MINISTRY OF HEALTH OF THE REPUBLIC OF MOLDOVA
***NICOLAE TESTEMITANU* STATE UNIVERSITY OF MEDICINE AND PHARMACY**

LABORATORY OF TISSUE ENGINEERING AND CELLS CULTURES
ORTHOPEDICS AND TRAUMATOLOGICAL CLINICAL HOSPITAL
HUMAN TISSUE AND CELLS BANK

The Materials of the National Scientific Conference with International Participation

„CELLS AND TISSUES TRANSPLANTATION. ACTUALITIES AND PERSPECTIVES. THE 2nd EDITION”

Chisinau, March 29-30th 2024

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AGENDA
Registration
March, 29, 2024

Opening ceremony 15:00 - 15:10

Romanciuc Grigore, Head of Transplantation Agency of Republic of Moldova.

Nacu Viorel, MD, PhD, Professor, Head of Human Tissue and Cells Bank Clinical Hospital of Orthopedics and Traumatology and responsable Laboratory of Tissue Engineering and Cells Cultures, SUMPh *Nicolae Testemitanu*.

DAY ONE – 29 March 2024
Session 1

Plenary meeting

Oral presentations

Moderators: Nacu Viorel, *MD, PhD* professor, *(Republic of Moldova)***, Țimbalari Tatiana**, *MD, PhD (Republic of Moldova).*

1. **15:10-15:30. Romanciuc Grigore**. Legislative aspects in tissue and cell transplantation. *Chisinau, Republic of Moldova.*
2. **15:30-15:50. Cusnir Valeriu**, **Lupan Valentina, Dumbraveanu Lilia, Andronic Sergiu, Cociug Adrian, Procopciuc Vitalie, Perlog Olga, Ciubara Cristina, Voina Maria, Nacu Viorel.** Tissue transplantation report in Ophtalmology for 2022 and 2023. *Chisinau, Republic of Moldova*.
3. **15:50-16:10. Iapascurta Victor**. Agent-Based Modeling: Revolutionizing Tissue Engineering. *Chisinau, Republic of Moldova.*
4. **16:10-16:25. Jian Mariana, Nacu Ana-Maria, Cobzac Vitalie, Mostovei Andrei, Ficai Anton, Nacu Viorel.** Collagen from umbilical-placental complex – the allogeneic biomaterial for medical applications**.** *Bucharest, Romania. Chisinau, Republic of Moldova.*
5. **16:25-16:40**. **Ceban Marina, Pisarenco Sergiu, Anghelici Gheorghe, Zugrav Tatiana, Vasiliev Radu.** The results of the treatment of trophic ulcers of the lower limbs by applying autologous platelet-rich fibrin. *Chisinau, Republic of Moldova.*
6. **16:40-16:50. Pașa Diana, Catereniuc Ilia.** Anatomical arterial variants of the upper limb**.** *Chisinau, Republic of Moldova.*

Session 2

Moderators: Sidorenko Ludmila, *MD, PhD (Republic of Moldova)***, Karl Mattias**, *MD, PhD (Germany).*

1. **16:50-17:10. Sidorenko Ludmila, Diaz-Ramirez Ivan, Rotaru Ludmila, Chornopyshchuk Roman, Badan Liliana, Wessel Niels.** The Vital Role of Vegetative Nervous System in Preventing Recurrent Arrhythmia in the Post-Interventional Regeneration Period. *Chisinau, Republic of Moldova. Berlin, Germany.*
2. **17:10-17:20. Mihaluta Viorica, Stoian Alina, Ignatov Olga, Raischi Ion, Verega Grigore, Nacu Viorel.** Amniotic membrane transplantation into lower limb ulcers. *Chisinau, Republic of Moldova.*

3. **17:20-17:30. Macagonova Olga, Cociug Adrian, Taralunga Tatiana, Ciobanu Vladimir, Braniste Tudor, Buza-Zueva Anastasia, Viorel Nacu.** Porcine dermis–a source for creating biomaterial by tissue engineering. *Chisinau, Republic of Moldova.*

4. **17:30-17:40. Iapascurta Victor**. The Combined Use of Agent-Based Modeling (ABM) and System Dynamics Modeling (SDM) for Tissue Engineering: A Raw Example of Interaction at Different Scales. *Chisinau, Republic of Moldova.*

5. **17:40-17:50. Fandofan Victoria, Bozul Uliana-Ariadna, Jeru Ion.** Features of microsurgical treatment in patients with pterygium. *Chisinau, Republic of Moldova***.**

6. **17:50–18:00. Chornopyshchuk Roman, Grebeniuk Dmytro, Nazarchuk Oleksandr, Burkovskyy Mykola, Kravchuk Vitalii, Sidorenko Ludmila, Rotaru Ludmila, Chornopyshchuk Nataliia.** Platelet-rich plasma in the treatment of burn patients**.** *Vinnytsya, Ukraine. Chisinau, Republic of Moldova.*

7. **18:00-18:10. Goreacii Ana, Nacu Ana-Maria, Taralunga Tatiana, Nacu Viorel**. Menstrual Blood-Derived Stem Cells: Milestones and Future Prospects for Regenerative Medicine. *Chisinau, Republic of Moldova.*

DAY TWO – 30 March 2024

Session 1

Moderators: Labuşca Luminita, *MD, PhD (Romania),* **Victor Palarie**, *MD, PhD (Republic of Moldova).*

1. **09:00-09:30. Labusca Luminita.** Stem cell sources in orthopedics-clinical practice between ortobiologics and advanced medicinal products. *Iasi, Romania.*

2. **09:30-9:45. Zara-Danceanu Camelia-Mihaela, Labusca Luminita, Herea Daniel, Minuti Anca Emanuela, Stavila Cristina, Chiriac Horia, Lupu Nicoleta**. Magnetoliposomes containing bioactive molecules as nanocarriers for biological applications. *Iasi, Romania.*

3. **09:45-10:00. Parii Sergiu, Ungureanu Alina, Eugeniu Nicolai, Cociug Adrian, Cabac Vasile, Valica Vladimir.** Preclinical research of otoprotective drugs. *Chisinau, Republic of Moldova.*

4. **10:00-10:15. Iacubitchii Vitalie, Vacarciuc Ion, Cojocaru Stefan, Buzu Dumitru, Nacu Viorel, Capros Nicolae.** Osteo-cellular graft in the wrist instability. Clinical case. *Chisinau, Republic of Moldova***.**

5. **10:15-10:30. Pisarenco Sergiu, Anghelici Gheorghe, Zugrav Tatiana, Ceban Marina, Vasiliev Radu.** Autolog transplantation of platelet rich fibrin in inguinal hernia repair in liver cirrhosis. *Chisinau, Republic of Moldova.*

6. **10:30-10:45 Croitoru Dan, Corobcean Nadejda, Visnevschi Sergiu**. Treatment in breast cancer using the CRISPR/Cas9 system. *Chisinau, Republic of Moldova.*

7. **10:45-11:00. Karl Mattias**. *In vitro* and *in vivo* Characteristics of a Bone Substitute for Ridge Preservation Procedures**.** *Hamburg, Deutschland.*

CONFERENCE CLOSING CEREMONY

Abstracts

STEM CELL SOURCES IN ORTHOPEDICS - CLINICAL PRACTICE BETWEEN ORTOBIOLOGICS AND ADVANCED MEDICINAL PRODUCTS

Labusca Luminita[1 2]
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[2]Magnetic Materials and Nanosensors National Institute of Research and Development for Technical Physics REGENERO Romanian Regenerative Medicine Association, Iasi Romania.

Background. The use of stem cells, particularly mesenhymal stem cells has emerged as an incoming tool for advanced therapeutics aiming to improve orthopedic practice.
Aim of the study. The presentation will introduce basic notion regarding stem cell types, fonction, and their importance for the rising field of regenerative orthopedics. The two major modalities to impleementing the use of stem cell use in clinical practice- third generation orthobiologics and stem cell based advanced medicinal products will be described and briefly presented.
Matherials and methods. The currently used tissue sources of stem cells in orthopedic: bone marrow derived mesenchymal stem cells, adipose derived strem cells, peripheral blood derived stem cells and existent modalities to procure them will be detailed. Several main indications and current limitations of using various sources of stem cells as injection therapy or as augmentation of existent orthopedic procedures will be briefly presented.
Conclusion. General considerations and reccomendation for the use of orthobiologics will be provided together with selected available results. In parallel, existent available stem cell-based products available for clinical use will be named along with principal regulatory landscape that govern their marketing approval.
Keywords: stem cells, mesenchymal stem cells, orthobiologics, orthopedics, advanced therapies medicinal products
ACKNOWLEDGEMENTS: Financial support was received from Ministry of Research, Innovation and Digitization, CNCS/CCCDI -UEFISCDI, project number ERANET-EURONANOMED-3-OASIs, within PNCDI III

TISSUE TRANSPLANTATION REPORT FOR 2022 AND 2023

Perlog Olga[2], Lupan Valentina[2], Dumbraveanu Lilia[2], Andronic Sergiu[2], Cociug Adrian[1], Procopciuc Vitalie[2], Ciubara Cristina[2], Voina Maria[2], Cusnir Valeriu[2], Nacu Viorel[1]

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[2]Department of Ophtalmology and Clinical Optometry, *Nicolae Testemițanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

Background. Approximately 185.000 cornea transplant surgeries are performed wordwide every year. A corneal graft can be utilized to improve vision and for the reconstruction of severe damages in the cornea. Additionally, cryopreserved amniotic membrane is used as a biological dressing in the treatment of various ocular surface disorders by promoting epithelialization and suppressing inflammation.

Aim of the study. To assess the dynamics of the number of corneal and amniotic membrane transplant surgeries throughout the 2022 and 2023 years.

Methods and materials. This is a secondary data analyzing study based on the Tissue Transplantation Reports at Ophthalmology Clinic No.2 for the years 2022 and 2023 in the SCM „*Sf. Treime*" Transplant Center.

Results. In 2022, a total of 90 tissue transplant procedures were performed at Ophthalmology Clinic No.2. 10% (9 recipients) of these were corneal grafts, and 90% (81 recipients) were amniotic membrane transplants. In 2023, there was a 19% increase in transplant surgeries (111 surgeries). Out of the totat number 16% were corneal transplants and 84% were amniotic membrane transplants. Over the course of 2 years of activity, 201 tissue grafts were ordered and transplanted to patients without any damage in the process or any returns to the bank.

Conclusion. The analysis of data from 2022 and 2023 shows a steady increase in the number of transplant procedures, with a 19% rise in total transplant surgeries. There were performed a total of 201 tissue grafts transplant surgeries, including 27 corneal grafts and 174 cryopreserved amniotic membrane grafts, over the 2-year of period.

Keywords: Corneal graft, amniotic membrane, tissue transplant.

THE COMBINED USE OF AGENT-BASED MODELING (ABM) AND SYSTEM DYNAMICS MODELING (SDM) FOR TISSUE ENGINEERING: A RAW EXAMPLE OF INTERACTION AT DIFFERENT SCALES

Iapascurta Victor [1,2]
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[2] Department of Anesthesia and Intensive Care, *Nicolae Testemițanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

Background. ABM can be used to model individual structures as cells, organs, systems, and their interactions, considering factors such as cell migration, proliferation, and differentiation. SDM can then help capture the overall dynamics of the tissue and organ system, incorporating factors like nutrient distribution, oxygen levels, and growth factors. By combining both models, researchers can comprehensively understand how cells/tissues/organs behave and interact. This paper explores how ABM and SDM can benefit tissue engineering, uncovering the potential for future models.
Materials and methods. The NetLogo integrated development environment (IDE) is used for this research. The "regular" part of this IDE is used to showcase some cell interactions and dynamics, and the system dynamic modeler serves to represent the interaction of three systems: (a) maternal, (b) fetoplacental system, and (c) the fetus.
Results. A hybrid model that combines ABM and SDM was created using the NetLogo programming environment. The ABM component visualizes the behavior of cells (i.e., erythrocytes) at the placental level. The SDM component consists of three subsystems: (a) the maternal system (primarily, elements that determine oxygen transport), (b) the fetoplacental system, and (c) the fetal system (with emphasis on the elements that determine oxygen delivery to the fetus, $D_{fetus}O_2$). The $D_{fetus}O_2$ value is influenced by the dynamics of the physiological parameters, which are the foundation of the three subsystems and can be monitored using traditional methods. Modifying specific parameters within each subsystem directly impacts $D_{fetus}O_2$, the central element of the model's graphical interface. In this way, one can continuously monitor oxygen delivery to fetal tissues. The demo version of the created model includes several scenarios: (a) state of anesthesia, (b) maternal pathology (e.g., anemia, heart failure, etc.), and (c) fetoplacental pathology (e.g., abruptio placentae). The model is available at https://modelingcommons.org/browse/one_model/6688#model_tabs_browse_info
Conclusions. This example demonstrates the successful integration of ABM and SDM that can serve as leverage for tissue engineering research, enabling a more comprehensive understanding of cell/tissue and system behavior and prediction of complex biological processes. By combining the strengths of both modeling approaches, researchers can gain deeper insights into tissue dynamics and design more effective interventions.
Keywords: agent-based modeling, system dynamics modeling, tissue engineering, oxygen delivery, maternal system, fetoplacental system, fetus.

AGENT-BASED MODELING: REVOLUTIONIZING TISSUE ENGINEERING

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Background. Tissue engineering is a rapidly evolving field that aims to create functional and viable tissues to replace or repair damaged organs. Achieving success in tissue engineering requires a deep understanding of complex cellular behaviors and interactions. Traditional research methods, while valuable, may not fully capture the intricate dynamics within a living system. In recent years, agent-based modeling (ABM) has emerged as a powerful tool for simulating and understanding these complex processes. This paper explores the use of ABM in tissue engineering and its potential to revolutionize the field.
Materials and methods. There are several ABM integrated development environments (IDE), to name a few: AnyLogic, Repast, MASON, Swarm, and others.
Results. For the purpose of this research, the NetLogo IDE is used. It can provide valuable insights concerning such aspects of tissue engineering as (a) Understanding Cellular Behaviors through modeling individual cells as autonomous agents, each with its own set of rules and behaviors; (b) Simulating Tissue Development by providing a dynamic model that can account for factors such as cell density, extracellular matrix composition, and mechanical forces, allowing for a more realistic representation of tissue formation; (c) Predicting and Optimizing Scaffold Design via the aid in predicting and optimizing scaffold design; (d) Studying Disease Progression and Treatment, (e) Bridging the Gap Between Experimental and Clinical Applications by reducing costs, time, and the number of animal experiments required, while increasing the likelihood of successful clinical translation. Some of the applications elaborated by the author that can serve as leverage for future models are available at https://modelingcommons.org/account/models/2495
Conclusions. Agent-based modeling offers a novel and powerful approach to the field of tissue engineering. By simulating and understanding cellular behaviors, tissue development, scaffold design, disease progression, and treatment strategies, ABM has the potential to revolutionize the way we approach tissue engineering challenges. The predictive capabilities of ABM can accelerate research, streamline experimental design, and ultimately lead to more successful clinical applications. As computational tools and techniques continue to advance, the integration of ABM in tissue engineering will undoubtedly play a pivotal role in shaping the future of regenerative medicine.
Keywords: agent-based modeling, tissue engineering, software applications, complex processes.

USE OF PLATELET-RICH PLASMA IN BURN PATIENTS

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[3] State University of Medicine and Pharmacy "*Nicolae Testemitanu",* Chisinau, Republic of Moldova.

Background. The use of platelet-rich plasma remains a promising area of medicine. The use of plasma, enriched with platelets, in the complex management of patients with burns, is of particular interest, especially in cases of thermal injuries and combined injuries.

Purpose. to analyze the feasibility and effectiveness of injectable administration of platelet-rich plasma in patients with deep burns injuries.

Materials and methods. 22 patients with partial thickness and full thickness deep burn injuries with an area of 15-20 % of the body surface and localization in the area of the lower limbs participated in the study. Local treatment of 12 patients in the observation group at the stage of wound preparation after radical necrosectomy for autodermoplasty included a daily change of bandages impregnated with a 0.02 % decamethoxin-based antiseptic solution. 10 patients of the main group were additionally injected with autologous plasma enriched with platelets during a similar period of treatment. The examination of the patients included a visual assessment of the condition of the wounds, the study of their microbial contamination, as well as the results of the skin grafting.

Results. The results of the statistical analysis show a significant reduction in the term of granulation formation of the affected tissue in patients of the main group ($p \leq 0.05$), whose wounds met the criteria of readiness for skin grafting. In patients of the observation group, a slower marginal epithelization, a longer period of cleaning of wounds from pathological layering with more intense wound secretions, as well as a higher microbial contamination of the wound surface were observed. Regarding the agents of microbial contamination, no significant difference between the studied groups was established ($p > 0.05$), just as the basic nature of the identified microbiota did not differ.

Conclusions. The obtained results convincingly confirm the effectiveness of the injection of autologous platelet-rich plasma in patients with deep thermal injuries who, in addition to necrosectomy, need the enhancement of preparation of wounds to restore the integrity of the skin by grafting.

Keywords: platelet-rich plasma, burns, effectiveness.

MAGNETOLIPOSOMES CONTAINING BIOACTIVE MOLECULES AS NANOCARRIERS FOR BIOLOGICAL APPLICATIONS

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Background. Proprietary magnetic nanoparticles (Fe_3O_4) with diameters around 40 nm were synthesized by the coprecipitation method and coated with oleic acid. The OA-Fe_3O_4 magnetic nanoparticles were formulated as magneto-liposomes containing ascorbic acid and dexamethasone with sizes below 210 nm. According to this study, magnetic nanoparticles loaded with bioactive molecules can be used to deliver bioactive molecules to osteoarthritic joints with minimal side effects.

Materials and methods. We investigated the magnetic behavior of magneto-liposomes by vibrating sample magnetometry (VSM). Using dynamic light scattering (DLS) and zeta potential measurements, magneto-liposomes were characterized in terms of their size, surface charge, and stability. A study of the in vitro biocompatibility, iron cell uptake, drug release, anti-senescence, and proliferation potential of the system was also conducted.

Results. The obtained magnetic nano-emulsions provided superior stability, magnetic properties, and biocompatibility when used as carriers for anti-inflammatory drugs such as dexamethasone and ascorbic acid.

Conclusions. This study showed enhanced ADSC migration potential along with chondrogenesis, which suggests magneto-liposomes containing dexamethasone could be used to alleviate symptoms of OA. Slow ascorbic acid release may further assist cartilage regeneration.

Keywords: magnetic nanoparticles, magnetoliposomes, bioactive molecules, drug-release, nanocarriers.

ACKNOWLEDGEMENTS: Financial support was received from Ministry of Research, Innovation and Digitization, CNCS/CCCDI -UEFISCDI, project number ERANET-EURONANOMED-3-OASIs, within PNCDI III

EVALUATION OF NON-VIABLE CORNEAL GRAFTS FROM THE HUMAN TISSUE BANK IN THE REPUBLIC OF MODOVA

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Introduction: Corneal preservation methods with the preservation of a maximum number of viable endothelial cells has been and remains one of the challenges of Eye Banks worldwide. There are three main approaches to the preservation and storage of corneas: the viable method, i.e. the culture medium, and non-viable – hypothermia, cryopreservation and lyophilization. Corneal preservation methods used in the Human Tissue Bank of the Republic of Moldova, such as lyophilization, being a non-viable method, in which cell viability is lost, only the architectural shell of the transplanted collagen fibers are preserved, which can be recellularized, only the epithelial layer. They are used in tectonic keratoplasties to restore the integrity of the sclera or some portion of the cornea. The most used preservation method is the tissue culture medium "C", Eussol "C" and Cary "C" with storage temperatures of 31° C and a duration of one month. During 11 years of activity, 435 corneas were transplanted, of which 4.5% (20 corneas) were lyophilized and transplanted through keratoplasty with tectonic purpose.

Material and methods. Morphological evaluation of non-viable cornea in culture media, lyophilized and preserved in glycerol in 20 rabbits and humans.

Results. Rabbit corneas preserved in 30, 50 and 80% glycerol at pH 7.4 and subsequently frozen at 80º C histologically by immunohistochemical staining with AE1/AE3 show disorganization of connective tissue architecture with fragmentation. Microelectronic scanning of freeze-dried human corneas determines the structural integrity of the connective tissue shell with layer persistence. Non-viable corneas from histological culture media by hematoxylin-eosin staining show intense edema of all layers predominantly in the stroma.

Conclusion. (1). The most preferred non-viable method of preserving the cornea is lyophilization with the maintenance of structural integrity, sterility and validity up to 2 years; **(**2). The glycerol preservation method at temperatures of - 800 C shows a destruction of the connective tissue casing due to the formation of ice crystals. **(**3). The non-viable preservation of the cornea shows a deep swelling of the layers and for its elimination, the Carry "C" detumescence medium is needed, which maintains the validity period of 2 months, being an expensive method.

Key words: preservation medium, validation, connective tissue.

References:

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NON-ENDOTHELIAL CD34 POSITIVE STEM CELLS OF THE UMBILICAL CORD AND PLACENTAL TISSUE

Globa Lilian[2,3], Globa Tatiana[1,2,4*], Pelin Elina[1,2], Globa Elena[5], David Valeriu[1,2]
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Background. Stem cells are unspecialized cells, but with a high capacity for differentiation, multiplication, and self-renewal, essential for the tissue regeneration. The placenta and umbilical cord are rich sources of stem cells, especially mesenchymal stem cells, which hold great promise for a regenerative medicine due to their plasticity and their immunomodulatory and anti-inflammatory properties. Mesenchymal stem cells can be easily collected from umbilical cord blood through non-invasive methods. However, one of the main obstacles in their use is the limited availability in umbilical cord blood.
Aim of the study. Studying the presence, characteristics, and distinctive features of potential hematopoietic mesenchymal stem cells within various regions of the umbilical cord and placental tissues.
Material and methods. The study included 56 umbilical cord and 26 placental specimens, resulting from normal vaginal deliveries at the Mother and Child Institute of the Republic of Moldova, during the period of 2012-2013. Hematopoietic precursor stem cells were quantified using anti-CD34 monoclonal antibody staining (clone QBEnd/10, prediluted, Leica Biosystem Newcastle Ltd, UK). Antigen retrieval used Bond Epitope Retrieval Solution 2 (Leica Biosystems, UK). Statistical analysis included calculating mean (X) and standard deviation (SD), with parametric Anova tests (F) for significant differences ($p<0.05$).
Results. In the umbilical cord, CD34+ cells were observed in arterial and venous vessels. Non-endothelial CD34+ cells were identified in the peripheral (14.19±2.14) and perivascular (5.92±1.13) zones of the Wharton's jelly. Morphologically, these cells were characterized by cytoplasmic extensions and a large oval/round nucleus, which was euchromatic. CD34 marker expression was membranous and/or cytoplasmic. H-score analysis revealed statistically significant differences between groups ($F=96.0299$, $p=<0.001$). In placental tissue, CD34+ cells were observed in placental vessels of chorionic villi and chorionic plate. In the stroma of villi, two populations of non-endothelial CD34+ cells with distinct characteristics of size and CD34 marker expression were identified.
Conclusions. Our data suggest that the umbilical cord and components of the placenta at term, such as the chorionic plate, amniotic epithelium, and stroma of chorionic villi, contain groups of hematopoietic cells that are not associated with fetal or maternal circulation and are distinct from endothelial cells expressing CD34.
Keywords: stem cells, CD34 positive cells, mesenchymal stem cells, umbilical cord, placenta.

IMPROVEMENT OF TRANSPLANT SERVICES AT THE REGIONAL LEVEL, PRIMARY FACTOR OF THE QUALITY OF HUMAN LIFE

Causan Corina[1], Ivan Daniel-Cornel[2], Radu Ghenadie[3].
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Background. In the context of the research of a wide range of applications in the field of transplantology, the promotion of this type of services is aimed at, as well as the formation of socio-economic thinking in accordance with the modern knowledge and trends of world medical science. Using the Data Bank at the national and international level, it was determined that in the Republic of Moldova this tool is still developing, but studying the impact of the innovative model and the action rates of the operations performed in the field of transplantation, we mention successes.
Materials and methods. The following research methods were used to achieve the aim and objectives outlined in this direction in the article: documentation, selection, analysis and bibliographic synthesis of statistical information from national and international medicine. The reports: «Eurotransplant 2023», to the Spanish National Transplantation Organization (ONT) and the World Health Organization (WHO). The impact of the innovative model on transplant action rates was studied.
Results. Currently, the importance of transplantation is one of the growing medical related fields. World practice shows the enormous picture of lives saved, especially of skilled labor, saving a child's life, etc. The article analyzes the impact of transplant services, in the context of the quality of human life. Currently, several liver and kidney transplant operations have been performed in the Republic of Moldova with an 80% survival rate.
Conclusions. The logistics of medical transplant services play a primary role in the quality of these services, resulting in the embodiment of the transplant to the patient, the time taken for the transplant and the recovery of the organism in the post-operative period, the period and methodology of transportation according to WHO protocols. The waiting list, the difficult connection, the legislation, the competence of local public bodies, different actors of this enormous process, diminish the methodologies of implementing the practice of advanced countries in this segment. Pertinent conclusions were drawn in favor of the maximum possible use of transplantology in the extreme conditions of the health of the patients with the respective traumas. An association of tools such as legislation, the management system of donation and transplantation of organs, cells and tissues, and its infrastructure, the share of GDP allocated to medical care in this segment, the public perception of the problem and the awareness of the population is significant.
Keywords: public health, transplant medical services, digital medicine, modern medical technologies, managerial tools, human life.

DECELLULARIZATION TECHNIQUES OF DENTAL PULP

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Background. Endodontic regeneration shows promise in treating dental pulp diseases, however, no suitable scaffolds exist for pulp regeneration. Acellular natural extracellular matrix is a favorable scaffold for tissue regeneration. This study investigated the characteristics of decellularized dental pulp from extracted wisdom teeth and evaluated whether it could mediate pulp regeneration. Decellularized dental pulp represents a suitable scaffold for improving clinical outcomes and functions of teeth with dental pulp diseases.
Materials and methods. The excised dental pulp was mounted to the perfusion system and washed with 1-1.5 liters of distilled water and subsequently decellularized by two methods: with decellularization agent – 0.25% or 0.5% sodium dodecyl sulfate (SDS) and the second method, in which we provided perfusion of the dental pulp with anticuagulant solution (citrate phosphate dextrose) before decellularization and then – decellularization with 0.25% or 0.5% SDS. Subsequently, the dental pulp was perfused with 1-1.5 L of 1% PBS solution. The segments of the intact and decelularized dental pulp were fixed in 10% formalin and subsequently was performed histological samples preparation and H-E staining. The extraction of nucleic acids was performed according to the QIAamp Blood Mini Kit extraction protocol (2003). Each sample was quantified by a spectrophotometer (Nano Drop 200 C Thermo Scientific). The hydroxyproline content was determined on a spectrophotometer based on the oxidation of hydroxyproline in pyrrole under the action of chloramine B.
Results. The macroscopic evaluation of the dental pulp at the experiment beginning, showed that after its washing with distilled water (first method) and with distilled water and citrate dextrose phosphate (second method) in the second one the dental pulp became to be more pale in comparision to the first one. However, visual differences in perfusion liquid color were observed: the perfusion liquid obtained after washing using the distilled and anticoagulant mixture has more intense brown color, which is explained by the more efficient removal of the blood clots.
Conclusions. The comparative evaluating of the DNA tissues content after decellularization by those two methods in relation to intact tissue proves that the method of decellularization of the dental pulp with SDS and washing with phosphate citrate dextrose shows better results.
The maintaining of connective architecture and collagen fibers, the higher content of hydroxyproline in ECM obtained by our method demonstrated their high feasibility for the subsequent use as bioengineering structure for recellularization process.
Keywords - decellularization, recellularization, dental pulp.

THE THERMAL STABILITY OF COLLAGEN EXTRACTED FROM THE UMILICAL-PLACENTAL COMPLEX

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Background. Collagen is the most abundant protein in animals. As part of the extracellular matrix it presents a true material for biomedical applications due to its versatility [1, 2]. An essential parameter of collagen sponges obtained for tissue engineering is their thermal stability [4].

Material and methods. The collagen was extracted by the modified enzymatic method according to Jian et all. [3] from the umbilico-placental complex taken from the Human Tissue Bank. In the experimental groups the extracted collagen was purified using the surfactants like 1% EDTA, 0.1% SDS, 1% SDC, and 1% CHAPS. The unpurified extracted collagen served as control. The collagen sponges were obtained by freezing the extracted collagen in Petri dishes at -20°C and lyophilized in the VaCo II system (Zirbus, Germany). The thermal analysis TG-DSC for the precursors was performed with a Netzsch STA 449C Jupiter tool. The samples were placed in an open crucible made of alumina and heated with 10 K min^{-1} from room temperature up to 900°C, under the flow of 50 mL min^{-1} of dried air. An empty alumina crucible was used as reference. Statistical analysis was performed with SPSS Version 23.0 statistic software package. The study was supported from the Project with No 23.70105.8007.01T: ”Obtaining and testing of composite biomaterials based on umbilical – placental collagen and hydroxyapatite for oral-maxillo-facial surgery”.

Results. Based on the thermogram analysis, all samples lost their initial mass up to 150°C, the process being accompanied by an endothermic effect on the DSC curve. Most likely this process was caused by the loss of residual water molecules from the samples. In the range of 150-460°C, an oxidative degradation of the organic material took place, a mass loss being recorded. The process was accompanied by a series of partially overlapping exothermic effects. This indicates that there were several types of partial oxidation reactions of organic compounds, accompanied by the fragmentation of polymer chains. After 460°C, the total oxidation of the carbon residue left from the oxidative degradation of the previous stage, took place. A mass loss was also recorded, the process being accompanied by exothermic effects.

Conclusion. When superimposing the results of the thermal analysis in the control and the experimental groups, the behavior was similar, thus indicating that the surfactants do not influence the thermal stability of the collagen.

Key-words. Thermal stability, collagen, umbilical-placental complex, tissue engineering

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AMNIOTIC MEMBRANE TRANSPLANTATION INTO LOWER LIMB ULCERS

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Background. There are many applications of the amniotic membrane in regenerative medicine, it serves as a source of stem cells and potent growth factors and like a very biocompatible natural scaffold; also the amniotic membrane serves as an efficacious nanorecipient for medicines delivery, due to its raised entrapment properties.
Materials and methods. Was performed a controlled clinical study, which were involved 10 patients, who suffered from neuropathic foot ulcers, and treated by amniotic membrane transplant. The age of patients was between 18-70 years and suffered from ulceration below the ankle for a month or more.
Results. The main result of this study was to assess the proportion of ulcers, that full closure in 9 weeks in treated with amniotic membrane. Thus, 78% of all patients obtained full closure.
Conclusion. The clinical application of amniotic membranes maintains the anatomical and structural configuraAmniotic membrane transplantation is a common practice in regenerative medicine due to its potential to provide stem cells and potent growth factors. It is also a biocompatible natural scaffold that can be used as an effective nanorecipient for delivering medicine.
Keywords. Neuropathic, amniotic, regenerative, ulcers.

THE USE OF AUTOTRANSPLANTED AND HOMOTRANSPLANTED SEPTAL CARTILAGE IN RHINOPLASTY AND RHINOSEPTOPLASTY SURGERIES

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Background. Surgical interventions for nasal reshaping, such as rhinoplasty and rhinoseptoplasty, have gained significant popularity among the population. Currently, these procedures are increasingly performed using both autotransplants and homotransplants. These surgical procedures are now enhanced through the use of advanced surgical techniques, specialized equipment, and high-performance instruments. Rhinoplasty surgeons have embraced a modern approach, abandoning traditional methods of dorsum nasi bone resection with chisel and hammer. Instead, a piezotome is used to perform median and lateral osteotomies, allowing for controlled fracturing of nasal bones along the greenstick fracture lines to obtain mobile fragments without displacement, and adjusting only the insertion angle. These aspects are crucial moments that previously presented multiple difficulties for surgeons. In many cases, it is necessary to fill depressions or tissue deficiencies on the nasal pyramid or adjust the position of the nasal tip using cartilaginous tissues. In such cases, nasal septal cartilage is a valuable resource. Rhinoplasty surgeons prefer to use the patient's own nasal septal cartilage whenever possible, but it is not always sufficient or may be absent, especially after previous nasal septal surgeries. In these cases, rib cartilage can be used, but some patients may refuse its harvesting or there may be contraindications. Consequently, the question arises regarding the use of homotransplanted nasal septal cartilage.This technique is well-known and successfully used by rhinoplasty surgeons. To benefit from homotransplanted cartilage, collaboration with a specialized tissue bank for human tissue transplants is necessary.
The aim of the study. Is to conduct comprehensive literature studies regarding the use of autotransplanted and homotransplanted nasal septal cartilage in rhinoplasty and rhinoseptoplasty surgeries. Materials and methods. In the analysis process, a total of 50 sources of information were evaluated, including those available on medical platforms such as Medlife, PubMed, Google Scholar, and ResearchGate. Among the highly relevant sources, several were highlighted, considered significant for this research domain, providing varied and detailed perspectives on the use of nasal septal cartilage in nasal aesthetic surgery and contributing to the comprehensive analysis of the subject. To achieve an advanced selection of bibliographic sources, several filters and criteria were applied. Full-text articles published in English and Russian between 2000 and 2024 were sought. After a preliminary analysis of the titles, original articles, editorials, and narrative, systematic, and meta-analysis synthesis articles were selected. These types of articles were chosen because they provide relevant information and contemporary concepts regarding the use of autotransplanted and homotransplanted nasal septal cartilage in rhinoplasty and rhinoseptoplasty surgeries.
Additionally, a supplementary search was conducted in the bibliographic reference lists of the initially identified sources to find additional relevant publications not included in the consulted databases. Information from the publications included in the bibliography was gathered, classified, evaluated, and synthesized to highlight the main aspects of contemporary views on the practices mentioned in the field of using nasal septal cartilage in aesthetic and reconstructive nasal surgeries. This approach allowed for exhaustive and updated research in the field of rhinoplasty and rhinoseptoplasty.
Results and discussions. According to the results obtained in these studies, in rhinoplasty and rhinoseptoplasty interventions, it was found that autotransplanted nasal septal cartilage was most commonly used, while homotransplanted cartilage, collected from other patients, and previously preserved at a human tissue bank for transplantation, was used less frequently.

Overall, the results were promising, with good integration and revitalization observed in both autotransplants and homotransplants.

Conclusions. The use of transplants, both autotransplants and homotransplants, represents the most efficient and commonly used method in rhinoplasty and rhinoseptoplasty surgeries. In rhinoplasty and rhinoseptoplasty surgeries, it was found that nasal septal cartilage is most frequently used compared to other types of transplants, such as auricular cartilage or costal cartilage. These transplants have the advantage of not being resorbed, maintaining their shape over time, and not causing inflammatory or allergic reactions, contributing to the success and durability of surgical interventions in these areas.

Keywords: autotransplantation, homotransplantation, rhinoseptoplasty, septal cartilage, rhinoplasty surgeries.

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AMNIOTIC MEMBRANE TRANSPLANTATION: IMPORTANCE AND CLINICAL INDICATIONS

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Background. Amniotic membrane transplantation has been recently gained wide-spread attention as a new method for reconstruction of the ocular surface. It is used in ophthalmology as a substrate for the growth of epithelial cells, for tectonic support in cases of small perforations and to cover large areas of corneal and conjunctival epithelial defects.
Material ant methods. A retrospective study was done from 2020 to 2023 included 43 patients with corneal pathologies of which: 31 (72,1%) men and 12 (27,9%) women hospitalized in the Department of ophthalmology *Timofei Mosneaga* Republican Clinical Hospital to examine the indications of amniotic membrane transplantation and the surgical techniques. All patients were adults. Patients ranged in age from 27 to 100 years, predominantly from rural areas
Results. The patients who underwent membrane transplantation had the following diagnoses: corneal ulcer (60,7%) followed by eye burns (14%), conjunctival neoformations (9,4%), pterygium (6,9%), symblepharon (5%), keratouveita after the contact lens (2%) and recurrent conjunctival melanoma (2%). Of the total number of patients, 27 patients had associated pathologies such as posttraumatic keratoveitis (26%), secondary glaucoma (18,5%), corneal leukemia (14,8%), purulent endophthalmitis (11,1%), pterygium gr I-II (11,1%), hypopyon (11,1%), uveitis (3,7%) and desmetocele (3,7%). The main surgical intervention was amniotic membrane transplantation to all patients and 15 patients underwent combined surgical intervention such as pterygium excision (26,7%), restoration of the corneal defect (33,3%), blepharorhaphy (33,3%) and restoration of the conjunctiva and sclera after trauma (6,7%). Vision at initial examination was light perception to 0 for 1 patients (2,4%), 1/p.l.incerta for 6 patients (13,9%), 1/p.l.certa for 21 patients (48,9%), 0.01 – 0,1 for 9 patient (20,9%) and 0,1 – 0,3 for 6 patients (13,9%). Predominantly patients aged between 60-70 years (27,9%), then 50-60 and 80-90 years (16,4%).
Conclusions. Amniotic membrane transplantation has high success rates and is clinically useful due to its unique structure, biocompatible composition, subsequent biological functions and has a multitude of ophthalmological indications such as persistent epithelial defects, partial limbal stem cell deficiency, bullous keratopathy and corneoscleral ulcers.
Keywords: amniotic membrane, transplant, ulcer, ocular surface.

Osteo-cellular graft in the wrist instability. Clinical case.

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Background. The wrist or carpal instability means any disturbance of the static and dynamic balance of forces at the wrist under the conditions of daily living [Linscheid, 1972]. The cause of wrist instability in 95% is of post-traumatic origin, the most of cases are around scaphoid bone [Watson, 1984]. The instability of the wrist joint causes the deforming osteoarthritis of the joint which in turn leads to chronic pain and disability [Azócar, 2021]. Wrist arthrodesis is a procedure performed in advanced arthritis with painful movement in wrist joint [Chhabra, 2010]. This surgery is a rescue one, and is made in order to remove the pain syndrome and increase the strength of the hand [Gelberman, 2000]. Aim of study was presentation the clinical case of scaphoid pseudarthrosis with deforming osteoarthritis of the wrist joint treated by arthrodesis using osteo-cellular graft (OCG).
Material and methods. Anamnesis, clinical and paraclinical data were taken from the hospital patient record. Were analyzed the laboratory examinations, radiography and MRI of the wrist joint of the patient.
Results. A 39-year-old man suffered repetitive fall trauma in the left hand: first time it was about 20 years ago and was performed conservative treatment, but 6 years later the pains started to appear. After another trauma 5 years ago, it was diagnosed scaphoid pseudarthrosis, but it was neglected. Now the patient presented at the Clinical Hospital of Traumatology and Orthopedics with severe pain, limitation of movements and deformity of the left wrist joint, he was admitted to the Division of Hand Surgery. The patient's radiological images and MRI reports - Scaphoid pseudarthrosis of the left hand with 2nd degree deforming osteoarthritis of the wrist joint. Together with patient it was decided to perform surgical treatment – scaphoidectomy and arthrodesis using osteo-cellular graft (OCG). Before surgery, harvesting of autologous mesenchymal stem cells and enrichment by tissue-engineering was carried out, which were combined with demineralized allograft obtaining OCG. According to preoperative planning, scaphoidectomy and 4-corner arthrodesis (capitate-lunate and triquetrum-hamatum) using OCG was performed. Remote imaging and clinical examinations showed a satisfactory outcome. The patient completely got rid of pain and began to work again.
Conclusion. The use of osteo-cellular graft in arthrodesis of wrist instability is a safe method with good results, the clinical study of this topic is imperative and needs to be researched further.
Keywords: wrist instability, scaphoidectomy, arthrodesis, osteo-cellular graft (OCG).

AUTOLOG TRANPLANTATION OF PLATELET RICH FIBRIN IN INGUINAL HERNIA REPAIR IN LIVER CIRRHOSIS

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Background. The objective of this study is to provide autologous platelet-rich fibrin transplantation in inguinal hernia repair in liver cirrhosis with ascites.
Materials and methods. A study was conducted on 28 patients with inguinal hernia combined with liver cirrhosis and massive ascites-peritonitis.
Group I: 14 patients with inguinal hernia associated with liver cirrhosis and massive ascites peritonitis underwent Lichtenstein type hernioplasty. Group II: 14 patients with inguinal hernia associated with liver cirrhosis and massive ascites peritonitis underwent Lichtenstein type hernioplasty with the application of autologous fibrin transplantation rich in platelets. All patients in both groups underwent laparoscopic lavage of the abdominal cavity with antibacterials and postoperative drainage with lavage.
Results. Seroma wounds postoperative wounds I group 3 cases, II group 0 cases. Postoperative wound suppuration I group 1 case, In group II – 0 cases. Recurrence of the hernia at 1 year was not observed in both groups. Mortality consists of 2 patients, who developed liver failure after 2 months of hospitalization, 1 patient from group I.
Conclusion. In patients with inguinal hernia and liver cirrhosis and ascites-peritonitis, the application of Lichtenstein-type surgical treatment with the application of autologous platelet-rich fibrin transplantation ensures safe local results, without postoperative complications in the postoperative wound (lack of seromaler and wound suppuration). Postoperative mortality does not determine a significant difference, being caused by liver reserves and liver failure. Surgical treatment without the application of autologous platelet-rich fibrin transplantation has an increased incidence of postoperative complications.
Keywords: inguinal hernia, liver cirrhosis, hernioplasty, autologous platelet-rich fibrin transplantation.

THE RESULTS OF THE TREATMENT OF TROPHIC ULCERS OF THE LOWER LIMBS BY APPLYING AUTOLOGOUS PLATELET-RICH FIBRIN

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Background. The most common cause of lower limb ulcers is chronic venous insufficiency.Up to 48% of patients with trophic ulcers are at the age of maximum productivity. 67% of patients with trophic ulcers become disabled, and in 81% the quality of life decreases considerably. Injection of autologous platelet-rich plasma (PRP) is an important factor in tissue regeneration and represents a new perspective in the treatment of trophic ulcers.
Material and methods. Prospective study. The study included 28 patients, divided into 2 groups, with trophic ulcers of the lower limbs with a duration of 6-24 months without epithelization dynamics, paraclinically confirmed the presence of chronic venous insufficiency. I group 14 patients combined treatment with PRF injection in venous ulcers. II control group – 14 patients who benefited from general basic treatment and local compressive treatment. All patients were monitored for 1 year.
On the 7th and 14th day of treatment, histological examinations of trophic ulcers were performed in both groups of patients, with a comparative evaluation of the results obtained. Platelet-rich fibrin membranes were obtained by centrifuging under special conditions the peripheral venous blood collected from the patient.
Results. In group I complete epithelialization after 12 months of treatment combined with platelet-rich fibrin was obtained in 10 patients and in 4 patients incomplete epithelialization was obtained (70% of the ulcerated surface) In group II control after 12 months of treatment epithelialization complete epithelialization was obtained in 7 patients and incomplete epithelialization in 7 patients (40% of the ulcerated surface)
The results of the histological examination demonstrated in Lot I the appearance of the neovascular network with granulation tissue in all patients. In batch II, the lack of formation of the neovascular network.
Conclusions. The use of autologous Platelet-Rich Fibrin is a simple and affordable method to use. PRF membranes initiate and accelerate granulation tissue formation and angiogenesis. As a result, complete epithelization of the ulcers occurs, improving the patients' quality of life.
Keywords: Platelet-Rich Fibrin, trophic ulcer, platelets, regeneration, PRF.

AMNIOTIC MEMBRANE IN OPHTHALMOLOGY

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Background. Amniotic membrane (AM) represents a thin membrane on the inner part of the placenta (A. C. Mamede, 2012) that can be used in ophthalmology, dentistry, urology, burn units, otorhinolaryngology, gynecology, and researches in stem cell technology (U. Sridhar, 2023). Growth factors and cytokines with anti-inflammatory, anti-bacterial, anti-immunogenic, anti-fibrotic, and promotion of epithelization qualities are delivered by the cells of AM (H. Elkhenany, 2022).
The study aims to give a brief overview of the clinical uses of AM in ophthalmology.
Methods and materials: Literature research was performed using the keywords "amniotic membrane transplant", "amnion AND cornea", "amnion AND ophthalmology", "amnion AND ocular surface" and "amnion AND retina".
There were selected articles written in English, until 01/03/2020.
Results. Due to its characteristics as nonimmunogenic, easily available, cosmetically acceptability, and good substrate for epithelial growth- the AM is used as a graft for epithelial cell growth, tectonic support for small perforations and thinning of cornea and sclera, and reconstruction for the ocular surface. Also, in vitreoretinal surgery, the applications of the AM have been extended, such as complicated retinal detachment, macular holes that failed to close, and end-stage age-related macular degeneration. All of these uses are now under investigation and its capacity to be assimilated into the retinal tissue without causing immunologic reactions or significant postoperative problems makes it a valuable basal membrane and a new strategy for treating various retinal diseases.
Conclusion. Nowadays, the amniotic membrane is widely used for the ocular surface with great postoperative results. For the vitreoretinal use, it is needed further prospective, randomized controlled studies to confirm the obtained results.
Keywords: amniotic membrane, cornea", ocular surface, retina, vitreoretinal surgery.

REHABILITATION OF PATIENTS WITH POST-SEQUESTRECTOMY OF THE JAWS WITH THE USE OF THE OSTEOSTIMULIN-C

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Background. Toxic osteomyelitis is an inflammatory origin pathology, which occurs in the jaws following the consumption of drugs with a high content of phosphorus and ephedrine, following treatment with bisphosphonates or radiotherapy. Its treatment is only surgical, it consists of sequestrectomy and results in a lack of bone tissue in the oro-maxillo-facial region.
After the interventions, patients are left with obvious sequelae and a significant lack of bone. For the rehabilitation of these patients, reconstructive surgery, orthopedic and prosthetic treatment, physiotherapy and pharmacotherapy are used. The use of osteogenetic stem cells has proven to be extremely effective, showing good results. A preparation that has demonstrated its effectiveness in appropriate clinical cases is Osteostimulin-C, which is an example of allogeneic embryofetal osteomedullary cells (CEFOMA).
Material and methods. The following study has been performed using the medical files of patients in the post-sequestrectomy state of the jaws, for whose rehabilitation the Osteostimuln-C drug was used.
Results. After the recovery of the patients and the healing of the operative field, it was rehabilitated by applying Osteostimulin-C. The success of this treatment allowed not only sufficient restoration of the jaw bone, as prosthetic treatment was possible, but also played a significant antibacterial role.
Conclusion. The utilization of CEFOMA allows the treatment of acquired bone pathologies, characterized by lack of continuity and bone substance via stimulating of new bone tissue growth, which allows a faster rehabilitation and a better quality of life for the patient.
Keywords: Toxic osteomyelitits of the jaws, sequestrectomy, osteogenetic stem cells, CEFOMA, rehabilitation.

PORCINE DERMIS - A SOURCE OF BIOMATERIAL MODELLING BY TISSUE ENGINEERING

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Background. Tissue engineering is a branch of regenerative medical technology that helps replace damaged tissue using appropriate scaffolds, living cells and growth factors. Collagen-based scaffolds are attractive products for various pharmaceutical, dermatological and tissue engineering applications such as wound healing. The use of purified collagen obtained from animal tissue can generate a large number of products that have applications in the medical field and in the manufacture of cosmetic products.

Aim of the study. In this article, we aimed to develop collagen scaffolds from decellularized porcine dermis by tissue engineering and evaluate the biomechanical properties for application in the field of dermatology.

Material and methods. In the case of dense tissues such as porcine dermis, it is extremely important to choose the decellularization protocol that is effective but not aggressive to the tissue in order to preserve the extracellular matrix and especially the proteins that enhance tissue regeneration. DAPI and hematoxylin and eosin stains were used to observe whether the cells were well removed and the scanning electron microscope to study its microstructure. Antigenic properties of collagen scaffolds obtained from porcine dermis were studied. Until a collagen biomaterial is obtained, the decellularized dermis has gone through five steps, such as: enzymatic digestion, extraction, solubilization, neutralization by dialysis, and lyophilization.

Results. (1) DAPI staining shows positive nuclear staining in native tissue indicating the presence of cells and negative nuclear staining in decellularized tissue indicating the absence of cells. (2) H&E staining indicates the presence of cells with purple nuclei in native tissue and decreased cells in decellularized tissue. (3) SEM shows a dense and non-porous native tissue and a cellular free 3D network structure. (4) Quantification of DNA in native and decellularized tissue indicating an approximately 91% decrease in DNA after decellularization. (5) An elastic and flexible sponge with a highly interconnected porous structure was obtained.

Conclusions. Porcine dermis can be processed in order obtain an elastic, flexible collagen sponge with an interconnected porous structure that would promote cell proliferation.

Keywords: porcine dermis, biomaterials, tissue engineering.

MENSTRUAL BLOOD-DERIVED STEM CELLS: MILESTONES AND FUTURE PROSPECTS FOR REGENERATIVE MEDICINE

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Background. Stem cell therapy is the future of medicine as research into incurable diseases and injuries continues to grow. Stem cells are difficult to obtain because of ethical conflicts, sampling difficulties or high costs. However, a line of menstrual blood-derived stem cells (MenSCs) shows great potential in address to these issues. Research on menstrual blood-derived stem cells is growing due to the properties they exhibit, including self-renewal, differentiation, angiogenesis, anti-inflammatory and immunomodulatory properties.
Aim of study. Reviewing the latest advances in researching menstrual blood stem cells (MenSC) and their potential for application. Finding convenient and efficient ways to isolate MenSCs and investigate their biological characteristics and proliferative capacities.
Methods and materials. This research is based on bibliographic analysis of the sources published in the period 2007-2022, 40 scientific sources were researched. The collection was carried out by means of the "Diva" menstrual cup. The menstrual blood of 3 women was isolated in the Tissue Engineering and Cell Culture Laboratory according to the researched protocols.
Results. The internal lining of the uterus - the endometrium - is a tissue with a strong regenerative potential located on the muscle-myometrium layer and is composed of the following layers: functional and basal. The human endometrium regenerates monthly, it has an approximate thickness of 0.5-1mm after menstruation, while at the end of the cycle 10-12mm. MenSCs obtained from women's menstrual blood were first reported in 2007, these stems are multipotent and can differentiate into a variety of cells including adipocytes, osteoblasts, chondrocytes and endothelial cells. In this study, similar to the results of revised sources, during the subculture, MenSCs showed a gradual increase of colonies up to 80% confluence after 3 days of seeding. Counting procedures were performed using a Neubauer chamber. MenSCs have beneficial properties including ease of acquisition, non-invasive collection procedures, large-scale expansion capabilities, rapid amplification abilities, genomic stability, and high proliferation rates without being tumorigenic or immunogenic.
Conclusion. The field of stem cells derived from menstruation is still growing, there is huge potential for the use of MenSC due to its multitude of benefits, but studies are needed to learn more about their mechanisms and their impact on people. At the same time, the influence of clinical and epidemiological factors, such as age, use of contraceptives or hormonal status, still requires further investigations to evaluate the collection and processing protocols of menstrual blood and their refinement under the conditions of the tissue engineering and cell culture laboratory.
Keywords: stem cells, menstrual blood, regenerative medecine.

A NEW APPROACH IN THE TREATMENT OF OPTIC NERVE ATROPHY USING MESENCHYMAL STEM CELLS. A SYSTEMATIC REVIEW

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Background. Tissue engineering is a progressing field that unites cells, biomaterials and biochemical factors focused at replacing, maintaining and substituting different kind of tissues. A major role is played by the use of the stem cells in various fields of medicine, including ophthalmology, namely in cases of the optic nerve atrophy. The optic nerve atrophy is the most important cause of decreased visual acuity and blindness. It is considered that the use of the stem cells can be an important new strategy in the treatment of the optic nerve atrophy, as the stem cells restore the structure and the function of the optic nerve due to the organotypic tissue induction and vascularization. The optic nerve atrophy is caused by irreversible apoptosis of the neuronal cells. In the absence of a specific treatment of the optic nerve atrophy, the current therapies are based on the etiological cause or complications. Considering the availability of the advanced therapies, the therapy using stem cells offers a new approach in the treatment of the optic nerve atrophy.
Aim of study. The evaluation of the latest advances of using mesenchymal stem cells based on clinical trials that included patients with optic nerve atrophy. Methods and materials. This study is a literature review, based on synthesis of clinical trials published in the period between 2009-2023. This article includes publications identified through Google Search Engines, PubMed Databases, National Bibliometric Tool, etc. The information was systematized, highlighting both aspects of the use of mesenchymal stem cells in the pathologies associated with the optic nerve atrophy, as well as the results of 24 clinical trials published on clinictrials.gov.
Results. Current treatment of the optic nerve atrophy is based on the etiological causes or late complications. Reviewing the accessibility of up to date therapies, stem cell therapy offers a new attitude in the treatment of the atrophy of the optic nerve. Being easy to collect and cultivate, mesenchymal stem cells are most often used in regenerative medicine, they can be induced to differentiate into cartilage, tendons, adipose tissue and other cell lines. Mesenchymal stem cell collecting has no ethical issues compared to embryonic stem cell harvesting. Also, mesenchymal stem cells are considered to be immunoprivileged because the major histocompatibility factor II is not expressed on their surface, and this great advantage allows the use of mesenchymal stem cells in autologous or allogenic form. Mesenchymal stem cells produce growth factors with paracrine action that are thought to activate endogenous repair mechanisms, due to these features mesenchymal stem cells have been used in several clinical studies in optic nerve disorders where immunomodulatory and neuroprotective properties have been revealed. All of the properties mentioned above stand for the clinical use of mesenchymal stem cells in case of optic nerve atrophy.
Conclusion. The clinical use of the stem cells is a significant chance for the regeneration of pathologically modified tissues. This fact requires further studies to establish how to use the cell therapy in the case of optic nerve atrophy.
Keywords: stem cells, optic nerve, atrophy, blindness.

BONE AUGMENTATION IN INTERNAL FIXATION OF CONGENITAL PATHOLOGIES, POST-TRAUMATIC DISORDERS (NON- OR MALUNIONS) AND PSEUDARTHROSIS TREATMENT ON UPPER LIMB

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Background. The paper explores the applicability and efficiency of bone augmentation in combination with internal fixation as a primary strategy in the treatment of malunited or non-united fractures and pseudarthrosis in the upper limb.

The aim is to evaluate the impact of this approach on improving bone consolidation and the functional recovery of patients.

Materials and Methods: The study includes a review of cases treated between 2019-2021, focusing on patients (N:39) with malunited (N:11) or non-united (N:6) fractures, congenital deformities (N:2), and pseudarthrosis (N:20) of the upper limb. Various internal fixation techniques (pins, plates (LC-DCP/T-DCP/LCP)), types of graft used (autograft from the iliac crest (N:6), allograft - bone block (21), demineralized bone graft (N:5), bone substitutes - autologous nucleated cellular suspension from bone marrow (N:8)) and their impact on the healing process are analyzed.

Results. The results obtained highlight a significant improvement in bone consolidation rates and the functionality of the treated limb, emphasizing the effectiveness of bone augmentation in combination with internal fixation. Depending on the type of pathology, valuable perspectives for optimizing future treatments are presented.

Conclusions. Bone augmentation accompanied by internal fixation represents an effective approach for managing deformity, malunited or non-united fractures and pseudarthroses of the upper limb. Selecting the appropriate method of augmentation and internal fixation, adapted to the specifics of each case, is crucial for achieving optimal bone consolidation and functional recovery.

Keywords: bone augmentation, internal fixation, post-traumatic deformities, non- and/or malunited fractures, pseudarthrosis, upper limb.

IMMUNOSTIMULATION OF LOCAL IMMUNITY IN THE COMPLEX TREATMENT OF CHRONIC TONSILLITIS IN CHILDREN

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Background. After healing the palatine tonsils in the complex conservative treatment of chronic tonsillitis, an important role is the stimulation of local immunity by applying autologous mononuclear cells. This is done by introducing these activated cells into the peritonsillar space. The application of this method does not produce immune conflict, transmission is excluded hemotransmissible pathologies, the bioethical problem is missing.
Objective. To examine the effect of applying local immunostimulation with activated autocells in chronic tonsillitis in children without complications at the distance.
Materials and methods. Clinical and immunological studies of the treatment of children with chronic tonsillitis without complications of other organs and (74 children) were investigated in the IP Mother and Child Center, *Emilian Cotaga* Clinic, ENT Department. The method of local immunostimulation (autologous mononuclear cells) was developed in the Tissue Engineering and Cell Cultures Laboratory of *Nicolae Testemițanu* SUMPh.
Results. After more than 2 months of treatment were highlighted decreases in IgE content, decreases in sensitization of T lymphocytes to *Streptococcus pyogenes* and pneumococcal antigens, decreases in IgG titers, decreases in the level of pro-inflammatory cytokines *TNF-alpha, IL-1-8 beta*, increases in cytokines anti-inflammatory *Il-4*. The presence of *Streptococcus pyogenes* in tonsillar surface smears was significantly reduced after treatment. Over the course of a year, the number of acute respiratory infections decreased in these children, as well as indications for antibiotic therapy, signs of chronic inflammation of the palatine tonsils (caseous masses in the hollows, hyperemia of the tonsil pillars, etc)
Conclusion. The method of local immunostimulation (with autologous mononuclear cells) in the case of chronic tonsillitis has a positive clinical impact, exerting a positive complex action on the reactivity of immune indices.
Keywords: chronic tonsillitis, autologous cells, children.

CELL VACCINES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA

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Background. Hepatocellular carcinoma is one of the most common forms of cancer globally (sixth most common cancer, in 2020), and represents an essential cause of mortality worldwide (third most common cause of death from cancer etiology), with approximately 905,677 new cases and 830,180 deaths in 2020 without effective treatment methods. Thus, the use of cellular vaccines in the treatment of hepatocellular carcinoma is a new therapeutic approach, aimed at acting on cancer cells and destroying them, by inducing efficient cellular responses mediated by specific antibodies for antigens selectively expressed by the tumor.
Aim of study. Studying the effectiveness of cell vaccines in the treatment of hepatocellular carcinoma, to increase the quality and duration of life.
Methods and materials. This study is a review of the specialized literature of the last 10 years on the selected topic. Electronic databases were used: NIH (5), Google Academic (2), PubMed (3), Medscape (1).
Results. The use of cellular vaccines in the treatment of hepatocellular carcinoma is a new therapeutic vision used by researchers, which appeared and was implemented less than a decade ago, and which is in continuous development, due to the positive results it has. There are several types of cellular vaccines: based on peptides, dendritic cells, based on viral vectors, DNA, mRNA, which have proven their effectiveness following clinical trials on patients. Thus, a meta-analysis of 11 studies including 396 patients reported a cumulative clinical response rate of 15.4% and that DC vaccines were well tolerated, and the survival rate increased in sick patients.
Conclusion. Cell vaccines for the treatment of cancer show substantial potential for the successful management and possible prevention of mortality from hepatocellular carcinoma. Cell vaccines need to be researched and applied in practice, especially in clinical trials, to evaluate the safety, efficacy and clinical relevance of these vaccines in cancer patients, to achieve long-term control of tumors and a lasting remission.
Keywords: cellular vaccines, hepatocellular carcinoma, immunotherapy, dendritic cell-based vaccines, peptide-based vaccines, mRNA-based vaccines, DNA.

THE PARTICULARITIES OF AMNIOTIC MEMBRANE TRANSPLANTATION ON THE OCULAR SURFACE. (LITERATURE REVIEW)

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Background. Amniotic membrane transplantation has emerged as a promising option for restoring vision, offering an alternative to corneal transplant procedures. This innovative technique involves transplanting the amniotic membrane, obtained from the innermost layer of the placenta, onto the surface of the eye.
The aim of the paper*:* Review of the thematic literature in the context of the analysis of current data on amniotic membrane transplantation.
Material and methods. A study of publications on the topic of amniotic membrane transplantation from the PubMed platform and other sources of scientific publications from the Republic of Moldova was carried out, with a period until 2024.
Results. When transplanted, the amniotic membrane has anti-inflammatory, anti-scarring, anti-angiogenic and possibly bactericidal. During the healing process, the amniotic membranes are integrated intraepithelially, subepithelially, or intrastromally. TAM improves visual outcome and reduces corneal neovascularization, symblepharon formation, and epithelialization time.
Conclusions. The implementation of the transplantation methodology is an innovative technology, having a positive impact on the patient's quality of life, and healthy life expectancy, enhancing work capacity. AM transplantation is a safe and effective procedure for the treatment of superficial eye diseases. The technically simple fixation of the AM with an overlock suture guarantees a stable position of the AM and a comfortable feeling for patients in the postoperative period. The authors agree with the opinion of the implementation of the surgical method of using the graft. Resulting in positive postoperative care from the patient's side.
Keywords: amniotic membrane, corneal ulcer, cornea.

FEATURES OF MICROSURGICAL TREATMENT IN PATIENTS WITH *PTERYGIUM*

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Bakground. *Pterygium* is clinically manifested by a triangular fold of the bulbar conjunctiva with the base towards the semilunar fold and the tip towards the cornea. The etiology and pathogenesis of *pterygium* is unknown. It would result from a corneo-conjunctival epithelial alteration, associated with a proliferation of fibrinogen tissue, progressing between the epithelium reduced to a few layers of cells and the perforated Bowman's membrane.
Aim. To assess the effectiveness of a modified method in the treatment of *pterygium,*stage II.
Objectives.1. To determine the effectiveness of the modified method using the free conjunctival flap plus subconjunctival administration of 5-FU (fluoruracil) in the treatment of patients with pterygium.
2. To appreciate the benefits of the modified method depending on the addressability of patients with *pterygium.*
Materials and methods. The study included 8 patients (4 men and 4 women) with pterygium aged 20-71 years who underwent pterygium removal according to a modified method. Thus, during the surgical intervention, a movable, free, rectangular flap with sides 5 x 3 mm was prepared inferiorly paralimbally, which was fixed conjunctivally paralimbally, nasally in the area of the body of the pterygium translocated to the superior or inferior fornix plus subconjunctival administration of 5-FU . It is important to position the formed conjunctival flap with a limbal orientation.
Discussions. The postoperative recovery was fast, but for several days after the operation the globe was hyperemic, irritating the suture fibers used to fix the conjunctival autograft. Antibiotic and anti-inflammatory in the form of eye drops are needed. Thus, in all patients, 3 months after the microsurgical intervention, no signs of recurrence of the operated pterygium were detected. In 2 late-presenting patients, the pterygium was extended onto the cornea, resulting in deep scarring. As a consequence, the radius of corneal curvature was changed with the decrease in visual acuity in the postoperative period. This is why surgery for *pterygium* should not have been delayed.
Conclusions:
1. The microsurgical method proposed for the treatment of *pterygium* is safe and effective, determining the lack of recurrence in the postoperative period.
2. Microsurgical intervention based on *pterygium* should be performed as early as possible.
Keywords: recurrent *pterygium*, free conjunctival flap, recurrence, postoperative period, 5-FU (fluoruracil).

Varia

EXPRESSION OF ANDROGEN RECEPTORS IN PROSTATE CARCINOMA

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Background. Androgens and their receptors are crucial for prostate development, maintaining glandular structure and function. Androgen receptors are present not only in epithelial but also stromal cells, comprising smooth muscle, fibroblasts, myofibroblasts, and macrophages. Their role in stromal cell regulation remains incompletely understood, yet they likely influence reactive stroma in prostate cancer. Comparative assessment of androgen receptor expression in stromal and epithelial cells in malignancy informs prostate cancer progression mechanisms.
Aim of the study. Assessment of the variation in AR receptor expression between stromal and epithelial cells in malignant prostate lesions.
Material and methods. The study included 73 prostate cancer specimens, collected by open surgery TURP in the clinical setting of the MSPI Institute of Oncology and MSPI Republican Clinical Hospital. The biopsy fragments, after fixation in 10% buffered formalin, were primarily processed following the standard procedures. Sections 5μm thick were sliced off each block, which were mounted on histological slides. The material collected was divided into 2 groups: acinar and non-acinar carcinomas. Histopathological profiling was performed on hematoxylin-eosin stained sections. Immunohistochemical study included the androgenic anti-receptor (anti-AR) monoclonal antibody. At the same time, to elucidate the types of AR-expressing stromal cells, the histological sections were subjected to Masson's trichrome staining and anti-αSMA immunohistochemical method.
Results. In all prostate carcinoma specimens, three patterns of AR expression were identified by the epithelial and stromal cells: diffuse nuclear, regional nuclear and focal nuclear. All three patterns were considered as a positive response to anti-AR immunoreaction. Most tumours were characterized by AR positive epithelial cells. However, in 21,9% (n=16) small AR negative tumour foci were observed. In the stroma, the density of AR positive cells decreased compared to benign lesions. The difference between the mean scores of histological carcinoma types was statistically significant (p=0,001). Based on the achieved results, the correlation between the total score of AR expression and Gleason score was recorded, obtaining a total and direct correlation (r_p=-0,86, p=0,001).
Conclusions. The decrease in stromal AR expression is dependent on tumour stage, Gleason score, and can be considered a marker of disease aggressiveness.
Keywords: androgen, prostate, prostate carcinoma, androgen receptors, stroma, Gleason score.

DIFFERENTIATED IMMUNOHISTOCHEMICAL EXPRESSION OF ANGIOGENIC FACTOR ANG2 IN THE GERMINAL STATUS OF UTERINE PREGNANCIES DISTURBED AT EARLY TERM

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Background. Angiopoietins contribute to vascular and angiogenic processes, playing a crucial role in establishing a functional placental vascular system that supports the intrauterine growth of the embryo and fetus. Changes in Ang2 expression disrupt the maturation and stabilization of the vascular network.
Aim of the study. Assessment of the immunohistochemical expression pattern of Ang2 in the chorionic villi germinal status of patients experiencing early-term pregnancy complications.
Methods and materials. Tissue samples were collected via uterine aspiration from 67 patients with early-term pregnancy disruptions at the Perinatal Center of the Mother and Child Institute's, during 2020. Patients were categorized into three groups: early spontaneous abortion (ESA) – 11 cases; missed abortions (MA) – 43 cases; and 13 cases of pregnancies terminated for social or personal reasons (TS or TD). All groups were further divided based on gestational age into 3-5 weeks, 6-9 weeks, and 10-12 weeks. Study methods included hematoxylin-eosin (H&E) staining, immunohistochemistry evaluating anti-Tie1. Immunohistochemical expression was analyzed in cellular expression sites: cytotrophoblast, syncytiotrophoblast, endothelial cells, Hofbauer cells, and stroma. Immunohistochemical intensity was graded from 0 (absent) to +3 (pronounced). Statistical analysis involved assessing intensity, statistical correlations (Spearman r_s), and Mann-Whitney (U) test.
Results. Cytoplasmic immunohistochemical expression was predominantly negative in all studied sites of the control group except for syncytiotrophoblasts (+3). SS and ASP groups showed negative cytotrophoblast expression and variable expression in Hofbauer and stromal cells (70,4/63,6%, 86,3/90,9%), except for endothelial sites, which exhibited differentiated immunostaining: SS – 56,1% positive *vs* ASP – 36,4% negative. Syncytiotrophoblast expression was predominantly positive (+3) in SS and ASP: 90,6%/90,9%. Significant statistical differences were found intergroup for the endothelial site in SS 6-9 weeks *vs* Control 6-9 weeks p=0,01; SS 10-12 weeks *vs* Control 10-12 weeks p=0,04; Control total *vs* SS total p=0,001 and ASP total *vs* Control total p=0,025. Correlations were observed in the total SS group, namely: TS with Hofbauer cells and stromal cells (r_s=0,54, p=0,002 and r_s=0,45, p=0,002); age with vascular endothelium (r_s=0,38, p=0,01).
Conclusion. During early-term pregnancy disturbances, Ang2 angiogenic environment in placental development mostly displays negative conditions, except for vascular endothelium in the MA group with prevalent positive expression. Cellular expression varies with gestational term and patient age, especially in the SS group.
Keywords: Ang2, placental implantation, pregnancy, early miscarriage.

DISTICTIVE IMMUNOHISTOCHEMICAL EXPRESSION OF ANG1 IN THE GERMINAL STATUS OF UTERINE PREGNANCIES DISTURBED AT EARLY TERM

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Background. Angiopoietins are part of vasculo- and angiogenesis with an important role in the formation of a functional placental vascular network, capable of supporting the intrauterine development of the embryo and fetus. Disruption of Ang1 expression is associated with the dysregulation of vascular network maturation and stabilization.
Aim of the study. Evaluation of the immunohistochemical expression profile of Ang1 in the choriovillary germinal status of patients with early-term pregnancy disturbances.
Methods and materials. Tissue samples from 62 patients experiencing early-term pregnancy disturbances were obtained via uterine aspiration at the Mother and Child Institute's Perinatal Center in 2020. Patients were categorized into three groups: early spontaneous abortion (ESA) – 8 cases; missed abortions (MA) – 39 cases; and 15 cases of pregnancy termination for social reasons/desire (TS or TD). Each group was further stratified by gestational age (3-5 weeks, 6-9 weeks, and 10-12 weeks). Methods included hematoxylin-eosin staining, immunohistochemistry assessing anti-Tie1. Immunohistochemical expression was evaluated in cytotrophoblasts, syncytiotrophoblasts, endothelial cells, Hofbauer cells, and stroma, graded from 0 to +3. Statistical analysis involved intensity assessment, Spearman's correlations (rs), and Mann-Whitney (U test).
Results. Cytoplasmic immunohistochemical expression ranged from 0 to +2, predominantly negative in controls (68,9%) versus 80% positivity in syncytiotrophoblasts. In the MA group, anti-Ang1 expression rose slightly to +2 (71,7%), peaking at 94,8% in villous syncytiotrophoblasts. ESA group showed significant positivity only in syncytiotrophoblasts (75%), with the rest within 50% positive-negative limits. Statistically significant differences were observed between ESA and control groups in syncytiotrophoblasts (p=0,02) and within MA 10-12 weeks versus MA 3-5 weeks: cytotrophoblasts (p=0,004), vascular endothelium (p=0,02), and cellular stroma (p=0,05); MA 10-12 weeks versus MA 6-9 weeks (p=0,01, p=0,02, and p=0,03). Cytotrophoblasts and vascular endothelium expression negatively correlated with gestational age (GA) (r_s=-0,33/0,02 and -0,32/0,02) and age (r_s=-0,41/0,01 and -0,36/0,01) in the MA group. In ESA 6-9 weeks, there was a strong positive correlation between age and cytotrophoblasts (r_s=0,89; p=0,02), and in ESA total between GA and syncytiotrophoblasts (r_s=-0,62/0,05).
Conclusion. During placental development, Ang1's angiogenic environment differs in pregnancies disrupted early, leading to a relatively weak angiogenic milieu. Cellular expression varies with gestational term and patient age.
Keywords: Ang1, placental implantation, pregnancy, early miscarriage.

PRECLINICAL RESEARCH OF OTOPROTECTIVE DRUGS

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Background. Drug treatment of Sensorineural Hearing Loss (SHL) is characterized by: administration of preparations from various pharmacological groups (nootropics, antioxidants, corticosteroids, etc.), combined prescription of drugs. The mentioned aspects indicate the need to use combined products in SHL pharmacotherapy.
Objectives. Determination of harmlessness and preclinical pharmacological efficacy in SHL of the combined product containing as active principle active principles – taxifolin, glycine (CAF-01).
Material and method. Acute toxicity and subchronic toxicity was performed on 72 mice and 54 male and female white rats by peroral and intraperitoneal administration with determination of physiological, hematological, biochemical and morpho-histological indices. Modeling of SHL induced by administration of gentamicine i/m and the determination of otoprotective effects was performed on 18 white rats with evaluation of Preyer's reflex, impedancemetry and otoacoustic emission (OAE). The research was carried out in collaboration with the Laboratory of Biochemistry and the Laboratory of Tissue Engineering and Cell Culture.
Results. The researched product shows reduced acute toxicity, being classified according to the Acute Toxic Class Method in toxicity class 5 with the average lethal dose (LD50) > 5000 mg/kg - practically non-toxic. In the context of subchronic toxicity, we determined that CAF-01 does not possess cumulative properties. There was a statistically significant increase ($p<0.01$) in the content of SH-groups of proteins and serum albumins. CAF-01 improves the balance between the pro- and antioxidant systems, the importance of dysfunctions in the respective systems for the etiology of SHL is known. The improvement of the Preyer reflex and the OEA parameters ($p<0.01$) was found, which indicates the improvement of the function of the inner ear of the animals that received the studied preparation.
CAF-01 inhibits POL (lipid peroxidation) hyperactivation and increases antioxidant activity by restoring glutathione, antioxidant enzyme activity (catalase, glutathione peroxidase and superoxide dismutase). Through the respective mechanisms, as well as through the elimination of the spasm of the arterioles and capillaries of the vascular stria from the membranous labyrinth, the beneficial otoprotective action on the sensorineural components of the organ of Corti, the auditory nerve, is distinctly outlined.
Conclusions. Estimating the effectiveness of drug treatment presents an innovative and forward-looking element in hearing recovery in patients with hearing loss. An important direction for the treatment of auricular diseases is the development and use in medical practice of combined medicinal preparations, which contain synthetic and natural substances. The researched combined medicinal product shows a high degree of harmlessness, does not lead to the development of toxic processes and at the same time has an otoprotective effect.
Keywords: sensorineural hearing loss, combined drugs, harmlessness, pharmacotherapy.

CURRENT FACTS IN THE TREATMENT OF GAUCHER DISEASE

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Background. Gaucher disease (GD) is a rare metabolic disease with autosomal recessive transmission, caused by the mutation of the GBA gene, which causes a deficient synthesis of the enzyme β-glucocerebrosidase. As result, glucocerebrosides is accumulated throughout the body, especially in the bone marrow, spleen and liver. Three forms of Gaucher disease have been identified, distinguished by the absence or presence and extent of neurological complications. Aim of the study is to evaluate the current therapies for the treatment of Gaucher disease.

Material and methods. Narrative synthesis of specialized literature from scientific databases: *PubMed, Gene Cards, National library of medicine, Google Scholar* and *Hinari* of the last 10 years.

Results. Enzyme replacement therapy is an effective way to treat Type 1 Gaucher disease. Treatment is done via infusion of imiglucerase – a synthetic glucocerebrosidase, to ensure the breakdown of accumulated lipids. Substrate reduction therapy uses a small molecule drug miglustat and eliglustat tartrate that inhibits the first committed step in glycosphingolipid biosynthesis. Chaperone therapy with non-inhibitory chemical chaperones can increase glucocerebrosidase levels and activity in lysosomes. Gene therapy as a potential therapeutic approach for treatment of GD type 1. Ex vivo autologous bone-marrow-derived GD 1 hematopoietic stem cells were genetically corrected by infection with self-inactivating lentiviral vectors expressing WT GBA1 induced by different cellular promoters. Hematopoietic stem cell transplantation, involving the replacement of affected stem cells with healthy stem cells is a treatment that can provide a permanent source of enzyme to people with Gaucher disease and is a considerably less expensive procedure. People with Type 3 Gaucher disease showed no further neurological deterioration. The important limitations of HSCT are the mortality and morbidity associated with the procedure and the non-availability of HLA matched donors.

Conclusions. The treatment of Gaucher disease is a subject under constant research, and research advances offer promising improvement in the life quality of patients with GD. Treatment should be personalized according to the severity of the disease and other associated medical conditions. Enzyme replacement therapy remains the most widely used and well tolerated form of treatment, and patients should be carefully supervised to prevent any unexpected complications.

Keywords: enzyme replacement therapy, Gaucher disease, glucocerebrosidase, lysosomal disease, GBA gene.

ANATOMICAL ARTERIAL VARIANTS OF THE UPPER LIMB

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Background. The terminal branches of the brachial artery, the radial and ulnar arteries have an applicative value. The radial artery is one of the main arteries of the forearm and hand. Usually, the brachial artery bifurcates in the cubital fossa, distal to the inter-epicondylar line of the humerus. Numerous variations are reported regarding the origin and branching patterns of the ulnar and radial arteries. Atypical origins are at the level of the arm, being called brachioradiales and brachiulnares with normal or superficial appearance. Their most common origin is the proximal half of the humerus.
Objective of the study. Evaluation of the prevalence of anatomical variations of the forearm arteries and their clinical relevance.
Material and Methods: The anatomical variations of the ulnar artery and radial artery were studied on 35 adults upper limbs at the Department of anatomy and clinical anatomy of SUMPh „Nicolae Testemițanu", Chisinau, Republic of Moldova. The variability of the arm and forearm arteries, their topography, course and diameters have been documented.
Results. Of the general number of members, 85.7% were male, 14.3% were female, right side was 48.6% and left side 51.4%. Males have an average bifurcation of the brachial artery distal to the elbow line of 29.83 mm, while females have an average bifurcation of 27.25 mm, 53.3% are on the right side and 46.7 % are on the left side. In one case, the bifurcation of the male left limb was proximal 33 mm to the elbow line. Overall average of trifurcation of the brachial artery distal to the elbow line was 35.67 mm. For males, it was 28.80 mm, and for females it was 70.00 mm. On the right side, both male patients had a brachioradiales artery that originated from the axillary artery. Brachiulnares artery was only found in one male case on the right side. The median artery was present in 14 cases, with 7 of them contributing to the formation of the superficial palmar arch, and 7 cases remaining on the forearm.
Conclusion. The present study revealed the significance of brachial artery variations for the composite tissue transfers and replantation in the microvascular surgery. An early diagnosis of the variants of the vascular structures and their pathology, such as aneurysm or thrombosis in the carpal tunnel, leads to a non-surgical approach.
Keywords: median artery, variations, radial artery, ulnar artery, brachioradialis, brachiulnares, superficial palmar arch.

ULTRASONOGRAPHY IN THYROID PATHOLOGY DIAGNOSTICS

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Background. In recent decades, a rejuvenation of the pathology of the thyroid gland has been observed, including thyroid tumors. The pathology of the thyroid gland has been increasing lately in our country, and one of the most valuable, safety, cost-efficient and optimal imaging methods used in thyroid gland examination is the ultrasonography.
Material and Methods. Our study was conducted on 92 patients (16 males and 76 females), aged between 1-72 years, with various functional problems of the thyroid gland, which were examined by ultrasonography in the Republican Diagnostic Center, during the period May 2021-January 2022.
Results. A series of thyroid diseases, among which the thyroid nodules (44.6%), the colloid cysts (7.6%), the autoimmune pathology (3.2%), and others (4.3%) were revealed. Out of the total number of patients diagnosed with thyroid nodules, 22% were males and 78% were females. Unilateral thyroid nodules were marked out in 65.9% of patients, with a male/female ratio of 18.5%/81.5%. Nodules of the right thyroid lobe were determined in 51.9%, with a male/female ratio of 28.6%/71.4% and nodules of the left thyroid lobe were determined in 48.1%, with a male/female ratio of 7.7%/92.3%. Bilateral nodules were present in 34.1% with a male/female ratio of 21.4%/78.6%. Multiple unilateral nodules were marked out in 19.5%. The morphometric parameters of the anteroposterior dimension of the right lobe (RL) of the thyroid gland varied between 1.03-2.34 cm, with a mean value of 1.66±0.27 cm, and that of the left lobe (LL) varied between 0.87-4.03 cm, with a mean of 1.66±0.37 cm. The transverse dimension of the RL were 0.68-2.03 cm, with a mean of 1.45±0.31 cm, and the transverse dimension of the LL were 0.83-8.6 cm, with a mean of 1.51±0.80 cm. The longitudinal dimension of the RL was 1.60-4.99 cm, with a mean value of 3.69±0.49 cm, and that of the LL was 1.64-4.96 cm, with a mean of 3.59±0.55 cm. The thyroid isthmus values varied between 1.5-6.6 mm, with a mean of 3.03±0.68 mm.
Conclusions. Both benign and malignant thyroid gland diseases had a higher rate in females, compared to males. Almost in a half of the examined patients were established thyroid nodules, with a twice-higher prevalence of the unilateral nodules and a slight prevalence of the nodules of the right thyroid lobe.
Keywords: thyroid gland, thyroid nodules, ultrasonography, morphometry.

MORPHOMETRIC PARAMETERS OF THE FACIAL NERVE TRUNK

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Background. In parotid tumor ablation, maxillo-facial surgery and mastoidectomy for preservation of the facial nerve trunk (FNT) integrity it is very important to identify the facial nerve (FN) course on its premandibular segment, but no less important are its morphometric parameters. The aim of the study was to determine the length and widths of the FNT on its premandibular segment, depending on the facial nerve branching pattern.
Material and methods. The research was conducted on 75 hemifaces (59 males/16 females) of adult formalized cadavers from the Department of anatomy and clinical anatomy of Nicolae Testemitanu State University of Medicine and Pharmacy of the Republic of Moldova. All the hemifaces were dissected and the course of the facial nerve was followed until the level of the facial trunk division into its primary branches. The morphometry of the FNT was carried out on all the samples and the obtained data were statistically analyzed using descriptive and inferential methods.
Results. Three main variants of the FNT course were characteristic on its premandibular segment: descending, horizontal and ascending one. Seven branching patterns of the FN were established. The mean length of the FNT in males was 11.3 mm (5-21 mm), and in females – 10.4 mm (5-16 mm); p=0.289. The same length of 11.1 mm of the FNT was determined on the both sides of the head, but on the right side the length varied from 5 mm to 18 mm, and on the left side it varied from 5 mm to 21 mm; p=0.981. Depending on the branching pattern the length of the FNT was as follows: type I – 12.2±3.33; type II – 11.0±2.54; type III – 11.3±2.93; type IV – 10.3±3.85; type V – 11.5±2.08; type VI – 10.1±2.06; atypical type NI – 11.5±3.11; p=0.578. The width of the FNT depending on the FN branching pattern was: type I – 2.7±0.49; type II – 2.6±0.37; type III – 2.7±0.31; type IV – 2.8±0.55; type V – 2.8±0.34; type VI – 2.7±0.57, atypical type NI – 3.0±0.80; p=0.950.
Conclusions. The mean length of the FNT in males was higher than in females. The highest length was established in type I and the lowest one – in type VI. The thickest trunk was determined in atypical type NI, and the thinnest one – in type II.
Keywords: facial nerve trunk, branching pattern, length, width, morphometry.

THE MORPHOFUNCTIONAL PECULIARITIES OF THE ESOPHAGO-GASTRIC JUNCTION IN CLINICAL ASPECT

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Background. The esophago-gastric junction (EGJ) has a physiological sphincter that enables the passage of the alimentary bolus and prevents the gastroesophageal reflux (GER). The medical community highlighted this junction as an important clinico-anatomical entity, due to its morphopathological substrate for several diseases, one of them being the gastroesophageal reflux disease (GERD). In order to determine the pathogenic link between the morphological structure of the EGJ and onset of the GERD, the patients were examined by paraclinical methods.
Materials and methods. The study was carried out on 250 patients, hospitalized at the MSPI CRH "Timofei Mosneaga" during the years 2019-2022. The endoscopic and radiological results were taken from the observation sheets of the patients and were statistically analysed.
Results. The patients included into the study were aged between 19-73 years (with a mean age of 55.5±2.3 years). The endoscopic examination was carried out on 121 patients (48.4%) and the radiological examination on 129 (51.6%). By endoscopic examination, non-erosive GERD was established in 62.8% of patients (with a mean age of 41.8±0.8 years) and erosive GERD – in 37.2% of patients (with a mean age of 48.02±0.5 years). The diagnosis of the erosive GERD was established depending on the degree of the mucosal changes. Non-confluent unique erosions were identified in 22.2% (degree I); confluent erosions with partial lesion of the mucosa – 33.4% (degree II); ulcerative lesions of the lower 1/3 of the esophageal mucosa – 24.4% (degree III); chronic peptic ulcer of the esophagus – 20% (degree IV). The incompetence of the inferior esophageal sphincter (IES), diagnosed endoscopically had the following rate: degree I – 28.3%, degree II – 33.9% and degree III – 37.8%. By barium sulfate x-ray examination were determined the types of the GER: high level (up to the C6 vertebra) – in 29.4%; middle level (up to T6) – 47.3%, and low level (up to T11-12) – 23.3%.
Conclusions. GERD is onset in case of incapacity of the anti-reflux mechanisms. In 2/3 of the endoscopically examined patients, a II-nd and III-rd degree failure of the IES was determined; in 1/2 of the radiologically examined patients a medium degree of the GER; in 1/4 – a high degree was revealed. Both endoscopic and radiological, diagnostic methods, are up-to-date and useful in GERD diagnostics.
Keywords: esophagogastric junction, inferior esophageal sphincter, gastroesophageal reflux disease.

TOPOGRAPHIC AND MORPHOMETRIC FEATURES OF THE AXILLARY ARTERY

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Background. Due to its large diameter and low risk of thrombosis, the axillary artery (AA) is lately used in carrying out the coronary angiography. Taking into consideration that the distal portion of the AA is the most frequently punctuated, among the complications that may occur at that level during its catheterization is the median nerve injury. The topographical relations of the median nerve towards the axillary artery and its morphometric parameters depending on gender were studied.
Materials and methods. It is a retrospective, descriptive study. The study group included 70 upper limbs taken from formalized adult human cadavers of both genders (37 males and 33 females), aged between 61-80 years, selected from the Department of anatomy and clinical anatomy of *Nicolae Testemitanu* SUMPh. By anatomical dissection, the syntopy of the AA in relation to the adjacent neurovascular elements was studied. For the measurements of the axillary artery dimensions, an anatomical probe with measuring units, a ruler, a protractor and a vernier caliper were used. The length of the axillary artery, its proximal and distal external diameters (ED), were determined.
Results. The mean length of the axillary artery was 9.2±0.16 cm and the median was 9.0 cm; in males (M) the mean length was 9.7±0.19 cm, in females (F) – 8.6±0.21 cm. The proximal ED of AA was 6.13±0.13 mm, the median – 6.0 mm; M – 6.54±0.17 mm, F – 5.67± 0.15 mm. The distal ED of AA had a mean of 5.52±0.11 mm, the median – 5.50 mm; M – 5.82±0.16 mm, F – 5.17±0.13 mm. At the level of union of the median nerve roots, the nerve was positioned anterolaterally to the axillary artery in 81.4% (51.4%/30% – male/female), medial to it – in 15.8% (4.4%/11.4% – male/female) and anteriorly to the brachial artery – in 2.8% of females.
Conclusions. The morphometric indices of the axillary artery in males had higher values than in females. The median nerve was most frequently positioned anterolaterally to the axillary artery, predominantly in males, and medial to it – predominantly in females. The relations of the median nerve towards axillary artery and knowledge of its dimensions are of great clinical significance for both surgeons and imaging specialists.
Keywords: axillary artery, morphometric parameters, median nerve, catheterization.

HEPATIC VEINS IN ANATOMICAL-SURGICAL ASPECT

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Background. Currently, complex liver pathology has imposed an increased need for surgical interventions at this level, which has required a detailed knowledge of hepatic blood circulation. An important place in this study belongs to the efferent venous circulation. Under normal conditions, the liver accumulates about 20% of the circulating blood volume and directs up to 1,200 ml of blood per minute into the inferior vena cava, which represents 50% of the breast volume returned through this vein. The advances made lately in knowing the anatomical distribution of the components of the hepatic, arterial and venous vascular tree have allowed a systematization of knowledge in the field of liver segmentation.The purpose of the present paper is to study the anatomical and surgical peculiarities of hepatic veins.
Material and methods. To establish the morphology of hepatic veins, the study was performed on a number of 11 macroscopic liver preparations. Macropreparations were taken from cadavers of both sexes who died at different ages, in which no diseases of the hilar or cavale area of the liver.
As working methods were used: plastic injection, which has solvent dust and green, yellow, blue and red paint, and corrosion step in hydrochloric acid solution.
Results. The trunks of the hepatic veins in all given cases are located intraorganically and flow into the inferior vena cava in its subdiaphragmatic portion. Depending on the size of the veins, large hepatic veins with a diameter of 7-18 mm and small diameters of 2-6 mm can be highlighted. The number of hepatic veins flowing into the inferior vena cava is variable.
Conclusions. The casts of the venous elements of the liver, obtained by polychrome injection and corrosion are very informative.
Keywords: liver, hepatic veins, plastic injection, corrosion.

ARTERIAL NUTRIENT FLOW OF THE LIVER IN PATIENTS WITH LIVER CIRRHOSIS

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Background. The progressive evolutionary forms of liver cirrhosis are especially characterized by the damage to the hepatic arterial.circuit. Although the blood flow through the hepatic artery is much lower than through the portal vein, the arterial blood provides the liver with more than 50% of the oxygen required. The hepatic artery constitutes the nutritional vasculature, reprezenting a branch of the celiac trunk that brings blood enriched with O_2 to the liver. The quadrate lobe is vascularized by the middle branch of the hepatic artery, and the caudate lobe by the right and left brances of the hepatic artery. The arteriolar sphincters are positioned anterior to the passage of arterial blood in the sinusoids.
Material and method. A study was conducted, including 32 patients with liver cirrhossis – 22 men and 12 women, average age - 48±0,37 years. The calculated linear parameters in the hepatic artery by Doppler quantification.
Result. The arterial circuit in 65% of patients included the dilation of the diameter of the hepatic artery, which was associated with a decrease in diastolic velocity (38%) and an increase in the volume velocity of blood flow in the studied segment (57%). A linear increase in blood flow by approximately 70% was revealed. The volume of blood flow speed in the hepatic artery was 269±115 ml/min. As the pathology progressed, the flow volume also increased: from 785±0.5 ml/min to -979±138 ml/min.
Conclusions. 1.The change in blood flow in the hepatic artery represents an informative hemodynamic parameter, which subsequently invokes the process of severe liver damage. 2.In these patients, the reduction of the elasticity and tone of the large arteries, the decrease in the filling of the small and medium caliber arteries of the liver with the modification of the gradient of the arterial circuit during systole was highlighted.
Keywords: liver cirrhosis, hepatic artery, volume velocity, diastolic velocity.

THE LESIONS TO HARD DENTAL TISSUES IN CHILDREN WITH CYSTIC FIBROSIS

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Background. Cystic fibrosis is a genetic disease that develops as a result of a mutation in a gene located on the long arm of chromosome 7 (Southern et al., 2007). The disease is based on a violation of the salt metabolism of epithelial cells of all exocrine glands of the body. Hyposalivation leading to stagnation of bacterial biofilm and disruption of the buffering properties of saliva lead to an increase (93% of cases) of dental caries in patients with cystic fibrosis (Castaldo et al, 2020). Among non-carious lesions, systemic enamel hypoplasia is the most common (Sinha et al, 2021).
Materials and methods. 29 children affected by cystic fibrosis with a moderate form (age 4-9 years; 17 males and 12 females) were examined at the Institution of Mother and Child. The prevalence of caries was calculated by determining the proportion of children with caries out of the number of those examined. Clinical examination of patients included of a survey, visual diagnostics, probing, as well as determining the hygienic status of the oral cavity, determining the prevalence of carious and non-carious lesions of hard dental tissues.
Results. Excessive plaque deposits indicate poor oral hygiene. Systemic hypoplasia was in 28% (8) cases. The study found that children with cystic fibrosis had a high prevalence of dental caries 93% (27) cases. Local hypoplasia was present in 10% (3) cases. The high prevalence of dental lesions may be related to the metabolic disease and the long-term pharmacological therapy to which they are exposed.
Conclusions. In patients with cystic fibrosis, the number of carious teeth exceeds the number of teeth with fillings, which indicates a low level of dental care. The results obtained rightfully suggest that it is necessary to develop and actively implement a set of treatment and preventive measures aimed at increasing the effectiveness of dental care and preserving the functions of dental organs and tissues in children with cystic fibrosis.
Keywords: cystic fibrosis, hypoplasia, caries.

THE INTERRELATION BETWEEN SPECIFIC AND NON-SPECIFIC IMMUNITY IN THE PATHOGENESIS OF ACUTE HERPETIC STOMATITIS

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Background. Acute herpetic stomatitis is accompanied by secondary immunodeficiency, associated with a functional insufficiency of cells, a decrease in their number or an imbalance of the components of the immune system.
The study aims to describe the role of immunity in the evolution and manifestation of acute herpetic stomatitis.
Materials and methods. A literature review used 45 scientific articles from PubMed, UpToDate, and NCBI, only works published in the last five years were selected.
Results. In herpetic stomatitis, the body's non-specific protective factors are the first to interact with the viral agent. Tissue macrophages are the cells involved in the immune response to the penetration of the viral agent into the microorganism, participating in both the specific and non-specific immune response. These cells capture and engulf pathogens, presenting antigenic proteins to T and B lymphocytes, which initiate the development of cellular and humoral immune responses. Macrophages respond to viral invasion by rapidly producing anti-inflammatory cytokines due to activation of neutrophils, monocytes, macrophages, NK cells and W lymphocytes, including the specific immune response. The concept of "oral tolerance" is based on a complex system of interactions between oral microflora, immunological protection and non-specific barrier mechanisms. The subepithelial lymphoid tissue represents a protective barrier against the penetration of foreign agents. The primary role is attributed to a protein (lysozyme), which acts as a mucolytic enzyme.
Conclusions. The state of the body's immune system plays a vital role in the clinical manifestation of HVS-1 infection, which influences the development of the infectious process in herpes infection by changing the proportions of viral components. The immune response of the microorganism is directed both against virus-infected cells and against the virus itself. It is determined by two defence mechanisms: specific immunity formed after the disease or artificial immunisation and natural resistance.
Keywords. Acute herpetic stomatitis, specific immunity, non-specific immunity.

SPECIFIC FEATURES OF THE INTERNAL ACOUSTIC MEATUS

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Background. The anatomical specific features of the internal acoustic meatus (IAM) are of high clinical significance in surgical access of the medial cranial fossa and in otologic surgery. The purpose of our study was to establish the anatomical variants and morphometric parameters of the internal acoustic opening (IAO) and of the IAM for a better comprehension of the course of the meatal segment of the facial nerve.
Material and Methods. The research was carried out on 82 dry temporal bones (41 right and 41 left) of unknown age and gender. The bones belonged to the Department of anatomy and clinical anatomy of Nicolae Testemitanu SUMPh. The external shape, length and angles that formed between the longitudinal axis of the temporal bone pyramid (LAP) and the anterior and posterior walls of the IAM were examined and measured by a ruler, a protractor and a vernier caliper. The descriptive and inferential methods of statistical analysis were used.
Results. The shape of the IAO varied from transverse and vertical oval shapes, to heart-like, semioval and quadrangular ones. In some cases, a partial or total septum of the IAM were revealed. The mean value of the transverse diameter (TD) of the IAO was 7.7±2.11 mm. On the right side the mean was 8.2±2.22, and on the left – 7.2±1.89 mm, p=0.031. The mean value of the vertical diameter (VD) of the IAO was 5.3±1.43 mm. On the right bones the mean was 5.6±1.58, and on the left ones – 5.0±1.22 mm, p=0.082. The mean length of the IAM was 10.1±2.83. On the right side the mean was 10.5±2.96, and on the left – 9.7±2.67 mm, p=0.214. The mean value of the angle that forms between the anterior wall of the IAM and the LAP was 21.4±13.67°. On the right side the mean was 22.2±14.62°, and on the left – 20.5±12.78°, p=0.564. The mean value of the angle formed between the posterior wall of the IAM and LAP was 82.4±8.02°. On the right bones the mean was 84.3±7.93, and on the left ones, it was 80.5±7.76°, p=0.032
Conclusions. Both the IAO and the IAM were variable. The morphological variants were characteristic for both sides' samples. All the examined parameters were higher on the right temporal bones.
Keywords: temporal bone, internal acoustic opening, internal acoustic meatus, morphometry.

TREATMENT IN BREAST CANCER USING THE CRISPR/CAS9 SYSTEM

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Background. Breast cancer is the leading cause of death in the oncological population of female gender and the second most prevalent cause of overall death in the United States of America and the third most prevalent cancer death in Europe. There is a trend for breast cancer in caucasian, hispanic and asian women. Numerous methods of treatment are accepted – chemotherapy, molecular targeted therapy, radiotherapy, immunotherapy, phototherapy and surgical interventions (lumpectomy, mastectomy). The genome editing methods – clustered regularly interspaced short palindromic repeats (CRISPR) technology is developed based on the protection systems found in bacteria, the one which is useful in treating cancer is the Cas9 protein thus defining the CRISPR-Cas9 system. It's main components are crRNA and tancrRNA (sgRNA) with the Cas protein.
Material and methods. We used the PubMed database in order the collect the information. After introducting the key-words „CRISPR-Cas9" and „breast cancer" we revealed up to 571 sources. We have reviewed the first 100 sources and have studied 18 of them. One source was added non-sistematically. Overall we have reviewed 19 sources.
Results. The CRISPR-Cas9 system can be delivered to the target cells via protein, lipid, polymer and inorganic based nanocarriers. Other method of delivery is via the lentiviral/adenoviral vectors. The most efficient ones are the gold nanocarriers (inorganic). The genome editing technology is based on plasmid systems that act via interference and activation thus making them useful for identifying biomarkers and in the diagnosis of breast cancer.The main genes that are targeted by the CRISPR-Cas9 system in breast cancer are BRCA1, BRCA2, MYC, CDK9, UBR5, ZNF319 kinome (HER2, PI3KCA and FGFR), CXCR4+CXCR7 (CXCL) and other tumour supressor genes (p53, PTEN, RB1 and NF1). The genes involved in metabolic pathways are upregulated in a secondary manner because of alterations in canceromatous states. Carcinogenesis, metastasis and resistance to drugs and radiotherapy is reduced after using this treatment method.
Conclusions. CRISPR-Cas9 system is efficient in breast cancer treatment and diagnosis. It has perspectives in order to be used as an adjuvant method in this condition without regard to it's high costs.
Keywords: CRISPR-Cas9, breast cancer, drug resistance, radioresistance.

THE EVALUATION ON *ANGUSTIFOLIA* LAVENDER EXTRACTS ACTION ON INDICES OF ANTIOXIDANT SYSTEM IN RATS BLOOD SERUM DURING CHRONIC INDUCED TOXICITY

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Background. In recent years, the extracts from medicinal plants gained an increased interest for wound healing. Thus, approximately 450 plant species have been identified with wound healing properties. The current knowledges about the wound healing process include coagulation, inflammation, proliferation, formation and accumulation of fibrous tissue, collagen deposition, epithelization, wound contraction with the formation of granulation tissues, remodeling and maturation [1].

Material and methods. As raw material were used wastes of the plants, left from the process of essential oil extraction. [2]. The chronic toxicity was induced by oral administration of *Lavandula Angustifolia* extracts to 18 Wistar rats divided into 3 groups. The LA extract was diluted with water and administered daily at the same time in successive doses for each separate group: the group I – 500mg/kg; the group II - 1000 mg/kg; and group III served as control, to which was administered just water without the investigated substance. Indices of the antioxidant system were apreciated: total antioxidant activity, catalase and superoxide dismutase (SOD). Statistical analysis was performed using IBM SPSS Statistics 17.

Results. The analysis of the results of the antioxidant system indices in the blood serum of rats with chronic induced toxicity, determined a statistically significant increase in both experimental groups, compared to the control group. The antioxidant system indices increased with 12% in group I ($p < 0.05$) and with 19% in group II ($p < 0.001$). It was also found that SOD enzyme activity showed a significant increase in group I – 10% ($p < 0.005$), while the catalase activity was significantly higher in both experimental groups compared to control ($p < 0.05$), in group I with 26% and in group II with 29%.

Conclusion. Lavander extracts present the antioxidant potential and needs to be studied further.

Keywords. Chronic toxicity, *Lavandula Angustifolia*, extract, antioxidant system.

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NERVOUS TISSUE DAMAGE IN PATIENTS INFECTED SARS-COV-19

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Background. The Covid-19 pandemic has become a global disaster with many dire consequences for the entire population. SARS-CoV-2 had a negative impact on the functionality of organ systems and homeostasis, while the new viral infection also affected nervous tissue. The incidence of central nervous system involvement is 25% of all reported cases of COVID-19. Pathogenetic pathways underlying damage to nervous tissue can be direct, through the olfactory bulb, hematogenous, lymphogenous, as well as indirect, suggesting the occurrence of some functional disorders of the central nervous system through a cytokine storm or an enhanced immunological response induced by the virus.
Materials and methods. Was analyzed retrospectively the clinical and neuropathological findings of the patients who were admitted in CMH ,,Arhanghel Mihail" between January 2022 and the end of December 2022. Neurological syndromes developing after the disease, which were likely to be associated with COVID-19, were included in the group of interest. The age, gender, neurological syndromes, post-COVID-19 period of persistence of neurological complications were determined.
Results. In a case series of 483 patients infected with COVID-19, the female gender predominates (67.2%) and the average age being of 66,56±2,3 years. The most common neurological consequence was post-COVID fatigue syndrome (362 patients), with the incidence of peripheral nervous system involvement being 65%. In most patients, a period of 3 to 6 months passed after acquiring the infection (302 patients). Other neurological manifestations associated with COVID-19 and persisting up to 1 year after infection were insomnia (56 patients), encephalopathy (96 patients), anxiety (76 patients), sensory disturbances of the lower extremities (14 patients).
Conclusions. Infection with SARS-CoV-2 can affect nerve tissue, and the consequences can last for a long time. Changes can occur at all levels: in the case of our study, the PNS was most affected (65%), followed by the VNS (21%) and the CNS with 14%.
Keywords: SARS-CoV-2, nervous tissue, neurological syndromes, neurological complications.

HYPERTROPHIC GINGIVITIS DURING ORTHODONTIC TREATMENT. CLINICAL CASE.

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Background. In the process of human evolution, the stomatognathic system has undergone significant changes, which led to the development of various pathological types of occlusion and tooth position abnormalities. As a treatment, different types of orthodontic appliances are used, and one consequence is hypertrophic gingivitis. Hypertrophic gingivitis is a chronic pathological process of proliferative type, with the involvement of the connective tissue and the gingival fibromucosa, not involving the bone tissue, but with the loss of the anatomical-morphological configuration of the gum presenting an aesthetic defect that has a negative impact on health oral cavity and the patient's quality of life.
The purpose of the work. Diagnosis and treatment of hypertrophic gingivitis induced by fixed appliance orthodontic treatment.
Materials and methods. Case presentation. Patient A.V., B./16 years, addressed the SRIMC, presenting aesthetic and functional complaints. Following the clinical examination, the diagnosis of chronic hypertrophic gingivitis was established.
Results. There are several causes to develop hypertrophic gingivitis, one of which is determined by the pressure of the orthodontic structure on the soft tissues of the periodontium, causing inflammation that becomes chronic. Another variant is also possible in which the main reason for the inflammatory reaction is enzymes and toxins produced by microorganisms from bacterial plaque accumulations. The treatment started with: 1. improvement of the main symptoms; 2. professional oral hygiene; 3. oral baths with chlorhexidine 0.06%, for one week; 4. administration of anti-inflammatory drugs and agents that normalize vascular tissue permeability: 5% butadiene ointment, 3% acetylsalicylic acid ointment, indomethacin in the form of gum applications; 5. electrophoresis.
Conclusions. Hypertrophic gingivitis during orthodontic treatment is induced by the response reaction of the gingival tissues to the fixed orthodontic appliance and poor oral hygiene. By timely prevention and treatment using drugs and physiotherapy, further complications can be avoided, as well as the structure and functionality of the periodontal tissues can be completely normalized.
Keywords: hypertrophic gingivitis, orthodontic treatment, bacterial plaque, aesthetic defect.

THE CARIOUS EXPERIENCE OF THE FIRST PERMANENT MOLAR IN A GROUP OF CHILDREN AGED BETWEEN 7-14 YEARS

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Background. The permanent first molar is the most vulnerable to caries due to its position, coronal morphology and early eruption in the oral cavity. The purpose of the study is to determine the prevalence of dental caries in the permanent first molar in a group of children aged between 7-14 years.
Materials and methods. A statistical study was carried out over a period of 1 year on a group of 53 children aged between 7-14 years. Each patient was questioned and examined, noting the dental status of the temporary and permanent teeth. Also, the COE index was calculated for each patient, noting the number of carious teeth and the number of extracted and filled teeth. The data were recorded and processed statistically with the Microsoft Excel program.
Results. The 53 children included in the study had a total of 184 erupted permanent first molars on the arch. Of these, 43.4% (80) were free of caries, 8.2% (15) had fissure caries, 21.7% (40) – simple caries, 2.7% (5) – complicated caries and 24% (44) – fillings. Regarding the gender distribution of caries of the first permanent molars, a predominance of boys is observed. However, in recent centuries, an important decrease in the prevalence of dental caries and the severity of molar caries in children can be observed in developed countries and even in countries with a disadvantaged socio-economic situation.
Conclusions. The particular vulnerability to caries of the permanent first molar imposes the need for permanent supervision, the rigorous application of dental caries prevention methods, the sealing of fissures and pits, as well as early therapeutic intervention. Since the prevalence of dental caries is very high for patients under the age of 10, it is necessary to adopt caries prevention strategies applied as early as possible.
Keywords: Dental caries, permanent first molar, prevalence, early eruption.

PSYCHOGENIC RISKS OF OBESITY

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Background. In many textbooks, the risk factors of obesity, the pathogenesis, how it affects the organ systems, are addressed, and less are analyzed the psychogenic risks of obesity on patients.
Materials and methods. The study was carried out based on 30 bibliographic sources from the databases: NCBI, PubMed, EMRO, Medscapes.
Results. The disease of obesity is associated with a significant psychosocial burden. Many individuals who have obesity also struggle with issues related to their mood, self-esteem, quality of life, and body image. This emotional distress likely plays a role in treatment seeking but also can impact successful treatment. With reference to the Republic of Moldova, 56% of adults (18 years +) are overweight, including 23% are obese. And the summary report data of the study assessing the health behaviors of school-age children (2014) show that 11% of children are overweight, including 2.2% – obese. Previous research suggests a relationship between excess body weight and depression. Persons with extreme obesity, for example, are almost five times more likely to have experienced an episode of major depression in the past year as compared with those of average weight. Disordered eating is common among persons with obesity. Many patients presenting for weight loss treatment report that they engage in eating for emotional reasons; others report having difficulty controlling the frequency of their eating, portion sizes.
Obesity also negatively impacts health-related quality of life. Individuals often report significant difficulties with physical and occupational functioning.
Persons who are obese are frequently subjected to discrimination in several settings, including educational, employment, and even health care settings. This persons are less likely to complete high school, are less likely to marry, and typically earn less money compared with persons of average body weight.
A small minority of individuals with obesity actively abusing substances. Approximately 10% of candidates with obesity report a history of illicit drug use or alcoholism, a percentage higher than seen in the general population.
Conclusions. Knowledge of the psychogenic risks of obesity is of significant importance in taking preventive measures and appropriate treatment of patients.
Keywords: Obesity, psychosocial burden, depression, eating disorders, quality of life.

Summary

Abstracts