especially coronary heart disease) and sudden death. Magnesium ( $Mg^{2+}$ ) plays a direct role in the functioning of the endothelial system, controls the contraction-relaxation processes of smooth muscle cells, affects the mechanisms of vascular wall calcification, the coagulation system, systemic inflammation, as well as the conduction system of the heart.

**Aim of study.** The research aims to analyze the bibliographic data regarding the benefits of  $Mg^{2+}$  salts in HT therapy.

**Methods and materials.** To carry out the study, 21 scientific articles were researched using the following databases: PubMed, MEDLINE, SciSearch, The Thomson Corporation and Cochrane Electronic Library, Google Academic.

**Results.**  $Mg^{2+}$  deficiency has been shown to correlate with a number of chronic cardiovascular diseases, including HT, diabetes mellitus, and hyperlipidemia in many studies. Unfortunately, it is impossible to ensure such an increased intake of  $Mg^{2+}$  only by changing the diet. For the long-term treatment of hypomagnesemia, drugs containing  $Mg^{2+}$  are used: tablets or oral solution. Thus, the drugs, containing inorganic salts of  $Mg^{2+}$ , have absorption of no more than 5%, therefore, to increase bioavailability,  $Mg^{2+}$ -salts are used in combination with vit.B6, with potassium and organic ones: aspartic acid, lactic acid, glutamic acid, citric acid, orotic acid. In case of  $Mg^{2+}$  deficiency, its additional administration is necessary (10-30 mg/kg per day). Depending on the clinical situation, 25% magnesium sulfate injection is given intravenously slowly in the health-care setting.

**Conclusion.** Magnesium is an essential electrolyte for living organisms. Magnesium has vasodilatory, anti-inflammatory, anti-ischemic and antiarrhythmic properties.  $Mg^{2+}$  supplementation may help reduce cardiovascular risk factors associated with HT caused by  $Mg^{2+}$  deficiency due to chronic diuretic use, inadequate intake, or both.

## 18. THE WAYS TO IMPROVE DRUG STABILITY



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**Introduction.** The stability of medicine represents capacity to maintain physical, chemical, biological and microbiological stability. It directly influences the effectiveness and safety of drugs.

**Aim of study.** To elucidate the possible way that can improve the drug stability.

**Methods and materials.** To accomplish the study there have been analyzed scientific articles, by accessing the MEDLINE databases, The Thomson Corporation and SciSearch, Cochrane Electronic Library.

**Results.** The pre-formulation studies are a crucial stage in the procedure of testing on drug substances available for absorption that would determine product safety and efficacy. In general, there are in fact five different types of stability: chemical, physical, microbiological, therapeutic, and toxicological. Excipient selection must be done carefully, because some excipients could interact with the substance, causing instability (phenobarbital with polyethylene glycols). Another way to improve drug stability is by selecting materials for packaging that guarantee protection from light, moisture, and oxygen. Proper container selection, especially utilizing dark glass or airtight containers (Vitamin B1, B6, B12, C, aminophylline), may avoid degradation caused by environmental factors. Lyophilization can be used to reduce water content and improve stability in some formulations. This is particularly helpful for biologics, such as proteins (interferon alpha – bifidobacterium, vaccines). Some pharmaceutical substances are sensitive to changes in pH (penicillin, adrenaline). Keeping the formulation's pH at the proper level can help prevent hydrolysis and degradation. Inert gases, such as nitrogen, can be used to displace oxygen in drug containers. Incorporating antioxidants into formulations can prevent oxidative degradation. Common antioxidants (sodium hydrosulfite, thiourea) play a crucial role in neutralizing reactive oxygen species that may otherwise lead to the degradation of drugs. Regularly monitor the stability of drug formulations through accelerated stability studies and real-time stability testing. This helps identify potential degradation pathways and allows for adjustments in formulation or packaging.

**Conclusions.** Stability analysis is the basis for all drug development and manufacturing. Implementing a combination of these strategies, tailored to the specific characteristics of each drug, is key to enhancing stability and prolonging the shelf life of pharmaceutical products.

**Keywords.** Stability, types of stability, drugs



***XIX. PHYSIOLOGY  
SECTION***

## 1. AUTONOMIC NERVOUS SYSTEM ACTIVITY PARAMETERS IN INDIVIDUALS WITH AFFECTIVE DISORDERS



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**Introduction.** Studies have shown a potential correlation between affective disorders and disturbances in the autonomic nervous system (ANS) activity, particularly heart rate variability (HRV). HRV is observed to be reduced in people suffering from affective disorders.

**Aim of study.** Highlighting the importance of using HRV as a biomarker for affective disorders.

**Methods and materials.** Research papers from the last 5 years, from specialized journals of the PubMed databases, were selected and analyzed using the following keywords: parasympathetic activity, sympathetic activity, affective disorders, autonomic nervous system, heart rate variability.

**Results.** Parameters known to quantify parasympathetic activity (e.g., high frequency (HF)-HRV and the root mean square of successive RR interval differences (RMSSD)) were observed to be lower in individuals with negative affect (emotions such as fear, anxiety and sadness). Moreover, reductions in the parasympathetic activity were shown to have a possible contribution to the onset and development of affective disorders, such as depression, through potential inflammatory pathways, increasing the level of pro-inflammatory cytokines. Low frequency (LF) and sympatho-vagal balance derived from the LF/HF ratio, used as indices of sympathetic activity, were revealed to be increased in individuals with negative affect, suggesting the involvement of the sympathetic outflow during those states. In comparison, studies imply that positive affect states may have less distinct signatures in heartbeat signals.

**Conclusion.** The consistent association between negative affect and a reduction in numerous HRV measures indicates a potential link between decreased parasympathetic activity and affective disorders. Variations in ANS activity could be a prospective biomarker for affective disorders, especially with the use of more complex non-linear models of the relationship between ANS and HRV, providing a promising path to understanding ANS and cardiac dynamics in affective disorders.





## 2. CHRONIC STRESS AND ITS INDUCING FACTORS IN A GROUP OF SECOND-YEAR MEDICAL STUDENTS

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**Introduction.** General medicine is one of the most prestigious academic fields in the Republic of Moldova. The study of general medicine is considered one of the most demanding, both in terms of the volume of information, knowledge, and skills required, and the psychological demands, competitive environment, and encounters with human suffering. All of the aforementioned factors and circumstances can lead to chronic stress among medical students. Stress is defined as a state of psychological, social, cognitive, and mental imbalance. Prolonged exposure to higher intensity stress can result in psychological problems such as fear, anxiety, panic attacks, depression, memory disorders, as well as somatic issues like insomnia, weight loss, weakness, breathing difficulties, palpitations. All the mentioned consequences contribute to a decrease in the quality of life for medical students.

**Aim of study.** Assessment of the level of chronic stress and the prevalence of its inducing factors among second-year medical students.

**Methods and materials.** Perceived chronic stress was assessed in a group of students (N = 240, age 19-22 years) in their second year of medical school (last week of the second semester). We utilized the MSSQ (Medical Stressor Questionnaire) for assessments. It measures stress factors distributed across 6 domains.

**Results.** Percentage distribution of stress levels in the analyzed group: mild - 10.4%, moderate - 25%, high - 49.6%, severe - 15%. The mild to moderate stress level is reasonable and can be well-managed, regardless of the stress factors in the six domains of the MSSQ scale. We observed that stress factors have different prevalence among subjects with high and severe stress levels: I - Academic stress factors: high stress level (47%); severe (13%); II - Intrapersonal and interpersonal stress factors: high stress level (18%); severe (3%); III - Teaching-learning process-related stress factors: high stress level (22%); severe (8%); IV - Social stress factors: high stress level (20%); severe (2%); V - Choices and desires-related stress factors: high stress level (12%); severe (4%); VI - Group activities-related stress factors: high stress level (20%); severe (3%).

**Conclusion.** The study found a high level of chronic stress among second-year medical students. There is a very high prevalence of academic stress factors and stress factors related to the teaching-learning process. The implementation of distress prevention programs and psychological counseling can serve as strategies to prevent chronic stress and its consequences: anxiety, depression, sleep disturbances, decreased attention.

### 3. CHRONOTYPE IN PATIENTS WITH SLEEP APNEA HEADACHES



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**Introduction.** Chronotype describes the hormonal schedule of an individual that makes them naturally inclined to a specific sleep pattern or period of alertness in a day, and unlike circadian rhythm, which describes a person's 24-hour clock that regulates their day-to-day physiological processes, it is genetic. In a way, we can say Circadian Rhythms stem from Chronotypes. While the latest scientific research suggests the PER3 gene is the genetic factor responsible for chronotypes, other factors such as age, environmental factors, work schedules, social obligations, and lifestyle choices could contribute to the evolution of chronotypes. These can, in turn, influence a person's sleep quality, mood, cognitive performance, and overall well-being. Hence, a complex association between the evolution of Sleep Apnea and headaches in specific Chronotypes is generated.

**Aim of study.** To further understand the prevalence of Sleep Apnea Headaches within a specific inherent Chronotype.

**Methods and materials.** Methods and Materials: An analytical review of the latest scientific research papers was conducted using online platforms, including – Google Scholar, PubMed and Elicit.

**Results.** Out of the three principle chronotypes known to exist, i.e. Morning type, Evening type and the Intermediate type, persons inclined to eveningness have been found to be at a higher risk for sleep complaints, including Sleep Apnea Headaches. Considering their natural tendencies to peak at their energy levels during the later part of the day while the norm of a person's lifestyle demands productivity and higher activity during the daytime, it is believed that evening-type persons tend to lack the balance needed to cope due to possible irregular sleep patterns and hence a disrupted circadian rhythm.

**Conclusion.** Although, for most of the part, Chronotypes are influenced genetically, they can still be evolved even if retraining or deliberately changing them is unachievable. Furthermore, their complex relationship with sleep Apnea and headaches still offers much scope for research.

**Keywords.** Chronotype, Sleep Apnea Headaches, PER3 gene.



#### 4. CIRCADIAN RHYTHM DISTURBANCES AND IMMUNE SYSTEM

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**Introduction.** The intricate dance between the immune system (IS) and circadian rhythm (CR) orchestrates a finely tuned symphony within the human body. IS is the body's vigilant defender against pathogens, relying on innate and adaptive components for immediate and targeted responses. The study aims to investigate the impact of circadian rhythm disturbances on immune system dynamics.

**Aim of study.** CR driven by the master circadian clock, regulates the rhythmic oscillations of physiological and behavioral processes over 24 hours and synchronizes various bodily functions, including sleep-wake cycles, hormone secretion, and metabolic activity. Also, immune cells exhibit circadian oscillations, influencing the body's susceptibility to infections, and conversely, immune challenges can disrupt CR. Understanding the nuances of this reciprocal relationship opens avenues for exploring how CR disturbances may impact immune responses and vice versa, shedding light on potential implications for human health and innovative therapeutic interventions.

**Methods and materials.** This systematic review synthesizes data from publications over the last decade, sourced from PubMed, PMC, and Google Scholar, focusing on the intricate relationship between normal and disturbed and the innate and adaptive ISN by analyzing approximately 51 relevant studies. The following keywords were used for the search: circadian rhythm, immune system, sleep disruption, clock genes, cytokines, melatonin, cortisol, shift work, immune regulation, and inflammatory response

**Results.** CR influences the innate and adaptive IS. It has been demonstrated that circadian clock proteins play a significant role in T cell differentiation. For example, CD4<sup>+</sup> T exhibits a rhythmic expression of clock genes, and the circulation of B and T cells increases at night and decreases throughout the day as they undergo extravasation. Cortisol, which peaks in the morning, stimulates wakefulness but, when chronically high, can inhibit the immune system. Melatonin, which rises in the evening, regulates the circadian rhythm and has anti-inflammatory properties, helping to maintain a healthy immune response during sleep. Sleep disruptions reduce the immune system's response by boosting cortisol and decreasing melatonin, increasing susceptibility to infections, encouraging inflammation, and limiting wound healing. Prioritizing healthy sleep patterns is critical for overall immune function support.

**Conclusion.** The circadian rhythm controls immunological responses by affecting clock gene expression, cytokine production, immune cell activity and levels of hormones like cortisol and melatonin. Coordination like this ensures an efficient and effective immunological response. Immune modulation may be impacted by disruptions to the circadian rhythm, emphasizing the significance of preserving a normal sleep-wake cycle.

## 5. MATERNAL CIRCADIAN RHYTHM AND SLEEP DISORDERS AS A RISK FACTOR FOR AUTISM SPECTRUM DISORDER



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**Introduction.** The prevalence of Autism Spectrum Disorder (ASD) in the Republic of Moldova and Israel is 0.49 and 0.36, respectively, reflecting a global increase in ASD cases. According to current literature, the prevalence has increased by 2.5 times since the first Autism and Developmental Disabilities Monitoring (ADDM) Network study in 2000.

**Aim of study.** The exact causation of ASD remains unclear, but emerging research emphasizes the role of maternal factors during pregnancy, specifically disruptions in CR and sleep patterns. Maternal CR and SD may impact the complex mechanisms that underlie embryonic neurodevelopment. SD are reported to affect 46-78% of pregnant women, with sleep quality deteriorating in the third trimester. This review delves into the association between maternal CR disturbances and the development of autism in the fetus. The study aims to investigate if pregnant mothers' circadian rhythm (CR) and sleep disorders (SD) are cofactors for the development of Autism Spectrum Disorder (ASD) in their offspring. Keywords: maternal circadian rhythms, melatonin, autism, neurodevelopmental disorders in children

**Methods and materials.** This review synthesizes data from approximately 70 publications over the last decade, sourced from PubMed, PMC, and Google Scholar.

**Results.** ASD development involves a multifactorial interplay of genetics, hormones, gut microbiota, immune dynamics, neural connectivity, neurotransmitters, and environmental exposures. Another important group of factors, but still undersized, are maternal CR disruptions, especially during pregnancy, and sleep difficulties in the second trimester, both of which increase the risk of neurodevelopmental disorders in children. There are a few underlying mechanisms, the most important are disrupted maternal melatonin secretion and the impact of stress and cortisol levels, which influence fetal development. Also, the dysregulation of a pregnant mother's physical activity during 24 hours could play an important role in ASD development because during physical activity pregnant woman releases growth hormone and insulin-like growth factor-1, promoting fetal growth through improved nutrient supply, exercise enhances fetal blood flow, reduces inflammation, oxidative stress, and increases growth factor levels, which improve neurodevelopment. Moderate to high-intensity physical activity during pregnancy positively affects newborn neurodevelopment.

**Conclusion.** In summary, maternal circadian rhythm disruptions and pregnancy-related sleep issues pose risks to offspring with ASD. Melatonin's role in fetal circadian rhythm and the impact of maternal stress are crucial. Maintaining moderate to vigorous physical activity throughout pregnancy benefits newborn neurodevelopment. Despite these findings, further research is essential to understand these intricate connections fully, shaping future research and therapies for ASD and neurodevelopmental disorders.





## 6. RESPIRATORY BIOFEEDBACK FOR ANXIETY REDUCTION THROUGH VISUALIZATION OF THE CHEST MOVEMENTS

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**Introduction.** Anxiety causes significant distress to patients and remains one of the most common complaints in primary healthcare. Family physicians often find themselves seeking the most effective treatment for patients, including free methods like biofeedback. Biofeedback is a therapeutic tool to facilitate the self-regulation of autonomous functions for health improvement. The respiratory biofeedback method is based on voluntary controlled respiratory movements in the form of a special breathing pattern.

**Aim of study.** This study aims to assess the efficiency of respiratory biofeedback, performed through slow abdominal breathing, with visual control of respiratory movements, on the anxiety.

**Methods and materials.** This study was conducted on a sample of 25 volunteers, students at *Nicolae Testemitanu* State University of Medicine and Pharmacy, 19 to 24 years old, mean age  $21.9 \pm 1.1$  years. Initially, a psychophysiological assessment of the study participants was conducted using State and Trait Anxiety Inventory Spielberger (STAI). The respiratory training for reduction of anxiety involved using abdominal breathing at a frequency of 6 breaths per minute. The onset of respiratory cycle phases (inspiration/expiration) was signaled by the metronome sound, strictly maintaining the ratio between the duration of inspiration and expiration at 5 seconds to 5 seconds. Thus, participants limited the amplitude of chest movements and increased the amplitude of abdominal movements, using instant visual feedback provided by the VISURESP application.

**Results.** The selected sample followed this special program for 14 days, with daily sessions lasting 15 minutes each. The results obtained in this study show that the majority of participants experienced a reduction in anxiety. A very significant decrease ( $p < 0.01$ ) in the trait score was recorded in 41.65% of subjects, a significant decrease ( $p < 0.05$ ) in 33.32% of subjects, and only 3 subjects did not show improvement in anxiety.

**Conclusion.** The visualization of the chest and abdominal movements during respiratory training helps ensure the correct execution of abdominal breathing. The outcome of this study supports the method of respiratory biofeedback as a complementary treatment for various anxiety disorders.



## 7. SIGNIFICANCE OF CIRCADIAN RHYTHM FOR CARDIAC HOMEOSTASIS.



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**Introduction.** Circadian rhythm plays a crucial role in the homeostasis of the cardiovascular system through hormonal secretion and the regulation of the nervous system's activity.

**Aim of study.** This research aims to understand the role of circadian rhythm in regulating cardiac homeostasis.

**Methods and materials.** The methodology relies on reading and analyzing 23 scientific articles published in PubMed and Google Scholar databases between 2019 and 2021, focusing on the source, publication date, and relevance to the topic. Keywords used include "cardiac homeostasis," "circadian rhythm," and "blood pressure variation."

**Results.** Research has shown the circadian rhythm's involvement in maintaining cardiac homeostasis, highlighting proteins such as BMAL1 and Clock. These proteins, binding to DNA sequences encoding circadian rhythm proteins (EBOX), not only initiate the synthesis of circadian rhythm-regulating proteins but also play a negative feedback role to ensure balance also their influence extends from regulating sympathetic (SNS) and parasympathetic (SNP) nervous systems to releasing hormones. The SNS, active during the day, generates positive inotropy, intensifying parameters like contraction force and heart rate. Conversely, the SNP, active during the dark phase, induces negative inotropy, moderating contraction force, conduction, and heart rate. Additionally, cyclically released hormones like aldosterone and cortisol cause vasoconstriction, adding a positive inotropic effect. These interactions become particularly significant in stressful situations, such as intense physical activity, where hormones inducing positive inotropy, via vasoconstriction, are released to meet the body's needs through neoglucogenesis stimulation, allowing glucose release into the bloodstream. These circadian rhythm oscillations also extend to metabolic processes, including increased synthesis of triglycerides and glycogen in the later part of the wakefulness phase, enabling the body to store reserves for the subsequent wakefulness phase. This phase also involves protein and phospholipid synthesis, contributing to cellular regeneration.

**Conclusion.** The results demonstrate that circadian rhythm-regulating proteins, such as BMAL1 and Clock, influence various aspects, from modulating nervous systems to releasing key hormones, impacting cardiac function. These interactions also extend to metabolic processes, emphasizing the extensive involvement of circadian rhythms in cardiovascular health. To optimize heart health, it is advisable to adopt regular lifestyle habits, such as maintaining consistent sleep schedules, promoting a balanced diet, and engaging in regular physical activity to support circadian rhythm and promote optimal cardiac homeostasis.

**Keywords.** Circadian Rhythms, Cardiac Homeostasis, Cardiac Function, Cardiovascular Physiology.



## 8. THE IMPORTANCE OF DAYLIGHT EFFECTS ON THE CIRCADIAN RHYTHM AND NEGATIVE CONSEQUENCES OF EVENING LIGHTENING OF DISPLAYS

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**Introduction.** Light is electromagnetic radiation with wavelengths between 400 and 700 nm visible to the human eye. Over recent years, a technological revolution has occurred in which conventional lightning has been replaced by light-emitting diodes (LEDs). The main sources of LED exposure are smartphones, TV and computer displays, and blue lightning sources (wavelengths between 400-500 nm). Nevertheless, natural light is considered the main “zeitgeber” that regulates circadian rhythm, sleep, mood, alertness and cognitive function by influencing photoreceptor cells in the retina (maximum sensitivity at 460-480 nm).

**Aim of study.** It is to establish the different effects on the circadian rhythm between natural light and light emanating from modern screens.

**Methods and materials.** An analysis of scientific sources between 2018 and 2023 was carried out using the PubMed search engines HINARI and Google Academic.

**Results.** Previous studies have shown that light effects depend on its physical characteristics, meteorological and atmospheric conditions, exposure time and intensity. Daylight contains all the visible spectrum, which changes throughout the day. The luminance of a sunny day varies between 20,000 and 100,000 lux, of a rainy day, between 3000 lux, and twilight up to 1000 lux. This variation regulates the circadian rhythm, the 24-hour sleep-wake cycle. Furthermore, sunlight stimulates the production of serotonin, and it is often associated with increased alertness and productivity. Blue light exposure in the evening hours from modern displays delays the time of the biological clock and thus sleep by suppressing melatonin secretion. Using the “night shift” or other filter modes of modern smartphones, the colour balance of the screen can be shifted to “warmer” (longer wavelength), which may reduce melanopsin activation by 67% at full display brightness. Nonetheless, dimming the smartphone to its minimum level reduces melanopsin activation to less than 1%. On the other hand, blue light therapy in the morning may be effective for seasonal affective disorders.

**Conclusion.** Due to the high sensitivity of the retina to blue light, the colour temperature and wavelength frequency the usage of blue light emitting technologies at night is deleterious. On the other hand, the spectral variety of natural light and changing intensity during the day facilitate the circadian rhythm regulation. However, more specific research is needed to differentiate the effects of light according to its biophysical characteristics.

## 9. THE IMPORTANCE OF MELATONIN IN THE DEVELOPMENT OF IDIOPATHIC SCOLIOSIS



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**Introduction.** Adolescent idiopathic scoliosis is a common disease, with a 0.47–5.2% prevalence. The female-to-male ratio ranges from 1.5:1 to 3:1 and is increasing with age. Untreated scoliosis can cause muscle imbalances, back pain, reduced mobility and respiratory or cardiovascular issues. This review aimed to assess the current information regarding the impact of melatonin on scoliosis pathogenesis by integrating specific genetic markers, molecular pathways, and clinical data.

**Aim of study.** Various hypotheses of idiopathic scoliosis's etiology have been put forth, such as neuromuscular dynamics, connective tissue structure, vestibular dysfunction, platelet microstructure, mechanical influences, growth-related and developmental aspects, asymmetry in the brainstem, genetic factors, equilibrium dysfunction, and impaired proprioception. Despite the conventional focus, recent research suggests a potential influence of melatonin on idiopathic scoliosis.

**Methods and materials.** A broad English search was undertaken of the Pubmed and Scopus databases for the terms "idiopathic scoliosis, circadian rhythm, melatonin." Articles from the period 2010-2023 were chosen.

**Results.** Melatonin may play a role in the pathogenesis of scoliosis through the neuroendocrine hypothesis, influencing muscle strength, which decreases at night and gradually increases in the morning. The physiological function of melatonin is to inhibit the intracellular  $Ca^{2+}$  receptor calmodulin, regulating actin-myosin interactions in skeletal muscle contraction. Studies have found that individuals with idiopathic scoliosis have higher levels of serum melatonin compared to controls matched for weight, age, and height, and the MT2 receptor has lower expression and is asymmetrically distributed in paravertebral muscles, with higher levels on the concave side of the spinal curve compared to the convex side. These modifications could lead to weakness and shortening of the muscles on the concave side, while on the convex side, there may be lengthening and hypertrophy of the muscles due to compensation.

**Conclusion.** The study provides evidence for melatonin's role in scoliosis development by inhibiting calmodulin because of its high serum levels and demonstrating asymmetrical receptor expression in paravertebral muscles, collectively indicating its potential contribution to scoliosis pathogenesis and providing insights for targeted therapeutic interventions and enhancing patient outcomes. And because melatonin is an essential factor involved in circadian rhythm regulation, further studies are needed to analyze the influence of circadian rhythm disorders in scoliosis etiology.



## 10. THE IMPORTANCE OF THE CIRCADIAN RHYTHM IN THE MUSCULOSKELETAL DEVELOPMENT OF CHILDREN

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**Introduction.** Bone and muscle cells have the same circadian rhythm as the rest of the body's cells, with 24-hour oscillations governed by the primary clock. This review aimed to determine if there is a correlation between circadian rhythm disturbances and musculoskeletal development during childhood.

**Aim of study.** The increasing use of blue-light-based devices amongst children increases the prevalence of circadian disruptions, leading to perturbed peripheral clocks.

**Methods and materials.** A comprehensive search of the Google Academic and PubMed databases was undertaken for the words "pediatric circadian rhythm", "circadian rhythm and muscle", and "circadian rhythm and bones"; publications from 2013-2023 were selected.

**Results.** Studies have shown that the circadian clock, primary and peripheral, is entrained by exercise, diet and sleep quality. Disruptions can lead to decreased muscle mass, reduced muscle strength, and increased osteoclast differentiation, leading to bone loss and tendon calcification. Other factors involved in circadian rhythm regulation like melatonin (stimulates osteoblastogenesis, inhibits osteoclastogenesis, promotes skeletal muscle growth, decreases muscle damage), growth hormone, estrogen, testosterone (increases bone and muscle mass and strength), calcium, vitamin D (increases bone mineral density, muscle strength) and their misalignment because of circadian rhythm dysregulation have been researched as potentiators of the musculoskeletal dyshomeostasis.

**Conclusion.** To understand in what way circadian misalignment affects the development of muscle and bones in children, further research should be done considering factors like circadian rhythm, sleep patterns, nutrition, physical activity, levels of hormones, and geographical regions. Also, future research should include development assessment methods like anthropometry, somatoscopy, spirometry, dynamometry and osteodensitometry correlated with circadian rhythm disruption.



## 11. THE INFLUENCE OF CIRCADIAN RHYTHMS IN THE EXACERBATION OF BRONCHIAL ASTHMA



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**Introduction.** Asthma is an inflammatory disease of the airways, affecting 334 million people globally, of whom 44-61% are prone to developing complications during the night. One of the most important diagnostic criteria for severe asthma, present in 5-10% of asthmatics, is nocturnal symptoms.

**Aim of study.** The purpose of the study was to highlight circadian variations in neurotransmitters and hormones that affect lung function and how disruptions in the internal clock can lead to worsening asthma. Rhythmic changes in respiratory functions are much more pronounced in asthmatic people than in healthy ones. Affecting sleep quality, decreasing productivity, and limiting social functions determined by nocturnal complications among asthmatics reveals the importance of understanding the physiological mechanisms of circadian rhythms on lung functions, which will allow the implementation of effective measures to prevent and alleviate symptoms.

**Methods and materials.** The research is a literature review based on the analysis of 20 articles published in the period 2014-2023 in the databases PubMed, Scopus and Google Scholar, based on the following keywords: "circadian rhythm, asthma".

**Results.** The predominance of the activity of the parasympathetic nervous system at night induces the intense release of acetylcholine on M3 muscarinic receptors, causing the formation of IP3 and increasing the concentration of Ca necessary for contraction, as well as the activation of M2 receptors coupled to the Gi protein, which inhibits adenylate cyclase A, favouring increasing the resistance of the pulmonary pathways. Similarly, stimulation of the ventro-lateral preoptic nucleus, which induces sleep through the release of GABA, inhibits locus coeruleus activity, amplifying the effects of vagal tone on the airways. Increasing serum melatonin concentration during the night increases the synthesis of cytokines, IL-2, IL-6 and IL-12, enhancing the inflammatory response of the pulmonary pathways in asthmatics. The evolution of bronchial asthma is also influenced by the circadian rhythm of cortisol, which inhibits the expression of pro-inflammatory genes. The decrease in cortisol concentration and glucocorticoid receptor affinity during the night intensifies inflammatory processes caused by IgE. Also, cortisol's circadian fluctuations decrease beta-adrenergic receptors' density by 33% during the night, diminishing the bronchodilator effects mediated by epinephrine.

**Conclusion.** Although many factors determine the pathogenesis of asthma, a complete understanding of the mechanisms by which circadian rhythms drive airway hyperresponsiveness to various peripheral modulators is essential. Proper hygiene of circadian rhythms: ensuring quality sleep, sequencing indoor work with exposure to natural light, and minimizing exposure to light from gadgets are other crucial factors in preventing asthma.





## 12. THE ROLE OF DYSFUNCTIONAL BREATHING IN THE PAIN SYNDROME. RESPIRATORY BIOFEEDBACK AND OTHER GUIDED BREATHING TECHNIQUES IN PAIN TREATMENT.

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**Introduction.** Chronic pain syndrome is a global health concern that significantly impacts patients' quality of life. It stems from various conditions, including degenerative joint diseases, neurological disorders, autoimmune diseases. Despite its widespread prevalence, the role of dysfunctional breathing in initiating and sustaining chronic pain is often overlooked, resulting in misdiagnoses and inadequate treatment. Recognizing the profound impact of breathing on pain and exploring methods to enhance patients' respiratory health is essential for improving their overall well-being.

**Aim of study.** To assess the impact of dysfunctional breathing in chronic pain syndrome and to explore the practical utility of technologies such as respiratory biofeedback and other guided breathing techniques in treating chronic pain.

**Methods and materials.** Bibliographic sources were analyzed using PubMed, Google scholar.

**Results.** The majority of analyzed clinical studies suggest a positive impact of a specific respiratory intervention on pain. Additionally, 4 of the analyzed studies did not apply the breathing technique independently of other potentially active therapeutic components, such as relaxation, massage, listening to the soothing sound of the sea, and meditation. In these studies, it is not clear how much each of the different interventions contributed to pain reduction or if the respiratory intervention contributed at all to the effect. Several factors in the analyzed clinical studies render it difficult to draw a general conclusion regarding the effectiveness of respiratory interventions, as well as the mechanisms that could determine a hypoalgesic effect. Firstly, it is evident that the quality, type, and intensity of the studied pain are highly heterogeneous in the analyzed clinical studies. Slow breathing exercises are unlikely to have the same outcome in different conditions, including burn pain, musculoskeletal pain, acute emergency pain, or labor pain. In several studies, the diversity of pain seems considerable even within a sample of patients from the same study.

**Conclusion.** Therefore, while there are study results supporting the benefits of breathing techniques in pain management, the direct relationship and specific mechanisms involved remain subjects for further investigation, underscoring the ongoing need for research in this field. It is advisable for future clinical studies to standardize and carefully report the applied breathing technique, as well as how it is instructed to patients.

### 13. TRAINING OF ABDOMINAL BREATHING ON PURPOSE OF REDUCING ANXIETY BY RESTRICTING THE CHEST MOVEMENTS



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**Introduction.** The respiratory biofeedback method is based on executing of paced voluntary respiratory movements in order to reeducate a dysfunctional breathing pattern into a physiologically normal one. Respiratory biofeedback includes manual and instrumental techniques, while the most efficient are proven to be the instrumental methods, which involve the use of technical devices. By auditory or visual signals, they provide feedback to the patient with the result of their voluntary actions on their breathing pattern.

**Aim of study.** This study aims to assess the efficiency of respiratory biofeedback, performed through slow abdominal breathing, with restricted chest movements, on the anxiety.

**Methods and materials.** To reduce anxiety, respiratory training involved abdominal breathing at a rate of 6 breaths per minute. The beginning of the phases of the respiratory cycle (inspiration/expiration) was given by the sound of a metronome, so that the ratio between the time of inspiration and that of expiration was strictly 5 to 5 seconds. Training of abdominal breathing with restriction of chest movements was performed with the Variteks REF 137 chest corset, on a group of 32 people, students of *Nicolae Testemitanu* State University of Medicine and Pharmacy, 19-24 years old, mean age  $21.4 \pm 1.1$  years. The anxiety was assessed using State and Trait Anxiety Inventory Spielberger (STAI). While using the corset which restricted the movements of the chest during the respiratory training sessions, it was possible to achieve abdominal respiration as it was demonstrated by recording these movements on 2 channels of VISURESP application.

**Results.** The selected sample of subjects breathed according to this program for 14 days, 15 minutes daily. The anxiety was assessed again using STAI. The outcome of the research showed that 56.25% of the subjects had a very significant decrease in score of trait anxiety ( $p < 0.01$ ), 12.5% of the subjects had significant decrease ( $p < 0.05$ ), for 3 subjects the level of anxiety did not improve and for one subject the level of anxiety had increased.

**Conclusion.** Restricting the chest movements with chest corset during the respiratory training helps to limit these movements in order to achieve abdominal breathing. This can serve as a tool for reducing anxiety, so this technique can be recommended as a nonpharmacological treatment for anxiety disorders.



## **XX. MENTAL HEALTH SECTION**

*"În călătoria noastră către sănătatea mintală, cercetarea este farul care ne călăuzește prin apele tulburi ale minții umane. Fiecare descoperire este o ancoră de speranță pentru cei care se luptă cu întunericul." (Sigmund Freud). „În adâncurile psihicului uman, descoperim atât umbre întunecate, cât și lumini strălucitoare de înțelegere. Prin cercetare și explorare continuă, ne eliberăm din labirintul tulburărilor mintale și ne îndreptăm către lumină și vindecare. În căutarea sensului și echilibrului, suntem redirecționați în adâncurile propriilor noastre minți, căci fiecare călătorie interioară aduce lumină în întunericul tulburărilor mintale. Pentru a avansa în înțelegerea și tratarea acestor afecțiuni, este esențial să ne implicăm activ în cercetarea științifică în domeniul sănătății mintale, transformând modul în care ne raportăm la aceste probleme și promovând o bunăstare mintală durabilă și accesibilă pentru toți."*

*"In our journey towards mental health, research is the beacon that guides us through the turbulent waters of the human mind. Each discovery is an anchor of hope for those struggling with darkness." (Sigmund Freud). „In the depths of the human psyche, we discover both dark shadows and bright lights of understanding. Through continuous research and exploration, we free ourselves from the labyrinth of mental disorders and move towards light and healing. In the search for meaning and balance, we are redirected into the depths of our own minds, for each inner journey brings light into the darkness of mental disorders. To advance in understanding and treating these conditions, it is essential to actively engage in scientific research in the field of mental health, transforming how we approach these issues and promoting sustainable and accessible mental well-being for all."*

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## 1. ANOREXIA AND BULIMIA NERVOSA



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**Introduction:** Eating disorders, which are mentally debilitating, life-threatening, and financially burdensome conditions, significantly compromise physical well-being and disrupt psychosocial functionality. Current diagnostic systems acknowledge six primary feeding and eating disorders [DSM (Diagnostic and Statistical Manual of Mental Disorders)]: anorexia nervosa, bulimia nervosa, binge eating disorder, avoidant-restrictive food intake disorder, pica, and rumination disorder. The impact of eating disorders on physical health is profound, leading to adverse effects on the cardiovascular, gastrointestinal, and endocrine systems. Anorexia nervosa is a severe mental disorder marked by an intense fear of weight gain and distorted body image. Individuals exhibit extreme dietary restrictions, purging, or excessive physical activity, with a unique focus on weight and shape concerns. Bulimia nervosa can occur at a normal or elevated weight; Key features include recurrent binge eating, loss of control, and compensatory actions to prevent weight gain, such as self-induced vomiting. Actuality: Anorexia and bulimia nervosa pose a significant disease burden in Moldova, impacting women's ability to maintain a positive self-image, attain a fulfilling social status, and experience happiness.

**Aim of study.** The aim of this research is to assess the impact of social-determinants and family-related factors on the initiation of eating disorders.

**Materials and methods.** The study involves scrutinizing 20 patient records obtained from a psychiatric clinical hospital, conducting a clinical case study through semi-structured interviews, and reviewing international articles sourced from databases such as PubMed, Research Gate, ScienceDirect, and the Psychiatry Manual of the Department of Mental Health, Medical Psychology, and Psychotherapy at USMF.

**Conclusion.** Individuals with anorexia nervosa endure a deep-seated fear of weight gain, leading to stringent dietary restrictions, while those with bulimia nervosa grapple with recurring binge-eating episodes and subsequent compensatory behaviors. Effective treatment for both disorders requires a comprehensive approach addressing distorted thoughts, physical health, and psychosocial factors. Acknowledging the formidable societal pressures related to body weight is pivotal, as individuals often contend with societal expectations that can contribute to the genesis and perpetuation of these disorders. Early detection and intervention remain crucial, underscoring the significance of holistic approaches that consider the societal context and pressures surrounding body weight.

**Keywords.** Eating disorders, anorexia nervosa, bulimia nervosa, social determinism, family factors.





## 2. ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN ADULTS

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**Introduction.** ADHD, or Attention-Deficit/Hyperactivity Disorder, is a neurodevelopmental disorder that affects both children and adults. It is characterized by symptoms such as inattention, hyperactivity, and impulsivity.

**Aim of study.** ADHD (Attention-Deficit/Hyperactivity Disorder) can have a significant impact on daily life, affecting various aspects of an individual's functioning. Relationships personal and professional, Work Performance, the challenges associated with ADHD, such as impulsivity and difficulty with self-regulation, can lead to feelings of frustration, stress, and low self-esteem.

**Methods and materials.** I evaluated articles from the last 5 years published in electronic sources recognized by the international medical society as: PubMed / NCBI, APA, CDC.gov, CHADD, Cognitive Behavior Associates, NIHR, DSM -V.

**Results.** It is estimated that approximately 4-5% of adults worldwide have ADHD. Incidence in adults varies across different age groups. The highest incidence is observed in the age group of 25-44, with a rate of 4.4%. The 18-24 age group follows closely with an incidence rate of 4.2%. The incidence decreases in older age groups, with the 45-64 age group having a rate of 3.9% and the 65+ age group having the lowest p rate of 1.9%. Research has shown that individuals with ADHD are at an increased risk of developing various mental health conditions, including anxiety, depression, and substance abuse disorders.

**Conclusion.** ADHD is not just a childhood disorder, as it can persist into adulthood and have significant impacts on individuals daily functioning and quality of life. The increasing incidence of ADHD in adults highlights the need for more research and resources to support adults with ADHD. It is important to understand the challenges faced by individuals with ADHD in order to develop effective strategies for managing the condition and improving overall well-being.



### 3. AUTISM SPECTRUM DISORDER SCREENING IN PRIMARY CARE



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**Introduction.** Autism Spectrum Disorder (ASD) is characterized by a series of deficits that originate in the first two years of life, including deficits in verbalization, socialization, and stereotypical behavior. ASD screening is the process of assessing the risk of autism through a questionnaire or direct observation.

**Aim of study.** To identify and evaluate the importance of screening in the initial detection of ASD in primary care settings.

**Methods and materials.** Articles published in the last 5 years from the electronic databases: PubMed, MDPI, and Scopus were selected and reviewed using the keywords: autism, screening, M-CHAT, primary care.

**Results.** The literature review showed that screening in the primary healthcare setting of children aged between 16 and 30 months significantly increased the rate of ASD diagnosis, despite the absence of warning signs. The gold standard in ASD screening is M-CHAT. This tool has an increased sensitivity in detecting presumptive cases. Children who are screened and test positive are several times more likely to be diagnosed with ASD compared to those without screening.

**Conclusion.** ASD screening is an effective first-line triage of suspected cases, allowing for early detection and intervention in ASD with improved quality of life.



#### 4. BORDERLINE PERSONALITY DISORDER IN CHILDREN AND ADOLESCENTS

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**Introduction.** Borderline personality disorder is one of the most common psychiatric diseases worldwide. The clinical features of the disorder vary a lot depending on age, onset, gender, social status, and other comorbidities. The diagnosis is difficult itself at any point the patient addresses, but within children and adolescents, the diagnosis is even more troublesome due to the fact that it is often overseen as "misbehaving" or troublesome teenager behavior associated with hormonal change and social or educational environment. There are multiple theories concerning the cause of the disorder, including genetics (especially alteration of hormonal secretion and response delay) and the most important environmental background. Factors such as avoidant attachment styles of parenting, trauma, sexual abuse, rape, and violence are cumulative factors that may cause the onset of the disorder. The risk associated with the condition is very high, considering that the suicide rate in patients with borderline disorder varies between 4 and 10%. Diagnosis is crucial for youth considering that there might be social groups liable for the condition due to poverty and abuse.

**Aim of study.** The aim of the study is to spread awareness in both civil and academic environments about borderline disorders and to help differentiate a tantrum or a "phase" from an ongoing psychiatric disorder.

**Methods and materials.** The study is an academic review of literature found on various academic platforms using key words such as: "borderline disorder", "children", "adolescents", and "youth."

**Results.** The available data on the topic shows that the diagnosis of the disorder is shown to be reliable only for children aged 11 years. The epidemiology data available at the moment shows a total of 3% of teenagers in the general population suffering from the disorder. The criteria for the diagnosis is the presence of the following manifestations (mostly common) in a one-year period: self-destructive behavior (body damage, substance abuse, indulging in abusive relationships), altered self-image, unstable social relations and interactions, paranoid behavior, emptiness, emotional instability, and anger crises. The importance of an early and precised diagnosis is crucial, as the treatment requires time and effort. The most effective treatments nowadays are DBT (dialectical behavior therapy) and CBT (cognitive behavioral therapy), assisted some cases with second-generation antipsychotics.

**Conclusion.** Borderline personality disorder remains a problem in terms of diagnosis and prevention due to poor awareness and variable manifestations. Early detection and an adequate response to treatment are lifesaving instruments for the patients involved in self-harm and suicidal behavior. The only method that has proved to be effective is therapy, which should be started as soon as possible to give an adequate result.

## 5. DEPRESSION AND ANXIETY IN PATIENTS WITH EPILEPSY



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**Introduction.** Depressive, anxious and other mood disorders are factors that, along with epileptic seizures, complicate the course of epilepsy and prevent full recovery of patient health even when remission is achieved seizures and significantly impair social adaptation of patients suffering from epilepsy. That's why study and early diagnosis of these disorders will allow us to choose the right therapeutic tactics of prevention and treatment, will facilitate psychosocial rehabilitation of such patients and, as a result, will help patients there in optimizing their quality of life - study, employment, family, etc.

**Aim of study.** Mood disorders associated with epilepsy are very common and overrepresented compared with other chronic medical conditions. Depression is a particularly common and worrisome comorbidity, especially because suicidality seems to be increased significantly in the context of epilepsy. Depression and epilepsy may exacerbate each other.

**Methods and materials.** In this research 54 patients were included. All patients were investigated at the department of epileptology within the Institute of Emergency Medicine from Chişinău. All the patients were hospitalized due to the worsening of their illness . The tools of analysis used were clinical data of the patients and results from general questionnaires and special for depression screening PHQ-9 and TAG 9 questionnaires. Patients were divided into groups depending on the severity of the depression/anxiety level.

**Results.** In our study, depressive disorder was detected in 66% of those examined, and 55,6% of them were female. The most patients 41,5% detected with mild depression severity, 34% healthy patients, without depressive disorders, 24,5% moderate depression, 5,5% moderately severe depression. Anxiety was present almost constantly in 73.9% of cases. 57,4 detected with moderate anxiety and 16,5 detected with severe anxiety. The most common plot was the fear of a recurrence of a seizure - 73.8% of patients, and in 41.6% of cases - in female patients.

**Conclusion.** Mood disorders, and particularly depression, are commonly associated with epilepsy. Principles of modern epilepsy therapy consist not only in achieving remission of epileptic seizures, but also helping the patient to optimize his quality life. identification of presence of depression will, by itself, go a long way toward improvement of quality of life for persons with epilepsy and comorbid mood disorder. Ultimately, treatment of comorbid mood disorder has important implications for outcome and quality of life, perhaps even more than treatment of epilepsy itself.



## 6. DEPRESSION IN SCHIZOPHRENIA

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**Introduction.** Schizophrenia is a mental disorder with pronounced symptoms in the form of mental disturbances, difficulties in communication, emotional reactivity and difficulty perceiving reality. Depression is a mood disorder characterized by apathy, lowered mood and social withdrawal. The presence of Depressive symptoms in schizophrenia, their diagnostic significance is equated with positive and negative symptoms. The frequency of depression among patients with schizophrenia is quite high, which emphasizes the relevance of this problem.

**Aim of study.** Studying the peculiarities of depressive symptoms in schizophrenia.

**Methods and materials.** Study and analysis of the scientific literature. Was interviewed with patients diagnosed with schizophrenia at the IMSP Clinical Hospital of Psychiatrists using the Calgary scale.

**Results.** Depression is the third most common syndrome in schizophrenia and significantly complicates the prognosis and course of the illness. The incidence of depressive disorders in schizophrenia is around 40%, but these figures are influenced by the stage of the illness, which can vary considerably. Depression in schizophrenia may be associated with increased frequency of psychotic episodes, more severe course of the illness, substance use, reduced quality of life and suicidal behavior. Depression is common in patients with schizophrenia and thus has an association with higher rates of disability, treatment resistance, and suicide-related mortality. The presence of depressive symptoms in patients with schizophrenia is associated with suicide attempts 20 times more often, as well as longer disease duration.

**Conclusion.** The presence of depression in schizophrenia requires a very careful differentiated diagnosis, which will also affect therapeutic tactics. At the same time, depressive symptoms are often presented both during periods of remission and during periods of exacerbation of the disease, which can significantly complicate the choice of therapeutic approach.

## 7. DIAGNOSTIC CRITERIA OF SUICIDAL AND PARASUICIDAL BEHAVIOR



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**Introduction.** Suicide behavior represents a totality of behaviors from suicide attempt to completed suicide. While, parasuicidal behavior is characterized by “any non-fatal, serious, deliberate self-harm with or without suicide intent”. The diagnosis of this type of behavior is a complex and delicate process that involves careful evaluation of specific criteria, which is crucial for taking appropriate intervention measures.

**Aim of study.** To explore the criteria used in diagnosing these behaviors, early identification and intervention to prevent the risk of suicide.

**Methods and materials.** Was identified national and international scientific literature which studies causes, criteria, coping mechanisms and treatment methods of patients with suicidal and parasuicidal behavior.

**Results.** One of the essential criteria in the diagnosis of suicidal behavior is the presence of suicidal thoughts or intentions expressed by the individual - desire to die, detailed planning of a suicidal act, or direct expression of the intention to seriously harm oneself or commit suicide. Another important criterion is the presence of previous suicidal or parasuicidal behaviors - suicide attempts or intentional self-harm, while parasuicidal behaviors involve self-injurious actions that are not ultimately aimed at suicide. Next important parameter includes the presence of psychological or sociodemographic risk factors, such as mental health disorders, substance abuse, social isolation, chronic stress, or family history of suicide. Also, there are two scales that assess the risk of suicide. C-SSRS evaluates the suicidal risk, and rates it from “wish to be dead” to “active suicidal ideation either specific plan”. Other scale SLAP - for specificity of the suicide plan, lethality of the means, availability of the means, and proximity of rescuers.

**Conclusion.** The diagnosis of suicidal and parasuicidal behavior should be conducted in a sensitive and empathetic manner, taking into account the individual context of each person. It is essential to involve mental health professionals in the evaluation process and to provide emotional support and appropriate treatment to those at risk. The criteria for diagnosing suicidal and parasuicidal behavior involve evaluating suicidal thoughts and intentions, previous behaviors, risk factors, and individual context. Early identification and intervention can play a crucial role in preventing suicide-related tragedies and promoting mental health and individual well-being.





## 8. DIET AND DEPRESSION

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**Introduction.** Depression is a mental disorder which is characterized by losing pleasure, mood or interest in activities usually for a long period of time. According to the World Health Organization approximately 280 million people worldwide have depression. Emerging research suggests that diet plays a crucial role in mental health outcomes, particularly in relation to depression. The study focuses on exploring the impact of nutritional factors on depressive symptoms and identifying potential mechanisms underlying this association.

**Aim of study.** The aim of this study is to highlight the relation between diet and depression.

**Methods and materials.** A comprehensive literature review was conducted to identify relevant studies examining the relationship between diet and depression. Various electronic databases, including PubMed, PsycINFO, Scopus, 3MedScape, Elsevier were consulted for articles published between 2010 and 2023

**Results.** People with depression sometimes have a diet which is far from adequate, so their nutritional habits might contribute to their disease. Diets characterized by high consumption of fruits, vegetables, whole grains, legumes, and lean proteins, such as the Mediterranean diet, were consistently associated with a lower risk of depression. Conversely, diets high in processed foods, saturated fats, and added sugars were linked to an increased risk of depressive symptoms. Nutritional deficiencies, including omega-3 fatty acids, B vitamins, vitamin D, zinc, and magnesium, were also identified as potential contributors to depression. Furthermore, some studies suggest that low level of serotonin increase risk for suicide, because decreased levels of this neurotransmitter can contribute to a diminished sensitivity towards future consequences, thereby promoting risky, impulsive, and aggressive behaviors that can ultimately culminate in suicide—an extreme manifestation of impulsive aggression directed towards oneself.

**Conclusion.** Diet plays a significant role in the development and management of depression. Adopting a healthy dietary pattern, consisting of nutrient-dense foods, may have a protective effect against depression. Conversely, nutritional deficiencies and unhealthy dietary choices appear to be associated with an increased risk of depressive symptoms. Further research is needed to better understand the underlying mechanisms and to develop targeted dietary interventions for individuals with depression

## 9. DISSOCIATIVE IDENTITY DISORDER- ETIOLOGY, SYMPTOMS, TREATMENT



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**Introduction.** According to the DSM-5, Dissociative Identity Disorder (DID) is identified as the existence of two or more distinct identity states, causing abrupt changes in self-awareness. These distinct identities are recognized to vary in sensory awareness, perceptual tendencies, emotional tone, emotional regulation, memory processes, thinking patterns, and behavioral responses.

**Aim of study.** Gaining a thorough understanding and enhancing awareness about this disorder needs a comprehensive exploration of its etiological factors, clinical manifestations, and treatment options.

**Methods and materials.** To achieve the study's aim, PubMed and Google Scholar were utilized, the most relevant articles were selected. A total of 319 articles were found using the keywords „Dissociative identity disorder”.

**Results.** DID emerges as a defensive response to traumatic experiences, giving rise to multiple identities with distinct memory access. Childhood traumas disrupt the ongoing development of a cohesive self, resulting in a fragmented identity as a defense against emotional and physical pain. Additionally, media influences, such as movies, books, and therapists' expectations, contribute to its information. DID syndrome include various dissociative symptoms, including amnesia, conversion symptoms, voices, depersonalization, trance states, derealization, presence of other personalities, identity confusion, flashbacks, auditory and visual hallucinations, first rank Schneiderian symptoms, and experiences of somatic passivity. Notably, there are no evidence-based treatment guidelines for DID. However, the International Society for the Study of Trauma and Dissociation recommends psychodynamic psychotherapy, consisting of three phases: I- ensuring safety and stabilizing symptoms; II- focusing on trauma treatment; III- integrating identity.

**Conclusion.** DID is a disorder insufficiently researched, especially in the Republic of Moldova, with childhood trauma being a significant etiological factor. It manifests through various dissociative symptoms, emphasizing its complex nature. Currently, there is no specific treatment, but psychodynamic psychotherapy is recommended.



## 10. EATING DISORDERS AMONG MEDICAL STUDENTS

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**Introduction.** Eating disorders lead to multiple somatic and psychiatric complications, thus affecting the quality of life of the general population. According to data published by NEDA (national eating disorders association), the prevalence of eating disorders increased from 3.5% to 7.8% between 2000 and 2018. In a nationally representative study in the US, up to 23% of people with Binge Eating Disorder attempted suicide, and almost all (94%) reported mental health symptoms in their life: 70 % mood disorders, 68% substance use disorders, 59% anxiety disorders, 49% borderline personality disorder, and 32% posttraumatic stress disorder. A meta-analysis found that atypical anorexia nervosa (AN) occurs more frequently than anorexia nervosa in community samples, however, fewer people with AAN are referred or admitted to specialty care for eating disorders.

**Aim of study.** The purpose of the research is to identify the socio-determining factors in the appearance of the eating disorders among medical students, to study the incidence,

**Methods and materials.** In order to achieve the proposed goal, the specialized scientific publications were analyzed, and also using the databases Google Search, Google Scholar and PubMed aiming at the studied problem. The articles published during the years 2011-2021 were selected as a filter, so 8,060 articles were found that address the topic "Eating disorders", "Medical students".

**Results.** For nutritional disorders such as overweight, the prevalence among males (30%) had a net predominance ( $p < 0.001$ ) over females (4.4%), while for underweight, it was prevalent only for female students (20.3%). Overweight was associated with low academic performance (odds ratio (OR)=7.2; 95% confidence interval (95% CI): 1-53.94), smoking (OR=2.4; 95% CI: 1-5.76) and binge drinking (OR=3; 95% CI: 1.26-7.25). We found a negative correlation between the number of sleeping hours per night and personal alienation ( $r = -.271$ ,  $p = .015$ ). The more hours the students sleep per night, the lower they score on personal alienation. Students who snack during nights have lower scores on body dissatisfaction ( $M = 7.48$ ) compared to those who don't ( $M = 10.83$ ).

**Conclusion.** This study elucidated the importance of medical students' eating habits. The factors that lead to the appearance of ED are sleep, alcohol, diets, fast food, stress, smoking. The issue of adjusting study hours with lunch breaks and snacks must be put on the forefront by universities to ensure a healthy living environment for students. In the same way, the psychological counseling of these students is important.

**11. EDUCATIONAL INTEGRATION OF CHILDREN WITH ADHD****Author:** Mădălina Bivol

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**Introduction.** Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental condition characterized by a persistent pattern of inattention, hyperactivity, and impulsivity. Although prevalence estimates vary widely (between 5% and 10%), there is a global trend indicating a decrease in incidence. According to recent systematic reviews, the prevalence of ADHD is 7.2% in school-age children, with an overall male-to-female ratio of 2-3:1. It stands among the most common neurobehavioral disorders of childhood, significantly impacting academic success, well-being, and social interactions in children. ADHD tends to persist into adulthood, even though with variable rates throughout life, and is therefore identified by long-term negative consequences, including an increased risk of substance abuse and dependence, antisocial and criminal behavior, and significantly higher personal and economic adversity. The practical implications of these findings underscore the need for individualized approaches in delivering education and educational support.

**Aim of study.** The research topic on ADHD and the difficulty of school integration is important and relevant in the context of knowledge. In a continually evolving society where the educational process becomes increasingly diverse and demanding, the recognition and profound understanding of the impact of ADHD in the school environment become vital. This research focuses on identifying and understanding the mechanisms contributing to the school integration difficulties of children with ADHD and explores personalized educational strategies and interventions to enhance their educational and social experience.

**Methods and materials.** The synthesis of relevant studies and systematic reviews on the research topic was conducted using the bibliographic databases (PubMed and GoogleScholar) from the recent period, specifically the last 5 years. This process resulted in a comprehensive synthesis of existing data, providing an updated perspective on the current state of knowledge in the respective field. The search terms included "ADHD," "school integration," and "academic performance."

**Results.** Following the examination of existing data, we highlighted that children with ADHD face difficulties in their school integration process due to complex and interconnected reasons. Multiple studies suggest that children with ADHD may exhibit dysfunctions in executive functions of the brain, such as impulse control, information organization, and planning. Concentration and attention maintenance difficulties can interfere with students' ability to process information efficiently and engage in academic tasks. Due to impulsivity and hyperactivity, children may encounter challenges in maintaining attention during group activities or social games, contributing to the deterioration of relationships with peers and teachers. According to research, these social difficulties can contribute to isolation and stigmatization among classmates, fostering an insecure and stressful school environment and, as a result, potentially affecting the integration of children with ADHD into the school community. Frustration caused by learning difficulties and challenging social interactions can lead to anxiety and stress. Additionally, issues of emotional self-regulation may arise, including rapid mood changes or impulsive reactions in conflict situations. Adapting to the school environment thus becomes a significant challenge. Longitudinal studies indicate that the difficulty of adaptation, insufficient academic performance, and poor educational outcomes associated with ADHD persist, thereby increasing the risk of dropout, repeating a grade, and ultimately leading to relatively low graduation rates from high school and post-secondary studies.

**Conclusion.** ADHD extends beyond the aspects of inattention, hyperactivity, and impulsivity; it brings forth a range of interrelated challenges associated with significantly lower academic performance, dysfunctional social relationships, and overall difficulties in adapting to the school environment.





## 12. GENDER DYSPHORIA: UNDERSTANDING AND ASSESSMENT

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**Introduction.** Gender dysphoria represents a profound incongruence between an individual's experienced gender and their assigned sex at birth, impacting their mental health, social integration and overall well-being. Understanding gender dysphoria necessitates a departure from rigid binary constructs and embraces a more fluid and inclusive perspective of gender identity.

**Aim of study.** To challenge social stigmatization and discrimination through education, promoting acceptance and respect for diverse gender identities. To identify effective methods of support, including mental health interventions and social frameworks that affirm and aid individuals experiencing gender dysphoria.

**Methods and materials.** Empirical studies based on original data 34%, 555 articles, including qualitative studies, cohort studies, case control studies and clinical trials. Meta-ethnography approach conducted a structured analysis for synthesizing research about the phenomenology of gender dysphoria in transgender individuals.

**Results.** Studies consistently demonstrate the positive impact of social support and acceptance on the mental health outcomes of individuals with gender dysphoria. Research underscores the detrimental effects of societal stigmatization and discrimination on individuals with gender dysphoria, leading to increased mental health challenges and decreased quality of life.

**Conclusion.** Positive social support and acceptance play a main role in the well-being of individuals with gender dysphoria. Creating inclusive and affirming environments is crucial in reducing stigma and supporting individuals in their journey. The experiences of gender dysphoria are diverse and intersect with various aspects of identity, including race, culture, socioeconomic status. Understanding these interactions is vital in providing inclusive and culturally competent care.



### 13. GENERAL ASPECTS REGARDING STUDENTS' ANXIETY



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**Introduction.** Anxiety, as defined by the World Health Organization, is a disorder characterized by excessive fear and worry, manifesting through disturbances in mood, cognition, behavior, and physiological activity. Anxiety, a global concern, impacts medical students uniquely due to the demands of their academic and professional journey. With a global prevalence of 33,8% among medical students in February 2019, anxiety remains an underexplored topic compared to depression in current literature. The curriculum exposes students to diverse stressors, starting from admission to the university, including the intense study workload, personal expectations, professors' pursuit of excellence, limited leisure time and various other stress-inducing factors. So, anxiety in medical students can impact overall well-being, affecting academic performance, interpersonal relationships, and long-term mental health outcomes.

**Aim of study.** The aim of this research was to study anxiety among medical students.

**Methods and materials.** A total of 319 medical students participated in the study (159- second-year students and 160- sixth-year students), including 216 females and 103 males. Students anonymously completed the DASS-21 questionnaire during the months of October-November 2023. The DASS-21 comprises 21 items and assesses three parameters: depression, anxiety, and stress.

**Results.** According to the statistical analysis, we identified that out of the total number of second-year students (159), 52.85% (84 students) did not exhibit anxiety, while 47.15% (76 students) showed varying degrees of anxiety: low level - 20.12% (32 students); moderate level - 19.49% (31 students); severe level - 7.54% (12 students). In the sixth year, out of the total number of respondents (160 students), 68.76% (110 students) had no anxiety, but in 31.24% (50 students), different degrees of anxiety were detected: low level - 10.62% (17 students); moderate level - 18.75% (30 students); severe level - 1.85% (3 students). Comparing the results obtained by female subjects with those of male subjects, we observed statistically significant differences: out of 216 surveyed females, 48.61% (105 females) had anxiety, while 51.39% (111 females) did not. Of the 103 males, 19.41% (20 males) had anxiety, while 80.59% (83 males) did not have anxiety.

**Conclusion.** Following the statistical analysis, it was observed that anxiety levels are higher among second-year students compared to their sixth-year counterparts. Upon comparing gender differences, it is noted that females exhibit higher levels of anxiety than males.



## 14. GENERALIZED ANXIETY DISORDER – CONTEMPORARY INTERVENTION.

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**Introduction.** Anxiety disorders are the most commonly encountered type of psychiatric disorders. Many patients with anxiety disorders report physical symptoms related to anxiety and then seek primary healthcare provider consultations. The pathogenesis of anxiety disorders is multifactorial, involving complex interactions between biological factors, environmental influences, and psychological mechanisms. Despite the high prevalence rates of generalized anxiety disorder, it is often underdiagnosed.

**Aim of study.** To identify the level of generalized anxiety in individuals seeking primary healthcare for various somatic problems.

**Methods and materials.** Articles published between 2010 and 2023 were studied on platforms such as PubMed, Mendeley, and Google Scholar.

**Results.** Generalized Anxiety Disorder (GAD) involves repeated feelings of nervousness, intense worries related to real situations or events, accompanied by symptoms such as fatigue, difficulty concentrating, and/or sleep disturbances. These manifestations must persist for at least 6 months. One of the primary risk factors is gender, which plays a certain role in the onset and progression of generalized anxiety disorder, with women having a risk 1.5 to 2 times higher than men to receive a diagnosis of anxiety disorder. Another risk factor is age; GAD is more commonly found in individuals aged 18 to 65, but it often begins in young individuals around 30 years old. Among patients with moderate to severe anxiety, those employed predominated, indicating that occupational status is a risk factor for GAD due to environmental factors affecting mental health, such as tense social relationships in the professional environment, society, low social support, or poverty, unemployment, discrimination, and human rights violations. Another significant risk factor is comorbidities; cardiovascular conditions such as hypertension, cardiomyopathies; digestive conditions such as chronic gastritis, pancreatitis, chronic cholecystitis; and endocrine conditions such as diabetes and hypothyroidism prevail. Screening tools such as GAD-7 are used to diagnose this disorder, and other instruments assess the severity of symptoms. Cognitive-behavioral therapy and exposure therapy to anxiety-provoking factors prove to be effective in GAD from mild to moderate. Selective serotonin reuptake inhibitors are first-line treatments in more severe forms with a response rate of 30 to 50%.

**Conclusion.** Generalized anxiety disorder proves to be a health problem affecting daily life, also involving considerable medical costs. Without treatment, patients may experience other conditions such as depression, social phobia, and separation anxiety disorder.

## 15. HOW MENTAL RETARDATION AND AUTISM SYMPTOMS ARE MORE PRONOUNCED IN BOYS WITH FRAGILE X SYNDROME DUE TO LACK OF GENETIC COMPENSATION



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**Introduction.** Fragile X syndrome is a genetic disorder that is inherited through the X chromosome. It is caused by a mutation in the FMR1 gene, which is located on the X chromosome. When a male inherits an X chromosome with the mutated FMR1 gene, they do not have the genetic compensation that girls have. This lack of compensation makes them more severely affected by the X-linked inheritance of the mutation. The main reason is Absence of Genetic Compensation in Boys: Girls, who have two X chromosomes, have the ability to undergo genetic compensation. The normal X chromosome can partially compensate for the effects of the mutated one, which is inactivated or turned off in each cell. As a result, the impact of the FMR1 gene mutation is more pronounced in boys, leading to more severe intellectual and developmental disabilities. The FMR1 gene contains instructions for the creation of the Fragile X Mental Retardation Protein (FMRP), which plays a crucial role in the brain's synaptic function and plasticity. In individuals with Fragile X syndrome, the mutation causes a decrease or absence of FMRP production, which negatively impacts synaptic communication and contributes to cognitive impairments.

**Aim of study.** Symptoms of autism, including challenges in social interactions, communication, and repetitive behaviors, are intensified in males affected by Fragile X syndrome. The lack of genetic buffering mechanisms worsens these difficulties, resulting in a more pronounced display of autistic characteristics.

**Methods and materials.** Hessler D, Nguyen DV, Green C, et al. conducted a study in 2008 in 217 children with FXS (age 6–17 years, 83 girls and 134 boys).

**Results.** The absence or insufficiency of FMRP in boys has a greater impact on neurodevelopment, resulting in more severe intellectual challenges. Boys with Fragile X syndrome experience more profound effects on cognitive functions, learning, and adaptive behaviors compared to girls, such as limitations in object discrimination learning and reversal tasks, visual-working memory, verbal short-term memory

**Conclusion.** To sum up, the absence of genetic compensation in males diagnosed with Fragile X syndrome intensifies the severity of cognitive impairment and symptoms of autism. It is essential for healthcare professionals, educators, and families to grasp the complexities of X-linked inheritance and its impact on neurodevelopment. Several factors, including the type of mutation, genetic background, and environmental influences, can influence the variability observed in individuals. Early detection, intervention, and continuous assistance play a critical role in enabling individuals with Fragile X syndrome, irrespective of their gender, to achieve their highest capabilities.



## 16. LIGHT THERAPY FOR SEASONAL AFFECTIVE DISORDER (SAD): A META ANALYSIS OF EFFICACY

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**Introduction.** Affective Disorder is a growing concern in mental health, and this study explores the effectiveness of light therapy. This meta-analysis delves into the efficacy of light therapy as a treatment for SAD. The research illuminates the diverse facets of SAD and its response to light therapy.

**Aim of study.** This study explores dynamics of Seasonal Affective Disorder, emphasizing its connection with seasonal changes and the resulting psychological impact of depression. Going beyond conventional approaches, it aims to understand how light therapy alleviates associated depressive symptoms.

**Methods and materials.** The research is conducted from sources like Google Scholar and ScienceDirect. Inclusion criteria prioritize studies specifically focused on light therapy for SAD.

**Results.** To determine the efficacy of light therapy for Seasonal Affective Disorder, a meta-analysis of 19 trials' data was carried out by researchers. With a standardized mean difference for depression ratings of -0.37 and a risk ratio for treatment response of 1.42, bright light therapy appears to be superior to placebo. A study presented an innovative perspective by investigating exposure to outdoor light as a potential adjunct or alternative for traditional artificial light therapy for SAD. Interestingly, using strong placebo controls to compare white and green light treatments highlights the difficulties in distinguishing therapeutic benefits from placebos. Furthermore, a study concentrating on short-wavelength (blue) light treatment shows that it is more effective than dimmer red light for reducing major depressive disorder symptoms in a seasonal pattern. The meta-analysis contributes valuable insights to the evolving understanding of SAD treatment efficacy and highlights the need for larger, high-quality clinical trials to further substantiate these findings.

**Conclusion.** This meta-analysis underscores the significance of light therapy as a viable treatment for SAD, providing valuable insights into its efficacy. The examination of existing research enhances our understanding of the role light therapy plays in addressing the psychological aspects of SAD, paving the way for informed interventions and future studies in this domain.



## 17. MANAGEMENT OF GENERALIZED ANXIETY DISORDERS IN PRIMARY MEDICAL CARE



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**Introduction.** Nowadays, anxiety disorders are some of the most common disorders. A multitude of people around the world suffer from various forms of anxiety, like phobias, panic attacks, post-traumatic stress or generalized anxiety. The effects of these disorders on both physical health and professional functioning have been well documented. Epidemiological studies denote that the lifetime prevalence of GAD is estimated to be between 5.8% and 9%. In Moldova, GAD is underdiagnosed in primary care, often the somatic symptoms of anxiety are attributed to medical conditions that simulate anxiety (angina pectoris, hyperventilation syndrome, hyperthyroidism, etc.). Identifying the GAD is a priority especially when they are accompanied by somatic symptoms and influence the diagnostic decision and the established treatment.

**Aim of study.** Identifying the level of generalized anxiety in people who come to primary health care with various somatic problems.

**Methods and materials.** Methods and materials. In order to study this topic more deeply, I decided to carry out an analytical, observational study. I realized an anonymous screening , questionnaire to 123 patients in the Primary Medical Care service at the IMSP University Clinic of AMP of USMF, *Nicolae Testemitanu*, who went to the family doctor between December and January, 2023. The examination of patients began by completing a general questionnaire which assessed different aspects of the patients' lives. After that, they filled up the TAG-7 Questionnaire, Zung's anxiety self-assessment scale (SAS), Hamilton scale (HAM-A) and Global Assessment of Functioning scale (GAF).

**Results.** Patients were classified into 3 groups according to TAG-7: The first group of 53 patients (53%) with a score of 5-9 points, mild anxiety; The second group of 11 patients (11%) with a score of 10-14 moderate anxiety points; The third group of 1 patient (1%) with a score of 15-21 severe anxiety points; And the remaining 35 (35%) patients accumulated a score of 0-4 points, classifying themselves as healthy patients. The majority of patients with moderate-severe anxiety presented accusations when addressing the family doctor, such as pain, this having a diverse location (headache, chest pain, epigastric pain, in the region of the right hypochondrium), in 33.3% nausea was detected as a symptom, the most often accompanied by dizziness, in 33.3% of cases the patients presented digestive symptoms (vomiting, heartburn, feeling of fullness), symptoms such as weakness and asthenia were manifested in 16.6%, and restlessness and nervousness only in 8, 3%. Among the primary risk factors are: gender-women having a 1.5 to 2 times higher risk than men, age- more often it starts at  $\pm 30$  years old. Another important risk factors are comorbidities, we noticed that cardiovascular diseases, digestive and endocrine disorders prevail.

**Conclusion.** Following the study, we detected a high prevalence (65%) of GAD among patients who came to the AMP with various complaints, other than anxiety. At the AMP level, anxiety often coexists with somatic diseases in 39%, which make it difficult to identify and diagnose it. Thus, the family doctor is the first specialist who can identify GAD in time after the presence of characteristic somatic symptoms and can at the moment be involved in the evolution of TAG through different methods. He will start with the non-pharmacological interventions such as training, education, counseling of the patient, psychological interventions, psychotherapies, but in severe cases medical treatment will be indicated.





## 18. NEUROPSYCHIATRIC SYMPTOMS IN PARKINSON'S DISEASE

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**Introduction.** BP is a major medical problem. According to World Health Organization (WHO) data, the number of cases of Parkinson's disease is increasing. By 2030, the prevalence of Parkinson's disease will exceed 9 million worldwide, making it one of the most common neurological conditions with an increase in neuropsychiatric symptoms.

**Aim of study.** To identify neuropsychiatric symptoms in Parkinson's disease and assess the impact of mental disorders on quality of life.

**Methods and materials.** In order to select the required publications, we accessed and explored academic databases such as PubMed, Google Scholar, Science Direct, USMF "*Nicolae Testemitanu*" scientific channels to ensure a comprehensive coverage of the existing literature and consulted a wide range of sources including scientific articles, scholarly books and research reports.

**Results.** Parkinson's disease is considered a multisystemic neurodegenerative disease, with damage to various neurotransmitter systems and a wide range of motor and non-motor disorders (neuropsychological, sensory, vegetative). Neuropsychiatric symptoms are quite common in patients with Parkinson's disease: depression, apathy, anxiety, anhedonia, fatigue, cognitive impairment, memory deficit, dementia, hallucinations, delusions, delirium, behavioral changes. Autonomic nervous system dysfunctions affect about 70%-80% of patients with Parkinson's disease and cause significant discomfort, leading to a decrease in both the quality and length of patients' lives. Depression, anxiety and sleep disturbances can be early signs of the disease. Depression occurs in 20-50% of patients, which exceeds the frequency of this disorder in the population and in other chronic diseases. Depression is the factor most closely associated with patients' poor quality of life indicators. Anxiety contributes to mental and somatic discomfort, as well as worsening existing motor symptoms. Patients will report that anxiety worsens pre-existing tremor or dyskinesia, and fear of falling has been associated with impaired postural stability. Apathy is characterized by a lack of motivation, interest or desire to engage in activities or events that previously would have been considered important or enjoyable. Cognitive impairments, memory deficits, dementia, psychotic episodes negatively influence the quality of life and daily functioning of patients with Parkinson's disease.

**Conclusion.** Neuropsychiatric manifestations play a major role in the quality of life of these patients. As pathology progresses, quality of life decreases. Because many of the motor, non-motor and psychiatric problems are interconnected, their optimal management requires coordination between those providing neurological, psychiatric care, family support and social services.

## 19. PSYCHOTRAUMA IN CORRELATION WITH DEPRESSION.



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**Introduction.** The XXI century is a century of dynamic events. Constant technical evolution, fast pace of life, fierce competition leads to physical and mental exhaustion, which subsequently forms psychotrauma, which in turn correlates with mental illnesses, mainly depressive and anxiety disorders.

**Aim of study.** The role of psychological trauma in patients with depressive disorder.

**Methods and materials.** Information was collected and analyzed in the electronic databases PubMed, Hinari, elsevier, e-library, cyberleninka. All sources over the past 10 years have been analyzed.

**Results.** As a result of international research over the past decade, it has been found that more than 50% of the general population has been subjected to psychological trauma, which, depending on the type of temperament and gender, led to a depressive disorder. It has been proven that the diagnosis of "depression" is established in female gender 2 times more often than in male. Analyzing temperament, studies have shown that the sanguine-choleric type is most often subjected to such trauma as the "loss of a loved one", while melancholics – to the "loss of former material stability and well-being". A correlation was also made between the genesis of depression and the threat of loss of social status for an uncertain or generally mixed type.

**Conclusion.** In each of these studies, it was found that depressive disorder is one of the most common conditions resulting from exposure to various psychotrauma. To date, there is a need for a more detailed study of traumatic events and their subsequent impact on the development of depression, depending on the age and experience of the person, the type of traumatic event, the degree of traumatic influence and individual psychological characteristics. This requires an in-depth study of the problem of psychotrauma in correlation with depression.



## 20. RETROSPECTIVE STUDY OF BORDERLINE PERSONALITY DISORDER DIAGNOSED AND HOSPITALIZED IN CLINICAL HOSPITAL OF PSYCHIATRY

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**Introduction.** Over the past five years, there has been a marked escalation in the incidence of borderline personality disorder (BPD) cases within the Republic of Moldova. The clinical landscape of BPD is characterized by intricate states exhibiting a polymorphic array of symptoms and signs, thereby giving rise to the potential for misdiagnosis or delays in both diagnosis and subsequent treatment. Hospitalization is reserved for instances manifesting delirious or suicidal behaviors.

**Aim of study.** The present study aims to document the experience of a single center (Clinical Hospital of Psychiatry) with patients diagnosed with BPD. Medical records were reviewed to determine baseline characteristics, patterns, clinical features, treatment and evolution of patients diagnosed with BPD.

**Methods and materials.** 28 patients with BPD diagnosed and/or treated in Clinical Hospital of Psychiatry between 2017-2023 were reviewed retrospectively using the data from Hospital Nursing Information System (SIAMS).

**Results.** Among the reviewed patients, 53% were female and 47% were male, within the age range of 17 to 50 years. A demographic breakdown revealed that 53% were from urban areas, while 47% from rural areas. 25% exhibited an exacerbated hereditary history marked by parental alcoholism. A comprehensive assessment indicated that all patients diagnosed with BPD had a history of suicidal attempts and self-harm. 15% presented comorbid eating disorders, and 4% grappling with a sexual identity disorder. 15% reported instances of bullying during their academic years. 53% had a history of alcohol and drug misuse. 10% disclosed a history of sexual abuse, and an equal proportion acknowledged maternal abandonment. 35% had a background of familial divorce. In terms of therapeutic interventions, all subjects underwent treatment following: one or two antipsychotic drugs, an antidepressant, a thymostabilizing agent and one benzodiazepine. Subsequent hospitalizations revealed the emergence of symptoms indicative of either bipolar disorder or schizotypal disorder.

**Conclusion.** Patients with BPD exhibit a diminished likelihood of hospitalization due to misdiagnosis or a high susceptibility to suicide. There is suggestive evidence that genetic predisposition and adverse life events contribute to BPD manifestation. Factors such as elevated rates of divorce, parental abandonment, bullying, and sexual abuse could be etiologic factors of BPD. The availability of inexpensive drugs and alcohol in society determines the comorbid substance abuse. Patients with BPD frequently contend with eating disorders. Suicidal attempts and self-mutilation emerged as recurrent patterns found in all reviewed cases. Due to lack of BPD management protocol, prescribed medications are commonly taken in overdose. Thus, further research is needed on the diagnosis, neurobiology, and treatment methodologies.

## 21. RISK FACTORS FOR DEMENTIA IN ALZHEIMER'S DISEASE



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**Introduction.** Alzheimer's disease is a progressive disorder that triggers brain regression and cell death in the cerebral cortex. Dementia in Alzheimer's disease presents one of the most widespread causes, making up about 50-60% of the total types of dementia. The incidence clinically diagnosed and reported in research ranges from 2.0 to 16.8 new cases of Alzheimer's disease per 1000 people for Europe, USA, China, Japan, and according to the World Health Organization, dementia has been declared a priority health problem.

**Aim of study.** Study of risk factors in the onset of dementia in Alzheimer's disease and their evaluation in the early development of the disease.

**Methods and materials.** The bibliographic analysis was carried out by synthesizing the international publications from the specialized literature, using the databases PubMed, Google Academic, Medline, the ResearchGATE network, MedScape.

**Results.** Age is the main risk factor, with the risk doubling every 5 years after age 65. Both genetic and environmental factors contribute to the phenomenon of family aggregation. In addition, some studies suggest that familial aggregation of Alzheimer's disease may be explained by genetic components such as the E4 allele, apolipoprotein E, being the only established genetic factor for dementia in both early-onset and late-onset Alzheimer's disease. Evidence indicates that immune cells of the monocyte family reach the central nervous system and can effectively clear beta amyloid from the brain. Various analyzes have progressively reported an increased risk of Alzheimer's dementia in association with vascular and metabolic diseases such as hypertension, hypercholesterolemia, obesity, diabetes and atherosclerosis. To the same extent, the impact of chronic bacterial infections in Alzheimer's disease was revealed. For example, syphilitic dementia caused by the spirochete-treponema pallidum bacteria, which accumulates in the cerebral cortex, produced neurofibrillary tangle-like lesions that led to devastating neurodegenerative disorders. In addition, the bacterium Chlamydia pneumonia can trigger dementia in late-onset Alzheimer's disease by activating astrocytes and cytotoxic microglia, disrupting calcium regulation and apoptosis, leading to impaired cognitive function and increasing its risk.

**Conclusion.** The consequences of dementia are varied: a decline in cognitive and behavioral abilities, which in turn makes it impossible for a person to function autonomously while performing certain tasks and living in the environment, which is also a problem for collective health, and cognition of risk factors allows early detection of the disease with reduced complications and provides a more favorable prognosis with an improved quality of life.





## 22. RISK FACTORS FOR VASCULAR DEMENTIA

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**Introduction.** Vascular dementia is a neurodegenerative disorder that occurs due to cerebrovascular disease and hypoperfusion. This can range from large vessel stroke to microvascular disease. The symptoms and presentation can be heterogeneous, depending on the extent of vascular lesions and the anatomical location. Lesions can be limited to a single site, multifocal, or diffusely distributed.

**Aim of study.** Updated information was analyzed to quantify the impact and importance of the risk factors of vascular dementia in order to demonstrate their influence in the prevention and management of the patients with vascular dementia.

**Methods and materials.** A synthesis analysis of international publications and specialized literature was performed using PubMed, Google Academic, Medline, ResearchGATE network, databases published during 2016-2022. With the usage of keywords dementia,vascular dementia, risk factors, stroke, hypertension.

**Results.** Through this study, it was highlighted that vascular dementia can be caused by small-vessel disease or by large-artery atherosclerosis with vascular lesions in strategic areas of the brain. In both cases changes in white matter are observed. Vascular factors like hypertension, stroke, diabetes, coronary artery disease, atrial fibrillation and atherosclerosis may increase the risk for vascular dementia by promoting inflammation, cerebral vascular disease, white matter lesions, and hippocampal sclerosis. It has been shown that depression, mutations in the APOE gene, use of saturated fatty acids, urban living, and lack of exercise were associated with independent risk of vascular dementia. Of biochemical risk factors, hyperhomocysteinemia (associated with low levels of folic acid and vitamin B 12), hyperlipidemia and low HDL cholesterol levels were found in both forms of vascular dementia. Some researches have argued that advanced age-the strongest risk factor for brain degeneration, male sex, smoking ,sleep apnea syndrome, pre-eclampsia history and migraine also increase the risk of developing vascular dementia.

**Conclusion.** Analyzing data from medical literature, I can conclude that reducing these two major, but modifiable risk factors-hypertension and stroke-could be a successful strategy for reducing the public health burden of cognitive impairment and vascular dementia. Lifestyle measures that maintain or improve vascular health including consumption of healthy diets, moderate use of alcohol and implementing regular physical exercise in general appear effective for reducing vascular dementia risk



### 23. SIDE EFFECTS OF BENZODIAZEPINE USE



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**Introduction.** BZDs are a class of psychoactive drugs known for their depressing effect on the central nervous system (CNS). Given the continuous increase in anxiety and sleep disorders over decades, BZDs remain the most prescribed class of drugs in the world. However, with this continued, widespread use comes the dark reality of BZD addiction and many side effects. This is worrying and requires attention.

**Aim of study.** It is to review the indications, the duration of treatment, to expose the adverse effects to long-term administration.

**Methods and materials.** We reviewed articles published in the last 10 years in Pubmed, Google Scholar, and specialized psychiatric books to gain a better understanding of what are the indications, and what are the side effects of long-term treatment.

**Results.** BZDs have significant side effects. According to several studies, the use of BZD increases with age, with long-term use being most prevalent in the 65-year-old and older population. Passaro et al. described an increased risk of falls in elderly hospital patients who were prescribed short-acting BZD. Many studies have examined the effects of benzodiazepines on cognition leading to psychomotor retardation, amnesia, and increased forgetfulness. Discontinuation after long-term use (more than two weeks) has even shown some people inability to return to the cognitive baseline. It has been associated with an increased risk of dementia. Long-term use of BZD leads to negative changes in the microstructure of sleep in patients with insomnia. Regular use of BZD has been shown to be addictive. Symptoms of withdrawal should be treated carefully with prolonged-acting BZD, with doses decreasing slowly over time.

**Conclusion.** BZDs are effective in improving the conditions indicated above. However, due to the severe potential for addiction and adverse effects, the guidelines for the recommended use do not exceed 2-4 weeks.



## 24. SUBSTANCE USE DISORDER IN INDIVIDUALS WITH SCHIZOPHRENIA

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**Introduction.** Schizophrenia can be defined as a mental disorder that affects a person's thoughts, actions, expression of the emotions, perception of reality, and relations with other people. Schizophrenia is one of the top 15 leading causes of disability. The World Health Organization (WHO) reports that worldwide, one out of every 300 individuals is affected by this disorder, and its prevalence on a global scale varies between 0.3-0.7%. The critical age of onset and behavioral manifestation for schizophrenia occurs at the end of adolescence or early adulthood, and it is notably lower in substance users compared to patients without any form of abuse. Drug consumption among patients with schizophrenia varies, but cannabis, alcohol and cocaine remain among the most commonly used substances, significantly impacting symptoms and disease management.

**Aim of study.** Schizophrenia and substance abuse commonly share overlapping risk factors, including genetic predisposition, environmental influences, and neurobiological vulnerability, contributing to their heightened co-occurrence. Their association is correlated with a higher frequency of relapses, extensive manifestations of positive symptoms, depression, cognitive impairments, less favorable outcomes, and ineffective responses to treatment. It is also notable that the age of onset for schizophrenia is significantly lower in drug users compared to patients without a history of abuse. The remarkable association between schizophrenia and substance abuse, especially among patients experiencing their first episode of the illness, is a significant and intriguing aspect in mental health research. Employing dual therapy, which integrates interventions addressing both mental health and substance dependency, is frequently crucial for ensuring a holistic and efficacious approach.

**Methods and materials.** An advanced search was performed in the PubMed and Medline databases, taking into account relevant articles, published in the last 10 years. We used the following keywords and word combinations to search for: "Substance abuse", "schizophrenia", "Substance use disorders".

**Results.** According to existing data in the specialized literature, the prevalence of substance use disorders (SUD) in individuals with schizophrenia is estimated to be between 20% and 65%, with variations across different studies. Patients with schizophrenia have a significantly higher risk of experiencing SUD compared to the general population. The relationship between SUD and schizophrenia is explained by four hypotheses, including the self-medication hypothesis, common vulnerability hypothesis, the theory of dysregulated dopaminergic reward system and the hypothesis of treatment side effects. However, the exact directionality of the relationship between substance use and schizophrenia remains unclear. Multiple studies suggest a high prevalence, approximately 35%, of substance abuse in the first episode of schizophrenia. The most commonly abused substances in schizophrenic patients were cannabis, followed by alcohol. Scientific research appears to indicate that a younger age of onset in the abuser group, male gender, lower education level, and the use of psychostimulants are factors associated with the onset of schizophrenia at an early stage of life, leading to a higher risk of dependence, increased severity of psychotic symptoms, and ultimately, a variety of poorer outcomes.

**Conclusion.** In conclusion, the intricate relationship between schizophrenia and substance abuse, particularly in the context of the first episode, underscores the need for a comprehensive understanding and integrated therapeutic approaches.

## 25. THE IMPORTANCE OF EARLY DIAGNOSIS IN AUTISM SPECTRUM DISORDERS



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**Introduction.** Autism Spectrum Disorders (ASD) are a group of developmental disabilities that can cause social, communication and behavioral impairments. Around 75 million people have autism spectrum disorder, that's 1% of the world's population. Centers for Disease Control and Prevention (CDC) finds that ASD affect an average of 1 to 36 children. 1 to 25 boys and 1 to 100 girls, report M:F- 3:1. CDC showed that 6,7 % of people with ASD have profound autism.

**Aim of study.** There are several types of autism, which are characterized by different manifestations, can affect each person differently and can vary in intensity. It is important to diagnose as early as possible, because the earlier the intervention is done, the higher the chances of the child to recover. Most children were diagnosed after age 4, although autism can be diagnosed by age 2. Through therapy, the child learns, in a structured way, how to speak, how to behave, how to be independent.

**Methods and materials.** Retrospective analysis of new data according to the CDC. Study and analysis of scientific literature. Quantitative and qualitative processing of results.

**Results.** By means of MRI it was highlighted : hyperexpansion of the cortex surface (between 6 and 12 months) and an increase in brain volume (between 12 and 24 months) in children subsequently diagnosed with ASD, a greater number of circumvolutions and anomalies in the white matter of the corpus callosum. It was found that the changes that occurred in the brain coincided with the period of the beginning of the installation of autistic behavior.

**Conclusion.** The maximum period of development of the human brain is approximately between the ages of 0 to 3 years. Early intervention for ASD is important because proper therapy can reduce difficulties while helping them learn new skills and make the most of their strengths. During this period, the effectiveness of treatment with the help of behavioral interventions is three times higher, the signs specific to the disorder are significantly reduced.



## 26. THE MAIN RISK FACTORS IN VASCULAR DEMENTIA

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**Introduction.** Worldwide, approximately 47 million people are living with a diagnosis of dementia. By the year 2050, this figure will increase approximately 3 times, the number being 134 million people. Vascular dementia is the second most common type of neurocognitive impairment after Alzheimer's dementia. Vascular dementia accounts for approximately 20% of all dementia cases. Certain risk factors can increase a person's chances of developing vascular dementia; avoiding and controlling these are the basic principles in dementia prevention.

**Aim of study.** The aim of our study is a literature review on the importance of risk factors in vascular dementia.

**Methods and materials.** A bibliographic study of scientific literature specialized at vascular dementia. Were used scientific publications and articles from the PubMed, Medscape, and database published during 2018-2023.

**Results.** Data from the scientific literature show the existence of many types of risk factors in vascular dementia. Some of the most important and common risk factors are strokes. Another significant factor that increases the risk of vascular dementia is the advanced age of the patient. After 65 years, there is a major risk of disease progression. Cerebral atherosclerosis is equally important as a risk factor; cholesterol deposits in vascular walls alter muscle elasticity and tone. Another factor is hypertension, which produces a defective regulation of cerebral flow. High blood glucose in diabetes increases the risk of stroke. Smoking actively participates in the breakdown of blood vessels. Obesity is the main cardiovascular risk, leading to vascular dementia. Atrial fibrillation promotes the formation of blood clots in the heart.

**Conclusion.** The influence of risk factors in vascular dementia is extremely important in the evolution of the disease. Their avoidance and control can enhance the patient's quality of life.

## 27. THE PLACEBO EFFECT IN THE TREATMENT OF MENTAL DISORDERS



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**Introduction.** In the modern world, there are high placebo response rates in various diseases, in particular in the field of psychiatry. Accordingly, there is an increasing demand from medical professionals for the development of new expert recommendations on the scientifically sound and ethical use of placebos in clinical practice.

**Aim of study.** a comparative study of the placebo effect in the treatment of mental disorders.

**Methods and materials.** Information was collected and analyzed in the electronic databases PubMed, Hinari, elsevier, e-library, cyberleninka. All sources over the past 10 years have been analyzed.

**Results.** The magnitude of the placebo effect varies depending on the psychological susceptibility of the participant and the type of mental disorder. There have been studies that have caused considerable resonance in the field of science, since the placebo effect was so pronounced that it formed the opinion that it should be used independently in the treatment of depressed patients with mild to moderate depression. In some studies, the response rate to placebo was almost as high as to antidepressants administration.

**Conclusion.** In a comparative analysis of the placebo effect in schizophrenia, BPD and BDR, we conclude that the use of the placebo effect is more appropriate for mood disorders than for schizophrenia. Despite the fact that the placebo effect remains an intriguing and widely studied topic, it requires more detailed consideration in the field of mental disorders in order to modernize treatment methods.





## 28. THERAPEUTIC INTERVENTIONS IN HYPOCHONDRIA

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**Introduction.** The prevalence of hypochondria in the society isn't well elucidated. AMP data assumes between 0.8 - 4.5%, covers a percentage considerable for a study based on treatment of the poorly elucidated condition. Hypochondria: a concern of having a serious illness based on a misinterpretation of symptoms, which complicates diagnosis and treatment. Marked depression and anxiety, often present, justifies additional diagnoses.

**Aim of study.** Hypochondriasis, also sometimes referred to as health anxiety, is much more common in general health wards than previously accounted for. Thus, an efficient way of its management needs to be formulated and this review article helps to shed light on the current treatment protocol available for hypochondriasis and their efficacy for the same.

**Methods and materials.** The study was based on speciality literature review, articles from electronic sources recognized by the international medical society: PubMed, NEJM, NCBI, and manuals (OxfordMedicine, Kaplan), national guidelines (MSMPS) and WHO.

**Results.** Despite technical advances, physicians still rely on development of the most individual approach for patients. Psychological therapies, especially CBT, being more effective in alleviating symptoms. Psychoanalytic therapy, which touches underlying problems of object relations and individual drives, etiological aspects. Drugs' role is limited by symptomatic effect. Efforts to improve treatment outcomes, transform hypochondria from a pathology that therapists avoid into a challenging but treatable disorder.

**Conclusion.** During analysis of bibliographic sources, study confronted an obstacle of deviating visions of DSM V and ICD 10, regarding the presence of hypochondria as a single entity and not as a grouping of conditions: somatic symptom disorder and nosophobic disorder. The literature lacks variability in psychotherapeutic treatment, denying the effectiveness of other methods, like hypnosis, autogenic training, etc. Anglo-Saxon or French literature is based on psychoanalysis, duration of which for years is significant, and medicinal corrections, such as the inclusion of SSRIs/SNRIs, neuroleptics in the list of preparations.

## 29. VIDEO GAMES IN PSYCHOSOCIAL REHABILITATION FOR SCHIZOPHRENIA PATIENTS



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**Introduction.** Schizophrenia is a lifelong and vigorously disabling condition, described by mental decline, positive and negative symptoms. While antipsychotic drugs and psycho-social interventions have shown efficacy in treating positive symptoms, negative symptoms and cognitive deficits often present ongoing challenges. Cognitive remediation therapies, specifically designed to address cognitive deficits in schizophrenia, have been proposed and found effective. Recent MRI studies indicate that commercial video games can induce changes in brain areas similar to those targeted by specialized training programs. The potential increase in gray matter and functional brain modulations, if translated into improved cognitive and everyday functioning, could make video game training an enjoyable and economically feasible treatment option for individuals with neuropsychiatric disorders. Nowadays video games, including virtual reality, are being explored as therapeutic tools for cognitive and social impairment in schizophrenia.

**Aim of study.** Schizophrenia, a chronic and severe mental disorder, poses unique challenges to both individuals diagnosed with the condition and the healthcare professionals tasked with their treatment. Traditional approaches to schizophrenia rehabilitation often involve a combination of medication, psychotherapy, and social support. However, as we delve into the 21st century, the intersection of technology and mental health is giving rise to innovative methods, with video games emerging as a promising tool in the rehabilitation of patients with schizophrenia.

**Methods and materials.** In a review of studies conducted between 2018 and 2023, the benefits of video games for individuals with schizophrenia and related disorders were examined.

**Results.** Active engagement with video games is associated with enhanced aerobic fitness and cognitive performance, potentially leading to improved functional outcomes and quality of life for individuals facing cognitive impairments and social challenges. Therapeutic software, designed for specific therapeutic goals in psychosocial rehabilitation, has demonstrated positive impacts on residual symptomatology, cognitive remediation, social skills, and everyday life activities in individuals with schizophrenia.

**Conclusion.** Thus, while computer-assisted therapy, video games, and virtual reality show promise as adjunctive therapies, their recommendation in the field of psychiatry, particularly for individuals with schizophrenia, remains premature due to the recent and preliminary nature of most studies. However, the evidence quality is low, and more data are required to establish the comparative effectiveness of cognitive approaches and traditional video games in schizophrenia treatment.



### 30. VIRTUAL REALITY IN PSYCHIATRY

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**Introduction.** Virtual reality (VR) is a computer simulation, a collection of images and sounds that form a real place or situation with which a person can interact using special electronic equipment. It allows to create therapeutically beneficial scenarios that are almost impossible to recreate in real life. These simulations give patients the confidence to deal with similar problems in real life. VR is gaining popularity as a promising tool for treating mental illness.

**Aim of study.** The purpose of the study is to analyze current information about the effectiveness of VR therapy in patients with mental disorders and identify areas of greatest effectiveness.

**Methods and materials.** Scientific articles from the PubMed and Google Scholar databases published during 2019-2023 were used.

**Results.** Several meta-analyses have reported the effectiveness of VR interventions in the treatment of various anxiety disorders and phobias (acrophobia, flying phobia, insect or animal phobia). On the contrary, the results obtained in the treatment of social phobia are still controversial and require further study. A meta-analysis of VR therapy for patients with PTSD reported significant reductions in PTSD and depressive symptoms after treatment. The effect of treatment lasted for 3–6 months. A meta-analysis of the treatment of compulsive overeating disorder showed that VR therapy leads to a change in a person's body image, increased self-esteem, and a decrease in compulsive overeating. These therapeutic effects lasted for about a year. A meta-analysis including only 6 studies found that applying VR to depressed patients can reduce the severity of their depression. Four studies examined different forms of VR in people with psychosis and schizophrenia. There is no clear evidence for or against using VR to encourage people with schizophrenia to take their medications.

**Conclusion.** Numerous studies provide evidence supporting the beneficial effects of VR therapy for several mental disorders. It is necessary to test how effective and safe VR therapy is compared to traditional treatment, and to establish the parameters of VR treatment that would be optimal for functional improvement in real life, and to identify the elements necessary for treatment. The problem with the availability of this type of therapy has remained relevant, mainly due to the high cost of developing a new clinical VR application and expensive technical support.

**Keywords.** Virtual reality, Mental health, Psychiatry, Meta-analysis.

### 31. WAR AND MENTAL HEALTH



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**Introduction.** The world's rhythm abruptly changed in 2022, opening the door to increasingly violent events. Conflicts between two powers, or WAR, inevitably cause hardship for the average person. This entails forcing two or more people to endure severe stress and suffering, which may finally result in post-traumatic stress disorder (PTSD). These were present dating back from the ancient wars, but they have been studied only recently. A war may finish on a global scale, but the internal conflict of those who fought in it or who survived it never ends.

**Aim of study.** To analyze the psychological consequences of wartime on individuals and to investigate their after-conflict lives, encompassing their interactions with partners, children, and society broadly.

**Methods and materials.** The book War and Public Health was looked at as a scholarly paper and publication within Google Scholar. This review focuses on Chapter 4 of Evan D. Kanter's manuscript, The Impact of War on Mental Health.

**Results.** Psychological conditions are the concealed scars of conflict. A neurological system injury that can be quite crippling is PTSD. Taking responsibility for individuals with PTSD implies a substantial budgetary cost, and it has detrimental impacts on communities and families as well. The tremendous impact it has on human civilization might persist for generations. Throughout the past three decades, there has been an enormous progress in our understanding of the psychological trauma of war. A certain amount of the negative impact will be alleviated by additional endeavors aimed at improving the identification and management of PTSD and other trauma-related conditions. The challenging task of providing significant intervention in war-torn societies in nations that are developing represents a challenge that is only recently beginning to be tackled. The prevention of war is, in the end, the intervention offering the greatest potential rewards.

**Conclusion.** In accordance with investigations published to this point, PTSD has been connected to enhanced concentrations of androgens and catecholamines in the Cerebrospinal as well as alterations in the amygdala that influence threat perception and provoke hyperreactivity. These astounding findings have resulted in the administration of anticonvulsants as valproic acid, which suppresses amygdala activity, as well as antiadrenergic medication, especially those that block alpha 1 receptors, as PTSD therapeutics. Drugs that cause sleep are also used, except that they solely relieve the symptoms and fail to recognize the root cause. PTSD along with additional psychological problems associated with warfare thus can be effectively addressed.



## **XXI. PUBLIC HEALTH SECTION**

***„În toate timpurile, sănătatea, tinerețea, dragostea și mintea au fost cele mai mari comori ale civilizațiilor. Este imperios necesar să le păstrăm, să le îngrijim și să luptăm pentru ele zilnic!”***

***"In all times, health, youth, love, and mind have been the greatest treasures of civilizations. It is imperative to preserve them, take care of them, and fight for them daily!"***

***Ion Băhnărel,***

*Professor, MD, PhD,*

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## 1. AN IN-DEPTH ANALYSIS OF ADOLESCENT BULLYING PATTERN IN SCHOOLS ENVIRONMENT OF THE REPUBLIC OF MOLDOVA



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**Introduction.** Throughout time, the term “bullying” has evolved, its root originating from the English word “bully”, which initially had a positive meaning, describing a pleasant, beloved person. Nevertheless, the term has taken on an increasingly ominous meaning, frequently “bullying” expresses acts of intimidation and terror. This shift in meaning has become prevalent globally, particularly in schools. Furthermore, the phenomenon of bullying in schools is commonly encountered in the Republic of Moldova, yet its particularities are less studied.

**Aim of study.** To explore the phenomenon of bullying patterns in the school environment among children and identifying potential consequences.

**Methods and materials.** A specialized search was conducted within the main reports, guides, and programs published by the Ministry of Education and Research of Moldova and UNICEF for the last 5 years. The keywords used were: bullying, children, school environment. The reported results were compiled in narrative form.

**Results.** Following reviewing the specialized literature sources, it becomes apparent that globally, half of pupils aged 13-15 faced different types of violence within the school environment. Statistics indicate that one in three children worldwide becomes a target of bullying on a monthly basis. A closer look at the situation in the Republic of Moldova during the 2022-2023 school year reveals alarming figures. In the first semester, there were reported cases of violence, including 1540 instances of physical violence, 988 cases of psychological violence, and 16 cases of sexual violence. Notably, there was a significant increase during the subsequent semester, with 1778 cases of physical violence, 974 cases of psychological violence, and 22 cases of sexual violence. In the context of bullying, a comprehensive research study highlighted that a staggering 86.8% of pupils in grades of 6 to 12 in the Republic of Moldova experience bullying. This translates to a troubling reality where any given school day, 8 out of 10 children aged 12-18 grapple with the detrimental effects of bullying. Manifestly, pupils subjected to various forms of bullying are especially prone to diverse emotional challenges, anxiety disorders, depression, eating disorders, self-harming tendencies, and distressingly, may even be at risk of suicide.

**Conclusion.** Bullying in the Republic of Moldova is often disregarded, yet its impacts are profound, irreversible, and at times fatal. In most instances, both aggressors and victims are identified within the school environment. It is crucial to underline existing methods promoting safety and well-being of children and update prevention through new research.



## 2. ASSESSMENT OF PARENTS' KNOWLEDGE OF THE USE OF CHILD RESTRAINT SYSTEMS

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**Introduction.** Currently, the number of traffic injuries among children has increased considerably in recent years, due to the increase in transport units and the incorrect use of safety systems for people under 12 years old.

**Aim of study.** The purpose of the study is to evaluate parents' knowledge regarding the use of safety systems among children to prevent road injuries.

**Methods and materials.** An observational study was conducted on the use of road safety systems among children in the Republic of Moldova, in 2022. 288 driver-parents and 356 children participated in the study. The data were collected by applying a questionnaire with 22 questions among the parents who brought or took their children from the early education institutions. 30 institutions were included in the study. Data collection was done in the morning (7.00-9.00) when the children were brought and, in the evening, (16.00-19.00) when the children were picked up.

**Results.** Seat belts were used by 148 (51.38 %) of 288 parent drivers. Of the 356 child passengers observed, 62.5% were properly restrained, 20.5% were seated in inappropriate child restraint systems, and 16.6% of the children were not using any restraint system. Most parents 174 (60.4%) use a car device for child protection, 36 (12.5%) because they are required by law and the rest did not use it because of the high price/accessibility. When they were asked from what age children can travel in the front seat, most parents answered that they did not know, 92 (31.9%) parents answered that from 12 years old, 32 (11.1%) that they must have at least 6 years. The majority of parents 159 (55.2%) consider that preschoolers should be positioned in the car seat, 85 (29.5%) parents confirm that the maximum age for using car seats is school children.

**Conclusion.** The obtained results will contribute to the development of actions to prevent road traffic accidents and traumas in order to convince car drivers to use road safety systems among children. Progress can be made to increase parents' knowledge and motivation to transport children safely and to ensure that safety seats are accessible and available.

### 3. ASSESSMENT OF SEXUAL AND REPRODUCTIVE HEALTH LITERACY AMONG ADOLESCENTS IN MOLDOVA



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**Introduction.** Despite significant progress in sexual and reproductive health (SRH) in Moldova, adolescents, particularly vulnerable populations such as refugees and the Roma minority, still face barriers to accessing accurate information and services. INTERSOS Moldova, Youth Friendly Center “Neovita”, “Nicolae Testemitanu” SUMPh, and two non-governmental organizations providing healthcare are collaborating to develop a digital resource to improve health literacy and access to healthcare among refugee and disadvantaged youth in Moldova.

**Aim of study.** To learn about adolescents’ and young refugees SRH needs in terms of knowledge and healthcare; to co-design an App content and to promote social cohesion and collaboration among local and refugee youth in addressing SRH challenges.

**Methods and materials.** Focus group discussions (FDG) were organized and conducted in 3 geographically distinct regions of Moldova, carried out by 2 experienced researchers in Romanian, Russian, or both and audio recorded with the participants permission. Each FDG groups lasted between 90 to 120 min. In total, 50 young participants from the Republic of Moldova, Ukrainian refugees, and Roma individuals aged between 15 and 24 years old get involved in. Interview guide had 12 opened questions related to: knowledge use of Apps and websites; what young people would like to know about SRH; where young people currently go for SRH information; where young people currently go for SRH care and digital health issues. The ethics committee’s approval was obtained.

**Results.** Participants demonstrated a strong reliance on social media, particularly platforms like Instagram, TikTok, and YouTube, for SRH information. Important gaps in awareness and a demand for improved education on contraception, sexually transmitted infections, male and female puberty, and menstruation were identified. Health professionals were considered credible sources, but shame and fear of dismissal hindered direct engagement. Anonymity, confidentiality, and the use of digital platforms, such as Apps, were identified as potential enablers for accessing SRH information.

**Conclusion.** The findings underscore the potential for a digital youth-focused SRH resource that adolescents can use independently. Clarity through easily understandable formats, including audio and video content were considered important features. Collaboration with health professionals and official health organizations is essential for credibility, and a resource incorporating opportunities for anonymous access to experts was proposed. To enhance SRH education, involving peer educators and facilitating direct interactions with younger health professionals in schools are recommended. Acknowledgement. The work reported in this publication was funded by the European Union. The authors gratefully acknowledge all members of INTERSOS Moldova and "Nicolae Testemitanu" SUMPh for their work on the project overall and for the contributions of project documentation used in this manuscript.



#### 4. BORON INTAKE OF THE POPULATION FROM DIFFERENT REGIONS OF THE REPUBLIC OF MOLDOVA

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**Introduction.** Boron is known as a trace element that could prevent osteoarticular diseases, especially osteoarthritis, rheumatoid arthritis, and osteoporosis. It is supposed that for obtaining its protective effect a dose of 3 mg of boron must be consumed daily.

**Aim of study.** The major sources of boron are water (30%) and diet (65%) with the remaining 5% for hygiene and home care products. World Health Organization recommends a limit of 2,4 mg/l of boron for drinking water with the possibility of an increase for countries where soils are rich in boron. In the Republic of Moldova, the limit of 1 mg/l in drinking water is set by the national legislation. The major food sources of boron are nuts and seeds, dried fruits, legumes, fresh fruits, and vegetables. This study aimed to estimate boron intake from water and food of the population from different regions of the Republic of Moldova and its protective effect for the osteoarticular system.

**Methods and materials.** To assess the boron intake of the population, the water and food sources were analyzed. For the first source, samples of deep drinking water were analyzed in the regional laboratories of the National Agency for Public Health, the results were collected, were evaluated and the regions with above-the-limit (more than 1,2 mg/l), limit (0,9-1,2 mg/l) and below the limit (0-0,8 mg/l) boron concentration in deep drinking water were detected. Boron-rich foods were selected based on the literature review of 120 sources. A sample of 425 patients with osteoarticular diseases – rheumatoid arthritis and osteoarthritis was selected and all of them completed a questionnaire that assessed their drinking water and food consumption habits. The statistical association between variables was established using Chi-Square Tests within the Epi Info™ 7 soft.

**Results.** 61,1% of the surveyed population drink water from the central water system and local wells, and 75% use this water for cooking. The boron intake for the population from above-the-limit, limit, and below-the-limit boron in drinking water area was calculated by summing the boron intake from water and the three most consumed rich in boron foods – nuts (75,3% population), legumes (79,5%) and seeds (57,4%). 52,9% of surveyed people drink 1,5-2 l of water per day, 41,9% consume 2-3 portions of vegetables per day, a portion of nuts and seeds per day is 15 grams for each, and legumes is 150 g a day with a boron concentration of 1,21 mg/100 g in nuts and seeds and 0,48 mg/100 g. Daily boron intake from water in the above-the-limit area (Comrat, Ceadir-Lunga) was 2,1-3,7 mg, in the limit area (Cahul, Vulcanesti) - 1,27-2,2 mg and below-the-limit area (Calarasi, Briceni, Drochia) – 0,45-0,6 mg. Total boron intake was 3,18-4,78 mg for the first area, 2,35-3,28 mg for the second, and 1,53-1,68 mg for the third.

**Conclusion.** Boron can have a protective effect on the osteoarticular system in the above-the-limit area, may have some benefits in the limit area, and can lack in effects in the below-the-limit area of the Republic of Moldova.



## 5. DISEASES PREVENTION AND CONTROL AMONG HEALTHCARE WORKERS



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**Introduction.** According to WHO Occupational health is an area of work in public health to promote and maintain the highest degree of physical, mental and social well-being of workers in all occupations. According to the national yearbook, the Republic of Moldova counts 12,214 doctors and 23,954 average medical staff, who play a crucial role in disease prevention, while being subject to the highest risk themselves.

**Aim of study.** The aim of the study was to investigate the factors that influence the health status and behavior of medical workers, as well as the existing measures and challenges in preventing infections and occupational diseases in their work environment.

**Methods and materials.** A cross-sectional descriptive study was initiated among 100 healthcare workers from different specialties and institutions in the period of September- October 2023, with application of the on-line and paper-based questionnaire consisting of 29 questions. The data were analyzed using descriptive and inferential statistics, such as frequencies, percentages, means, standard deviations.

**Results.** The results showed that medical workers face various risks and problems related to their health and work, such as exposure to biological and chemical hazards, physical and mental stress, lack of personal protective equipment, insufficient motivation. Among the participants, 59.1% had not experienced any illnesses due to their working conditions in medicine in the last 12 months; 30.3% had, and 10.6% were unsure. A high or very high level of stress at work was reported by 76.6% of the participants, while 23.4% reported a moderate level. Half of the participants (50.8%) had a neutral perception of the psychological climate at work, while 33.8% had a positive one and 15.4% had a negative one. The study also revealed that medical workers have different levels of knowledge, attitudes, and practices regarding the prevention of diseases, depending on their age, gender, education, and experience. The majority of the participants (64.1%) rated their colleagues' infection prevention awareness as high, while 35.9% rated it as medium.

**Conclusion.** The responses indicate that medical workers want better pay and conditions, more respect and support from others, psychological help, relaxation and recreation activities, and improved work organization and management. The study concluded that there is a need for improving the conditions and quality of work, as well as the health education and promotion of medical workers, in order to reduce the incidence and prevalence of diseases among them.





## 6. DUAL-ENERGY X-RAY ABSORPTIOMETRY /DEXA, THE STANDARD IN THE DIAGNOSIS OF OSTEOPOROSIS

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**Introduction.** Osteoporosis is a problem of global importance, clinically asymptomatic and has been placed by the World Health Organization in the list of diseases related to the aging of the population. This pathology is of great economic importance and is characterized by the compromise of mechanical resistance and damage to the bone's microarchitecture, resulting in fractures.

**Aim of study.** Assessment of bone mineral density, a method for the early detection of osteoporosis.

**Methods and materials.** This literary review was written after analyzing articles, guides and reports from PubMed, Google Scholar, Hinari databases. Only full and open access publications were analyzed. Reference period – the last five years.

**Results.** Analysis of prospective cohort studies allowed establishing the direct link between decreased bone mineral density and increased fracture risk. In addition, there is a strict correlation between the increase in bone mineral density on the background of anti-osteoporotic treatment and the decrease in the frequency of subsequent fractures. Dual energy X-ray absorptiometry (DEXA), the standard in the diagnosis of osteoporosis, is currently used to assess the state of bone tissue. Based on several studies, the effectiveness of this method for the assessment of fracture risk has been demonstrated. The basic indicators of bone tissue mineralization by the DEXA method are: bone mineral content, the amount of mineralized tissue (g) by scanning the bones determined by the length of the scanned surface (g/cm) and the density of mineralized bone tissue in the scanned area (g/cm<sup>2</sup>). Currently, bone mineral density is appreciated using two scores T and Z. The World Health Organization relies on the determination of bone mineral density by the T score, and defines osteoporosis as the presence of a bone mineral density of 2.5 standard deviations below the mean for young women. Before the widespread application of DEXA, osteoporosis was rarely diagnosed, only in women with symptomatic vertebral fractures or osteopenia observed radiographically for other reasons. The FRAX tool was developed to assess 10-year fracture risk. It is a questionnaire that integrates associated risks and bone mineral density measured by DEXA at the level of the femoral neck. Questions included are: sex, age, height, weight, presence/absence of previous fractures and rheumatoid arthritis, glucocorticoid administration, risk factors smoking and consumption of 3 or more units of alcohol per day. FRAX was developed from the study of population-based cohorts in Europe, North America, Asia and Australia.

**Conclusion.** In the absence of osteoporotic fractures, the physical examination may not reveal any particularity. Bone hardness and resistance to fractures depend on bone mineral density, its assessment by DEXA and FRAX is of major importance for early diagnosis and prognosis.

## 7. EFFECTIVENESS OF EAR ACUPUNCTURE TREATMENT OF SMOKING TEMPERANCE SYNDROME DEPENDING ON SMOKING PERIOD



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**Introduction.** Tobacco use is one of the biggest threats to the worldwide public health and is the leading cause of death (7 million people per year worldwide), associated diseases (including cancer, chronic lung disease, cardiovascular disease) and impoverishment that can be prevented. Smoking eradication is an important global health issue approached by the World Health Organization (WHO). The difficulty for smokers to quit is due to the strong addiction to nicotine, psychological, sociological factors. Drug elimination methods, replacement therapy, hypnosis, psychotherapy do not provide the expected results. The use of acupuncture to suppress addiction and eliminate withdrawal symptoms has steadily increased in recent years and is showing significant results.

**Aim of study.** Studying the effectiveness of auricular acupuncture treatment in patients with smoking temperance syndrome, according to the clinical-psychological symptoms and the duration of smoking period.

**Methods and materials.** This study was carried out for 1 year on a group of 71 persons of different ages and smoking experience.

**Results.** The elucidation of the clinical-psychological manifestations allows the differentiated evaluation of the patients' condition and, in accordance with this, the prescription of a certain treatment. In patients with a smoking experience of up to 10 years, the first version of the abstinence syndrome is predominating (the pronounced ideational-mental component and the absence of distinct affective disorders). From 10 to 20 years of smoking - the second version (pronounced ideational-mental component and manifest sub-depressive anxiety disorders) and when smoking for more than 20 years, the third version is more frequent (pronounced ideational-mental component and dysphoric disorders). The obtained data reveal that, in order to provide an individualized treatment to patients, it is necessary to take into account the duration period of smoking. The use of auricular acupuncture as monotherapy is highly effective for patients with the first version of temperance syndrome. Placebo treatment has no clinical efficiency. The dynamic monitoring of the condition of the patients over the course of a year showed that the effective correction of ideation and emotional disorders and the stabilization of the obtained positive effect are possible after two, and sometimes three, treatment courses.

**Conclusion.** The treatment of smoking can be individualized, depending on the clinical-psychological version of the smoking temperance syndrome expressed by the patient and the duration period of smoking, which is mutually related to the prevalence of certain affective disorders. Auricular acupuncture as a monotherapy is effective for people with a smoking history of up to 10 years and the first version of the temperance syndrome (pronounced ideational component and the absence of distinct affective disorders).



## 8. EPIDEMIOLOGICAL TRENDS AND CHARACTERISTICS OF HUMAN RABIES CASES IN THE REPUBLIC OF MOLDOVA, 1950–2022

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**Introduction.** Rabies is a zoonotic viral disease responsible for the death of approximately 59,000 people worldwide, with more than 3.7 million disability-adjusted life years lost annually. Due to acute progressive encephalitis, rabies is fatal once clinical signs appear. Rabies is present on all continents except Antarctica. Rabies remains endemic in Moldova and has high public health importance.

**Aim of study.** Analysis of the epidemiological situation on the territory of the Republic of Moldova regarding the circulation of the rabies and high risk areas.

**Methods and materials.** We obtained data from the National Agency for Public Health archive for the period 1950-2022. The data included demographic information regarding the patient's origin, age, and gender. Clinical data included estimated date of animal exposure, site of bite, type of exposure, incubation period.

**Results.** 117 data on human rabies deaths reported to the ANSP were analyzed to explore trends in human rabies over time. The highest number of cases was reached in 1951 ( $n = 15$ ; 0.38 per 100.000), 1953 ( $n = 8$ ; 0.20 per 100.000), and in 1955, 1966, 1976 there were 6 cases or 0.15 cases per 100.000. It is important to note that from 1991 to 2022 there were only 3 cases of human rabies in the entire country (in the years 2003, 2016 and 2019). According to the territorial distribution, we can mention that the most cases were recorded in the districts in the north of the country: Edinet - 9 cases, Soroca - 7 cases; and the center – Criuleni, Orhei has 6 cases each. There was a higher number of deaths from rabies in males compared to females (81% vs 19%). Among the victims who died of rabies, 62% were adults, most cases being in the 51-60 age group ( $n=15$ ; 30%); 38% children, most cases ( $n = 15$ ; 45%), registering in children aged between 11-15 years. Dogs represented the majority of exposure sources ( $n = 47$ ; 46%), followed by foxes ( $n = 41$ ; 40%) and cats ( $n = 11$ ; 10.7%). The incubation period of rabies ranged from 5 days (the shortest incubation period) to 635 days (the longest incubation period), with an average of 79 days. The median rabies incubation period was 46 days (range: 7–135 days) in cases with head and neck exposure sites; 85 days (range: 5–635 days) for upper limbs; and 100 days (range: 9–210 days) for the lower limbs. 52% of cases had an incubation period between 31-90 days, 17% - 15-30 days and 16% - 91-180 days.

**Conclusion.** Although there are still cases of rabies in the country, there have been only 3 cases in the last 30 years. The most cases were recorded in the districts in the north of the country, among adults (62%). The average of the incubation period is 79 days. Dogs represented the majority of exposure sources 46%, followed by foxes 40% and cats 10.7%. Strengthening and promoting cross-sectoral involvement through the One Health approach is essential for the sustainability of the rabies elimination programme in the Republic of Moldova.

## 9. EPIDEMIOLOGY OF MUMPS AT THE CURRENT STAGE



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**Introduction.** The national epidemiological situation regarding parotitis or mumps remains unfavourable. It should be noted that increased mumps morbidity occurs even in communities of children and adolescents with high vaccination coverage. In the last outbreaks of epidemic parotiditis, the clinical picture of this disease and the distribution of patients by age group has changed. Nowadays, mumps has become a re-emerging disease, which requires a detailed analysis of its contemporary peculiarities, development and implementation of specific surveillance and prevention measures .

**Aim of study.** Assessment of the current epidemiological situation of epidemic mumps.

**Methods and materials.** According to data provided by the National Public Health Agency at present time and National Statistical Office.

**Results.** Vaccination saves more than three million lives worldwide every year. When vaccination coverage is high (above 95%), the number of people contracting the disease is greatly reduced. In the absence of vaccination or when vaccination coverage falls below 90%, diseases and epidemics are likely to recur. The Republic of Moldova is today at the 90% limit. According to data provided by the National Bureau of Statistics, cases of epidemic parotitis have varied in recent years, suggesting the impact of vaccinoprophylaxis and contemporary anti-vax trends.

**Conclusion.** There are conflicting arguments around the world about the need for vaccination. But as the medical system, the scientific environment and society's desire for a better life evolve, it is becoming increasingly clear that neglecting immunization can have tragic consequences. This is especially true for children, who are going through a complicated period of health and life risks in their first years of life.



## 10. EVALUATION OF THE CONSUMPTION OF FOOD PRODUCTS CONTAINING SUGAR AMONG YOUNG PEOPLE

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**Introduction.** Sugar consumption among young people is a major public health problem with long-term negative health effects. The World Health Organization recommends that added sugar intake should not exceed 10% of total caloric intake. However, studies show that young people consume on average is twice as much sugar as is recommended.

**Aim of study.** Assessment of dietary habits and awareness of sugar consumption among young people.

**Methods and materials.** A survey was conducted in which 159 people between the ages of 18 and 30 participated, from urban (74.8%) and rural (25.2%) localities of the Republic of Moldova. Male respondents – 17.6%, female – 82.4%.

**Results.** The daily consumption of food products with a high sugar content was reported by 52.2% respondents, 35.8% – 2-3 times a week, 12% – once a week. The main sources of sugar in the diet were: fruits (81.1%), sweets (78.6%), pastries (66.7%), soft drinks (22.6%). Factors that influenced the decision to buy low-sugar food products: personal health (59.1%), taste (56.6%), recommendations from friends or family (27%), advertising and promotion (19.5%), price (14.5%). Young people reported that they are aware of the sugar content of food products in 51.6% of cases, moderately aware – 47.2% and young people who are not aware of the problem – 1.2%. 39.6% respondents have a lot of knowledge about the effects of excessive sugar consumption on health, moderate knowledge - 54.7%, little knowledge - 5.7%. The most information about the impact of sugar on the health of young people was received from school / university (73.6%), mass media (72.3%), doctor (28.3%). Young people reported that it is important to be given more information about the risks of excessive sugar consumption: yes – 89.3%, no – 8.2%, sometimes – 2.5%. Thus, young people are aware of the risks associated with excessive sugar consumption, but are still prone to consuming foods high in sugar. This is partly because soft drinks, sweets and pastries, which are major sources of sugar, are accessible, cheap and tasty. To reduce sugar consumption among young people, it is important to combine several strategies, including: (1) Awareness campaigns. (2) Education in schools. (3) Access to healthy alternatives. These strategies could help reduce sugar consumption among young people and improve their long-term health.

**Conclusion.** Excessive sugar consumption among young people is a complex problem with serious health consequences. Awareness campaigns should inform young people about the risks associated with excessive sugar consumption and motivate them to make healthy food choices. Youth education programs should include information on nutrition, the negative effects of excessive sugar consumption, and ways to adopt a healthy lifestyle.



## 11. EXAMINING GENDER-BASED VIOLENCE RESPONSE STRATEGIES IN MOLDOVA



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**Introduction.** In a constantly evolving society, the issue of gender-based violence is a topic of crucial importance, with a profound impact on the individual and the community as a whole. The Republic of Moldova, being a territory where social and cultural changes are palpable, faces specific challenges regarding the response to gender-based violence. This complex phenomenon requires a comprehensive and coherent approach.

**Aim of study.** To identify the strengths and weaknesses of health care infrastructure related to the response of GBV among the population in the Republic of Moldova.

**Methods and materials.** A specialized search was conducted within the google scholar with reference to the response to gender violence in the Republic of Moldova, according to the inclusion and exclusion criteria previously set-up. The keywords used were: gender based violence, violence. In the analyses, 15 bibliographic references published in the last 5 years in the Republic of Moldova were included.

**Results.** The Republic of Moldova is in the top of the countries in Europe with the most cases in which women have been psychologically or sexually abused at least once in their lives. In the Republic of Moldova, practically 3 out of 4 women (73%) have experienced one form or another of family violence during their lifetime. About 30 women die each year from these abuses. The review reveals significant progress in the legislative field, with the adoption and amendment of laws to protect the rights of victims of gender-based violence. However, there are still challenges in the consistent implementation and enforcement of these laws. Important efforts have been made in developing support and counseling services for victims of gender-based violence. However, access to these resources remains a problem in some areas, and public awareness of the existence and usefulness of these services can be increased.

**Conclusion.** The literature review reveals progress in addressing gender-based violence in the Republic of Moldova, but challenges remain related to cultural norms, unequal access to resources and the need for continued awareness. This research can contribute to the development of more effective preventive measures, thus consolidating the progress already made in building a fairer and safer society. Acknowledgement. The work reported in this publication was funded by the National Institutes of Health - Fogarty International Center at the University of Iowa (Grant Agreement: 5D43TW007261-17). The authors gratefully acknowledge all members of the iCREATE grant for their work on the project overall and for the contributions of project documentation used in this manuscript.



## 12. FREQUENCY AND TYPE OF DOMESTIC INJURIES AMONG CHILDREN UNTIL 12 YEARS

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**Introduction.** Domestic injuries are nowadays a major medical and social problem which is constantly increasing. Globally, domestic accidents are the leading causes of disability and morbidity among children. According to the World Child Injury Prevention Report, worldwide, more than 2,000 children die every day from unintentional injuries, but most of them are preventable. Although injuries at home are a common problem among children in rural areas, their mothers, according to studies, do not have sufficient knowledge regarding the causes, prevention and first aid in dealing with these injuries.

**Aim of study.** The major objective was the analysis and assessment of injury through accidents and domestic trauma among children under 12 years of age in the Republic of Moldova and the development of their preventive measures.

**Methods and materials.** A study was carried out using a questionnaire to assess knowledge, attitudes, and practices regarding domestic accidents. The population included in the study were parents, grandparents and other caregivers that look after children aged between 0 to 12 years. After analyzing the results obtained from the questionnaire, we collected the following information: data on child supervision - aspects regarding the degree of supervision of children; storage conditions for household goods, risk factors in the household; and data on knowledge of first aid measures in child injury situations.

**Results.** In total, 481 parents participated, their children are up to 12 years of age, the majority aged between 26-35 (62.7%), with higher education (78.3%), of which 94.8% were women, most from the urban environment (80%). Almost 68.3% respondents believe that their child could injure themselves at home, namely by accident (86.9%), followed by 37.1% who believe that their child could consume something risky. In 46.3% of cases, it is difficult for children to get sharp objects, drugs, and harmful solutions, in 12.6% - it is simple. Falls accounted for 76% of child injuries in the past year. Parents claim that they can always see and hear their children, according to 48.3% of parents, although there are times when they leave their children alone for a while. However, they occasionally leave them in the care of their grandparents (58.3%) or other people (23.7%). When a child was injured at home, 46.7% of parents treated their child at home, while 36.9% went to the doctor, of which 34.1% were examined and discharged without treatment. After the accident, 74.8% of people rated the child's condition as good, and 27.5% as acceptable.

**Conclusion.** With the help of this study, we identify the risks to which children can be exposed at home, inform and educate the general population about first aid, in various domestic traumas among children.

### 13. HEALTH PROMOTION AT WORKPLACE IN THE REPUBLIC OF MOLDOVA



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**Introduction.** Health promotion is a movement that enables the population to have control over the determinants of health and create their overall health. It aims to reduce current differences in health status and ensure equality of opportunity and resources to enable all people to reach their full health potential.

**Aim of study.** In this study we aimed to evaluate the practice of the Republic of Moldova in promoting health at the workplace, to elucidate the strategies and mechanisms involved in encouraging a healthy work environment and supporting the well-being of employees.

**Methods and materials.** The specialized literature on the topic of health promotion was analyzed: studies in the last 10 years, using the PubMed, NCIB, Medscape, Mendeley databases, using the keywords: "health promotion", "workplace", "evaluation", "questionnaire". As well as guides, manuals, monographs, the order of the Government of the Republic of Moldova regarding health promotion, the Ottawa Charter for health promotion.

**Results.** Based on the analyzed literature, we developed a questionnaire in Google Forms that addressed the working population of the Republic of Moldova, which aimed to evaluate health promotion. The questionnaire included closed type questions, which allowed the collection of general data about the participant, yes or no type questions and mixed type questions, where the participants could choose the answer option or propose their own option. Based on the results of these questionnaires, we formulated the following conclusions.

**Conclusion.** The Republic of Moldova faces various challenges: with the worsening of economic pressures and the increase in the costs of health services, the risk of social exclusion increases and in the future, the key to success could be changing the mentality of decision-makers, service providers and members of society, so that the health service health should no longer be perceived as simple actions for the treatment of diseases, but a mechanism that places the emphasis on the promotion of health and well-being.



## 14. HEALTH PROMOTION IN THE PRACTICE OF THE FAMILY DOCTOR

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**Introduction.** The family doctor plays an important role in all stages of a patient's life. In the 21st century, he has an important role in promoting the health of his patients. He is the one who has the function of promoting a healthy way of life and explaining the risks and consequences of the obtained pathologies. The family doctor is the first to take care of the patient's ongoing education, such as educating a patient with hypertension, a patient with diabetes, a pregnant woman, and advice on a necessary diet for the patient.

**Aim of study.** The proposed study aims to evaluate the effectiveness of health promotion strategies in family physician practice, focusing on improving the general health status of patients.. The research will also expand on the implementation of preventive practices to identify key aspects that contribute to the promotion of a healthy lifestyle. The obtained results will provide useful information for the optimization of primary medical services and will support the development of a proactive approach in health care.

**Methods and materials.** This research was developed by applying a questionnaire developed by the author. The questionnaire consisted of the following sections: socio-demographic data, behavioral risk factors with an impact on health, determination of the population's sources of information about disease prevention and health promotion and individual attitude, which contains 32 questions. The sample included 112 randomly selected patients aged 18-65 years. The survey was confidential and was researched with the consent of each respondent.

**Results.** Harmful factors at work: Overcooling (53.1%), overheating (45.3%), vibration (37.5%), radiation (59.4%), heavy metals (39.1%), toxic, chemical factors (tobacco, pesticides, paints,etc.) (59.4%), hard physical work (50%). How often the family doctor is consulted: weekly (2.7%), monthly (8.1%), once a semester (51.4%), once a year (16.2%), don't go to the family doctor (9.5%). Present health problems: cardiovascular diseases (10.8%), hypertension (24.3%), obesity (10.8%), diabetes (12.2%). The family doctor spends up to 10 minutes of the visit to promote a healthy lifestyle (39.2%). (71.6%) would change their diet; (51.4%) would lose weight; (55.4%) would do sports; (29.7%) would quit smoking. (40.3%) believe that the family doctor could have helped them.

**Conclusion.** A large number of patients suffer from metabolic pathologies such as hypertension, obesity, diabetes, cardiovascular diseases that are subject to a negative risk due to exposure to harmful factors at work. This study demonstrated the importance of the family doctor in promoting health among patients in order to reduce the risk of some pathologies or to improve the health status of an already present pathology.

## 15. HEALTHCARE-ASSOCIATED INFECTIONS IN PEDIATRIC PATIENTS- AN UNDERESTIMATED PROBLEM OF HUMANITY



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**Introduction.** Healthcare-associated infections (HCAIs) are the most frequent cause of morbidity and mortality in children, contributing to prolonged hospitalization and increased healthcare costs.

**Aim of study.** The aim of the study is to evaluate the bibliographic data regarding the situation of HCAIs in pediatric patients.

**Methods and materials.** A bibliographic study was carried out, the search engine included the keywords: "Healthcare Associated Infections" and "infections in pediatric units" on the search platforms Pubmed, Google Scholar and Hinari. Over 100 sources were analyzed. Of them, 19 sources were relevant to the research topic and met the inclusion criteria.

**Results.** At the global level, it is estimated that a lot of hospitalized children suffer from HCAIs, with incidence rates ranging from 3.5% to 12% in developed countries and 5.7% to 19.1% in low- and middle-income countries. The result of a study carried out in 29 European countries, demonstrates that the range of prevalence of HCAIs in children in Europe is between the values of 4.0–10.7%, the average incidence for Europe being 6.1%. Pediatric intensive care units (15.5%) and neonatal intensive care units (10.7%) have the highest prevalence of HCAIs, followed by neonatology wards (3.5%), pediatric surgery (3.4%) and general pediatric wards (1.8%). A study conducted in India demonstrated that the rate of HCAI in pediatric intensive care units was 20%. Bloodstream infections (37.3%), pneumonia (30.5%), and urinary tract infections (25.5%) were the most common and were almost always associated with the use of an invasive device. Another study done in Turkey determined the occurrence of 311 (9.1%) episodes of HCAIs in 3420 hospitalized pediatric patients. 77.8% of them-were less than 1 year old. Annually, in the Republic of Moldova, about 60 cases of HCAIs in children aged 0-17 years old are reported to the National Public Health Agency. But no matter to this, studies that would demonstrate the real epidemiological situation through HCAIs in children in the country, have not been carried out.

**Conclusion.** HCAIs in pediatric departments represent a primary public health problem. Despite all the efforts to register, monitor and control pediatric HCAIs, until the moment the incidence of these infections is underestimated, the real incidence being much higher.

**Keywords.** Healthcare-associated infection, pediatric patients, incidence, morbidity, mortality.





## 16. HISTORICAL REFLECTIONS ON DRINKING WATER: HYGIENIC AND SOCIAL SIGNIFICANCE

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**Introduction.** Drinking water has always been a vital resource for the survival and development of human societies. Historically, access to clean water has significantly influenced the health, culture, and social structures of communities.

**Aim of study.** The study aims to explore how hygienic practices and social perceptions related to drinking water have historically changed, as well as the impact of these changes on public health and social structures.

**Methods and materials.** The analysis is based on an extensive review of historical documents and socio-cultural studies. The methods include comparative analysis of water treatment practices from different cultures and eras, and the evaluation of their impact on health and social organization.

**Results.** The study highlighted a varied evolution in drinking water hygiene. Initially, prehistoric purification relied on simple sedimentation and sand or gravel filtration, removing visible impurities but not microorganisms. Ancient civilizations like Egypt and Rome advanced these methods. Egyptians settled particles from the Nile in cisterns, while Romans used aqueducts and lead or stone filters. Yet, lacking microbial knowledge, these techniques were limited in disease prevention. In the Middle Ages, water purification saw little progress. Boiling became common, recognized for killing certain pathogens despite a lack of understanding of microorganisms. The Renaissance era, however, marked significant advancements. Distillation techniques improved for purer water, influenced by early microbial studies. The industrial period brought breakthroughs. The early 20th century's introduction of chlorination revolutionized water hygiene. John Snow's 19th-century work in London, linking water quality to cholera, spurred filtration and purification system development. Rapid sand filtration and widespread chlorination significantly cut waterborne disease rates. The 20th century's growing grasp of microorganisms and chemical pollutants led to stricter hygiene standards. Techniques like reverse osmosis, effective in removing salts and contaminants, emerged. Activated carbon filtration became prevalent for chlorine and organic substance removal. This evolution profoundly influenced public health, drastically reducing water-related diseases like cholera and typhoid fever, especially in areas with purified water access. Technological advances also improved drinking water availability in resource-limited regions, enhancing health standards and life quality.

**Conclusion.** The study emphasizes that the hygiene of drinking water is a key factor in human health and development. The evolution of purification methods reflects technological progress and awareness of health risks, being essential in disease prevention and life quality improvement.

## 17. IN VITRO BIOFILM FORMATION BY *S. AUREUS* ISOLATED FROM ORAL INFECTIONS AND THEIR ASSOCIATION WITH ANTIMICROBIAL RESISTANCE



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**Introduction.** *Staphylococcus aureus* is an opportunistic pathogen most commonly involved in skin and soft tissue infections. It is part of the normal microflora of the nasopharynx, skin, eyes, intestines, and urogenital tract. However, it can breach the barriers of the skin and mucous membranes through injuries or surgical incisions, leading to infection. Additionally, it has the ability to adhere to and form biofilms on tissues or medical devices.

**Aim of study.** Aim of study was to study the in vitro biofilm-forming ability of *S. aureus* isolated from oral infections and their association with antimicrobial resistance.

**Methods and materials.** The study was carried on 64 samples isolated from oral infections. The microbial strains involved in the process were isolated in pure cultures, under laboratory conditions, and subsequently identified by classical microbiological methods and Vitek2 Compact system (BioMerieux), based on the morpho-biological, coloring and biochemical properties. The antimicrobial susceptibility and biofilm-forming ability testing was performed using the Kirby-Bauer disk diffusion technique and the quantitative adhesion test, respectively. Strains that showed resistance to three or more antibiotic groups were considered poly-resistant ones.

**Results.** The antibiotic susceptibility tests of *S. aureus* strains isolated from oral infections showed a high level of resistance to drug preparations. Of the 64 microbial strains isolated, 42 (65.6%) strains produced detectable biofilms ( $OD > 0.112$ ). As regarding the biofilm status, 13 (30.9%) isolates produced strong biofilms ( $OD > 0.220$ ), 26 isolates (61,9%) – moderate biofilms ( $OD 0.112-0.220$ ) and 3 isolates (7.2%) – weak biofilms. The antibiotic resistance of biofilm-forming compared to non-biofilm-forming strains showed that biofilm-forming strains had a higher resistance to all groups of drugs tested.

**Conclusion.** The study results revealed a higher biofilm formation capacity at the strains isolated from oral infections, as well as higher rates of antimicrobial resistance in biofilm-producing strains compared to non-producing ones. The obtained data proves a strong correlation between biofilm formation capacity and antimicrobial resistance patterns. The implementation of the relevant antimicrobial susceptibility testing of biofilm-producing strains will improve the management of infections caused by these microorganisms, as well as provide feasible strategies to prevent their spread.



## 18. INTERCULTURAL COMMUNICATION IN THE FRANCOPHONE EUROPEAN YOUTH COMMUNITY

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**Introduction.** Intercultural communication remains an important necessity and a method of getting to know one another among French-speaking young people in the European community. Intercultural communication is at the basis of the relations between the young people of the European community through the symbiosis and variability created by the system of values, traditions, customs, way of life and thinking, religion and the environment as factors of external influence.

**Aim of study.** The presentation of a research carried out at the level of the European youth community and the description of the most important aspects that unite students from different countries of the world, who study at different universities on the European continent.

**Methods and materials.** Questionnaires and specialist information justifying research results. The literature was studied on the aspects of intercultural communication and the methods of manifestation necessary for effective communication.

**Results.** Intercultural communication is the basis and foundation of solid and long-lasting relationships. From the first teaching, cultural, sports, scientific and entertainment activities, francophone students are integrated into the big family of the European Youth Community through the Platform for Francophonie, Multilingualism and Cooperation in Europe and thanks to the intercultural communication that is also the basis of the training the communication skills needed to create interpersonal relationships. The Festival of Young Francophones in Central and Western Europe, the Colloquium of Young European Francophones „Ecological Issues in European Higher Education” and the Francophone European Scientific Research Symposium are events that stimulate and promote intercultural dialogue and represent the perfect space and atmosphere for young people to build lasting friendships and relationships through cross-cultural communication. AUF-University Agency of Francophonie and ESFAM-Francophonie Management School represent the environments favorable to the development of these interpersonal relationships and which combine the pleasant and the beautiful and offer students different opportunities to express themselves and overcome linguistic and emotional barriers, as the main barriers of intercultural communication.

**Conclusion.** Intercultural communication is the foundation of human relations in the European student community. The multitude of didactic, scientific, sports and cultural activities in which students from the bachelor's, master's and doctoral study programs are involved demonstrates the need to have effective intercultural communication.

## 19. KNOWLEDGE, ATTITUDES, AND PRACTICES REGARDING HEPATITIS B AND C AMONG STUDENTS AT "NICOLAE TESTEMIȚANU" STATE UNIVERSITY OF MEDICINE AND PHARMACY



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**Introduction.** Viral hepatitis B and C represent significant global public health challenges with a profound impact on the population. Students at the "*Nicolae Testemitanu*" State University of Medicine and Pharmacy (USMF) are future medical professionals who will play a crucial role in the prevention, diagnosis, and treatment of these conditions. In this context, emphasizing the knowledge, attitudes, and practices of students regarding viral hepatitis B and C becomes essential for developing effective educational programs and awareness strategies.

**Aim of study.** The aim of this study is to assess the level of knowledge, attitudes, and practices among USMF students regarding viral hepatitis B and C, identifying potential gaps and providing a foundation for improving education and awareness in the field.

**Methods and materials.** To achieve the stated objective, a cross-sectional study was conducted using a structured questionnaire randomly distributed to USMF students from years 1 to 6. The questionnaire included questions about basic knowledge of hepatitis B and C, attitudes towards affected patients, and practices related to hepatitis prevention and control. Data were collected and analyzed using statistical methods, Microsoft Excel, and EpiInfo.

**Results.** A total of 152 students were surveyed. The cause of infection with hepatitis B and C was correctly mentioned by 93.4% and 92.1%, respectively, while others cited bacteria or drugs. 82.9% believe that HBV can be prevented through vaccination, 48.7% believe that HCV can be prevented through vaccination, 56.6% believe that HBV can be treated, and 51.3% believe that HCV can be treated. 96.1% and 94.1%, respectively, consider blood and amniotic fluid to pose a risk of infection with viral hepatitis B and C. 21.7%-25.0% consider urine to be a way of transmission, 36.2%-34.2% consider hepatitis B and C can be transmitted through saliva. 47.4% of respondents believe that HBV can be transmitted through breast milk, while 44.1% mentioned HCV. 65.1% believe that HBV can be transmitted from mother to fetus during pregnancy, and 60.5% mentioned HCV. 85.5% believe that HBV can be transmitted sexually, and 80.3% believe the same for HCV.

**Conclusion.** The study highlights the urgent need to improve the education level and awareness of USMF students regarding viral hepatitis B and C. The implementation of training programs, along with the promotion of non-stigmatizing attitudes and effective prevention practices, represents critical directions for the future. Active involvement of faculty and educational authorities is essential to ensure the proper training of future medical professionals.



## 20. LEGAL INSTRUMENTS FOR THE PROTECTION OF CHILDREN'S RIGHTS AGAINST ACTS OF VIOLENCE

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**Introduction.** Violence against children is still a widespread phenomenon in the Republic of Moldova, as only in 2020, 26% of girls and 35% of boys were subjected to physical violence by the age of 18. In the 2020-2021 academic year, throughout the country, teachers identified 6,949 cases of violence, of which 2,775 were physical violence.

**Aim of study.** The paper aims to highlight the importance of the legal system in ensuring the protection of children's rights for their harmonious development.

**Methods and materials.** An analytical study of international and national legislation on the protection of children's rights, including against acts of violence, was carried out.

**Results.** The Universal Declaration of Human Rights guarantees every human being the right to life, liberty and security. The UN Convention on the Rights of the Child ensures children's rights at home and in society, including the right to be free from violence and sexual exploitation. By ratifying the UN Convention on the Rights of the Child, the Republic of Moldova undertook to provide children with good social security and conditions for intellectual and physical development as comprehensive as possible. The European Convention on Human Rights, also ratified by the Republic of Moldova (1997), is the most important instrument developed by the Council of Europe to guarantee fundamental human rights. The Constitution of the Republic of Moldova is the Supreme Law and ensures the respect of the rights of all citizens, including children. In the Republic of Moldova, the child's interests are protected by means of the Law on the Rights of the Child, which establishes the legal status of the child (up to 18 years) as an independent subject and provides for ensuring the child's physical and spiritual health and guaranteeing the right to life and physical and mental inviolability. The state is committed to protecting the child against any form of violence and exploitation, discrimination, physical or mental violence, cruel behavior, including from parents or legal surrogates and through Law no. 140/2013 regarding the special protection of children at risk and children separated from their parents and Government Decision no. 270/2014. The response of the health system to cases of violence against children is regulated by the Order of the Ministry of Health no. 445/2015.

**Conclusion.** The rights of the child, including the right not to be subjected to acts of violence, are protected through international UN standards. Although the Republic of Moldova has special legislation on the protection of children, violence against them, especially physical violence, is still a frequently recorded phenomenon. In order to ensure the reduction of the incidence of this phenomenon, the population must be educated in the spirit of respecting the rights of the child, and the professionals trained in providing an adequate response to cases of violence against children, arising from their ultimate interest.

**Keywords.** Physical violence, children, international standards, legal norms.



## 21. MEASURING AND EVALUATION – BASIC TOOLS IN PUBLIC HEALTH



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**Introduction.** The problem of preservation of the health of the population is considered a top priority for public health, which requires the development of coordinated actions to improve the health and quality of life of the population. The health profile is the most effective tool for providing evidence for the development of health policies at the community level.

**Aim of study.** The aim of the study was the evaluation of the Health Profile tool implementation in the activity of the Public Health Center and Public Authority of the Balti Municipality.

**Methods and materials.** The methodology of the National Guide on developing the Health Profile of population at the territorial-administrative unit level, approved by order of the Ministry of Health of the Republic of Moldova no. 1363 from 01.12.2014 was applied. There were analyzed 42 statistically relevant indicators for M&E of non-communicable diseases (NCDs) and determining factors as well as the decisions issued by the Public Administration of the Balti Municipality regarding public health issues. The observation period covers the years 2016-2020.

**Results.** The development process of the health profile of the Balti municipality was started in 2014 and includes the analysis of the health status of the population and the determining factors in their multi-annual dynamics, during the years 2007-2014. In the routine monitoring, public health specialists applied the statistical indicators, available in the open-access databases. The epidemiological analysis of 42 statistical indicators recorded in the period 2015-2020 highlighted trends that differ from those identified in the previous period, in the positive aspects. The Public Administration of the Balti Municipality adopted 16 decisions based on the evidence from the health profile.

**Conclusion.** The health profile is an effective M&E tool in public health. Currently, only 40% of the indicators provided for by the National Guide are collected, mostly focused on non-communicable diseases. It is important to involve and support the Local Public Authority, which can provide truthful data for completing the territorial health profile with their use in the process of planning and evidence-based decision-making, at the moment being rated at a medium average level.



## 22. MICROBIAL RESISTANCE TO ANTIBIOTICS

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**Introduction.** The use of antibiotics (ABs) in the treatment of pathologies caused by microorganisms has saved many human lives, but subsequently, bacterial infections have again become a severe threat due to antimicrobial resistance, causing 1.27 million deaths globally in recent years.

**Aim of study.** Identifying and studying current data from the field literature regarding the incidence, etiology, mechanisms of development of bacterial resistance and evaluating strategies to counter this problem.

**Methods and materials.** We conducted a systematic search of the modern literature, using the databases: MedLine, PubMed, Up to Date, Research gate to identify relevant articles with reference to "pathogenic microorganisms", "antibiotics", and "microbial resistance to antibiotics".

**Results.** Based on the studied literature. We summarized 7 bibliographic sources. The era of antibiotic therapy dates back to 1928, when A. Fleming discovered penicillin. Since then ABs have transformed modern medicine and saved millions of lives. In the 1950s penicillin resistance became a clinical problem, necessitating the development and implementation of new beta-lactam ABs. In 1962 in the USA the first case of methicillin-resistant *Staphylococcus aureus* was described and the pharmaceutical industry introduced many new ABs to solve the problem. Antimicrobial resistance (AMR) occurs when microbes: develop protective mechanisms to antimicrobial drugs (AMBD), survive exposure to ABs and can be the cause of random mutations, the latter being the consequence of prolonged use of AMBD. A major cause of ABR is the lack of rapid and adequate identification of pathogens, especially in patients with severe infections (sepsis, infective endocarditis, pneumonia, etc.), which leads to the excessive use of broad-spectrum AB, sometimes in inappropriate doses and short duration to eradicate the infection. Another cause is the abuse of AMBD in the treatment of any common cold. Microorganisms resistant to several AMBD can be: extensively multiresistant or totally resistant. Resistant microbes are difficult to treat, requiring higher doses or alternative drugs that can be more toxic and expensive.

**Conclusion.** Antimicrobial resistance represents a serious danger for patients with critical infections, influencing the effectiveness of treatment, disfavoring the evolution and prognosis of the disease. Prompt and correct differential diagnosis of diseases, implementation of key investigations, appropriate treatment with complete eradication of the infection are essential to counteract this phenomena and protect public health. Preventing the abuse of antimicrobial drugs leads to a significant reduction of microbial resistance to antibiotics facilitating a promising future.

## 23. NOSOCOMIAL INFECTIONS IN SURGICAL PRACTICE



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**Introduction.** Nosocomial infections (NIs), also referred to as healthcare-associated infections (HAIs), are presently a major concern in surgical practice. The rates of nosocomial infections serve as a crucial indicator of the quality of healthcare provision in surgical units. Hence, examining the incidence of NIs and identifying the pathogens more frequently associated with them contributes to a deeper understanding of this issue.

**Aim of study.** To review articles that addressed nosocomial infections in surgical practice.

**Methods and materials.** A review of relevant articles was conducted on the incidence of nosocomial infections and pathogenic agents within surgical units.

**Results.** A recent study (Olof Jannach et al., 2015) revealed that among 358 patients, of which 42% with pancreatic resection, 25% cases with hepatic resection 29%—gastric resection (3%), and esophageal resection—33.5% patients developed one or more surgical site infections (SSIs). The most prevalent were intra-abdominal septic infections (16.5%) and postoperative surgical wound infections (12.3%). The main causative agents were *E. coli* (12.4%), coagulase-negative staphylococci (12.2%), and *Enterococcus faecium* (9.7%). According to other authors (Wondemagegn Mulu et al., 2012), the incidence of surgical site infections in aseptic and contaminated operations was 3.3% and 12.8%, respectively. A total of 42 bacterial pathogens were identified, with *Staphylococcus aureus* being the predominant strain in 26.2% cases, followed by *E. coli* and coagulase-negative *Staphylococcus* species, making up 21.4%. About 100% of Gram-positive bacterial isolates and 95.5% of Gram-negative isolates exhibited resistance to two or more antimicrobial drugs. In the study conducted by (N. Capsamun, 2013), focusing on the pediatric neurosurgery unit as a model, it was found that the incidence of nosocomial infections (NIs) is directly correlated with the length of surgical interventions. Specifically, patients with a surgery duration of 0-1 hour had a NI incidence of 2.12%, those who underwent surgery for 2-3 hours showed- 12.76%, and patients with a surgery duration of 3-4 hours or more had the highest incidence of 44.68%.

**Conclusion.** NIs pose a significant medical and social challenge due to their increased incidence, diverse etiological factors, and high resistance of causative agents to antimicrobial drugs.

**Keywords.** Nosocomial infections, surgery-associated nosocomial infections.



## 24. OCCUPATIONAL STRESS FOR THERAPEUTIC AND SURGICAL DOCTORS. COMPARATIVE STUDY

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**Introduction.** Occupational stress represents a significant problem for doctors in the therapeutic and surgical fields, having a profound impact on their mental health and the quality of the medical act. Occupational stress among doctors is a major problem in the 21st century, where a large part of doctors are subjected to an overload related to the excessive number of night shifts or the large number of patients over a period of time, which denotes the appearance of pathologies such as insomnia, hypertension, diabetes, obesity, the occurrence of cardiovascular diseases, the nervous system, the digestive tract, etc.

**Aim of study.** The comparative study focuses on the impact of occupational stress on doctors in the therapeutic and surgical fields. By looking at factors such as workload, time pressure and patient experiences, the research highlights significant differences between the two specialisms. Deep understanding of these issues can help create a healthier and more balanced professional environment for doctors in both fields.

**Methods and materials.** This research was carried out by applying a questionnaire developed by the author. The questionnaire consisted of the following sections: socio-demographic data, Risk factors at work and their impact on personal health, Knowledge and skills about occupational stress, Measures to combat and prevent occupational stress, which contains 38 questions. The sample included 135 randomly selected patients aged between 25 and 65 years. The survey was confidential and was researched with the consent of each respondent.

**Results.** The research included (40.7%) surgical doctors and (59.3%) therapeutic doctors. The majority of doctors work 51-65 hours per week (25.2%). (50.4%) of doctors have 1-2 shifts per week. (34.1%) of doctors come into contact with 31-40 patients per week. (77%) are not satisfied with the salary received. (25.9%) acquired diabetes, (31.1%) hypertension, (22.2%) gastric ulcer, (46.7%) acquired neurosis, (53.3%) insomnia. (82.2%) of doctors selected that the volume of work is the most frequent source of stress in their work. (66.7%) consider that the workplace caused the emergence of health problems. (48.1%) of doctors had moments when occupational stress had a negative impact on medical decisions.

**Conclusion.** Occupational stress is a major problem in the 21st century that seriously affects the health of surgical and therapeutic doctors. Most doctors, as a result of the effect of stress and over-requests, acquire pathologies that will subsequently decrease the level of quality of life. Occupational stress at work is considered a major cause of early deaths among doctors.

## 25. ORGANIZATION OF LEGAL MEDICINE IN THE REPUBLIC OF MOLDOVA AND ABROAD



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**Introduction.** The harmonious organization of the forensic medical service leads to a well-functioning institution that ensures respect for human rights in relation to crimes against human life, health and dignity. Efficient organizational management of forensic institutions, including forensic medicine, is a priority of the state, which assumes the protection of fundamental human rights.

**Aim of study.** The aim of the study consists in analysis of the organizational systems of forensic services, in particular forensic medicine, in Moldova and abroad.

**Methods and materials.** The work is based on normative acts from Moldova, Romania, including institutional organization and functioning, a report on "Functional analysis of the national system of judicial expertise institutions in the Republic of Moldova" and other sources were analyzed.

**Results.** The system of public forensic expertise institutions in Moldova is coordinated by the Ministry of Justice and includes three large, specialized institutions: National Centre for Forensic Expertise (Ministry of Justice), Centre of Forensic Medicine (Ministry of Health) and Technical-Criminalistic and Forensic Expertise Centre (Ministry of Internal Affairs). The state may establish other institutions, public subdivisions, such as Directorate 4 of the General Directorate of Operational Assurance of the National Anti-Corruption Centre, the Directorate of Document Expertise under the General Inspectorate of Border Police. The Centre of Forensic Medicine, is a unique public institution of forensic expertise in Moldova, specialized in forensic medicine and forensic psychiatric expertise, with the mission to provide scientific-practical means of evidence to contribute to the dispensation of justice and the improvement of healthcare in order to respect human rights. The structure of the forensic expertise system in Romania and other countries, like in the Republic of Moldova, involves multiple institutions from the Ministries of Justice, Interior Affairs, and Health. However, forensic medicine comprises entities like the Institute of Forensic Medicine "Prof. Dr. Mina Minovici" in Bucharest, forensic medicine institutes in university medical centers, and county forensic medicine services and offices, fostering collaboration.

**Conclusion.** The Forensic Medicine in the Republic of Moldova is organizationally similar to most forensic systems in other countries, but even if it is organized and regulated by a set of normative acts, it needs more improvements oriented towards the quality of forensic and psychiatric forensic services.





## 26. EPIDEMIOLOGICAL FEATURES OF INFECTIONS CAUSED BY CLOSTRIDIUM DIFFICILE

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**Introduction.** *Clostridium difficile* has been intensively studied in recent years due to the rapid increase in the number of people affected by the virulence of this bacterium. The bacterium has become very resistant to different treatment methods, epidemiological studies prove that there are several factors that have contributed to this phenomenon: the administration of antibiotics without medical prescription and the appearance of a new strain known as PCR ribotype 027 (sometimes referred to as BI/NAP1/027).

**Aim of study.** We analyzed the epidemiological data from the Republic of Moldova and globally regarding the level of knowledge of the population and medical workers regarding the adverse effects of antibiotics, which is a risk factor in triggering the multiplication of the bacterium *Clostridium difficile*. The epidemiological data that demonstrate the rapid and partially uncontrolled spread of the bacterium.

**Methods and materials.** Epidemiological data analysis was based on articles published on Google Scholar, PubMed, Journal.ohrm and other platforms.

**Results.** *Clostridium difficile* - a "dangerous" gram-positive, anaerobic, mobile, sporogenous bacterium that is in the normal flora of every human's intestine. The CDI bacterium forms spores that are extremely resistant in the external environment (several months), increased resistance to alcohol disinfectants and sensitive to chlorine-containing disinfectants. The normal flora of the small intestine contains over 2000 types of bacteria that are essential for health. Exposure to certain aggressive factors trigger the colonization and multiplication of the pathogenic bacterium *Clostridium difficile*. This bacterium was studied for the first time in 1970, until now worldwide it causes approximately 500,000 cases of illness, in the Republic of Moldova CDI is not monitored epidemiologically, but it has become one of the most frequent infections acquired between hospitals. It mainly affects people over 60-65 years admitted to the hospital, the reason being the suppression of immunity. In Romania, due to the dramatic increase in the number of infected people, an "ATLAS" Score was launched, used to analyze the evaluation of the disease after confirmation, the parameters of this score are: age, fever, number of leukocytes, albumin, the antibiotic administered. A study presented by Garcia et al. demonstrated that after 30 days of illness the patient who has a score of <3 points were treated without sequelae 100%, the patients with the score: >8 died 100%, the patients with the score between 4 and 7 points are subjected to surgical treatment which consists of intestinal resection, with a 70.1% survival rate.

**Conclusion.** It is necessary in the Republic of Moldova to implement methods of identification, monitoring and reporting of the number of cases of infection with CDI, in order to be able to control the infection.

## 27. PERSONAL HYGIENE: HABITS OR PREVENTION



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**Introduction.** Maintaining physical, moral, and social well-being involves adopting conduct habits known as personal hygiene. Thus, knowledge, attitude, and practices related to personal hygiene become essential as a primary intervention in preventing the onset of diseases, especially in the context of interaction with pathogens such as viruses, bacteria, and parasites.

**Aim of study.** This study investigated the association between personal hygiene habits as a method of preventing communicable and non-communicable diseases, as well as the level of implementation of these practices in everyday life.

**Methods and materials.** An analysis of specialized scientific sources in Romanian, English, and French was conducted using Google Scholar, PubMed, and Mendeley search engines, accessing a total of 50 sources. For a more detailed search, keywords such as "personal hygiene," "disease prevention," "hygiene," "correct hygiene habits," "communicable diseases," and "non-communicable diseases" were used. The reference period for this research covered the years 2013-2023.

**Results.** According to the World Health Organization, "Hygiene refers to conditions and practices that help maintain health and prevent the spread of diseases." For people to live in health and well-being, the development of healthy lifestyle habits is crucial. Primarily, the risk communication approach is considered relevant in the context of personal hygiene habits and in preventing communicable and non-communicable diseases. Secondly, personal hygiene practices and disease prevention are influenced by information provided by expert sources, and finally, proper education plays a crucial role in shaping correct thinking about preventive behaviors. The daily need to interact with different people, spaces, and living organisms has created hygiene habits that ensure protection against harmful factors. Among these, we enumerate basic practices such as handwashing, disinfection and care of surfaces, safe water supply and consumption, use of personal hygiene items, and daily cleaning of clothing and footwear.

**Conclusion.** We emphasize the importance of hygiene as a fundamental tool in preventing communicable and non-communicable diseases. It is not only an essential practice for maintaining health but also a crucial element for establishing a proper balance between the individual and the surrounding environment. Although there are multiple ways to reduce the risk of illness and disease transmission, there is no single solution that ensures 100% efficiency in prevention. Therefore, it is necessary to adopt and maintain various hygiene habits to minimize the risk and protect our health.



## 28. PLAYGROUND DANGERS: A COMPREHENSIVE INVESTIGATION INTO CHILDHOOD INJURIES AND PARENTAL PERSPECTIVES

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**Introduction.** Playgrounds represent environments that occupy a significant point in shaping children's daily activities by providing room for social interaction and self-development. However, this role comes with a spectrum of associated risks, rendering playgrounds to potential injuries. Therefore, falls are depicted as the prevailing mechanism of harm across various types of playground equipment, with the incidence ranging from 58.7% for seesaw injuries to 90.1% for climbing equipment injuries.

**Aim of study.** The overall aim is assessing children's safety at the outdoor playground and parents' behaviour regarding children's safety at the playground.

**Methods and materials.** An observational mixed study using a questionnaire for evaluating outdoor playgrounds and a qualitative study using face-to-face interviews with parents of children under 7 years of age. Coding was done using MaxQDA qualitative research software in conjunction with narrative analysis. Parents or other carers of children under 7 were the study unit. The data were collected over 3 months and assess the hygiene aspects of outdoor playgrounds within Chisinau municipality, randomly selected from all 5 districts. A checklist was used to assess the state of hygiene and playground equipment in Chisinau municipality. For face-to-face interviews with parents, a guide with questions related to children's safety at outdoor playgrounds.

**Results.** In this research study, individual interviews were conducted near playgrounds in close proximity to playgrounds. Parents identified slides (7 out of 18), sandboxes (5 out of 18), and swings (4 out of 18) as the most hazardous play elements. Concerns raised by parents included insufficient sun protection, challenges in observing or maintaining vigilance over children at elevated heights, and the belief that a playground is only safe under constant supervision. The documented trauma incidents occurred during the summer of 2022. Contributing factors to these accidents were found to be parental inattention and the presence of aging elements in the playground. Parents reported accidents stemming from their children falling from elevated positions, such as slides, or slipping due to loose gravel.

**Conclusion.** This is the first research in the Republic of Moldova on playground injuries and is an encouragement to study this problem. The analysis of the interviews with parents gave a general idea about their knowledge in different aspects (from their perspective about the playground elements to the injuries that occurred or first aid). The study showed that playgrounds in Chisinau have more disadvantages than advantages. Based on this research, further preventive measures will be taken.

## 29. PSYCHOEMOTIONAL HEALTH OF MEDICAL WORKERS DURING PANDEMIC PERIOD



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**Introduction.** Health worker burnout was a crisis long before COVID-19 arrived. More than half of health workers report symptoms of burnout, and many are contending with insomnia, depression, anxiety, post-traumatic stress disorder, or other mental health challenges. Overwhelming requirements, a high degree of work, and prolonged exposure to emotionally demanding circumstances in work and life settings can lead to burnout syndrome.

**Aim of study.** The aim of study is to highlight burnout syndrome and its associated factors among medical workers during the COVID-19 pandemic.

**Methods and materials.** With this broad perspective in mind, to grasp the complexity of the problem, was analyzed a narrative review. A systematized review of literature was performed without date restrictions; it was conducted on Pubmed, Hinari, Google Academic.

**Results.** During the COVID-19 pandemic, healthcare workers have reported increased stress, depression, anxiety, sleep disturbances, and post-traumatic stress disorder conditions that are also associated with burnout. The crisis didn't start with COVID-19, but the last three years have exacerbated persistent mental unwellness and trauma among those workers. Due to permanent changes in the healthcare field, the conditions for mental tension and burnout change simultaneously with the reactivity to stress. Burnout results from job stress that accumulates over time and results in fatigue, cynicism, and a lost sense of control, contributing to disruptive behavior, lost workdays, and ultimately resignation or early retirement. The causes of burnout in the health professions are numerous, and the impact reverberates negatively throughout the organization and for their patients. The effects of burnout are not isolated to the workplace but often carry over into the health professional's personal life, impacting both the family and self. Health professionals, including nurses, physician assistants, pharmacists, and physicians, are more susceptible to burnout than the general population due to moral stress, increased regulations and bureaucratic requirements, excessive hours and on-call responsibilities, and increased productivity requirements.

**Conclusion.** The COVID-19 pandemic has worsened the mental health of healthcare workers. The combination of increased workload, decreased resources to care for patients and feeling unsupported by leadership has led to unprecedented dissatisfaction. Since the problem is multifaceted, physician burnout is a major threat to health care quality, patient outcomes, and the vitality of the medical workforce. Burnout represents a harmful condition that is plaguing modern medical institutions. Such occurrences represent a potential danger to the foundation of the medical professional, loss of possible revenue stream to the organization, and diminished patient care.



### 30. ROAD SAFETY KNOWLEDGE, ATTITUDES AND PRACTICES AMONG PEDESTRIANS

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**Introduction.** Road safety is an essential aspect in our modern society. Whether we are drivers, pedestrians or passengers, we are all involved in traffic and must be aware of the dangers and risks associated with it. Their knowledge, attitudes and practices play a key role in preventing accidents and ensuring safe mobility.

**Aim of study.** Assessment of pedestrian knowledge, attitudes and development of road safety measures among pedestrians.

**Methods and materials.** The given study is a descriptive, cross-sectional epidemiological study among students aged between 19-30 years. 150 young people from USMF "*Nicolae Testemitanu*" participated in the study. Students were exposed to a 15-question questionnaire assessing pedestrian safety knowledge, attitudes and practices.

**Results.** Most of the respondents included in the study are between 21-24 years old, the average being  $20.4 \pm 5$ . Of the total number of respondents, 23% answered that they frequently have to drive on the street because of illegally parked cars, 28% of them frequently avoid streets and dangerous intersections for crossing and 15% frequently listen to music through headphones while crossing the street or walking on the street. As pedestrians, 12% of them are very often disturbed by car drivers, in 8% by motorcyclists and in 2% by cyclists. When asked about the consumption of alcohol as a pedestrian, 30% believe that this very often can lead to an increased chance of accidents. Regarding the number of places intended for crossing the streets, the respondents reported that in 44% of cases they are rarely satisfied with it, they are not satisfied in 11% of cases.

**Conclusion.** Road safety for pedestrians largely depends on their knowledge, attitudes and practices. Continuous education and the promotion of a responsible attitude among pedestrians are essential to reduce the number of accidents. Every individual has a role to play in creating a safe road environment, and investing in pedestrian education is an investment in shared road safety.



### 31. THE CLIMATE CHANGE PROBLEM IN THE VIEW OF MEDICAL STUDENTS



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**Introduction.** Climate change has a significant impact on human health. Information about climate change is essential to identify, prevent and treat health problems that may be exacerbated or triggered by phenomena such as extreme heat, increased pollution levels or increased risk of infectious diseases. In light of these reasons, knowledge about climate change is essential for training future physicians, helping them to provide more comprehensive care and contributing to health promotion in a manner that takes into account the impact of climate change on human health.

**Aim of study.** Assessing medical students' level of knowledge about climate change and the importance of its study.

**Methods and materials.** A cross-sectional epidemiological study was carried out using an online questionnaire. In the study participated 122 2nd and 3rd year medical students. The data was collected throughout 2023 and was processed via Excel.

**Results.** The average age of the students was  $20.5 \pm 1.3$  years. 27.9% male respondents participated in the study, respectively 72.1% - female respondents. The analysis of the questionnaire data elucidates the following picture: 97% of the respondents believe that climate change is a problem impacting the health of the population. Respondents stated that extreme temperatures (93.3%), drought (83.3%), air pollution (95.5%), the hole in the ozone layer (68.2%), floods (60.6%) are caused by climate change. The main sources from which students get information about the issue of climate change are: the Internet (92.4%), television (39.4%), conferences/symposia (19.7%), family/friends (4.5%), courses held within educational institutions (25%). Regarding the need to include topics about this specific problem in the educational program, 94% of the students spoke favorably, the most requested topics being food and water security (60.6%), extreme temperatures (57.6%), air pollution (65.2%), vector-borne diseases (60.6%) and mental health (60.6%). Students consider it appropriate for these topics to be discussed during theoretical courses (39.4%), conferences (51.5%), fieldwork and activities (45.5%) and practical work (28.8%).

**Conclusion.** Climate change is a major concern for human health and should be studied and discussed in medical school courses with the purpose of training future physicians to manage and prevent its damaging effects on public health.



## 32. THE EPIDEMIOLOGICAL APPROACH TO WOMEN'S REPRODUCTIVE HEALTH

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**Introduction.** Multiple studies have been conducted on the risk factors that influence women's reproductive health: hormonal changes, fertility and different pregnancy outcomes, for example, miscarriage, congenital malformations, perinatal mortality, birth weight, alcohol consumption, smoking, obesity, infections. However, gynecological cancers are an increasingly prevalent and well-studied malignancy in today's world of female reproductive health.

**Aim of study.** Epidemiological study of reproductive health in women in the general population

**Methods and materials.** Articles from the last 5 years concerning reproductive health in women were selected and analyzed, using the PubMed, Medscape, NCBI databases

**Results.** The researched studies mention that there are a multitude of risk factors that act on reproductive health in women. From the review of studies dealing with women's exposure to chemical agents, pesticides, physical agents, ergonomic factors and stress, it appears that the evidence is currently sufficient to warrant maximum protection of pregnant women against several well-documented occupational risks. Smoking cessation interventions help reduce smoking, and both individual and group interventions to increase folic acid intake improve pregnancy outcomes. Behavioral factors and clinical and biomedical interventions affect a range of women's health conditions.

**Conclusion.** Representing half of the world's population, women help manage the epigenetic legacy of future generations through healthy pregnancies. There is also an urgent need to educate women about the importance of understanding the need to modify their lifestyle to avoid exposure to potentially harmful chemicals during pregnancy. Positive prevention in family planning is needed, including health education, regular screening and appropriate treatment of diseases of the reproductive system in women.

### 33. THE GLOBAL EPIDEMIOLOGY OF TETANUS



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**Introduction.** Tetanus, a bacterial toxin generated by *Clostridium tetani*, is the cause of the potentially fatal infectious disease. The illness damages the central nervous system, leading to severe muscle spasms and paralysis. Despite not being directly transmissible between people, tetanus remains a major global health concern.

**Aim of study.** Overview looks at the up-to-date information about the tetanus epidemic worldwide.

**Methods and materials.** A literature review was conducted. Analysis of literature sources and scientific articles retrieved from databases such as NihGov, PubMed, NCBI, ScienceDirect, World Health Organization reports and national statistics.

**Results.** The incidence of tetanus has demonstrated a notable decline over the past two decades, with rates decreasing from 6.9 per 100,000 total population in 2002 to 0.9 in 2022. The most significant improvements have been observed in countries within the African, South-East Asia, and Western Pacific regions. These countries, which were late adopters of immunization programs and experienced high infection rates, have achieved particularly commendable results. However, the incidence of tetanus exhibits notable spatial variation, especially in areas with limited medical infrastructure and restricted access to vaccines, where infection is more susceptible to widespread. Despite vaccination efforts, tetanus remains a health concern in some developing countries, where poor hygiene conditions and unclean wounds facilitate bacterial entry into the body.

**Conclusion.** Tetanus, though controlled through vaccination and improved medical care, faces challenges. Sustaining collective immunity and universal coverage are crucial. Initiatives for tetanus eradication are needed due to unequal access to medical care and immunizations. Key actions involve modifying health policies, assessing vaccination efficacy, and monitoring incidence rates. Challenges persist in achieving a tetanus-free world, requiring international coordination, resources, and community education.



### 34. THE IMPACT OF MODERN HOUSEHOLD CHEMICALS ON HUMAN HEALTH IN THE REPUBLIC OF MOLDOVA

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**Introduction.** In the modern world, household chemicals are an integral part of the life of every person, therefore the influence of household chemicals on human health is an actual problem. Modern household chemicals include such dangerous chemicals as: chlorine, phosphates, formaldehyde, phenol, phthalates (DIDP, DNOP), polymers, silicates. According to research, household chemicals cause the greatest harm to the skin, respiratory and reproductive systems. The respiratory system is most affected by volatile substances such as acetone, benzene, formaldehyde, which are part of cleaning sprays. The harm of these substances is associated with a high risk of developing asthma. The harm of detergents designed to remove grease and mold is directly linked to the development of eczema and dermatitis. A group of chemicals called endocrine disrupting chemicals (EDCs), found in many cleaning products, can affect the quality of sperm and eggs.

**Aim of study.** The aim of the study was to find out the awareness of part of the population of the Republic of Moldova about the dangers of household chemicals, about compliance with protective measures when using household chemicals.

**Methods and materials.** For the purpose of the study a social questionnaire was created. The survey included 150 people, aged from 16 to 50 years, male and female, from different localities of the Republic of Moldova.

**Results.** The majority of respondents were women – 68,6%, compared to men-31,4%. Age of the people ranged from 16 to 50 years, with an average age of  $28.4 \pm 0.3$  years. According to the survey, 97% of respondents use household chemicals every day. Unfortunately, only 25% of respondents read the chemical composition of detergents when purchasing. According to the data obtained, 88% of respondents are aware of the possible dangers of household chemicals. Approximately 68% of respondents know about safety measures when using household chemicals, but only 17% of respondents comply with these measures. Regrettably, only 24% of people (most of whom are students and medical workers) know how to provide first aid for acute poisoning from household chemicals. Also, approximately 61% of respondents know about the existence of alternative household cleaning products.

**Conclusion.** The use of modern household chemicals by the majority of the studied population in the Republic of Moldova can have serious health consequences, since most people do not pay attention to the composition of household chemicals when purchasing, do not know about safety measures when using household chemicals and the existence of alternative cleaning methods.

### 35. THE PSYCHOLOGICAL IMPACT OF NOSOCOMIAL INFECTION: A SYSTEMATIC REVIEW



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**Introduction.** Nosocomial infections are a burden on society and a public health problem. The diagnosis of a serious somatic illness is a strong stressor. At this stage, the man is gripped by fear and despair. Restlessness and helplessness create the conditions for severe emotional stress. The association of a nosocomial infection during treatment causes an additional series of personality changes, which leads to an increase in the degree of psycho-emotional instability: anxiety, depression, behavioral disorders, suicide, etc., as well as poorer social reintegration.

**Aim of study.** Systematic review of bibliographic references on the psychological impact of nosocomial infections.

**Methods and materials.** A bibliographic study was carried out, the search engine included the keywords: nosocomial infection, psychological impact, depression, on the search platforms PubMed, Google Scholar and EMBASE. Over 100 sources were analyzed, of which 17 met the research themes and inclusion criteria.

**Results.** According to Abbate & Di Giuseppe's research, the most difficult nosocomial infections to treat are the MDR ones, such as *S.aureus* MRSA positive and *Cl.difficile*. Superinfection has been found to be associated with prolonged length of hospital stay, additional costs to the health sector internationally and increased mortality. At the same time, according to Peterson's studies, it has been shown that stress increases susceptibility to infections, but also post-operative recovery, tissue regeneration. According to Kaptein & Broadbent's research, the person perceives the disease on a cognitive and emotional level. Following the systematic analysis of the specialized literature, the anxiety and depression scales applied to patients were highlighted in order to evaluate the emotional impact following isolation measures in the case of the addition of nosocomial infections. Thus, following empirical analysis and meta-analysis, cumulative mean difference estimates were determined for the anxiety scale ( $P=0.15$ ) and for the depression scale ( $P=0.09$ ). Results from meta-analysis and empirical analysis of psychological burden determined that isolated patients with nosocomial infections showed more pronounced personality effects than non-isolated patients or without nosocomial infections. The estimated implied cost per day of anxiety and depression in terms of quality-adjusted life years (QALYs) is approximately \$10.

**Conclusion.** The interdisciplinary application of sanitary-hygienic measures to prevent nosocomial infections, but also the psychological support of patients, is the key to success in achieving their physical and psycho-emotional well-being.





### 36. THE ROLE OF NUTRITION AND PHYSICAL ACTIVITY IN THE DEVELOPMENT OF OBESITY AMONG PRESCHOOLERS

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**Introduction.** According to the Republic of Moldova's Summary Report about the preschooler's health behaviors 11% of children suffer from ponderability, also 2,2 % from obesity. Nowadays it has become the fourth cause of death, which induces the importance of studying this subject.

**Aim of study.** To identify the role of alimentation and physical activity regarding obesity in children aged 3-7 years.

**Methods and materials.** Were used „Pubmed MEDLINE,, database to select relevant articles published from 2014-2023, using the key words „children obesity”, alimentation of children, risk factor of obesity . Were found 213 sources: 174 articles, 30- reviews, 4- Clinical trials, 5-meta analysis.

**Results.** For the last 9 years a continuously increasing rate of obesity among children has been highlighted, becoming a pressing public health concern. Unhealthy dietary habits and lack of physical exercises remain decisive factors to this alarming trend. Parents do not know how to provide a safe model of nutrition in order to prevent obesity and educators, as well people who provide medical services do not inform about this important component of a healthy lifestyle. The impact of this lack of action on the part of the trainers of children's health habits is huge. It extends beyond the physical and mental well-being of children and increases the risk of developing chronic diseases in adulthood.

**Conclusion.** Childhood obesity between preschoolers requires a multicentric approach that involves healthy behaviors promotion and the community involvement in order to create conducive environments to active living and choices about nutrition. A good way to prevent this global issue is to induce changes in three levels : attitude of parents,educators,doctors also physical activity and energy intake. It is a duty of everyone to improve the health system by improving first their lifestyle, educating healthy habits in their children's lifestyle and in the limits of their possibility to guide the parents and educators in this line.

### 37. THE WATER – SOURCE OR VEHICLE FOR SPREADING ANTIMICROBIAL RESISTANCE?



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**Introduction.** Antimicrobial resistance is considered a threat to public health by the World Health Organization, and by 2050 it could become a hazard causing up to 10 million deaths yearly. It is all the more dangerous as it involves all elements of the environment, both as a reservoir and as a mode of transmission of resistant bacteria or their components (MGEs and ARGs) known as resistome. Water is considered to be the main vehicle for spreading the antimicrobial resistance, as 92% of ARGs found in water is also found in other environmental elements.

**Aim of study.** To elucidate the role of water in the development of antimicrobial resistance and its dangerousness as a reservoir of various resistomes.

**Methods and materials.** 372 articles were retrieved from PubMed (n=225) and Scopus (n=147) databases using the keywords “antimicrobial resistance”, “resistome”, “water” and “ARGs”. In the final research, 16 full-text articles were included.

**Results.** Seven studies claim that wastewaters either hospital or urban are the main source of antimicrobial resistance in the environment and other water bodies. Groundwaters are often contaminated with ARGs from wastewaters and consumed without treatment. Liu et al. determined over 1000 ARGs belonging to 37 ARG types in the global groundwater, dominated by rifampicin and quinolone resistance genes. Another paper from Liu et al. argues that freshwater lakes are the main reservoir of ARGs and resistomes due to their long retention in the water, hence the extended possibilities of antimicrobial resistance evolution in bacteria. The paper of Spänig S. analyzed the ARGs detected in 274 European lakes and showed that lakes from Romania, Germany and France are important reservoirs of cephalosporin resistance genes. On the other hand, Lee et al. consider the rivers to be the main channels for human exposure to antimicrobial resistant bacteria or their elements. They identified a resistome comprising 65 ARG subtypes, but

**Conclusion.** Aquatic environment has an important role in spreading and maintaining the AMR cycle as all waterbodies collect the ARGs and resistant bacteria from other environments and its roles as source and spreading vehicle can't be dissociated. Also, each type of water body carries its own resistome that endangers human health and environmental safety.



### 38. VIOLENCE PREVENTION IN PHARMACIES

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**Introduction.** Pharmacists, being the healthcare team members most easily reachable and commonly interacted with, may face a higher risk of encountering violence compared to other healthcare professionals. Violence against pharmacists can have various negative outcomes, affecting individuals, communities, and the healthcare system as a whole. It may contribute to decreased job satisfaction and a negative work environment, leading pharmacists to reconsider their career choices. Constant fear of violence can contribute to burnout, negatively affecting the overall well-being of pharmacists.

**Aim of study.** Workplace violence can include physical violence, verbal abuse or other forms of aggressive behaviour. Preventing violence can ensure a safe working environment for pharmacists. Implementing effective strategies and developing appropriate behaviour can significantly reduce the risk of violence.

**Methods and materials.** A cross-sectional descriptive study among 155 pharmacists aged 20 to 60 years was conducted from February 2022 to May 2023 using the online questionnaire "Workplace violence surveillance among pharmacists". The questionnaire included three sections (general information, most serious event in your experience and prevention strategies).

**Results.** The survey interviewed 155 pharmacists, 82.5% of whom were women and 17.5% men. Within the past 16 months, the respondents encountered incidents of violence in community pharmacies. Verbal violence was reported in 49.0% of cases, acts of theft with violence - 29.6% of cases. Out of the total number of respondents, 80.6% did not participate in training on prevention of violence at work. According to the questionnaire, 62.5% answered that the pharmacy contributes to the reduction of violence through CCTV systems, alarms, security, and lighting of dangerous areas. However, 44.5% mentioned that other forms of ensuring safety in the workplace are also necessary.

**Conclusion.** Training employees on violence and undertaking all safety measures can contribute to a favourable working environment. Efforts to prevent violence against pharmacists include implementing security measures, providing training in conflict resolution, and promoting awareness about the importance of a safe working environment. Community education and collaboration with law enforcement can also contribute to reducing the incidence of violence in pharmacies. It is crucial for healthcare institutions, law enforcement, policymakers, to collaborate in creating a safe and supportive environment for pharmacists to fulfill their vital role in healthcare delivery.

### 39. WEIGHT SELF-PERCEPTION IN ADOLESCENTS: EVIDENCE FROM A POPULATION-BASED STUDY



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**Introduction.** Exploring the nuanced relationship between weight and self-perception in adolescents is a crucial aspect of understanding their mental and physical well-being. Through a population-based study, we delve into the evidence surrounding how adolescents perceive their weight and its impact on their overall self-image.

**Aim of study.** To assess misperceptions regarding weight among adolescents and identify links between self-perceived weight and socio-demographic factors, screen time, self-assessed food quantity and quality, weekly breakfast frequency, and the consumption of both healthy and unhealthy foods.

**Methods and materials.** This study is based on a study in which a questionnaire was used that was answered by 101 students aged 15-18.

**Results.** Nearly half (53,1%) of the adolescents with overweight/obesity did not evaluate their weight properly. Associating perceptions of being thin or carrying excess weight was notably influenced by multiple factors. These inclinations were linked to gender, particularly females, individuals grappling with overweight/obesity, self-assessed diet quality as poor/very poor, and a habit of consuming snacks  $\geq 3$  times per week. Moreover, a pattern emerged where daily breakfast consumption appeared to reduce the likelihood of perceiving oneself as thin. On the other hand, excessive eating habits seemed to heighten the likelihood of this perception. Interestingly, those consuming cookies/crackers  $\geq 3$  times per week seemed less inclined to perceive themselves as having excess weight. 46.9% of teenagers believe that weight loss diets can have a negative impact on health. (56.3%) say that among the negative effects of weight-loss diets, the most important is the impact on mental health, (46%) of teenagers consider that the previous weight returns after the interruption of the diet and (33.3%) that there are important nutritional deficiencies. However, the biggest finding is that (89.1%) of teenagers say that they have never been guided by a specialist in choosing a weight loss diet.

**Conclusion.** Greater weight misperception was found in overweight/obese adolescents. Self-rated food quantity/diet quality, weekly frequency of breakfast and some unhealthy foods were associated with self-perceived weight. Conclusively, the prevalence of weight misperception among overweight/obese adolescents underscores the need for targeted interventions to address this issue. The significant associations discovered between self-perceived weight and various socio-demographic attributes, coupled with the misconception regarding weight loss diets among teenagers, signal a crucial need for comprehensive education and guidance on healthy lifestyle practices. Moreover, the concerning revelation that a vast majority of adolescents have never sought guidance from specialists when opting for weight loss diets demands urgent attention. The present findings could contribute to health promotion strategies targeting adolescents.



## ***XXII. RADIOLOGY SECTION***



## 1. IMAGING DIAGNOSIS IN RECTAL CANCER



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**Introduction.** Rectal cancer represents a significant weight in oncological pathology, constituting around 4-5% of all cancers, being one of the most common locations of cancer in the human intestine. It predominantly affects the elderly, with most cases occurring in people aged 50 and over. According to the latest WHO data published in 2020, rectal cancer deaths in the Republic of Moldova reached 1,030 or 2.67% of the total number of deaths. The age-adjusted death rate is 17.43 per 100,000 inhabitants. One year after rectal cancer detection, in the Republic of Moldova, approximately 98 (18%) diagnosed patients die. This disease predominantly affects individuals from the urban residence, mostly men, the ratio between men/women being 1.11/1.. In this context, imaging plays a primary role in establishing the diagnosis and subsequently the treatment strategy of rectal cancer. Such investigations as Irigoscopy, Colonoscopy, MRI, CT represent the basic source in providing information regarding the pathology.

**Aim of study.** Assessment of imaging informativeness in the diagnosis of rectal cancer in order to establish the optimal imaging method.

**Methods and materials.** The study carried out in the imaging diagnosis of rectal cancer was based on the research of specialized literature and medical files from the archive of the Oncological Institute.

**Results.** According to the gender the diagnosis of rectal cancer is more common among men than women, the age that this disease occurs varies between 50 - 60 years old.

**Conclusion.** Each imaging modality has its own strengths and limitations, and the choice of imaging technique depends on the specific clinical scenario and the information needed for treatment planning. In the Republic of Moldova the golden standard for diagnosing rectal cancer is colonoscopy.



## 2. IMAGING DIAGNOSIS OF MULTIPLE SCLEROSIS

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**Introduction.** Multiple sclerosis (MS) is a chronic and disabling autoimmune disease of the nervous system that affects more than 2.9 million people worldwide. Early detection of MS is essential to initiate appropriate therapy and management strategies that can help slow disease progression and prevent disability. The main role in the diagnosis of MS is occupied by imaging methods.

**Aim of study.** To identify the imaging methods used in the diagnosis of MS and to underline the imaging particularities of the pathological changes characteristic of MS.

**Methods and materials.** A literature review was done, by searching the scientific articles on Google Scholar, PubMed, Cochrane, Elsevier, published in the last 5 years, using keywords “diagnosis of MS”, “MRI changes in MS”, “cerebral changes”, “MRI criteria”.

**Results.** MRI is the most common imaging method for diagnosing MS, providing high-quality images of the brain, optic nerve and spinal cord to identify lesions. Other radiological and imaging techniques used in the diagnosis are positron emission tomography, single photon emission computed tomography and optical coherence tomography, fluid attenuated inversion recovery, MR spectroscopy. Imaging methods can detect areas of demyelination in the brain and spinal cord, which are the main characteristics of MS, these areas appear as hyper-, hypointense spots on MRI, specific signs are "black holes", "Dawson's fingers", as another manifestation cerebral atrophy may occur. Based on these imaging changes and clinical manifestations, the McDonald diagnostic criteria were created.

**Conclusion.** Imaging methods are widely used in the evaluation of patients with MS and provide important imaging data for clinical and differential diagnosis, staging and later aid in effective management.

### 3. TACTICS OF IMAGING INVESTIGATIONS IN THE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA



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**Introduction.** Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for approximately 85-90% of all cases. It is unique among malignancies shown on imaging investigations, allowing an accurate diagnosis without an invasive biopsy.

**Aim of study.** Analysis and determination of optimal investigations in the detection of hepatocellular carcinoma.

**Methods and materials.** A literature review of the scientific literature specialized in hepatocellular carcinoma imaging was done. There were used scientific articles from PUBMED, NCBI, Radiopedia databases.

**Results.** A significant sensitivity has been reported using ultrasonography, ranging from 34 to 100%. Another attractive method is computed tomography (CT) with contrast substance, as it allows the detection, characterization and clinical staging of liver lesions. One study from the USA found that CT scanning showed increased sensitivity for HCC detection compared to USG or AFP, while another study found US and CT to have comparable sensitivity and specificity. In recent years, magnetic resonance imaging in angiographic mode has been noted for better detection of liver lesions. Lesion detection rates of 80% for nodules >2 cm, 50% for nodules 1–2 cm, and 33% for lesions <1 cm were reported in one study that concluded that MRI was insensitive for detecting HCC nodules <2 cm in patients with cirrhosis. However, a more recent study in cirrhotic patients reported that the presence of delayed hypointensity in patients with arterial-enhancing liver lesions had a sensitivity of 80% and a specificity of 95% for small (<2 cm) HCC.

**Conclusion.** The diagnosis of HCC is based on the assessment of attenuation differences on CT and signal intensity on MRI, these being the optimal investigations in detection of liver cancer. However, for a better diagnosis, it is necessary to perform at least two investigations: USG/CT, USG/MRI or CT/MRI, especially in the case of small formations in the liver.



#### 4. THE ROLE OF NUCLEAR MEDICINE INVESTIGATIONS IN DIAGNOSIS AND MANAGEMENT OF BREAST CANCER

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**Introduction.** It should be pointed out that breast cancer is the most common pathological tumor among women worldwide. Nuclear medicine investigations, such as whole-body bone scintigraphy, offer possibilities for diagnosis, personalized treatment and post-treatment follow-up. Based on the fact that breast cancer most often metastasizes to the bones, we can analyze the importance of nuclear medicine screenings.

**Aim of study.** For over five decades, radiopharmaceuticals have been employed to study breast cancer according to recent guidelines. The role of nuclear medicine, which began in the 1990s when the radiotracer Tc-99m was first used to directly detect breast cancer, is seeing progress. Bone scintigraphy is the classic method of confirming metastasis to the skeleton.

**Methods and materials.** The retrospective descriptive study included 42 patients with diagnosed, histopathological proven breast cancer. They were investigated with administration of the radioactive tracer Tc99m-MDP by WB bone scintigraphy at Gamma Camera AnyScan S in the Nuclear Medicine Laboratory of the Oncological Institute of the Republic of Moldova during May-July 2023.

**Results.** The study enrolled 42 patients with breast cancer, with an average age of  $62.07 \pm 10.91$  years. Among the participants, 4 patients (9.52%) exhibited metastatic skeletal bone lesions. In 22 cases (52.38%), suspicious changes for secondary involvement were identified, necessitating further imaging investigations, including radiography (Roentgen), computed tomography (CT), and magnetic resonance imaging (MRI) to confirm the diagnosis. For 16 patients (38.10%), the nuclear medicine investigations revealed non-specific findings for secondary spread. The results highlight the potential of nuclear medicine investigations in early detection of metastases in the bone system.

**Conclusion.** In conclusion, the results of this study emphasize the significant role of nuclear medicine investigations in diagnosing and managing breast cancer, particularly in the context of skeletal bone metastases. WB bone scintigraphy offers essential information, which has efficacy in influencing therapeutic decisions and potentially improving patient outcomes. These findings underscore the importance of integrating nuclear medicine into the comprehensive care of breast cancer patients for more personalized and effective treatment approaches.

## 5. ULTRASONOGRAPHIC DIAGNOSIS OF THYROID NODULES



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**Introduction.** Thyroid nodules are very common in the general population, the diagnostic method is easily accessible with a high prevalence found in the ultrasound examination (US), ranging from 20% to 76% in the adult population. The specificity was 92.3% and 88.7% respectively. Differentiation of malignancy is an important clinical process, as malignancy occurs in 7-15% of detected thyroid nodules, depending on various risk factors. Various combinations of ultrasonographic (US) features are increasingly used to classify thyroid nodules. Ultrasonography is one of the most sensitive and widely used methods for detecting thyroid nodules.

**Case statement.** Ultrasonographic diagnosis of thyroid gland nodules will allow the early identification of both malignant and benign tumors of the thyroid gland. The study was carried out based on examinations of 20 patients. We studied the quality of ultrasonographic diagnosis in the detection of thyroid gland nodules and we evaluated the success of the ultrasonographic method in the diagnosis of thyroid gland nodules by comparing other methods, such as ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), radiography. We have identified the factors that affect the results of the diagnosis of thyroid gland nodules, such as the size of the nodules, their location, the presence of visualization complications.

**Discussions.** Currently, real-time high-resolution US not only detects the presence, location, number and size of thyroid nodules, but also clearly shows the characteristics of thyroid nodules. Some authors have reported the ultrasound diagnosis of thyroid nodules of all types with relatively high sensitivity ranging from 74% to 81%, but no formulas based on feature analysis are available to predict malignancy. Therefore, we prospectively evaluated the US characteristics of thyroid nodules and analyzed the probability of malignancy based on multiple logistic regression analysis.

**Conclusion.** An ultrasonographic examination is a safe, non-invasive and rapid imaging technique: it is quite sensitive for detecting thyroid nodules of various sizes and identifying suspicious features and can be used to plan further investigations and management. Considering that the average prevalence of thyroid nodule malignancy is variable and ranges from 4.0% to 6.5%, accurate estimation of the risk of malignancy in the US could minimize the detection of advanced stage cancer.





## **XXIII. MEDICAL REHABILITATION SECTION**

***„În reabilitarea medicală, cel mai important lucru de înțeles este că fiecare pas înainte contează. Recuperarea este un maraton, nu un sprint. Răbdarea împreună cu perseverența sunt cheile succesului în acest domeniu.”***

***"In medical rehabilitation, the most important thing to understand is that every step forward counts. Recovery is a marathon, not a sprint. Patience along with perseverance are the keys to success in this field."***

***Oleg Pascal,***

*MD, PhD, Professor*

*Head of Department of Medical Rehabilitation, Physical Medicine and  
Manual Therapy*

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## 1. FUNCTIONAL PECULIARITIES IN THE RECOVERY OF PROSTHETIC GAIT IN PATIENTS WITH UNILATERAL TRANSTIBIAL AMPUTATIONS



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**Introduction.** Recovery of functional abilities caused by amputation is an important indicator of medical rehabilitation and a functionally independent person is more motivated for social life. Prosthetics appreciably improves the functional status of the lower limb amputee, and gait patterns are often adaptive and aimed at maintaining balance, static and dynamic coordination.

**Aim of study.** Was to analyze the impact of active kinetic methods on gait rehabilitation outcomes after transtibial amputations.

**Methods and materials.** The study included 140 individuals after unilateral, transtibial amputation of diabetic genesis, randomly divided into two groups of 70 patients. Both groups received conventional rehabilitation treatment and the experimental group was involved in active kinetic programs with a focus on prosthetic gait balance re-education. Integral functional abilities were assessed by using the Tinetti Scale and gait outcomes, the qualitative (points) and quantitative (seconds) "Up & GO" test, and gait autonomy scale at admission, after 1 and 6 months.

**Results.** The mean age of the individuals was  $60.4 \pm 2.9$  years, and 79.5% were men. Improvement in the quality of the prosthetic gait was observed from the first month in both groups - with a decrease in the maximum value of 25 seconds of the quantitative "Up & GO" test. There was an increase in the proportion of people who recorded values of 11-15 seconds after the first month of treatment (by 25% compared to the control group with this level maintained after 6 months. The qualitative "Up & GO" test in dynamics recorded maximum values of 10-12 points in 18.6% of cases in the control group versus 68.3% in the experimental group. The Tinetti Scale gait balance registered a positive dynamic after 6 months by reaching a maximum score of 7 points in 45.8% of the control group and 21.4% of the experimental group. Also gait autonomy was achieved for 38.9% of the experimental group compared to 12.9% of the control group.

**Conclusion.** Comprehensive rehabilitation programs, with active kinetic methods, significantly enhanced the functional status after transtibial amputations. The integration of kinetic active techniques positively influenced both qualitative and quantitative parameters of prosthetic gait, with a notable difference of 28% in the dynamics of the "Up & GO" test and 24.4% for the Tinetti test in favor of the experimental group.

**Keywords.** Transtibial amputations, prosthetic gait, medical rehabilitation, prosthetics.



## 2. MEDICAL REHABILITATION PROGRAMMES FOR MUSCULOSKELETAL DISORDERS IN PATIENTS WITH DIABETES MELLITUS

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**Introduction.** Background. Diabetes is a global burden and can have fatal consequences for human health and a significant impact on the health system economy. Diabetes is a metabolic disease that can cause severe complications and mortality if not treated effectively and quickly. Musculoskeletal disorders in patients with diabetes are a significant concern in the management of this chronic condition.

**Aim of study.** Objective of the study. Improving medical rehabilitation programmes for diabetes patients with musculoskeletal disorders, including the development and introduction of new high-tech methods of treatment and prevention of its complications.

**Methods and materials.** 35 selected scientific publications were analyzed from PubMed, Hinari, MedScape and Medline.

**Results.** Kinetotherapy is an important step in the rehabilitation of diabetic patients, the main beneficial effects include: improved glycemic control, increased insulin sensitivity with decreased insulin requirements in insulin-dependent patients, improved plasma lipoprotein profile and weight loss through reduced fat mass. Magnetolaser therapy influences the metabolic parameters of diabetes mellitus, contributing to lower blood glucose, lower hyperlipidaemia and improved microcirculation. Pulse frequency is 37-50 Hz, exposure is gradually increased from 2.5-3 to 7.5 minutes. The method is indicated for patients with micro and macroangiopathy of the lower extremities grade I-III, disorders of the microcirculatory system, spastic disorders and atonic vascular states. Electrostimulation helps prevent muscle atrophy, increase contractility, muscle tone and performance. Indications for electrostimulation programming: impaired glucose tolerance, metabolic syndrome, diabetes in the compensated stage, osteochondrosis, arthrosis. Ozone therapy is a non-invasive method with immunomodulatory, anti-inflammatory, antibacterial, antiviral, analgesic and antifungal effects. Intravenous ozone therapy in combination with physiotherapy reduced mean fasting blood glucose indices by 18.7%. A study of patients with type 1 diabetes who underwent exercise in combination with autologous bone marrow stem cell transplantation shows a significant decrease in mean HbA1C.

**Conclusion.** Medical rehabilitation programmes are an essential component in the comprehensive approach to diabetes and musculoskeletal conditions. A multidisciplinary, personalized and education-oriented approach that has a significant impact on patients' health and quality of life.

**Keywords.** Diabetes mellitus, rehabilitation, musculoskeletal disorders, glycaemia, immunomodulator, angiopathy, microcirculation, therapy.

### 3. PHYSICAL-KINETIC REHABILITATION METHODS IN TREATMENT OF SCAPULOHUMERAL PERIARTHRITIS.



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**Introduction.** Periarthritis of the shoulder joint, commonly known as frozen shoulder syndrome, is prevalent in 80% of rheumatic shoulder diseases and mostly affects women aged 40-60. It significantly reduces mobility and increases shoulder joint pain, impacting daily activities and quality of life. Conventional treatments often don't fully alleviate symptoms, highlighting the need for physical-kinetic rehabilitation methods that focus on improving shoulder functionality and reducing pain through tailored exercise programs.

**Aim of study.** This literature review aims to evaluate the effectiveness of physical-kinetic rehabilitation methods in scapulohumeral periarthritis.

**Methods and materials.** A comprehensive search was performed in databases like PubMed to identify studies on the effectiveness of physical-kinetic rehabilitation methods in treating scapulohumeral periarthritis.

**Results.** Literature data suggest the importance of physical therapy for scapulohumeral periarthritis. Studies have shown that physical therapy is crucial for managing scapulohumeral periarthritis, studies showing its effectiveness, either alone or alongside other treatments, in improving shoulder function and reducing pain. Therapy varies by phase: the freezing phase focuses on pain management and gentle mobilization, the frozen phase on improving range of motion with active exercises, and the thawing phase on restoring full functionality with intensive exercises. These techniques are personalized to individual patient needs and may be combined with other treatments like medication and manual therapy techniques.

**Conclusion.** The review concludes that effectively treating frozen shoulder requires a combination of various physical therapy interventions tailored to each stage of the disease. This approach emphasizes the importance of personalized rehabilitation strategies in managing frozen shoulders, adapting therapy to the specific needs and progress of the patient at each stage of the condition.



#### 4. THE IMPACT OF KINESIOTHERAPY TECHNIQUES ON PATIENTS WITH PRIMARY CHRONIC LOW BACK MUSCULOSKELETAL PAIN.

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**Introduction.** The treatment with kinesiotherapy techniques for patients with primary chronic low back musculoskeletal pain reflects a comprehensive and effective approach to its management and recovery. Currently, the significant importance of personalized kinesiotherapy exercises and techniques is emphasized in reducing pain, restoring functionality, and improving the quality of life for patients. These techniques not only address symptoms but also provide long-term benefits, contributing to the prevention of recurrence and enhancing individual capacity for adaptation and management of chronic musculoskeletal pain. The integration of kinesiotherapy into treatment plans is becoming increasingly relevant, standing out as an essential role in the rehabilitation of patients with such conditions.

**Aim of study.** Assessing the impact of kinesiotherapy techniques on patients with primary chronic musculoskeletal low back pain.

**Methods and materials.** Musculoskeletal functional deficiencies were assessed in 40 patients with primary chronic musculoskeletal low back pain. The pain was initially evaluated and reassessed after kinesiotherapy interventions using the Visual Analog Scale, and quality of life – through the EQ-5D-5L Health Questionnaire.

**Results.** Initially, primary chronic musculoskeletal low back pain was observed in 100% of cases, with 14.2% of cases experiencing mild pain, 65.4% - moderate pain, and 20.4% severe pain. After rehabilitation interventions using kinesiotherapy techniques, pain decreased to 33.4% of cases, including 14.3% with moderate pain, 17.41% of cases with mild pain, and 2% of cases with severe pain. The EQ-5D-5L Health Questionnaire initially presented the following levels: Level 1 - 0.41%, Level 2 - 20.5%, Level 3 - 58.5%, Level 4 - 6.6%, and Level 5 - 0.81%. In the final assessment, the distribution was as follows: Level 1 - 3.8%, Level 2 - 54.3%, Level 3 - 45.1%, Level 4 - 4.8%, and Level 5 - 0.80%.

**Conclusion.** Kinesiotherapy techniques had a significantly positive impact on patients with primary chronic musculoskeletal low back pain by improving the initial functional status, reducing pain, and enhancing the quality of life.



## 5. THE INFLUENCE OF CHRONIC PAIN ON QUALITY OF LIFE, FUNCTIONAL IMPAIRMENT, AND MOOD IN PATIENTS WITH SPINAL CORD INJURY



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**Introduction.** Chronic pain is a pervasive challenge in patients with spinal cord injury (SCI), significantly impacting their overall well-being. This theoretical study aims to explore the intricate relationship between chronic pain, quality of life (QoL), functional impairment, and mood in individuals living with SCI.

**Aim of study.** To study the influence of Chronic Pain on Quality of Life, Functional Impairment, and Mood in Patients with Spinal Cord Injury.

**Methods and materials.** This theoretical exploration involves a comprehensive review of existing literature on chronic pain in SCI patients. Relevant articles, studies, and clinical reports were analyzed to elucidate the multifaceted connections between chronic pain, QoL, functional impairment, and mood. To analyze and achieve the set goal of the study. So something is taken from the following sources: PubMed, ScienceDirect and Biomedcentral databases. For advanced selection of literature sources were applied articles (preclinical, clinical and experimental studies) in English.

**Results.** The review highlights the profound influence of chronic pain on the QoL of individuals with SCI, encompassing physical, emotional, and social dimensions. Functional impairment, both directly related to SCI and exacerbated by pain, contributes to a cascade effect on overall well-being. Mood disturbances, depression and anxiety, emerge as common consequences of chronic pain in this population.

**Conclusion.** Understanding the intricate dynamics of chronic pain in individuals with SCI is imperative for developing effective interventions that address not only the physical aspects but also the broader dimensions of their well-being, such as quality of life, psycho-emotional support and help with life adjustment. Research should attempt to validate and refine the theoretical insights provided herein, guiding the development of targeted interventions for this vulnerable population.



## **XXIV. STOMATOLOGY SECTION**

***„Stimați participanți la Congresul Medical Internațional pentru Studenți și Tineri Medici MedEspera 2024,***

***Din numele Profesorilor Facultății de Stomatologie vă aducem sincere Felicitări pentru implicarea voastră în acest important Congres! Este o dovadă a dedicării și pasiunii voastre de a căuta în continuă dezvoltare a cunoașterii și aprofundării științifice în domeniul medicinei moderne. Participarea voastră la acest eveniment nu numai că vă oferă oportunitatea de a vă îmbogăți cunoștințele și de a vă întâlni cu colegi din întreaga lume, dar și de a contribui la progresul inovativ medical. Să vă bucurați de această experiență, să împărtășiți idei și să vă inspirați unii pe alții în călătoria voastră academică și profesională. Fie ca fiecare prezentare, discuție și interacțiune să vă aducă mai aproape de realizarea visurilor voastre în domeniul medicinei. Succese în toate prezentările voastre și să fiți plini de noi cunoștințe și perspective care să vă îmbogățească parcursul științific medical! Să continuați să vă îndrumați unii pe alții să vă susțineți reciproc în drumul vostru către succese și împliniri profesionale. Vă doresc succese tuturor și inspirație în toate eforturile voastre.”***



***"Dear participants of the International Medical Congress for Students and Young Doctors MedEspera 2024,***

***On behalf of the Faculty of Dentistry professors, we extend our sincere congratulations for your involvement in this important Congress! It is a testament to your dedication and passion for continuous pursuit of knowledge and scientific exploration in the field of modern medicine. Your participation in this event not only provides you with the opportunity to enrich your knowledge and meet colleagues from around the world but also to contribute to innovative medical progress. Enjoy this experience, share ideas, and inspire each other in your academic and professional journey. May each presentation, discussion, and interaction bring you closer to realizing your dreams in the field of medicine. Success in all your presentations and may you be filled with new knowledge and perspectives to enrich your medical scientific journey! Continue to guide each other, support one another in your path towards professional success and fulfillment. Wishing you all success and inspiration in all your endeavors."***

***Oleg Solomon,***

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## 1. ABSOLUTE ANCHORAGE BY ORTHODONTIC IMPLANTS IN THE TREATMENT OF DIFFERENT DENTAL MALPOSITIONS. CASE REPORT

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**Introduction.** Absolute anchorage using orthodontic implants represents a new orthodontic paradigm and is perhaps the most important advancement in recent times, as it provides orthodontics with the principle of "action without reaction," virtually eliminating Newton's third law. Microimplants are screws that are inserted into the jaw and serve as a support for the movement of the teeth that need to be corrected during orthodontic treatment.

**Case statement.** Patient C. L., 14 years old, diagnosed with Angle class I dento-maxillary anomaly, associated with upper and lower incisor-canine crowding, deep occlusion degree 1 in the frontal region, ectopy and entopia in the frontal region, dolichocephalic growth, the patient suffering from sdr. Marfana. The treatment plan was made thanks to the thorough examination: photostatic examination, orthopantomography, telerradiography, intraoral scanning and study models. The patient benefited from orthodontic treatment with the self-ligating Damon System/ Damon Q technique. During the orthodontic treatment stage, the retention of d. 47 was confirmed by OPG. The extraction of d. 48 was performed. After 4-6 months, a Vector Tas 10mm x 2mm orthodontic mini-implant was inserted in the retromolar region. The button was also fixed on d. 47 the distal surface. Orthodontic forces were applied on the same day. After 2 months, the button was reattached in the mesial region of d.47, and the position of the mini-implant was not changed. No complications were observed after orthodontic implant insertion.

**Discussions.** The malposition of tooth 47 was corrected with the help of the orthodontic mini-implant, later its alignment was realized using the self-ligating Damon System/ Damon Q technique. The orthodontic mini-implant treatment lasted approximately 8 months.

**Conclusion.** Orthodontic implants used as absolute skeletal anchorage in orthodontic treatment contribute to obtaining faster results in terms of time and effectiveness. The insertion technique is quick and painless.

## 2. ACUTE DIFFUSE PULPITIS. ETIOLOGY AND TREATMENT METHODS



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**Introduction.** Dental pulp inflammation (pulpitis) represents the most commonly encountered emergency in dentistry, characterized by severe pain, and it occupies one of the first places in dental conditions, with a major risk towards periodontal complications leading to tooth loss. Acute diffuse pulpitis evolves rapidly and often in an intense manner, characterized by extensive inflammation of the dental pulp. This condition can be triggered by a variety of factors, including deep cavities, dental injuries, bacterial infiltrations, or other forms of pulp irritation. Clinical experience has shown that the microorganisms causing tooth decay are the most common etiological factor in the disease of the pulp tissue. Therefore, the medical approach in choosing appropriate treatment methods, as well as their subsequent practical implementation, represents essential steps in the correct management of acute diffuse pulpitis.

**Aim of study.** The examination of etiological factors that contribute to the onset of acute diffuse pulpitis and the identification of treatment methods to prevent complications.

**Methods and materials.** In this study, 13 patients diagnosed with acute diffuse pulpitis, aged between 18 and 45 years, including 7 women and 6 men, were included in the analysis and treatment. The patients were evaluated through clinical examinations, based on which a comprehensive diagnosis and treatment plan were formulated. Thus, 9 patients were treated by the vital extirpation method and 4 patients by the non-vital extirpation method, with the use of paraformaldehyde-based mummifying paste.

**Results.** After the treatment, favorable results were obtained in 13 patients, of which one patient treated with the non-vital extirpation method did not show up on time and experienced complications. Therefore, the vital method is better to use because it can be performed in a single session.

**Conclusion.** In the practical applications, we concluded that treating acute diffuse pulpitis through vital extirpation and three-dimensional sealing of the root canals yields high-performance results and minimizes post-treatment complications.

**Keywords.** Acute diffuse pulpitis, treatment, vital extirpation, non-vital extirpation.





### 3. ACUTE NECROTIZING ULCERATIVE GINGIVITIS

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**Introduction.** Acute necrotizing ulcerative gingivitis (ANUG) is a relatively rare and yet specific infectious disease of the gingival tissue characterized by gingival necrosis and ulceration, gingival pain, and bleeding, affecting <1% of the population. Although the prevalence of this disease is not high, its clinical importance is clear, as it represents the most serious of the diseases associated with dental biofilm, which, if left untreated, can lead to severe complications such as necrotizing ulcerative periodontitis or noma, which is usually fatal.

**Case statement.** This report presents a clinical case of ANUG and its clinical management.

**Discussions.** An 18-year-old male patient presented to the Department of Dentistry with complaints of gingival pain and bleeding, a fetid odor from the oral cavity, and nutritional deficiencies. History of the disease: oral hygiene has definitely been ignored; he smokes up to 20 cigarettes a day. The intraoral examination revealed the clinical picture characteristic of ANUG: swelling and edema of the gums, which bleed easily when touched; multiple ulcerative erosions covered with fibrin deposits; and an unpleasant odor from the oral cavity. Silness Loe plaque index = 3. Submandibular lymph nodes are enlarged and painful to palpation. Microbiological investigations demonstrated the excessive presence of *Fusobacteria* and *Porphyromonas* species. Emergency treatment was administered in the dental office, and home treatment was prescribed. Recommendations were directed towards a complete general examination, strict adherence to personal oral hygiene, and smoking cessation.

**Conclusion.** Although it is quite rare in medical practice (<1%), the complications of ANUG are quite severe, from necrotizing ulcerative periodontitis to noma. By presenting this clinical case, we draw the attention of the dental community to the risks to which patients are exposed in the case of ignoring personal oral hygiene and the importance of common risk factors, such as smoking, in the occurrence of ANUG.

#### 4. ANALYSIS OF THE CONSEQUENCES OF FIXED DENTURES ON PERIODONTAL HEALTH



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**Introduction.** Dental health is an important aspect of general health. Various environmental and dietary factors can adversely affect the balance of the oral cavity, leading to inflammatory and destructive diseases of the teeth. These diseases, known as periodontal diseases, are a widespread and persistent problem affecting people of all ages. However, current methods of diagnosis and treatment often do not take into account the presence of orthopaedic structures or the influence of these structures on local immunity. This problem arises primarily from the prevalence and severity of this disease in the population. Current methods used to diagnose periodontal diseases usually overlook the influence of orthopaedic structures and only determine the presence of inflammation without identifying the root cause. Different materials with different chemical composition, manufacturing techniques and uses are commonly used in dentistry to replace missing teeth. However, introducing these materials into the oral cavity can disturb the natural balance, leading to oral health problems.

**Aim of study.** The aim of this study is to investigate the impact of different structural materials used in fixed dentures on the periodontium.

**Methods and materials.** In the study we selected a sample of 10 patients aged 30-60. We used cobalt-chromium ceramic prostheses fabricated by the conventional method, cobalt-chromium ceramic prostheses fabricated by a CAD/CAM technique and zirconium prostheses fabricated by a CAD/CAM technique. Fixation is achieved by cementation. As research methods we used detailed clinical examinations, including measurement of periodontal pocket depth by means of periodontal probes, also intraoral radiographs for bone level assessment.

**Results.** It was found that the average duration of use of the prosthesis is 8.8 years, providing insight into the period of functionality of the prosthesis. The prevalence of complications and/or failures of fixed prostheses, which can include a range of problems such as: shade mismatch, overcontact, marginal opening, caries, periodontal disease, gingival bleeding, conjoined margins, fractured porcelain, discomfort, pain, periapical injury, occlusal wear, pontic fracture.

**Conclusion.** This study highlights the need for patient education on rigorous oral hygiene and the need for regular monitoring to detect and manage potential complications in the early stages. It can be concluded that there is a vast need to improve the success and survival of fixed prostheses by formulating effective methods of pathology control. In addition, dentists require improvement of their clinical skills, their knowledge of biomaterials and understanding of laboratory techniques.



## 5. ANESTHESIA IN THE ORO-MAXILLO-FACIAL REGION IN PATIENTS WITH HYPERTENSION

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**Introduction.** Arterial hypertension (HTN) is a commonly encountered condition in patients requiring dental treatment, which can significantly influence the management of conditions in the oro-maxillo-facial region using local anesthesia. Due to the increased risk of cardiovascular complications in patients with HTN, it is crucial to carefully choose the anesthetic substance, method, and technique that are safest for this patient category.

**Aim of study.** To analyze the specific considerations in choosing the type of anesthetic and to assess their effectiveness in managing patients with arterial hypertension (HTN).

**Methods and materials.** In the present study, 14 patients with arterial hypertension who sought dental intervention with local anesthesia were included. The study was conducted at the Department of Oro-Maxillo-Facial Surgery and Oral Implantology, "Arsenie Gutan." Two types of local anesthetics were used: "Septanest" (active substance articaine 4% with adrenaline concentration 1:200,000) and vasoconstrictor-free anesthetic "Scandonest" (active substance mepivacaine 3% without adrenaline content). Continuous monitoring of blood pressure was performed using the classic automated sphygmomanometer "Microlife."

**Results.** Among the 14 patients with hypertension (HTN) aged between 44 and 71 years, 5 (35.71%) were female, and 9 (64.28%) were male. 4 (28.57%) patients required dental implants, 7 (50.0%) underwent tooth extractions, 2 (14.28%) received endodontic treatment, and 1 (7.14%) underwent a cystectomy for a radicular cyst on tooth 4.6. Regarding the anesthesia technique, infiltrative anesthesia was used in 8 (57.14%) patients, and block anesthesia was used in 6 (42.85%) patients. The anesthetic "Scandonest" was administered in 4 (28.57%) cases, while "Septanest (1:200,000)" was administered in 10 (71.42%) cases. In all cases, both during and after the intervention, the sphygmomanometer did not register changes in the initial blood pressure. None of the patients reported pain during the intervention.

**Conclusion.** Based on this study involving a cohort of 14 patients with hypertension, the use of high-quality anesthetics that ensure operator comfort is recommended. These include "Septanest" (articaine 4% with adrenaline concentration 1:200,000) and vasoconstrictor-free anesthetic "Scandonest" (mepivacaine 3% without adrenaline content) for local anesthesia in patients with hypertension.

## 6. BIOSTIMULATION THERAPY IN THE COMPLEX TREATMENT OF PERIODONTAL DISEASE



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**Introduction.** In periodontal disease (PD), the advanced stage of damage to the periodontal elements is often irreversible. This necessitates a comprehensive treatment approach for gingivitis and periodontitis, including medication administration, surgical procedures, and maintenance treatment, including biostimulation therapy (PRP therapy). In the context of the therapeutic effects of platelet-enriched autologous plasma, the use of biostimulation therapy in PD can be justified by its beneficial properties, attributed to the content of growth factors and other biologically active substances that initiate the regeneration and recovery processes of partially or totally damaged tissues. The present growth factors stimulate and initiate the regeneration and recovery processes of affected tissues precisely in the area and location where the autologous plasma (injectable form) is introduced, through the interaction mechanism between the specific growth factor and the tissue receptors of the recipient area. The effect of biostimulation therapy begins within 30 minutes, and after a course of treatment, it persists from 6 months to 1 year.

**Aim of study.** Introducing biostimulation therapy into the complex treatment plan of periodontal disease.

**Methods and materials.** The "Plasmodent" technology was used as the material for biostimulation therapy (EBA-20 centrifuge, standardized Plasmodent tubes, accessories for collecting venous blood from the patient, consumables). Thirty-two patients with PD were included (9 with plaque-induced gingivitis and 23 with marginal periodontitis (MP) of various severity degrees, including severe MP/stage IV).

**Results.** As a result of using injectable biostimulation therapy in patients with PD at all stages of complex treatment, including the maintenance phase, good and very good clinical outcomes were achieved, expressed by a noticeable reduction in inflammation, suppression of gingival bleeding, reduction in tooth mobility, and an extension of the remission period in PD treatment (gingivitis, MP).

**Conclusion.** 1. Biostimulation therapy is a modern adjunctive method in the complex treatment of PD. 2. Autologous plasma used in biostimulation therapy serves as a safe and harmless "biological tool" for initiating and accelerating all natural regeneration and tissue recovery processes. 3. When using biostimulation therapy, any allergic reaction is excluded (as it is self-produced), and it is accessible and straightforward for use in the dental office.



## 7. CAD/CAM TECHNOLOGY IN DIFFERENT FIELDS OF PROSTHETIC DENTISTRY

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**Introduction.** CAD/CAM (computer aided designing and manufacturing) technology was introduced in dentistry in the year 1989, by Mormann & Brandestini in Germany and today it is widely used in all the branches of prosthodontics. Using these CAD/CAM technologies, various types of restorations and dental prostheses can not only be designed but also machined with accuracy and precision. Over the past 10 years, CAD/CAM technology has become extremely popular. The introduction and evolution of computer aided designing and manufacturing (CAD/CAM) technology in dentistry has greatly revolutionized treatment concepts and prostheses fabrication.

**Aim of study.** To analyze the existing literature research on advantages and limitations to the use of CAD/CAM technology in different fields of prosthetic dentistry.

**Methods and materials.** A comprehensive review of the literature was done through the MEDLINE and PubMed database for research articles with keywords “CAD/CAM technology”, “prosthetic dentistry”, “advantages”, “limitations”. The inclusion criteria for selection were clinical studies, laboratory technical research papers, case reports, and review articles with a comparison between CAD/CAM and conventional processing techniques for dental prostheses fabrication.

**Results.** The electronic research through MEDLINE and PubMed resulted in more than 90 titles in the English language literature, and 10 were relevant to determine the advantages and limitations of CAD/CAM techniques for dental prostheses fabrication. The advantages of using the CAD/CAM systems are: no traditional impressions, less appointment, high precision and accuracy, improve the qualities of restoration, eliminates the use of the laboratory equipment required for conventional LOST-WAX technique, speed, ease of use, and quality digital scans, faster design and fabrication, natural appearance of CAD/CAM restorations. The Limitations of using the CAD/CAM systems are the initial high cost of CAD/CAM systems and time and cost investment to master the technique. The CAD/CAM is used in different fields of prosthetic dentistry: removable prosthodontics, fixed prosthodontics, implant prosthodontics, maxillofacial prosthodontics.

**Conclusion.** The analysis of literature showed that CAD/CAM technology has large prospects in modern dentistry due accuracy and post manufacture process shrinkage. The quality of CAD/CAM milled dental prostheses surpasses the quality of conventional dental prostheses. So, there is improvement at the branch of digital prosthodontics and much more precision.



## 8. CHARACTERISTICS OF CLINICAL MANIFESTATIONS IN ACUTE HERPETIC STOMATITIS IN CHILDREN



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**Introduction.** Acute herpetic stomatitis in children, mainly caused by herpes simplex virus type 1 (HSV-1) of the family Herpesviridae, is characterized by a high infectiousness. The diversity of clinical manifestations of this condition complicates the diagnostic process, being able to hide the presence of other serious diseases, including systemic infections. Therefore, it is crucial to analyze the symptoms of stomatitis in detail in order to obtain an accurate diagnosis and develop an effective treatment plan adapted to each individual case.

**Aim of study.** Analysis of the clinical manifestations of acute herpetic stomatitis in children in various evolutionary phases and providing relevant information for early diagnosis and for the development of effective therapeutic approaches.

**Methods and materials.** A literature review was made using 55 scientific articles from PubMed, UpToDate, NCBI, ESMO databases for a period of 10 years. A clinical study was conducted including 30 children aged between 3 months and 3 years and were analyzed the clinical aspects of acute herpetic stomatitis according to the severity of the process.

**Results.** The clinical study carried out revealed five stages in the evolution of acute herpetic stomatitis: incubation, prodromal, clinical manifestation, attenuation and convalescence. A variation in clinical manifestations has been observed depending on the stage of the disease, from mild symptoms in the incubation phase to more severe manifestations in the later stages.

**Conclusion.** Acute herpetic stomatitis, regardless of its form, is an infectious disease that requires early detection to prevent spread and ensure effective healing, thus contributing to the rapid recovery of patients.



## 9. CHRONIC APICAL PERIODONTITIS. METHODS OF DIAGNOSIS AND TREATMENT.

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**Introduction.** Chronic apical periodontitis is a frequent pathology in the periapical area, usually caused by complications of teeth with pulp necrosis, whose prevalence depends on the country and population. In the case of chronic apical periodontitis, the clinical and paraclinical examination is important for establishing the diagnosis and differential diagnosis of different forms of pathology and will determine the tactics and treatment plan, which may include extraction, root canal treatment or other methods.

**Aim of study.** Aim of the study is to identify the factors in the development of chronic apical periodontitis and to highlight the methods of diagnosis, differential diagnosis and treatment.

**Methods and materials.** The study included 51 patients with chronic apical periodontitis, aged between 18 and 66 years, of which 35 were men and 16 were women. The average age was 31 years. The diagnosis was based on the clinical ( objective and subjective ) and paraclinical ( Orthopantomography and CBCT ) examination. The periapical index (PAI) was also used to analyze the apical lesions. Treatment included the use of rotary instruments, irrigation with 5.25% sodium hypochlorite and subsequent sealing of the root canals.

**Results.** Apical periodontitis is preceded in most cases by the presence of an intraradicular infection and a poor root canal treatment. After the study, it was established that 86.3% of the patients came for aesthetic/pain/functional reasons, and only 13.7% came for a systemic visit. The gender distribution showed a predominance of men over women with a ratio of 2.19, which could be explained by the higher incidence of dental trauma among men. Following the analysis of the Periapical Index (PAI) - the most recorded scores are 3 (45.1%) and 4 (31.4%), indicating that patients mostly seek treatment in advanced stages of periodontitis.

**Conclusion.** Apical periodontitis is a pathology that occurs as an inflammatory response to microbial aggression, involving the destruction of periapical tissues, often in teeth with root canal treatment in the past. Although there may be other factors that contribute to the development of periodontitis, inadequate root canal treatment and the quality of the seal remain the most common causes, leading to a persistent infection. This pathology is often overlooked in orthopantomography but can be more easily identified using cone-beam computed tomography (CBCT), and detecting it at an early stage will allow the choice of optimal treatment strategy.

## 10. CLINICAL EXPERIENCE OF USING ICON RESIN IN THE TREATMENT OF POST-ORTHODONTIC AND NON-POST-ORTHODONTIC WHITE SPOT LESIONS



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**Introduction.** Dental caries is one of the most widespread conditions globally, affecting more than 3.5 million people. Current trends in the treatment of early carious lesions are focused on preserving the integrity of the hard dental structures. An effective method of masking and stopping the clinical evolution of early carious lesions is their infiltration with Icon resin, a preparation of DMG, Germany. Studies in the field demonstrate that starting the treatment as early as possible of early post-orthodontic or non-post-orthodontic carious lesions can have very promising results.

**Case statement.** Evaluation of the esthetic efficacy of using the Icon resin infiltration method in the treatment of post-orthodontic and non-post-orthodontic white spot lesions. Two adolescent patients: a 17-year-old boy with post-orthodontic white spot lesions on the vestibular surfaces of the incisors, and an 18-year-old girl with non-postorthodontic white spot lesions, also on the vestibular surfaces of the incisors, were treated with resin Icon and were supervised for six months. The treated teeth show an excellent aesthetic result immediately after applying the resin, an effect that is already maintained for six months, and the progression of the clinical evolution in both cases seems to be stopped.

**Discussions.** Icon resin infiltration, being a non-invasive method, does not require anesthesia of dental hard tissues, is well tolerated by patients and easy to use in dental practice. The treatment of post-orthodontic and non-post-orthodontic white spot lesions has a significantly greater masking effect than other treatment methods, such as natural remineralization or regular application of fluoride varnishes and can be recommended in the treatment of early post - orthodontic or non-post-orthodontic carious lesions.

**Conclusion.** Although the use of the infiltration method of early post-orthodontic or non-post-orthodontic carious lesions with Icon resin is quite effective on the vestibular surfaces of the teeth, its use for the proximal surfaces is still quite limited and requires further studies.



## 11. COMPARATIVE ANALYSIS OF PALATAL WOUND MANAGEMENT TECHNIQUES POST FREE GINGIVAL GRAFTING

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**Introduction.** The use of the hard palate mucosa as a donor area is considered the gold standard in gingival plastic surgery today. Following palatal grafting, various methods have been proposed for managing the postoperative wound, such as protecting it with a blood clot, using collagen-based biomaterials, or utilizing PRF membranes.

**Aim of study.** To determine the optimal method in the management of the palatal wound following palatal grafting surgery.

**Methods and materials.** This study was conducted between 2022 and 2023 at the "Omnicent" clinic. It involved 15 patients aged between 20 and 45 years who required palatal grafting intervention. Following the palatal graft harvesting procedure, the patients were divided into two groups: the intervention group, consisting of 5 patients who received PRF membrane and 5 patients with collagen-based biomaterial (Kolapol KP-3), and the control group comprising 5 patients whose palatal wound was under the protection of a blood clot. In each case, patients were reviewed at 7-, 14-, and 30-days post-operation and examined based on the following criteria: wound bleeding, re-epithelialization level, shape and size of the wound, presence or absence of postoperative complications, and pain intensity assessed using the Numeric Rating Scale (NRS).

**Results.** A significant difference was observed between the control group and the intervention group; a substantial difference in wound re-epithelialization was noticed by day 14. For patients with the PRF membrane and Kolapol, values were 60% and 10% for the control group, respectively. At 30 days post-operation, complete re-epithelialization of 100% was observed in all cases. Among patients who received the PRF membrane and Kolapol KP-3, no major differences were noted. The morbidity level among the control group patients was higher compared to the intervention group. According to the Numeric Rating Scale at 14 days post-operation, the control group indicated values between 4-6, whereas the intervention groups reported values ranging from 1-4.

**Conclusion.** The results have demonstrated that both the PRF membrane and collagen-based biomaterials accelerate the healing of the palatal wound compared to cases where the wound protection is solely achieved by a blood clot. Additionally, patient morbidity is reduced through a shorter healing time.

## 12. COMPREHENSIVE ANALYSIS IN THE DETECTION OF CARIES SUSCEPTIBILITY IN CHILDREN WITH DENTAL FLUOROSIS



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**Introduction.** Dental fluorosis is the most common and prominent early-stage symptom of chronic fluorosis, which is caused by excessive fluoride intake during tooth development. Numerous studies have shown that patients with dental fluorosis suffer from dental caries less often, and the most common forms of dental caries at the age of 12 and 15 years are early and superficial. There is also a trend that fluorosis teeth with higher scores are more prone to caries due to more severe post-eruptive changes.

**Aim of study.** A comprehensive literature review in the detection of caries susceptibility in children with dental fluorosis.

**Methods and materials.** The study is based on the analysis of publications from the scientific databases of the national and international libraries for the period 2015-2023. All studies that reported data on the susceptibility of permanent teeth to dental caries in children with dental fluorosis were included in this review. The web databases were searched for publications like PubMed, Google Scholar, SCOPUS, and Hinari.

**Results.** Although the pathogenesis of dental fluorosis is not fully elucidated, the causative factor is well known. Excess fluoride ingested by the child in the first years of life causes dental fluorosis. Much attention has been paid to the composition and structure of fluorotic enamel, and fluorine has been assigned the role of the chemical element with the highest anticariogenic potential. The relationship between fluorine intake during the period of development of dental hard tissues and the anticarious resistance of teeth has been recognized. At the same time, less attention has been focused on other factors that can intervene in the anticarious resistance of fluorotic teeth, such as the concentration and quality of salivary nitrites, individual masticatory patterns, dietary habits, etc. The results of the literature review demonstrate the role of salivary nitrites in the prevention of dental caries, which increase the resistance against salivary acidification *in vivo* and *in vitro*, thus preventing the development of caries in patients with dental fluorosis. Additionally, it has been suggested that fluoride presented in the oral cavity may delay bacterial growth and metabolism by inhibiting enolase and ATPase. Another mechanism that may explain the low prevalence of caries in patients with dental fluorosis is the much slower and longer chewing pattern due to compromised enamel.

**Conclusion.** To be able to explain in more detail the balance between caries progression and reversal in patients with dental fluorosis, which is a more complicated one, further studies are needed.

**Keywords.** Tooth susceptibility, dental caries, dental fluorosis.





### 13. CONSERVATIVE AND SURGICAL TREATMENT OF CHRONIC PERIAPICAL LESIONS

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**Introduction.** Chronic apical periodontitis is an osseous lesion of the apical periodontium affecting the apical alveolar bone and the root apex by necrosis and resorption under the influence of granulation tissue, which appears as reaction tissue. It is one of the most current problems in contemporary dental therapy. If etiopathogenetic is not treated correctly, it will progress with the destruction of adjacent tissues, evolving from one form to another, frequently resulting in severe complications. Conservative treatment methods do not always completely remove the focus of odontogenic infection. Thus, in cases where an endodontic lesion cannot be resolved by conventional endodontic (re)treatment, surgical treatment is the treatment of choice to save the tooth. Apical resection is one of the best options, helping preserve the teeth on the dental arch.

**Aim of study.** To evaluate the clinical effectiveness of endodontic treatment with the calcium hydroxide preparation "Apexdent" in root canals with periapical changes for tissue regeneration, as well as the therapeutic tactics in teeth that do not respond to endodontic treatment.

**Methods and materials.** The study comprised 10 patients, 6 women and 4 men aged between 35 and 50 years, who were examined clinical and paraclinical. The patients were subjected to root canal treatment performed with the calcium hydroxide preparation "Apexdent". Given the diversity and severity of clinical forms of apical periodontitis, 3 of the 10 cases were not treated with the help of calcium hydroxide preparations, requiring surgical treatment.

**Results.** The clinical study determined that the calcium hydroxide preparation "Apexdent" contributed to the destruction of the pathogenic flora in the root canal. In cases where the periapical processes were not cured with the help of root canal treatment, surgical treatment was resorted to.

**Conclusion.** Calcium hydroxide preparations proved favourable results in the treatment of apical periodontitis. However, in some cases, the pathological processes were stopped using surgical treatment methods.

## 14. CONTEMPORARY RHINOPLASTY METHODS: ACTUALITIES AND CHALLENGES



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**Introduction.** Rhinoplasty is a surgical procedure utilized to improve and reconstruct damaged or badly conformed nasal structures by grafting or by transplanting a portion of skin from another part of the body. Nasal surgical access can be obtained through two types of incisions: incisions made inside the nose (endonasal approaches) or through incisions made outside the nostrils (external approach). In recent years, two more types of non-surgical rhinoplasty have been introduced - rhinoplasty with dermal fillers and ultrasound.

**Aim of study.** This review aims to investigate the existing rhinoplasty techniques, methods and indications.

**Methods and materials.** A literature review of the scientific literature was made using PUBMED, Medline.plus , Medline.com, Google Scholar, PlasticSurgery.org, TripDatabase, Science Direct databases, for a period of 5 years. The review was supplemented with a manual search using the keywords: “nose rhinoplasty, grafts, methods” (PR) during the 2018 to 2023 time span. A study was carried out which included 5 patients ( 4 men and 1 woman, N=5), aged between 28-38 years old ( average age-33 years old) diagnosed with septum deviation (N=1), asymmetric nasal tip (N=1), asymmetric alar cartilage (N=1), nasal bone fractures (N=1). Contemporary rhinoplasty techniques such as endonasal, external and non-surgical with dermal fillers were applied to these patients.

**Results.** Following the analysis of scientific articles and specialised works, contemporary rhinoplasty methods were analysed. According to a study carried out by Hyi Seong Kim, it was determined that the open rhinoplasty method is more precise, better outcomes were also obtained compared to closed rhinoplasty due to the transcolumellar incision which allows a more accurate evaluation of the anatomy of the nose. On the other hand, the author Cárdenas-Camarena L highlights that endonasal rhinoplasty could be a better method to prevent edema and bruising. Taking into account that a patient satisfaction survey was not performed, such as the NOSE and ROE scores, it is difficult to obtain scientifically accurate information about which technique is more likely to show better outcomes.

**Conclusion.** Nasofacial aesthetic ideals are culturally variable, and they are influenced by the passage of time. Therefore, it is difficult to state the correct definition of what constitutes an aesthetically pleasing nose. The contemporary techniques used in this study proved to be effective through a minimally invasive approach, with no postoperative complications. It has been noted that the quality of life was significantly improved from a morpho-functional point of view. Besides nasal appearance, respiratory function can also be notably improved by these techniques.



## 15. DECOMPRESSION - METHOD OF TREATMENT OF GIGANT CYSTS OF THE UPPER JAW. CLINICAL CASE.

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**Introduction.** Reaching large sizes, cysts located on the upper jaw often affect the neighboring anatomical formations, such as the maxillary sinus, the floor of the nasal cavity, penetrating them and thus affecting their function. During its invasive growth, the cyst affects the palate and neighboring vital teeth. The classical method of treatment - cystectomy has a number of shortcomings: during the operation communication with the maxillary sinus, nasal cavity, palatal, vestibular region of the alveolar process can be achieved, as well as it involves preliminary endodontic treatment of the teeth included in the cystic cavity and their apical resection. In order to avoid these shortcomings, firstly, the cyst can be treated by the decompression method until the volume of the cyst is reduced and the volume of the lost bone is restored, and then cystectomy can be performed without the danger of damaging the surrounding anatomical formations.

**Case statement.** Patient C., aged 25, went to the dental clinic "Omni Dent" for surgical treatment - extraction of the root of tooth 24. Clinical signs were not present. Paraclinical examination (OPG and CBCT) revealed an area of radiopacity - bone destruction. Preventive diagnosis was established - giant radicular cystic of tooth 24. The decision was made that the patient should be treated by the decompression method. A decompression device was manufactured according to the individual parameters of the patient with the help of CAD/CAM system and inserted to the patient at the place of extracted tooth 24. The decompression device consists of the tube, which through the socket of the extracted tooth enters into the cystic cavity, and the fins, with the help of which the device is fixed to the neighboring teeth. The patient was monitored according to certain criteria: size of the cyst, bone supply, vitality of the teeth, complications.

**Discussions.** The duration of decompression was 6 months, during which time the patient underwent lavage. The patient was monitored during decompression to assess volumetric changes of the cyst to determine the timing of cyst enucleation. Analyzing the given method according to the proposed criteria we can say that after 6 months of decompression: the cyst shrank in volume (from 4.83 cm<sup>3</sup> to 1.3 cm<sup>3</sup>); bone restoration occurred in the region of the nasal cavity, maxillary sinus and neighboring teeth; teeth remained vital, during treatment complications did not occur. Cystectomy with augmentation (Kolapol) was performed. After 6 months the patient underwent implant-prosthetic restoration with Megagen Anyone implant size 4.5x13. Although the duration of treatment is longer, the method of decompression reduces the risk of complications, such as perforation of the nasal cavity floor and maxillary sinus, and allows the vitality of the teeth included in the cyst to be preserved.

**Conclusion.** This method of treatment can be considered minimally invasive because the method of decompression of gigant cysts allows us to preserve the vitality of the teeth included in the cyst and reduces the risk of damage to surrounding anatomical structures. Due to the use of the decompression device for 6 months, the cystic cavity reduced in size, which facilitated the enucleation of the cyst and helped avoid intraoperative complications such as perforation of Schneider's membrane and nasal mucosa.

## 16. DENTAL CARIES IN PERMANENT TEETH IN CHILDREN. INCIDENCE STUDY



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**Introduction.** The topic is relevant due to a continuous increase in the number of dental caries cases, the worsening of the issue, and the potential negative impact of dental caries, both locally and throughout the whole body. Dental caries is one of the most common dental diseases in the human body, affecting both temporary and permanent teeth. In some cases, the teeth are affected immediately after an eruption.

**Aim of study.** To assess the incidence of dental caries in permanent teeth in children and to increase the efficiency of diagnosis during prophylactic examinations.

**Methods and materials.** A group of 49 students from the theoretical "Ioan Vodă" high school in Cahul were included in the study. The average age of the patients in the study was between 13 and 16 years. The examination was performed according to the WHO methodology by direct and indirect inspection with a dental mirror and palpation with a dental probe. To determine approximal caries, dental floss was applied, namely the silk floss sign. The inspection and observation findings were registered in dental health records.

**Results.** Of the 49 subjects examined, 47 schoolchildren (95.92% of cases) had dental caries in their permanent teeth. The diagnosis of dental caries was established in 5 subjects by combining clinical and complementary examinations and using the method of the silk floss sign (10.20%).

**Conclusion.** 1. The incidence of dental caries in children in the study, aged between 13 and 16, is high, accounting for 95.92%. 2. The use of the additional test, the silk floss sign, helped establish a definitive diagnosis in 10.20% of cases.



## 17. DENTAL CARIES OF CHILDREN WITH CONGENITAL CARDIAC MALFORMATIONS

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**Introduction.** Congenital heart malformations (CHM) affect approximately 8-10 of every 1000 births worldwide. Dental caries (DC) is one of the most common diseases, in the etiology of which the impact of the microbial agent is recognized, and its association with systemic diseases such as cardiovascular diseases can cause severe complications in children, because chronic foci of odontogenic infection can increase the risk of developing infective endocarditis (EI). At the same time, the research dedicated to DC affecting children with cardiac pathology and in particular, CHM, are less numerous, the data of different authors being often contradictory.

**Aim of study.** The aim of the present study was to carry out a review of the specialized literature regarding the impact of dental caries on children with congenital heart malformations.

**Methods and materials.** In order to achieve the purpose of the study, the search for scientific publications was carried out according to the keywords: "children with heart diseases", "congenital heart disease", "valvular heart disease", "infective endocarditis", "oral microbiota", "dental caries", "oral health". From the 108 sources obtained, "Free full text" articles were selected, which were 36 in total, but 28 articles published during the last 10 years were selected for analysis.

**Results.** Current research in the field has shown that cardiac pathology, including EI, is increasing over the last 10-15 years. Several studies have shown that *Streptococcus mutans* from multiple carious lesions could migrate into cardiac tissue. Thus, there was a need to develop effective methods to prevent *Streptococcus mutans* from invading the bloodstream and, ultimately, the endothelium of cardiac tissues. Since these methods are still not progressing, preventive techniques such as oral hygiene, which can ensure the elimination of these bacteria, is the only approach that can be followed by most patients.

**Conclusion.** A relationship between *Streptococcus mutans* bacteremia and the worsening of cardiovascular diseases, especially EI, has been demonstrated in several studies. Therefore, severe dental caries may be an important risk factor for bacterial colonization in cardiac tissues. Thus, studying the level of dental caries in children with CHM is important not only for researchers in the field of cardiology, but also for the dental community in order to develop effective methods to prevent DC.



## 18. DENTAL DISCOLORATION. MODERN METHODS OF TREATMENT.



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**Introduction.** Dental discoloration represents any modification of tooth colouring which can vary from minor pigmentation or local discoloration to significant changes of entire tooth colour. These modifications can affect the tooth enamel or dentine and can be caused by both external and internal factors. Extrinsic dyschromia appears due to the deposition of colouring substances on the surface of an erupted tooth, while intrinsic dyschromia is mainly of a general etiology. Aim of study: Identification of causes leading to the appearance of dental dyschromia and the methods of treating it.

**Aim of study.** Identification of causes leading to the appearance of dental dyschromia and the methods of treating it.

**Methods and materials.** According to the study, the majority of patients demonstrated dental discoloration caused by food consumed. As a method of treatment we applied the dental whitening procedure with the help of a teeth whitening system "Light Whitening" and with an ultraviolet rays lamp. We used subjective evaluations of those participating in the study, as well as objective measurements of dental nuance before and after the treatment procedure.

**Results.** Following the dental whitening procedure with the help of a UV lamp, visible results have been obtained.

**Conclusion.** Nowadays, in the modern world when people wish to have teeth as white as possible, dental discoloration represents a major problem in their lives. The discovery of teeth whitening techniques represents an efficient solution for treatment of dental dyschromia. The teeth whitening by means of ultraviolet rays lamp is an excellent and well tolerated procedure for obtaining a radiant and healthy smile.

**Keywords.** Dental discoloration, tooth discoloration, UV lamp



## 19. DENTAL TRANSPOSITION. DIAGNOSTIC AND TREATMENT GUIDELINES

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**Introduction.** Tooth transposition is a rare anomaly in orthodontics, presenting a distinctive challenge that demands precision and expertise. This phenomenon, characterized by the interchange of positions between two adjacent permanent teeth within the same quadrant of the dental arch, has sparked a growing interest in diagnostic and treatment methodologies, because of the various factors that need to be taken into consideration in the treatment selection options such as cooperation, aesthetics, functionality and age, influencing decisions on whether the treatment should involve tooth extractions, aligning the teeth according to the transposition order, or correcting the transposition through orthodontics.

**Aim of study.** The main purpose of this review is to evaluate the optimal diagnostic and treatment features of patients with dental transposition.

**Methods and materials.** In order to fulfill the specified goal, were analyzed several electronic databases such as PubMed, ResearchGate, Google Scholar, Sci-Hub and NCBI, using the following keywords: “tooth transposition”, “dental developmental anomaly”, “ectopic eruption”.

**Results.** Transposition can affect both genders equally, and although it can occur in the maxilla or mandible, the frequency of permanent involvement of the upper canine is the highest. In the maxilla, the canine is most commonly transposed with the first premolar (70%), less frequently with the lateral incisor (20%), rarely followed by the central incisor or second premolar. It has been reported that maxillary tooth transposition occurs in approximately 1 out of 300 hundred orthodontic patients. Unilateral transpositions are more commonly found than bilateral transpositions and show a left-side dominance. Transposition of the upper canines and first premolars was identified in a group of 73 individuals with cleft lip and palate, where 3 patients (4.1%) exhibited this anomaly. Diagnosing and treating dental transposition pose various challenges, many of which can be effectively tackled using CBCT. The severity of transpositions and the imposed alveolar limitations, in turn, can define the level of difficulty and treatment duration, potentially affecting the biomechanical strategy that needs to be employed.

**Conclusion.** Tooth transposition, once a perplexing challenge, is now being tackled with a modern and multidisciplinary approach. Advances in diagnostic tools, treatment modalities, and patient education contribute to the evolving landscape of managing this unique dental condition.

## 20. DENTAL TRANSPOSITION: DIAGNOSTIC CONDUCT AND TREATMENT IN ADULTS



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**Introduction.** Dental transposition is a rare dental anomaly involving the misalignment and positional exchange of two adjacent teeth within the same dental arch. Although it has a low incidence rate (0.33%), the orthodontic realignment challenges posed by this anomaly, particularly in adult patients, can present a genuine challenge for orthodontists.

**Aim of study.** To determine predisposing factors and diagnostic methods to enhance interdisciplinary treatment for patients with dental transpositions.

**Methods and materials.** The study encompassed 5 patients (4 females and 1 male) aged between 19 and 32 years, who sought orthodontic consultation due to complaints of dental crowding and dentoalveolar disharmony. The inclusion criterion was the clinical and radiological presence of partial or complete dental transposition.

**Results.** Patients underwent clinical and paraclinical examinations and received orthodontic treatment lasting between 17 to 32 months, with an average duration of 23 months. Treatment in all cases involved a dual-jaw fixed adhesive system. Incomplete dental transposition transformed into complete transposition was the functional and aesthetic choice for treating adult patients. The prevalence of dental transposition among orthodontic patients was 0.54%.

**Conclusion.** Orthodontic correction of transposition is suitable for cases of incomplete transposition involving only the dental crown. Identifying predisposing factors and hereditary factors is crucial for treatment predictability. Treatment method selection relies on radiological examination, allowing three-dimensional visualization of the dental apex projection. Partial transposition in adult patients is often transformed to total transposition, where orthodontic treatment is complemented by restorative therapy.



## 21. DENTIGEROUS CYSTS: DIAGNOSIS AND TREATMENT STRATEGIES

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**Introduction.** Odontogenic cystic formations are not uncommonly discovered on routine X-rays. There are a number of various cyst-like lesions seen on radiographs, presenting as a notorious image: a well-defined radiolucent area surrounded by a halo of more opaque tissue, inside the maxillary or mandibular bone, involving an adjacent tooth or even encapsulating it. One of these many lesions is the dentigerous cyst, also known as a follicular cyst. Dentigerous cysts are pseudotumoral benign lesions resulting from impaired odontogenesis, presenting as the proliferation of the reduced adamantine epithelium and accumulation of cystic fluid between the crown of the tooth and the epithelium, or between the outer and inner layers of the epithelium.

**Aim of study.** Dentigerous cysts are one of the most common cystic formations in humans, also being one of the top benign odontogenic lesions in all ages. If left untreated, a dentigerous cyst can extend its margins into the surrounding bone tissue causing inflammation and bone destruction.

**Methods and materials.** The following search engines were used for the research: PubMed, Google Scholar, Web of Science. The keywords were dentigerous cyst, odontogenic follicular cyst, odontogenic cyst. There was shown a number of 809 articles according to the keywords entered, 10 of which were selected, which included the full case presentation, diagnosis and treatment and classified the dentigerous cyst according to the WHO classification. 10 patients (2 female and 8 male), ages 18-53 years old, diagnosed with dentigerous cyst were given the plan of treatment of either enucleation or marsupialization, according to each individual case's characteristics. The aim of the review was to study the individual characteristics of dentigerous cysts in order to correctly formulate a diagnosis, therefore to establish the strategy of treatment comparing the advantages and disadvantages of each technique.

**Results.** The diagnosis was made based on histological analysis and the treatment plan was chosen according to the patient's situation: from the 10 cases, 2 were treated by marsupialization and following orthodontic traction of the enclosed tooth; the other 8 cases were treated by enucleation (cystectomy and following odontectomy of the enclosed tooth).

**Conclusion.** Dentigerous cysts are cystic lesions occurring in an unerupted tooth due to perturbed odontogenesis. This type of cystic formation can be detected in both young and old patients. During pathogenesis, the cyst develops due to pathological proliferation of the reduced adamantine epithelium and the accumulation of cystic fluid between the epithelium and the crown of the tooth, or between the layers of the adamantine epithelium. Currently, dentigerous cysts are a problem due to their asymptomatic development and large incidence in various age groups. The key points of diagnosis are radiographs and histological analysis. Keywords: dentigerous cyst, enucleation, marsupialization, follicular cyst.

## 22. DIAGNOSIS, TREATMENT AND PROPHYLAXIS OF DEEP CARIES



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**Introduction.** Dental caries is a dental disease with the longest evolution worldwide. It has a high frequency and the ability to expand, which gives it an endemic-epidemiological character. About 91% of people aged between 20 and 64 years old have dental caries. Deep caries is an infectious process that is characterized not only by the breakdown of the enamel but also of the dentin, so that a thin layer of healthy dentin remains between the carious cavity and the pulp chamber. In this case, dentinal canaliculi serve as a gateway for bacteria and their products into the pulp chamber, leading to pulp inflammation. The therapeutic tactics should be chosen depending on the type of pulp inflammation (reversible or irreversible). For these reasons, it is necessary to establish a correct diagnosis, relying on anamnesis, inspection, probing, radiological examination, electronic odontometry, and thermometry. The treatment of deep caries consists of applying a thin layer of calcium hydroxide filling (up to 1mm) in the deepest area of the cavity floor. Calcium hydroxide filling material has an odontotropic, remineralizing and bactericidal effect.

**Aim of study.** To study the methods of prophylaxis and diagnosis, as well as the modern methods of treatment of deep caries, which can increase the life of the tooth and reduce the risk of local and general complications among the patients.

**Methods and materials.** In the study, 20 patients with deep caries were examined and treated, of whom 12 men and 8 women aged between 19 and 45 years (20 teeth - 2 canines, 5 premolars, 13 molars). The patients were diagnosed with deep caries using clinical and paraclinical examinations. In order to increase the effectiveness of the treatment, to avoid accidental opening of the pulp chamber, and to increase the life of the tooth in deep caries, the Stepwise technique (two-step) was used. At the first stage, the deep carious cavity was extended within the affected dentin. Only the affected dentin was removed, after which Ultra-Blend plus curative calcium hydroxide filling was applied, which has odontotropic, antiseptic, bactericidal, and antitoxic effects. The tooth was restored with a temporary filling. The cavity was accessed again after 6-12 months, removing the remaining carious process up to the healthy dentin, and then the tooth was permanently restored with composite.

**Results.** Of all the examined and treated patients, only four had complications such as acute pulpitis. Thus, the use of the Stepwise technique and Ultra Blend plus curative calcium hydroxide filling had a success rate of 80%, making it effective in the treatment of deep caries if diagnosed correctly.

**Conclusion.** If a definitive diagnosis of deep caries is established and the signs of irreversible pulpitis are excluded, the Stepwise technique (two-step) shows high effectiveness, thus avoiding the accidental opening of the pulp chamber and only the affected dentin being removed. Due to the favorable properties of Ultra-Blend plus curative calcium hydroxide filling material, the carious activity was inactivated and dentinogenesis was stimulated, thus increasing the dentin layer between the carious cavity and the pulp chamber and providing the opportunity to remove the compromised dentin without any risks at the second stage, thus, increasing the life of the tooth and and reduce the risk of local and general complications among the patients.





### 23. DIAGNOSTIC AND TREATMENT FEATURES OF PALPEBRAL XANTHELASMA.

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**Introduction.** Xanthelasma palpebrarum is the most common manifestation of cutaneous xanthoma, with a prevalence of approximately 0.3% in men and 1% in women. This benign proliferation presents as soft, semi-solid, yellow papules or plaques resulting from infiltration of histiocytes with intracellular lipid deposits into the reticular dermis. Palpebral xanthelasma can occur in the context of both primary (type II and IV) and secondary hyperlipidemia (hypothyroidism, diabetes mellitus), as well as in association with a normal lipid profile. Various treatment methods, including simple surgical excision, cryotherapy, trichloroacetic acid chemical peels, radiofrequency, and laser, are used for the treatment of palpebral xanthelasma.

**Case statement.** A 62-year-old female presented to the oro-maxillo-facial surgery department with aesthetic disorders and the presence of an upper eyelid formation. During the clinical examination, a yellow, painless papule with a semi-solid consistency was identified in the medial canthus area of the upper eyelid. Differential diagnosis was performed with necrobiotic xanthogranuloma, atheroma, syringoma, and palpebral sarcoidosis. Based on the clinical examination, the presumptive diagnosis of upper eyelid xanthelasma was established. Laboratory tests (hemoglobin, glucose, cholesterol, triglycerides, HDL, liver function tests) showed no pathological changes, thus excluding the systemic cause of dyslipidemia. A surgical intervention through simple excision was recommended. Histopathological examination confirmed the preoperative diagnosis, revealing the specific features of xanthelasma: the presence of a perivascular inflammatory infiltrate in the reticular dermis composed of mono- and multinucleated foamy histiocytes, characterized by cytoplasm with lipid vacuoles.

**Discussions.** Opting for surgical excision as the most optimal method of treatment, normal lipid profile, deep dermal involvement, size >5 mm, semi-solid consistency, onset >1 year, and the presence of skin laxity and blepharochalasis were considered. Postoperatively, the wound was covered with sterile strips and a compressive dressing. The patient was prescribed antibiotic prophylaxis with Ciprofloxacin, Tobrex eye drops and wound treatment with chlorhexidine. No postoperative complications were reported.

**Conclusion.** The surgical approach to palpebral xanthelasma requires special attention due to its direct location on the medial canthus, with increased potential for epicanthus development. To minimize this risk in cases with excess skin, it is recommended to perform two semilunar incisions and skin detachment without applying excessive traction.

## 24. EFFICIENCY OF THE CARRIER-MOTION APPLIANCE IN THE TREATMENT OF CLASS II MALOCCLUSION. CASE REPORT.



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**Introduction.** The Carrier Motion Appliance is a non-invasive device. It delivers a light, uniform force, moving and distalizing the whole canine to the molar segment as a unit and correcting the first molar rotation, before braces or aligners therapy. Treatment takes approximately six months and can improve the outcome of orthodontic therapy.

**Case statement.** Patient R.C. Age: 14 years old. Chief complaint: esthetic and functional disorder; profile: convex; normodivergent facial pattern; vertically growing chin; skeletal class II pattern; class II molar, canine relations; increased overjet; protruded and proclined upper incisors; proclined lower incisors; upper diastema d.11-21, spaces between d.11-12, d.12-13, d.22-23; lower diastema d. 31-41, spaces between d. 31-32, d.32-33, d.41-42, d. 42-43. Diagnosis: Angle Class II division 1 malocclusion. The first phase of treatment: molar and canine distalization with the Carrier Motion Appliance. Second phase: fixed bimaxillary orthodontic appliance.

**Discussions.** Using the Carrier Motion Appliance in the first phase of treatment of class II/1 malocclusion brings an undeniable benefit.

**Conclusion.** Upper first molars rotate into the correct position. Class I molar and cuspid relationships achieved. Overjet and overbite corrected. Total treatment time was greatly reduced.

**Keywords.** Carrier Motion Appliance, Class II Malocclusion, Distalization.



## 25. ETIOLOGY OF TEETH ERUPTION DISTURBANCES

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**Introduction.** Tooth eruption is a complex process during which teeth, initially positioned intraosseously, move along the alveolar process to the oral cavity, establishing contacts with the antagonists. Any deviation from the physiological pattern of tooth eruption signifies a disturbance of this process. Chronological changes of tooth eruption are represented by early eruption, delayed eruption and tooth impaction. All these disturbances can negatively influence the harmonious development of the craniofacial complex.

**Aim of study.** This study aims to carry out a literature review and to identify the etiological factors contributing to the occurrence of dental eruption disturbances.

**Methods and materials.** The analysis of 20 scientific articles on the PubMed and Google Scholar platforms was carried out using the keywords "early tooth eruption", "delayed tooth eruption", "tooth impaction".

**Results.** The analysis highlighted the multifactorial nature of the tooth eruption etiology. Early tooth eruption is usually caused by general factors such as endocrine disorders like hyperthyroidism and juvenile acromegaly, congenital syphilis, exposure to toxic compounds such as dibenzofuran or the hereditary factor which favors the superficial position of the tooth bud. Endocrine disorders are also the cause of delayed eruption. The most common are hypothyroidism which affects 1/5000 children, hypoparathyroidism, hypogonadism. Genetic causes of delayed eruption are Down syndrome, ectodermal dysplasia, Apert syndrome. Tooth eruption can be delayed in malnutrition especially associated with hypovitaminosis D and A. The administration of certain medications, such as acetylsalicylic acid, ibuprofen disrupts osteoclastic activity by inhibiting the activity of prostaglandins, which later leads to delayed eruption. General factors, as a rule, affect the eruption time for the majority of teeth or all of them while local factors affect the eruption of a single tooth or a small group of teeth. The main local factor that causes delayed eruption or tooth impaction is represented by physical obstruction which is the presence of an obstacle in the path of tooth eruption. The obstacle can be a supernumerary tooth such as mesiodens, odontogenic or nonodontogenic tumors, odontogenic cysts, gingival hyperplasia, mucosal barriers, the presence of scars following trauma or surgical interventions, ankylosis. Another local factor is the lack of space necessary for tooth eruption or its reduction, caused by the migration of neighboring teeth, macrodontia, transverse narrowing of the jaws.

**Conclusion.** Both general and local factors are involved in the etiology of dental eruption disturbances. In the case of early eruption, general factors prevail, while in delayed eruption both factors play a great role. Dental impaction, in most cases, is caused by local factors. Knowing the factors that can cause disturbances in the tooth eruption process enables their early detection and the initiation of appropriate treatment, thus preventing further complications.

## 26. EVALUATION OF GUIDED BONE REGENERATION AND BONE GRAFTING WITH AUTOGENOUS LAMINATES IN ORAL SURGERY



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**Introduction.** Oral rehabilitation, using dentures fixed on dental implants, has made a revolution in modern dentistry. However, it is often found that patients have significant bone atrophy of the alveolar processes of the jaws, which creates unfavorable conditions for the placement of dental implants. In these cases alveolar bone rehabilitation is the solution. It is considered that the “golden standards” of alveolar process atrophy rehabilitation are Guided Bone Regeneration (GBR) and bone grafting with autogenous laminates according to the method of Prof. Khoury.

**Aim of study.** The aim of this study is evaluation of bone regeneration techniques based on postoperative outcomes and complications.

**Methods and materials.** In this study, 20 patients aged 40-67 years, including 11 women and 9 men, with alveolar process atrophy of the mandible were registered. 10 patients underwent GBR surgery, with initial average bone width of  $\pm 4,14$  mm, and 10 patients - bone grafting with autogenous laminates, with initial average bone width of  $\pm 3,20$  mm. In case of GBR “Evolution Ostiobiol” membrane was used with the mix of autogenous and xenogenous bone grafts. In other case autogenous bone laminate was fixed vestibular with “Konmet” screws. The results of the surgeries were evaluated after 6 months based on CT data according to the following criteria: bone tissue growth, bone tissue resorption and complications.

**Results.** The study of both bone regeneration techniques showed no significant differences in bone gain 6 months after surgery. However, the use of bone rehabilitation with autogenous laminates demonstrated less bone resorption. Measurements made based on the control CT showed average resorption of 1,97 mm in case of GBR and 1,05 mm in case of regeneration with autogenous laminates. Analysis of postoperative pain level showed that a greater number of patients with severe postoperative pain was found in the group where bone regeneration with autogenous laminates was performed. In the case of GBR, 8 patients presented mild pain and only 2 patients – strong pain. In other techniques only 1 patient presented mild pain and 9 patients – severe pain. Postoperative swelling was not significantly different in both study groups with slightly longer duration in case of bone grafting technique with autogenous laminates. The average duration of swelling after the GBR surgery was 4 days, but in the case of bone grafting technique with autogenous laminates it was 6 days. There was only 1 case of temporary neurosensory disturbance out of the total number of patients reported only in case of augmentation with autogenous bone laminates. It's associated with bone laminate harvesting. In this case, sensitivity was fully restored after 4 weeks.

**Conclusion.** Bone grafting with autogenous bone laminates has a more favorable outcome in the amount of bone obtained and less resorption compared to GBR, both presenting similar postoperative complications.



## 27. EVALUATION OF THE PATHOLOGY OF THE FIRST PERMANENT MOLAR IN CHILDREN FROM LOCATIONS WITH LOW CONCENTRATIONS OF FLUORINE IN DRINKING WATER

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**Introduction.** The low concentration of fluoride in drinking water can have negative effects on children's oral health. For a maximum cariopreventive effect, fluoride must be administered endogenously during the mineralization period of the teeth.

**Aim of study.** Evaluation of the pathology of the first permanent molar in subjects aged 12 and 15 years from a geographical region of the Republic of Moldova with low fluoride concentration in drinking water.

**Methods and materials.** The medical records of 126 children aged 12 and 15, living in an area in the south of the Republic of Moldova, where the concentration of fluoride in drinking water is low, were analyzed. The subjects were ordered into 2 age groups: I group - 12 years (59 subjects) and II group - 15 years (67 subjects), later each group was subdivided into 2 other subgroups: A - girls and B - boys, depending on gender. Respectively, 31 subjects were included in group I A, subgroup I B - 28 subjects, II A - 32 subjects and II B - 35 subjects. Dental caries frequency indices, DMFT and DMFS caries intensity index, molar incisor hypoplasia (MIH) frequency index and missing first permanent molar were analyzed in both study groups.

**Results.** In the given locality the concentration of fluoride in the drinking water is low  $\cong 0.5$  ppm. The frequency of dental caries was 100% in all four study subgroups. The intensity of dental caries varied according to age: in the 1st group the DMFT index = 4.5, and the DMFS index = 8.1. In study group II, the DMFT index = 6.3, and the DMFS index = 12.9. The MIH frequency was 8.73% overall, and the highest frequency was in the group of 15-year-old boys – 11.42%. Premature loss of the 6-year-old molar was diagnosed in 12.69%, and missing first molar was most frequently diagnosed in 15-year-old boys – 17.5%. The serious case was diagnosed in a 15-year-old male subject who was missing 3 first permanent molars.

**Conclusion.** In areas with low fluoride concentration in drinking water, the frequency of dental caries is very high - 100%. The values of the dental caries intensity indices, both DMFT and DMFS exceed the values of the average level of dental caries intensity, placing these subjects in the group of subjects with high dental caries intensity. MIH falls within the global MIH frequency limits. Premature loss of the first permanent molar reaches alarming levels of up to 17.5%. Consumption of water with a low concentration of fluoride during the period of formation and mineralization of dental hard tissues presents an increased risk of dental caries and premature loss of permanent teeth.



## 28. FACIAL ARCH IN THE REHABILITATION OF COMPLETELY EDENTULOUS PATIENTS



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**Scientific advisor:** Alina-Ramona Dimofte, MD, PhD, Assistant Professor; Kamel Earar, MD, PhD, Professor

**Aim of study.** The key element ensuring successful prosthetic therapy is the possibility to determine and record the position of the maxilla relative to the skull base in bimaxillary totally edentulous patients.

**Methods and materials.** Four patients aged between 71 and 88 years were examined at the University Center of Dental Medicine of the Municipality of Galati and diagnosed with total bimaxillary edentulousness. To determine the intermaxillary relationships it was decided to use the facial arch with an arbitrary hinge axis. After this step, the models were mounted in the articulator by two methods: with and without records determined with the facial arch.

**Results.** After comparative analysis of the two types of mountings, a difference was found between the inclination and direction of the recorded prosthetic orientation plane. The intermaxillary relationships determined with the facial arch, subsequently mounted in the articulator, were closest to the actual intraoral clinical situation.

**Conclusion.** The use of the facial arch by the dentist and its corresponding articulator by the dental technician has proven its usefulness in total adjunctive prosthetic therapy.

**Keywords.** Total edentulous, facial arch, semi-adaptable articulator



## 29. GINGIVITIS FOLLOWING ORTHODONTIC TREATMENT. METHODS OF DIAGNOSIS AND TREATMENT

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**Introduction.** Periodontal disease is currently one of the most common diseases of the dental and jaw systems. The rapid increase in the incidence and frequency of this disease, its severe onset, its progressive tendency, the impairment of the general condition of the body and the decrease in the quality of life make this disease one of the most widespread pathologies today. This leads to massive tooth loss. According to the OMS, tooth loss due to periodontal disease is five times more common than tooth decay and its complications.

**Aim of study.** Aim of study was studying methods of diagnosis and treatment of gingivitis in patients with orthodontic appliances.

**Methods and materials.** In this statistical study descriptive methods were used for the analysis of clinical cases. The aim of this study is to clarify the involvement of promoter factors in the development of gum disease in patients wearing orthodontic appliances. For this study, patients underwent subjective and objective clinical examinations, collecting detailed anamnestic data to determine the triggers and determinants of gingivitis development, they also underwent paraclinical examinations. A thorough analysis and correct diagnosis of a patient with gingivitis provides an opportunity to start a comprehensive treatment. Determination of bacterial plaque index and determination of bleeding gums on probing with periodontal probes was performed. Based on the results obtained we established the diagnosis of gingivitis and its type.

**Results.** Regular monitoring of gum health, patient training in effective oral hygiene techniques and promoting a healthy diet are essential elements in the preventive approach to gingivitis. Proper hygiene of dental surfaces and orthodontic appliances is crucial to prevent bacterial plaque build-up and reduce the risk of gum inflammation.

**Conclusion.** Integrated approach to gingivitis in orthodontic treatment requires close collaboration between patient and doctor. Ongoing patient education on oral hygiene, close monitoring of gum health and early intervention if inflammation develops are key to maintaining long-term oral health during and after orthodontic treatment.

### 30. GUIDED BONE REGENERATION USING LAMELLAR AUTOGENOUS BONE BLOCK.



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**Introduction.** Nowadays, restoring edentulous areas by inserting implants is becoming increasingly popular. Successful implant placement requires an adequate alveolar ridge dimension, this is one of the mandatory requirements to provide aesthetics and functionality on the long term. To provide the required amount of bone tissue for implantation, guided bone regeneration procedures using allogenic as well as xenogeneic grafts are often used. However, the obtained results often are insufficient due to poor integration of grafting material. One of the techniques that allow the restoration of three-dimensional crestal defects is the Khoury technique - which offers the advantage from the following perspectives: the structural stability gained by using autogenous bone blocks, also offering the advantage of integrating bone blocks through faster postoperative tissue adhesion (due to the autogenous nature of the graft) and the low volume of inflammatory complications.

**Case statement.** The study was centred on a female patient of 60 y(o), that addressed with the absence of the right lower molars in the mandible. After clinical and paraclinical evaluation, it was determined that the posterior sector of the mandible presents a horizontal defect of the alveolar ridge – class C-w by Misch, limited amount of medullary bone, thin gingival phenotype, and an implant crown-ratio close to 1:1. of two bony wall defects. In order to restore the defect, bone augmentation using autogenous lamellar bone blocks harvested from the region of wisdom molar was used. The lamellar bone from the donor site was harvested with piezotome and stabilized with microscrews, while the obtained space between block and recipient site was grafted with porcine graft and covered with biphasic cement. Postoperative x-rays were made at the end of the healing period (4 months), before implant placement.

**Discussions.** The augmentation method performed showed a sufficient amount of bone obtained. In comparison with Khoury technique, in this particular case porcine graft and biphasic cement were used to fill the gap. During the preparation of the implant site, no difference between the native bone and porcine graft were observed. The implants were inserted in one-surgical step and soft tissue grafting was performed in the same surgery.

**Conclusion.** The usage of xeno- or porcine graft in combination with autogenous lamellar bone blocks offer good results and can be considered an alternative to the pure autogenous grafting material. The presence of autogenous bone at the edge of the grafted area ensures both osteogenic properties and hard support of the obtained scaffold.



### 31. HISTOLOGICAL ASPECTS OF BONE RECONSTRUCTION IN ORTHODONTICS

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**Introduction.** Understanding the mechanisms of bone growth is crucial for orthodontists. Craniofacial development involves intricate processes of bone formation, sutural growth, and changes in the shape and size of facial structures. Orthodontists must be well-versed in the normal patterns of craniofacial development to diagnose and address abnormalities. There are 2 important process of bone formation: bone modeling and remodeling. The modeling refers to the process of bone formation and adaptation during growth. In orthodontics, it is particularly relevant to the shaping of bones in response to mechanical forces, such as those applied by orthodontic appliances. Also it plays a significant role in achieving desired tooth movements and jaw adjustments. The remodeling is the continuous process of bone resorption and formation throughout life. It is essential for maintaining bone density, responding to functional demands, and repairing micro-damage. Orthodontic treatments can influence bone remodeling, especially in cases where teeth are moved or repositioned.

**Aim of study.** Was to explain the bone structure and its density in performing orthodontic treatment. Understanding of this can lead to more targeted and efficient approaches, potentially reducing treatment times and optimizing outcomes.

**Methods and materials.** We accessed relevant literature from sources such as NihGov, PubMed, NCBI and ScienceDirect from 2018-2023. The information was gathered also from histology and dentistry books. The keywords used for the search included “orthodontics, bone structure, bone remodeling, bone growth and bone density in orthodontics”.

**Results.** After studying the sources and analyzing their reliability, we have determined that orthodontic tooth movement involves the repositioning of teeth within the alveolar bone to achieve proper alignment. The success of orthodontic tooth movement is closely linked to the remodeling of the alveolar bone surrounding the tooth roots. This process includes the resorption of bone tissue on the compressive side and the deposition of new one on the tension side. Both, labial (towards the lips) and lingual (towards the tongue) movement of anterior teeth leads to changes in the alveolar bone. Notably, these changes in alveolar bone height and thickness primarily occur at the cervical level.

**Conclusion.** Ongoing and future research in the field, including histological studies, is crucial for advancing orthodontic care. This research contributes to a deeper understanding of the complex interactions influencing bone histology. Also, this statement emphasizes the dynamic nature of orthodontics, where understanding bone histology is crucial for providing effective and personalized care for patients across different age groups and health conditions. Advances in research, especially in the realm of genetics, hold the potential to further refine and enhance orthodontic treatments on an individual basis.

## 32. ICON-AN INNOVATIVE APPROACH TO FLUOROSIS TREATMENT.



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**Introduction.** Minimally invasive treatment serves as a progressive outlook in the field of dentistry, and it has valuable scientific importance. It serves as a support to create adequate conditions for the maximum preservation of dental tissue. The infiltrative method based on the ICON system offers promising results in fluorosis treatment.

**Aim of study.** Efficiency evaluation of infiltrative methods based on the ICON system in fluorosis treatment.

**Methods and materials.** The study includes patients with unaesthetic discoloration of enamel, including the involvement of both superior and inferior maxilla due to fluorosis. All the patients were treated using the infiltrative method based on the ICON system. The results were analyzed through clinical assessment before and after the treatment.

**Results.** As a result, the study demonstrated the aesthetic effect of the treatment with preservation of the enamel surface relief. Hence, the patients obtained a monochrome and shiny, avoiding the hyperesthesia phenomenon; therefore the patients were satisfied.

**Conclusion.** The aesthetic appearance of the teeth affected by fluorosis can be recovered successfully using a conservative treatment that relies on the infiltrative method based on the ICON system. Its application provides satisfactory outcomes in a short period of time, additionally ensuring the maximum preservation of dental tissues.





### 33. IMMUNE SYSTEM RESPONSE TO ORTHODONTIC TOOTH MOVEMENT

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**Introduction.** Dental movements during orthodontic treatment are generated by a mechanical force that induces an aseptic inflammatory response in the tissues of the periodontal system, which subsequently generates the process of bone resorption and apposition. Knowing the immune system mechanisms involved in tooth movement can be useful in orthodontic practice, regarding the selection of the treatment method, the management of forces applied to the periodontal units and the correct application of biomechanical principles.

**Aim of study.** Analyzing the interaction of the immune system with tooth movements in orthodontic treatment, which helps to gain vast insights into shortening the treatment period and reducing the number of complications.

**Methods and materials.** The study involved a detailed review of the literature to highlight recent findings in the field of the interaction between the immune system and orthodontic movements. Clinical and experimental studies that assessed the immune response in the context of orthodontic treatment were also reviewed.

**Results.** The literature review reveals that orthodontic movements can activate local immune responses, causing the release of cytokines, prostaglandins and other mediators of inflammation, which subsequently play a significant role in triggering bone remodeling processes around the teeth subjected to the applied forces. According to some researchers, orthodontic forces induce synthesis and secretion of endogenous prostaglandins by local cells, which in turn stimulates the osteoclastic process of bone resorption. Pain associated with orthodontic movements has also been found to be related to local inflammation and changes in intercellular interaction.

**Conclusion.** The response of the immune system to orthodontic movements is a complex phenomenon, in which the interactions between immune cells, dento-periodontal tissues and biological processes are closely related. Understanding these mechanisms is an essential component for optimizing orthodontic treatment, both from the perspective of effectiveness and patient comfort. Also, identifying ways to manage the inflammatory response may contribute to the development of more personalized and better tolerated therapeutic strategies.

### 34. IMPORTANCE OF AN IMAGISTIC EXAMINATION OF TEMPOROMANDIBULAR JOINT



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**Introduction.** Medical imagistic techniques have evolved significantly in recent years, which has led to an increase in both the quality of the images obtained and the quality and accuracy of diagnosis. Therefore, imagistic examination of the TMJ (temporomandibular joint) remains a subject of interest in dentistry and is expected to continue to evolve in the near future as a result of the development of medical technologies. Imagistic examination of the TMJ is mandatory for the diagnosis of conditions such as arthritis, temporomandibular dysfunction, joint dislocation and soft tissue tumors. Using various medical imagistic techniques such as CBCT (cone-beam computed tomography), MRI (magnetic resonance imaging), or USG (ultrasonography), it is possible to obtain a detailed picture of the anatomy and structure of the TMJ.

**Aim of study.** To determine the indications and contraindications, as well as the possibilities of using different types of imagistic examinations of the temporomandibular joint.

**Methods and materials.** In this study, such imagistic examinations as panoramic radiography, CBCT (cone-beam computed tomography), USG (ultrasonography) and MRI (nuclear magnetic resonance) were evaluated and compared, along with the particularities of each method, their advantages and disadvantages, and their importance in relation to TMJ disorders. Examples of comparative physiological and pathological anatomical aspects of TMJ were presented.

**Results.** After reviewing the articles, it was found that the selection of the imagistic technique should be carefully made by the practitioner in correlation with the clinical signs and symptoms. Each method has its own indications, and by correctly understanding the tissue biology, we can distinguish when one method or another would be preferable. CBCT and MRI are currently the most commonly used imagistic techniques. CBCT is effective in the diagnosis of bone changes, and MRI is effective in the examination of the articular disc. High-resolution USG is indicated in the evaluation of articular disc position.

**Conclusion.** TMJ disorders have a high prevalence rate among the population and because these disorders are often accompanied by pain, they can significantly affect the quality of life. Therefore, it is of great importance to accurately and timely diagnose these disorders in order to achieve effective treatment or at least to mitigate the consequences.



### 35. INFLAMMATORY PROCESSES IN THE ORO-MAXILLOFACIAL REGION. STUDY OF ANTIBIOTICOGRAMS AND STATISTIC DATA.

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**Introduction.** Inflammatory processes in the OMF region provide a serious risk to patients because of its proximity to the head and neck region's organs. Due to the OMF area's high vascularization, infections can spread easily, leading to serious and occasionally fatal consequences such as meningitis, thrombophlebitis, sepsis, and mediastinitis. Since the OMF region is an aesthetic area, early diagnosis and prompt surgical intervention are crucial to the patient's overall physical and psychological well-being. Only 4–10% of cases have microorganisms from non-odontogenic sources as the etiological component, while the majority of cases (90–96%) - odontogenic infection. For a considerable amount of time, the primary cause of inflammatory illnesses with an odontogenic origin was thought to be facultative anaerobic microflora, such as streptococci and staphylococci, and aerobic pyogenic microflora. Later, when new techniques for microbiological diagnosis emerged, it was determined that staphylococcus is present in 15%, streptococcus - 6%, and anaerobic bacteria - 79%.

**Aim of study.** Analysis of the optimal medicamentous method of treatment based on contemporary literature and antibioticogram data.

**Methods and materials.** The study included 4538 patients (2777 men and 1761 women), aged 18-90 in the period 2018-2023 with the diagnosis of inflammatory processes. The most often detected were phlegmons - 2609, followed by abscesses - 1030 and furuncles - 592 cases.

**Results.** Following the analysis of the antibioticograms the most common pathogen determined was staphylococcus epidermidis - 32.48%, followed by streptococcus group G - 18.53% and streptococcus group C - 10.69%. The basic principles of antibiotic therapy must be adhered to: selecting antibiotics based on microbiological research; optimizing dosages and administration methods; periodically substituting commonly used drugs with newly developed; continuously analyzing strains of microorganisms and their sensitivity in the hospital environment. The analysis of antibioticograms showed their sensitivity to antibiotics, so we obtained the following data: staphylococcus epidermidis sensitive to azithromycin, erythromycin, gentamicin, streptococcus group G sensitive to amoxicillin, amoxycylav, azithromycin, moxifloxacin and streptococcus group C- benzylpenicillin, amoxicillin, amoxycylav.

**Conclusion.** The antibiotics used in dental practice, penicillins, proved to be the antibiotics most frequently prescribed by dentists; the most popular antibiotic was amoxicillin, followed by azithromycin and the combination of amoxicillin and clavulanic acid.

### 36. INTERACTIVE METHODS OF PROMOTING ORAL HEALTH IN CHILDREN



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**Introduction.** The promotion of oral health is currently a necessity, it directly contributes to educating, changing the behavior of the population, creating a healthy family environment and adopting a healthy lifestyle, with proper oral hygiene practices.

**Aim of study.** Evaluation of the effectiveness of interactive methods to promote oral health in rural school-aged children.

**Methods and materials.** The study was carried out in the premises of an educational institution in the municipality of Râșcani, on a sample of 54 children, aged between 11 and 14 years. Children were clinically examined, clinical data were collected in accordance with World Health Organization criteria. Oral hygiene status was assessed using the OHI-S (G. Green, I. Vermillion 1964). The evaluation of the children's initial knowledge was carried out using the questionnaire method (Questionnaire 1). Afterwards, the children received an interactive educational session in the classroom, dedicated to oral hygiene training and dental disease prevention dedicated to oral hygiene training and dental disease prevention that included an interactive presentation, the True or False game, demonstration of an instructional video film, demonstration of tooth brushing technique on casts. Questionnaire 2 was used to evaluate the effectiveness of health education. In the questionnaires, the usual language was used, the questions were short, neutral and clearly formulated. The study was conducted in accordance with ethical requirements, with the written consent of the children's parents being obtained. The analysis of the obtained data was carried out using parametric and non-parametric tests of Excel and Epi Info Software, with the help of their functions and modules.

**Results.** Following the evaluation of the state of oral hygiene, it was found that in the children included in the study, the average value of the OHI-S index was  $1.46 \pm 2.28$ . The satisfactory state of oral hygiene was appreciated in 53.7%, and unsatisfactory - in 14.81% of the children. The statistical processing of Questionnaires 1 revealed that only 29.62% of the children interviewed mentioned that they brushed their teeth twice a day, 57.42% of the children - only once a day, and 12.96% stated that they brush your teeth a few times a week. Following the application of interactive methods to promote oral health, the number of children who brush their teeth twice a day increased by 42.6%, and those who regularly sanitize their oral cavity decreased by 7.4%. The state of oral hygiene improved 1.43 times, the average value of the OHI-S index becoming  $1.02 \pm 1.14$ .

**Conclusion.** Interactive methods of promoting oral health are efficient motivating children and boosting the activities of proper hygienic care of the oral cavity. The implementation of interactive methods to promote oral health in groups organized by children is necessary to be carried out within health education programs implemented at the community level.



### 37. MANAGEMENT OF ZYGOMATIC COMPLEX FRACTURE

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**Introduction.** Zygomatic complex fracture is a prominent type of maxillofacial trauma in the Republic of Moldova. This type of trauma is severe due to potential complications that can adversely affect a person's overall health (diplopia, enophthalmos, difficulty in mouth opening). In recent years, there has been a trend of increasing incidents of this type of trauma. This trend is associated with an increase in car accidents, aggressive incidents, and activities resulting in falls.

**Aim of study.** To conduct a retrospective analysis of data over the last 2.5 years for patients with zygomatic complex fractures. To analyze statistics and identify the prevalence of this type of trauma, as well as its seasonality, age and gender characteristics.

**Methods and materials.** A retrospective analysis was conducted for the period from 19.01.2021 to 20.06.2023, using patient records from the Maxillofacial Surgery Department archive at the Emergency Medical Institute. The statistical data were based on patients diagnosed with “zygomatic complex fracture” upon admission.

**Results.** From 19.01.2021 to 20.06.2023, 42 patients with zygomatic complex fractures were admitted, making up 33.6% of all maxillofacial traumas in this period. Zygomatic complex fractures ranked second in frequency among all traumas in the maxillofacial region for this period. The male-to-female ratio is 4:1 (34:8), explained by the fact that the most common etiological factors are assaults and sports activities, often accompanied by falls. In 2021, there were 12 cases, in 2022 - 25 cases, and in the first half of 2023 - 5 cases (29%, 60%, and 12%, respectively). The majority of patients were admitted during the summer (38%). April, June, and August being the most common months for this type of injury, each of these months accounts for 15%. The least common months were September with 0 cases and December with 1 case (0% and 2%, respectively). The average age of patients was  $36\pm 6$  years, with the most common age group being 25-44 (47%), and the least common age group being 60-74 (6%). No cases were identified in the age group over 75 during this period.

**Conclusion.** A descriptive retrospective study was conducted using data from the archive of the Emergency Medical Institute over the last 2.5 years, revealing the prevalence, seasonality, and age and gender characteristics of this type of trauma.



### 38. METHODOLOGY OF USING THE OCCLUSAL KEY IN CLINICAL PRACTICE



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**Introduction.** The special significance of personalization is manifested in the meaning of the anatomical, topographical, and constitutional characteristics of patients. Therefore, the search for new materials and technologies for “invisible” dental restoration in therapeutic activities is justified. The methodology of using the occlusal key involves reproducing the original anatomy of the tooth structure by simulating the original unprepared tooth structure. The technique is used where, before the restorative procedure, the occlusal surface is practically undamaged.

**Case statement.** One of the ways to reproduce the structure of the cusps and fissures is to make an occlusal key using a liquid rubber dam from the chewing surface. In the clinic, it can be used in cases where, in the presence of carious lesions, the main area of the chewing surface is preserved. I present a clinical case of making a template for caries. Intact chewing surface. It is assumed that the occlusal key will be removed using a liquid rubber dam, followed by the preparation of the cavities and filling them with a photocurable composite.

**Discussion.** An analysis of the effectiveness of restoring the chewing surface of teeth using the “occlusal key” technique showed that the material filled the mouths of the fissures and covered the slopes and cusps of the chewing surface. When evaluating the finished restoration made using the “occlusal key” technique, the chewing surface of the finished work completely reproduced the chewing surface of the tooth before preparation. When checking the occlusal contacts, the restoration was in full interaction with the antagonist's teeth.

**Conclusion.** Thus, the use of individual occlusal keys in the clinical practice of a dentist in specific situations is an excellent alternative option for modeling the occlusal surface of individual teeth. The “occlusal key” technique simplifies the dentist’s work, saves time on modeling the restoration, and avoids its lengthy occlusal adaptation and grinding compared to the free modeling technique.



### 39. METHODS OF DIAGNOSIS AND TREATMENT OF CHRONIC FIBROUS PERIODONTITIS

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**Introduction.** Chronic apical periodontitis is one of the main problems of contemporary endodontic therapy. Fibrous periodontitis occurs as a result of acute periodontitis, previously treated pulpitis, or stress caused by edentation or joint trauma associated with the reduction of cellular elements and the increase of fibrous tissue - a diffuse thickening of the periapical portion of the periodontium.

**Aim of study.** To determine the effectiveness of the treatment of chronic fibrous periodontitis, including the sterilization, drying and perfect sealing of the root canal system and the preservation of the functional tooth in the healthy bone.

**Methods and materials.** A group of 18 patients, aged between 35 and 50 years, who were treated or were undergoing treatment were clinically and paraclinical examined to determine the presence of periapical changes and obtain clinical and radiological data on affected teeth. The final treatment of the tooth is possible only when the periapical tissues are free of apical inflammation.

**Results.** Endodontic treatment complying with the stages of root canal preparation, qualitative sterilization and filling represents a complex therapeutic solution to restore the morpho-functional integrity of the teeth in the dental arch.

**Conclusion.** The clinical study was of great importance in the treatment of chronic fibrous periodontitis and highlighted the need for qualitative and effective treatment to stop and heal pathological apical processes. Successful results of the therapeutic approach to patients with periapical conditions depend on an early diagnosis and treatment plan.

## 40. METHODS OF DIAGNOSIS AND TREATMENT OF SUBMANDIBULAR ABSCESS



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**Introduction.** Infectious processes localized within the fascial spaces of both the maxillary and mandibular regions represent a clinically challenging case, even in the current stage, regardless of medical technological and scientific advancements. In the vast majority of clinical cases involving infection with subsequent suppuration of the Oro-Maxillo-Facial region, both odontogenic infections and periodontal conditions are implicated as etiological factors. From the category of fascial spaces located in the lower jaw, the submandibular space is more frequently involved in purulent-inflammatory processes of dento-parodontal origin, with the causative teeth often being the lower molars. The treatment of submandibular abscess involves a comprehensive approach, consisting of a surgical component, the incision and drainage of the purulent collection.

**Case statement.** Patient O.G., female, 58 years old, presented at the Emergency Medicine Institute, complaining of pain and swelling in the left submandibular region. According to the patient, six days ago, she experienced pain in the region of tooth 38, and she sought dental care where tooth extraction was performed, followed by antimicrobial and analgesic treatment. Subsequently, she developed pain in the post-extraction region, accompanied by trismus. Swallowing disturbances appeared, and gradually, the swelling and pain in the left submandibular region progressed. The patient has no personal pathological history or associated illnesses. Upon objective clinical examination, extraorally, an oval facies with asymmetry due to inflammatory edema in the left submandibular region was observed. Palpation revealed suppleness, with the covering skin being edematous, hyperemic and painful. Mouth opening was limited to approximately 2.0 cm due to severe trismus. Intraorally, the oral mucosa appeared pink-pale and intact, except for the swollen, and painful trigone retromolar region on the left. In the alveolus of tooth 38, there was a grayish-gray endoalveolar clot. Paraclinical investigations included Computed Tomography, revealing a radiolucent area at the left submandibular angle. Based on the results of the clinical and paraclinical examinations, a diagnosis of left submandibular odontogenic abscess, post-extraction of tooth 38, was established. A comprehensive treatment plan was devised, involving medical therapy: administration of antimicrobial, anti-inflammatory, detoxifying, desensitizing, and analgesic medications. Surgical treatment was performed under local infiltrative anesthesia with 1% Lidocaine - 20 ml and intravenous sedation. The skin incision in the left submandibular region was approximately 5-6 cm long, penetrating through layers into the submandibular space, obtaining purulent exudate, and collecting samples for bacteriological examination. Wound irrigation with antiseptic solutions, placement of two perforated polyethylene tubes, and aseptic dressing were performed. Postoperatively, the patient showed improvement in symptoms, with treatment focused on medical therapy and physiotherapeutic procedures.

**Discussions.** Based on the study of contemporary literature and treatment outcomes, it has been observed that submandibular abscess most commonly has odontogenic etiology, with the lower molars being frequently involved.

**Conclusion.** Infections of fascial spaces constitute a medical emergency due to the complex anatomy of the Oro-Maxillo-Facial territory and the potential complications that may arise in the evolution of the septic process. Therefore, early and accurate diagnosis of submandibular space abscess contributes to the development of a specific treatment plan, given its complex nature. The surgical component is the primary method, with the highest level of efficiency, and the medicinal aspect, which is complementary.



## 41. METHODS OF MAKING TEMPORARY PROSTHETIC CONSTRUCTIONS AND THEIR APPLICATION IN DENTAL PRACTICE

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**Introduction.** An important issue for patients with bulky coronal dental lesions is the emotional and aesthetic impact of coronal lesions, which can influence a person's self-confidence and social interactions.

**Aim of study.** Studying the importance and particularities of provisional prosthetic constructions in the pre-prosthetic preparation stage.

**Methods and materials.** In the elaboration of this new thesis we used the information resources of the Medical Scientific Library of the *Nicolae Testemitanu* State University of Medicine and Pharmacy, which included publications from peer-reviewed journals in the searchable base of electronic library sources PubMed, Medline, MedScape, Google Scholar, Wikipedia and Hinari.

**Results.** Depending on the indication and the expected time in clinical service, there are a variety of materials and manufacturing techniques available. Depending on the fabrication technique provisional prosthetic constructions (PPC) can be divided into direct and indirect restorations. The different technologies have an influence on the individual wearing time of PPC. Fabricated using the direct technique are recommended for a wearing period between one and three months, while PPC fabricated using indirect techniques can be in service for up to two years. Particularly in clinical settings requiring changes in the vertical or horizontal dimension of the occlusion of all the materials needed to construct a provisional prosthetic construct by the direct method the most common is light-curing composite material, but by the indirect method – CAD/CAM polymers based on polymethyl methacrylate (PMMA) resins. According to some authors, the choice of material for fixation of provisional restorations is of little clinical importance; however, the use of a suboptimal cement can lead to a number of complications, including increased marginal permeability, development of secondary caries, loss of fixation of the restoration, displacement of restored, adjacent and antagonizing teeth, and fracture of the restoration; therefore, the following factors should be considered when selecting a cement: clinical conditions, caries index, preparation form, mechanical stresses, type of preparation, and the type of cement used in the restoration. To prevent the complications described above, special attention must be paid for each patient individually when selecting the optimal cement for fixation of provisional restorations.

**Conclusion.** A provisional prosthetic construction is necessary to protect the denture-ready teeth against thermal and chemical irritation, bacterial invasion (a risk factor), to reduce dentin sensitivity, as well as to prevent mechanical defects and ensure a healthy periodontium.

## 42. MINIMALLY INVASIVE MANAGEMENT OF DENTAL FLUOROSIS IN ADOLESCENTS: CASE REPORT



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**Introduction.** Dental fluorosis is the most common and prominent early-stage symptom of chronic fluorosis, which is caused by excessive fluoride intake during tooth development. It is characterized by the presence of bilateral, diffuse, thin and horizontal striations ranging from immaculate white to brownish brown. In the most severe cases, the enamel may erode or have areas of massive destruction. This condition can affect the quality of life and have psychosocial effects on patients. Aesthetic discoloration of fluoridated teeth can be managed by bleaching, micro-abrasion, infiltration, veneering, or crowning.

**Case statement.** This report presents a case of clinical management of dental fluorosis. A 13-year-old boy presented to the Department of Pediatric Dentistry with complaints of unaesthetic defects on the surface of the teeth. According to the parents, the child is affected by the appearance of the teeth and requests the doctor's intervention to correct the dental aesthetics. The patient was born and lived in a locality with an optimal concentration of fluoride in the drinking water, but every year he spent the three months of his summer vacation at his grandmother's in a locality with a high concentration of fluoride in the drinking water of 5 ppm. The intra-oral examination revealed the characteristic clinical picture of dental fluorosis. The permanent dentition is established. Oral hygiene is perfect. The Tooth Surface Index of Fluorosis score was 4. Taking into account the young age of the patient, it was decided to apply the microabrasion method in combination with the infiltration method of hard dental tissues with resin.

**Discussions.** Microabrasion is indicated for surface opacities, while bleaching can treat opacities deep within the tooth. When these techniques have failed to achieve the desired result, camouflaging the opacity with composite resin may be helpful. New techniques, such as infiltration or opacity sealing, can alter the refractive index of enamel, providing additional treatment options.

**Conclusion.** When selecting the method of aesthetic treatment of teeth with dental fluorosis, the age of the patient, the form of dental fluorosis, and the patient's expectations will be taken into account. The safest, most effective, and minimally invasive methods are enamel microabrasion, resin infiltration, and tooth whitening. Severe forms require more drastic methods, such as dental restorations and crowding, which inevitably require enamel grinding.





### 43. MODERN CONCEPTS ON THE CLINICAL ASPECTS OF THE CUNEIFORM DEFECT

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**Introduction.** The cuneiform defect is the most common non-carious lesion of hard dental tissue. It is usually located in the cervical region of the teeth and the vestibular surfaces of maxillary premolars. The geometry of the lesion is represented by a cone (from the Latin *cuneus* - wedge), this is where the name of the condition comes from. The lesion causes over time dentinal hypersensitivity, aesthetic discomfort and dystrophic pulp changes. Repeated exposure to stress leads to the increase in size of the defect.

**Aim of study.** Analysis of the particularities of the clinical appearance of the cuneiform defect according to the geometric shape of the lesion.

**Methods and materials.** The study included 13 patients with cuneiform defects in the limits of enamel and dentin, both in the upper and lower jaw. The wedge- or V-shaped lesions (less area of stress concentration under load) was identified in 4 patients and the U-shaped lesion (with a flattened tip - where the forces are dispersed) was identified in 9 patients. The analysis was based on the use of inspection, percussion and sensibility tests such as heat pulp testing (HPT) and cold pulp testing (CPT).

**Results.** According to the results, V-shaped lesions were associated with hypersensitivity, recently appeared aesthetic defects, jaw pain and temporomandibular joint (TMJ) noises. In the cases associated with U-shaped cuneiform defects, a long evolution of the lesions was observed and patients reported only aesthetic changes. Also, some of the patients claimed suffering of the gastrointestinal tract, such as acute gastritis episodes or gastro-intestinal reflux.

**Conclusion.** The geometric shape of the lesion plays an important role in the stress distribution to the teeth. U-shaped cuneiform defects are more frequently associated with a chronic evolution and erosive etiological factors. The V-shaped lesions are associated with an acute and rapid evolution, with pathological occlusal forces and muscle hyperfunction. These aspects are important in clinical practices because they guide the clinician to the right treatment tactics. Additionally, they offer the possibility to transform lesions with sharp geometry into rounded cavities, thus preventing further loss of dental tissue during the restoration.

#### 44. MOLAR INCISOR HYPOMINERALIZATION ASSOCIATED WITH SUPERNUMERARY TEETH



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**Introduction.** Molar incisor hypomineralization (MIH) is a qualitative enamel defect that usually occurs on one or more permanent first molars with or without involvement of the permanent incisors, with reported rates ranging from 2.5% to 40.2%. Although the exact cause of MIH is still unknown, some authors believe it to be complex. An odontostomatologic anomaly known as supernumerary teeth (ST) is defined as having more teeth than is typical for a given dental formula. The prevalence of ST has been reported at 0.2–3% in primary and permanent dentition. There are many theories about the development of ST etiology, even if they are not fully explained, such as dental lamina hyperactivity or tooth bud dichotomy. The molecular mechanism during the early phase of tooth development may be a reason for a single ST. Several STs occur more frequently in relatives of affected patients than in the general population.

**Case presentation.** Is a clinical case of association between MIH and two permanent upper central incisors.

**Discussions.** This study reports a clinical case of association between MIH and two supernumerary central incisors in a 7-year-old girl who presented for dental care at the Department of Pediatric Dentistry. The intra-oral examination revealed the characteristic MIH clinical picture of all permanent first molars and the presence of temporary upper incisors without mobility. The maxillary lateral incisors were completely erupted. To clarify the diagnosis, CBCT was performed, which revealed the presence of two impacted maxillary central incisors, placed posteriorly to the primary central incisors. In addition, CBCT also confirmed the presence of two supernumerary teeth, also placed behind the impacted central incisors. Both MIH and ST are major challenges in pediatric dental practice due to the complexity of clinical symptoms and the long-term effects these conditions can produce. The causes are different, and the management of each condition will take into account the presence of the other. Management of ST depends on the type, location, outcome, and potential influence on adjacent teeth. Tooth sensitivity in cases of MIH can cause a child to neglect oral hygiene, resulting in susceptibility to caries. The medical condition may be linked to persistent pulpal inflammation. Concerns about appearance are prevalent, particularly when the anterior teeth are involved.

**Conclusion.** There is a need for early emphasis on preventive measures to avoid post-eruptive enamel breakdown in cases of MIH. The choice of treatment method in such cases must take into account the type of additional tooth, the distance from the permanent germ to the supernumerary tooth, and the availability of space inside the arch for an unerupted tooth..



## 45. MORPHO-FUNCTIONAL RESTORATION OF THE LATERAL GROUP OF TEETH

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**Introduction.** The health and aesthetics of teeth are a determining indicator of the quality of life for all humanity. Therefore, nowadays aesthetics has become a primary concern for patients, with an increasing number turning to this branch of dental medicine, through which the morpho-functional restoration of teeth occurs with the help of dental restorations. These, in turn, provide patients with healthy dental structures, a healthy periodontium, as well as normal neuro-muscular functions. Additionally, they offer a new shape to the teeth along with a charming smile that restores self-confidence. Sometimes, a charming smile can even represent the 'ace up the sleeve' in social situations, where outcomes often depend on image, regardless of the nature of the relationships, whether diplomatic or affective. Aesthetics here becomes the final foundational puzzle piece in fostering beautiful relationships and impressions.

**Aim of study.** Identification and highlighting of modern aspects regarding the preparation and methods for the morpho-functional restoration of the lateral group of teeth, as well as the utilization of materials for restorations.

**Methods and materials.** In this study, 15 patients aged 21-46 years, including 9 women and 6 men, were examined and treated. After the paraclinical and clinical examination, At 5 patients, direct dental restorations were performed on posterior teeth using the composite material "Charisma Classic," while at 10 patients, restorations on posterior teeth were carried out using the composite material "G-aenial Posterior." Both materials provide excellent aesthetics and good adaptation to hard dental tissues. Charisma Classic Gluma 2 Bond, G-aenial Posterior and G-aenial Universal Flo Syringe were used to ensure an effective treatment. Also, for these restorations was used the Microbrush Stamp Technique, the method that involves the anatomical reconstruction of the tooth structure.

**Results.** Patients exposed to the morpho-functional restoration treatment of the lateral group of teeth, through the Microbrush Stamp Technique, using state-of-the-art composite materials, showed satisfactory results and remarkable dental aesthetics.

**Conclusion.** The dental restorations performed on these patients, using the Microbrush Stamp Technique, significantly reduced the treatment time and restored the exact anatomy of the occlusal surface of the molars, providing remarkable aesthetics due to modern working methods and standards.

**Keywords.** Teeth, smile, restoration, image.

## 46. MORPHOLOGICAL CHARACTERISTICS OF TEMPOROMANDIBULAR JOINT HEADS ACCORDING ORTHOPANTOMOGRAMS



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**Introduction.** One important problem in the dental system is TMJ pain caused by joint deformation. Numerous articles discuss TMJ pathologies like arthrosis and arthritis, but information on the relationship between joint shape/size and tooth loss is lacking

**Aim of study.** Collection and analysis of literature on the topic of the study, as well as a comparative study of the morphological characteristics of the articular heads in various adentia on digital orthopantomograms.

**Methods and materials.** 35 articles from the electronic database (<https://cyberleninka.ru/>) were used along with existing literature for analysis. The study involved 56 adult patients who underwent visual assessment of articular heads' shape and size using digital orthopantomograms. Among the patients, 5 had intact dentitions while the remaining 51 had partial adentia of I-III classes according to Kennedy.

**Results.** OPTG showed round articular heads of medium and large size in patients without dental defects. In OPTG of patients with adentia, flat articular heads accounted for 39.2% and round articular heads accounted for 60.8%. In terms of size, the distribution was: small - 37.2%, medium - 33.33%, large - 29.4%. OPTGs with flattened articular heads were more common in patients with extensive adentia of I-II class according to Kennedy, likely due to cartilage surface abrasion. Narrow articular heads in the lower jaw are more prevalent in extensive adentia with severe alveolar process atrophy.

**Conclusion.** The morphology and pathology of the jaw joint heads are linked to dentition condition and adentia type. More extensive adentia often leads to flattened joint heads and greater atrophy of alveolar processes, resulting in narrower joint heads.



#### 47. OPEN BITE MORBIDITY IN SCHOOL-AGED CHILDREN

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**Introduction.** The study of open bite is relevant due to the increase in the incidence of dento-maxillary anomalies in recent years caused by the complexity of functional disorders and orthodontic treatment difficulties. An open bite is a dento-maxillary anomaly characterized by vertical plane disturbances and the lack of contact between the two antagonistic dental arches in various ways, affecting swallowing, phonation, mastication, and physiognomy.

**Aim of study.** To assess open bite morbidity in school-aged children.

**Methods and materials.** A descriptive study was carried out based on 115 medical records, including exo- and endooral clinical examination data on school children, aged 11-15, within an educational institution in Chisinau. To determine the incidence of open bite, the schoolchildren were stratified using mathematical calculations.

**Results.** The data were analyzed, and the occlusal parameters were described according to the reference planes. Most of the children had sagittal malocclusion. The incidence of Angle class I malocclusion made up 75.65% of cases, class II malocclusion - 16.52%, and class III malocclusion - 7.83%. The clinical-morphological signs of dental occlusion in the vertical plane were assessed. The assessment revealed deep occlusion in 20.87% of cases and an open bite in 2.61%. The occlusal relationship in a transverse plane was examined, revealing laterognathia in 5.22%.

**Conclusion.** An open bite is a less common dento-maxillary anomaly. The assessment of morbidity in the study found 2.61% of cases, a fact contradicted by the complex anatomic-functional semiology of the anomaly. The study is of particular relevance because it emphasizes the importance of early diagnosis of open bite to provide appropriate etiopathogenic orthodontic treatment.



## 48. ORAL HEALTH BEHAVIORS OF CHILDREN FROM DENTAL FLUOROSIS ENDEMIC AREAS



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**Introduction.** Currently, dental fluorosis is one of the most common causes of aesthetic dysregulation of the stomatognathic system, which causes changes in the psycho-emotional balance of children. In the Republic of Moldova there are several endemic areas, where the fluoride content in drinking water exceeds the maximum permissible values. At the same time, most patients with dental fluorosis do not have sufficient information for the proper care of the oral cavity and the annihilation or reduction of the consequences of chronic fluoride poisoning.

**Aim of study.** Evaluation of the level of information and behavior towards oral health of children in endemic areas of dental fluorosis.

**Methods and materials.** To carry out this study, an educational institution from the city of Rîșcani was selected, being an endemic area of fluorosis, and the level of fluoride varies within the limits of 7-10 mg/l. 78 children between the ages of 7 and 18 who were born and live permanently in this locality were included in the study. The objective clinical examination of the oral cavity was performed, and the children's sanogenic attitudes and behaviors were evaluated by means of a questionnaire developed by us. The questionnaire included questions regarding the knowledge about the causes and risk factors for dental fluorosis, and his attitude towards the aesthetic appearance of the teeth, the smile, the frequency of visits to the dentist, the particularities of the hygienic care of the oral cavity and measures to prevent dental fluorosis and maintain health oral. The research was carried out in accordance with the ethical requirements, with the written consent of the parents being obtained for the children's participation in this study. The analysis of the obtained data was carried out using Software Excel and Epi Info, with the help of their functions and modules.

**Results.** Of the total number of children examined, 74.36 % of the subjects showed signs of dental fluorosis. In the study it was found that 11.53% of children have not visited the dentist in the last 2 years, 48.72% do not know whether the toothpaste contains fluoride or not, 58.97% - do not have any information about the effect of fluoride on dental hard tissues, 52.56% do not know the causes and risk factors for dental fluorosis, 51.28% do not sanitize the oral cavity daily, 75.64% - feel psycho-emotional discomfort due to the appearance of teeth affected by fluorosis, 88, 46% - want to change the aesthetic appearance of the smile.

**Conclusion.** In this study, the insufficient level of information of 58.97% and the inappropriate behavior of at least 51.28% of the children in endemic areas of dental fluorosis were detected. Taking into account the impressive number of the population of the Republic of Moldova that permanently lives in endemic areas of dental fluorosis, it is necessary to initiate and carry out educational and oral health programs aimed at preventing dental diseases and strengthening the health of the growing generation.



## 49. OSTEOMYELITIS OF THE LOWER JAW

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**Introduction.** The problem of osteomyelitis has a long history. Despite certain successes in the fight against purulent infection, osteomyelitis of the jaws remains a pressing problem in modern medicine. This is due to the prevalence of the disease, the severity and duration of the pathological process. In this regard, it is necessary to constantly update and develop methods for the diagnosis and treatment of osteomyelitis of the jaw, as well as increase public awareness of this problem.

**Aim of study.** The study of statistical data over the past 5 years to identify trends in the prevalence of osteomyelitis in various age groups, genders and regions.

**Methods and materials.** Is a retrospective study performed in the period from 2018-2023 using the archive of the Department of Oral-Maxillofacial Surgery of IMSP IMU of patients hospitalized with a diagnosis of “osteomyelitis of the lower jaw of various etiologies”.

**Results.** Over the past 5 years, from 2018 to 2023, 193 cases diagnosed with osteomyelitis were reported. Over 5 years, the highest incidence rate was recorded in 2017, amounting to 38.3%. The majority of patients seeking surgical help are urban residents (63%). According to the research work, it was revealed that men get sick more often than women, which amounted to 52%. Most often, patients in the age category from 31 to 40 years suffer, which is a percentage of 22%. The leading etiological factor is odontogenic infection (62%), and it is the 7th tooth that causes the spread of infection. Most patients visited the Department of Oral-Maxillofacial Surgery on their own, and 71% of all patients had health insurance. According to the study, 90% of patients underwent surgical exploration, and the hospital stay ranged from 1 to 5 days, accounting for 59%.

**Conclusion.** According to the analysis of the archive of the Department of Oral-Maxillofacial Surgery, it was revealed that many people living in urban areas are most often ill. This can be explained by the fact that there are more medical institutions in the city and patients are treated more often than in rural areas.

## 50. PREDISPOSING FACTORS IN THE DEVELOPMENT OF TRANSVERSE MALOCCLUSIONS



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**Introduction.** Transverse malocclusions represent conditions that encompass a discrepancy in the alignment of teeth and maxillae in the transverse plane. Their etiology involves multiple aetiological factors that interact with each other. Knowing and identifying them in daily practice constitutes one of the key elements in establishing an accurate diagnosis and devising an individualized and successful treatment plan.

**Aim of study.** To emphasize the importance of predisposing factors in the development of transverse malocclusions.

**Methods and materials.** The specialized literature sources studied for this review were selected through scientific databases: PubMed, Google Scholar, Research Gate, and ScienceDirect. The following keywords were used: predisposing factors, transverse malocclusions, crossbite.

**Results.** The study of specialized literature highlighted the impact of vicious habits, such as: poor posture, thumb or object sucking, and interposition of the tongue between the dental arches, on the development of transverse malocclusions. However, several authors ascribe a more significant role to oral breathing, resulting from nasal airway obstruction, and atypical swallowing. The impact of these predisposing factors lies in the disruption of the balance between the forces exerted on the dental arches by the extraoral and intraoral musculature. Adaptive modifications occur at the level of the mandible, tongue, buccinator and orbicularis oris muscles, which subsequently lead to repercussions on the development of the dento-maxillary apparatus and the onset of changes in both the transverse and vertical as well as sagittal planes

**Conclusion.** Oral vicious habits, oral breathing and atypical swallowing are among the factors that predispose or aggravate transverse malocclusions depending on the intensity, duration and frequency with which they are performed. This underscores the importance of early detection of these factors and the need for an interdisciplinary approach in order to prevent or treat already established malocclusions.



## 51. PREVALENCE OF CORONAL DENTAL TRAUMA OF YOUNG PERMANENT TEETH IN CHILDREN FROM FLUOROSIS ENDEMIC AREAS

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**Introduction.** Hard tissue trauma is a common problem among children and adolescents, having a significant impact on long-term oral health. The influence of prolonged exposure to fluoride on the child's body in general and on dental hard tissues in particular and the association with dental trauma has become a topic of increased interest in fluorosis endemic communities. Due to the long exposure to high concentrations of fluoride during the formation and development of dental hard tissues, the structure and strength of tooth enamel changes, becoming more fragile and more susceptible to fractures.

**Aim of study.** Evaluation of the prevalence of dental coronal trauma of young permanent teeth in children and adolescents from fluorosis endemic areas.

**Methods and materials.** The study material served the data obtained as a result of the examinations of 299 children: 144 (48%) boys and 155 (52%) girls from two age groups: 163 (54.5%) 12-year-old children and 136 (45.5%) of 15-year-old adolescents from different fluorosis endemic areas of the Republic of Moldova. The methodology of the examination of the patients included the collection of accusations and data from the anamnesis and the objective clinical examination. The data were obtained by specialists in pediatric dentistry and included in the patient record. The type of trauma was determined according to the TDP Classification according to the WHO. The data was collected during the years 2022-2023.

**Results.** Coronary dental traumas were diagnosed in 30 (10.03%) subjects from the total number of examined children. The prevalence of trauma increased with age: dental trauma was detected in 5 (16.7%) 12-year-old children and in 25 (83.3%) 15-year-old children. Also, the prevalence of trauma increased with the severity of dental fluorosis - in 6.7% of cases dental trauma was present in subjects with questionable or incipient forms of fluorosis, and 93.3% of cases in subjects with erosive or destructive forms of dental fluorosis.

**Conclusion.** Although fluoride is the main chemical element in the prevention of tooth decay, its excess can cause dental fluorosis. The higher the dose of fluoride, the more essential are the changes in the tooth enamel structure. In severe forms of fluorosis, teeth can be susceptible to the action of mechanical factors and can easily be fractured.

## 52. RELATIONSHIP BETWEEN VISUAL IMPAIRMENT AND EYELID PTOSIS



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**Introduction.** Eyelid ptosis develops in many patients as they age. The cause is mainly age-related changes in the skin and formation of fat hernias, the reason for which is weakening of the turgor of the eye muscle. Most patients complain of eyelid asymmetry.

**Case statement.** Five clinical cases of patients with eyelid ptosis were studied at the Department of Oral and Maxillofacial Surgery and Oral Implantology „Arsenie Guțan”. All patients had ptosis and fat hernias in the upper eyelid area. The age of the patients ranged from 45 to 55 years old, all patients were female. The complaints were of aesthetic discomfort. When collecting anamnesis it was revealed that these clinical cases also had visual impairment: myopia, hyperopia or both at the same time. According to the conclusion of ophthalmologists, all these patients were found to have visual impairment. During clinical examination it was revealed that hernias in the upper eyelid area appear mainly in the area of the eye that sees better, and in the area of the eye where vision is worse hernias are detected to a lesser extent. This is explained by the fact that the eye muscle is strained less and atrophies faster, and when the other eye is overstretched, the muscle eventually weakens and therefore fat hernias are formed. Asymmetry of eyelids in patients was combined with different visual acuity. Eyelid ptosis also depended on the degree of cosmetic care of eyelid skin and protection from direct sunlight.

**Discussions.** To study clinical cases of patients with visual impairment and severity of eyelid ptosis.

**Conclusion.** Examination of data from current literature as well as clinical cases revealed that asymmetry in the eye area, various skin redundancies, and the presence of hernias depend on visual acuity impairment as well as the thoroughness and frequency of eyelid care.





### 53. SELECTION OF PULPAL TREATMENT METHODS OF PRIMARY TEETH

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**Introduction.** The health of primary teeth is crucial for the harmonious development of the child's stomatognathic system and overall development. Pulpitis of primary teeth often present a real challenge in the practice of the pediatric dentist.

**Aim of study.** The purpose of this literature review. The synthesis of data from the specialized literature to identify and analyze the most contemporary treatment strategies for pulpitis of temporary teeth, the materials used for this purpose and the factors that influence their choice in different clinical situations.

**Methods and materials.** The study is based on the analysis of publications from the scientific databases of the national and international library, for the period 2018-2023. All studies that reported data on treatment strategies for pulpitis of temporary teeth were included in this review. Publications were searched in the online databases PubMed, Google Scholar, SCOPUS, Hinari and Sci-hub.

**Results.** Based on the data from the current specialized literature, we mention that vital pulp therapies can be divided into three treatments: indirect pulp treatment, which can be used in deep caries cavities, and direct pulp capping and pulpotomy, which can be used in pulp perforations. The factors that contribute to the selection of the treatment method for temporary teeth pulpities are the child's age, the degree of caries activity, the stage of formation or resorption of the dental roots, the child's health group. The most indicated treatment strategy for pulpitis of temporary teeth is vital amputation and the most indicated materials are calcium hydroxide-based materials (Pro Root MTA, Thera Cal LC, Biodentin, Trioxident) the effectiveness of this method is up to 80% over 3 years. The main characteristics of these preparations are: tolerance to moisture, high hermitizing properties, high biocompatibility with human tissues, the ability to activate the synthetic activity of cells, producing mineralized tissues, low cytotoxicity, the possibility to complete the treatment in one visit. Preparations based on paraformaldehyde used until now, are accused of possible carcinogenic actions on the body.

**Conclusion.** The preliminary data of the specialized literature analysis suggest the selection of preparations for the treatment of pulpitis of primary teeth in favor of those based on calcium hydroxide and against those based on paraformaldehyde.

## 54. SINGLE-VISIT TREATMENT OF ACUTE PULPITIS



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**Introduction.** Pulpitis represents the reactions and processes that occur in the dental pulp under the action of pathogens that act intensely on the tooth or that come into direct contact with the dental pulp. Following the long-term action of these pathogens, biochemical, functional and structural changes occur in the dental pulp, which are similar to connective tissue inflammation. The method of single-visit treatment of pulpitis is the most common and frequently used method of complete removal of the pulp, both coronal and radicular, after the pulp has been anesthetized with an anesthetic.

**Aim of study.** To determine the optimal and effective treatment plan for patients with clinical signs of pulpitis.

**Methods and materials.** A group of 10 patients, aged between 20 and 50 years, with pulpitis symptoms were selected and clinical and paraclinical examined. The treatment of pulpitis was carried out by surgical extirpation of the dental pulp, both coronal and radicular, after applying anesthetics, which helped to carry out the complex treatment in a single visit, thus shortening the treatment time, preventing root canal infection, and ensuring favorable biological conditions for the healing of the remaining pulp abutment within the apical foramen after removing the pulp.

**Results.** The study ascertained the benefits of the anesthetics used in the treatment of pulpal diseases.

**Conclusion.** The clinical study demonstrated a positive, favorable, efficient, and qualitative impact using the method of pulpitis treatment in a single visit under anesthesia.



## 55. SPECIFICITIES OF THE ORAL FLUID COMPOSITION IN CHILDREN WITH CLEFT LIP AND PALATE

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**Introduction.** Cleft lip and palate (CLP) are the most common congenital facial deformities that significantly affect the structure and functions of the oral cavity. Individuals with CLP may experience severe functional impairments during eating, speaking, and breathing, leading to a significant aesthetic disruption of the face, posing a major obstacle to the social integration of children of various ages. Liquid biopsy is an attractive approach for diagnosing multiple pathologies, and oral fluid (OF) can become a useful diagnostic tool for the early detection of various dental conditions due to its multiple advantages: simple, rapid, safe, and non-invasive collection, avoidance of the risk of infection, easy transport, and better acceptance and collaboration with anxious patients.

**Aim of study.** To investigate the specificities of the oral fluid composition in children with cleft lip and palate.

**Methods and materials.** In a case-control clinical study, 48 children aged 1 to 17 years were included. The research group (L1) consisted of 16 children with cleft lip and palate (CLP). Out of the total of 16 children, 12 (75%) had unilateral CLP, and 4 (25%) had bilateral CLP. In the control group (L0), 32 conventionally healthy children were included, selected proportionally to the subjects in L1 by age, living environment, and gender. All children underwent clinical examination, assessing oral health status, dental hygiene level, and OF collection. OF pH and viscosity were assessed. The levels of TNF- $\alpha$ , cortisol, IL-8, and sIgA in OF were determined by the immunoenzymatic analysis method. The study was conducted in compliance with ethical standards, and written consent from parents for their children's participation in the study was obtained. Parametric and non-parametric tests were used for statistical data analysis using Epi Info<sup>TM</sup> 7.0.

**Results.** Comparative analysis of OF indicators revealed a significant increase in viscosity, cortisol, and TNF- $\alpha$  levels, as well as a decrease in pH and sIgA levels in children with CLP compared to healthy subjects of the same age. The decrease in OF biomarker levels reflecting local immune protection and the increase in those indicating an unfavorable state of oral health were correlated with the results of the objective clinical examination.

**Conclusion.** Assessing the specificities of OF composition represents an innovative non-invasive analysis for the early detection and prognosis of dental conditions necessary for correcting preventive and treatment measures within the framework of comprehensive and personalized medical care and rehabilitation for children with CLP.

## 56. STATISTICAL DATA AND IMAGING METHODS USED IN THE DIAGNOSIS OF OSTEOMYELITIS OF THE UPPER JAW



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**Introduction.** Osteomyelitis of the jaw is an infectious purulent-necrotic inflammatory disorder of the bone tissue that affects the periosteum and surrounding soft tissues in addition to the bone marrow and bone itself. It was discovered that the mandible exhibits a far higher frequency of the development of inflammatory bone disorders compared to the maxilla in connection to the anatomical and structural particularities. This prevalence is explained by the difference between the anatomical characteristics of the upper and lower jaw, such as the abundant vascularization of the maxilla, which ensures high resistance to infections, and the thin cortical plates that provide advantageous drainage.

**Aim of study.** To review the published literature for investigating the particularities of osteomyelitis of the upper jaw, to determine the etiological factors and the imaging methods of choice for establishing the diagnosis.

**Methods and materials.** Study of the contemporary bibliography and archive data within the IMSP Institute of Emergency Medicine, Department of Oral-Maxillo-Facial Surgery and Oral Implantology "Arsenie Guțan", during the years 2018—2023. The study included 137 patients (75 men and 62 women), aged 19-81, diagnosed with jaw osteomyelitis.

**Results.** The study indicates that odontogenic, posttraumatic, and toxic factors are mostly responsible for osteomyelitis development. The immunosuppression of the body is the result of the persistence of predisposing factors, such as concomitant diseases or harmful habits represented by excessive alcohol consumption or drug dependence. Systemic conditions that compromise an individual's immune system, such as diabetes, malnutrition, and chemotherapy use, are factors that can lead to osteomyelitis. In order to establish the diagnosis of osteomyelitis and the treatment plan, it is necessary to use both imaging and laboratory paraclinical methods. The most commonly used methods include panoramic radiography, computerized tomography, and magnetic resonance imaging, which allow for the determination of the infectious focus, localization, and involvement in relation to adjacent anatomical structures. It was found that 11 patients (8%) had upper jaw osteomyelitis and 126 patients (92%) had mandibular osteomyelitis. It was shown that odontogenic osteomyelitis, which affected 61 patients (44%), was the most prevalent form. Post-traumatic osteomyelitis affected 37 patients (27%), while osteomyelitis associated with bisphosphonates was less common, with three patients diagnosed (2%).

**Conclusion.** After statistical data analysis, it was concluded that osteomyelitis of the upper jaw is a rare occurrence in comparison to osteomyelitis at the mandibular level. It is considered that it results from a combination of etiological factors and the body's low immunoreactivity. The most popular ones for the upper jaw are magnetic resonance imaging and computed tomography, but panoramic radiography for the mandible.



## 57. SURGICAL MANAGEMENT OF THE LOWER THIRD MOLAR IMPACTION

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**Introduction.** The study emphasizes the importance of understanding the complex nature of impacted third molars, their potential complications, and the considerations for their removal in clinical practice.

**Aim of study.** The thesis aims to analyze the surgical removal of impacted third molars. It evaluates the existing classification and difficulty index of these teeth, discusses factors related to impaction, and assists in decision-making for surgery by understanding the risks and presenting options to patients.

**Methods and materials.** This retrospective study, conducted from January 2021 to October 2023 at the Dental Imaging Centre in Avidor, Israel, analyzed panoramic and periapical radiographs of 55 patients, aged 16-65, focusing on impacted third molars. It assessed factors like age, gender, location, angulation, position, and impaction level using Winter's and Pell and Gregory classifications. Exclusions included patients under 16, with incomplete records, systemic diseases, craniofacial anomalies, or trauma history. The study mainly addressed angulation, position, and depth of impacted mandibular third molars.

**Results.** This study involved 55 patients (46% female, 54% male) and examined 175 molars. It analyzed the distribution of third molars by gender and age, with the highest occurrence in the 20-29 age group. The study revealed that as age increased, the number of third molars decreased, and more males had third molars than females. It also categorized 175 third molars into erupted, partially impacted, and completely impacted, noting differences in the mandible and maxilla. Gender-based distribution showed no significant difference. Additionally, 38 teeth had issues like pericoronitis and caries. The study provided insights into the distribution, impaction types, and symptoms of third molars, which is crucial for dental professionals in assessing and managing these teeth.

**Conclusion.** M3 (third molar) impaction is commonly linked to various oral health issues, leading to recommendations for early removal. The prevalence of associated pathologies varies across studies. Causes include limited jaw space, inadequate skeletal growth, and larger tooth crown size. Dental attrition and dietary habits also play roles in creating space for these teeth. Managing impacted third molars involves decisions about removal timing, surgical techniques, and postoperative care. The complexity of surgery and potential complications, such as nerve injuries and infection, necessitate careful planning and consideration of the dentist's expertise and patient's condition. The risks of leaving impacted M3s are uncertain due to varying incidence rates of complications in studies. Common complications from surgical removal include dry socket, nerve damage, and infection. The relationship between dental arch size and M3 impaction is under-studied, with factors like arch crowding and mandible growth being significant.



## 58. THE ADVANTAGES AND BIOCOMPATIBILITY OF ZIRCONIUM IN UNIDENTAL PROSTHETIC CROWNS



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**Introduction.** Currently, prosthetic treatment with zirconium dental crowns has become increasingly popular due to its superior aesthetics. This material has great clinical success due to its mechanical and chemical properties, computer manufacturing technology. Aim of study. Assessment of the properties, advantages and biocompatibility of zirconium in the treatment with single crowns.

**Aim of study.** Key words: zirconium dental crown, advantages of zirconium, biocompatibility of zirconium.

**Methods and materials.** For this study, 15 publications were taken from the PubMed database, including clinical cases and specifications of the analysis of structure, biocompatibility and physical properties in order to study them and form a conclusion about the effectiveness of zirconium in prosthetic treatment. 114 adult patients with structural and aesthetic teeth defects were examined. These patients were examined at 3 months, 6 months, 12 months and 18 months, to highlight the properties and biocompatibility of the material over time.

**Results.** In this study at the follow-up examination were evaluated the gingival index, probing depth, marginal crown integrity and wear of abutment teeth, antagonist teeth, contralateral teeth in all cases. The results related to the marginal adaptation in all 114 patients were identified as perfect, due to digital fabrication techniques, CAD-CAM / 3D printing, resulting in a 100% excellence rate. 4 patients were identified with chipping of the zirconium dental crown as a result of bruxism. In 2 of all examined patients, it was identified the presence of cracks in the enamel of the teeth opposing the zirconium dental crown.

**Conclusion.** Zirconium for fixed unidental prosthetic treatment indicates a good success rate with minimal complications thanks to its aesthetics, physical, mechanical and chemical properties. This material is superb, due to its resistance to compression and cracking, to physical action, this material has only presented faults in patients where the masticatory function overloads the material of the crown, resulting in chipping. None of the patients presented any adverse effects following the prosthetic treatment with zirconium dental crowns, which demonstrates the biocompatibility of this material in patients with perfect general health and in patients with systemic diseases. In vivo and in vitro laboratory research has been carried out that demonstrates maximum biocompatibility with human biological structures.



## 59. THE EFFECT OF ANTI-INFLAMMATORY MEDICATION ON ORTHODONTIC TOOTH MOVEMENT

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**Introduction.** It is now well-known that orthodontic tooth movement (OTM) is possible due to the biological response to the applied mechanical forces. The new studies have revealed its inflammatory nature. This in turn raises the question of whether the orthodontic treatment can be altered by anti-inflammatory medication. And if yes, should it be a concern for orthodontists?

**Aim of study.** Among the patients who seek orthodontic help there can always be some who are simultaneously undergoing an anti-inflammatory treatment. While not all the anti-inflammatory drugs have been thoroughly studied, we now know a few which can indirectly alter either the process, or the results of OTM. Taking into consideration the common use of this medication, it would be beneficial for orthodontists to know how these drugs can affect the treatment and if their influence on OTM can be managed.

**Methods and materials.** A systematic review of articles and textbooks in English have been made. Only the original content without translation was used. Platforms containing medical articles were used as a database: PubMed, ScienceDirect, Research4Life, Oxford Academic. The keywords were: orthodontic tooth movement, anti-inflammatory drugs. Articles that contained the terms 'Orthodontic appliances', 'Biomechanics' were excluded.

**Results.** Most NSAIDs non-selectively inhibit the formation of prostaglandins (PGs), which results in suppression of any inflammatory process and a delay of OTM. Acetaminophen acts on the central nervous system, leading to a slight decrease of PG' levels, having no significant effect on the rate of OTM. A few original studies addressed the use of COX-2 inhibitors during orthodontic treatment. An original human study conducted by Villa et al. in 2005 showed that the tooth movement patterns in patients receiving placebo and those administered with nabumetone were almost identical. Animal experiments revealed the inhibiting effect of the glucocorticoids (GCs) on the osteoblasts' function. This led to decrease of bone formation, resulting in accelerated OTM, as well as in compromised retention period. Most review articles highlight the elevated risk of osteoporosis in patients receiving GCs.

**Conclusion.** A thorough literature review makes it clear that the antiinflammatory drugs have a considerable influence on the rate of OTM which however can be successfully managed. The administration of the non-selective NSAIDs will lead to a significant decrease in OTM. Acetaminophen is the only known exception. A COX-2 blocking NSAID (nabumetone) has been shown to also have no influence on OTM rate. More research in this field is needed. Glucocorticoids medication will lead to an acceleration of OTM, but will also compromise the retention period. Therefore orthodontists may want to reduce the orthodontic force, to make the control visits more often and to provide an enhanced retention method.

## 60. THE INFLUENCE OF GENETIC FACTORS ON THE DEVELOPMENT OF CLASS III MALOCCLUSION ACCORDING TO ANGLE



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**Introduction.** The diagnosis of malocclusion is an increasingly common issue in orthodontics, reflecting a growing need for interventions and treatments in this field. Class III malocclusion, of skeletal and non-syndromic nature, represents a particular concern and is largely influenced by genetic factors. Among the most common hereditary factors is autosomal dominant transmission.

**Aim of study.** This study aims to determine the influence of genetic factors on the development of Class III malocclusion.

**Methods and materials.** This study investigated 26 scientific articles addressing key terms such as Class III malocclusion, genetics, locus, phenotype, development, and etiology. Research sources included scientific platforms such as Google Academic, PubMed, ScienceDirect, WileyOnlineLibrary, Scirus, and Medline.com.

**Results.** Investigations into the genetic association of Class III malocclusions have identified specific loci, with the 1p36 locus often correlated with this condition. Genes located in this locus, such as *Matrilin*, *HSPG2*, *ALPL*, and *EPB41*, play essential roles in cartilage development, craniofacial formation, and cytoskeleton-associated functions. The existence of genes 12q23 and 12q13 has also been described as correlating with bone and cartilage development, highlighting the complexity of molecular pathways influencing mandibular size. Other candidate genes, such as *IGF1*, *HOXC*, *COL2A1*, and *DUSP6*, have been identified in association not only with mandibular prognathism but also with maxillary deficiency. Additionally, single nucleotide polymorphisms in *FGFR2* and *COL1A1* present a higher risk for skeletal Class III malocclusion, while the *TBX5* gene is associated with a reduced risk for this condition.

**Conclusion.** Exploring these genetic aspects and the relationship between heredity and Class III malocclusion makes significant contributions to optimizing therapeutic approaches and improving outcomes in orthodontic practice. These factors are key elements in understanding the origin and evolution of Class III malocclusion, providing the foundation for the development of personalized diagnostic and treatment strategies.



## 61. THE PSYCHO EMOTIONAL STATUS OF SUBJECTS WITH GINGIVAL DISEASE

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**Introduction.** In dentistry there is a circumstance that influences the conduct of a procedure that is widespread among patients - odontophobia. Often this condition is underestimated and insufficiently studied by clinicians and researchers.

**Aim of study.** Oral care methods can diminish the risk of periodontitis - a chronic multifactorial disease with gum infection that can lead to tooth and bone loss.

**Methods and materials.** The cross-sectional study consisted of clinical examination and questionnaires by Ten-Item Personality Inventory (TIPI), Rozenberg self-esteem scale (SES), Fear Questionnaire (FQ), The Dental Patient Satisfaction Survey (PSS) and oral hygiene behavior - teeth brushing (TB) and interdental care (IDC).

**Results.** In the group of 54 subjects over 18 years of age, healthy gums, gingivitis and periodontitis were detected, after which they were divided into group I who performed TB and IDC 2 times a day and II-irregular oral hygiene. In group I and II 37,1 vs 7,4% were healthy, with gingivitis - 13,0vs 22,2, and 1,9 vs 18,5% had periodontitis stage 2. The responses to items in TIPI were predominantly self-disciplined 55.5%, followed by conventional-35, 2, extraverted-3.7 and careless only 5.6% cases. Rozenberg SES found out self- esteem medium – 77,8, high- 14,8 and low-7,4% cases. At the same time FQ demonstrated slightly disturbing fear – 38,8, definitely fear – 31,5 and very disturbing fear – 29,6% cases. Through the dental PSS, the appreciation given by the patients of the office, hygiene and the doctor was good – 75,9, liked – 20,4 and least-3,7% cases.

**Conclusion.** Agreeableness prevails in TIPI and only 5.6% are negligent. According to FQ, the phobia of injections and minor surgery in the dental patient satisfaction survey prevailed the best note about the office, professionals and the doctor. Moreover poor oral hygiene increases the risk of periodontitis, which can be reduced by performing it. Patients were unsure to stay in this dental office in 9.2%, agree - 88.9 and disagree expressed only 1.9% subjects.

## 62. THE RISK OF DENTAL CARIES IN CHILDREN BORN PREMATURE



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**Introduction.** Premature birth represents a major public health problem, associated with increased neonatal morbidity and mortality. Premature birth is a current problem, following it, the fetus is diagnosed with a series of functional disorders from different systems of organs, including the stomatognathic system. According to clinical observations, children born prematurely are susceptible to dental caries (CD). In this sense, it is current the study which evaluates the risk of caries in children born prematurely.

**Aim of study.** Personalized assessment of the risk of dental caries in newborns premature.

**Methods and materials.** A clinical study was carried out on a sample of 68 children aged between 1 and 3 years, divided into 2 identical groups according to structure. The research group (Gr 1) consisted of 34 children born prematurely (according to the anamnesis data). The control group (Gr 0) was identical in structure to Gr 1 and consisting of 34 conventionally healthy children. Children were clinically examined, and the clinical data recorded according to the criteria of the World Health Organization. Behavioral risk factors from the family environment of children were identified (the particularities of food and hygienic care, the level of knowledge regarding oral health and mothers' sanogenic attitudes, etc.). Acidogenic bacterial plaque was identified and estimated rates of frequency and intensity of dental caries. Complex caries risk assessment was performed using the Cariogram Software application. The study was conducted in accordance with ethical requirements, with the written consent of the children's parents or their legal representatives.

**Results.** Dental caries was detected in 47.06% of children from Gr 1 and in 29.41% of subjects from Gr 0. The personalized assessment of the caries risk with the Cariogram Software application allowed us to analyze comparing the risk of dental caries in subjects from Gr 1 and Gr 0. Thus, in the children born preterm high and very high caries risk prevailed and was 32.57% higher, comparatively with conventionally healthy children. In most children from Gr 1, the cumulative influence of a complex of risk factors: the impact of systemic pathology and its medication, as well as unsatisfactory state of oral hygiene, number of *Streptococcus mutans* in saliva  $>5 \times 10^5$  CFU/ml, decreased flow of oral fluid. The lack or insufficiency of the implementation of preventive measures detected in children from both groups.

**Conclusion.** Personalized and complex CD prediction revealed high and very high caries risk in most premature babies. Personalized caries risk assessment is necessary for the development and application of effective CD prevention methods.





### 63. THE ROLE OF COLLAGEN GRAFTING IN SOCKET PRESERVATION

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**Introduction.** The implant prosthetic rehabilitation became an ordinary and most accepted method for treatment of edentulism. According to the literature, bone atrophy in the first year after the tooth extraction can occur up to 40%. Different biomaterials and techniques have been proposed for socket preservation to decrease the atrophy. However, the results of healing after using xenogenic or synthetic biomaterials in a postextractional socket often lead to a poor bony tissue, which may affect the implant's integration. Thus, in case of 2 or 3 bone wall defects, the preservation of the socket becomes a necessity in order to maintain the height and width of the bone crest.

**Case statement.** The study was based on a 65 years old patient who accused pain and mobility of the bridge in the right posterior side of the mandible. According to the X-ray, a radiolucency all around the second molar was noticed. The radiological signs of inflammation around the failing tooth reached the close proximity of the inferior alveolar nerve, with defect of buccal and lingual plates. In order to minimize the postoperative defect, a modified approach was applied. After removing the bridge and the tooth, the surrounding invaginated tissue were detached with the flap elevator from the bottom, preserving at least one contact with the marginal mucosa, and hemostasis has been performed. The created space was filled with resorbable collagen material with HA, lincomycin and metronidazole. The tent was created from the tissue that surrounded the tooth and sutured to the marginal mucosa. Medicamentous treatment was prescribed, and the patient was monitored for the next 6 months. The newly formed bone and soft tissue quality obtained after 6 months showed a good regeneration with insignificant atrophy.

**Discussions.** In conventional teeth extractions, the soft tissue from the socket are usually removed. That creates big defects during healing, especially in such situations with 2 or 3 bone walls defects. Except periapical granulomas, the invaginated tissue from marginal periodontium which surrounds completely the teeth roots can be successfully used as a tent to minimize the soft tissue defects and enhance the epithelization. On the other hand, the collagen resorbable materials offer a porous scaffold which allows the surrounding bone to proliferate easier inside the grafted space and lead to a better bony tissue in comparison with other ones.

**Conclusion.** In case of soft tissue invagination around the failing teeth, the tunneling technique and their usage as a tent with collagen preservation of the socket minimize the postoperative defects and show predictable results.

## 64. THE ROLE OF MODERN SUTURE MATERIALS IN ORAL SURGERY



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**Introduction.** The development of contemporary suturing materials has led to the creation of numerous categories, including braided, non-resorbable, resorbable, monofilament, multifilament, natural, and synthetic suture materials. These materials can be employed in a wide range of circumstances to guarantee full recovery. In order to maximize wound healing, minimize ischemia, remove excessive wound tension, and prevent tissue damage, surgeons must choose the best suture materials while also taking into account factors like salivary flow, oral functions like chewing, swallowing, and speaking, as well as the high vascularization of the oral tissues.

**Aim of study.** Current data on contemporary suture materials was examined to assess how to use them as well as their physical and biological properties.

**Methods and materials.** A review of literature published in Pubmed, Google Scholar, Science Direct, and Medscape databases.

**Results.** Contemporary suture materials provide increased stability, minimize wound infection risk, shorten recovery periods, shorten surgical times, and maximize the restoration of the targeted tissue's appearance and functionality. Their enhanced adaptability makes them more useful in the wide range of clinical scenarios that surgeons face. Oral surgery uses resorbable sutures more frequently. The most widely used types of resorbable sutures are chromic catgut, catgut, which are natural, and vicryl, polyglycolic acid (PGA), polydioxanone, which are synthetic. Because catgut sutures are prone to enzymatic breakdown, polyglycolic acid and chromic catgut sutures are used more frequently. The most common non-resorbable suture materials used in oral surgery are polyester and silk. Although silk is inexpensive and widely available, its braided structure, which is more traumatic and prone to bacterial buildup, frequently results in tissue inflammation. Polyester suture materials, such as polypropylene and polytetrafluoroethylene, are less traumatic and reduce the chance of bacterial growth due to their monofilament configuration.

**Conclusion.** Thanks to current innovation, surgeons today have access to a wide variety of suture materials. A thorough understanding of the physical and biological properties of the suture material used, as well as the location, thickness, elasticity, and rate of healing of the damaged tissue, is essential for effective rehabilitation following oral surgery.



## 65. THE SIGNIFICANCE OF RESTORING THE FRONT TEETH'S CONTACT POINT

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**Introduction.** The contact point is a small area where the proximal surfaces of two neighboring teeth meet. It protects the interdental papilla and helps maintain the stability and correct position of the teeth in the dental arch, preventing the build-up of bacterial plaque, which can lead to the development of initial caries. The contact point contributes to the natural and harmonious contour of the teeth and their aesthetic appearance. Therefore, it is necessary to choose a highly aesthetic composite material and apply it according to the contemporary approach and the selected treatment method.

**Aim of study.** To evaluate the methods of restoring the contact point of the front teeth, considering the morpho-functional particularities of the front teeth and the aesthetic criterion, which is indispensable for the front teeth.

**Methods and materials.** A group of 12 patients, 7 women and 5 men aged between 30 and 50 years, were examined clinically and paraclinically. The restoration of the interdental point of the front teeth was performed with the injectable composite material Beautifil Flow Plus and the supra-nano filled composite materials Estelite Equick A3 and OA3.

**Results.** The clinical study determined that the light-curing composite materials contributed to restorations with unique aesthetic features, which helped achieve an efficient and durable contact point.

**Conclusion.** The contact point plays an essential role in direct restorations of the anterior teeth. The restoration of the functional, morphological, and aesthetic integrity of the interdental point can be achieved due to the higher restorative characteristics of the composite materials used, as well as the treatment method selected according to each clinical case.

## 66. THE USE OF BIPHASIC CEMENTS IN PERI-IMPLANT CONTOUR GRAFTING



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**Introduction.** Tooth loss over time leads to bone atrophy in the edentulous area, which involves bone degradation in thickness, width and height. This aspect served as a starting point for the discovery of different materials, which resemble the natural bone structure, biocompatible with the human body and suitable for restoring lost bone volume. However, integration of the grafting materials does not always correspond to the expected results. In order to isolate the periosteum from the graft different membranes are used, which increase both surgical difficulty and the cost of the surgery.

**Case statement.** The case presentation is based on a female patient (39 years old) who complained about a missing tooth on the upper jaw (first premolar). After clinical and paraclinical (CBCT) examination, a bone defect was observed from the buccal aspect (class B by Misch) which required contour grafting. A biphasic cement was used as grafting material. After performing incision and flap reflection, the implant site was performed with osseo-densification drills in order to preserve as much bone as possible, a 4,0-12mm implant was placed with an insertion torque of 40Ncm. Biphasic cement was applied to the buccal side until the level of neighboring teeth buccal profile. After drying with a gauze, the flap was sutured and no membranes were used. An individual healing abutment was made. Control x-rays were performed postoperatively and 6 months later in order to evaluate the obtained results.

**Discussions.** The obtained results showed good restoration of the alveolar ridge and stable result after 1 year follow-up. Due to its property to harden during drying, it was easy to handle and no membrane was necessary for isolation of the graft. Insignificant postoperative edema was present 2 days after the surgery. At 1 year follow-up, the level of alveolar ridge in the region of the implant preserved its contour, similar to the neighboring area.

**Conclusion.** In small one-wall defects, the usage of biphasic cement showed good and predictable results. Beside the resorbable properties of this biomaterial, it can be a good option for contour grafting and can significantly decrease the operative time and costs due to hardening properties, which exclude the necessity of membrane usage.



## 67. THE USE OF COMPOSITE MATERIALS IN THE MORPHO-FUNCTIONAL AND AESTHETIC RESTORATION OF THE ANTERIOR TEETH

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**Introduction.** Dental traumas, caries, and injuries of the anterior teeth have an impact on the patient's physical and psychological well-being, requiring prompt functional and aesthetic restoration. Aesthetic tooth restoration differs from conventional dental filling primarily in that, instead of only restoring the functional appearance of the tooth, the aesthetic tooth restoration uses a material that exactly reproduces the dentin, enamel, transparency, and colour range of the tooth. Aesthetic modeling and dental restoration solve two problems simultaneously, namely restoring dental functionality and providing a clearly superior aesthetic appearance. Teeth affected by carious or non-carious lesions are usually restored using composite materials. Currently, resin-based composites are a popular option for direct restoration of anterior and posterior teeth. Physical appearance, such as colour match and polish, is very important for anterior teeth. Composite materials used for anterior teeth usually have small filler particles, which increases smoothness but also reduces the Young's modulus and fracture toughness of the material.

**Aim of study.** To assess modern techniques and methods of treatment of coronal odontal lesions using composite materials.

**Methods and materials.** To achieve the purpose of the work, a clinical study was performed. All patients were examined clinically and paraclinically. The diagnosis of coronal odontal lesions was made, and the treatment plan was established in mutual agreement with the patients. The anterior direct restoration technique was applied in the given study. The restorative materials used to restore the front teeth were as follows: GC GRADIA DIRECT AO2, GC GRADIA DIRECT A2.

**Results.** The patients who underwent the morpho-functional and aesthetic restoration of the anterior teeth with composite materials according to the latest techniques presented good aesthetic results, restoring the integrity of the tissues and the shade of the tooth colour.

**Conclusion.** The dentist must choose between direct and indirect techniques when determining the most qualitative and effective treatment for patients with aesthetic issues of the anterior teeth. Direct composite restoration should be strongly considered in circumstances where conservative treatment is possible. Advances in direct restorations, as well as the use of new bonding agents and new highly aesthetic direct resin systems, can all have a favourable impact on treatment. The direct method is considered a method of improving the aesthetics and reducing the working time.



## 68. THE USE OF TRANSSINUS AND PTERYGOID IMPLANTS ON THE UPPER JAW AS AN ALTERNATIVE TO THE CLASSIC ALL-ON-4/6 PROTOCOL



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**Introduction.** The problem of the "all on 4/6" operation on the upper jaw arises in complex clinical situations, such as the inability to achieve primary implant stability due to maxillary sinus pneumatization, significant atrophy of the alveolar process, and decreased bone density. The use of an alternative method by using nasal, transsinus, and pterygoid implants of considerable length (18-25 mm) allows to carry out the operation without the need for bone grafting (sinus lifting) and the use of more invasive zygomatic implants.

**Case statement.** A 65-year-old patient has turned to a dentist for total rehabilitation. CT showed a complete secondary adentia on the upper jaw, marked atrophy of the alveolar process in both horizontal and vertical planes (Cawood and Howell). Bone density was at level 3-4 (Lekholm and Zarb) with significant maxillary sinus pneumatization. It was decided to use a modified protocol for total rehabilitation with the application of transsinus and pterygoid implants. Transsinus implants were placed in the region of the 5th teeth, while the implant apex was fixed in the frontonasal buttress. Pterygoid implants were placed in the pterygoid process of the sphenoid bone in the region of the 7th teeth and also achieved high primary stability. Inclined implants of 18-25 mm in length, passing through the maxillary sinus into the pterygoid process, provided high primary stability more than 70 Ncm. Anterior implants, placed in the lateral incisor region, achieved stability of approximately 25 Ncm. Immediately after the surgery, an impression was taken, and a temporary acrylic prosthesis was fabricated on a metal framework.

**Discussions.** Patient's rehabilitation proceeded as planned with predictable satisfactory results, despite the difficulties. The high primary stability of inclined transsinus and pterygoid implants allows their use in cases where the traditional "all on 4/6" procedure is not feasible. This method helped to avoid bone grafting and significantly reduced patient treatment time, being cost-effective, which is quite important. The total torque obtained with inclined implants and two direct implants in the anterior part of the upper jaw allows the safe loading of these implants in a short time and the fabrication of complete dental prostheses with 14 teeth.

**Conclusion.** The implantological treatment of this patient using long implants demonstrated good results and allowed rehabilitation in a case where the use of the traditional protocol is not possible. Despite the advantages of this method, there are several serious complications that may pose risks to this upper jaw restoration approach.



## 69. TOPOGRAPHICAL CHANGES OF THE MANDIBULAR CANAL, CAUSED BY THE RADICULAR CYST. CLINICAL CASE.

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**Introduction.** The mandibular canal is one of the main anatomical structures, representing the key point of the functionality and vitality of the mandibular anatomical elements. For oral-maxillo-facial practice, the topographic relationships of the lower teeth with the mandibular canal are particularly important. Some pathological processes at the level of the roots of the lower teeth (cysts) can also have harmful consequences on the anatomical elements of the mandibular canal.

**Case statement.** A 64-year-old, male patient came to the SRL "OMNI DENT" clinic with complaints of pain while chewing in the region of tooth 46. Following the clinical and paraclinical, radiological examination through OPG and CBCT, the diagnosis of radicular cyst was established at tooth 46. The topographical changes of the mandibular canal caused by the chronic mechanical pressure exerted by the cystic formation and the perforation of the mandibular lingual cortex at the level of the cyst were also highlighted. Then, the endodontic treatment of the teeth 46,45,44, and the surgical intervention of cystectomy and apical resection of the teeth 46,45,44 roots were performed.

**Discussions.** Pre-operative, immediately post-operative, and at 10 months post-operative, OPG and CBCT were performed, in which the cystic formation was identified, and comparing the topographic ratios of the mandibular canal in quadrant III, with healthy dentition, with the topographic ratios in quadrant IV, topographical changes of the mandibular canal were observed in quadrant IV, mainly under the cystic formation. The measurements were performed in the region of the teeth 36 and 46, being reference teeth. Thus, a deviation of the measured values was observed. As bony landmarks having the basilar margin (BM), the alveolar margin (AM), the vestibular cortex (VC) and the lingual cortex (LC). The dental landmarks being the apexes of the teeth (TA). Pre-operative: – tooth 36: BM= 6.30 mm; AM= 14.66 mm; VC=6.81 mm; LC=1.20 mm; TA=3.85 mm; – tooth 46: BM= 2.98 mm; AM=19.07 mm; VC=3.98 mm; LC=2.70 mm; TA=9.40 mm; Immediately post-operative: – tooth 36: BM=6.48 mm; AM=15.53 mm; VC=7.02 mm; LC=1.43 mm; TA=4.81 mm; – tooth 46: BM=3.17 mm; AM=19.07 mm; VC=4.22 mm; LC=2.62 mm; TA=12.34 mm; At 10 months post-operative: – tooth 36: BM=5.88 mm; AM=15.35 mm; VC=7.22 mm; LC=1.14 mm; TA=4.11 mm; – tooth 46: BM=6.02 mm; AM=16.63 mm; VC=5.23 mm; LC=1.85 mm; TA=10.59 mm; The comparison of these values, obtained from the topographical analysis of the mandibular canal in the regions of teeth 36 and 46, shows us the topographical changes of the mandibular canal towards the basilar edge, and the vestibular cortex of the mandible, in quadrant IV, region of the tooth 46, under the influence of chronic mechanical pressure in the presence of the cyst. Likewise, the topographical changes of the mandibular canal in quadrant IV, can be observed in the dynamics, after 10 months post-operative, returning to the topography similar to quadrant III, in the absence of the cystic formation.

**Conclusion.** Dynamic CBCT monitoring of the patient with a radicular cyst allowed us to evaluate the topographical changes of the mandibular canal under the influence of the pressure exerted by the cyst and later in its absence, thus demonstrating the human body's capabilities for adaptation and bone remodeling.

## 70. TREATMENT OF BURNS AND THEIR CONSEQUENCES IN THE FACE AND NECK AREA



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**Introduction.** The skin is vital, ensuring homeostasis and defending against environmental threats. Its complex functions regulate water balance, temperature, and facilitate signal perception. Additionally, it plays a crucial role in producing and activating hormones, neuropeptides, and cytokines. Burns present a medical challenge by compromising the skin's barrier, elevating infection risk. Ongoing clinical advancements improve thermal injury treatment efficacy, addressing disorders and methods at various stages. Burn injuries frequently induce trauma to multiple organs, exacerbating the complexity of the condition and extending the overall recovery duration.

**Case statement.** One year ago, a 23-year-old woman was admitted to a burn center following a car accident at a gas station, resulting in a third-degree burn affecting 70% of her total body surface area. Subsequently, a free flap-plasty procedure was performed. Post-surgery, the patient exhibited scarring, microstomia, obliterated facial contours, and an erased lip contour. One year later, the patient initiated scar treatment under the care of the Department of Maxillofacial Surgery. Examination of the face and neck revealed scar tissue with a pale color, accompanied by areas of hyperemia due to the distinct color of the grafted skin. Palpation indicated dense tissue with heightened elasticity. Both invasive and minimally invasive techniques were employed for treatment. Local flap surgery was utilized to augment the skin area and address microstomia, dermabrasion was employed to smoothen scars, and hyaluronic acid injections were administered to restore facial contours.

**Discussions.** A positive healing outcome was observed ten days after dermabrasion, with successful removal of microstomia and well-defined contouring of the lower lip. The only challenging area for healing was identified on the right side of the chin following local flap surgery. According to various authors, this difficulty may be attributed to alterations in platelet structure and blood coagulation. This phase represents the initial stage of treatment, with future plans including plastic surgery and additional dermabrasion procedures.

**Conclusion.** The care of burn patients is entrusted to an interprofessional team, comprising a surgeon, intensivist, burn specialist, dietitian, physical therapist, nurses, wound care specialists, and plastic surgeon. The primary focus is on preventing complications and reinstating functionality. The prognosis for burn patients is contingent upon the degree and extent of the burn.



## 71. TREATMENT OF CHRONIC APICAL PERIODONTITIS IN WHICH CANAL SECRETION PERSISTS

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**Introduction.** Chronic apical periodontitis presents destructive periapical lesions of a varied extent, occurring in areas of a minor but long-lasting infection, often leading to the development of fistulas in places of low resistance. The occurrence of pus discharge is a sign of a reaction to a pathogenic bacterial infection, and the presence of purulent discharge in the canal impedes the root canal filling.

**Aim of study.** To determine the effectiveness of curative calcium-hydroxide dressings with iodoform in the regeneration of periapical tissues and therapeutic tactics in teeth with a persistent purulent discharge in the root canals.

**Methods and materials.** A group of 15 patients were clinical and paraclinical examined, being subjected to endodontic root canal treatment with calcium-hydroxide paste containing iodoform over a period of 1-3 weeks. Iodine released from the medicated paste helped sterilize the root system and remove the purulent discharge from the root canals.

**Results.** Medicated calcium-hydroxide dressings with iodoform applied in the root canals over a period of time destroy the pathogenic flora in the root system, having a favorable prognosis.

**Conclusion.** The clinical study highlighted the importance of medicated calcium hydroxide dressings with iodoform as an effective remedy for teeth with a purulent discharge in the root canals.

## 72. USES OF MINERAL TRIOXIDE AGGREGATE IN ENDODONTIC TREATMENT



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**Introduction.** Mineral trioxide aggregate (MTA) is an endodontic cement with hydrophilic and biocompatible properties having the ability to stimulate healing and osteogenesis. Its composition includes a fine powder of trioxides such as tricalcium oxide, silicon oxide and bismuth oxide, along with other hydrophilic particles such as tricalcium silicate and tricalcium aluminate, which are responsible for the chemical and physical characteristics of MTA. Mineral Trioxid Agreggant has been proposed as a preferred option in a variety of procedures including apical filling, pulp capping, pulpotomy for primary teeth, apical barrier formation in teeth with necrotic pulp and open tips, perforation repair and apexification. For each of these applications, numerous clinical studies have been conducted to evaluate the performance of MTA.

**Case statement.** Evaluation of the effectiveness of using Mineral Trioxide Agreggant (MTA) to optimize endodontic treatment.

**Discussions.** Evaluation of using Mineral Trioxide Agreggant (MTA) to develop an optimal algorithm in endodontic treatment found that this sealing material of root canals have superior biocompatibility properties and interact effectively with dental tissue. The study included patients with pulpal disease caused by dental caries, and after clinical and paraclinical examinations, endodontic space damage was observed. MTA was the preferred optimum for endodontic treatment, demonstrating good adaptability and notable healing capacity in interaction with dental tissues. These results support the use of MTA in optimizing endodontic treatment, providing significant benefits in the context of acute pulpal disease. The results obtained after an effective root canal treatment were analyzed by using clinical and paraclinical tests (radiography), thus demonstrating the effectiveness of mineral trioxide agreggant (MTA) in smoothing and sealing the canals.

**Conclusion.** Mineral Trioxid Agreggant (MTA) has been successfully used in a number of endodontic procedures such as apical filling, pulp capping, pulpotomy for permanent teeth, according to radiographic data, showed uniformly filled canals without any gaps.





## ***XXV. SURGERY SECTION***

***„Dacă ai decis să devii chirurg, TREBUIE:***

- 1. Să cunoști la perfecție medicina (anatomia)***
- 2. Să te grăbești să faci bine fără să te gândești la arginți***
- 3. Să înveți ce e mai bun de la alții***
- 4. Cugetul să-ți meargă înaintea mâinilor***
- 5. Să fii permanent cu gândul la Dumnezeu“***

***"If you have decided to become a surgeon, you MUST:***

- 1. To know medicine (anatomy) perfectly***
- 2. To rush to do good without thinking about money***
- 3. To learn the best from others***
- 4. Let your mind go before your hands***
- 5. To be constantly thinking about God"***

***Gheorghe Ghidirim,***

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## 1. 3D MODELING IN BONE GRAFT SUBSTITUTES, INCLUDING DEVICES FOR IMPLANTATION



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**Introduction.** The first documented bone transplant took place in 1686 by a Dutch surgeon, Job van Meekeren, when he used dog cranium to repair a soldier's skull defect. Today, more than two million bone transplants are performed worldwide each year. The use of 3d printing in bone graft substitutes including implantation devices is gaining more and more importance day by day. It has a significant impact on preparation of patients for surgery, probability of rejection and other complications.

**Aim of study.** The data that was accessible from clinical trials were gathered, and a meta- analysis and comprehensive review were carried out to evaluate the procedure of 3d modeling in bone graft substitutes.

**Methods and materials.** Researched and Obtained from articles that could be found using the keywords "3d modeling" "bone graft substitutes" "devices for implantation" etc. in databases (PubMed, NCIB, pubmed central, frontiers,...etc.).

**Results.** Bone defects can be caused from accidents, neoplasms, infection, malunion or nonunion from fracture healing and if they try to let them heal on their own it can lead to a lot of defects like shortening or loss of full functioning. Autografts were considered as the best treatment, however the complications such as availability, difference of bone structure in different parts ...etc. indicate need for newer methods like 3D printing. It can be used to make personalized implants which fits to specific needs of individual patient size and shape. 3d printing can also make functional tissues and organs for transplants. It can also create custom individual fit prosthetics that are light, strong and comfortable than all other prosthetics. They can also create replicas of patients' anatomy and perform training before they do the actual surgery. It is also used to make specific surgical instruments like scissors, forceps ...etc.

**Conclusion.** In orthopedics and traumatology 3d printing can be an innovative substitute to all other traditional methods. It can solve most of the problems such as tissue source, rejection of organs, transmission of diseases, contamination ...etc. this innovative method can be used in reconversion of normal bone structure of both compact and spongy bones. Even though there is scarcity in studies and experiments, also there is more improvement to be made, it is certain that 3D printing is the future of transplant medicine



## 2. A CASE OF BOERHAAVE SYNDROME- CHALLENGES IN DIAGNOSIS AND TREATMENT

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**Scientific advisor:** Caragia Eugen MD, Panțiri Sergiu MD

**Introduction.** Boerhaave syndrome is a rare yet dangerous condition and one of the most lethal diseases of the gastrointestinal tract marked by transmural esophageal perforation. It is often preceded by forceful vomiting. Early diagnosis and treatment is mandatory for the possibility of a good outcome. Boerhaave syndrome can be associated with Mackler's triad: vomiting followed by severe chest pain and subcutaneous emphysema.

**Case statement.** We present the case of a 41-year-old male patient, who presented to the hospital for chest pain, dyspnea, tachycardia, pain when swallowing and hoarse voice. The symptoms appeared after the patient forced himself to vomit after swallowing a candy that got stuck. The presumptive diagnoses were acute gastroduodenitis, laryngeal edema and intercostal neuralgia. Treatment with Analgin, Dimedrol was started. On the second day, the patient began to present subcutaneous emphysema. A fibrogastroduodenoscopy was performed and it revealed an esophageal perforation in the lower third and the patient was diagnosed with Boerhaave syndrome. Papaverine, Cefazolin, Pantoprazole, Clemastine and Maalox were added to the treatment scheme and the patient was transferred to the surgery department. Urgent surgery was performed on the third day with posterior mediastinal debridement and irrigation. Unfortunately the patient developed mediastinitis and is currently in ICU in critical condition with leukocytosis, fever, tachycardia and a high CRP.

**Discussions.** In this case, the uncommon cause of esophageal perforation and the common symptoms for a wide range of diseases led to a delayed diagnosis and the patient developing mediastinitis. The late surgical treatment resulted in a bad prognosis.

**Conclusion.** Boerhaave syndrome can be challenging to diagnose because of the lack of classic symptoms. The mortality rate can reach over 75% if the diagnosis is not made within the first 12-24 hours and reaches 100% if left untreated. Despite the treatment, the late intervention led to a worse outcome.

### 3. ASPECTS OF DIAGNOSIS AND TREATMENT OF DUODENAL INJURIES IN ROAD ACCIDENTS



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**Introduction.** Injuries in road accidents present a major problem with a significant impact on human health. Annually, 1.3 million people die, and up to 50 million are traumatized, with serious health consequences. In the context of these accidents, duodenal injuries represent a challenge in promptly identifying internal injuries and providing the necessary treatment.

**Aim of study.** Identifying the causes of late detection of duodenal lesions in traffic accidents.

**Methods and materials.** The research included a retrospective study of 34 patients with duodenal injuries following road accidents, hospitalized in the IMU. The B/F ratio 79.41% (27)/ 20.58% (7), aged 18-80. Trauma-hospitalization time: <1h-13 (38.23%), <6h-11 (32.35%), <12h-5 (14.70%), <24h-1 (2.94%), 24h –48 h 1 (2.94%), >48h-3 (8.82%), with stable hemodynamics-16 (47.05%) and unstable-18 (52.94%). As diagnostic instrumental methods were: abdominal x-ray-5 (14.7%), chest x-ray-13 (38.23%), skull x-ray-8 (23.52%), pelvis x-ray-8 (23.52%), USG-18 (52.94%), CT-15 (44.11%), laparocentesis-2 (5.88%), laparoscopy-8 (23.52%).

**Results.** Post-investigations signs of duodenal injury were: retroperitoneal hematoma-2 (5.88%), diffuse peritonitis-1 (2.94%), definite duodenal injury-1 (2.94%). Intraoperatively, the following were found: hemoperitoneum-30(88.23%), retroperitoneal hematoma-26 (76.47%), retroperitoneal phlegmon-3 (8.82%), diffuse peritonitis-6 (17.64%), imbibition retroperitoneal bile-4 (11.76%). Surgical treatment was performed according to the degree of duodenal damage. In the first degree: duodenorrhaphy-12 (35.29%), evacuation of retroperitoneal hematoma-1 (2.94%). In the II degree: duodenoraphys-5 (14.07%), antrumresection with a GEA-1 (2.94%). In degree III: duodenoraphs-5 (14.07%), with a GEA according to Braun – 2 (5.88%), In degree IV: duodenoraphs-2 (5.88%) with the exclusion of the duodenum from the passage and GEA. In grade V: exclusion of the duodenum with GEA with EEA -1 (2.94%). Postoperative complications were manifested by wound suppuration-2, suture dehiscence-4, duodenal fistula-4, retroperitoneal phlegmon-1, intraperitoneal abscesses-5, evolving peritonitis-8, sepsis-2. Relaparotomy as a result of the complications occurred in 13 patients, the lethality constituting 16 cases.

**Conclusion.** Duodenal lesions represent a challenge in diagnosis, having non-specific symptoms and lack of obvious signs. The study emphasizes the severity of these injuries in abdominal trauma, with a great influence on lethality. Early identification and appropriate surgical intervention are essential to improve the prognosis of patients with duodenal injuries caused by road traffic accidents.



#### 4. CHRONIC VENOUS INSUFFICIENCY AND THE PROBABILITY OF TROPHIC ULCER DEVELOPMENT

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**Introduction.** Chronic venous disease represents one of the predominant vascular conditions in the current era. With the rise in comorbidities and the association of risk factors such as sedentary lifestyle, obesity, smoking, and arterial hypertension, the number of affected individuals is steadily increasing. It is important to note that with the high recurrence rate of this pathology, it progressively evolves towards complications that often require prolonged treatment and frequent hospitalizations, impacting the quality of life for patients.

**Aim of study.** To identify the most effective methods for treating venous trophic ulcers.

**Methods and materials.** The study is based on the analysis of the most current and relevant scientific sources (PubMed, National Library of Medicine).

**Results.** The main mechanism in the development of venous leg ulcers is chronic venous insufficiency manifested by reflux, venous hypertension, and microangiopathy, caused by congenital diseases, primary and secondary venous disease. In the presence of venous hypertension, a series of pathological biochemical changes occur, further aggravating the process with the development of chronic inflammation and specific skin alterations. The treatment of venous ulcers is a complex process, involving multiple resources, specialists, and psychosocial support. Often, the treatment is prolonged, involving postural therapy for the lower limb, compressive therapy, and local topical treatment. Based on several observations, the recurrence rate of ulcers is higher after conservative treatment compared to surgical treatment. However, compressive therapy remains a key component of the overall treatment regardless of the clinical classes in which the patient fit according to the CEAP classification. Recommended compressive therapy methods for patients with chronic venous disease include elastic bandages and compressive elastic stockings. Surgical treatment is recommended after the failure of conservative therapy, aiming to reduce venous stasis and improve patient symptoms. As surgical interventions, perforator ablation or perforator ablation in combination with saphenectomy can be employed.

**Conclusion.** Surgical techniques, combined with compressive treatment, have proven to be highly effective in the long-term improvement of patients' quality of life and with a low recurrence rate.



## 5. COMPLEX INNOVATIVE MANAGEMENT OF THE GIANT ABDOMINAL HERNIA



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**Introduction.** Giant ventral incisional hernia is a challenging topic in general surgery, as the ideal approach has not been developed due to the high perioperative morbidity (abdominal compartment, frequent recurrences and lowered quality of life). A modification of the classic retromuscular Stoppa technique was described to improve the results of surgical management.

**Aim of study.** To improve the results of the surgical treatment of large incisional hernias by 1) implementing the technique of posterior components separation with transversus abdominis release procedure (TAR) and prosthetic augmentation, 2) developing an innovative preoperative management and preparation protocol, and 3) performing examination (work-up approach consideration).

**Methods and materials.** The TAR procedure was performed during the period between 2019 and 2022 on 12 patients with giant ventral incisional hernias, classified according to EHS (2009 in): M1W3 (n=1), M2W3 (n=2), M3W3(n=4), M4W3 (n=2), M5W3 (n=1) and L2W3 (n=2).

**Results.** The proposed procedure is based on the principal goals of abdominal wall reconstruction: the restoration of abdominal wall functionality by preserving autologous tissue combined with mesh reinforcement and non-tension midline closure. Thus, the TAR technique combined with polypropylene mesh placed in retromuscular/preperitoneal space provides positive results in reconstruction of the abdominal wall. In our study patients developed the following postoperative complications: parietal wound infection (n=4) and intestinal fistula formation (n=1). 1 year follow-up identified 2 cases of hernia recurrence.

**Conclusion.** TAR technique provides satisfactory postoperative outcomes. It could serve as an effective solution for treatment of complex abdominal wall defects. Additionally, it ensures structural and functional restoration of the abdominal wall.

**Keywords.** Giant ventral incisional hernia, posterior component separation, prosthetic mesh augmentation.



## 6. CONTEMPORARY APPROACHES IN THE DIAGNOSIS AND MANAGEMENT OF CHOLEDOCHOLITHIASIS

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**Introduction.** Cholelithiasis, also known as common bile duct stones, is a common condition characterized by the presence of gallstones in the common bile duct. Diagnostic modalities for cholelithiasis include ultrasound, magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography. The management of cholelithiasis necessitates a multidisciplinary approach, encompassing medical therapy, endoscopic interventions, and surgical treatment, with the choice contingent on various factors.

**Aim of study.** To conduct a contemporary literature review and elucidate various factors for treating patients with cholelithiasis.

**Methods and materials.** Multiple articles from the PubMed database have been reviewed over a span of ten years.

**Results.** The treatment of cholelithiasis primarily involves the removal of obstructing stones through endoscopic procedures. Endoscopic retrograde cholangiopancreatography, typically performed in the prone position, allows the insertion of a duodenoscope into the duodenum, advancing a catheter and guidewire into the common bile duct. Using a sphincterotome, the papilla is cut with cautery, enlarging the ampulla of Vater to release stones. Various tools, such as snares and baskets, aid in stone removal, and a balloon catheter can sweep the common bile duct. Surgical removal is indicated for large, stuck, or numerous stones, requiring laparoscopic or open common bile duct exploration. An elective cholecystectomy during the same admission prevents future cholelithiasis episodes.

**Conclusion.** The focus of cholelithiasis treatment revolves mainly around a minimally invasive approach. Treatment factors involve using tools for stone removal, sphincterotomy, balloon catheterization, and stent placement to manage remaining stones and prevent obstructive jaundice.

## 7. CONTEMPORARY MANAGEMENT OF THYROID NODULES



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**Introduction.** Thyroid nodules are becoming more common every year. In 90-95% of cases they are benign formations.

**Aim of study.** The clinical picture of patients with a thyroid nodule can be completely different, being asymptomatic in 80% of cases, which makes it extremely difficult to identify malignancy in the early stages. The frequency of detecting thyroid nodules in preventive ultrasound investigations ranges from 11.5% to 50.5%, necessitating the development of new tactical approaches in their diagnosis and treatment.

**Methods and materials.** "Management of Thyroid Nodules and Differentiated Thyroid Cancer 2018" Sanziana A. Roman, Julie Ann Sosa. И.В. Слепцов. "Узлы щитовидной железы. Современные принципы диагностики и лечения".2017 г. .Flore Varcus " Nodulul tiroidian , etiopatogenie, diagnostic, tratament" 2008;

**Results.** Firstly, blood tests are performed to assess hormone levels, indicating the thyroid gland's function and feedback with the hypothalamic-pituitary system. At the same time, an increase in antibody titers occurs in less than 15% of the global population and does not always indicate the presence of an autoimmune process. However, in comprehensive investigations, it is essential for the diagnosis of autoimmune thyroiditis. In some cases of nodules, blood analysis for calcitonin levels is conducted, as an increase in this hormone may indicate the presence of medullary carcinoma in the patient. Ultrasound is the first investigation of a thyroid nodule. This method can indirectly indicate the malignancy of the process through TI-RADS classification. Scintigraphy is an important investigation for assessing the functionality and localization of the nodule, particularly significant in cases of ectopic nodular locations. For all nodules with suspected malignancy, Fine Needle Aspiration Biopsy is indicated, which has the highest specificity of 93.5% and a sensitivity of 74.2%. CT and MRI allow identifying the structure, consistency, invasion into adjacent organs and metastases in cases of cancer.

**Conclusion.** Due to the introduction of contemporary investigative methods, the treatment strategy has changed significantly within the last 20 years. The number of surgeries has decreased because of the introduction of new technologies for monitoring and controlling this pathology.



## 8. DIAGNOSIS AND TREATMENT OF ISOLATED DUODENAL INJURIES

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**Introduction.** The low incidence of isolated duodenal trauma results from its anatomic retroperitoneal location. When establishing the diagnosis of isolated duodenal trauma, investigative imaging methods have the highest priority.

**Aim of study.** The identification of diagnostic and treatment methods in isolated duodenal trauma.

**Methods and materials.** This is a retrospective study that includes 21 patients with isolated duodenal trauma, hospitalized in the IMU. The group included a distribution of 17 men and 4 women, between the ages of 18-70 years.

**Results.** The applied diagnostic methods were abdominal radiography (n=11), chest x-ray (n=5), USG (n=14), CT (n=5), laparocentesis (n=1), laparoscopy (n=4), FEGDS (n=2). Indirect signs of isolated duodenal injury were hemoperitoneum (9,5%), pneumoperitoneum (19,1%), retroperitoneum (14,3%), retroperitoneal hematoma (4,8%), obvious duodenal injury (4,8%), diffuse peritonitis (19,1%), aerocoly (9,5%), liquid in BO (38,1%), postbulbar ulcer (4,8%). Hemoperitoneum (19,1%), retroperitoneal hematoma (23,8%), retroperitoneal phlegmon (28,6%), diffuse peritonitis (71,4%) were intraoperatively established. The detected duodenal lesions were located on the anterior wall (52,4%), posterior wall (33,3%), as well as their association (14,3%). The frequency of traumatized duodenal segments was: D1- 33,3%, D2- 33,3%, D3-23,8%, D4-14,3%. The degrees of duodenal injury according to the AAST classification were the following: 1st group - 1 (4,76%), 2nd - 11 (52,38%), 3rd - 6 (28,57%), 4th - 3 (14,28%). The surgical treatment was carried out depending on the location, the damage degree and the hemodynamics of the patient. First patient had the duodenal deserosis sutured (4,76%); six patients in the second group (28,57%) dealt with duodenorrhaphy and exclusion of the pylorus [n=1(4,76%)], pyloroduodenoplasty [n=2(9,52%)], and the evacuation retroperitoneal hematoma [n=2(9,52%)]. Four third degree patients (19,04%) had the following performed: duodenorrhaphy with gastric resections; excluding the pylorus Şalimov procedure; Konishi gastric transposition, and duodenal pyloroplasty by Miculici [n=2 (9,52%)]. Severe degrees of injury (IV-V) requested following techniques: duodenorrhaphy [n=2(9,52%)] with GEA Von-Hacker and Jejunostomy Witzel; Konishi technique of exclusion of duodenum after with retrocolic GEA, and evacuation of retroperitoneal hematoma [n=1(4,76%)].

**Conclusion.** Isolated duodenal trauma presents an atypical clinical picture, with major difficulties in establishing the diagnosis. The applied investigation methods identified the presence of indirect signs of isolated duodenal injury.

## 9. DIFFUSE AXONAL INJURY IN A PATIENT WITH POLYTRAUMA



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**Scientific advisor:** Gălbineanu Simona

**Introduction.** Diffuse axonal injury of the brain is primary diffuse traumatic effect, caused by mechanisms of impact and inertial dynamics. In more cases, the patients are unconscious with minimal lesions visualized on the initial CT scans. MRI with sequences sensitive to hemorrhagic lesions/ cytotoxic oedema and is able to visualize DAI by detecting even microscopic amounts of blood or nonhemorrhagic lesions secondary to axonal strain in deep white matter.

**Case statement.** Patient P.R. 30 y male, no relevant medical history, collision accident polytrauma (as driver), medical assistant in Emergency room. He was found scoring 5 points on GCS, with symmetrical and reactive pupils, hypothermic. He was then intubated and transported to Emergency where the CT-trauma protocol was performed. Diagnosis on admission: Polytrauma following collision road accident, TCC with accumulation bleeding at the level of the brain scythe, Intracerebral contusions, Diffuse cerebral oedema, Acute respiratory failure, Pulmonary contusions bilateral, Anemia. ISS: 43 points, APACHE II: 11 points, SOFA: 7 points. The patient is admitted to the ICU comatose, under continuous sedation, afebrile, intubated and mechanically ventilated, hemodynamically stable, with urine output. Admission screening tests were sampled, started specialized treatment under monitoring and support of the vital functions. Evolution: On Day 1-3, patient under continuous sedation On Day 4-7, altered neurological status On day 8, the patient begins to open his eyes spontaneously, exhibits tonic-clonic movements and demonstrates brainstem reflexes. On the 10th day, tracheostomy is performed. On day 12, the patient has anisocoria without evidence of any significant lesions on CT scans, further MRI highlights multiple areas with diffuse axonal lesions. Following very slow progress, the patient watches and follows with his eyes, spontaneously moves his right hand, is weaned from the ventilator and continues the respiratory and motor physiotherapy. On day 30, He is maintained swallowing deficient, and we decided to perform a gastrostomy On day 70, the patient with improved general condition, afebrile, stable respiratory and circulatory, conscious, spontaneously moves all limbs, is transferred to the Neurology Department for further treatment and medical recovery.

**Discussions.** Although the neurological status was uncertain for a very long time and the emotional impact for the whole staff was important, for us, our colleague is a real fighter. Despite the large duration of initial hospitalization followed by multiple admissions in recovery clinics, now the patient is conscious, cooperative, and reintegrated into society.

**Conclusion.** The treatment adapted to the patient's needs, early neuromodulator and neurotrophic treatment, intense physiotherapy at the patient's bedside, attentive nursing and family involvement gave the patient an extra chance.





## 10. EXTRA-ANATOMIC BYPASSES: A SOLUTION FOR COMPLEX CLINICAL SCENARIOS IN VASCULAR SURGERY

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**Introduction.** The extra-anatomic bypass is defined as a vascular reconstruction with tunneling of the graft outside the normal anatomical trajectory of the major arteries. We present three clinical cases, demonstrating the utility of extra-anatomic reconstructions in different clinical situations.

**Case statement.** First patient (male, 40 years old) was admitted in emergency with infected femoral artery pseudoaneurysm, caused by repeated injections of illicit drugs. Excision of the aneurysm with triple arterial ligation (external iliac, femoral and deep femoral artery) was performed and limb was revascularized via ilio-femoral bypass. The PTFE graft was tunneled through obturator foramen and non-infected tissue planes. Groin wound required serial debridement and application of negative pressure therapy. In the second case an axillary-to-femoral artery bypass with reinforced PTFE graft was performed in an 83 years old male patient with chronic limb threatening ischemia. Anatomic type of reconstruction was considered unsuitable due to the extreme aorto-iliac calcification (“porcelain aorta”) and patient frailty. Third patient (male, 57 years old) was operated for giant recurrent sarcoma in the inguinal region with invasion in femoral artery, nerve and vein. Wide excision of the tumor and ligation of the femoral vessels wa

**Discussion.** Extra-anatomic bypasses are relatively rare performed in vascular surgery. Despite slightly inferior long-term patency and increased technical difficulty these reconstructions can be a unique solution in high-risk situations.

**Conclusion.** For patients with complex clinical scenarios extra-anatomic bypasses represent an alternative approach and offer acceptable results.

## 11. HIATAL HERNIA, AN UPDATE OF DIAGNOSIS AND TREATMENT



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**Introduction.** Hiatal hernia is a rather common ailment in the general population. It is caused by increased intra-abdominal pressure, which causes the stomach and other abdominal viscera to protrude into the mediastinum.

**Aim of study.** Hiatal hernia (HH) is quite common in the general population and is characterized by a variety of non-specific symptoms, the majority of which are connected to gastroesophageal reflux symptoms. The most recent guideline for the care of hiatal hernia was published in 2013 by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). This review seeks to provide clinical practitioners with the most recent developments on the diagnostic and therapy of hiatal hernia.

**Methods and materials.** The following research was carried out using PubMed searching medical keywords as “Hiatal hernia”, “Management”, “Treatment”. Prospective, randomized trials, systematic reviews, and original articles were among the papers we investigated.

**Results.** This review includes fresh data on hiatal hernia diagnosis and management. While the diagnosis process has remained mostly constant, new information about the surgical therapy of hiatal hernia has emerged. We discuss the imaging modalities used to diagnose it, as well as the medicinal and surgical treatment that are now available.

**Conclusion.** In the last five years, there has been extensive research in the field of hiatal hernia management, particularly surgical treatment. However, there are still outstanding questions, and solid modifications to the recommendations have yet to be developed. More randomized studies on subsets of patients stratified by age, gender, symptoms, and comorbidities are needed to address issue.



## 12. IMMUNOPATHOLOGY OF LIVER TRANSPLANTATION

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**Introduction.** Liver transplantation is a new lead in surgery and hepatology domains. This procedure requires drastic changes in the human immune system to ease the recipient's graft for the donor, including immunodeficiency for both parties. This way the transplant implies lesser risks for graft rejection, even though complications happen at a moderate rate.

**Aim of study.** Based on scientific data from special literature there is a need to determine the cause factors of the incompatibility reactions in liver transplant failure and see the possibilities to observe both the transplantation and recovery after. Therefore, this literature research tends to make a retrospective on the immune modifications and complications in the process of getting a liver transplant.

**Methods and materials.** This study presents a literature review, published on scientific platforms, such as PubMed, USA National Library of Medicine, JSTOR, and Google Scholar, that refer to liver transplantation and its immune-modulations. This paper includes results based on 10 publications.

**Results.** One study presents that 19% of recipients of liver grafts show failed immunosuppression, and yet another study determined that only 12 out of 20(60%) of children recipients present successful immunosuppression, with no portal inflammation. Donors' and recipients' body immune modulation determines the favorable outcome of the liver transplant, which requires immunodeficiency for 3 types of antigens: ABO, major HLA, and minor HLA. Not suppressing enough, the liver graft can cause donor T-cell-specific intolerance at the interaction of hepatic/portal antigens with endotoxins produced by intestinal bacteria. This results in the secretion of pro-inflammatory substances: cytokines, IFN- $\gamma$ , and co-stimulatory agents that induce major liver inflammation, necrosis, and graft rejection. Another immunopathological mechanism in liver transplantation is the interaction between the donors' and recipients' HLA antigens, resulting in excess production of IgG, especially IgG3, presented in the Baylor group study on patients with chronic liver transplant rejection.

**Conclusion.** Liver transplant has a great impact on the human body. The recipient goes through life immune suppression in order to minimize the chances of graft failure, but eventually, ABO and HLA incompatibility can result in severe immunopathologies. Studies present that most allografts show different stages of rejection. Acute and chronic rejection yield under proper immunosuppressing treatment, the recommended combination being: calcineurin inhibitors (cyclosporin), antimetabolite agents (azathioprine) corticosteroids, and mammalian target of rapamycin inhibitors (sirolimus).

### 13. INNOVATION IN THE TREATMENT OF MYELOMENINGOCELE: ADVANCED APPROACH TO CORRECTION THROUGH FETAL SURGERY



**Author:** Săbăduș Eric Christian

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**Introduction.** Fetal surgery, also known as intrauterine surgery, has evolved significantly over the years. This specialized branch of surgery focuses primarily on treating congenital conditions and abnormalities of the developing fetus. Prenatal repair of myelomeningocele (MMC), the most common and severe form of spina bifida, is an exceptionally delicate surgical procedure in which fetal surgeons open the uterus and close the opening behind the baby while it is still in the womb. Because spinal cord injury progresses throughout the gestational period, prenatal repair of myelomeningocele can prevent further damage.

**Aim of study.** The research was conducted on PubMed using the keywords "fetal surgery," "spina bifida," "myelomeningocele," and "prenatal."

**Methods and materials.** Scientific papers were selected based on inclusion criteria, which involved patient groups treated with both prenatal and postnatal surgery, recovery period, postoperative well-being of patients, operating time and the effectiveness of the procedure itself. Articles mentioning patients with major complications were excluded. Risk of bias was not assessed, and PRISMA criteria were used for data synthesis. Within the carefully curated selection of 12 articles, we have delved into two impactful studies that contribute significantly to the field. The initial study, led by the esteemed National Institute of Child Health and Human Development (NICHD), meticulously scrutinized a cohort of 183 patients treated between 2010 and 2020. Notably, 91 patients underwent prenatal surgery, while 92 underwent postnatal intervention. The second study, conducted at the Saint Louis Fetal Care Institute, methodically investigated a cohort of 58 patients, all of whom received prenatal treatment, spanning the years 2011 to 2017.

**Results.** According to the first study, children from the group that underwent prenatal surgical intervention showed a significantly higher likelihood of achieving independent mobility (44.8% compared to 23.9% in the group that underwent surgery after birth). Subsequent research indicates that prenatal repair of myelomeningocele improves motor outcomes at the age of 30 months compared to postnatal repair. Within the cohort of 58 patients analyzed in the second study, 2 unfortunately succumbed to prematurity (3.44%), and 30 required treatment for hydrocephalus (51.72%).

**Conclusion.** Fetal surgery for spina bifida brings remarkable benefits, notably reducing the need to divert fluid from the brain, enhancing mobility, and increasing the likelihood of independent walking for the baby. This intervention addresses and mitigates the effects of spina bifida, a congenital condition impacting the spinal cord. By surgically repairing the myelomeningocele (MMC) prenatally, the procedure contributes to improved long-term outcomes for affected individuals, preventing ongoing damage and fostering a foundation for healthier development. This proactive approach underscores the transformative impact of medical innovation on the lives of those with spina bifida.



#### 14. INTERNAL OSTEOSYNTHESIS OF POSTERIOR PELVIS INJURIES. EVALUATION OF RESULTS 2020-2024

**Author:** Sirghi Grigore

**Introduction.** Lesions of the posterior part of the pelvic ring can occur in trauma, resulting in instability of the posterior part of the pelvic ring. The goals of invasive treatment include adequate reduction and stable fixation to ensure pelvic ring stability.

**Aim of study.** Evaluation of the results of internal osteosynthesis treatment in lesions of the posterior part of pelvic ring, establishment of the complication rate, evaluation of long-term results.

**Methods and materials.** We analyzed 70 clinical cases: 40 men and 30 women; The average age was 51.8 years. All suffered from unstable pelvic fractures type B and C, according to the Tile classification, as well as fractures due to osteoporosis. The causes of the trauma were: 42 cases of road accidents, 18 cases of catatrauma, 4 cases of crushing and 6 cases osteoporotic fractures. 52 patients had strictly pelvic injuries, 18 patients were polytraumatized. The average period of hospitalization constituted an average of 15.5 days. All patients underwent internal osteosynthesis surgery (60 patients - ilio-sacral fixation, 1 patient - underwent bilateral spino-pelvic fixation, 6 patients - underwent triangular fixation, 3 patients - underwent sacro-iliac fixation with anterior plate). 6 patients underwent percutaneous surgery, 38 patients underwent open surgery for other present pelvic lesions, 18 underwent surgeries on other segments of the locomotor system.

**Results.** All patients were followed up at post-surgery. Degradation of osteosynthesis occurred in 3 patients, incorrect placement of implants - 3 patients, lethal outcome in the postoperative period occurred in 3 patients caused by severe trauma and comorbidities.

**Conclusion.** The best results and fewer complications were achieved when all pelvic injuries were fixed in a timely manner and a good patient's compliance.



## 15. INTERNAL OSTEOSYNTHESIS OF THE PUBIAL SYMPHYSIS INJURIES. RESULTS EVALUATION 2020-2024



**Author:** Sirghi Grigore

**Introduction.** Diastasis of the pubic symphysis represents the injury consisted of the loss of the connection between the pubic bones, resulting in the instability of the anterior pelvic ring. The lesion with diastasis exceeding 25 mm is considered the lesion requiring surgical intervention. The goals of treating symphysis diastasis include adequate reduction and stable fixation to ensure pelvic ring stability.

**Aim of study.** Evaluation of the results of osteosynthesis treatment in pubic symphysis lesions, determination of the complication rate, evaluation of long-term results.

**Methods and materials.** We analyzed 31 clinical cases: 27 men and 4 women; The average age was 51.23 years. All were investigated by pelvic CT. All suffered unstable pelvic fractures type B and C, according to the Tile classification. The cause of trauma was: 19 cases of road accidents, 9 cases of catatrauma, 2 cases of crushing. The average hospitalization period was 27.64 days and 9.76 days in 13 people with strict pelvic injuries. All studies underwent surgical treatment (1 – external fixation, 5 – external fixation with subsequent conversion, 8 –osteosynthesis of the anterior part of pelvic ring, 19 – anterior osteosynthesis supplemented by fixation of the posterior part of pelvic ring).

**Results.** All studies were followed post-surgery for 1, 3, 6, 12 months. Osteosynthesis degradation occurred in 3 patients, postoperative infection in 4 patients, lethal results in 4 patients caused by severe trauma and comorbidities.

**Conclusion.** The best results and fewer complications were achieved in a close and personalized approach to the cases, with both pelvic halves fixed and a good patient's compliance.



## 16. MALPRACTICE IN PLASTIC SURGERY: BIOETHICAL ASPECTS

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**Introduction.** Currently, plastic surgery is a very popular field as a method of correcting patients' external appearance problems. Despite the advantages of plastic surgery, one of the biggest and acute problems is the manifestation of malpractice and its bioethical dimension in this field.

**Aim of study.** Analysis of bioethical aspects in plastic surgery. Highlighting the causes of malpractice and methods to solve them.

**Methods and materials.** For this study, medical sources available on the PubMed platform were used. Statistical data were analyzed from patients who suffered from malpractice in plastic surgery. The literature on similar cases of medical malpractice has been studied.

**Results.** In the 1960's, when malpractice lawsuits increased exponentially, a defensive medicine practice was created and developed in the 1970's. Over the past 20 years, the number of medical malpractice lawsuits has declined, but the practice of defensive medicine has lingered. 5 medical articles on the respective topic were studied. It was found that a large number of surgeons accused of malpractice worked in private clinics. The main ethical and medico-legal consequences of complications were analyzed, as well as the appropriate actions of the plastic surgeon, alternative approaches to medical ethics, the definition of bioethical limitations, the principles of medical ethics related to plastic surgery.

**Conclusion.** Malpractice is a very important and always a relevant issue in medicine, including plastic surgery. The adoption of new laws, data collection, creation and publication of malpractice statistics in plastic surgery will improve the quality of services provided in this field.

## 17. MANAGEMENT OF ABDOMINAL COMPARTMENT SYNDROME IN THE CONTEXT OF POSTOPERATIVE EVENTRATIONS



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**Introduction.** Abdominal compartment syndrome, known in the literature as Batzner's syndrome, plays an important role in the surgical treatment of postoperative eventrations, its importance being illustrated by the increased rate of postoperative complications. The repositioning of the contents of the hernial sac in the abdominal cavity and the reconstruction of the abdominal walls with parietal defects over 10-15 cm, contributes to the increase in intra-abdominal pressure above the normal values, which can result in cardiovascular, respiratory and hemodynamic disorders.

**Aim of study.** Elucidation of preventive measures and their effectiveness in the context of compartment syndrome in patients with incisional hernias.

**Methods and materials.** For the purpose of the study, were monitored 40 patients, aged between 50-60 years, admitted to the "Timofei Mosneaga" Republican Clinical Hospital with the diagnosis of postoperative eventrations, who presented a risk of triggering intra-abdominal hypertension. There were studied methods of prevention, their effectiveness at the preoperative, intraoperative and postoperative stages.

**Results.** The prevalence of intra-abdominal hypertension was 45% (18 patients). They were divided into three categories depending on the intra-abdominal pressure values, subsequently: 22.5% (9 patients) developed intra-abdominal hypertension degree I - values between 10-15 mmH<sub>2</sub>O, 12.5% (5 patients) intra-abdominal hypertension degree II - values between 16-25 mmH<sub>2</sub>O, 10% (4 patients) intra-abdominal hypertension grade III - values between 26-35 mmH<sub>2</sub>O. Intra-abdominal hypertension with values higher than 35 mmH<sub>2</sub>O were not detected. Postoperative curative management followed a controlled respiratory ventilation.

**Conclusion.** The management of the diagnostic and curative complex for patients with postoperative eventrations lower the number of severe abdominal hypertension and the rate of early and late complications.



## 18. MANAGEMENT OF AXILLARY ARTERY INJURY

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**Introduction.** The axillary artery injuries are considered to be an uncommon trauma, accounting for about 15-20% of all vascular injuries of the upper limb. The distinguishing feature of this type of trauma is that it represents less than 5% of all civilian vascular injuries. In a similar context, slightly more than 5% of all arterial injuries are caused by fracture and dislocation of the shoulder. Among the contemporary modalities to repair injuries of axillary artery the specialized literature emphasizes the following surgical approaches: the interposition of different type of grafts (saphenous or basilic veins, as well as prosthetic grafts), direct repair and endovascular treatment using stent grafts.

**Aim of study.** The objective of this study was to present the role of clinical characteristics and to assess postoperative results of the surgical management of patients with traumatic axillary artery lesions.

**Methods and materials.** We conducted a retrospective study that includes 9 patients hospitalized at Vascular Surgery Clinic, Institute of Emergency Medicine, Chisinau (Republic of Moldova), from October 2018 to February 2022 with axillary artery lesions. The study cohort was stratified by trauma type, trauma-surgery time, Rutherford's acute limb ischemia classification, coexisting of nerve plexus injury, vascular reconstruction methods, and postoperative clinical evolution. Descriptive statistics were performed on all variables.

**Results.** The study group included 8 male and one female patient; mean age – 58.7 (ranged 28 – 80 years). In 44.5% (n=4) patients trauma was caused by bone fracture and in 55.5% (n=5) – by shoulder dislocation. Acute ischemia of the upper limb was established in all patients, corresponding to stage I – 33.3% (n=3) or stage II – 66.7% (n=6) according to Rutherford classification. Also, 44.4% (n=4) patients was diagnosed with concomitant nerve plexus injury. Vascular injury was confirmed by imaging exam: computed tomography angiography (n=6) or duplex scan (n=3). In most of cases the time from trauma onset up to vascular reconstruction varied between 9 hours and 70 hours, while in one case – it was about 112 hours, because of late patient's presentation. The rate of primary open surgical approach was 77.8% (n=7). Autologous venous graft interposition was performed in 3 cases, and the primary repair by creating a T-T anastomosis was practiced in 4 observations. The primary endovascular approach was attempted in two patients, but was completed successfully in only one. Another case required interposition of a venous graft. There were no cases of death, amputation or other major complications in the early postoperative period.

**Conclusion.** The axillary artery trauma may require a varied curative approaches. Regardless of the method used for revascularization, the short-term postoperative clinical results are favorable in most cases.

## 19. MINIMALLY INVASIVE REPAIR TECHNIQUES IN BARLOW'S MITRAL VALVE DISEASE.



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**Introduction.** Barlow's disease is a challenge for minimally invasive cardiac surgery which represents a clinical form of mitral valve insufficiency characterized by dilation of the mitral valve annulus, valve prolapse and excessive myxomatous tissue.

**Aim of study.** Analysis the scientific bibliographic sources of the speciality literature with reference to the evaluation of the success and durability of the intraoperative results and postoperative survival after minimally invasive cardiac surgery in Barlow's mitral valve disease.

**Methods and materials.** Multilateral and complex study by analyzing the speciality literature in the data bases: PubMed, Ovid MEDLINE, Google Scholar according to the following search terms: Barlow, minimally invasive cardiac surgery, prolapse, mitral valve insufficiency. Have been selected relevant studies in English from 2018 to the present.

**Results.** The literature analysis allowed the identification of 112 publications noting an increase in interest towards this topic. Echocardiography was the essential examination in establishing indications for surgical treatment. Various complex surgical techniques were analyzed: Carpentier's slip plasty, edge-to-edge (Alfieri) techniques, neochord (Loop) techniques, chordal transfer or shortening, leaflet flip techniques, and "non-sectional" annuloplasty approaches. Regardless of the surgical technique applied in Barlow's disease the minimally invasive approach ensures intraoperative time, extracorporeal circulation and the aortic clamp. The decrease in postoperative complications was established: hemorrhage, vascular accidents, infections and the rate of surgical reintervention.

**Conclusion.** Minimally invasive surgeries in Barlow's disease are performed safely with excellent long-term results and confirmed valvular performance echocardiographic remains stable over time. The results of the surgical techniques can be comparable but remain superior to the conventional cardiac surgical treatment, so surgeons practicing the minimally invasive cardiac surgical approach can use any technique based on their own experience.

**Keywords.** Barlow, minimally invasive cardiac surgery.





## 20. MULTIMODAL TREATMENT IN GASTRIC CANCER

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**Introduction.** Worldwide, gastric cancer is the fourth most common cancer and has a poor prognosis with a 5-year survival rate of 20-25%. Highest incidence rates are observed in East Asia, Central Asia, Eastern Europe, and the Pacific Coast of South and Central America, whereas the lowest incidence rates are found in Northern Europe and North America. Although the course of multimodal treatment has improved, radical resection is still the current main treatment for gastric cancer. When diagnosed at an early stage, the success rate with minimally invasive resection, such as endoscopic, laparoscopic, and robotic surgery, is high. Advanced gastric cancer for which radical resection is not indicated is primarily treated with chemotherapy. Results of treatment in these neoplasms are strictly dependent on tumor stage.

**Aim of study.** The principle of operative intervention for gastric cancer is to achieve complete resection of the primary tumor with an en bloc regional lymphadenectomy. Gastric surgery can be classified as total, distal, pylorus-preserving, and proximal gastrectomy. Lymph node dissection is decided according to clinical T and/or N factor, and D1 or D1+ dissection is indicated for cT1 lesions and D2 dissection for cT2 lesions. A total gastrectomy may be indicated when the extent or location of the primary tumor is such that adequate margins of resection are not possible with a subtotal gastrectomy.

**Methods and materials.** A literature review using full-text articles on PubMed, World Journal of gastroenterology, HHS, Asia Journal of Surgery, International Journal of Surgery, MEDICINE and several other articles using the relevant keywords.

**Results.** D1 partial gastrectomy is the classic operation for distal gastric cancer. After a distal partial gastrectomy, the remaining stomach can be anastomosed to the mobilized duodenum or the first loop of jejunum, and is described as a Billroth I and II. A further alternative reconstruction is with a Roux-en-Y loop. Also, several meta-analyses show that patients have better survival rates with D2 lymphadenectomies in advanced disease. D2 subtotal gastrectomy is particularly suitable for small gastric tumors involving the pylorus and distal third of the stomach. Except in early gastric cancer, a total gastrectomy becomes necessary for all but antral tumors. Perioperative chemotherapy is essential in advanced stages.

**Conclusion.** In conclusion, gastric cancer remains a significant global health challenge with late presentation especially in the western world. Surgical resection, particularly radical resection, continues to be the primary curative approach. Advancements in minimally invasive and robotic techniques offer promising outcomes, including faster recovery and reduced morbidity.

## 21. PERIHILAR CHOLANGIOCARCINOMA. SURGICAL DIAGNOSIS AND TREATMENT



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**Introduction.** Even though cholangiocarcinoma is a rare hepatobiliary malignancy, with an incidence of <1 case per 100,000 people, which represents 3% of all gastrointestinal malignancies worldwide, the patients with PHC are usually hospitalized with severe, painless jaundice and are diagnosed at an advanced stage, which means an unfavorable prognosis and a short life span. Preoperative diagnosis and available surgeries provide the opportunity to intervene promptly, respectively improving survival.

**Aim of study.** The aim of the study is to compare staging, assess resectability and identify the diagnostic and therapeutic approach to perihilar cholangiocarcinoma.

**Methods and materials.** A descriptive, retrospective study was carried out on a group of patients with Klatskin cholangiocarcinoma. Between 2020 and 2023, 17 patients were admitted to the surgery clinic of "Timofei Moșneaga" IMSP SCR\* (\*Public Medical-sanitary Institution Republican Clinical Hospital "Timofei Moșneaga"). The research of the study was based on the statistical method accompanied by clinical, paraclinical examination including laboratory tests and instrumental investigations (necessary for tumor localization, pre-surgical staging and resectability identification). Non-invasive (ultrasonography, CT, MRCP), and invasive (CPGRE) diagnostic methods are used. The parameters evaluated were as follows: tumor staging, technical variants applied.

**Results.** According to the Bismuth - Corlette classification, Klatskin tumors type I and II – 2 cases, type IIIA – 3 cases, IIIB – 2, and 10 cases were recorded in type IV. Surgical treatment was performed in 7 (41.1%) patients. Left hepatectomy was performed in 2 patients, right hepatectomy in 2 patients with restoration of digestive tract continuity by applying hepatico-jejunal anastomosis in Y a la Roux and extension to the caudate lobe. In the other 3 cases, resection of the main bile ducts was used with the application of bi hepatico-jejunal anastomosis.

**Conclusion.** The examination algorithm for patients with Klatskin tumors will include – clinical examination, laboratory and instrumental examination. Ultrasound, CT, MRCP and CPGRE shall be used as a choice). Due to the aggressive nature of the Klatskin tumor and the late onset of symptoms, only 41.1% of patients are surgically resectable at diagnosis. Surgery is the only curative option, but long-term survival is reduced.



## 22. POSTOPERATIVE URINARY RETENTION: RISK FACTORS AND PREVALENCE

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**Introduction.** Postoperative urinary retention (PUR) is a known and frequent complication of the immediate period after surgery, representing the inability to urinate postoperatively despite the presence of a full bladder. PUR can be a source of stress for the patient or can go unnoticed. Recognized early and with appropriate management, PUR is reversible, rarely having long-term consequences.

**Aim of study.** Assessment of the prevalence and identification of risk factors for the development of postoperative urinary retention with the development of a prevention strategy.

**Methods and materials.** A literature review of the Google Scholar, PubMed, Elsevier, Cochrane databases, was done with the selection of articles from the last 10 years.

**Results.** In the specialized literature, the prevalence of PUR varies a lot, values between 5% and 70% being quoted. The variability with which the phenomenon is registered can be explained by the lack of a standardized definition for PUR, each clinical study adapting different definition criteria. Risk factors involved in the development of PUR may be related to medical procedures: type of surgery (previous pelvic surgery may increase the risk, probably as a result of direct damage to the nerves innervating the lower urinary tract), anesthetics used (general anesthetics cause bladder atony by interfering with the autonomous nervous system), duration of the intervention (this finding may be associated with the volume of intravenous fluids administered and the increase in opioids used), volume therapy (the administration of intravenous fluids more than 750 ml in the perioperative period increased the risk of PUR by 2.3 times) or with the patient: comorbidities (DM has been implicated in impairing capacity and decreased contractility), age (patients over 50 years of age have 2.4 to 2.8 times higher chance of having this complication), gender (higher incidence was reported in men (4.7%) compared to women (2.9%)) and preoperative urinary function (80% of patients who developed PUR had some form of prior urinating difficulty).

**Conclusion.** The diagnosis of PUR is often arbitrary, the real prevalence of the phenomenon remains unknown. By identifying and stratifying patients at risk for PUR and the implementation of ultrasound monitoring of bladder volumes, PUR can be prevented, with the implicit reduction of its associated morbidity. Failure to identify RUP in a timely manner can lead to significant morbidity: prolonged hospital stay, urinary tract infections, detrusor muscle dysfunction, delirium, cardiac arrhythmias, permanent bladder dysfunction, etc.

## 23. POSTOPERATIVE VENTRAL HERNIAS



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**Introduction.** Postoperative ventral hernias are protrusions of organs or other structures through the abdominal wall that occur after abdominal surgery in the area of the surgical scar and are often the result of the weakening or inability of the abdominal wall to heal properly after surgery. Treatment may involve surgery to repair the defect and strengthen the abdominal wall.

**Case statement.** Patient X, 52 years old, diagnosed with chronic obstructive pulmonary disease (COPD), type II diabetes mellitus (DM) and grade II obesity (BMI 38.5 kg/m<sup>2</sup>), underwent abdominal surgery for the resection of a tumor benign in the colon. Approximately six months after the operation, he presented with abdominal pain and swelling in the area of the surgical scar. Clinical examination revealed a deformity with a parietal defect located in the lower abdomen, which became more pronounced with coughing. The patient reported discomfort and pain in the respective area. Medical imaging, including computed tomography, confirmed the diagnosis of postoperative ventral hernia.

**Discussions.** Being with serious comorbidities, persistent symptoms and risks of complications, such as strangulation of the hernia, the decision was made for the patient to undergo a ventral hernia repair intervention, with the use of a polypropylene mesh to strengthen the abdominal wall. The treatment plan involved addressing the ventral hernia through corrective surgery, considering complicating factors such as COPD and DM that were corrected and monitored preoperatively as well as postoperatively to prevent further complications. In the immediate postoperative period, the patient showed a favorable recovery, with a gradual decrease in pain and discomfort. A period of rest and avoidance of exertion was recommended. Intense physical activity, daily measurement of blood sugar and administration of antitussives. The patient was closely monitored for signs of any potential complications. At the following follow-up consultations, the patient's evolution was favorable and the symptoms of the hernia decreased significantly. The healing process continued, and the patient was encouraged to gradually resume his normal activities, under the close supervision of the medical team.

**Conclusion.** The case highlights the importance of careful postoperative monitoring and management of ventral hernias to prevent complications and ensure optimal patient recovery.



## 24. POTENTIAL APPLICATIONS OF NANOTECHNOLOGIES AND BIOENGINEERING IN DUPUYTREN'S DISEASE TREATMENT

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**Introduction.** Dupuytren's disease, characterized by the formation of knots and cords in the palm and finger fascia of the hand, needs significant challenges in treatment due to its progressive nature and tendency for recurrence. In recent years, nanotechnology and bioengineering have emerged as a promising avenue for addressing the complexities of this condition.

**Aim of study.** The review explores the emerging applications of nanotechnologies and bioengineering in the treatment of Dupuytren's disease, by examining recent advancements.

**Methods and materials.** A comprehensive search of electronic databases including *Google Scholar*, *PubMed*, *Scopus*, and *Web of Science* was conducted to identify relevant studies in the period of time 2020-2024. The search strategy employed a combination of keywords related to nanotechnology, bioengineering, Dupuytren disease, and treatment modalities.

**Results.** Key areas of focus include targeted drug delivery using engineered nanoparticles, that can be designed to deliver therapeutic agents directly to affected tissues, increasing treatment effectiveness while minimizing side effects. The development of nanostructured scaffolds, that are designed to support tissue regeneration and inhibit contracture progression in affected areas of the hand, present a promising approach for tissue engineering. These scaffolds can mimic the extracellular matrix and provide a supportive environment for cells to grow and regenerate, potentially offering a novel approach to treating Dupuytren disease. Nanoparticle-based imaging involves the use of nanoparticles as contrast agents for advanced imaging techniques such as magnetic resonance imaging, computed tomography, or ultrasound. These nanoparticles are designed to specifically target and accumulate in areas affected by Dupuytren disease, providing enhanced visualization of disease-related structures and processes. By harnessing the unique properties of nanomaterials, researchers aim to enhance the efficacy of current treatments, minimize side effects, and ultimately improve outcomes for patients with Dupuytren's disease.

**Conclusion.** Despite the early stage of research in this field, the potential of nanotechnology and bioengineering to revolutionize Dupuytren's disease treatment highlights promising advancements. However, further studies are needed to optimize these approaches, evaluate their long-term safety and efficacy, and develop clinically feasible methods for their application in Dupuytren disease.

**Keywords.** Dupuytren Disease, Nanotechnologies, Bioengineering.



## 25. RELEVANCE OF COLOR DOPPLER EXAMINATION IN THE ASSESSMENT OF THYROID NODULES



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**Introduction.** The utilization of color Doppler examination facilitates the exploration of changes in the frequency of ultrasonic waves reflected by the bloodstream. This method is employed in assessing the vascularity of thyroid nodules.

**Aim of study.** The preoperative differential diagnosis between benign and malignant thyroid nodules is quite important for assessing the extent of the surgical intervention.

**Methods and materials.** The study included 124 patients with thyroid nodules examined ultrasonographically using color Doppler, ranging in age from 19 to 71 years. There were 20 male patients (16.13%) and 104 female patients (83.87%). Nodules were categorized as non-vascularized, with peripheral vascularization, intranodular vascularization, and mixed vascularization.

**Results.** As a result of color Doppler examination, thyroid nodules were detected with mixed vascularization in 53 patients (42.7%), peripheral vascularization in 30 patients (24.2%), intranodular vascularization in 24 patients (19.4%), and without vascularization in 17 patients (13.7%). In patients with malignant thyroid nodules confirmed by definitive histopathological examination, mixed vascularization was identified preoperatively.

**Conclusion.** Color Doppler examination is crucial in determining the malignancy of thyroid nodules. Mixed vascularization of thyroid nodules is characteristic of thyroid gland cancer.



## 26. REVASCULARIZATION OF THE LOWER EXTREMITIES USING TRANSOBTURATOR BYPASSES

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**Introduction.** Transobturator bypass is a surgical technique used as an alternative option for lower extremity revascularization. The passage of the vascular graft through the obturator foramen, thus bypassing the inguinal region, is a suitable option for patients who cannot safely benefit from an arterial bypass with an anatomic route of the conduit (previous vascular surgery, graft infections or inflammation in the groin area, tumors with metastases in the regional lymph nodes, pseudoaneurysms). The purpose of the current study was to identify the clinical circumstances in which revascularization of the lower limbs were performed through transobturator bypass and to assess early postoperative results.

**Case statement.** The case series included three male patients operated between 2020-2022 at the Vascular Surgery Clinic, Institute of Emergency Medicine, Chisinau, Republic of Moldova. Vascular diseases were diagnosed by computed tomography angiography. The following conditions were established: (#1) traumatic injury of the left common femoral artery, (#2) pseudoaneurysm of the right common femoral artery in a drug addict and (#3) limb-threatening ischemia of the left lower extremity caused by occlusion of the native femoral artery and failure of two previous femoral popliteal bypasses (one with autologous vein and another - with PTFE graft). In first two cases opting for extra-anatomic bypass was conditioned by the infection in the groin area, and in case #3 – by the multiple postoperative scars in the infrainguinal region. The external iliac artery served as the inflow source in all cases; whereas, after passing through the obturator foramen, the venous (#1) or prosthetic (#2, #3) graft was anastomosed with the superficial femoral artery (#1, #2) or popliteal artery (#3). In the latter case, a composite bypass was applied - the dacron graft being connected to the P3 segment of the popliteal artery via an additional reversed vein fragment. The postoperative period passed without major events, except for case #2 where vacuum-assisted wound closure therapy was necessary for the management of the residual cavity after the excision of the infected pseudoaneurysm.

**Discussions.** Transobturator bypass is an older and less frequently used revascularization method for improving the circulation to the lower extremities.

**Conclusion.** Arterial bypass through the obturator foramen remain a viable technique for revascularization of the lower limbs with local (groin) risk factors, regardless of the nature of the latter.

## 27. STAGED SURGICAL CORRECTION IN PATIENTS WITH "FUNCTIONALLY" UNIVENTRICULAR HEARTS



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**Introduction.** "Univentricular" heart is a term used to describe complex cardiac anomalies, which are characterized by the presence of a single ventricle with pumping function. Patients with univentricular heart face major challenges because they do not have both ventricles co-relatively developed to support normal blood circulation. Staged hemodynamic surgical correction is a complex, stepwise surgical approach in the treatment of patients with a "functionally" univentricular heart, requiring successive surgical interventions to improve hemodynamics and ensure efficient blood flow in the body, and is represented by 3 stages: intersystemic anastomosis/pulmonary artery banding, Glenn anastomosis, and Fontan surgery. Thus, staged surgical correction is often an option to improve and improve life expectancy in this category of patients.

**Aim of study.** The aim of the study is to evaluate the efficacy, safety and long-term impact of this complex surgical approach, based on the 10-year survival of patients operated by this method.

**Methods and materials.** Literature review of the PubMed electronic database, 7 articles for the terms "Functioning univentricular heart", "Staged univentricular intervention" and 2 BMJ journals articles .

**Results.** After reviewing the basic literature, it is found that after early Glenn surgery, early survival is on average 87%, and after late survival is about 65%. In 30% cases after Glenn anastomosis complications are possible such as: superior vena cava syndrome, hilarothorax, pleurisy, anastomosis thrombosis, cardiac arrest. As the last stage of univentricular correction, Fontan operation is performed, which post-operatively presents with the following complications: pulmonary thrombembolism, arrhythmias, progressive postoperative cyanosis, protein-losing enteropathy, liver dysfunction, etc. However, the average survival rate in these patients is high, after analysis of the articles the average survival estimated at 5, 10 and 20 years after Fontan operation was 95%, 91% and 82%.

**Conclusion.** Although the treatment of patients with "functionally" univentricular hearts is complex and carries a substantial risk of mortality, it is often the only possible route of treatment, which when performed in a timely manner and in accordance with inclusion criteria, gives patients a life expectancy of up to 50 years.



## 28. SURGICAL TREATMENT OF ACROMIOCLAVICULAR JOINT INJURIES

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**Introduction.** Acromioclavicular joint (ACJ) injuries represent a challenge for modern medicine. ACJ injuries represent >40% of all shoulder injuries with an incidence of 9.2/1000 people a year. This review presents the results of coracoclavicular ligament plasty (CCLP) method using non-absorbable ultra-high molecular weight polyethylene double sutures.

**Aim of study.** Result analysis of surgical treated patients with coracoclavicular ligament plasty (CCLP) using durable and non-absorbable double suture.

**Methods and materials.** 48 patients with ACJ injuries Rockwood type III, IV and V were treated surgically using CCLP with ultra-high molecular weight polyethylene sutures.

**Results.** Patients age between 16 and 65 years old; 43 (89.6%) men and 5 (10.4%) women. Type III dislocation was noted in 24 (50.0%) cases, type IV- 18 (37.5%) and type V- 6 (12.5%) cases. 44 patients had surgery (91.7%) in first 7 days after injury. Surgical treatment was performed in 24 (50.0%) cases of type III dislocation. Only vertical instability was determined afterwards, horizontal stability was partially secured by deltoid and trapezius muscles. 18 (37.5%) patients with type IV had a CCLP with additional acromioclavicular stabilization for a 6 week period, due to a deltoid muscle trauma and to maintain anterior and posterior clavicle stability. In type V dislocations, collar bone was moved cranially >200%, deltoid and trapezius muscles desinsertion was determined intraoperative. Old traumas were determined in 4 (8.3%) cases: one patient- type III dislocation, 2 patients- type IV dislocation, one patient- type V dislocation. These patients were treated with acromioclavicular joint opening and acromioclavicular joint revision with scars removal. Intraarticular disc removal was performed in one patient. Systematic clinical assessment for 36 months after surgery was performed. Shoulder immobilization after surgery period was 28 days, hospitalization period was 6 days. Long distance complications: 3 cases (6.3%) pin tract infection type IV dislocation at a 3 week period, subluxation- 4 (8.3%). After 3 months, Taft score results were: very good- 10 (20.8%), good- 31 (64.6%), satisfying- 7 (14.6%). Constant and Murley score results were: very good- 8 (16.7%), good- 27 (56.3%), satisfying- 13 (27.1%).

**Conclusion.** CCLP with ultra-high molecular weight polyethylene double sutures has proven a good clavicle stability that doesn't need a reintervention for implant extraction. Very good and good results were obtained in type III dislocation, for type IV and V required additional acromioclavicular stabilization with percutaneous K-wire for a 6 week period. Long distance results were very good and good after Constant and Murley score, and Taft score.

**Keywords.** Acromioclavicular joint, dislocation, coracoclavicular ligament plasty, with ultra-high molecular weight polyethylene double sutures.



## 29. SURGICAL TREATMENT OF PATIENTS WITH MORBID OBESITY



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**Introduction.** Class III obesity, formerly known as morbid obesity, is a complex chronic disease in which a person has a body mass index of 40 or higher or a BMI of 35 or higher and is experiencing obesity-related health conditions. These include Type 2 diabetes mellitus, cardiovascular diseases, metabolic syndrome, chronic kidney disease, hyperlipidemia, hypertension, nonalcoholic fatty liver disease, certain types of cancer, obstructive sleep apnea, osteoarthritis, and depression.

**Aim of study.** Analysis of surgical treatment methods for patients with morbid obesity based on bibliographic research and clinical observations.

**Methods and materials.** Seven patients with morbid obesity who required surgical intervention, were supervised, monitored, and performed the necessary investigations during one year. The study included 3 women (42.8%) and 4 men (57.2%) with a body mass from 105 kg to 175 kg and a BMI from 35.49 to 57.8. Obesity due to caloric excess was the most common etiological cause (7 patients), associated with genetic predisposition in 57,14% (4 patients). In addition to being overweight, the patients also accused other comorbidities: Type 2 diabetes mellitus (5 patients, 71,4%); arterial hypertension (6 patients, 85,7%); osteoarthritis with severe pain performing physical effort (4 patients, 57,1%); obstructive sleep apnea (4 patients, 57,1%); heartburn (2 patients, 28,6%); hyperlipidemia (3 patients, 42,8%) and nonalcoholic fatty liver disease (5 patients, 71,4%). Therefore, the following laparoscopic surgeries were performed: in two patients (28,6%) the Mini Gastric Bypass was performed, and in the other five (71,4%) the Gastric sleeve was done.

**Results.** The patients were monitored for 6 months postoperatively. After the intervention, all patients presented a good general condition, without complications and were discharged after 2-4 days. Also, all patients noted weight loss, with a result from 14 to 42 kg: patient N.1 obtained a BMI from 35.49 to 25.35; N.2 from 35.8 to 31.48; N.3 from 57.8 to 44.59; N.4 from 48.85 to 35.26; N.5 from 44.08 to 36.36; N.6 from 54.88 to 42.99; N.7 from 46.09 to 33.27. Five of patients noted the decrease and stabilization of blood sugar. According to the lipidogram, at 3 patients it was noted the stabilization of the lipid indices. Also, patients communicate about the disappearing of arthralgia. The systolic and diastolic blood pressure values reached the normal or normally high blood pressure.

**Conclusion.** Bariatric surgery ensures long-term weight loss and body mass index related with the improvement and successful treatment of comorbidities associated with morbid obesity. Laparoscopic surgery, also known as minimally invasive surgery, is an effective method, with minor postoperative complications and quick recovery compared to traditional open surgery. Sleeve gastrectomy has become one of the most commonly used bariatric procedures worldwide.





### 30. THE APPROACH OF HEMORRHAGE OF THE SUPERIOR DIGESTIVE TRACT IN EMERGENCY MEDICINE DEPARTMENT (2021-2022)

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**Introduction.** Although we are in the 21st century when medicine has seen great advances in various branches, even today we are faced with massive uncontrolled hemorrhages that shatter human lives. Bleeding management today continues to be a debatable issue that offers controversial solutions.

**Aim of study.** To identify the hemostatic techniques used in the approach of hemorrhage of the superior digestive tract in the emergency department (ED) of the Institute of Emergency Medicine (IEM).

**Methods and materials.** This review was based on the study of 31 patients during the period of (2021-2022), that suffered from superior digestive tract hemorrhage, from which applied hemostatic solution, that differs between Thrombin 500 international units or Alcohol 2ml 70%.

**Results.** Patients that were suffering from superior digestive tract hemorrhage, during their endoscopic investigation and verification, were administered initially Thrombin 500 UI dissolved in 10 ml of NaCl 0.9%. In 10% from total cases the procedures were done up to 4 times, with the maximum dosage of 2000 IU of Thrombin. In around 32,2% from total patients, needed more than thrombin after the maximum dosage and were also administered with Sol. Alcohol 70% with the concentration of 2 ml with 8 ml of NaCl 0.9%. up to 2 rounds. The method is done by an endoscopist. All 31 patients were provided successfully endoscopic hemostatic treatment.

**Conclusion.** The application of the correct hemostatic solution in time of investigating Endoscopic-ally is one of the most important approaches to superior digestive tract hemorrhage.

### 31. THE IMPACT OF DELAYED DIAGNOSIS IN RETROPERITONEAL DUODENAL TRAUMA



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**Introduction.** The issue of diagnosing traumatic retroperitoneal duodenal injuries is current and quite significant, considering the vague clinical signs, the ensuing complications, and the associated postoperative mortality.

**Aim of study.** Studying the diagnosis of evolutionary peculiarities of traumatic retroperitoneal lesions of the duodenum by analyzing the methods used for establishing the clinical diagnosis.

**Methods and materials.** This retrospective study comprises the examination of medical files from 29 patients with retroperitoneal duodenal trauma who were hospitalized at the Institute of Emergency Medicine between 1992-2017. Ratio: M:W- 25:4, age 18-70 years. Among these patients, 18 (62.06%) presented with polytrauma, while 11 (37.9%) had isolated abdominal trauma. Trauma mechanisms included road accidents in 10 cases (34.48%), falls from height in 3 cases (10.34%), physical assaults in 5 cases (17.24%), injuries due to foreign bodies in 1 case (3.44%), knife wounds in 7 cases (24.13%), firearm injuries in 2 cases (6.89%), waterjet-related trauma in 1 case (3.44%), and injuries necessitating interhospital transfer in 9 cases (31.03%). Regarding hospital admission, 25 patients (86.2%) were hospitalized within 6 hours, 4 patients (13.79%) after 48 hours, and 11 patients (37.93%) were admitted after 72 hours with signs of intoxication. Hemodynamic stability was noted in 15 patients (51.7%), while 14 patients (48.27%) presented with hemodynamic instability. Diagnostic evaluations were performed in 22 of the patients (75.8%).

**Results.** Clinical diagnostics were tailored to each case, including abdominal X-rays in 10 patients (detecting pneumoperitoneum and retroperitoneal abnormalities), USG in 14 patients (free fluid in 10), and CT scans in 7 patients (revealing one duodenal lesion, free fluid in 4, pneumoperitoneum in 3, retroperitoneal changes in 4, and one retroperitoneal hematoma). Diagnostic laparoscopy in 5 patients identified conditions like hemoperitoneum (2 cases), peritonitis (2 cases), and duodenal lesions (1 case). Intraoperatively, duodenal lesion locations were determined: D1 in 7 cases (13.7%), D2 in 13 (41.82%), D3 in 10 (34.48%), and D4 in 2 (8.33%). The mortality rate was 55.17%.

**Conclusion.** This comprehensive analysis underscores the criticality of tailored diagnostic approaches in managing traumatic retroperitoneal duodenal injuries, highlighting a notable mortality rate of 55.17% that emphasizes the urgent need for early detection and intervention in these complex cases.



## 32. THE MINIMALLY INVASIVE APPROACH TO MECHANICAL JAUNDICE

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**Introduction.** The current issue in hepatopancreatobiliary surgery involves the diagnosis and treatment of mechanical jaundice (MJ) resulting from cholestasis, caused by inflammatory processes, tumors, and iatrogenic injuries. MJ in 35-42% is a consequence of choledocholithiasis, 71-93% due to strictures of the extrahepatic bile ducts, and tumor-related cases range from 21-90%. The treatment objective involves normalizing bile flow through decompression, The methods are dependent on etiology of MJ. Minimally invasive techniques in the initial stage prevent severe complications, creating subsequent conditions for surgical treatment.

**Aim of study.** To investigate the efficacy of minimally invasive methods of biliary decompression in mechanical jaundice (MJ).

**Methods and materials.** The study included 82 patients with mechanical jaundice (MJ) treated between 2021 and 2023. The male-to-female ratio was 43/39, with a mean age of  $62.4 \pm 2.7$  years. Patients presented with jaundice for an average duration of  $44.38 \pm 11.23$  days, accompanied by epigastric and right hypochondrial discomfort (64.8%), cutaneous pruritus (44.5%), and pain (52.8%). Eighteen patients experienced cholangitis. Initially, total bilirubin levels ranged from 40 to 523  $\mu\text{mol/L}$ , with elevated transaminases in 67.9% of cases. The prothrombin level was low at 52.7% ( $63.8 \pm 8.47\%$ ). As per EUS, CT, and MRI findings, the origin of jaundice was tumoral in 47.6% of cases, while the remainder resulted from biliary strictures and duodenal diverticula. Primary biliary decompression was achieved by retrograde stenting of the bile ducts in 67 patients for both malignant and benign jaundice, and in 15 patients through transparietohepatic drainage.

**Results.** The positive effect of biliary decompression was established in 96.4% of cases. A significant decrease in bilirubin levels was observed with retrograde drainage of the bile ducts compared to transparietohepatic drainage ( $148.26 \pm 48.52 \mu\text{mol/L} \rightarrow 45.88 \pm 19.33$  vs.  $137.43 \pm 36.22 \rightarrow 61.32 \pm 24.35 \mu\text{mol/L}$ ). Complications were recorded in 28.4% of cases, primarily associated with transparietohepatic decompression (62.4%). The mortality rate was 5.6%. The study indicates that patients with mechanical jaundice resulting from drainage procedures have real chances of reducing bilirubin levels, with each method being determined by the etiology of jaundice.

**Conclusion.** Biliary decompression in mechanical jaundice (MJ) represents the primary intention method in preventing complications, especially hepatic insufficiency. Transduodenal stenting shows a lower frequency of complications compared to transparietohepatic drainage.

### 33. THE USE OF PLATELET-RICH FIBRIN IN THE REGENERATIVE TREATMENT OF REFRACTORY CHRONIC ULCERS OF THE LOWER LIMBS



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**Introduction.** Chronic refractory ulcer is defined as a skin defect, with or without involvement of adjacent tissues that persists for more than 6 weeks and does not improve for more than 3 months following proper treatment. Chronic refractory ulcers of the lower limbs are a medico-social problem, leading the patient to disability, requiring time and increased finances for cure. PRF is an alternative therapeutic method that enhances soft tissue regeneration thanks to platelets - the main source of growth factors and cytokines.

**Aim of study.** Evaluation of the safety and effectiveness of PRF use in the regenerative treatment of lower limbs chronic refractory ulcers, of various etiologies, using an accessible, non-invasive and inexpensive technology.

**Methods and materials.** This study is a review of the last 10 years of published specialty literature on the selected topic. The following electronic databases were used: Google Academic, PubMed, Cochrane Library, Scopus. The key words used are: "platelet-rich fibrin", "platelet concentrate", "chronic skin ulcer". In total, 475 articles were identified, 115 articles met the inclusion criteria. From these, 50 reports were included in the research.

**Results.** PRF is a simple, inexpensive cellular therapeutic method that shortens the healing time of chronic ulcers, does not require hospitalization, and has an increased healing potential over soft tissue, bone tissue, tendons, and ligaments. Its properties are due to platelets - central cells in wound healing. They release more than 20 growth factors and cytokines that trigger the process of angiogenesis and tissue regeneration. In PRF the concentration of platelets is approximately 3-5 times higher than in the patient's blood, and this fact explains the potency of the increased regenerative effect.

**Conclusion.** PRF is an effective method in the regenerative treatment of chronic refractory lower limb ulcers, regardless of etiology, with no reported adverse effects.



### 34. TREATMENT OF BILIARY OBSTRUCTION- ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY VS TRADITIONAL SURGERY

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**Scientific advisor:** Hogeia Mircea, MD, Assistant Professor, Transilvania University of Brasov

**Introduction.** Cholecystolithiasis with obstruction of the bile duct is a common medical issue. Endoscopic retrograde cholangiopancreatography (ERCP) and laparotomy with choledochotomy are commonly used in treating this condition. ERCP is a minimally invasive procedure allowing for the assessment and treatment of biliary tract problems, whereas laparotomy with choledochotomy is the traditional method involving a large incision in the abdomen. This review aims to compare these two surgical methods.

**Aim of study.** The research was conducted on PubMed using the keywords "gallstone," "ERCP," "choledochotomy," and "stone extraction."

**Methods and materials.** Scientific papers were selected based on inclusion criteria, which involved patient groups treated with both ERCP and laparotomy, hospitalization period, recovery period, postoperative well-being of patients, operating time and procedure effectiveness. Articles mentioning patients with major complications and individuals over the age of 70 were excluded. Risk of bias was not assessed, and PRISMA criteria were used for data synthesis.

**Results.** Out of the total of 18 articles found, 10 studies were selected. The cohort comprised 1423 patients, with 712 treated using ERCP and 712 through traditional surgery. The patient group treated with ERCP had a hospitalization period of 1-2 days, with postoperative pain that was easier to manage and an operating time of approximately 15 minutes. Meanwhile, the group treated with the traditional method experienced moderate to intense pain, and the hospitalization period ranged from 7 to 20 days and with an operating time of approximately 90 minutes. Minimally invasive surgery patients had a recovery period of up to 3 weeks compared to the other group, where the maximum recovery period was 7 weeks.

**Conclusion.** ERCP represents a less invasive alternative to laparotomy with choledochotomy in the treatment of gallstone disease. Understanding the advantages offered by ERCP, such as rapid recovery, reduced complications, and diagnostic precision, makes this method an attractive option in the management of gallstones. These advantages also encourage further research into these treatment methods.



### 35. TREATMENT OF VARICEAL UPPER GASTROINTESTINAL BLEEDING



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**Introduction.** Variceal upper gastrointestinal bleeding is a direct complication of portal hypertension and adequate management is essential in positive outcome of patients prognosis and prevention of hemorrhage relapse. Upper varices include esophageal and gastric varices, the first ones being the most frequent. Other causes of upper variceal bleeding, besides cirrhosis, can be occlusion of portal or splenic vein, schistosomiasis, non-cirrhotic fibrosis of portal vein, previous endoscopic or surgical variceal management, tumors of the hepatobiliary area. Nowadays, the endoscopic treatment is widely used in variceal management, and it includes: sclerotherapy, obturation with cyanoacrylate and lipidol, ligation with removable loops, injection of thrombin, combined therapy (loop ligation and cyanoacrylate obturation), sonographically guided endoscopic therapy, hemospray.

**Case statement.** A 73 y.o. male was admitted urgently to the surgery department within Gheorghe Paladi Municipal Clinical Hospital on 11.10.2019, with the following symptoms: vomiting with fresh blood, hematochezia, loss of consciousness, general weakness, abdominal pain, BP 90/60 mmHg, heart rate 100 bpm, respiratory frequency 17/min. The onset occurred 12 hours prior to hospitalization with no history of previous such episodes. The clinical and paraclinical examination established jaundice, swollen abdomen with ascitis, melena, HGB 62 g/l, RBC  $1.8 \times 10^{12}/l$ , HCT 0,21/l, WBC  $11 \times 10^9/l$ , ESR 20 mm/h, albumin 38 g/l, total protein 60 g/l, ALT 120 U/l, AST 150 U/l, ALP 500 U/l, urea 12 mmol/l, creatinine 156 mmol/l, glycemia 4,2 mmol/l, total bilirubin 87 mcmmol/l (direct 50 mcmmol/l, indirect 37 mcmmol/l), PT 30%, fibrinogen 2 g/l, INR 1.8. Diagnostic endoscopy proved esophageal and gastric varices GOV 2, F2, grade 2. Endoscopy haemostasis has been made with paravariceal injection of 500 units of thrombin. The patient remained under observation for 6 days, was discharged in a satisfactory condition, with no relapse of bleeding.

**Discussions.** Although some experts advise the use of cyanoacrylate in variceal management, paravariceal thrombin administration proves to be an effective procedure as well. However, there is yet to be established an agreed-upon primary and secondary prophylaxis of gastrointestinal variceal bleeding, as the subject is still studied, and the treatment must be customized to each individual.

**Conclusion.** Upper gastrointestinal variceal bleeding is a medical emergency that needs endoscopic management on a first episode, and preferably surgical intervention whenever multiple episodes occur.



### 36. TWISTED COLON: A REVIEW OF SIGMOID VOLVULUS

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**Introduction.** Sigmoid volvulus (SV) is a pathological condition characterised by the torsion of the distal segment of the colon, resulting in the blockage of the intestinal passage and affecting the vascular perfusion of the affected colon.

**Aim of study.** Assessing the significance, informativeness of epidemiology, clinical presentation, diagnostic techniques, and modern therapeutic and surgical strategies of SV.

**Methods and materials.** PubMed, PubMed Central, Medline, Google Scholar databases for assessing the management of sigmoid volvulus, keywords used „twisted colon”, „sigmoid volvulus”, „intestinal passage”.

**Results.** A total of 55 full articles were studied and analysed. The articles containing information about the etiopathogenetic mechanisms of sigmoid volvulus, the clinical and paraclinical findings, diagnostic methods, as well as the curative management of patients with sigmoid volvulus were selected. The etiology of SV is multifactorial and controversial. The main symptoms are abdominal pain, distention and constipation. The diagnosis of SV is established by clinical, radiological , endoscopic and sometimes operative findings.

**Conclusion.** This thesis concludes and offering a thorough summary helps to further knowledge of this complicated illness and attempts to assist medical professionals in making the best decisions possible for patients who come with sigmoid volvulus. Keywords. Sigmoid volvulus, twisted colon, management.

## **XXVI. UROLOGY SECTION**



***Urologia, ca specialitate medicală, se bucură de cercetări dinamice, iar aspectele inovative sunt orientate spre îmbunătățirea actului medical. Cercetarea în urologie acoperă subiecte de actualitate axate pe utilizarea posibilităților tehnologiilor avansate în plan diagnostic, tratament și profilaxie. Prin colaborarea dintre clinicieni și cercetători, descoperirile fundamentale sunt implementate cu succes în clinică, aducând beneficii tangibile în tratarea afecțiunilor urologice și îmbunătățirea calității vieții pacienților.***

***„Urology, as a medical specialty, enjoys dynamic research, with innovative aspects aimed at enhancing medical practices. Research in urology covers contemporary topics focused on utilizing the possibilities of advanced technologies in diagnostics, treatment, and prevention. Through collaboration between clinicians and researchers, fundamental discoveries are successfully implemented in clinics, bringing tangible benefits in treating urological conditions and improving the quality of life for patients.”***

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## 1. ACUPUNCTURE IN THE TREATMENT OF PSYCHOGENIC ENURESIS

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**Introduction.** Enuresis is an ongoing inability to control urination commonly we can say urinary incontinence. The most prevalent kind of urine incontinence, known as stress urinary incontinence (SUI), is the involuntary leakage of urine brought on by physical activity, such as coughing or sneezing and also under stress. SUI affects a person's life in social, psychological, physical, and economically. SUI can have a significant negative influence on one's capacity to perform daily tasks, which can lead to social isolation, sleeplessness, and shame. It's possible that patients with SUI are less inclined to engage in physical activity, which can negatively affect general health as inactivity is a risk factor for numerous illnesses.

**Aim of study.** To find out how safe and effective acupuncture is for treating psychogenic enuresis in adults.

**Methods and materials.** From the time of their creation until April 2020, pertinent databases such as MEDLINE, Cochrane Library, EMBASE, Chinese National Knowledge Infrastructure, PubMed, Chinese Biomedical Literature Database, and the Chongqing VIP Chinese Science and Technology Periodical Database will be retrieved.

**Results.** We identified 233 studies. Of these, 32 were published in Chinese. Of these, 22 were deemed potentially eligible, and 211 were excluded because they did not include acupuncture, did not include randomised controlled trials, or did not include self-inflicted pain in the participants. Of the 22 studies that remained, we excluded 20 for various reasons, designated one for further assessment, and included one study.

**Conclusion.** The findings show that acupuncture successfully reduces the maximal and average urine speed during symptoms of SUI and additionally studies have demonstrated that acupuncture methods paired with muscle building techniques like kegel exercises for the pelvic floor, herbal remedies (jin Gui Shen Qi Wan, Gi ji nourishing tablets), Vit, etc. have led to advancement in SUI.

## 2. BLADDER INSTILLATIONS WITH SODIUM HYALURONATE IN THE MANAGEMENT OF URINARY TRACT INFECTIONS: A CASE REPORT STUDY



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**Scientific advisor:** Donath-Miklos Imola, Department of Physiology, Faculty of Medicine, "Vasile Goldis," Western University of Arad.

**Introduction.** Recurrent urinary tract infections (UTIs) present a significant challenge, particularly in conjunction with neuro-muscular dysfunction of the bladder and chronic pelvic pain syndrome. Traditional interventions frequently result in limited success, necessitating an investigation into alternative therapeutic modalities. In this case study, the focus is on assessing the effectiveness of bladder instillation with sodium hyaluronate 40mg/50ml in managing the intricate urological challenges faced by a 66-year-old female patient diagnosed a decade ago with cervical cancer. The evaluation aims to shed light on the potential of sodium hyaluronate in addressing recurrent UTIs and related complications, taking into account the patient's history of cervical cancer surgery.

**Case statement.** The patient underwent total hysterectomy with bilateral adnexectomy and received adjuvant radiotherapy and chemotherapy. A recurring issue manifested in the form of UTIs caused by *E. coli* accompanied by right renal colic. Diagnostic investigations, including ultrasound and contrast-enhanced CT scans, revealed a diagnosis of right ureterohydronephrosis resulting from ureteral stenosis at the iliac level. Additionally, retroperitoneal fibrosis was identified following prior radiotherapy. The initial intervention involved the insertion of a double J catheter, but the patient exhibited intolerance to the stent, experiencing severe low urinary tract symptoms (LUTS), renal colic, and recurrent UTIs. Long term stenting failed to ameliorate the ureteral stenosis, and the patient exhibited a rapid decline in renal function on the affected side over time. Consequently, a decision was made to proceed with nephrectomy. Simultaneously, bladder instillations with sodium hyaluronate 40 mg/50 ml were initiated, involving four weekly instillations initially, followed by monthly sessions for a duration of 12 months. Following nephrectomy and a year of treatment, the recurrence rate of UTIs exhibited a slower progression compared to the initial stages of therapy. Presently, the patient performs instillations every 2-4 months, resulting in a reduced frequency of UTIs appearing at this interval, as opposed to the previous monthly reappearance.

**Discussions.** The discussion delves into the challenges encountered in managing the patient's condition and the rationale behind incorporating bladder instillations with sodium hyaluronate. Analyses of previous treatments, surgical interventions, and the recurrent nature of UTIs underscore the need for alternative therapies. Emphasis is placed on the evolving clinical response observed post-sodium hyaluronate instillations, addressing the multifaceted aspects of the patient's urological complications, including neuro-muscular dysfunction and chronic pelvic pain syndrome.

**Conclusion.** Bladder instillation with sodium hyaluronate emerges as a promising adjunct in the management of recurrent UTIs and associated urological complexities. The observed improvements in symptomatology, particularly in reducing UTI recurrence, neuro-muscular dysfunction symptoms, and chronic pelvic pain, highlight the potential efficacy of sodium hyaluronate. These findings suggest a novel avenue for addressing challenging urological cases, though further research is essential to validate these preliminary outcomes.





### 3. COMPLICATIONS IN PATIENTS WITH URETHRAL OBLITERATIONS

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**Introduction.** Urethral obliterations is a condition characterized by the narrowing of the urethra, which can cause problems with urine flow and related complications. It can be caused by factors such as injury, infections, inflammation and medical procedures. Urethral strictures can lead to various complications that greatly impact the health and quality of life of patients. These complications include difficulties, with urination challenges in using catheters, kidney problems, urinary tract infections and abscesses in the urethra. Some of these conditions can be life threatening, such as tract infections and kidney dysfunction. Different factors like strictures narrowing at the back of the urethra, strictures and the absence of symptoms related to lower urinary tract issues have been found to contribute to higher rates of complications.

**Aim of study.** To carry out a contemporary literature review and to elucidate the complications of patients with urethral obliterations.

**Methods and materials.** Several articles over a period of ten years from the PubMed database have been reviewed.

**Results.** According to the literature, Patients with strictures can experience severe complications. Acute urinary retention (AUR) can be a complication of neglected cases of urethral stricture ,occurs when a narrowing of the urethra obstructs the normal flow of urine, leading to the sudden inability to urinate, the management of AUR due to urethral stricture typically involves procedures such as urethral dilation to widen the narrowed segment of the urethra or the placement of a suprapubic tube (SPT) to bypass the obstruction and allow for urine drainage. In instances where there is a stricture and urinary extravasation there is a possibility of developing a periurethral abscess. If the corpus spongiosum experiences extensive thrombophlebitis it can lead to the formation of a stricture. The presence of an periurethral abscess may contribute to the development of a dense stricture that has an unfavorable prognosis.Urethral stricture increases the risk of developing necrotizing infection and Fourniers gangrene, an infection that affects the urethra or the tissues surrounding it. Furthermore urosepsis, an infection associated with an abscess, in or, around the urethra can occur. Additionally when urethral stricture causes retention it can lead to impaired kidney function and bilateral hydronephrosis, which may also be linked to infections.

**Conclusion.** The complications associated with urethral strictures are diverse and can have significant impacts on patient health and quality of life. Acute complications such as urinary retention, difficult catheterization, urethral abscess, and urosepsis can necessitate immediate medical intervention.The management of urethral strictures and their associated complications requires a more in depth approach, including timely diagnosis, appropriate treatment, and long-term follow-up.

#### 4. DESCRIPTIVE STUDY OF DIAGNOSTIC FINDINGS IN MALE WITH SEVERE OAT SYNDROME AND AZOOSPERMIA



**Author:** Palamarciuc Luminita, Dumbrăveanu Ion, Arian Iurii

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**Introduction.** It has been established that one of the most prevalent causes of male subfertility is oligoasthenoteratozoospermia (OAT). About 1% of men in the general population and 10%–15% of men who are infertile have azoospermia. Azoospermia exists in two forms: obstructive and non-obstructive. The diagnosis of male infertility, ranging from mild OAT to complete azoospermia, requires a comprehensive evaluation to ascertain the underlying causes.

**Aim of study.** The aim of the study was to do the analytical description of diagnostic findings in male with severe OAT syndrome and azoospermia.

**Methods and materials.** This retrospective analysis encompassed 90 patients diagnosed with severe OAT syndrome and azoospermia. Inclusion criteria were based on semen quality parameters: sperm concentration  $\leq 5$  million/mL, inclusive of azoospermia and cryptozoospermia. Evaluated factors included age, body mass index (BMI), comprehensive semen analysis, serum vitamin D3 levels, scrotal ultrasonography, and targeted genetic assessments (karyotyping, AZF microdeletions, and CFTR mutations). Participants were split into two subgroups, with 45 individuals in each, for the qualitative and quantitative analysis of seminal material in the study group: severe OAT and azoospermia.

**Results.** The average age was  $32.83 \pm 5$ , calculated BMI ( $27.1 \pm 4$ ) indicating overweight. In the group with severe OAT, the average values for both the concentration and total sperm count were  $1.77 \pm 2$  and  $5.59 \pm 8$ , respectively. The total motility ( $12.64 \pm 16$ ), progressive motility ( $7.93 \pm 12$ ), vitality ( $13.64 \pm 18$ ), and morphology ( $1.02 \pm 2$ ) were significantly reduced. In this group, agglutination was absent, and mild aggregation was present in 4.4% of cases. An elevated number of germ cells and leukocytes in semen ( $4.1 \pm 8$  and  $1.71 \pm 3.3$ , respectively) were observed. Vitamin D levels were deficient ( $29.37 \pm 9.3$  ng/ml). The levels of FSH and LH were elevated ( $14.55 \pm 13.22$  IU/L and  $8.42 \pm 5.3$  IU/L, respectively). The ultrasound evaluation of the scrotum was conducted, estimating the average volume of the right testicle ( $12.50 \pm 5.47$ ) and the left testicle ( $12.30 \pm 5.09$ ). Changes in echotexture and echogenicity of the right testicle were identified in 24.6% and 31.5%, respectively. For the left testicle, altered echotexture was present in 15.6% and abnormal echogenicity in 25.5%. Testicular calcifications were present on the right in 4.4% and on the left in 7.7%. Varicocele on the left of varying degrees was identified in 17.7%. Genetic evaluations revealed Y chromosome microdeletions in 4.4%, with 92.2% having a normal karyotype and 7.8% exhibiting karyotypic abnormalities. A single case of a CFTR gene mutation was identified.

**Conclusion.** Males with severe OAT syndrome and azoospermia has higher BMI, FSH and LH levels comparable with normal range limit, but deficit of vitamin D being noticed. Genetic abnormalities were found in 13.3% of the cases.



## 5. ERECTILE DYSFUNCTION IN PATIENTS WITH PERIODONTAL DISEASE

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**Introduction.** Erectile dysfunction (ED) is the inability to achieve or maintain an erection for a sufficient duration for sexual intercourse. Periodontal disease is primarily the result of infection and inflammation of the gums and bone that surround and support the teeth. There is growing evidence that periodontal disease may affect male sexual health (erectile function). However, clinical studies showing a link between male sexual health and periodontal disease are limited.

**Aim of study.** The aim of this study was to evaluate the relationship between periodontal disease and erectile dysfunction.

**Methods and materials.** The study was based on a systematic review of publications over the last decade on selected topics using Google Academic, PubMed and Scopus electronic databases, combining keywords related to periodontal disease and words describing erectile and reproductive dysfunction. A total of 410 articles were retrieved, 45 of which met the inclusion criteria.

**Results.** A total of 20 studies were included and analyzed the systematic review. The ages of the study participants ranged from 18 to 95 (mean age 41.2 years). In six studies, the age of the participants was not specified. Only three studies have evaluated the relationship between sex hormone levels and periodontitis, and two of them showed that patients with periodontitis should have high levels of testosterone. Two of the five studies showed a significant association between semen quality and periodontal disease. Finally, out of nine studies, eight found a significant association between erectile dysfunction and periodontal disease. Studies do not show the direct mechanism of erectile dysfunction, but draw attention to correlations between periodontal diseases and cardiovascular or metabolic diseases, more common in these patients. It is also mentioned that dental extraction can improve the function of the vascular endothelium.

**Conclusion.** This systematic review found a significant association between periodontal disease and erectile dysfunction, but the mechanism is still unclear. Further research is needed to determine the mechanisms of interaction between these diseases.

## 6. ETIOLOGICAL FACTORS AND THERAPEUTIC PERSPECTIVES IN DISTAL RENAL TUBULAR ACIDOSIS



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**Introduction.** Distal renal tubular acidosis (DRTA) is characterized by decreased acid excretion in the distal tubule, resulting in metabolic acidosis. Complications such as bone disease, growth failure, urolithiasis, and hypokalaemia are associated with this rare pathology. However, due to its rarity, treatment lacks standardization, leading to contradictory reported outcomes. While corticosteroids are commonly used, various other immunosuppressive drugs are suggested for treatment.

**Aim of study.** This study aimed to investigate the etiopathogenetic factors involved in DRTA development. The objective was to determine pathogenesis peculiarities, and therapeutic strategies associated with this condition. This study aimed to understand better and possibly find new ways to prevent and treat the condition.

**Methods and materials.** Research articles from 2018 to 2023 were gathered using keywords like "distal tubular renal acidosis" and "inheritance." Initially, 164 primary sources were identified, and 14 were selected for analysis, forming the basis of this review.

**Results.** Triggers of DRTA include genetic factors affecting kidney acid-base regulation (mutations in ATP6V0A4, ATP6V1B1, FOXI1, SLC4A1, WDR72), autoimmune diseases (e.g., Sjögren's syndrome, lupus), medications (certain diuretics, anti-retrovirals, and antibiotics), CKD, obstructive uropathy, sickle cell disease, and primary hyperparathyroidism. Therapeutic strategies focus on individualized plans, managing acid-base imbalances, and addressing associated complications. These strategies involve alkali therapy (oral supplements like potassium citrate or sodium bicarbonate), electrolyte balance maintenance (especially potassium), calcium and vitamin D supplementation for bone health, treatment of underlying conditions (autoimmune diseases, CKD), kidney stone monitoring and prevention, and dietary modifications.

**Conclusion.** The study revealed that several factors contribute to the development of DRTA in various ways. Genetic mutations, autoimmune conditions, medications, and various pathophysiological states emerged as potential triggers. The treatments, though personalized, focus on fixing acid levels in the body and handling problems that come with the condition. Despite corticosteroid usage, treatment variability persists, warranting further exploration of alternative immunosuppressive agents for optimal efficacy. This review aims to deepen understanding of DRTA, potentially guiding the development of targeted preventive strategies and more effective therapeutic interventions. Standardized protocols are essential, necessitating continued research and clinical trials to enhance outcomes and elevate the quality of life for individuals affected by DRTA.





## 7. FROM GENES TO STONES: EXPLORING GENETIC COMPONENTS IN CALCIUM OXALATE UROLITHIASIS

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**Introduction.** Calcium oxalate urolithiasis, characterized by the formation of kidney stones, presents a significant health burden worldwide. While environmental and dietary factors contribute to stone formation, recent studies highlight the pivotal role of genetic components in predisposing individuals to this condition. This research aims to explore the genetic underpinnings associated with calcium oxalate urolithiasis, elucidating the intricate interplay between genes and stone formation.

**Aim of study.** The primary objective of this study is to investigate the genetic factors involved in the pathogenesis of calcium oxalate urolithiasis. We aimed to identify specific genetic markers, pathways, and variations associated with stone formation. This exploration intends to provide a deeper understanding of the genetic landscape underlying this condition, potentially paving the way for targeted preventive strategies and therapeutic interventions.

**Methods and materials.** This abstract drew from research articles retrieved between 2015 and 2023 using keywords like "genetics," "Calcium oxalate urolithiasis," and "inheritance." Initially, 54 primary sources were identified, and 12 were chosen for analysis, forming the basis of this review's exploration into the genetic facets of calcium oxalate urolithiasis inheritance.

**Results.** Our investigations on urolithiasis revealed a spectrum of genetic variations within key genes involved in oxalate metabolism, calcium regulation, and renal transport mechanisms. Related to calcium oxalate urolithiasis there were identified the following genes: AGXT (involved in oxalate metabolism), SLC26A (oxalate transport in the kidney), 1CLCN5 (calcium transport), SLC34A1 (renal transport of calcium and phosphate), GRHPR (glyoxylate metabolism pathway), HOGA1 (metabolic pathway of hydroxyproline). Significantly higher frequencies of specific SNPs in these genes were observed in the urolithiasis cohort compared to the control group. Information related to mutations in these genes can help to identify drugs for personalized treatment.

**Conclusion.** The findings from this study underscore the substantial role of genetic components in calcium oxalate urolithiasis etiology. Identifying genetic variations and pathways associated with stone formation provides crucial insights into the underlying mechanisms. These discoveries hold promise for the development of targeted interventions, personalized treatment strategies, and improved risk assessment tools for individuals susceptible to calcium oxalate urolithiasis.

**Keywords.** Genetics, Calcium oxalate urolithiasis and inheritance.



## 8. HISTOLOGICAL OUTCOME AFTER CONVENTIONAL TESTICULAR SPERM EXTRACTION VS MICROSURGICAL TECHNIQS IN PATIENTS WITH AZOOSPERMIA



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**Introduction.** The 2021 AUA/ASRM Guidelines on Diagnosis and Treatment of Infertility in Men recommend micro-TESE for men with NOA undergoing sperm retrieval. The 2021 European Association of Urology (EAU) Guidelines on Male Sexual and Reproductive Health recommend conventional or micro-TESE.

**Aim of study.** The study aimed to perform a comparative analysis of the success sperm retrieval rate and histological outcome between tissue samples obtained through conventional and micro-TESE.

**Methods and materials.** The study included 45 men with a mean age of  $33.4 \pm 5.6$  years. According to the internal protocol, patients with presumed obstructive azoospermia underwent conventional TESE (22 men), while those with non-obstructive azoospermia underwent micro-TESE (23 men). The criteria for presuming the type of azoospermia were: medical history, testicular volume, hormones and genetic findings. A comparative analysis of the success sperm retrieval rate and histological outcome was conducted in both groups.

**Results.** In the group undergoing classical extraction intervention, the success sperm retrieval rate was 81.8% (18), respectively 18.2% (4) yielding a negative result. Histological analysis revealed normal spermatogenesis in 68.2% (15), reduced spermatogenesis in 22.7% (5), and maturation arrest in 9.1% (2). We observed that 9.1% (2) with reduced spermatogenesis had a negative success rate due to the classical method used. In the group subjected to micro-TESE methods, the success rate was 21.7% (5) versus 78.3% (18) where sperm cells were not identified. Histological examination identified mixed atrophy in 13.6% (3), hypo-spermatogenesis in 8.7% (2), Sertoli cell-only syndrome in 56.5% (13), and tubular fibrosis in 21.2% (5).

**Conclusion.** Both conventional TESE and micro-TESE are effective methods when patients are pre-selected based on the presumed type of azoospermia. For better efficacy, the possibility of switching to the microsurgical method should be considered for patients planned for the classical method.



## 9. MALE UROGENITAL INFLAMMATION STATUS SHOULD BE CONSIDERED IN INFERTILE COUPLES WITH RECURRENT PREGNANCY LOSS

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**Introduction.** Male urogenital infections are one of the causes that can lead to infertility in men. It is believed that nearly 15% of couples with RPL suffer from multiple infections in the urogenital tract. Recurrent pregnancy loss (RPL) is the loss of at least two consecutive pregnancies in the first 20 weeks of gestation. Numerous bacteria and viruses can result in male genital infection, which is considered to have a negative impact on sperm function and quality.

**Aim of study.** Comparative analysis of semen, hormones, and inflammatory/infectious parameters in men from couples with PRL vs. non-RPL.

**Methods and materials.** The retrospective study included 30 men from couples with RPL, mean age  $33.76 \pm 6.62$ , and 35 non-RPL, mean age  $32.11 \pm 7.48$ , as a control group. A comparative analysis of semen, hormones (FSH, LH, PRL, TT, E2), urogenital inflammation status, the presence of conditionally pathogenic infections, and specific flora in semen and urine was done. The data were analyzed using IBM SPSS Statistics 23.

**Results.** The mean values of semen parameters in both groups were within the normal range, but with higher numbers in the study group: sperm concentration:  $70.26 \pm 11.29$  vs  $53.54 \pm 13.45$ ; progressive mobility:  $34.63 \pm 8.32$  vs  $33.22 \pm 10.65$ . Meares-Stamey 2 glasses test found no significant inflammation in both groups ( $8.37 \pm 9.51$  vs.  $8.08 \pm 10.15$  for the first voided sample and  $8.55 \pm 12.32$  vs.  $10.11 \pm 11.21$  for the second voided sample). Sexually transmitted infections that were more frequently found in both groups are *Ureaplasma* species (16.6% vs. 14.2%), *Gardnerella vaginalis* (13,3% vs. 8,5%) and *Mycoplasma* species (6,6% vs. 2,8%). The prevalence of infections within the study group was observed. Also, there is a significant difference between groups in the prevalence of non-specific infections: 10 (58.82%) vs. 3 (8.57%). The total testosterone value was lower in the study group compared with the control group:  $323.26 \pm 72.59$  vs.  $379.25 \pm 45.69$ . FSH ( $4.22 \pm 3.21$  vs  $5.60 \pm 3.41$ ), LH ( $4.46 \pm 2.79$  vs  $4.13 \pm 4.28$ ), PRL ( $224.37 \pm 186.34$  vs  $244.69 \pm 201.17$ ), and E2 ( $31.95 \pm 18.02$  vs  $34.44 \pm 15.74$ ) were in the normal range limit.

**Conclusion.** Men from couples with RPL present more often with specific and non-specific infections of the urinary tract, with a prevalence of *Ureaplasma* species, *Gardnerella vaginalis*, and *Mycoplasma* species, most of the cases with multiple infections.

## 10. METASTATIC MATURE TERATOMA ASSOCIATION WITH AZOOSPERMIA DUE TO BILATERAL CRYPTORCHIDISM AND TESTICULAR BENIGN TERATOMA: CASE REPORT



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**Introduction.** Azoospermia, the most severe type of male infertility, is caused by numerous untreatable testicular problems. Approximately 10% to 15% of all male infertile individuals suffer from azoospermia, which affects approximately 1% of all men. The phenomenon known as growing teratoma syndrome is considered to be relatively uncommon. It is characterized by the enlargement of a residual mass that has been histologically confirmed to be a mature teratoma.

**Case statement.** We present the case of a 37-year-old male with difficulty conceiving. The patient has a history of bilateral cryptorchidism, for which orchidopexy was performed at the age of 6. 4 years ago, the patient presented a testicular mass. Scrotal ultrasonography (sUSG) revealed an asymmetric enlargement of the right testicle with multiple microcalcifications and peripheral vascularity, measuring 3.2x3.0x2.2 cm, indicative of primary testicular cancer, with normal serum tumor markers. Semen evaluation revealed azoospermia. Subsequent chest and abdomen contrast enhanced CT (CECT) scans showed an unremarkable chest scan, while the abdomen CECT identified a thin-walled, well-circumscribed, cystic mass compressing the anterior aspect of the inferior vena cava, measuring up to 7 cm in diameter. Right orchiectomy was performed. The surgical pathology report (SPR) reveals benign teratomatous elements within the testis, a central cystic component containing necrotic material, that occupies ~75% of testicular volume. The remaining seminiferous tubules show absent spermatogenesis and Leydig cell hyperplasia. Afterwards, resection of the retroperitoneal mass was performed. The SPR confirms the diagnosis of a mature teratoma with metastasis to a precaval lymph node. Notably, paracaval, intra-aorto-caval, and para-aortic lymph nodes show no signs of metastasis. The patient maintained regular screening, undergoing abdomen and pelvis CECT scans biannually. The present patient examination involved the assessment of hormones, spermogram and sUSG. The relevant abnormal hormonal results: Tt-191, FSH-65, LH-25, Prolactin-732. The spermogram evidences azoospermia. sUSG reveals left testicle volume 3.4 cm<sup>3</sup>, irregular contour, inhomogeneous “geographic” echo structure. Doppler USG reveals increased vascularity. Micro-TESE was performed on left testis with negative sperm retrieval results, histology – tubular fibrosis and Sertoli cell-only syndrome.

**Discussions.** Metastatic mature teratoma is frequently observed in both radiological and histopathological examinations following chemotherapy for metastatic non-seminomatous germ cell cancers. The primary explanation for these remaining tumors is the distinct resistance of teratomas to chemotherapy compared to the heightened sensitivity of the embryonal components. Resection of metastatic mature teratomas is recommended due to their malignant potential and occasional progression to growing teratoma syndrome, which involves the invasion of surrounding structures.

**Conclusion.** Azoospermia due bilateral cryptorchidism is a common clinical situation. However, there’s no evidence of concomitant metastatic mature teratoma and testicular benign teratoma related to this condition.



## 11. THE COMPARATIVE STUDY BETWEEN ENDOUROLOGICAL AND MINIMALLY INVASIVE TREATMENT OF RENO-URETERAL LITHIASIS

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**Introduction.** Lithic urological obstruction is ranked 3rd among urological diseases worldwide, following renal infectious pathologies and prostate pathologies. At the national level, it is the most prevalent urological disease.

**Aim of study.** The aim of this study is to compare the benefits, efficacy, and potential complications of endourological and minimally invasive methods for treating reno-ureteral lithiasis.

**Methods and materials.** A retrospective descriptive study was conducted on a group of 148 patients with reno-ureteral lithiasis who were treated at the urology clinic of IMSP SCM "Sfânta Treime" between January 2023 and July 2023. The first study group included 59 patients (39.8%) who were treated with semi-rigid ureteroscopy. Of these, 37 patients had 1/3 middle ureteral lithiasis and 22 patients had lithiasis of the juxtavesical segment. The second group consisted of 89 patients (60.2%) with pyelocalyceal lithiasis who were treated with NLP (percutaneous nephrolithotomy). The study also utilized statistical methods, clinical and paraclinical examinations, including laboratory tests (complete blood count, urinalysis, blood biochemistry analysis, uroculture, coagulogram), as well as other instrumental investigations such as conventional imaging methods (SRVR, renal USG, IUR, retrograde ureteropyelography). In some cases, more complex imaging methods were used, such as abdominal CT, spectrometric analysis of the removed stones to evaluate the appropriate treatment approach for each patient.

**Results.** The criteria used to analyze the results of the study were the success rate, number of failures, type of anesthesia, time of stone removal, and complications and their management. The study included 148 patients (96 men and 52 women) between the ages of 19 and 78, with a median age of  $46 \pm 10.7$ . In the first group, the "stone free" rate was 70%, with an intervention time of 25-40 minutes using local anesthesia and no associated complications. In the second group, the "stone free" rate was 87%. However, due to factors such as excess weight, volume and location of the kidney stones, and access to the stone, the intervention time was longer at 45 minutes to 1 hour and 30 minutes, with spinal or general anesthesia. There were also secondary complications, including 3 cases of exacerbation of chronic pyelonephritis and 7 cases of subcapsular renal hematomas. The patients with hematomas were closely monitored and did not require additional surgical intervention.

**Conclusion.** The most effective treatment for renal stones is NLP. Compared to semi-rigid ureteroscopy, NLP has a higher success rate in completely removing the stones due to its more precise targeting. With semi-rigid ureteroscopy, it can be challenging to capture all the fragmented stone pieces. Additionally, the use of a ureteroscope to access the stones through the urinary tract results in a quicker recovery time, lower complication rates, shorter hospital stays, and faster return to work for the patient compared to NLP treatment.



## 12. THE ROLE OF PROSTATIC INFLAMMATORY PATHOLOGIES ON MALE FERTILITY



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**Introduction.** Inflammation significantly impacts prostate health, contributing to issues like prostatitis. Triggered by infection, autoimmune response or other factors, it can compromise sperm quality or cause prostate dysfunction, affecting male fertility. This review explores prostatitis, focusing on infections and reported seminal quality changes.

**Aim of study.** High occurrences of male infertility are common among infertile couples, and inflammation in the prostate, regardless of its cause, can significantly impair the reproductive capabilities. Given the prevalent occurrence of prostatitis in males, its impact on infertility is substantial.

**Methods and materials.** A literature review study about the impact of prostatitis on male fertility was performed. The source selection prioritized detailed coverage, including research and case studies. Emphasis was placed on up-to-date publications from PubMed etc. The search strategies, utilizing keywords, aimed to refine results and provide a thorough understanding of prostatitis and infertility.

**Results.** Male urogenital infections impact fertility, with conflicting effects on sperm quality noted in the 2023 UAE protocol. Studies on STIs show limited evidence of a strong link to infertility. Prostatitis, the third most common urinary tract disease, is challenging to treat. Seminal analysis is crucial for evaluating infections and assessing sperm quality. P(+)leukocytes  $>10^6$ /mL suggest inflammation; PCR analysis is recommended for specificity. Ureaplasma significantly affects male fertility. Viruses may impact sperm quality. Leukocytospermia's connection to infertility varies;  $>10^6$ /mL indicate infection, but alone doesn't confirm infertility. Chronic prostatitis harms sperm parameters, with Ureaplasma often found in infertile men. Pathogens (C. Trachomatis and Ureaplasma) can reduce sperm parameters, including DNA damage. The role of bacterial infections in forming antisperm antibodies remains uncertain.

**Conclusion.** In summary, it is evident that exploring underlying prostatitis is warranted in cases of male infertility, particularly considering its often asymptomatic nature. In this regard, a comprehensive semen analysis, with a focus on leukospermia in the prostatic fluid, along with accurately collected prostatic fluid cultures, is crucial.



