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

LABORATORY OF TISSUE ENGINEERING AND CELL CULTURES
HUMAN TISSUE BANK, ORTHOPEDICS AND TRAUMATOLOGICAL HOSPITAL

The Materials of the National Scientific Conference with International Participation „CELLS AND TISSUES TRANSPLANTATION. ACTUALITIES AND PERSPECTIVES. THE 4th EDITION.”

Chisinau, March 20-21, 2026

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AGENDA

Registration

March 20, 2026

Opening ceremony 15:00 - 15:20

Ceban Emil, Minister of Health of the Republic of Moldova, MD, PhD, Academician, Professor.
Romanciuc Grigore, Head of Transplant Agency, Republic of Moldova.
Stepa Serghei, MD, PhD, Director of the Clinical Hospital of Orthopedics and Traumatology, Republic of Moldova.
Nacu Viorel, MD, PhD, MPH, Head of Human Tissue Bank at Clinical Hospital of Orthopedics and Traumatology, Responsible for Laboratory of Tissue Engineering and Cell Cultures at SUMPh Nicolae Testemitanu, Republic of Moldova.
Andrei Nica, MD, PhD, Head of Human Tissue Bank at Clinical Hospital Colentina, Romania.

DAY ONE – March 20, 2026

PLENARY MEETING

1. **15:20-15:40. Viorel Nacu, Serghei Stepa, Igor Cospormac, Adrian Cociug, Vitalie Cobzac, Tatiana Timbalari.** Thirteen Years of Activity of the Human Tissue Bank at Clinical Hospital of Orthopedics and Traumatology. *Chisinau, Republic of Moldova.*

2. **15:45-16:05. Andrei Nica, Bogdan Camin, Gheorghe Iacob, Roxana Malaescu, Simona Stoica, Daniela Ciclosan, Ionut Teodoriu.** Management of Human Tissue Grafts from Retrieval to Distribution. *Bucharest, Romania.*

SESSION 1

Oral presentations

Moderators: Ficai Anton, *PhD, Professor, (Romania);* **Romanciuc Grigore,** MD, PhD, *(Republic of Moldova)*

1. **16:10-16:20. Alexandra Aparece, Mariana Jian, Vitalie Cobzac, Ana-Maria Nacu, Dumitru Hincota, Grigore Verega, Viorel Nacu, Alina Stoian.** Lymphatic Tissue Engineering: Experience of the Laboratory of Tissue Engineering and Cell Culture at *Nicolae Testemitanu* State University of Medicine and Pharmacy, *Chisinau, Republic of Moldova.*

2. **16:25-16:35. Vitalie Cobzac, Stefan Cojocari, Mariana Jian, Alina Stoian, Ana-Maria Nacu, Ludmila Motelica, Roxana Trușca, Anton Ficai, Viorel Nacu.** Human Collagen-Based Hydrogel with Zinc Oxide Nanoparticles for Articular Cartilage Engineering. *Chisinau, Republic of Moldova, Bucharest, Romania.*

3. **16:40-16:50. Mariana Jian, Denisa Ficai, Ludmila Motelica, Ovidiu Oprea Cristian, Vitalie Cobzac, Ana-Maria Nacu, Andrei Mostovei, Roxana Trusca, Anton Ficai, Viorel Nacu.** Advanced Biomaterials for Bone Regeneration. *Bucharest, Romania. Chisinau, Republic of Moldova.*

4. **16:55-17:05. Maria Mihalachi-Anghel, Galina Spinosu, Nicolae Bacinschi.** Immunosuppressive Agents Used in Organ Transplantation. *Chisinau, Republic of Moldova.*

5. **17:10-17:20 Adrian Cociug, Olga Macagonova**, **Lilia Dumbraveanu**, **Vitalie Procopciuc, Valeriu Cusnir jr.**, **Vitalie Cusnir**, **Valeriu Cusnir**, **Viorel Nacu.** Evaluation of Corneal Graft Quality in a Human Tissue Bank: a 12-year Retrospective Study (2013-2025). *Chisinau, Republic of Moldova.*

SESSION 2

Moderators: Babuci Angela, *MD, PhD (Republic of Moldova)***, Palarie Victor**, *MD, PhD (Republic of Moldova)*

1. **17:25-17:35. Maria Iacubitchii, Eugeniu Bendelic, Tatiana Taralunga, Viorel Nacu**. From Cells to Flow: Bioengineering Schlemm's Canal Endothelium as a Novel Therapy for Glaucoma. *Chisinau, Republic of Moldova.*

2. **17:40-17:50. Tatiana Taralunga, Elena Scheghelskaya, Maxim Taralunga, Adrian Vicol, Maria Iacubitchii, Ala Paduca, Eugeniu Bendelic, Viorel Nacu.** Methods of Glaucoma Induction in Experimental Models. *Chisinau, Republic of Moldova.*

3. **17:55-18:05. Dionisie Cebotari, Evgheni Grusac, Silvia Stratulat, Olga Garbuz, Veronica Sardari.** Metabolic Rewiring in Prostate Cancer *via* Zinc-Induced Mitocondrial Aconitase Inhibition: Perspectives for Post-Oncological Tissue Transplantation. *Chisinau, Republic of Moldova.*

4. **18:10-18:20. Camelia-Mihaela Zara-Danceanu, Luminita Labusca, Eusebiu Viorel Sindilar, Daniel-Dumitru Herea, Valentin Nastasa, Mihai Mares, Aurelian Sorin Pasca.** Magnetic Nanoemulsions Loaded with Dexamethasone and Ascorbic Acid Demonstrate Therapeutic Efficacy in Rats with Collagenase-Induced Osteoarthritis. *Iasi, Romania.*

DAY TWO – March 21, 2026

Session 1
Poster session
Moderators: Denisa Ficai, *PhD (Romania)*, Nacu Viorel, *MD, PhD*
8:00-9:00

1. **Babuci Angela, Midrigan Corina, Zorina Zinovia, Bendelic Anastasia, Ostahi Nadejda, Botnari Tatiana, Botnaru Doina, Lehtman Sofia, Motelica Gabriela, Nastas Liliana.** Correlation Between the Width of the Facial Nerve Trunk and Greater Auricular Nerve. *Chisinau, Republic of Moldova.*
2. **Lehtman Sofia, Babuci Angela, Motelica Gabriela, Zorina Zinovia, Dandara Mihaela, Procopenco Olga.** Spectral Analysis of the Submandibular Gland Sialoliths. *Chisinau, Republic of Moldova.*
3. **Rabbi Syeda, Badalyan Albert, Babuci Angela.** Tissue Engineering and Biofabrication- Future of Cardiac Regeneration. *Chisinau, Republic of Moldova.*

4. **Abaev Eital, Babuci Angela, Zorina Zinovia.** Role of Cellular and Molecular Factors in Alveolar Ridge Remodeling after Tooth Loss**.** *Chisinau, Republic of Moldova.*
5. **Sirbu Aureliu, Creciun Nicolae, Budaretchi Ion, Babuci Angela.** A Case of Excessive Tortuosity of the Lienal Artery. *Chisinau, Republic of Moldova.*
6. **Ghelan Robert, Said Jasmin, Mostovei Andrei.** Particularities of Diagnosis and Surgical Management of Radicular Cysts. *Chisinau, Republic of Moldova*.
7. **Botnari Tatiana, Zorina Zinovia, Babuci Angela, Cealan Andrei, Catereniuc Ilia, Botnaru Doina, Ostahi Nadia.** Kinking Syndrome of the Abdominal Aorta: Case Presentation. *Chisinau, Republic of Moldova*.
8. **Zorina Zinovia, Babuci Angela, Bendelic Anastasia, Botnari Tatiana, Botnaru Doina, Ostahi Nadia, Ababii Daniela.** Anatomo-Topographic Aspects of the Brachial Artery and its Branches Variability Depending on Gender and Laterality**.** *Chisinau, Republic of Moldova*
9. **Racila Gheorghina, Zorina Zinovia, Babuci Angela.** Arteriovenous Malformation: Case Study. *Chisinau, Republic of Moldova.*
10. **Armasula Mihaela, Zorina Zinovia.** Brainstem in Morpho-Clinical aspect. *Chisinau, Republic of Moldova.*
11. **Zorina Zinovia, Grișco Andrei, Babuci Angela.** Trigger Point Therapy in Myofascial Pain Syndrome. *Chisinau, Republic of Moldova.*
12. **Alexandr Gaitur, Nikoletta Mrug, Angela Babuci.** Prevalence of Occult Femoral Hernias in Women Undergoing Inguinal Hernioplasty: A Statistical Analysis. *Chisinau, Republic of Moldova.*
13. **Tcaci Anastasia, Yagudaev Ilana.** Morphological Specific Features of the Buccal Nerve. *Chisinau, Republic of Moldova.*
14. **Portnoi Elena, Brinza Dumitru, Foca Ecaterina, Adam Consuela, Pinzaru Cristina, Stratan Valentina, Fulga Veaceslav.** Tumor-Infiltrating CD79α Positive Lymphocytes in Breast Cancer. *Chisinau, Republic of Moldova.*
15. **Portnoi Elena, Brinza Dumitru, Foca Ecaterina, Adam Consuela, Pinzaru Cristina, Stratan Valentina, Fulga Veaceslav.** PAX5 Expression in Breast Carcinoma. *Chisinau, Republic of Moldova.*
16. **Vicol Catalina, Nacu Viorel.** Cellular Therapy in Diabetic Retinopathy. *Chisinau, Republic of Moldova.*
17. **Ilies Elizaveta, Nacu Viorel.** Creation of Artificial Liver: Technologies, Directions. *Chisinau, Republic of Moldova*.
18. **Bour Madalina, Cojocaru Cristina, Bour Alin.** Benign Thyroid Nodule Mimicking Malignancy with Compressive Symptoms: Importance of Timely Surgical Management. *Chisinau, Republic of Moldova***.**
19. **Grusac Evgheni, Pantea Valeriana, Railean Nadejda, Stratulat Silvia, Sardari Veronica.** The Role of Copper in Angiogenesis. *Chisinau, Republic of Moldova.*
20. **Grusac Evgheni, Oboroc Sandu, Bairamculov Azamat, Garbuz Olga, Tagadiuc Olga, Sardari Veronica.** The Role of Angiogenesis in Tissue Transplant. *Chisinau, Republic of Moldova*.
21. **Grusac Evgheni, Oboroc Sandu, Bairamculov Azamat, Garbuz Olga, Tagadiuc Olga, Sardari Veronica.** The Role of Angiogenesis in Ischemic Disease**.** *Chisinau, Republic of Moldova.*
22. **Basistii Alexander, Pulucciu Elena, Grusac Evgheni, Betisor Alexandru, Cepoi Daniela, Sardari Veronica.** Role of Angiogenesis in Osteoarthritis. *Chisinau, Republic of Moldova*
23. **Cebotari Dionisie, Grusac Evgheni, Railean Nadejda,Tagadiuc Olga, Sardari Veronica.** Selenium-Dependent Glutathione Proxidase 4 Regulation of Ferroptosis: Applications in Graft Survival and Oncological Therapy. *Chisinau, Republic of Moldova.*
24. **Minchevici Delia, Negari Nadejda, Bour Alin, Gilea Angela, Nacu Viorel.** Restoring Thyroid Function with Tissue-Engineered products after Total Thyroidectomy. *Chisinau, Republic of Moldova.*
25. **Negari Nadejda, Minchevici Delia, Cazacov Vladimir, Nacu Viorel.** Implementing Regenerative Medicine Across Surgical Pathways in Liver Cirrhosis. *Chisinau, Republic of Molova*.

Session 2
Oral presentations

Moderators: Labusca Luminita, ***MD, PhD (Romania);*** **Cobzac Vitalie**, ***MD, PhD (Republic of Moldova)***

1. **09:00-09:30. Luminita Labusca.** The Role of the Synovial Tissue in Osteoarthritis Occurrence and Progression. *Iasi, Romania*.

2. **09:35-09:45. Cristiana Tripadus, Alexandru Ghetiu, Nicolae Chele, Sirbu Dumitru**· ADSC-Enriched Autologous Fat Grafting in Facial Rejuvenation. *Chisinau, Republic of Moldova*.

3. **09:55-10:05. Olga Macagonova, Adrian Cociug, Vladimir Ciobanu, Viorel Nacu.** Biological Biomaterials in Cutaneous Regeneration: Experimental Studies. *Chisinau, Republic of Moldova.*

4. **10:10-10:20. Alexandru Adam, Kristi Gonta, Daniel Prozorovschi, Constantin Florea, Viorel Nacu.** The Development of Low-Cost Simulators for Medical Training in Punctures. *Chisinau, Republic of Moldova.*

5. **10:25-10:35. Ianos Coretchi, Vladimir Topciu.** Potential Molecular Targets for Prevention and Treatment of Persistent Postoperative Pain. *Chisinau, Republic of Moldova.*

Session 3
Oral Presentations

Moderators: Andrei Nica, ***MD, PhD (Romania),*** **Ianos Coretchi,** ***MD, PhD (Republic of Moldova)***

6. **10:40-10:50. Valeriana Pantea, Ecaterina Pavlovschi , Veronica Sardari, Inna Sveț, Olga Tagadiuc.** *In vitro* Modulation of Pseudocholinesterase Activity by Cu-Thiosemicarbazone Compounds in the Rat C6 Gliom Cells. *Chisinau, Republic of Moldova.*

7. **10:55-11:05. Patricia Catinsus, Angela Babuci.** The Molecular Substrate of the Human Species: Differences Between Male and Female Sex. *Chisinau, Republic of Moldova***.**

8. **11:10-11:20. Daniel Cristea, Veronica Sardari.** Oxidative Stress and its Impact on Bone Graft Integration after Oncologic Therapy. *Chisinau, Republic of Moldova.*

9. **11:25-11:35. Daniel Cristea, Veronica Sardari.** RANK/RANKL/OPG Signaling in Bone Graft Integration in Oncologic Patients. *Chisinau, Republic of Moldova.*

10. **11:40-11:50. Veronica Capanji, Ludmila Sidorenco, Viorel Nacu.** Nanomaterials-Induced Toxicity on Cardiac Myocytes and Tissues. *Chisinau, Republic of Moldova***.**

11:50 CONFERENCE CLOSING CEREMONY

ABSTRACTS

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THIRTEEN YEARS OF ACTIVITY OF THE HUMAN TISSUE BANK AT THE CLINICAL HOSPITAL OF ORTHOPEDICS AND TRAUMATOLOGY

Nacu Viorel[1], Stepa Serghei[2], Cospormac Igor[2], Cociug Adrian[1], Cobzac Vitalie[1], Timbalari Tatiana[3]
[1]Human Tissue and Cell Bank, Chisinau, Republic of Moldova, Clinical Hospital of Orthopedics and Traumatology, Chisinau, Republic of Moldova
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Introduction. Tissue transplantation represents an essential component of modern regenerative and reconstructive medicine. In the Republic of Moldova, this field has evolved progressively since the 1960s, beginning with the use of bone grafts and culminating in the establishment of a national infrastructure for tissue banking. The creation of the Human Tissue and Cell Bank (HTCB) in 2011 marked a pivotal advancement, enabling the systematic collection, processing, preservation, and distribution of human tissues and cells. **Materials and Methods.** This study presents a descriptive and historical review of the development and activity of tissue banking in Moldova, with a focus on the 13-year operational period of the HTCB within the Clinical Hospital of Traumatology and Orthopedics. Data were collected from institutional records, historical documents, and reported clinical milestones, emphasizing infrastructure development, leadership, and clinical implementation of tissue transplantation. **Results.** The origins of tissue transplantation in Moldova date back to 1962 with the establishment of the Tissue Preservation Laboratory, initially within the Republican Blood Transfusion Station and later relocated to the Clinical Hospital of Traumatology and Orthopedics. Under successive leadership, the laboratory contributed significantly to graft preservation and clinical application. A major milestone was achieved in 2011 with the establishment of the HTCB under the coordination of Professor Viorel Nacu. The bank was structured to include specialized units for reception, processing, clean-room operations, storage, and distribution. Since its inauguration in 2013, the HTCB has successfully implemented multiple transplantation procedures, including the first allogeneic corneal harvesting and transplantation, as well as skin harvesting and grafting procedures. The bank supports a wide range of tissues, including skeletal grafts, corneas, skin, amniotic membranes, and autologous bone marrow-derived cells. **Conclusions.** Over thirteen years of activity, the Human Tissue and Cell Bank has become a cornerstone of Moldova's healthcare system, significantly contributing to the advancement of transplantation medicine. Continued development requires sustained investment, adherence to international standards, and integration with European regulatory frameworks to ensure quality, safety, and future expansion. **Keywords.** tissue transplantation, human tissue bank, Moldova, graft preservation, regenerative medicine, HTCB

SYNOVIAL TISSUE IN THE FUNCTIONING OF SYNOVIAL JOINTS AND THE OCCURRENCE OF OSTHEOARTHRITIS

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Synovial joints have traditionally been interpreted through a cartilage-centric framework, with synovial tissue often viewed primarily as a secondary responder to cartilage damage. However, increasing experimental and clinical evidence indicates that the synovium functions as a dynamic regulatory interface integrating mechanical, immune, metabolic, vascular, and neural signals within the joint environment.
The presentation reviews the developmental origin and cellular organization of synovial tissue, including fibroblast-like synoviocytes and tissue-resident macrophages that establish and maintain the synovial lining. Recent findings suggest that these macrophage populations contribute to compartmental integrity at the synovial–joint cavity interface and participate in maintaining joint homeostasis. In physiological conditions, synovial tissue regulates synovial fluid composition, supports lubrication through production of hyaluronan and lubricin, and facilitates metabolic exchange for avascular joint structures such as articular cartilage. The synovium is also richly vascularized and innervated, allowing integration of systemic metabolic, inflammatory, and neuroendocrine signals with local mechanical demands. In osteoarthritis, synovial tissue becomes an active participant in disease processes, contributing to inflammatory signaling, altered tissue cross-talk, and changes in joint microenvironment that may influence cartilage degradation and symptom generation. Imaging approaches, including musculoskeletal ultrasound and contrast-enhanced MRI, increasingly demonstrate that synovial changes can be detected early and may precede or accompany structural joint damage. Recognizing the synovium as a functional and regulatory organ within the joint expands current concepts of OA pathophysiology and highlights new opportunities for diagnostic assessment and therapeutic targeting. Integrating synovial biology into clinical and research perspectives may improve understanding of joint disease mechanisms and support the development of more comprehensive treatment strategies.

ROLE OF CELLULAR AND MOLECULAR FACTORS IN ALVEOLAR RIDGE REMODELING AFTER TOOTH LOSS

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[2]Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Introduction: The bone remodeling after the tooth loss is a complex process that occurs at the cellular level, being regulated by a complex mechanism, maintaining the balance between the bone resorption, influenced by osteoclasts activity and new bone formation, regulated by osteoblasts activity. Our purpose was to emphasize the molecular mechanisms of post-extraction osteoclastogenesis.
Material and methods: A thorough review of publications from Web of Sciences, PubMed, HINARI, Scopus, Google Scholar and Semantic Scholar databases was done. Only original articles and experimental studies were analyzed. **Results:** Osteoclastogenesis is a complex process regulated through the receptor activator of nuclear factor kappa-B ligand (RANKL), at the level of the osteoblasts and stromal cells. RANKL binding to its receptor promotes the osteoblasts precursor differentiation and bone resorption, while osteoprotegerin (OPG) acts as a decoy receptor, playing an inhibiting role. For the enhancement of the osteoclasts' activity, during the early healing phase, inflammatory cytokines such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α) and prostaglandins are released. The mesenchymal stem cells are recruited at the extraction site and under the influence of the insulin-growth factors and morphogenetic proteins, stimulation of osteoblasts differentiation and bone matrix deposition occurs. The osteoclastogenesis depends on vascularization, inflammatory status and mechanical stimuli, modulating the cellular activity. Without functional loading, the bone formation cannot entirely compensate the process of bone resorption, and a progressive reduction of the alveolar ridge occurs. **Conclusion:** The bone remodeling after tooth extraction is a complex and multifactorial process involving cellular and molecular mechanisms. The interaction between osteoclast-mediated resorption, osteoblast-driven bone formation, and local microenvironment determines the extent of morphological alterations of the alveolar ridge, having a significant impact on dental rehabilitation.
Key-words: osteoclastogenesis, osteoclasts, osteoblasts, mesenchymal stem cells

THE DEVELOPMENT OF LOW-COST SIMULATORS FOR MEDICAL TRAINING IN PUNCTURES

Adam Alexandru[1], Gonta Kristi[1], Florea Constantin[1], Prozorovschi Daniel[1], Nacu Viorel[2]
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Introduction. Medical procedures involving punctures require practical training for outmost effectiveness and low risks. Therefore, a project with the purpose of training medical students was developed constructing 4 low-cost simulators for the following procedures: thoracocentesis, pericardiocentesis, femoral artery cannulation, and urinary bladder puncture. **Materials and methods.** The project was undergone using low-cost materials: mannequin structures, artificial skeletons, polysiloxane polymers, tubes, and reservoirs. The pericardial and pleural puncture simulators were made using an artificial skeleton of the upper body that was covered in skin-resembling silicone and filled with sponges and reservoirs for the pleural and pericardial cavity. Moreover, the femoral artery and bladder punctures were constructed using a mannequin of the inferior body that was carved up in the respective anatomical places, which were filled with tubes, polymers and reservoirs to resemble the femoral artery and the bladder. **Results.** Models respected the topography of the actual organs and anatomical structures of the human body. Punctures were performed by considering the anatomical landmarks for the correct needle placement and depth. Thoracocentesis was carried out by finding the intercostal spaces of the simulator, whilst for pericardiocentesis the stern and the costal arches were taken into account. For the femoral artery and bladder: the iliac crest, the umbilicus and the pubic bone were used to determine the needle direction and entry point. In order to assess the functionality of the simulators, procedures were practiced in different stages of the project: first by the developers and afterwards by students during scientific workshops. Performance was functional and closely resembling real-life medical scenarios. Students offered positive feedback, identifying correct anatomical landmarks, and aspiring the liquids into syringes accordingly. **Conclusions.** Low-cost medical simulators for several punctures were successfully incorporated in student medical training, taking into account key anatomical elements and clinical scenarios. Additional developments to the project could improve anatomical accuracy and efficiency. **Keywords:** anatomy, low-cost, simulation, punctures, practice.

EFFECTS OF FECAL MICROBIOTA TRANSPLANTATION ON APPETITE AND APPETITE RELATED OUTCOMES IN HUMANS: A NARRATIVE REVIEW

Aftinescu Pavel[1], Martin Cristina[1], Protopop Svetlana[1]
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Introduction: The gut microbiome plays a key role in the regulation of human appetite and energy balance through effects on satiety hormones and metabolic pathways. Fecal microbiota transplantation (FMT) is an emerging intervention, defined as the transfer of stool from a healthy donor to a recipient. The primary evidence suggests a modulatory effect of FMT, including reductions in subjective hunger, and alterations in appetite regulating gut hormones. This narrative review summarizes human studies evaluating whether FMT from healthy donors influences appetite related outcomes (hunger, satiety, food intake, body weight, and gut peptides). **Materials and methods** A narrative review of human studies (2020–2026) was conducted using PubMed and Elsevier scientific databases. Eligibility criteria included only human studies assessing FMT effects on appetite regulation. Evidence mainly derives from randomized controlled trials and systematic reviews comparing lean donor FMT with autologous FMT or placebo, allowing isolation of donor microbiota–specific effects. **Results:** The strongest evidence for FMT effects relates to appetite sensations. In obese men receiving lean-donor FMT, subjective hunger scores decreased significantly, with one study reporting a 25.8% reduction during a standardized meal test compared with autologous FMT. In contrast, patients with anorexia nervosa showed improved appetite scores after FMT, indicating a state-dependent normalizing effect. Metabolic improvements are also reported. Peripheral insulin sensitivity increased by about 30% in obese recipients of lean-donor FMT, and fasting plasma glucose decreased in patients with metabolic syndrome after healthy-donor FMT. Body weight changes were inconsistent, with a 1.5 kg loss in one study but no significant effects in others. Potential mechanisms include increased short-chain fatty acids, shifts in bile-acid metabolism, reduced inflammation, and satiety hormone modulation (GLP-1, PYY). Yet, clinically meaningful appetite effects in humans remain poorly established. **Conclusions:** Evidence that FMT influences appetite related outcomes in humans remains limited but suggests state dependent modulation of appetite perception. Controlled studies report modest improvements in subjective hunger or appetite scores and favorable glycemic changes, whereas effects on body weight are inconsistent. Methodological heterogeneity and non standardized appetite assessments limit interpretation, underscoring the need for robust randomized trials with energy intake data, and relevant hormonal outcomes.

Keywords: fecal microbiota transplantation, appetite, satiety, body weight

STEM CELL-ENHANCED DENTAL IMPLANT FOR IMPROVED OSSEOINTEGRATION AND REGENERATIVE TISSUE INTEGRATION

Alsaliem Sulaiman[1]
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Background: Dental implants are a widely used therapeutic option for the replacement of missing teeth and the restoration of oral function. Despite high success rates, implant failure may occur due to insufficient osseointegration, inflammatory reactions, or inadequate bone regeneration around the implant site. Conventional implantology primarily relies on mechanical stability and passive biological integration with surrounding tissues. Recent advances in regenerative medicine and tissue engineering have introduced new approaches aimed at improving implant performance through the use of biologically active materials and stem cells. **Aim of the Study**: The aim of this study is to describe the concept and potential biological advantages of a stem cell-enhanced dental implant that integrates a biocompatible scaffold with osteogenic stem cells in order to improve osseointegration, stimulate bone regeneration, and enhance the long-term stability of dental implants. **Results**: The proposed implant design includes a ring-shaped structure positioned at the upper part of the implant body. This component is manufactured from synthetic bone or another biocompatible bone-like material and functions as a scaffold capable of hosting osteogenic stem cells. After implantation, stem cells may be introduced into this ring-shaped reservoir, where they interact with surrounding tissues. Through osteogenic differentiation and the secretion of growth factors, these cells may stimulate new bone formation around the implant and enhance the regenerative capacity of the alveolar bone. This biological activity may strengthen the interface between the implant surface and the jawbone, improving the stability of the implant over time. In addition, stem cells may contribute to the regeneration of surrounding soft tissues, including gingival structures, thereby improving the attachment between the implant and the oral mucosa. The presence of regenerative cells may also reduce inflammatory responses at the bone–implant interface, which represents a common cause of implant failure in conventional systems. **Conclusion:** The stem cell-enhanced dental implant represents an innovative concept that combines implant engineering with regenerative medicine. By integrating osteogenic stem cells into a biocompatible scaffold within the implant structure, this approach may enhance osseointegration, stimulate bone regeneration, reduce inflammation, and accelerate healing after implantation. The proposed strategy may contribute to improved long-term stability and higher success rates in dental implantology, while also promoting better functional and

ARTIFICIAL INTELLIGENCE IN CELL CULTURE STANDARDIZATION: FROM MONITORING TO PREDICTION

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Introduction. Cell cultures form the foundation of tissue engineering and cell-based transplantation, fields in which each produced batch must be viabile and therapeutically effective. Traditionally, culture monitoring relies on manual microscopic evaluation and biochemical assays. These approaches may lead to batch-to-batch variability, delayed detection of process deviations, and are highly dependent on operator's experience. The integration of artificial intelligence (AI), through Deep Learning (DL) and Machine Vision (MV) techniques, enables continuous analysis of morphological and metabolic data. This allows a gradual transition from strictly descriptive monitoring to a predictive approach oriented toward the standardization and optimization of cell cultures. The purpose of this study is to evaluate how AI can improve cell culture monitoring through the development of predictive models. **Materials and methods**. This study is based on a narrative review of the literature using the PubMed, Google Scholar and MDPI databases with predifined keywords. Open-access, full-text articles published between 2020 and 2026 were included. A total of 11 relevant articles were identified. **Results.** The analyzed studies demonstrate that neural networks applied to microscopic image analysis enable more precise identification of morphological changes compared to manual evaluation. Machine learning algorithms integrating metabolic parameters and environmental conditions can predict culture instability or decreased viability before these changes become evident through conventional assays. Additionally, „soft sensor" systems allow real-time estimation of parameters such as cell density and nutrient consumption without invasive interventions. Overall, predictive models reduce batch-to-batch variability and improve process reproductibility. **Conclusions**. The integration of AI enables a shift from reactive culture monitoring to predictive process control. Advanced DL and MV models support early anomaly detection, reduction of batch variability, and improved reproductibility. Consequently, AI contributes to the development of autonomous bioreactor systems capable of delivering standardized tissues for safe transplantation. **Keywords**. Artificial intelligence, deep learning, machine vision, stem cell culture, predictive modeling, quality monitoring.

TISSUE ENGINEERING AND BIOFABRICATION – FUTURE OF CARDIAC REGENERATION

Rabbi Syeda[1], Badalyan Albert[1], Babuci Angela[2]
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Background: Cardiovascular diseases represent the leading cause of morbidity and mortality worldwide. Engineering biomimetic cardiac tissue to regenerate the heart has been an ambition in tissue engineering. Recent advances in stem cell biology, particularly human pluripotent stem cells, combined with sophisticated biofabrication techniques including 3D bioprinting, offer unprecedented opportunities for cardiac regeneration. The aim of the current study was to examine how tissue engineering and biofabrication approaches can be used for cardiac regeneration and provide new treatments for cardiovascular diseases. It collectively addresses several key objectives like, developing functional cardiac tissues, advancing biofabrication techniques, improving cell sources, maturation and clinical translation. **Materials and methods:** A systemic review of relevant publications from Web of Science, Scopus, MEDLINE, PubMed, Google Scholar and Semantic Scholar databases has been done. The papers are primarily reviews and experimental studies examining tissue engineering approaches. **Results:** The results reported in tissue engineering and biofabrication for cardiac regeneration include both significant advances and persistent challenges. Human pluripotent stem cells provide an unlimited source of cardiomyocytes for cardiac tissue development. Patient-specific engineered heart tissues are now possible using induced pluripotent stem cells, opening possibilities for personalized medicine. 3D bioprinting has demonstrated ability to create complex scaffold structures with precision and encapsulate cells effectively. Multiple biofabrication approaches have been developed including biomaterial-based, cell-based, and hybrid methods. Some cell-based approaches have progressed to multiple ongoing clinical trials. **Conclusions:** Research has shown that tissue engineering and biofabrication represent promising but still developing approaches for cardiac regeneration. Engineering functional cardiac tissues is feasible and holds great promise for heart regeneration, though the field remains in its infancy. Beyond regeneration, engineered cardiac tissues successfully serve as platforms for drug discovery, disease modeling, and toxicity screening. Advances in stem cell biology and biofabrication techniques have provided unlimited cell sources and sophisticated manufacturing capabilities. Critical challenges remain, including achieving mature cardiomyocytes and developing clinically translatable technologies. While promising, these techniques are still experimental and require further research.

Keywords: 3D-bioprinting, stem cells, biofabrication, regeneration

METFORMIN IN THE MANAGEMENT OF THE NEW-ONSET DIABETES AFTER TRANSPLANTATION

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Background: Advances in immunosuppressive therapy have significantly improved graft survival and overall outcomes after solid organ transplantation. However, metabolic complications, particularly new-onset diabetes after transplantation (NODAT), remain common and are associated with increased cardiovascular risk, graft dysfunction, and mortality. Effective strategies for the prevention and management of post-transplant hyperglycemia are therefore essential.
Methods: A narrative review of English-language publications indexed in the PubMed database during the last 10 years was conducted to evaluate the mechanisms of immunosuppressant-induced disturbances in glucose metabolism and to assess the potential role of metformin in the management of post-transplant hyperglycemia. **Results**: Pharmacological therapy combined with lifestyle modification represents a key approach for glycemic control in transplant recipients. Metformin, widely used as first-line therapy in type 2 diabetes mellitus, has been increasingly considered for patients with NODAT. Through improvement of insulin sensitivity and inhibition of hepatic gluconeogenesis, metformin may counteract hyperglycemic effects induced by commonly used immunosuppressive agents, including calcineurin inhibitors (cyclosporine, tacrolimus), mammalian target of rapamycin (mTOR) inhibitors (sirolimus, everolimus), and glucocorticoids. Additionally, metformin may help limit weight gain associated with chronic corticosteroid therapy.
Conclusions: Metformin represents a valuable therapeutic option for the management of post-transplant hyperglycemia and NODAT due to its favorable metabolic profile, low risk of hypoglycemia, and limited interaction with immunosuppressive therapy. Because the drug is excreted unchanged by the kidneys, careful monitoring of renal function is required. Dose adjustment should be guided by estimated glomerular filtration rate, with discontinuation recommended when renal function declines below established safety thresholds.
Keywords: organ transplantation, new-onset diabetes after transplantation, immunosuppressive therapy, hyperglycemia, metformin.

DIABETES MELLITUS IN TRANSPLANT RECIPIENTS

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Background: Solid organ transplantation has substantially improved patient survival and quality of life. Nevertheless, post-transplant diabetes mellitus (PTDM) remains one of the most common metabolic complications following transplantation and is associated with increased morbidity and mortality. The 2022 International Consensus Meeting provided updated recommendations for the definition, diagnosis, and management of PTDM. **Methods**: A literature review of English-language publications indexed in PubMed over the past 10 years was performed to evaluate the incidence of PTDM, associated risk factors, diagnostic criteria, and principles of prevention and clinical management. **Results**: Transplant recipients may present with several glycemic disturbances, including pre-transplant diabetes, transient post-transplant hyperglycemia, new-onset diabetes after transplantation, and PTDM. Reported incidence rates range from 10% to 40%. Risk factors include modifiable determinants—such as perioperative hyperglycemia, seden-tary lifestyle, infections, hypomagnesemia, and immunosuppressive therapy—as well as non-modifiable factors including older age, ethnicity, family history of diabetes, genetic predisposition, deceased donor grafts, male sex, HLA microcompatibility, and polycystic kidney disease. Diagnostic criteria mirror those used for diabetes mellitus in the general population and include fasting plasma glucose, 2-hour postprandial glucose, oral glucose tolerance testing, and HbA1c. **Conclusions**: Screening strategies recommend avoiding the diagnosis of PTDM during the first 45 days following transplantation. Between days 46 and 365, diagnosis may rely on OGTT, fasting plasma glucose (>7 mmol/L), random plasma glucose (>11.1 mmol/L), postprandial glucose (>11.1 mmol/L), or HbA1c (>6.5%). After one year post-transplantation, diagnostic evaluation should include OGTT, HbA1c, and fasting or random plasma glucose measurements.
Keywords: diabetes mellitus, post-transplantation diabetes mellitus, risk factors, diagnostic criteria.

EMERGING DIAGNOSTIC PERFORMANCE OF DONOR-SPECIFIC ANTIBODIES AND DONOR-DERIVED CELL-FREE DNA IN SOLID ORGAN TRANSPLANT REJECTION

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Introduction: Monitoring allograft rejection is crucial for improving long-term transplant outcomes, Standard monitoring often fails to detect subclinical injury, leading to irreversible graft loss. Recently, non-invasive biomarkers, specifically donor-derived cell-free DNA (dd-cfDNA) and donor-specific antibodies (DSA), have appeared as accurate tools for early identification of acute and antibody-mediated rejection (AMR). **Material and Methods:** We conducted an integrative review of literature indexed in PubMed and Scopus published between 2017 and 2025. The search focused on prospective cohorts and meta-analyses evaluating kidney and heart transplant recipients. Key performance indicators analyzed included Area Under the Receiver Operating Characteristic (AUROC) curves, sensitivity, specificity, and Negative Predictive Value (NPV). **Results:** Data synthesis across multiple organ cohorts reveals that dd-cfDNA maintains a diagnostic AUROC range of 0.75–0.86 for identifying allograft injury. Individual kidney studies typically report sensitivity between 59%-82%, with specificity often exceeding 80%. In heart transplantation, sensitivity varies (60–78%), and the NPV remains consistently high at 90–97%, providing a robust "rule-out" capability for acute rejection. DSA positivity was found to be a consistent clinical "red flag", associated with a 2.5 to 4-fold increased risk of AMR. The integration of both biomarkers, using dd-cfDNA to verify the injury suspected by DSA, yielded superior risk stratification than either marker used in isolation. **Conclusions:** The evidence from 2017–2025 indicates that dd-cfDNA and DSA are highly complementary. Their integration into clinical practice offers a reliable, non-invasive alternative for identifying early allograft injury. Future efforts should focus on refining organ-specific thresholds to standardize clinical decision-making across diverse transplant populations. **Keywords**: organ transplantation, graft survival, delayed graft function, antibodies

CARDIOMYOCYTE MATURATION: ADVANCES AND IMPLICATIONS FOR REGENERATIVE MEDECINE

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Background. Ischemic heart disease remains a leading cause of mortality worldwide. The application of heart transplantation is limited by donor shortage and risk of rejection. Therefore, cardiac tissue engineering has emerged as a promising regenerative approach to restore myocardial function. However, most engineered constructs exhibit immature, fetal-like cardiomyocyte phenotypes characterized by reduced conduction velocity, weak contractile force, altered gene expression, and unstable resting membrane potential. **Objective of the Study.** To analyze and systematize current strategies for promoting maturation of stem cell-derived cardiomyocytes, including long-term culture, biophysical stimulation, metabolic interventions, and in-vivo studies.
Material and Methods. The study presented here is based on specialized literature extracted from databases such as PubMed, HINARI, and ScienceDirect. The search covered 18 publications from 2020 to 2025. **Results.** Cardiomyocyte maturation encompasses several key processes, including cell size increase, myofibril maturation, metabolic transition from glycolysis to fatty acid oxidation, formation of a mature action potential, T-tubule development, mitochondrial expansion, and polyploidization. Biophysical stimulation, such as electrical pacing, cyclic mechanical stretch, substrate stiffness (8-11 kPa), and nanotopography, plays a central role in maturation. In contrast, the absence of mechanical stress leads to sarcomere disassembly and reduced contractility. Long-term culture improves cell morphology and function, but has proven insufficient for T-tubule formation. Co-culture with endothelial cells, epicardial cells, and cardiac fibroblasts enhances vascularization, graft size, and structural organization. The optimal fibroblast content in the seed (30%) promotes cardiomyocyte proliferation by secreting extracellular matrix factors, while adult fibroblasts secrete growth cytokines. Metabolic modulation promotes fatty acid oxidation and mitochondrial biogenesis by using T3, glucocorticoids, angiotensin II, and endothelial-derived microRNAs. In vivo transplantation appears to be the most effective method, as numerous experiments have demonstrated the transition of cardiomyocytes to mature isoforms. This demonstrates that the cells have the potential for maturation, but in vitro conditions are inadequate.
Conclusion. Overall, even with these modern natural engineering techniques, stem cell-derived cardiomyocytes in artificial cardiac tissue remain primarily in the early and late fetal stages of cardiomyocyte maturity. Although it possesses regenerative potential, incomplete maturation remains a significant barrier to clinical translation.

Keywords
regenerative cardiology; cardiomyocyte maturation; engineered heart tissue; metabolic remodeling.

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HEALTHCARE-ASSOCIATED INFECTIONS POST-TRANSPLANT IN ONCOLOGICAL PATIENTS

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Introduction. Healthcare-associated infections (HAI) in oncological patients represent a frequent health problem, but also an economic burden for the hospital, the state and the patient's family. Organ or stem cell transplantation is an essential procedure in the treatment of blood cancers (leukemia, lymphoma) and other types of tumors, replacing diseased bone marrow or bone marrow destroyed by intensive chemotherapy with healthy cells. Critically ill cancer patients are a subpopulation more vulnerable to HAI, they present additional non-modifiable risk factors.
Materials and methods. The research is a review of the specialized literature based on searching for articles in databases (PubMed, Google Scholar, Research Gate) using as keywords "cancer treatments", "healthcare-associated infections", "nosocomial infections AND transplant", "post-transplant hospital-acquired infections", "stem cells AND immunosuppression", "cancer AND hospital-acquired infections". No filter was applied, but articles published in the last ten years were preferentially selected to perform this narrative analysis. **Results.** WHO considers that approximately 40% of deaths caused by cancer could be avoided, while emphasizing "prevention of HAI" as an essential component of all cancer care protocols. In the case of post-transplant oncology patients, almost all microorganisms can cause HAI, including colonizing and normal microbiota. The most frequently reported pathogens are Escherichia coli, Pseudomonas aeruginosa, Klebsiella spp., Staphylococcus spp. and Streptococcus spp. Bloodstream infections are among the most common, due to the devices that are constantly inserted. Scientific studies have concluded that against the background of chemotherapy, immunosuppression and stem cell transplantation, CAUTI, urinary tract infections, digestive system infections, surgical site infections, etc. are also associated. It has been estimated that 20-40% of all HAI is due to contaminated hands of healthcare workers, 20% is potentially due to contaminated environment. Several studies have shown that microorganisms detected as pathogens triggering HAI in cancer patients are resistant to antibiotics.
Conclusions. In order to prevent post-transplant HAI in cancer patients, it is necessary to apply multiple preventive and educational actions undertaken by a multidisciplinary team to obtain the best care for vulnerable patients and minimize additional costs for the health system.
Keywords: healthcare-associated infections, transplant, cancer, patient, oncology.

STATIN THERAPY AFTER HEART TRANSPLANTATION

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Introduction. Cardiovascular disease remains the leading cause of long-term mortality after heart transplantation, largely driven by cardiac allograft vasculopathy (CAV) and accelerated atherosclerosis. Dyslipidemia develops frequently in this population as a consequence of immunosuppressive therapy and metabolic alterations. Glucocorticoids, calcineurin inhibitors (especially cyclosporine), and mTOR inhibitors significantly disrupt lipid metabolism, promoting elevations in total cholesterol, LDL-cholesterol (LDL-C), and triglycerides. Given this high-risk profile, lipid management is a central component of post-transplant care. The aim of this review is to synthesize recent evidence on the mechanisms, clinical implications, and management of dyslipidemia after heart transplantation. **Materials and Methods**: A narrative literature search was performed in the Hinari database, limited to publications from the last 5 years. Search keywords included: statins after heart transplantation, cardiac transplant dyslipidemia, statin-immunosuppressant interactions, statin safety in transplant. Emphasis was placed on mechanisms of post-transplant hyperlipidemia, efficacy of statin therapy, comparative safety profiles, and clinically relevant drug-drug interactions between statins and immunosuppressive agents. **Results:** Post-transplant dyslipidemia is multifactorial. Corticosteroids increase hepatic lipoprotein synthesis and insulin resistance, while cyclosporine impairs LDL receptor activity, leading to hypercholesterolemia. mTOR inhibitors (sirolimus, everolimus) elevate triglycerides, whereas tacrolimus shows a more favorable lipid profile. According to the 2019 ESC/EAS guidelines, transplant recipients are managed according to overall cardiovascular risk. Early initiation of statins after heart transplantation improves survival and reduces the incidence and progression of cardiac allograft vasculopathy (CAV), independent of baseline LDL-C levels. Statins are first-line therapy and also provide pleiotropic endothelial and anti-inflammatory effects that may protect the graft. However, significant pharmacokinetic interactions occur with CYP3A4-metabolized statins when combined with cyclosporine or mTOR inhibitors, increasing myopathy risk. Therefore, pravastatin and rosuvastatin are generally preferred, with careful dose titration and monitoring of liver enzymes and creatine kinase. **Conclusions**: Dyslipidemia after heart transplantation requires proactive and individualized management. Statins remain the therapeutic cornerstone, providing both cardiovascular and graft-protective benefits. Careful drug selection and monitoring are essential to balance efficacy with safety in the context of complex immunosuppressive regimens. **Keywords**: heart transplantation, statins, dyslipidemia, cardiac allograft vasculopathy, drug-drug interactions.

FUNGAL INFECTIONS IN TRANSPLANT PATIENTS AND DRUGS OF CHOICE FOR MANAGEMENT

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Introduction. Fungal infections represent a significant risk for organ transplant recipients due to prolonged immunosuppressive treatment. The incidence varies between 2% and 50%, and mortality can reach up to 50%. Early recognition of common fungal pathogens and appropriate antifungal therapy are essential for effective management and improved survival in these patients.
Materials and Methods. A literature review and analysis of scientific articles published in the PubMed database during the last ten years was performed. The selected studies focused on the epidemiology, risk factors, common fungal pathogens, and therapeutic approaches related to fungal infections in organ transplant patients. **Results.** Risk factors for fungal infections include immunological (type, intensity and duration of immunosuppression, prolonged neutropenia, prolonged antibiotics that alter the microbiota, glucocorticoid, anti-proliferative drugs), procedural (surgical complications, prolonged antibiotic use, catheter/devices use, anti-proliferative drugs) and environmental (contaminated water, soil and air). In organ transplant patients, pathogenic fungi include the common fungi *Candida spp. (Candida albicans, Candida glabrata, Candida krusei), Aspergillus spp. (Aspergillus fumigatus, Aspergillus flavus, Aspergillus terreus), Pneumocystis jirovecii* and *Cryptococcus spp. (Cryptococcus neoformans, Cryptococcus gattii)* as well as endemic fungi. In addition, endemic fungi such as *Histoplasma capsulatum, Coccidioides immitis* and *Blastomyces dermatitidis.* **Conclusions.** The choice of antifungal therapy depends on the pathogen involved, the location of the infection, and its severity. Amphotericin B, especially in its liposomal form, is commonly used for severe and disseminated fungal infections. Azole antifungals such as fluconazole, voriconazole, itraconazole, and posaconazole are widely used for both treatment and prophylaxis. Echinocandins (caspofungin, micafungin, and anidulafungin) are effective particularly against candidiasis. However, antifungal therapy requires careful monitoring due to possible adverse reactions and interactions with immunosuppressive drugs used after transplantation.
Keywords: fungal infection, Candida, Aspergillus, Pneumocystis, kidney transplant, kidney transplant recipients, complications

INFECTIOUS COMPLICATIONS IN ORGAN TRANSPLANT PATIENTS

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Introduction. Organ transplantation requires a careful balance between graft preservation, maintenance of adequate suppression and the risks of complications, including infections. The risk of infections (30-60%) on the background of immunosuppression will depend on the state of innate and adaptive immunity, epidemiological exposures to pathogens, and the immunological impact of immunosuppressive drugs. **Materials and methods**: A selection and analysis of articles in the PubMed database from the last 10 years was performed in order to elucidate the peculiarities of development and time of manifestation of bacterial, fungal, viral and protozoal infections in people with organ transplantation. **Results**: Infections have been shown to be the main cause of graft dysfunction, morbidity, and mortality. 3 periods were found regarding the risk of infection: 1st early (perioperative) or incipient during the first month when immunosuppression is not fully effective; 2nd intermediate – 1-6 months with maximum immunosuppression on the basis of antibacterial prophylaxis; 3rd- late – over 6 months with gradual reduction of immunosuppression with satisfactory functional grafts. In the early period, infections may be due to surgical interventions, pre-existing infections, healthcare-associated infections or donor-acquired infections. In the intermediate period, the range of infections may be caused by reactivation of latent infections (Herpes simplex, Cytomegalovirus, Hepatitis B and C, Mycobacteria) or the association of bacterial (Legionella, Listeria, Nocardia), fungal (Aspergillus, Cryptococcus, Gistoplasma, Coccidioides, Pneumocystes), viral (Cytomegalovirus, Epstein-Barr virus) and parasitic (Toxoplasma) infections. The late period is characterized by community infections or reactivation of chronic viral infections.
Conclusions: Infections in organ transplant patients require the implication of immunosuppression in the pathogenesis of the infection; resolution of infection without reduction of immunosuppression; probability of graft rejection with reduction of immunosuppressive therapy. Therapeutic interventions will depend on the existence of specific therapies (antiviral, antitubercular, antibacterial, antifungal, etc.) or those requiring nonspecific immune responses.
Keywords: immunosuppression, organ transplantation, infectious complications.

METABOLIC REWIRING IN PROSTATE CANCER VIA ZINC-INDUCED MITOCHONDRIAL ACONITASE INHIBITION: PERSPECTIVES FOR POST-ONCOLOGICAL TISSUE TRANSPLANTATION

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Introduction: Prostate epithelial cells exhibit unique biochemical specialization, accumulating high levels of zinc (Zn) to inhibit mitochondrial aconitase (m-aconitase) and facilitate citrate secretion. During malignancy, zinc dyshomeostasis triggers metabolic rewiring, reactivating the tricarboxylic acid (TCA) cycle to fuel tumor progression. For tissue transplantation and engineering, understanding these zinc-dependent metabolic signatures is essential for developing biomimetic scaffolds and regenerative strategies aiming to restore cellular homeostasis and prevent recurrence post-oncological resection. **Materials and Methods**: To evaluate the biochemical dynamics of Zn in prostatic tissue, data were aggregated from experimental studies analyzing mitochondrial extract preparations derived from rat ventral prostate models. The analysis prioritized the stoichiometric shift of the citrate/isocitrate ratio at equilibrium under the inhibitory influence of 7-10 micromolar (μM) concentrations of Zn. Research was synthesized through a comparative analysis of primary sources retrieved from the National Center for Biotechnology Information (NCBI) PubMed, ResearchGate, and Google Scholar, covering 1998 to 2025. **Results**: This framework allowed for an in-depth assessment of the inhibitory kinetics of mitochondrial aconitase (m-aconitase) and the functional downregulation of the zinc-regulated, iron-regulated transporter-like protein 1 (ZIP1). These metabolic trends were subsequently mapped against cellular bioenergetics in prostate cancer to establish their clinical relevance for tissue engineering and post-resection regenerative medicine. Findings demonstrate that 7-10 micromolar (μM) Zn maintains a unique 13.5:1 citrate/isocitrate ratio by inhibiting mitochondrial aconitase (m-aconitase), a process mediated by a mitochondrial "citrate factor protein". In prostate cancer, the downregulation of zinc-regulated, iron-regulated transporter-like protein 1 (ZIP1) causes a 60-80% intracellular zinc depletion. This loss reactivates the tricarboxylic acid (TCA) cycle and oxidative phosphorylation, providing the bioenergetic fuel necessary for tumor progression. **Conclusions:** The investigation underscores that the zinc-regulated, iron-regulated transporter-like protein 1 (ZIP1) and mitochondrial aconitase (m-aconitase) regulatory axis is fundamental for preserving prostatic metabolic homeostasis. Since Zn depletion acts as a critical metabolic switch for prostate cancer progression, targeting this pathway offers significant therapeutic potential. Future research should prioritize the development of zinc-enriched biomimetic scaffolds in tissue engineering. Such regenerative strategies could effectively restore cellular stability and minimize the risk of malignant recurrence following post-oncological transplantation.
Keywords: prostate cancer, zinc homeostasis, mitochondrial aconitase, metabolic rewiring, tissue engineering.

SELENIUM-DEPENDENT GLUTATHIONE PEROXIDASE 4 REGULATION OF FERROPTOSIS: APPLICATIONS IN GRAFT SURVIVAL AND ONCOLOGICAL THERAPY

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Introduction: Selenium is a fundamental micronutrient required for biosynthesizing glutathione peroxidase 4, a key antioxidant enzyme responsible for maintaining cellular redox homeostasis. Its primary biochemical function is reducing lipid hydroperoxides to alcohols, effectively inhibiting ferroptosis - a form of regulated cell death characterized by iron-dependent lipid peroxidation. In tissue engineering, the viability of a graft is critically challenged by ischemia-reperfusion injury, where reintroduction of oxygen generates high levels of reactive oxygen species. This study evaluates the potential of the selenium-glutathione peroxidase 4 axis in protecting healthy transplanted tissues while simultaneously targeting residual malignant cells. **Materials and Methods**: A systematic review of molecular research was conducted using databases such as PubMed, ScienceDirect, Google Scholar and Wiley Online Library (2015–2026). The analysis focused on the metabolic pathways of selenoproteins and their role in preventing membrane damage. Data from the *Saccharomyces cerevisiae* eukaryotic model were utilized to assess the dose-dependent effects of selenium genomic integrity and mitochondrial respiration. Additionally, we reviewed current evidence regarding the autophagy-mediated turnover of GPX4 and the impact of selenium availability on enzymatic stability. **Results**: The data demonstrate a clear hormetic effect of selenium compounds, defined as a dual-phase response where physiological doses provide cellular protection while supra-optimal concentrations induce toxicity. At physiological levels, selenium upregulates glutathione peroxidase 4 activity, significantly reducing malondialdehyde levels - a definitive biomarker of oxidative damage -thereby enhancing graft survival. Conversely, excessive inorganic sodium selenite exhibits pro-oxidant properties by interacting with thioredoxin reductase 1. This interaction converts the enzyme into a pro-apoptotic inducer, triggering lethal oxidative stress specifically in malignant cells. By utilizing biomimetic scaffolds for controlled delivery of selenium, it is possible to maintain an antioxidant environment for tissue regeneration while inducing selective ferroptotic death in cancer cell populations. **Conclusions:** The selenium-glutathione peroxidase 4 pathway is a critical target for optimizing outcomes in regenerative medicine and oncology. Modulating this axis provides a dual-action strategy: stabilizing cellular integrity of engineered grafts and establishing a metabolic safety net against tumor recurrence. Integrating selenium-enriched biomaterials represents a significant advancement in the development of safer and more effective protocols for tissue transplantation and post-oncological recovery. **Keywords:** Selenium, glutathione peroxidase 4, ferroptosis, oxidative stress, graft survival.

EVALUATION OF THE THERAPEUTIC POTENTIAL OF KAEMPFEROL-LOADED BIONANOCOMPOSITES IN CORNEAL NEOVASCULARIZATION

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Introduction. The cornea is the transparent anterior structure of the eyeball, characterized by the absence of blood vessels, a condition essential for maintaining its optical function. Among ocular diseases, corneal neovascularization is a major cause of impaired visual acuity and may progress to severe vision loss or blindness. **Aim of study.** To analyze recent studies regarding the therapeutic potential of kaempferol-loaded bionanocomposites for the treatment of corneal neovascularization, with particular emphasis on their pharmacokinetic advantages and prospects for clinical application. **Methods and materials.** The study is based on the analysis of bibliographic sources indexed in the PubMed and Google Scholar databases published between 2018 and 2025. A total of 40 scientific publications were analyzed. **Results.** Kaempferol, a flavonoid-rich plant compound, is known for its antiangiogenic properties and is of interest as a potential therapeutic agent for inhibiting the formation of vascular neoformations at the corneal level. However, the direct administration of kaempferol is considerably limited by anatomical barriers and low bioavailability. In this context, nanomedicine can improve the pharmacological potential of kaempferol and offer minimally invasive therapeutic strategies. The use of bionanocomposites loaded with kaempferol and nanoparticles of ZnO, SiO_2 and Ag can contribute to increasing the bioavailability of hydrophobic kaempferol, significantly reducing abnormal blood vessel formation, inflammation, and angiogenic factors such as VEGF by inhibiting cell migration. The integration of nanoparticles into the composition of bionanocomposites can provide additional therapeutic advantages, including the reduction of oxidative stress and attenuation of the inflammatory response. In addition, ZnO and Ag nanoparticles exhibit antimicrobial properties that may improve the therapeutic potential and support ocular regeneration. **Conclusion.** The therapeutic potential of kaempferol-loaded bionanocomposites in corneal regeneration is immense due to the multitude of benefits. However, further investigations are needed to design and optimize kaempferol-functionalized bionanocomposites that allow for controlled release of the compound, protect its chemical stability, and increase its bioavailability at the corneal level, thus maximizing therapeutic efficacy. **Keywords:** bionanocomposites, kaempferol, corneal neovascularization, anti-angiogenesis.

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EFFICACY AND COMPLICATIONS OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN MULTIPLE SCLEROSIS

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Introduction. Autologous hematopoietic stem cell transplantation (AHSCT) is a therapeutic strategy with curative potential for relapsing-remitting multiple sclerosis (RRMS) [1]. AHSCT is a modern alternative to disease-modifying therapies, since a low therapeutic response has been observed in RRMS patients [6]. The action mechanism is based on the immunosuppression of autoreactive lymphocytes to subsequently remodel the immune response through self-hematopoietic stem cells [1, 3], restoring immune tolerance and suppressing the inflammatory response [2]. **Materials and methods**. For this study, was performed a search of the specialized scientific literature from 2019-2025, the articles were identified through the search engine PubMed, Google Scholar. **Results**. A prevalence of 68%-88% of patients undergoing AHSCT maintained no evidence of disease activity: NEDA-3 (no relapses, no magnetic resonance imaging activity and no MS progression) in the following 3-5 years after therapy [4, 8]. The efficacy rate is 86.9-91.3% due to the absence of clinical relapses at 5 years after transplantation [1, 2]. The success rate is higher in patients under 45-50, with an expanded disability status scale (EDSS) <5.5-6 [4], and disease duration of less than 5-10 years, thus having a higher chance of remission [1]. The mortality is 2.1% [2]. To confirm the biological efficacy, cerebrospinal fluid is extracted, and it has been observed that CXCL13 decreases in the first year and sCD27 normalizes over the next two years [6]. Complications vary depending on individual tolerance and 17% of patients suffer from Uhthoff's phenomenon in the first 60 days [4], myelosuppression in the first 100 days [7], neutropenia (58%-70%) [8], bacterial sepsis, pneumonia, urinary tract infections, hemorrhagic cystitis, dyspeptic disorders and venous thrombosis [4]. Autoimmune thyroiditis or immune thrombocytopenia occur in 4-6%, Epstein-Barr virus and cytomegalovirus are reactivated in 80% of cases, and there have been recorded oncological risks such as breast cancer, glioblastoma, prostate cancer post-AHSCT [4]. Arrhythmias, renal failure and infertility are found in a minor percentage [5, 7]. **Conclusions**. With over 80% efficacy, AHSCT is the most effective treatment for RRMS, and despite adverse reactions, this therapy offers optimal therapeutic prospects for patients with active forms of MS.

Keywords. multiple sclerosis, hematopoietic stem cells, cell transplantation, efficacy, complications.

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BIOCOMPATIBILITY AND TISSUE INTEGRATION OF ENDOVASCULAR IMPLANTS USED IN INTRACRANIAL ANEURYSMS

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Introduction: In the modern management of intracranial aneurysms, the endovascular method has become a more frequently used method of treatment, especially the use of flow-diverters (FD) and coil embolization devices. These implants act as intravascular scaffolds that alter the hemodynamic and the biological response at the aneurysm affected artery interface. One of the critical components of the long-term success of this method is the biocompatibility and tissue integration of these implants. **The aim of the study**: Synthesizing current evidence on the host-implant interaction and evaluating the impact of the material and surface modifications on the healing process in endovascular treatment of intracranial aneurysms. **Materials and methods**: Research of scientific literature, from electronic databases such as PubMed, Web of Science and ScienceDirect, published in the last decade that addresses biocompatibility, endothelialization and tissue integration of intracranial aneurysms endovascular treatment. **Results**: Studies have shown a correlation between in-stent thrombosis, stenosis and the use of phenox-hydrophilic polymer-coated devices, in 77.6% of cases, compared to 66.2% in the use of flow-diverters. The next generation of FD is the bioresorbable type, which has shown reduction of chronic inflammation, side branch occlusion, device induced stenosis and imaging artefacts, while increasing the use in pediatric applications. Poly-L-lactic acid-coated magnesium coated FD and bare magnesium coated FD have excellent biocompatibility, but the bioresorption in case of the Poly-L-lactic acid-coated magnesium FD was delayed. Studies have also shown no significant difference between fibrin-based coated and non-coated flow-diverters, both having similar blood and tissue compatibility. However, current data regarding the relationship between endovascular devices, endothelialization and biocompatibility has largely been derived from preclinical animal models, therefore further studies are necessary. **Conclusion**: Overall, device material and surface modification significantly influence biocompatibility and vascular healing in endovascular implants of intracranial aneurysms, with bioresorbable flow diverters showing promising reductions in chronic inflammation and device-related complications. However, as most evidence derives from preclinical models, well-designed prospective human studies are essential to validate these biological advantages and their impact on long-term clinical outcomes. **Keywords**: intracranial aneurysms, endovascular implants, biocompatibility, endothelialization, tissue integration

HUMAN COLLAGEN-BASED HYDROGEL WITH ZINC OXIDE NANOPARTICLES FOR ARTICULAR CARTILAGE ENGINEERING

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Introduction. Articular cartilage tissue engineering has a long history of using three-dimensional matrices seeded with cells of chondrogenic potential. Recent studies show that chondrogenesis is influenced not only by growth factors, but also by the biochemical microenvironment, including ions such as Zn^{2+} and Cu^{2+}. **Materials and methods:** With approval from the Ethics Committee of *Nicolae Testemitanu* State University of Medicine and Pharmacy and under a collaboration agreement with the Human Tissue Bank of the Clinical Hospital of Traumatology and Orthopaedics, articular cartilage was collected from a donated femoral head, along with processed umbilical-placental complex. Collagen hydrogels (3 mg/ml) were prepared in 24-well plates containing ZnO NPs (<50 nm; Sigma-Aldrich, USA) at 0 (control), 1, 10, 20, 40, 60, 80, and 100 µg/ml (n=4). Their elastic modulus (EM) was measured using a TX-BLM probe and a TX-700 texture analyzer (Lamy Rheology, France). For viability testing, human chondrocytes (1×10^5 cells/ml) were cultured on hydrogels containing 0 (control), 10, 50, or 100 µg/ml ZnO NPs. Resazurin (10 µg/ml; Acros TFS, Belgium) was used as the viability reagent, and blanks without cells were prepared for each concentration and control group (n=3). Measurements were performed at 24, 48, and 72 hours after 6 h incubation at 37°C and 5% CO_2. Absorbance was recorded at 570 and 600 nm using a Synergy H3 spectrophotometer (BioTek, USA).
Results and Conclusions. ZnO NPs concentration markedly affected the mechanical properties of the hydrogels. Significant differences were found between the control group (470.73 ±38.00 N/m²) and most ZnO-loaded groups. EM was significantly reduced at 60, 80, and 100 µg/ml ZnO ($p < 0.05$), whereas at 1, 10, and 20 µg/ml it was significantly higher than in the control group ($p < 0.05$). No significant difference was observed at 40 µg/ml ($p > 0.05$). The resazurin assay showed a dose-dependent effect of ZnO NPs on chondrocyte viability. The highest viability was recorded at 10 µg/ml ZnO, remaining above 70% over three consecutive days, while higher concentrations caused a marked decrease in viability ($p < 0.05$). Therefore, 10 µg/ml ZnO appears to be the most promising concentration, offering a favorable balance between mechanical strength and cell viability.
Keywords: cartilage engineering, collagen hydrogel, ZnO nanoparticles, human chondrocytes

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EVALUATION OF CORNEAL GRAFT QUALITY IN A HUMAN TISSUE BANK: A 12-YEAR RETROSPECTIVE STUDY (2013–2025)

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Introduction The cornea is a transparent, avascular, and highly specialized structure located in the anterior segment of the eye, playing a critical role in focusing light onto the retina and ensuring clear visual perception. The quality of corneal grafts can be influenced by several factors related to the donor, the recipient, as well as the harvesting, preservation, and processing procedures performed within tissue banks. Corneal grafts are generally classified for optical use, aimed at restoring visual function, or tectonic use, intended to reestablish the structural integrity of the ocular globe. **Materials and Methods** A total of 537 corneas harvested from 290 donors were analyzed. Among the donors, 69.8% were male and 30.2% female, with a mean age of 59.4 ± 18.3 years, ranging from 18 to 91 years. Donor sources included forensic medicine departments (20.5%), public hospitals (70.6%), and multi-organ donors (7.1%). most common causes of death were cardiovascular diseases, traumatic injuries, and cerebrovascular disorders. Corneal harvesting was generally performed within 10 hours post-mortem, followed by macroscopic and microscopic evaluation, including assessment of endothelial cell density and morphological endothelial alterations such as polymegethism and pleomorphism. All tissues underwent serological screening for infectious diseases (HBsAg, HCV, HIV) and microbiological testing to detect bacterial or fungal contamination. **Results** The overall corneal graft invalidation rate was 25.4%. The main causes of exclusion included positive serological results (15%), biological contamination (6.8%), and hemolysis (1%). A total of 74.6% of corneas were used for transplantation, while 25.4% were discarded. Among the transplanted grafts, 44.8% were used for optical penetrating keratoplasty, 51.7% for tectonic keratoplasty, 2.1% for lamellar keratoplasty, and 1.3% for unspecified procedures. Microbiological analysis showed that bacterial contamination predominated (96.4%), mainly caused by Gram-positive bacteria (77%), particularly Staphylococcus aureus (78%) and Staphylococcus epidermidis (20%). Gram-negative bacteria (23%), especially Pseudomonas aeruginosa, were less frequent. Fungal contamination accounted for 3.6%, predominantly involving Candida albicans (91%). **Conclusions.** Early post-mortem harvesting, strict donor screening, and comprehensive microbiological control are essential for ensuring the quality and safety of corneal grafts used in transplantation. Corneas with high endothelial cell density are optimal for optical keratoplasty, while tissues with lower endothelial density remain valuable for tectonic reconstruction when preserved appropriately. **Keywords:** penetrating keratoplasty, polymegethism, cellular pleomorphism

ZINC OXIDE NANOPARTICLES IN CARTILAGE TISSUE ENGINEERING: A COMPREHENSIVE MAPPING OF THE LITERATURE

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Introduction: Osteoarthritis and focal osteochondral defects represent a major clinical challenge due to the avascular nature and limited regenerative capacity of articular cartilage. While mesenchymal stem cell (MSC)-based therapies offer immense potential, directing their specific chondrogenic lineage remains a bottleneck. Zinc oxide nanoparticles (ZnO-NPs) have emerged as promising bioactive agents providing structural reinforcement and osteochondrogenic signaling cues.
Material and Methods: A comprehensive mapping of the literature was conducted, analyzing extensive pre-clinical data (~300 citations) to evaluate the therapeutic efficacy, physicochemical properties, and cytotoxicity profiles of ZnO-NPs in cartilage tissue engineering. Data were systematically clustered based on nanoparticle morphology, concentration, signaling pathways, and scaffold integration. **Results:** The therapeutic window of ZnO-NPs is strictly dose- and morphology-dependent. Concentrations below 10–15 µg/mL demonstrate excellent biocompatibility and promote MSC chondrogenesis without inducing apoptosis. However, smaller (<30 nm) and spherical NPs accelerate Zn^{2+} burst release, increasing the risk of acute reactive oxygen species (ROS) generation and cytotoxicity. Conversely, anisotropic and streamlined ZnO-NPs exhibit a gradual ion release, offering sustained biological effects and enhanced rheological properties in hydrogels. Molecularly, ZnO-NPs effectively upregulate key chondrogenic markers (SOX9, COL2A1) and modulate critical pathways (TGF-β, Wnt/β-catenin). Furthermore, integrating ZnO-NPs into synthetic, natural, or 3D-printed scaffolds significantly improves biomechanical stability and cellular integration in various *in vivo* models. **Conclusions:** ZnO-NPs represent a highly versatile platform for cartilage regeneration, actively driving chondrogenic differentiation while suppressing hypertrophic degeneration. Standardizing their physicochemical parameters (size, shape, dose) is essential to maximize therapeutic efficacy, avoid nanotoxicity, and accelerate successful clinical translation.
Keywords: zinc oxide nanoparticles, cartilage regeneration, tissue engineering, nanotoxicity.

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RANK/RANKL/OPG SIGNALING IN BONE GRAFT INTEGRATION IN ONCOLOGIC PATIENTS

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Introduction: Bone grafting is frequently required in oncologic patients after tumor resection, management of pathological fractures, or reconstruction following metastatic bone destruction. Successful graft integration depends on a tightly regulated balance between bone resorption and bone formation, processes controlled primarily by the receptor activator of nuclear factor kappa-B (RANK), its ligand RANKL, and the decoy receptor osteoprotegerin (OPG). In malignancy-associated bone disease, this regulatory axis is often disrupted, resulting in excessive osteoclast activation and structural instability. The objective of this study was to elucidate the molecular mechanisms through which imbalance of the RANK/RANKL/OPG signaling pathway affects bone graft integration in oncologic patients. **Material and methods:** A structured narrative literature review was conducted using 10 peer-reviewed articles published between 2016 and 2026. Data were collected from biomedical databases including ScienceDirect, PubMed Central, BioMed Central, and related scientific sources. Experimental studies, translational research, and clinical investigations evaluating alterations in RANK, RANKL, and OPG expression in primary bone tumors and bone metastases were analyzed. Particular emphasis was placed on molecular signaling pathways, cytokine-mediated regulation, and their implications for bone remodeling and graft incorporation. **Results:** Malignant cells and tumor-associated stromal elements promote increased RANKL expression while suppressing OPG production, leading to enhanced osteoclastogenesis. This imbalance accelerates bone resorption, degrades extracellular matrix integrity, and weakens mechanical stability at the graft-host interface. Pro-inflammatory cytokines such as interleukin-6 (Il-6) and tumor necrosis factor-α (TNF-α) further stimulate osteoclast differentiation and amplify osteolytic activity. Sustained bone turnover interferes with osteoblast-mediated mineralization and delays graft incorporation. Emerging evidence indicates that targeted modulation of the RANK/RANKL/OPG pathway may reduce pathological bone resorption and create a more favorable microenvironment for graft integration. Furthermore, disruption of this signaling balance alters cellular communication within the bone niche, prolonging catabolic remodeling and increasing the risk of incomplete graft stabilization. **Conclusion:** Dysregulation of the RANK/RANKL/OPG axis represents a central biochemical mechanism contributing to impaired bone graft integration in oncologic patients. Improved understanding of this pathway may support the development of molecularly guided therapeutic strategies aimed at enhancing reconstructive outcomes and long-term graft stability. **Keywords:** RANK/RANKL/OPG, bone graft integration, osteoclastogenesis, oncology, molecular imbalance, bone remodeling.

OXIDATIVE STRESS AND ITS IMPACT ON BONE GRAFT INTEGRATION AFTER ONCOLOGIC THERAPY

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Introduction: Bone tissue regeneration following grafting is a complex biochemical and cellular process that requires balanced osteoblast activity, controlled osteoclast resorption, and adequate vascularization. In oncologic patients, chemotherapy and radiotherapy significantly disrupt systemic redox homeostasis, leading to excessive production of reactive oxygen species (ROS). Elevated oxidative stress may interfere with normal bone remodeling and compromise graft incorporation. The objective of the study was to elucidate the biochemical mechanisms through which oxidative imbalance affects bone graft integration after cancer treatment. **Material and methods:** A narrative literature review was performed, using 10 articles from 2016-2026, including data from ScienceDirect, PubMed Central, Biomed Central, MedScape, and others, focusing on experimental and clinical studies evaluating oxidative stress biomarkers, mitochondrial dysfunction, and alterations in bone cell metabolism in patients undergoing oncologic therapy. Molecular pathways related to ROS generation, antioxidant defense systems, and intracellular signaling involved in osteoblast and osteoclast regulation were examined. **Results:** Increased ROS levels activate intracellular signaling cascades that promote osteoclast differentiation and enhance bone resorption. At the same time, oxidative stress inhibits osteoblast proliferation, reduces collagen type I synthesis, and decreases alkaline phosphatase activity, impairing extracellular matrix formation and mineral deposition. Chemotherapeutic agents induce mitochondrial dysfunction and reduce cellular energy availability, further compromising regenerative capacity. Radiotherapy contributes to vascular damage, reduced osteocyte viability, and persistent inflammatory signaling within bone tissue. Diminished antioxidant defenses, including superoxide dismutase and glutathione-dependent pathways, exacerbate oxidative injury. This biochemical imbalance weakens early graft stabilization and increases the risk of delayed healing or graft failure. Moreover, oxidative stress alters angiogenic signaling pathways, reducing vascular endothelial growth factor (VEGF) expression and impairing neovascularization essential for graft survival. Experimental findings suggest that modulation of oxidative stress may partially restore osteoblastic activity and improve structural graft incorporation. **Conclusion:** Oxidative stress represents a significant biochemical determinant of impaired bone graft integration in oncologic patients. Targeting redox imbalance may offer supportive therapeutic potential in reconstructive protocols. Further clinical investigations are required to establish evidence-based antioxidant strategies capable of improving transplantation outcomes. **Keywords:** oxidative stress, reactive oxygen species, bone graft integration, chemotherapy, bone regeneration, oncology.

COMPLICATIONS AND GRAFT REJECTION AFTER KERATOPLASTY: CLINICAL OUTCOMES AND RISK FACTORS IN A TERTIARY OPHTHALMOLOGY SERVICE

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Introduction. Corneal blindness is a major cause of visual impairment, and keratoplasty is often the only option to restore corneal transparency and function. Despite advances in surgical techniques, postoperative complications and graft rejection still limit long-term graft survival. This study aimed to characterise complications after keratoplasty, estimate the incidence and timing of graft rejection, and identify major clinical risk factors in a tertiary ophthalmology centre.**Materials and Methods.** We performed a retrospective observational study including 76 eyes of 72 patients who underwent penetrating or lamellar keratoplasty at the Ophthalmic Surgery Centre *Ovisus*, Chișinău, between 2019 and 2024. Demographic data, indication for keratoplasty, surgical technique, pre-existing ocular status, postoperative course and clinical signs of rejection were extracted from medical records. Best corrected visual acuity (BCVA), graft transparency, postoperative complications and episodes of rejection were analysed. Associations between potential risk factors and rejection were assessed using odds ratios (OR) with 95% confidence intervals (95% CI) in univariate and multivariate models, with statistical significance set at $p < 0.05$. **Results.** Mean age at surgery was 52.6 ± 14.3 years; 56.9% of patients were male. The main indications were corneal dystrophies (28.9%), ectatic disease including keratoconus (23.7%), post-infectious corneal scars (19.7%) and postsurgical endothelial decompensation (17.1%). Lamellar keratoplasty was performed in 57.9% of eyes (DALK 21.1%, DSAEK 19.7%, DMEK 17.1%), while 42.1% underwent penetrating keratoplasty. At least one postoperative complication occurred in 44.7% of eyes; early events (25.0%) were mainly transient corneal oedema (15.8%), suture-related problems (11.8%), infectious keratitis (3.9%) and ocular hypertension (9.2%). Graft rejection was documented in 18.4% of eyes (14/76), more frequently after penetrating than lamellar keratoplasty (25.0% vs 13.6%). Independent predictors of rejection were postoperative inflammatory or infectious episodes (adjusted OR 4.92; 95% CI 1.48–16.31) and non-adherence or premature tapering of topical corticosteroids (adjusted OR 4.21; 95% CI 1.19–14.87). **Conclusions**. Keratoplasty provides meaningful visual rehabilitation, but nearly half of grafts experience postoperative complications and almost one fifth develop rejection. Careful preoperative risk assessment, strict control of postoperative inflammation and infection, and reinforcement of adherence to corticosteroid therapy are essential to improve long-term graft survival and visual outcomes.

Keywords: corneal transplantation; keratoplasty; graft rejection; postoperative complications; risk factors; corneal dystrophy; lamellar keratoplasty

POSTOPERATIVE AUTOLOGOUS MONONUCLEAR CELL THERAPY IN PEDIATRIC HYPERTROPHIC RHINITIS: COMPARATIVE CLINICAL OUTCOMES FOLLOWING LASER DIODE AND BIPOLAR CAUTERIZATION

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Introduction. Hypertrophic chronic rhinitis in children is frequently associated with inferior turbinate enlargement, leading to persistent nasal obstruction, sleep disturbances, and reduced quality of life. Surgical reduction techniques such as laser diode and bipolar cauterization are widely used; however, postoperative inflammation and delayed mucosal recovery remain clinical challenges. Cell-based regenerative approaches may enhance tissue repair and functional restoration. The aim of this study was to evaluate the efficacy and safety of postoperative autologous mononuclear cell therapy in children undergoing inferior turbinate reduction. **Materials and methods.** A prospective comparative study included 40 children aged 7–17 years diagnosed with hypertrophic chronic rhinitis. Patients were allocated into four parallel groups (n=10 each): laser diode (LD), laser diode plus cell therapy (LD+CT), bipolar cauterization (CB), and bipolar cauterization plus cell therapy (CB+CT). Autologous mononuclear cells were obtained from peripheral blood and administered locally in the early postoperative period under endoscopic guidance. Patients were followed for 24 months. Primary outcomes included symptom severity (NOSE score), rhinomanometric nasal resistance, and endoscopic evaluation of edema and crusting. Secondary outcomes included acoustic rhinometry parameters, complications, and recurrence rate. Statistical analysis involved repeated-measures models and intergroup comparisons with $p<0.05$ considered significant. **Results.** All groups demonstrated postoperative improvement; however, patients receiving adjunctive cell therapy showed significantly greater and sustained symptom reduction. At 24 months, mean NOSE scores decreased from 73 to 14 in the LD+CT group compared with 30 in LD alone and 36 in CB. Rhinomanometric resistance showed greater reduction in LD+CT (0.45 to 0.20 $Pa/cm^3/s$) compared to non-cell therapy groups. Postoperative inflammatory signs and recurrence rates were lower in both cell therapy groups, with the most favorable outcomes observed in the laser diode plus cell therapy combination. **Conclusions.** Postoperative autologous mononuclear cell therapy enhances mucosal recovery, reduces inflammation, and improves long-term functional outcomes in pediatric hypertrophic rhinitis. The combination of laser diode surgery and cell therapy demonstrated the best clinical profile over 24 months, supporting further development of regenerative strategies in rhinologic surgery. **Keywords:** hypertrophic rhinitis; inferior turbinate; autologous mononuclear cells; laser diode; bipolar cauterization; pediatric rhinology; regenerative therapy.

AUTOLOGOUS *vs* ALLOGENEIC SEPTAL CARTILAGE GRAFTING IN RHINOLOGIC SURGERY: CURRENT EVIDENCE, BENEFITS, RISKS, AND FUTURE DIRECTIONS (NARRATIVE REVIEW)

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Introduction. Septal cartilage grafting is a fundamental technique in rhinoplasty and rhino-septoplasty for restoring nasal structure, correcting contour defects, and improving airway function. When autologous septal cartilage is insufficient or unavailable—particularly after prior septal surgery—allogeneic cartilage from tissue banks may represent an alternative. This review summarizes current evidence on autologous and allogeneic septal cartilage transplantation in rhinologic surgery, focusing on clinical outcomes, safety, and future regenerative perspectives. **Materials and methods.** A narrative literature review was conducted using PubMed, Google Scholar, and ResearchGate. Publications from 2000 to 2024 were screened. Inclusion criteria comprised full-text articles in English, Romanian, or Russian addressing rhinoplasty or rhino-septoplasty with autologous or allogeneic septal cartilage grafting. Original studies, reviews, editorials, and meta-analyses were analyzed. Additional relevant sources were identified through reference screening. Due to methodological variability, findings were synthesized qualitatively. **Results.** Autologous septal cartilage remains the preferred graft material in rhinologic surgery due to high biocompatibility, structural stability, and low immunologic risk. Clinical reports describe predictable integration and high patient satisfaction regarding both functional and aesthetic outcomes. Allogeneic cartilage is less frequently used but may be valuable when autologous tissue is limited. Reported risks include infection and rejection-like reactions, necessitating careful case selection and informed consent. Advances in harvesting and implantation techniques, including endoscopic approaches, improve visualization and postoperative recovery but require surgical expertise. **Conclusions.** Both autologous and allogeneic septal cartilage grafts are effective in rhinologic procedures. Autologous cartilage remains first-line due to its safety profile, while allogeneic grafts provide a viable alternative in selected cases with access to certified tissue banks. Future directions include refinement of surgical techniques, standardization of outcome assessment, and exploration of regenerative strategies to enhance graft integration and tissue remodeling. **Keywords:** septal cartilage; autologous graft; allogeneic graft; rhinoplasty; rhino-septoplasty; tissue banking

THE SYNERGY OF PHACOEMULSIFICATION AND BIO-GRAFTS: A NEW ERA IN ACUTE GLAUCOMA MANAGEMENT

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Introduction. Acute angle-closure glaucoma (AACG) presents as an ophthalmic emergency characterized by abrupt, severe increases in intraocular pressure (IOP), leading to irreversible apoptosis of retinal ganglion cells. Contemporary approaches increasingly support definitive lens extraction as an adjunct to conventional pressure-lowering therapies. In addition, the incorporation of biological tissue modulation strategies is being explored to optimize ocular hemodynamics and promote neural survival, preventing the risk of surgical failure caused by fibrosis. **Methods and materials.** This study analyzed literature on MIGS and biological grafting from articles (2016-2026) using PubMed. Search optimization utilized MeSH terms (“Phacoemulsification”, ”Amniotic membrane”) and keywords. The review incorporated national protocols and international data on amniotic membrane and MSC derivatives. **Results.** Early phacoemulsification resolves pupillary blockage, maintaining a mean post-operative IOP of 14.2 mmHg. Utilizing an amniotic membrane (AMT) as a “bio-shield” correlates with a 23% success rate increase ($p< 0.01$) by modulating wound healing and preventing subconjunctival fibrosis. In Republic of Moldova this synergy reduced post –operative inflammation by 40%. Research on MSC-derived exosomes shows a 26% improvement in ganglion cell density, suggesting a potential for functional neuroregeneration. **Conclusions.** The evolution of acute glaucoma management is marked by a transition from mechanical pressure control to biological reconstruction. The synergy between phacoemulsification and bio-grafts provides an objective framework for both pressure control and structural neuroprotection. This evidence-based approach confirms the viability of advanced regenerative protocols as a sustainable evolution in acute glaucoma management.
Keywords: Acute glaucoma; Phacoemulsification; Amniotic membrane; Neuroregeneration; Bio-grafts; Tissue Engineering.

THE ROLE OF OBESITY AS AN IMMUNOMETABOLIC FACTOR IN TISSUE AND CELL TRANSPLANTATION

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Background. Obesity has a critical global public health challenge, characterized by excessive accumulation of adipose tissue and a state of chronic systemic inflammation that disrupts metabolism and immune function. The low-grade inflammation and immunometabolic dysfunction typical of obesity involve an imbalance of adipokines and pro-inflammatory cytokines, which can affect host immune responses and graft tolerance after transplantation. In this context, the molecular mechanisms of obesity, including activation of the NF-κB pathway and insulin resistance, may influence both graft survival and the risk of rejection. The aim of the study is to evaluate the role of obesity as an immunometabolic determinant of tissue and cell transplant success. **Material and Methods.** Articles from the MDPI, PubMed, Researcher, NCBI, WILEY, Science Direct databases published between 2020 and 2026 were analyzed. Observational studies and systematic reviews were included to estimate current evidence about the impact of obesity on the immunometabolic homeostasis in the context of tissue and cell transplantation. **Results.** Current evidence suggests that the inflammatory and immunometabolic status associated with obesity correlates with significant alterations in the post-transplant microenvironment. Elevated levels of TNF-α, IL-6, and leptin, together with decreased adiponectin, have been associated with persistent activation of the NF-κB pathway and amplification of the proinflammatory immune response, promoting increased allo-reactivity of T lymphocytes and reduced regulatory T cell function. This proinflammatory immune polarization contributes to enhanced acute rejection and progression of chronic rejection. Furthermore, insulin resistance has been linked to endothelial dysfunction, increased oxidative stress, and impaired angiogenesis in the transplanted tissue, with affecting graft perfusion and integration. A microenvironment characterized by excess reactive oxygen species and mitochondrial dysfunction promotes activation of apoptotic pathways and fibrotic remodeling of the transplanted tissue, mechanisms involved in reduced long-term graft survival. **Conclusion.** In the case of cellular transplantation, the obesity-associated proinflammatory state has been correlated with decreased engraftment rates. Overall, these biochemical and immunometabolic changes support the association between obesity and an increased risk of post-transplant complications, rejection, and graft loss. **Keywords:** obesity, immunometabolism, inflammation, insulin resistance, oxidative stress, engraftment

THE ROLE OF ANGIOGENESIS IN TISSUE TRANSPLANT

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Background. Ischemia reperfusion injury (IRI) is one of the most important mechanisms involved in delayed or reduced graft function after transplantation. It is a complex pathophysiological process, followed by a pro-inflammatory response that enhances the immunogenicity of the graft and the risk of acute rejection. Tracheal, cartilage and skin allotransplantation have historically been unfeasible because of the absence of a vascular pedicle for anastomosis. Stimulating angiogenesis may be a solution. **Objective of the study**. To elucidate the mechanism of angiogenesis in order to combate ischemia reperfusion injury in transplants. **Materials and methods**. A review of the literature from 2016-2026 was performed, using 11 articles, including data from ScienceDirect, PubMed Central, Biomed Central, MedScape, and others. **Results**. Angiogenesis is the process of new blood vessel formation from pre-existing network through *endothelial cell* (EC) migration and proliferation playing a crucial role in post-transplant recovery and organ function, with decreased activity potentially indicating graft failure. In rewieved literature have been mentioned effectiveness of supplementing transplants with *Fibroblast Growth Factor 2* (FGF-2) or *Vascular Endothelial Growth Factor (*VEGF), VEGF hydrogel, fibrin precipitate, *sphingosine-1-phosphate* (S1P), erythropoietin, *induced pluripotent stem cells* (iPSCs). Unfortunately, these methods promote the formation of small-caliber vessels that are prone to stenosis and thrombosis. While angiogenesis is induced by hypoxia and results in new capillaries, arteriogenesis is induced by physical forces, most importantly fluid shear stress and mast cells in orchestrating leukocyte function in this process. Fluid shear stress, induce the adherence of platelets to ECs, a process mediated by the interaction of the platelet receptor *Glycoprotein Ib α* (GPIbα) with the endothelial *von Willebrand factor* (vWF). Subsequently resulting in *platelet–neutrophil aggregate* (PNA) formation and neutrophil extravasation. **Conclusions.** In conclusion it may be effective to use physical methods in promoting arteriogenesis. For example, vacuum aspiration of the plague before skin-graft transplantation. On other hand it may be efficient to supplement transplants with preconditioned mast cells originate from hematopoietic stem cells.

Key-words: Neoangiogenesis, Arteriogenesis, IRI, Fluid shear stress.

FROM CELLS TO FLOW: BIOENGINEERING SCHLEMM'S CANAL ENDOTHELIUM AS A NOVEL THERAPY FOR GLAUCOMA

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Introduction. Glaucoma is a progressive visual neuropathy that is often linked to elevated intraocular pressure. It is primarily brought on by a malfunction in the normal outflow of aqueous humour. Even while the majority of current treatments use medicine or surgery to lower intraocular pressure, they do not address the underlying biological cause, which is damage to the structures that control outflow. The Schlemm's canal endothelium, a specialized endothelium with properties halfway between the vascular and lymphatic systems, has been shown to play a crucial role in maintaining intraocular pressure homeostasis in recent years. Increased drainage resistance in glaucoma is directly caused by its malfunction. The purpose of the research is to analyze the Schlemm canal endothelial bioengineering using stem cells and its promise as a regenerative treatment approach for glaucoma. **Materials and methods.** Databases as PubMed, Scopus, Web of Science were used to conduct a narrative literature review. Included were reviews and experimental papers from the past 20 years on regenerative applications in glaucoma, three-dimensional culture models, "eye-on-a-chip" microfluidic systems, and stem cell differentiation into Schlemm's canal-like endothelial cells. Analysis was done on biomechanical characteristics, phenotypic markers, biological mechanisms, and reported functional outcomes. **Results.** According to research, mesenchymal stem cells and induced pluripotent stem cells can develop into Schlemm's canal-specific endothelial cells that exhibit distinctive markers and react to mechanical stress similarly to natural tissue. Their incorporation into microfluidic devices and three-dimensional models has made it possible to improve outflow and partially recreate the drainage pathway. Real therapeutic promise has been suggested by experimental models that demonstrate a decrease in drainage resistance and a return to normal intraocular pressure. There are still restrictions on tissue integration, immune response regulation, and long-term survival, though. **Conclusion.** A promising approach to regenerative therapy for glaucoma is the bioengineering of the Schlemm canal endothelium, which aims to restore the drainage pathway's physiological function rather than merely reduce intraocular pressure symptoms. Preclinical findings are promising, but more research is required to confirm safety and clinical suitability.

CREATION OF ARTIFICIAL LIVER: TECHNOLOGIES, DIRECTIONS. REVIEW

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Introduction. The artificial liver support system (ALSS) is a therapeutic approach and an important direction in biomedical research, involving the use of an external device to replace or support liver functions in patients with acute or chronic liver failure who require liver transplantation. This study aims to review and synthesize current technologies and research directions in the development of artificial liver systems that sustain the lives of patients with acute and chronic liver failure. **Material and methods**. A review of 32 bibliographic sources from the specialized literature published over the past 10 years was conducted using the databases Google Scholar, PubMed, National Institutes of Health (NIH), BioMed Central (BMC), SpringerLink, and ScienceDirect, focusing on technologies and research directions in artificial liver systems. **Results.** There are three main categories of ALSS: 1.) non-biological artificial liver (NBAL) – hemoperfusion, plasmapheresis, MARS, Prometheus, SPAD, SEPET, that operate on the principles of dialysis and adsorption. 2.) bioartificial liver (BAL) - ELAD, HepaCure-BAL, AMC-BAL, that integrate hepatocytes (porcine, human, tumor HepG2 and its derivative C3A, immortalized, stem cells: embryonic (ESCs), induced pluripotent (iPSCs), human mesenchymal (MSCs)) in bioreactors to reproduce the liver's biosynthesis and detoxification functions. 3.) hybrid artificial liver (HAL) - HepatAssist, MELS, Li-HAL, that combines efficient detoxification of NBAL with metabolic functions of BAL. **Conclusions.** Artificial liver support systems improve survival rates among patients with acute or chronic liver failure awaiting liver transplantation and, in individuals with preserved hepatic regenerative capacity, promote full functional recovery.
Keywords: artificial liver, liver failure, NBAL, BAL, HAL.

INTERNEURON TRANSPLANTATION – A NEW TREATMENT PERSPECTIVE IN DRUG-RESISTANT EPILEPSY

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Introduction. Nowadays, adequate seizure management represents a challenge, as approximately 30-40% of patients with epilepsy fail to control them. The loss or malfunction of inhibitory interneurons in the cortex and hippocampus causes persistent hyperexcitability. Interneuron transplantation, a minimally invasive approach, aims to restore inhibitory pathways in the epileptic subjects. The purpose of the research was to elucidate the mechanisms by which interneuron transplantation could insure the treatment of epilepsy. **Materials and Methods.** 11 scientific articles from the PubMed database, published between 2016-2026, were analyzed. **Results.** The treatment of drug-resistant epilepsy represents a challenge for clinicians and common surgical interventions, performed for therapeutic purposes, due to their invasive nature, could be accompanied by complications, such as neurological deficits. Transplantation of gamma-aminobutyric acid (GABA)ergic interneurons was proposed as an alternative treatment for epilepsy refractory to pharmacological therapy. Researchers have identified a significant benefit with spontaneous seizure suppression (up to 84-92%) and reduced mortality in the mouse model of mesial temporal lobe epilepsy (MTLE), Stargazer mouse model of absence epilepsy or models lacking a voltage-gated potassium channel (Kv1.1), where the cells used were derived from medial ganglionic eminence of the ventral telencephalon of the embryo. After transplantation into cortical and hippocampal regions, these cells survived (up to 20-22%), migrated locally from injection site (up to 5 mm) and were integrated into host cerebrum to form inhibitory circuits, and were found to have morphological similarities to native interneurons, but did not proliferate in the host brain. Also, in preclinical research, this intervention was associated with a significant reduction in dentate granule cell dispersion, a pathological feature of MTLE, but the effects were dose-dependent.
Conclusions. Interneuron transplantation is a cell therapy that was tested in various rodent models of epilepsy, demonstrating positive results, but further studies are needed to prove its clinical utility and safety in patients. Currently, the studies are limited due to ethical concerns and potential physiological incompatibility.
Keywords: interneuron, epilepsy, cell transplantation, inhibition

VULVAR CANCER ASSOCIATED WITH RENAL TRANSPLANTATION

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Introduction. Chronic immunosuppression, required after renal transplantation, significantly increases the risk of developing vulvar cancer. This type of cancer is frequently associated with persistent HPV infection and tends to have a more aggressive clinical course than in the general population. Identification of molecular markers may contribute to the development of personalized therapeutic strategies and the optimization of immunosuppressive regimens. **Materials and Methods.** A narrative literature review was conducted to synthesize current evidence on vulvar cancer in renal transplant recipients, examining relevant studies identified through electronic databases such as *PubMed*, *Scopus*, and *Web of Science*. **Results.** Most tumors examined in the context of renal transplantation were HPV-positive, predominantly genotypes 16 and 33. Overexpression of the p16 protein was observed in more than two-thirds of patients, indicating an HPV-dependent mechanism. The proliferative index Ki-67 was elevated, correlating with high-grade histology and rapid disease progression. Activation of the *PI3K/AKT/mTOR* signaling pathway was more frequent in patients treated with calcineurin inhibitors, and *PD-L1* expression was detected in 30–35% of tumors, suggesting a potential role for immunotherapy, although limited by the risk of graft rejection. Conversion of the immunosuppressive regimen to mTOR inhibitors was associated with better tumor control and reduced recurrence. In addition, *PTEN* loss correlated with *PI3K/AKT/mTOR* pathway activation and aggressive histological features. Integration of these markers allowed individualized therapeutic approaches, including immunosuppression adjustment, targeted therapy, and radiotherapy planning. Data analysis showed that approximately 40% of patients with multiple positive molecular markers experienced recurrence within 12 months, compared to only 15% of those without marker combinations, indicating a significantly increased risk of rapid disease progression. **Conclusions.** Vulvar cancer post-renal transplantation exhibits a distinct molecular profile, dominated by HPV-dependent mechanisms and *PI3K/AKT/mTOR* pathway activation. Systematic molecular testing may guide personalized therapy and immunosuppressive management, highlighting the importance of a multidisciplinary oncologic and transplant approach. **Keywords:** vulvar cancer, renal transplantation, molecular markers.

BIOLOGICAL BIOMATERIAL IN CUTANEOUS REGENERATION: EXPERIMENTAL STUDIES

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Introduction. Biological biomaterials derived from decellularized extracellular matrix (ECM) represent an important direction in regenerative medicine due to their structural similarity with native tissue and their ability to support cellular adhesion, proliferation, and tissue remodeling. The present study aimed to develop and experimentally evaluate biological wound dressings obtained through tissue engineering techniques and to assess their regenerative potential in cutaneous wound healing. **Materials and Methods**. Biomaterials were obtained from porcine dermis and small intestinal submucosa (SIS) using decellularization protocols based on Triton X-100 and sodium deoxycholate treatments to remove antigenic cellular components while preserving the ECM architecture. *In vitro* biocombatibility was evaluated using the MTT assay on human dermal fibroblasts. The regenerative capacity of the biomaterials was investigated *in vivo* using a full-thickness excisional wound model in Wistar rats. Wound healing progression was monitored macroscopically and microscopically at 7, 14, and 21 days. Histological and immunohistochemically analyses included CD31 for angiogenesis, CD68 for inflammatory response, collagen IV for basement membrane reconstruction, and AE1/AE3 for epithelial regeneration. **Results**. The MTT assay demonstrated high cellular compatibility of the biomaterials, with fibroblast viability reaching approximately 103 % after 72 hours compared to control cultures. *In vivo* experiments revealed accelerated wound healing in animals treated with biological dressing compared with saline-treated controls. The SIS-based collagen scaffold combined with povidone –iodine induced enhanced angiogenesis, with average vascular density of approximately 45 CD31-positive vessels per microscopic field, whereas wounds treated with decellularized dermal matrices combined with gentamicin presented about 30 vessels per field. CD68 staining showed an initial macrophage aggregation in the early inflammatory response and progressive stromal organization. Collagen IV immunostaining revealed more continuous basement membrane reconstruction in the SIS-based biomaterial group. AE1/AE3 staining confirmed progressive re-epiteliazation and restoration of epidermal architecture during advanced healing stages. **Conclusions.** Biological dressings derived from porcine extracellular matrices demonstrated good biocompatibility and significantly improved cutaneous regeneration by stimulating angiogenesis, extracellular matrix remodeling, and epithelial restoration. The findings support the potential clinical application of ECM-based biomaterials in regenerative medicine and reconstructive surgery for the treatment of complex skin wounds. **Keywords:** tissue engineering, extracellular matrix, biological dressings, skin regeneration, angiogenesis, wound healing.

IMMUNOSUPPRESIVE AGENTS USED IN ORGAN TRANSPLANTATION

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Introduction. In recent decades, organ transplantation has become increasingly accessible for saving patients' lives, and the development of immunosuppressive drugs has played a key role in improving postoperative care, patient survival and quality of life. In this context, efforts are needed to broaden the spectrum of immunosuppressive drugs used for induction and maintenance therapy based on advances in immunology and better understanding of their mechanism of action. **Materials and methods**. A selection and analysis of articles published in the PubMed database over the last 10 years was performed in order to elucidate the groups of immunosuppressants, their mechanisms of action and their impact on the immune system. **Results**. The main classes of immunosuppressive agents used in organ transplantion include: the calcineurin inhibitors (CNIs-cyclosporine and tacrolimus); mammalian target of rapamycin (mTORi-sirolimus, everolimus); antiproliferative or antimetabolite agents (azathioprine, mycophenolate mofetil); glucocorticosteroids (GC-prednisolone, methylprednisolone); biological immunosuppressive drugs (basiliximab, alentuzumab, rituximab, eculizumab, tocilizumab etc.). Calcineurin inhibitors bind to intracellular proteins (immunophilins), leading to the inhibition of calcineurin and gene transcription in the nuclear factor of activated T-cells pathway in a wide range of cells, including T cells, B cells and all myeloid lineage cells. Mammalian target of rapamycin inhibitors form a complex with the intracellular protein and inhibit the activation of mTOR serine-threonine kinase. This disruption of the IL-2 receptor signaling pathway impairs the proliferation of B and T lymphocytes. Mycophenolate inhibits inosine monophosphate dehydrogenase which results in impaired purine synthesis with broad effects on T cells, B cells, dendritic cells, monocytes, and macrophages. Azathioprine is metabolized to 6-methyl-MP and 6-thioguanine that inhibits DNA synthesis, impairing B- and T-cell proliferation. Glucocorticoids interact with intracellular specific receptors and alter gene regulation leading to changes in cell function, indirect effects via alterations of cytokine release and cell signalling. Belatacept is a fusion protein composed of a modified extracellular domain of the cytotoxic T-lymphocyte antigen 4 and selectively inhibits T-cell activation. Basiliximab, IL-2 receptor monoclonal antibody, inhibits IL-2 binding to IL-2 receptor and thus inhibiting IL-2 dependent T-cell proliferation. Alentuzumab, anti-CD52 monoclonal antibody, binds to CD-52 producing antibody dependent lysis of T-cells and B-cells. Rituximab, anti-CD20 monoclonal antibody, binds to CD-20 producing B-cell depletion via a variety of mechanisms including antibody dependent cytotoxicity and antibody- dependent cellular cytotoxicity. Eculizumab, anti-complement (C5) monoclonal antibody, prevents cleavage of C5 into C5a and C5b and prevents formation of membrane attack complex. Tocilizumab, IL-6 receptor antagonist, inhibits the action of cytokine IL-6. **Conclusions**. The analysis showed that most immunosuppressive agents markedly inhibit cellular immunity (T-cells), while humoral immunity was most strongly afected by GC and rituximab, followed by CNIs, antimetabolites, alemtuzumab. In contrast, mTORi and IL-6 receptor antagonists exerted minimal effect on humoral immunity. Innate immunity was effectively diminished by GC and eculizumab. **Keywords**: organ transplant, immunosuppressive agents, mechanism of action, cellular immunity, humoral immunity.

DIABETOGENIC EFECT OF IMMUNOSUPPRESSIVE DRUGS IN TRANSPLANT RECIPIENTS

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Introduction. In organ transplant patients, new onset diabetes mellitus after transplantation (NODAT) has been found to be a frequent and serious complication. The use of immunosuppressive drugs after transplantation has been shown to be one of the most significant risk factors for the development of NODAT. It has been estimated that the pathogenetic links of NODAT are reduced to impaired insulin secretion, insulin resistance and damage of the pancreatic beta-cells. **Materials and methods**. A selection and analysis of english-language articles in the PubMed database from the last 10 years was performed in order to elucidate the pathogenic mechanisms of glucose metabolism disorders in the use of immunosuppressive drugs for allograft preservation. **Results**. Calcineurin inhibitors (cyclosporine, tacrolimus) produce hyperglycemia by decreasing insulin secretion, increasing insulin resistance and direct toxic damage to beta-cells. Insulin resistance increases due to dysregulation of genes responsible for insulin sensitivity in myocytes and adipocytes, as well as by decreasing the number of GLUT-4 transporters in muscle and adipose cell membranes. The diabetogenic effect becomes more pronounced when combined with glucocorticoids. Tacrolimus has proven to be more effective than cyclosporine as an immunosuppressant, but also with a more pronounced diabetogenic effect. mTOR (mammalian target of rapamycin) inhibitors, such as sirolimus and everolimus, may induce hyperglycemia through multiple mechanisms, including increased insulin resistance due to impaired insulin signaling, direct β-cell dysfunction with reduced insulin secretion, and enhanced hepatic gluconeogenesis. Glucocorticoids can contribute to the development of NODAT by: increasing insulin resistance; decreasing insulin secretion; stimulating gluconeogenesis in the liver; inducing beta-cell apoptosis. Studies have shown that short-term post-transplant glucocorticoid pulse therapy continued with low-dose maintenance therapy reduces the risk of NODAT. Antimetabolites (azathioprine, mycophenolate mofetil) are not considered to have diabetogenic effect. At the same time, these drugs may reduce the diabetogenic effects of calcineurin inhibitors and glucocorticoids by allowing the use of lower doses of these immunosuppressants. Belatacept showed a lower incidence of NODAT, but also reduced the hyperglycemic effects of calcineurin inhibitors.
Conclusions. Immunosuppressants used in the post-transplant period, calcineurin inhibitors, mTOR inhibitors and glucocorticoids, may be responsible for disturbances in glucose metabolism and the development of NODAT. The incidence may increase with the combined use of these immunosuppressants. Belatacept demonstrated a low incidence of hyperglycemia, and antimetabolites did not show a diabetogenic effect. The combination of immunosuppressive agents at lower doses may potentiate the therapeutic effect and reduce the incidence of hyperglycemia.
Keywords: organ transplantation, immunosuppressive drugs, new onset diabetes mellitus after transplantation, calcineurin inhibitors, mTOR inhibitors, antimetabolites.

RESTORING THYROID FUNCTION WITH TISSUE-ENGINEERED PRODUCTS AFTER TOTAL THYROIDECTOMY

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Introduction: Post-thyroidectomy hypothyroidism is a common complication of total thyroid removal, traditionally managed with lifelong hormone replacement therapy. Thyroid models developed through tissue engineering represent innovative approaches to restore endocrine function. This study summarizes recent advances in thyroid tissue engineering and compares the efficacy and practical potential of various methods. **Materials and Methods:** We conducted a narrative review using articles published between 2009-2025, focusing on autologous thyroid transplants, stem cell-derived thyrocytes, organoids, hydrogel scaffolds, and decellularized matrices. Preclinical and in vitro outcomes assessed included thyroid hormone production (T3, T4, TSH), follicular architecture, vascularization, and long-term stability. We synthesized the data descriptively to compare functional restoration and practical feasibility. **Results:** Autologous thyroid cell sheets transplanted into pre-vascularized, retrievable Cell Pouch™ devices restored serum T3 and T4 to 95-100% of baseline in rat models within 4-7 weeks. Histology attested 95% normal follicular architecture and angiogenesis in all grafts, with endocrine function maintained till 20 weeks. Pluripotent stem cells differentiated into thyroid follicular cells expressed NKX2-1 and PAX8 in >90% of cells. These cells secreted T4 at 80- 85% of what native tissue produces in vitro, but in vivo endocrine rescue reached only 30-40% of normal serum T4. Decellularized human thyroid scaffolds and hydrogel matrices increased cell survival by 70-80%, maintained follicular organization in ~85% of constructs, and encouraged blood vessel growth. Thyroid organoids from fetal and adult tissues proved over 90% efficiency in forming follicles and produced hormones reaching 75-80% of normal T4 output. Comparative analysis indicates that autologous transplantation in vascularized devices currently provides the strongest restoration of thyroid function. Meanwhile, stem cell and organoid-based strategies have significant potential for personalized regenerative therapies. **Conclusions:** Tissue-engineered methods can restore post-thyroidectomy endocrine function, with autologous thyroid cell transplantation in pre-vascularized devices demonstrating good efficiency in preclinical studies. Stem cell-derived thyrocytes, organoids, and hydrogel scaffolds give complementary platforms for functional restoration and future clinical applications. Further exploration is necessary to optimize scalability, vascularization, immune compatibility, and long- term safety for human implementation. **Keywords:** thyroid tissue engineering, thyroid regeneration, post-thyroidectomy hypothyroidism, stem cells.

PERINATAL STEM CELLS IN REGENERATIVE MEDECINE AND TRANSPLANTATION: CURRENT APPLICATIONS AND FUTURE PERSPECTIVES

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Introduction. The preservation of perinatal biological materials - umbilical cord blood, umbilical cord tissue, and placental tissue - has become one of the most important developments in modern preventive and regenerative medicine. These tissues represent a unique biological resource rich in hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs). Compared with adult stem cells, perinatal stem cells demonstrate higher proliferative potential, broader differentiation capacity, and lower immunogenicity. Since the first successful umbilical cord blood transplantation in 1988, the clinical field of stem cell transplantation has expanded rapidly. To date, more than 40,000 cord blood transplants have been performed worldwide. Beyond hematological diseases, increasing scientific attention is focused on the role of perinatal stem cells in regenerative medicine, tissue engineering, and advanced transplantation technologies. Their biological characteristics make them a promising platform for future personalized therapeutic strategies. **Materials and Methods.** This analytical review was conducted using systematic literature searches in major biomedical databases including PubMed and ClinicalTrials.gov. Key search terms included: umbilical cord blood banking, perinatal stem cells, mesenchymal stem cells, regenerative medicine, and tissue transplantation. More than 600 scientific publications were initially identified. Following relevance screening and quality assessment, 12 peer-reviewed clinical studies and experimental reports were selected for detailed analysis. The review focused on clinically validated therapeutic applications of perinatal stem cells as well as emerging experimental approaches in regenerative transplantation and tissue bioengineering. **Results.** Hematopoietic stem cells obtained from umbilical cord blood are currently used in evidence-based clinical practice for the treatment of more than 80 diseases, including leukemias, lymphomas, inherited metabolic disorders, and immune deficiencies. Mesenchymal stem cells derived from umbilical cord tissue and placenta demonstrate strong regenerative, anti-inflammatory, and immunomodulatory properties. These characteristics make MSCs particularly attractive for regenerative therapeutic strategies. Recent experimental clinical studies suggest potential applications of perinatal stem cells in neurological injuries, including spinal cord trauma, where stem cells may contribute to neuronal repair and functional recovery. In orthopedic and traumatology practice, MSC-based therapies are increasingly investigated for enhancing tissue regeneration following joint replacement procedures and severe musculoskeletal injuries. At the same time, regenerative medicine is moving toward organ bioengineering. Researchers at Tel Aviv University and Sheba Medical Center have successfully developed human kidney organoids derived from stem cells that remained stable for up to 34 weeks under laboratory conditions and demonstrated developmental characteristics similar to fetal kidney tissue. **Conclusions.** Perinatal stem cell banking represents a strategically important biomedical resource capable of expanding the therapeutic potential of modern cell and tissue transplantation. The integration of cryopreserved perinatal stem cells into regenerative medicine, trauma recovery protocols, and organ bioengineering may significantly transform future treatment strategies for severe diseases and complex injuries. As regenerative technologies continue to evolve, access to high-quality perinatal stem cells is likely to become a decisive factor shaping the future of personalized medicine and transplantation science. **Keywords:** Perinatal stem cells, umbilical cord blood, regenerative medicine, mesenchymal stem cells, cord blood banking

TRANSLATIONAL PERINATAL MEDICINE IN NON-IMMUNE FETAL HYDROPS: FROM PRENATAL TO MODERN CELLULAR THERAPIES

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Introduction. Non-immune fetal hydrops (NIHF) represents one of the most severe conditions in fetal medicine, characterized by the pathological accumulation of fluid in at least two fetal compartments and associated with high perinatal mortality. Its heterogeneous etiology includes genetic anomalies, cardiovascular pathologies, congenital infections, and idiopathic causes. Recent advances in prenatal diagnostics have improved early etiological identification; however, therapeutic options remain limited. Translational perinatal medicine aims to integrate insights from cellular biology and regenerative medicine into fetal management, including the use of cellular therapies and intrauterine transplantation strategies. The objective of this study is to evaluate the potential role of modern cellular therapies in the management of NIHF. **Materials and Methods.** A narrative review of recent scientific literature published between 2022 and 2025 in PubMed, Scopus, and Web of Science was conducted, including review articles and experimental studies. Data were synthesized descriptively, and results from experimental studies were analyzed comparatively. **Results.** Current literature confirms that the prognosis of NIHF largely depends on the prenatal etiological diagnosis and the timeliness of therapeutic intervention. The development of stem cell–based therapies, including transamniotic administration of mesenchymal and hematopoietic stem cells, has shown promising effects on fetal hematopoiesis, placental inflammation, and fetal survival in experimental models. Innovative strategies, such as transamniotic stem cell therapy, enable systemic fetal cell distribution through minimally invasive approaches. Furthermore, extracellular vesicles derived from amniotic fluid–derived stem cells have demonstrated regenerative potential in compromised fetal lung development, a mechanism relevant to the progression of fetal hydrops. These approaches support a transition from purely supportive care toward targeted biological interventions. **Conclusions** The integration of advanced prenatal diagnostics with cellular therapies represents a promising approach in managing non-immune fetal hydrops. Translational perinatal medicine enables the shift from understanding pathogenic mechanisms to fetal regenerative interventions. Future studies are needed to validate the safety and efficacy of intrauterine cellular transplantation and improve neonatal outcomes. **Keywords:** non-immune fetal hydrops, prenatal diagnosis, stem cell therapy, fetal therapy, translational medicine

IMPLEMENTING REGENERATIVE MEDECINE ACROSS SURGICAL PATHWAYS IN LIVER CIRRHOSIS

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Introduction: Liver cirrhotic patients often face surgical and interventional procedures, such as hepatectomy with modulation of future liver remnant, portoenterostomy in cases of biliary atresia, transjugular intrahepatic portosystemic shunt, and liver transplant. Regenerative medicine is progressively tested for the improvement of liver regeneration, prevention of progression of liver fibrosis, and reduction of liver failure. **Materials and methods:** A systematic review (2020-2026) was performed in PubMed/Medline, Scopus, and ClinicalTrials.gov using "cirrhosis", "mesenchymal stem cells/MSC/umbilical cord", "liver-derived progenitor/HALPC/HepaStem", "organoid/iPSC/hepatocyte-like cells", and procedural terms like "Kasai", "transplantation", "hepatectomy", "portal vein embolization", "ALPPS", "future liver remnant". The information was collected regarding population, time frame, delivery method, evaluation criteria, and safety. The selection was made using descriptive statistics due to heterogeneity in results. **Results:** Allogeneic infusion of umbilical cord-derived mesenchymal stem cells has been performed in postoperative cirrhotic patients after Kasai portoenterostomy, allowing the short-term monitoring of liver function. The perioperative administration of MSC has been tested in a controlled form in transplant patients to modulate alloimmune responses, reduce inflammatory damage, and boost graft recovery of function. Liver-derived progenitor products: the development of human allogeneic liver-derived progenitor cells (HALPC/HepaStem) in severe cirrhosis-related syndromes such as ACLF gave a regulated development platform that could be potentially applied to surgical mitigation. Regenerative liver surgery, including portal vein embolization, liver venous deprivation, and ALPPS-based procedures, represents the most established strategy to enhance the growth of the future liver remnant in selected patients with compromised liver parenchyma to reduce the risk of post-hepatectomy liver failure. In contrast, the iPSC-based graft strategies have been in the field of translation, thus limiting the perioperative use of such methods. **Conclusions:** Regenerative strategies for operative cirrhosis remain advanced for surgical interventions that stimulate pre-hepatectomy hypertrophy, while MSC and liver-derived progenitor cell-based regenerative therapies remain in early-phase, safety-focused trials for the post-Kasai and peri-transplant context. Future research should focus on standard product, procedure-specific timing, endpoints such as MELD/Child-Pugh, portal hypertension, post-hepatectomy liver failure, and properly powered randomized trials within surgical pathways.**Keywords:** liver cirrhosis; regenerative medicine; mesenchymal stem cells; umbilical cord MSC; future liver remnant

PANCREATIC ISLET CELL AUTOTRANSPLANTATION AS A THERAPEUTIC OPTION IN CHRONIC PANCREATITIS COMPLICATED BY PANCREATIC PSEUDOCYST

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Introduction. In the management of chronic pancreatitis (CP), pancreatic pseudocyst (PCP) is a complication that requires the attention of surgeons, provided that it is non-neoplastic, recurrent, >6 cm in size, persists >4 weeks, has calcifications, causes ductal strictures, is refractory to endoscopic drainage and endoscopic ductal decompression. When CP is complicated by such a PCP, which progressively destroys the parenchyma, total pancreatectomy with pancreatic islet cell autotransplantation (PACT) can be opted for. **Objectives**. To analyze the relevance of using PACT in patients with PCP who opt for total pancreatectomy, to evaluate the clinical success and post-operative risks. **Materials and methods.** Research of scientific literature, from electronic databases such as PubMed, Web of Science and ScienceDirect, was conducted for the last decade. **Results**. ACIP represents the last therapeutic step when all other medical alternatives fail. The non-functional pancreas is completely removed, the islets are isolated from the extracted pancreas, and the islets are retransplanted into the portal vein, thus preserving the reserve of insulin and C-peptide secretion . To increase the therapeutic yield, it is necessary to comply with several clinical conditions: severe CP, basal glycemia <200 mg/dL, HbA1c <8%, islet-positive patient, age <60 years, absence of terminal diseases and advanced cirrhosis. The major contraindication is the presence of type 1 diabetes, since there is a risk of immune rejection of the islet transplant. Post-ACIP results are promising with clinical improvement of up to 90%. Beneficial effects include: reduced risk of insulin dependence and avoidance of severe hyperglycemia, maintenance of normal HbA1c for at least 12 months, pain relief and opioid withdrawal (59%), and total insulin independence when IEQ/kg > 5000 (48%). Post-ACIP risks include: endocrine morbidity (18.6%), postoperative hemorrhage (10%), exocrine symptoms (43.5%), postpancreatectomy pancreatogenic diabetes (<1%), portal vein thrombosis (5%) and mortality (1.6%) . Perioperative morbidity is 50%, with the need for surgical reintervention in 16% of patients. **Conclusions**. ACIP offers an advantageous therapeutic combination for patients with pancreatic complications, such as PCP: it relieves pain, allows preservation of endocrine function and the perioperative risk is minimal. **Keywords**: chronic pancreatitis, pancreatic pseudocyst, transplantation, islet cells, pancreatogenic diabetes

FECAL MICROBIOTA TRANSPLANTATION IN METABOLIC SYNDROME

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Introduction. Metabolic syndrome (MetS) is a multifactorial disease, and the gut microbiota plays an important role in its pathogenesis. Moreover, recent studies suggest associations between gut dysbiosis and components of MetS. **Materials and methods.** A descriptive review was conducted on the effects of FMT on MetS components, based on the specialized literature from the period 2015-2025, selected from the PubMed, Springer Nature, BMC databases. **Results.** The aim of the study is to evaluate the impact of fecal microbiota transplantation (FMT) on patients with MetS. Most of the reviewed studies, in the first 6 weeks after FMT, reported changes in the composition of the gut microbiota and improvements in some clinical parameters: reduction in glycemia, insulinemia and glycated hemoglobin (HbA1c) levels, and increase in HDL-cholesterol levels. Regarding LDL-cholesterol, triglycerides, anthropometric parameters and blood pressure, most studies did not identify significant changes. These results suggest that FMT may improve some metabolic parameters in the short term. Regarding long-term effects, fewer studies have been conducted and their results are controversial. At least 2 studies associate FMT with reduction in abdominal adiposity and changes in the overall composition of the gut microbiota at 26 weeks after FMT. The improvement in insulin sensitivity, reduction in blood glucose, HbA1c and LDL-cholesterol were transient and, in most cases, statistically insignificant. Also, there were no significant differences in weight and body mass index compared to the placebo group. **Conclusions.** Fecal microbiota transplantation, as an adjuvant therapy, may be useful in the treatment of metabolic syndrome. However, further studies are needed to better understand the molecular mechanisms by which gut microbiota metabolites influence laboratory parameters and clinical conditions of metabolic syndrome

LUNG TRANSPLANTATION IN THE MANAGEMENT OF CYSTIC FIBROSIS

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Introduction. Cystic fibrosis (CF) is an autosomal recessive genetic disorder caused by mutations in the *CFTR* gene, affecting multiple organs, particularly the lungs, and leading to progressive respiratory failure. Despite therapeutic advances, some patients progress to advanced stages of the disease, for whom lung transplantation represents the only option with a significant impact on survival. **Materials and Methods.** A narrative synthesis of specialized literature was conducted using GeneCards, PubMed, the National Library of Medicine, and Hinari, focusing on publications from the past 10 years. **Results.** Analysis of the specialized literature indicates that lung transplantation in patients with advanced CF leads to significant improvements in respiratory function and quality of life. Post-transplant survival is estimated at 80–90% at one year, 78–82.8% at three years, and 69–77% at five years, while long-term survival at 10 years ranges between 50–62%, with a median of approximately 10–10.7 years. Clinical factors, including chronic infections and post-transplant rejection, influence prognosis, whereas lung retransplantation is associated with lower survival compared to primary transplantation, highlighting the importance of rigorous patient selection and optimal timing of intervention. Optimization of perioperative management and personalized immunosuppressive therapy contributes to complication reduction and improved survival. Multidisciplinary coordination of patient management further enhances clinical outcomes and long-term survival. **Conclusions.** Lung transplantation represents an essential intervention for patients with advanced CF, significantly improving life expectancy. Rigorous perioperative management, personalized immunosuppressive therapy, and multidisciplinary coordination contribute to the reduction of post-operative complications and improved clinical outcomes. Post-transplant risks persist, requiring continuous monitoring and adaptive interventions. **Keywords:** Cystic fibrosis, lung transplantation, post-transplant survival.

STRATEGIES FOR MITIGATING OXIDATIVE STRESS IN TRANSPLANTED CELLS

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Introduction. Transplantation is a vital treatment for organ failure, degenerative diseases and severe tissue injuries. Challenge being, the poor function, survival of transplanted cells caused by oxidative stress. During the transplantation, ischemia and reperfusion injury generates reactive oxygen species (ROS). These highly reactive molecules damage lipids, proteins, and nucleic acids, leading to mitochondrial dysfunction and apoptosis. Oxidative stress leads to graft failure. This study explores strategies to mitigate oxidative stress for improving the survival of transplanted cells. **Materials and Methods**. A literature review was synthesized from Google scholar, PubMed, Scopus, and Web of Science, focusing on oxidation and antioxidant-based protective strategies from articles between 2010 and 2024. Research regarding transplantation and organ preservation was included. Data on pharmacological treatments and cellular preconditioning were collected and compared. Descriptive analysis was applied to summarize the protective effects reported. **Results.** Pharmacological antioxidants like N-acetylcysteine serve as vital glutathione (GSH) precursors, replenishing the intracellular thiol pool to facilitate peroxide detoxification, while vitamin C and vitamin E scavenge ROS and protect cells. Activation of the nuclear factor erythroid 2-related factor 2 (Nrf2), a master transcription factor regulating cellular defense against oxidative and electrophilic stress, controls over 200 genes, including antioxidant enzymes like superoxide dismutase and catalase, increasing expression and preventing oxidative damage in transplanted tissues. Cellular preconditioning and antioxidant supplementation before transplantation improve mitochondrial membrane potential and reduce apoptosis. Advanced biomaterial scaffolds and preservation solutions enriched with mitochondria-targeted antioxidants also reduce oxidative injury during the procedure. Specifically, these combined interventions not only preserve structural cellular integrity but also significantly enhance early engraftment rates. By maintaining mitochondrial homeostasis and preventing lipid peroxidation, targeted therapies effectively suppress ROS-induced inflammatory signaling. This synergistic approach -bolsters intrinsic defenses while providing extrinsic ROS scavenging- minimizes acute rejection risks and promotes robust, long-term functional recovery of the graft. **Conclusions.** Mitigating oxidative stress improves the survival of transplanted cells. Strategies such as antioxidant therapies and the activation of endogenous protective pathways show promising results in reducing graft injury. Future research on targeted antioxidant approaches can enhance long-term graft outcomes.
Keywords: Oxidative stress; reactive oxygen species; antioxidant therapy; Nrf2; transplantation; graft survival.

IMPACT OF DONOR AGE ON 10-YEAR GRAFT SURVIVAL IN DECEASED-DONOR KIDNEY TRANSPLANTATION: A MODERN REGISTRY ANALYSIS

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Introduction: The growing shortage of donor kidneys has led to the increased utilization of older deceased donors. Age-related structural changes in the renal parenchyma may reduce graft longevity, raising clinical concerns regarding long-term outcomes. This study evaluated the association between donor age and graft survival using large-scale registry data to refine organ allocation strategies. **Material and Methods**: Data were obtained from the United Network for Organ Sharing (UNOS) and Eurotransplant registries for adult deceased-donor kidney transplants performed between 2011 and 2016. This range ensured a minimum 10-year follow-up for all subjects by late 2025. Recipients were stratified by donor age: <40, 40–59, and ≥60 years. The primary outcome was ten-year death-censored graft survival (DCGS). Multivariable Cox proportional hazards models, adjusted for Kidney Donor Profile Index (KDPI), cold ischemia time (CIT), and recipient comorbidities, were used to calculate adjusted hazard ratios (aHR). **Results:** Increased donor age was significantly associated with progressively lower graft survival. Ten-year DCGS rates were 72% for donors <40, 61% for 40–59, and 42% for those ≥60 years. Donors in the ≥60 age group exhibited a significantly higher risk of graft loss (aHR 2.04; 95% CI, 1.81–2.29; $p < 0.01$). While older grafts were associated with higher rates of delayed graft function (DGF), modern "old-for-old" allocation and the increased use of machine perfusion during the 2011–2025 period partially mitigated early failure rates in the elderly cohort. **Conclusions**: Donor age is a critical determinant of long-term kidney graft survival. While older donors remain essential for expanding the donor pool, the significant decline in ten-year survival highlights the need for optimized preservation techniques, such as machine perfusion. These findings support the continued refinement of age-matching strategies to maximize the utility of available organs. Future research should focus on the molecular markers of renal aging to better predict the longevity of "expanded criteria" organs. **Keywords:** kidney transplantation, donor age, graft survival, delayed graft function.

LYMPHATIC TISSUE ENGINEERING: EXPERIENCE OF THE LABORATORY OF TISSUE ENGINEERING AND CELL CULTURE AT NICOLAE TESTEMITANU STATE UNIVERSITY OF MEDECINE AND PHARMACY

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Introduction: Lymphedema (LE) is a chronic and progressive disease caused by damage to lymphatic vessels and/or lymph nodes (LNs). Conservative treatment includes complex decongestive therapy, physiotherapy, exercise, and skin care, while surgical treatment options include lymphovenous anastomosis, vascularized LN transfer, and reductive procedures such as liposuction and excisional techniques. Although these approaches provide symptomatic relief, they do not restore damaged lymphatic structures. Lymphatic tissue engineering (LTE) represents a promising regenerative strategy, combining biomaterials, scaffolds, cells, growth factors, and *in vitro* and *in vivo* models to promote the regeneration of lymphatic structures. **Materials and methods:** This work is based on a literature review in LTE and presents our experience in LNs-based TE. The literature review focused on current strategies in LTE, with an emphasis on LNs decellularization, decellularized scaffold, lymphatic endothelial cell culture, and preclinical animal models. Articles were selected from PubMed, Google Scholar, and Scopus, without time restrictions. Our experience at the Laboratory of Tissue Engineering and Cell Culture involves decellularization method applied to nonvascularized lymph nodes (NLNs) in small animal models, assessing their potential for regenerative applications. **Results:** Anatomical studies of the lymphatic system in small animal models (rats) were performed to identify suitable models for LN-based TE. Among the LN examined, the axillary LN was found to be the most practical and accessible for experimental procedures. A low-concentration detergent protocol was developed for decellularization of NLNs. This protocol allowed effective removal of cellular components while preserving the extracellular matrix architecture, providing a suitable scaffold for potential regenerative applications, as demonstrated in our previous experience. The literature review revealed that similar approaches have been explored in other preclinical models, showing that decellularization and decellularized scaffold-based strategies can preserve LN microarchitecture and support regenerative applications. **Conclusion:** (i) Axillary LN in small animal models are practical for LN-based TE; (ii) Low-concentration detergent decellularization preserves extracellular matrix structure, providing scaffolds for regenerative applications; (iii) Preclinical studies support these strategies, highlighting their potential to promote lymphatic regeneration and improve treatments for lymphedema.

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APPLICATIONS OF NEURAL STEM CELLS-LITERATURE REVIEW

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Background. Neural stem cells (NSCs) are multipotent progenitor cells capable of self-renewal and differentiation into the principal cellular components of the central nervous system, including neurons, astrocytes, and oligodendrocytes. In the adult brain, NSCs are primarily located in the subventricular zone and the hippocampal dentate gyrus, where they contribute to limited physiological neurogenesis. Advances in stem cell biology, molecular neuroscience, and regenerative medicine have significantly increased interest in the therapeutic potential of neural stem cells. Numerous experimental studies and emerging clinical trials have explored the capacity of NSCs to promote neural regeneration and functional recovery in a wide range of neurological disorders. The unique biological properties of neural stem cells, including their proliferative capacity, migratory behavior, and ability to integrate into neural circuits, make them promising candidates for cell-based therapies aimed at restoring damaged nervous tissue. **Aim of the study**. The aim of this literature review is to analyze current scientific evidence regarding the applications of neural stem cells in regenerative medicine and neurological disease treatment, with emphasis on their mechanisms of action and therapeutic potential. **Results**. The reviewed literature demonstrates that neural stem cells have been investigated in several neurological conditions, including neurodegenerative diseases, cerebrovascular disorders, traumatic injuries, and demyelinating diseases. In neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis, NSCs have shown the potential to replace damaged neurons and provide neuroprotective support through the secretion of trophic factors. In stroke and traumatic brain injury models, neural stem cell transplantation has been associated with improved functional recovery by stimulating endogenous neurogenesis, promoting angiogenesis, and reducing inflammatory responses. In spinal cord injury, NSCs may contribute to neuronal replacement, remyelination, and reconstruction of neural pathways. Furthermore, research suggests that neural stem cells can play a role in the treatment of demyelinating diseases such as multiple sclerosis by differentiating into oligodendrocytes and promoting remyelination. In addition to therapeutic applications, NSCs are widely used in disease modeling, drug screening, and neural tissue engineering. **Conclusion**. Neural stem cells represent a promising strategy for the treatment of various neurological disorders due to their regenerative and neuroprotective properties. Although preclinical and early clinical studies demonstrate encouraging outcomes, further research and well-designed clinical trials are required to establish the safety, efficacy, and long-term therapeutic benefits of neural stem cell–based therapies.

METHODS FOR INDUCING GLAUCOMA IN ANIMAL MODELS: EXPERIMENTAL APPROACHES AND RESEARCH APPLICATIONS

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Introduction. Glaucoma is a leading cause of irreversible blindness worldwide, characterized by progressive optic neuropathy and retinal ganglion cell loss, often associated with elevated intraocular pressure. Experimental animal models are essential for understanding disease mechanisms and evaluating novel therapeutic strategies. This study aims to review and systematize the principal methods used to induce glaucoma in animal models. **Materials and Methods.** A narrative review of the literature was conducted using major biomedical databases, including PubMed, Scopus, and Web of Science. Relevant studies describing experimentally induced glaucoma in animals were selected and analyzed. Methods were classified based on the mechanism of intraocular pressure elevation and anatomical or functional alterations. No statistical analysis was applied, as this study is descriptive in nature. **Results.** Several experimental techniques for inducing glaucoma were identified. The most commonly used methods include laser photocoagulation of the trabecular meshwork, episcleral vein cauterization, microbead or viscoelastic injection into the anterior chamber, and genetic manipulation in transgenic models. Laser-based models allow controlled and reproducible intraocular pressure elevation but require specialized equipment. Episcleral vein occlusion produces sustained pressure increase, though variability may occur. Microbead injection is minimally invasive and widely used due to its reproducibility and adaptability. Genetic models provide insight into molecular mechanisms but may not fully replicate acquired glaucoma. Each model presents specific advantages and limitations depending on the research objective. **Conclusions.** Animal models of glaucoma are indispensable tools in ophthalmological research, enabling the investigation of pathophysiological processes and therapeutic interventions. The selection of an appropriate induction method should be guided by the study's aims, reproducibility requirements, and available resources. Future research should focus on refining models to better mimic human glaucoma and improve translational applicability. **Keywords** glaucoma, animal models, intraocular pressure, experimental ophthalmology, trabecular meshwork, retinal ganglion cells, laser photocoagulation, microbead injection

ADSC-ENRICHED AUTOLOGUS FAT GRAFTING IN FACIAL REJUVENATION

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Introduction: Autologous fat transfer (AFT) is widely applied in facial rejuvenation due to its biocompatibility and capacity to restore age-related volume loss. Although patient satisfaction remains high, long-term predictability is limited by graft survival, with traditional techniques demonstrating approximately 50–60% volume retention at one year. To improve these outcomes, stromal vascular fraction (SVF) – enriched grafting, also referred to as cell-assisted lipotransfer (CAL), incorporates adipose-derived stem cells (ADSCs) in order to enhance tissue integration, angiogenesis and regenerative capacity. This paper analyzes the biological mechanisms and clinical outcomes of ADSC-enriched autologous fat grafting in facial rejuvenation. **Material and Methods:** A structured literature review was performed focusing on publications from 2015 to 2025. Thirty-five records were identified through searches in PubMed, HINARI and Google Scholar using combinations of the terms "autologous fat grafting", "adipose-derived stem cells", "stromal vascular fraction", "cell-assisted lipotransfer" and "facial rejuvenation". After screening titles and abstracts, full-text articles were evaluated according to predefined inclusion criteria and eighteen publications met the eligibility criteria. **Results:** ADSC enrichment improves graft performance through multiple mechanisms. These include stimulation of angiogenesis via increased secretion of vascular endothelial growth factor and fibroblast growth factor, reduction of oxidative stress and modulation of inflammatory pathways that facilitate tissue regeneration. Enhanced neovascularization improves oxygenation during the critical early ischemic phase, thereby supporting graft survival. Reported retention rates for CAL reached up to 88%, compared with 50–60% in conventional AFT, 6 months post-procedure. Patient satisfaction increased from approximately 81% with traditional grafting to 91.1% following ADSC enrichment. Histological findings demonstrated increased collagen and elastin deposition, improved dermal thickness and enhanced vascularization. While complications were not eliminated, they appeared reduced. Traditional AFT is associated with fat resorption, necrosis and infection, whereas CAL primarily reported lower incidence of these events and rare vascular embolism. **Conclusions:** ADSC-enriched fat grafting enhances angiogenesis, dermal remodeling, and long-term volume stability compared with conventional techniques. Standardization of protocols and larger controlled studies remain necessary to define optimal clinical guidelines and confirm long-term safety and efficacy.
Keywords: autologous fat grafting, adipose-derived stem cells, stromal vascular fraction, cell-assisted lipotransfer, facial rejuvenation.

COMPLEX RECONSTRUCTION OF THE POSTOPERATIVE CAVITY IN TYPE B1 TYMPANIC PARAGANGLIOMA USING AUTOLOGOUS TISSUES

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Introduction. Tympanic paragangliomas are rare, highly vascular tumors that can resemble chronic ear infections, which may delay diagnosis and treatment. Removing large tumors can leave wide tissue defects and carries a high risk of bleeding. Safe and effective reconstruction is therefore essential. This paper presents a clinical case of complex reconstruction of a large postoperative cavity using combined autologous tissues. **Materials and Methods**. We present the case of a 63-year-old woman from an urban area whose symptoms began in 2006. She reported hearing loss, ear pain, pulsatile tinnitus, vertigo, and poorly controlled hypertension. For about 15 years, she was treated for right chronic suppurative *otitis media*. During this period, she developed severe right-sided ear bleeding that required emergency care. Otomicroscopy showed a red, pulsating mass blocking the external auditory canal. Magnetic resonance imaging revealed a hypervascular lesion (1.1 × 0.9 cm) in the external auditory canal and middle ear. Computed tomography confirmed a type B1 tympanic paraganglioma according to the Fisch classification. The tumor was surgically removed. The postoperative defect was reconstructed by filling the cavity with autologous abdominal fat, placing auricular cartilage for support, and using temporalis fascia to rebuild the tympanic membrane and restore the middle ear. The combined use of these autologous tissues helped control bleeding and reduced the risk of postoperative hemorrhage. **Results**. The postoperative recovery was good, with no bleeding or infection. The grafts healed well, successfully closing the cavity and providing stable support. The anatomical and clinical outcomes were satisfactory. **Conclusions**. Reconstruction with abdominal fat, auricular cartilage, and temporalis fascia is a safe and effective method for treating large defects after tympanic paraganglioma removal. Autologous tissues are well tolerated, provide good structural support, and help prevent bleeding complications. This approach is a valuable option in reconstructive ear surgery. **Keywords:** tympanic paraganglioma; autologous grafts; middle ear reconstruction; postoperative cavity; otologic surgery

CELLULAR THERAPY IN DIABETIC RETINOPATHY

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Introduction. Diabetic retinopathy is one of the most common microvascular complications of type 1 and type 2 diabetes and a major cause of visual impairment and blindness in adults. Its pathogenesis involves complex mechanisms, including chronic hyperglycemia, oxidative stress, inflammation, and microvascular dysfunction, which cause progressive deterioration of retinal structures. Although conventional treatments, such as anti-VEGF agents, laser photocoagulation, or intravitreal corticosteroids, can slow disease progression, they do not regenerate the affected retinal cells. In this context, stem cell therapy represents a promising avenue of research in regenerative medicine. The objective of this study was to evaluate and synthesize the recent studies on the efficacy of cell therapies in diabetic retinopathy. **Material and methods.** This work was conducted through a review of the national and international literature. Eighty references published between 1989 and 2025 were analyzed. They were selected from scientific databases such as PubMed, ClinicalTrials.gov, Elsevier, Google Scholar, and Medscape. The analysis included original articles, preclinical studies, and clinical trials related to the use of cell therapies in diabetic retinopathy, as well as the pathogenic mechanisms involved in the development and progression of this disease. **Results.** The literature review highlights the therapeutic potential of various types of stem cells, particularly mesenchymal stem cells derived from bone marrow, adipose tissue, umbilical cord blood, and perinatal tissues. These cells exert beneficial effects through multiple mechanisms, such as the secretion of paracrine factors, modulation of the inflammatory response, reduction of oxidative stress, and stimulation of tissue regeneration. Preclinical studies have shown that stem cell transplantation or the administration of stem cell-derived exosomes can protect retinal structure, reduce neuronal degeneration, and improve microvascular integrity. Preliminary clinical studies suggest that cell therapies could improve visual function and reduce retinal inflammation, but the results remain limited and require validation. **Conclusions** Cell therapy represents an innovative and promising strategy for the treatment of diabetic retinopathy. It could target the pathogenic mechanisms of the disease and promote the regeneration of affected retinal structures. However, further studies are needed to evaluate the safety, efficacy, and long-term clinical applicability of these therapies. **Keywords:** diabetic retinopathy, cell therapy, regenerative medicine, mesenchymal stem cells.

Varia

BRAINSTEM IN MORPHOCLINICAL ASPECT

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Introduction. Morphoclinical analysis of the brainstem is essential due to its structural complexity and the severity of associated disorders. Stroke represents the main acute neurological pathology, presenting a wide range of symptoms with major implications for vital and functional prognosis. Purpose of the work: Evaluating the morphological particularities of the brainstem in patients with stroke by correlating clinical findings with imaging data. **Material and methods.** The study included a total of 30 patients diagnosed with vertebrobasilar stroke and hospitalized at the Institute of Emergency Medicine, Chișinău (2020-2025). The investigation analyzed demographic characteristics, associated risk factors and comorbidities, clinical manifestations, stroke types and subtypes, brainstem lesion location and vertebrobasilar arterial variants. **Results.** The study group included 63% male patients (M) and 37% female patients (F), stratified by age: 31-40 years – 9% (all F), 41-50 years – 13% (6.5% M, 6.5% F), 51-60 years – 13% (10% M, 3% F), 61-70 years – 33% (23% M, 10% F), 71-80 years – 30% (23% M, 7% F), 81-90 years – 2% (all F). Area of residence: urban – 53.5% (33.5% M, 20% F), rural – 46.5% (30% M, 16.5% F). Main risk factors: arterial hypertension – 83.5%, diabetes mellitus – 20%, smoking – 23.5%. Frequent clinical manifestations: motor deficits – 73.5% (57% M, 16.5% F), speech and swallowing disorders – 80% (63% M, 17% F), dyspeptic manifestations – 60% (27% M, 33% F). All patients underwent brain CT, 40% had CT angiography and 3.5% MRI. Stroke types: ischemic – 63.5% (40% M, 23.5% F), hemorrhagic – 36.5% (23.5% M, 13% F). Lesion location: medulla oblongata – 18% (12% M, 6% F), pons – 55% (30% M, 25% F), midbrain – 27% (20% M, 7% F). Ischemic stroke subtypes: lacunar – 26.5% (21.5% M, 5% F), silent – 5% (all M), involutive – 16% (11% M, 5% F), established – 5% (all F), progressive – 47.5% (27% M, 20.5% F). Frequent vertebrobasilar variants: unilateral vertebral artery hypoplasia (58.5%), tortuosity of the vertebrobasilar arterial system (17%). **Conclusions.** Stroke is the primary acute brainstem pathology and a significant public health concern. Correlating clinical findings with brainstem lesion location highlights the importance of symptom analysis in evaluating stroke severity and neurological prognosis.

Keywords: brainstem, vertebrobasilar stroke, stroke severity, morphoclinical analysis

CORRELATION BETWEEN THE WIDTH OF THE FACIAL NERVE TRUNK AND GREATER AURICULAR NERVE

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Introduction. Surgical repair of the facial nerve trunk (FNT) after iatrogenic injures, trauma or tumor removal is one of the primary goals in head and neck surgery. As grafts for facial nerve repair in large nerve defects the sural, the greater auricular nerve (GAN), and anastomosis with the hypoglossal and masseteric nerves are used. Considering the proximity of the GAN to FNT and the fact that harvesting of GAN is comfortable for both surgeons and patients, the goal of our study was to determine the correlation between the widths of the FNT and GAN depending on sex, laterality and cephalometric type. **Materials and Methods.** The study was carried out on 70 dissected formalized adult hemiheads at the Department of Anatomy and Clinical Anatomy of *Nicolae Testemitanu* State University of Medicine and Pharmacy. The measurements of the FNT and GAN widths were done by a caliper. For statistical analysis, Pearson correlation coefficient was applied. **Results.** The mean value of the FNT width was 2.7±0.47 mm, and that of the GAN – 2.9±0.51 mm. A strong and positive correlation ($r=+0.86$), statistically significant ($p<0.001$), between the FNT and GAN widths was established. A positive and very strong correlation between the widths of both nerves was characteristic depending on sex. In males the correlation was positive ($r=+0.78$), $p<0.001$, while in females it was positive and stronger ($r=+0.98$), $p<0.001$. A strong bilateral correlation between the FNT and GAN widths was found. On the right hemiheads Pearson correlation coefficient was ($r=+0.93$) and on the left samples it was ($r=+0.81$), $p<0.001$. The correlation was higher on the right side, $p=0.05$. Depending on the cephalometric type, the lowest correlation was characteristic of mesocephalic type ($r=+0.84$), followed by the brachycephalic type ($r=+0.91$) and the highest value was determined in dolichocephalic type ($r=+0.94$). The correlation coefficient was statistically significant for all cephalometric types: for mesocephalic type ($p<0.001$) and for each of the brachycephalic and dolichocephalic types ($p=0.002$). **Conclusions.** The facial nerve trunk was thinner to 0.2 mm compared to the width of the greater auricular nerve. A strong and statistically significant correlation between the FNT and GAN widths depending on sex, laterality and cephalometric type was established. **Keywords:** facial nerve trunk, greater auricular nerve, cephalometric type, correlation

THE ROLE OF ANGIOGENESIS IN OSTEOARTHRITIS

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Background. *Osteoarthritis* (OA), a degenerative joint disease, involves synovial inflammation, subchondral bone erosion, and cartilage degeneration affecting nowadays more than 630M people worldwide for which there is currently no cure. The aim of the study was to elucidate the role of angiogenesis (ANG) in OA in order to find prevention and treatment methods of this disease.

Materials and methods. Literature review from 2016-2026 was performed, using 13 articles, including data from ScienceDirect, PubMed Central, MedScape, and others.

Results. ANG is regulated by the balance of proangiogenic and antiangiogenic factors, which is modulated by the presence of either a facilitating or inhibitory extracellular matrix environment. The articular cartilage and inner meniscus are avascular structures alimented via diffusion and convection by dense capillary networks of periosteum and synovium. During progressive inflammation in OA, chondrocytes, synovium and subchondral bone produce proangiogenic factors such as *vascular endothelial growth factor* (VEGF), *cysteine rich protein 61* (CYR61) and *wingless-type mouse mammary tumor virus integration site family 1* (WNT1) *inducible signalling pathway protein 3* (WISP3), contributing to synovitis, increased vascular penetration, disruption of the osteochondral junction, endochondral ossification, and increased sensory nerve densities. On other hand recently was shown good results of *platelet-rich plasma* (PRP) and *mesenchymal stem cells* (MSCs) transplantation which produce growth and angiogenic factors. *Transforming growth factor*-β (TGF-β) and *fibroblastic growth factor-2* (FGF-2) showed to enhance the expression of type-II collagen and aggrecan. But VEGF and the *platelet-derived growth factor* (PDGF) have shown to promote successful cartilage healing via induction of proteoglycan deposition. Also it have been shown greater metabolite buildup and ANG of *blood flow restriction* (BFR) training which present exercise technique in which blood flow to a muscle is partially restricted using a cuff or band while performing low-load resistance exercises.

Conclusions. To conclude both angiogenic and antiangiogenic therapies are potential in osteoarthritis, depending on stage and etiology of injury. Antiangiogenic methods are genicular artery embolization, VEGF-blocking antibodies (bevacizumab and ranibizumab) and receptor tyrosine kinase inhibitors (sunitinib, vandetanib and sorafenib). Then, angiogenic methods are *blood flow restriction* training, *platelet-rich plasma* and *mesenchymal stem cells* transplantation.

Key-words: Angiogenesis, ostheoarthritis, MSCs, blood flow restriction training.

KINKING SYDROME OF THE ABDOMINAL AORTA: CASE PRESENTATION

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Introduction: Abdominal aortic kinking syndrome is a rare congenital malformation characterized by angulation of the abdominal aorta (AA), which, depending on the degree of inflection, can alter the origin and trajectory of its branches, including the renal arteries, causing blood flow disorders. The diagnosis of abdominal aortic kinking syndrome is based on imaging studies that provide accurate data on the morphofunctional appearance of the aorta and its branches. Purpose: Case presentation of abdominal aortic kinking syndrome involving the renal arteries. **Materials and methods:** A 45-year-old patient diagnosed with arterial hypertension underwent abdominal aortic angiography at CDM ScanExpert, Chisinau, Republic of Moldova, to determine the cause, which revealed kinking syndrome. **Results:** On the imaging sequences obtained following AA CT angiography, two curves of the abdominal segment of the aorta were identified: the first located at the middle of the L3 vertebra; the second at the AA bifurcation (upper edge of the L5 vertebra). At the same time, bilateral accessory renal arteries were identified. The origin of the left renal artery (LRA) was determined at the middle of L2, and that of the accessory LRA (originating from the AA) at the lower edge of L2. This supernumerary artery crossed the LRA in an ascending trajectory and entered the renal parenchyma of the upper pole. The right renal artery (RRA), originating from the AA at the lower edge of L2, had a sinuous ascending trajectory caused by the first curvature of the AA, thus corresponding to the lower edge of L1 at the renal hilum. The accessory ARD started from the AA slightly below the main renal artery, described a trajectory parallel to it, and penetrated the kidney in the same way through the hilum. Morphometric: the length of the ARS was 39 mm, the diameter was 5 mm; the length of the accessory ARS was 65 mm, diameter – 2.6 mm; the length of the ARD was 25 mm (due to the convexity of the aorta), its diameter – 4 mm; the length of the accessory ARD was 33 mm and its diameter – 3 mm. **Conclusions:** One of the causes of hypertension may be angulation of the abdominal aorta, sinuous course of the renal arteries, presence of accessory renal arteries that intersect and compress the main renal arteries. Imaging methods such as Doppler sonography and CT angiography are considered the "gold standard" in identifying kinking syndrome.

Keywords: kinking syndrome, abdominal aorta, renal artery

MEDICATION NON-ADHERENCE IN CHRONIC CONDITIONS

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Introduction: Medication adherence in chronic diseases is conceptualized as a multidimensional, longitudinal construct encompassing initiation, implementation, and discontinuation of therapy. Failure to initiate prescribed treatment constitutes primary medication non-adherence (PMN), whereas suboptimal implementation or premature discontinuation reflects secondary non-adherence. Refill-based measures primarily assess secondary non-adherence, whereas PMN remains insufficiently studied due to challenges in linking prescribing and dispensing data, despite its significant clinical and economic impact. Against this background, the present study aims to review the prevalence and determinants of primary and secondary non-adherence in chronic diseases and to elucidate their clinical implications. **Material and methods**: A narrative literature review was conducted using electronic databases including EBSCOhost and HINARI. Peer-reviewed articles published within the last five years were screened. Keywords used in the search strategy included: "medication adherence," "persistence," "discontinuation," "chronic diseases". Observational studies, systematic reviews, and clinical studies addressing determinants and outcomes of non-adherence in adult populations were included. **Results:** Primary non-adherence rates in chronic conditions are commonly reported between 14-20%, while persistence frequently declines below 50% within the first year of therapy. Non-adherence is consistently associated with increased emergency department utilization, higher morbidity, mortality, and avoidable healthcare expenditures. Across conditions, adverse drug reactions and the perception of medication-related harm represent prominent barriers affecting both initiation and continuation. Depression and psychological distress are repeatedly linked to reduced adherence across multiple chronic diseases. Multimorbidity, disease burden, regimen complexity, medication cost, and emergency care utilization further increase discontinuation risk. Facilitators of adherence are primarily relational and systemic, including trust in the healthcare team, continuity of care, sufficient consultation time, access to services, health education, social support, and perceived treatment benefit. A strong therapeutic alliance and effective communication help counteract negative beliefs and enhance long-term persistence. **Conclusion:** Non-adherence in chronic diseases is a multidimensional and phase-specific phenomenon influenced by clinical, psychological, and system-level determinants. Identifying the underlying barrier motivating non-adherence is more clinically meaningful than merely detecting its presence. Standardized methodological approaches and integrated health system strategies are essential to design targeted interventions aimed at improving initiation, implementation, and persistence in long-term pharmacotherapy. **Keywords*:*** non-adherence, primary medication non-adherence, chronic diseases, initiation, persistence.

THE MOLECULAR SUBSTRATE OF THE HUMAN SPECIES: DIFFERENCIES BETWEEN MALE AND FEMALE SEX

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Introduction. Delegates of the same species – Homo Sapiens, males and females present strong contrasts which concern cognition, passions, goals and lifestyle. These differences are beyond the two completely unsimilar reproductive systems, term well-known in science as *sexual dymorphism*. The aim of study is to evidentiate the variations between the two sexes, which automatically translate into distinct behavioral patterns. **Materials and Methods.** The current study reveals the analysis and synthesis of articles published in the following databases: PubMed, ScienceDirect, ResearchGate, Google Scholar, uncovering the molecular, anatomical and neurophysiological substrates that divide the human species into two groupes – male and female sex. **Results.** On a cell level, the X chromosome genes offer females immune advantages, elevated stress resistance and angiogenic capacity. Their cardiomyocytes have a greater regenerative capacity, which explains the lower ratio of cardiovascular diseases for women.

The single bone structure that makes a significant difference between sexes constitues the pelvis, evolutionarily more voluminous for females, in order to satisfy birth demands. The other bones follow the principle „the bigger the body, the larger the structures", typical of masculine sex. Males' brain is 8-15% more massive, followed by greater dimensions for the majority of neural parts. They also possess a greater amygdala, which leads to impulsivity in actions and the tendacy to attack. Due to its effects on the amygdala and the orbitofrontal cortex, the testosteron is also responsible for social dominance, agression and for risk-taking behavior. Mens' steroid hormone has an anabolic effect on scheletic muscles, binding to specific androgen receptors, resulting in massive protein synthesis and a great number of myofibrils nuclei. Therefore, males appear stronger, conceived to fight, gain food and protect dear ones. Women show a larger lymbic cortex, suggesting a deeper sense for emotions. Higher quantity of adipose tissue, especially in the femuro-gluteal regions, assures survival in lack of energy, as a benefit for reproduction. **Conclusion.** The way they had been designed – males and females represent two distinct individualities, from an molecular, anatomical, physiological and neuropsychological view. Owing to this fact, despite the struggle for gender equality, these two can never be totally similar, although they are entities intended to coexist harmoniously and to complete reciprocal.

Keywords. sexual dimorphism, steroid hormones, estrogen, testosteron, behaviour, emotions, cognition, longevity.

DECREASED MELANOGENIC ACTIVITY CORRELATE WITH ENHANCED AGGRESSIVENESS OF CUTANEOUS MALIGNANT MELANOMA

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Introduction. Cutaneous malignant melanoma exhibits marked heterogeneity in clinical behaviour and histopathologic appearance. Although tumour thickness, Clark level, and invasive growth patterns remain key prognostic indicators, the significance of melanocytic pigment synthesis remains incompletely defined. Amelanotic melanomas are often associated with delayed diagnosis and poorer outcomes. Loss of pigmentation may reflect melanocytic dedifferentiation, altered melanogenesis pathways, and enhanced invasive potential. The relationship between pigmentation status and established markers of aggressiveness has not been consistently quantified. This study investigates the relationship between pigmentation status and histopathologic indicators of tumour aggressiveness in superficial spreading melanoma.

Materials and Methods. A retrospective analysis was performed on 47 cases of superficial spreading melanoma from the Oncology Institute of Chisinau. Histopathologic evaluation included tumour thickness, Clark level, ulceration, mitotic activity, microsatellitosis, pigmentation status, lymphovascular invasion, perineural invasion, and lymph node involvement. Pigmentation was assessed on hematoxylin–eosin–stained sections and classified as pigmented or non-pigmented. Correlations were analysed using Pearson correlation coefficients, with significance set at $p \leq 0.05$. **Results.** The cohort included 47 patients (mean age 65.6 ± 12.15 years), comprising 24 females (51.1%) and 23 males (48.9%). Pigmented melanomas accounted for 34 cases (72.3%), while 13 cases (27.7%) were non-pigmented. Pigmentation status demonstrated statistically significant inverse correlations with several established histopathologic markers of tumour aggressiveness. A moderate negative correlation was observed between pigmentation and tumour thickness ($r = -0.42$, $p = 0.0001$), indicating that non-pigmented melanomas were associated with increased tumour thickness. Similarly, pigmentation was inversely correlated with Clark level ($r = -0.38$, $p = 0.001$). Pigmentation showed significant negative associations with both, lymphovascular invasion ($r = -0.26$, $p = 0.04$) and perineural invasion ($r = -0.24$, $p = 0.05$), suggesting a higher frequency of invasive features in non-pigmented tumours. No other parameters showed significant correlations. **Conclusions**. Loss of pigmentation in superficial spreading melanoma is associated with a more aggressive histopathologic profile, including greater tumour thickness, higher Clark level, and increased invasive features. Pigmentation status may serve as an additional prognostic indicator and warrants careful evaluation in routine histopathologic assessment. **Keywords:** cutaneous malignant melanoma, pigmentation, tumour aggressiveness, prognostic factors.

TUMOUR THICKNESS AS A PROGNOSTIC FACTOR IN THE EVOLUTION OF CUTANEOUS MALIGNANT MELANOMA

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Introduction. Cutaneous malignant melanoma is a biologically heterogeneous neoplasm characterized by marked variability in clinical behaviour and prognosis. Although, multiple histopathologic parameters are incorporated into contemporary risk stratification models, tumour thickness remains one of the most reliable predictors of disease progression and patient outcome. Evaluation of its association with additional clinicopathologic features may further fortify its role as a key determinant in melanoma aggressiveness. The present study assesses the prognostic significance of tumour thickness in superficial spreading melanoma by analysing its correlations with established markers of tumour progression. **Materials and Methods**. A retrospective analysis was performed on 47 cases of superficial spreading melanoma obtained from the Oncology Institute of Chisinau. All specimens underwent comprehensive histopathologic review to assess tumour thickness, Clark level, ulceration, mitotic activity, microsatellitosis, pigmentation status, and lymph node involvement. Tumour thickness was measured on routine haematoxylin–eosin-stained slides. Statistical analysis of correlations between tumour thickness and clinicopathologic features was performed using Pearson correlation coefficients, with significance defined as $p \leq 0.05$. Results. The cohort included 47 patients with a mean age of 65.6 ± 12.15 years; 24 patients (51.1%) were female and 23 (48.9%) were male. Pigmented melanomas accounted for 34 cases (72.3%), while 13 cases (27.7%) were non-pigmented. Tumour thickness demonstrated statistically significant positive correlations with several indicators of tumour aggressiveness, including Clark level ($r = 0.60$, $p = 0.001$), ulceration ($r = 0.29$, $p = 0.03$), lymphovascular invasion ($r = 0.54$, $p = 0.001$), microsatellitosis ($r = 0.36$, $p = 0.01$), and advanced tumour stage ($r = 0.45$, $p = 0.001$). In contrast, tumour thickness showed a significant inverse correlation with pigmentation status ($r = -0.42$, $p = 0.05$), indicating that thicker tumours were more frequently non-pigmented. No additional clinicopathologic parameters reached statistical significance level.

Conclusions. Tumour thickness is strongly associated with multiple histopathologic features of aggressive behaviour in superficial spreading melanoma. Its correlation with invasive parameters and advanced tumour stage, along with its inverse association with pigmentation, underscores its central prognostic value. These findings support the continued use of tumour thickness as a key prognostic marker and highlight the importance of integrating morphologic parameters in melanoma risk stratification.

Keywords: cutaneous malignant melanoma, tumour thickness, prognostic factors, tumour aggressiveness, superficial spreading melanoma, histology.

CONTEMPORARY APPROACHES IN ANAL CANCER RADIOTHERAPY: BALANCING EFFICACY AND SAFETY

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Introduction. The treatment of localized anal cancer was initially surgical; however, studies by Dr. Norman Nigro demonstrated that neoadjuvant chemotherapy combined with radiotherapy (5-fluorouracil and mitomycin C) can achieve complete responses, reducing the need for immediate surgical intervention. Technological advancements, including intensity-modulated radiation therapy (IMRT) and image-guided radiotherapy, have improved treatment precision and reduced toxicity. This review summarizes the evolution of radiotherapy and explores modern strategies for treatment personalization aimed at optimizing oncologic outcomes. **Materials and Methods.** In this review, we analyzed the scientific literature available through Google Scholar to summarize the evolution of radiotherapy in anal cancer. The focus is on current guidelines for IMRT contouring and planning, as well as strategies aimed at reducing toxicity and personalizing treatment. Criteria for defining target volumes, CTV and PTV margins, methods for protecting organs at risk, and dose delivery techniques, including the use of a simultaneous integrated boost, are also examined. **Results.** Chemoradiotherapy remains the standard treatment, achieving complete responses in the majority of patients. Modification or reduction of chemotherapy from the classical regimen in order to decrease toxicity may negatively impact oncological outcomes. Technological advances in radiotherapy enable the delivery of higher and more precise doses, while reducing both acute and late adverse effects. Contouring of all elective nodal regions is recommended in most stages, with the exception of selected early-stage tumors, and the dose delivered using the simultaneous integrated boost (SIB) technique should be adapted to the primary tumor and involved lymph nodes. Recent research also explores the role of proton therapy and personalized treatment approaches in locally advanced or recurrent disease. **Conclusions.** Treatment of anal cancer should be individualized, adjusting the intensity of therapy according to the stage and characteristics of the tumor. Modern radiotherapy technologies, including IMRT and image-guided radiotherapy, allow for dose optimization and reduction of toxicity. Emerging strategies, such as proton therapy and precise adjustment of target volumes, offer opportunities for treatment personalization and improvement of oncologic outcomes, while the application of contouring guidelines and atlases supports the safe and effective delivery of therapy.
Keywords: anal cancer, radiotherapy, IMRT, proton therapy, toxicity, personalized treatment

TRIMETAZIDINE – A METABOLIC MODULATOR IN PERFORMANCE SPORTS

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Background: Trimetazidine, used in the treatment of angina pectoris, is a metabolic modulator that optimizes cellular myocardial energy metabolism in hypoxia. Due to its potentially ergogenic effects, in 2014 it was included in the World Anti-Doping Agency (WADA) class S4 Hormones and Metabolic Modulators list of prohibited substances. **Objective of the study:** To elucidate the metabolic effects of trimetazidine at the cellular and tissue level, its influence on physical performance, and the potential health risks associated with its unauthorized use in competitive performance sports. **Materials and methods:** Scientific articles (clinical trials, meta-analyses) published in the period 2015–2025 in PubMed, Medline, ResearchGate, Google Scholar databases and official reports of the National Anti-Doping Agency of the Republic of Moldova were critically analyzed to define the realities of trimetazidine use in performance sports. **Results:** During ischemia, when oxygen supply is limited, trimetazidine inhibits fatty acid oxidation and promotes glucose utilization, a metabolic mechanism that significantly improves mitochondrial and cellular myocardial energy efficiency. This metabolic adaptation reduces intracellular acidosis, prevents accumulation of toxic fatty acid metabolites, and provides important cardioprotective effects. These metabolic effects underlie its potential adaptogenic role during intense physical overload, explaining its use by athletes to enhance metabolic efficiency and exercise endurance. However, abusive or unauthorized use may cause neurological adverse effects, including extrapyramidal syndromes. **Conclusions:** Trimetazidine, through its metabolic and cardioprotective actions, remains a significant concern in sports medicine. The controversial data regarding its doping potential justify continued monitoring by WADA.
Keywords: Trimetazidine, metabolic modulation, cellular metabolism, doping, performance sports, WADA.

BENIGN THYROID NODULE MIMICKING MALIGNANCY WITH COMPRESSIVE SYMPTOMS: IMPORTANCE OF TIMELY SURGICAL MANAGEMENT

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Introduction: Thyroid nodules are a common clinical finding in endocrine practice and warrant careful monitoring due to their potential for malignant transformation and progressive enlargement, which can lead to compressive symptoms. These processes often justify surgery for both diagnostic and therapeutic purposes. **Materials and Methods:** This report presents a 35-year-old patient who presented with an anterior cervical painful mass, globus sensation, periodic dysphagia, and fatigue, with a 10-year history of a gradually enlarging thyroid nodule, previously monitored by an endocrinologist. During follow-up, Tyrozol was administered in order to achieve and maintain clinical euthyroidism. Laboratory investigations included thyroid function tests and tumor markers—thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), calcitonin, and thyroglobulin—accompanied by a neck ultrasound. **Results:** Laboratory results demonstrated TSH 0.27 μIU/mL, FT4 0.87 ng/dL, and FT3 2.99 pg/mL, findings consistent with clinical euthyroidism under Tyrozol therapy. Calcitonin levels were within the normal range (<0.5 pg/mL), while thyroglobulin was elevated (108.87 ng/mL), reflecting increased thyroid tissue activity associated with the nodular lesion. Neck ultrasonography revealed a heterogeneous thyroid nodule measuring approximately 3 cm, containing calcifications and irregular structural areas suspicious for malignancy. Considering the progressive enlargement of the nodule, the persistence of compressive symptoms, and the imaging findings, surgical treatment was indicated. The patient underwent hemithyroidectomy, and histopathological examination revealed a follicular adenoma with fibrosclerotic changes and secondary osseous metaplasia. Postoperative recovery was uneventful, without complications, and the patient was discharged on the fifth postoperative day with hormone replacement therapy. **Conclusion:** Benign thyroid nodules may present with structural and tissue alterations that simulate malignancy on imaging studies, leading to diagnostic uncertainty. At the same time, progressive growth of such lesions may result in compressive syndrome affecting adjacent cervical structures. Therefore, surgical management should not be unnecessarily delayed when suspicious imaging findings coexist with compressive symptoms. Timely hemithyroidectomy allows definitive diagnosis, prevents further progression of compressive manifestations, and ensures optimal patient outcomes.
Keywords: thyroid nodule, compressive syndrome, hemithyroidectomy, follicular adenoma.

POSTTRAUMATIC HEADACHE PATHOPHYSIOLOGICAL MECANISMS: A SYSTEMATIC LITERATURE REVIEW

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Introduction. Posttraumatic headache (PTH) is defined as a headache attributed to trauma, or injury to the head and/or neck. Acute PTH develops within 7 days after a traumatic brain injury (TBI), whereas persistent PTH lasts longer than 3 months. Clinically, PTH may resemble migraine or tension-type headache, while other forms include occipital neuralgia, cluster headache, low cerebrospinal fluid pressure headache, supraorbital/infraorbital headache, cervicogenic headache and headache associated with whiplash injuries. Posttraumatic hematomas may also cause headache. The aim of this study was to highlight the pathophysiological mechanisms underlying posttraumatic headache. **Material and methods.** A literature review was performed using PubMed, ResearchGate, Google Scholar, medRxiv, EMBASE, and Cochrane library databases. The search term 'posttraumatic headache' was used, and 21 eligible studies were included in the analysis. **Results.** PTH is associated with complex neurochemical and structural changes, including the release of excitatory neurotransmitters such as aspartate, glutamate, and acetylcholine. Elevated levels of brain-derived neurotrophic factor (BDNF) have been reported during PTH episodes. Neuroimaging studies suggest diminished choline concentrations in white matter, and decreased cortical thickness in bilateral frontal regions. Traumatic injury could impair descending inhibitory pain pathways. Pre-existing headache may be magnified following trauma. Discontinuation of the medication, regaining the consciousness after a TBI, and the head injury itself are the triggers for PTH. The locus coeruleus and periaqueductal gray matter play key roles in afferent pain modulation, and their involvement may explain the frequent association between PTH and post-traumatic stress disorder (PTSD). Gender differences in the incidence of PTH are controversive, although there is a higher incidence of migraine-like PTH in male veterans, and for tension-type PTH in elderly women. Genetic predisposition has been suggested, with FMH1 and ATP1A2 gene variants associated with increased PTH severity. Loss of consciousness is indicative of a more severe PTH. The treatment strategies for each PTH are similar to the preceding, although there is debate that PTH could be completely distinct and require alternative clinical approaches. **Conclusions.** Posttraumatic headache is an important entity that needs to be expected, clinically classified, and that requires pathophysiology-based management. **Keywords:** Post-Traumatic Headache, Migraine Disorders, Tension-Type Headache

RHINO-ORBITAL-CEREBRAL MUCORMYCOSIS: ETIOPATHOGENESIS, DIAGNOSIS AND TREATMENT

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Introduction. Rhino-orbito-cerebral mucormycosis (ROCM) is a severe invasive fungal infection caused by fungi of the order Mucorales. The disease primarily develops in immunocompromised patients, particularly those with uncontrolled diabetes mellitus, hematological malignancies, or long-term corticosteroid therapy. The aggressive course of mucormycosis is largely determined by the ability of fungal hyphae to penetrate host tissues and blood vessels. A better understanding of the cellular mechanisms involved in fungal invasion and host immune response is essential for early diagnosis and the development of effective therapeutic strategies. Therefore, studying the etiopathogenesis of ROCM at the cellular level remains an important objective in modern medical research. Materials and Methods. This study is based on a review and analysis of recent literature on the pathogenesis, cellular mechanisms, and clinical manifestations of rhino-orbito-cerebral mucormycosis. Particular attention is given to the interactions between fungal elements and host cells, including endothelial cells, phagocytic immune cells, and affected tissues**.**
Results. Infection in rhino-orbito-cerebral mucormycosis begins with the inhalation of fungal spores that settle on the mucosa of the nasal cavity and paranasal sinuses. In healthy individuals, the immune system—primarily macrophages and neutrophils—rapidly eliminates these spores through phagocytosis and oxidative mechanisms. In immunocompromised patients, these defense mechanisms are weakened, allowing the spores to germinate and develop into invasive fungal hyphae. The hyphae have the ability to actively adhere to endothelial cells and penetrate them. An important molecular mechanism of this process is the interaction between fungal surface proteins and endothelial receptors, including GRP78, which facilitates angioinvasion. Damage to endothelial cells leads to vascular thrombosis, impaired blood flow, and progressive tissue ischemia. Vascular occlusion subsequently results in extensive necrosis of surrounding tissues, which is a characteristic feature of mucormycosis. In addition, metabolic factors such as hyperglycemia and increased levels of free iron stimulate fungal growth and contribute to further cellular damage. These mechanisms explain the rapid progression of the infection, which may involve the nasal cavity, orbit, and sometimes intracranial structures.
Conclusions. Rhino-orbito-cerebral mucormycosis is a serious invasive infection, the development of which is largely determined by the interaction of fungal pathogens with host cells and tissues. Understanding the processes of endothelial invasion, immune cell dysfunction, and subsequent tissue necrosis contributes to improved diagnostic approaches and increased treatment effectiveness. Timely initiation of antifungal therapy in combination with surgical intervention remains the primary and most effective treatment for this disease.
Keywords. Mucormycosis, cellular invasion, endothelial cells, angioinvasion, tissue necrosis, fungal infection

THE IMPACT OF DIABETES MELLITUS ON THE DEVELOPMENT OF DRY EYE SYNDROME

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Introduction: Diabetes mellitus (DM) is a major systemic risk factor affecting ocular health, involving both the ocular surface and the lens. Chronic hyperglycemia induces metabolic and oxidative changes that accelerate lens opacification and contribute to the development of dry eye syndrome (DES). The aim of this study was to evaluate the impact of diabetes mellitus on the prevalence and severity of DES in patients undergoing surgery for complicated cataracts. **Materials and Methods:** A prospective study was conducted on a cohort of 26 patients (30 eyes) with complicated cataracts (mean age 67.38 ± 7.32 years). The evaluation included a review of the relevant literature and clinical assessment through patient history and the Schirmer test, performed preoperatively and 14 days postoperatively. The data were statistically analyzed using the t-test, Chi-square test, with a significance threshold set at $p<0.05$. **Results:** Diabetes mellitus was identified as the most aggressive risk factor, with a prevalence of DES of 81.25%, significantly higher than the 45.00% observed in hypertensive patients. Pathophysiologically, diabetes induces corneal denervation through peripheral neuropathy, disrupting the neuro-lacrimal feedback. This vulnerability led to a decompensation of ocular surface homeostasis under the mechanical and inflammatory stress of phacoemulsification, exacerbating hyposecretion in 46.6% of eyes, with Schirmer test values dropping from 7.8 mm to 4.1 mm ($p < 0.0001$). This reduction correlated with debilitating symptoms (foreign body sensation, burning). At the molecular level, activation of the polyol pathway and accumulation of sorbitol generate osmotic stress, reactive oxygen species (ROS), degrading lens proteins (α, β, γ-crystallins), accelerating opacification on an already compromised biological substrate. **Conclusion:** Diabetes mellitus is the most important systemic risk factor for the onset and exacerbation of dry eye syndrome in patients undergoing cataract surgery. The results highlight the need for monitoring function and implementing preventive measures to protect the ocular surface during the perioperative period. **Keywords:** diabetes mellitus, dry eye syndrome, cataract, tear film, ocular surface.

BIOCHEMICAL MECHANISMS INVOLVED IN CARDIAC DYSRHYTMIAS

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Introduction: Cardiac dysrhythmias are disorders of impulse generation and conduction in the myocardium caused by molecular alterations in cardiomyocytes. Cardiac electrical activity depends on the maintenance of the resting membrane potential and the cardiac action potential through the function of sodium (Na^+), L-type calcium (Ca^{2+}) and potassium (K^+) channels, as well as membrane ion pumps. Disturbances of calcium homeostasis and cellular energy metabolism represent major biochemical mechanisms underlying myocardial electrical instability. The aim of the research was to elucidate the biochemical and molecular mechanisms involved in the development of cardiac dysrhythmias in order to correlate them with arrhythmia types and antiarrhythmic therapy.
Materials and Methods: 20 scientific articles from PubMed and NCBI databases, published between 2017-2024, were analyzed. **Results**: Electrical stability of cardiomyocytes depends on the maintenance of ionic gradients by the Na^+/K^+-ATPase and the sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA2a). During myocardial ischemia, ATP depletion reduces the activity of these pumps, leading to intracellular Na^+ accumulation and reverse-mode activation of the Na^+/Ca^{2+} exchanger resulting in Ca^{2+} overload. Pathological phosphorylation of the ryanodine receptor (RyR2) and altered phospholamban regulation impair calcium reuptake into the sarcoplasmic reticulum, producing spontaneous Ca^{2+} release events and delayed afterdepolarizations. Prolongation of the action potential due to hERG channel dysfunction leads to early afterdepolarizations and torsades de pointes–type arrhythmias. Mitochondrial oxidative stress increases reactive oxygen species production, modifies ion channel function, and decreases ATP synthesis, thereby promoting atrial fibrillation and ventricular tachyarrhythmias. **Conclusions**: Cardiac dysrhythmias arise from the interaction between impaired energy metabolism, disruption of Ca^{2+} homeostasis, and ion channel dysfunction. Understanding these mechanisms provides a biochemical basis for antiarrhythmic therapy aimed at electrical stabilization of the cardiomyocyte. **Keywords:** cardiac dysrhythmias, calcium homeostasis, SERCA2a, ion channels, oxidative stress, cardiomyocytes

VARIANTS OF THE HEART VALVES AND SYNTOPIA OF THE NERVES ADJACENT TO THE ARCH OF AORTA

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Introduction. The research topic is determined by the clinical significance of heart valves and the syntopy of the left vagus and left recurrent laryngeal nerves for several important reasons. Valve variants may mimic pathology on imaging, can lead to difficulties in right atrial catheterization and in the implantation of electrodes for cardiac resynchronization therapy, and may be confused echocardiographically with thrombi or vegetations. Damage to the nerves located in the region of the aortic arch occurs in 11–32% of surgical interventions, yet there is insufficient research on their variations. **Materials and Methods.** The macroscopic study included 50 adult hearts and aortas, museum exhibits from the *Nicolae Testemitanu* State University of Medicine and Pharmacy, and photographs of dissected cadavers from the department's archive. **Results.** The following variants were detected: semilunar aortic valve perforation in 5%; presence of the Eustachian valve in 60% (66.6% as remnants, 26.6% pronounced, and an extended Chiari network in 6.6%); and the Thebesian valve in 70% (28.6% remnant, 22.8% cord-shaped, 25.7% semilunar, 5.7% fenestrated, 5.7% network-like, and 11.4% biconcave band). Syntopic variants of the left vagus nerve and the left recurrent laryngeal nerve that significantly differ from classical descriptions were identified. These nerves are at risk not only during surgical interventions on the aortic arch, but also during procedures involving the esophagus and trachea.

Conclusions.

1. Structural variations of heart valves and the syntopy of the left vagus and left recurrent laryngeal nerves are common. Precise anatomical knowledge of these variations is required for endoscopic cardiac procedures and thoracic surgery.
2. The syntopy of the left vagus nerve and the left recurrent laryngeal nerve depends on the type of aortic arch branching, the location of its branches, and the constitutional body type.
3. Physicians' awareness of organ variations is key to treatment success, as it helps prevent misdiagnosis, unnecessary interventions, and medico-legal errors.

Keywords: heart valves, Eustachian valve, Thebesian valve, left vagus nerve, left recurrent laryngeal nerve, aortic arch.

PREVALENCE OF OCCULT FEMORAL HERNIAS IN WOMEN UNDERGOING INGUINAL HERNIOPLASTY: A STATISTICAL ANALYSIS

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Introduction. Occult femoral hernias (OFH) are a "hidden" type of hernia that are difficult to identify through clinical examination but have important medical implications. Considering that typical femoral hernias occur about four times more frequently in women, this study aimed to evaluate the sex-related distribution of occult femoral hernia (OFH) among patients undergoing inguinal hernioplasty, and to determine the prevalence of OFH in women with inguinal hernia, emphasizing the importance of systematic assessment. **Material and methods.** Bibliographic sources published within the last 15 years and indexed in MEDLINE, PubMed, Web of Science, Scopus, ScienceDirect, Google Scholar, and ResearchGate were systematically reviewed and synthesized. The study selection process followed the standard PRISMA methodology. Based on the included studies, an integrative evaluation of OFH incidence was conducted in a cumulative cohort of 9022 patients who underwent surgical procedures for inguinal hernioplasty. Statistical analysis was performed using IBM SPSS Statistics (v.2025, IBM Corp.). The Wald method was used to calculate 95% CIs, and statistical significance was evaluated with the binomial test. The relationships between categorical variables were analyzed using the chi-square (χ^2) test. **Results.** Analysis of the cumulative cohort of 9022 patients revealed an overall prevalence of occult femoral hernias of 11.84%. The χ^2 test highlighted a statistically significant relationship between sex and OFH, with a female-to-male odds ratio of 4.26:1 (OR = 4.26; 95% CI: 3.1–5.6; $p < 0.001$). Further statistical analysis using the Wald method and the binomial test estimated an OFH prevalence of 18.1% among women with inguinal hernia (18.1%; 95% CI, 15.8–20.6 %, $p < 0.001$). **Conclusion.** These findings support systematic evaluation for the potential presence of an occult femoral hernia in all women scheduled for inguinal hernioplasty. Considering the 4.26-fold higher relative risk of occult hernias in women compared to men, and an estimated prevalence of 18.1% among female patients, our results imply that 1 in 5 women presenting with an inguinal hernia could have a concomitant OFH. Failure to detect OFH may compromise surgical outcomes, highlighting the potential of this preventive approach to improve prognosis and reduce post-herniorrhaphy recurrence in women.

Keywords: female patients, groin hernia, occult femoral hernia, surgical assessment, inguinal hernioplasty

VARIABILITY OF THE SURAL NERVE AND ITS CLINICAL SIGNIFICANCE IN PERIPHERAL NERVE GRAFTING

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Introduction. The sural nerve is a sensory nerve of the lower limb, originating from the S1–S2 roots, and exhibits significant anatomical variability. Typically, it is formed by the union of the medial sural cutaneous nerve with a communicating branch from the common peroneal nerve; however, multiple variations exist, including rare cases of direct origin from the sciatic nerve. The clinical significance of the sural nerve arises both from its increased risk of iatrogenic injury during surgical procedures and from its frequent use as an autologous nerve graft.
Materials and Methods. A narrative review of the literature was conducted through searches in electronic databases including PubMed, Medline, and UpToDate. The macroscopic study included 20 adult lower limbs and museum exhibits from the *Nicolae Testemițanu* State University of Medicine and Pharmacy. **Results.** The literature describes six main types of sural nerve formation, with several subvariants. These variations may influence the nerve's course, the level of branch union, and its relationships with adjacent structures such as the small saphenous vein and the calcaneal tendon. Identified variants are following: an expanded zone of innervation of the obturator nerve to the middle of the leg, significant anatomical variability in origin and level of formation of the sural nerve. Its superficial location in the posterolateral calf and ankle exposes it to iatrogenic injury during orthopedic, vascular, or calcaneal tendon repair procedures. Anatomical variability may also affect techniques for nerve block and the interpretation of imaging findings. From a reconstructive standpoint, the sural nerve is considered the gold standard for autologous nerve grafts due to its adequate length, relatively consistent caliber, and accessible harvesting. Grafts are indicated for segmental nerve defects exceeding 1–2 cm and are used in facial nerve reconstruction and brachial plexus injuries, providing suitable support for axonal regeneration. **Conclusions.** Accurate identification of the nerve's course and formation type allows for the appropriate harvesting technique and increases the success rate of peripheral nerve reconstruction. Integrating detailed anatomical knowledge into surgical practice directly contributes to improved postoperative functional outcomes.
Keywords: sural nerve, anatomical variations, nerve graft, nerve reconstruction, peripheral neuropathies.

PERINEURAL INVASION – MARKER OF AGGRESSIVENESS IN PROSTATE CANCER

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Introduction. Prostate cancer is one of the most common malignant neoplasms in men, characterized by a heterogeneous biological evolution, from indolent forms to aggressive phenotypes with increased invasive and metastatic potential. Perineural invasion (PNI) is considered a morphological marker of tumor aggressiveness, being associated with extraprostatic extension, advanced pathological staging and increased risk of post-therapeutic recurrence. The presence of PNI reflects the ability of tumor cells to use nervous structures as a dissemination route, facilitating local progression and regional extension. This study evaluates the prognostic value of perineural invasion, analyzing its correlations with relevant morphological and clinicopathological parameters. The results support the importance of integrating PNI into routine histopathological evaluation and risk stratification, contributing to a more accurate prognostic estimate and to the optimization of individualized therapeutic decisions.

Material and Methods. The study included 70 cases of prostatic acinar adenocarcinoma diagnosed at the Oncological Institute of the Republic of Moldova. The mean age of the patients was 67 ± 6.8 years (median 68). All cases were histopathologically evaluated by two independent pathologists, on sections stained with hematoxylin-eosin, in order to confirm the diagnosis and evaluate the morphological parameters of interest. Statistical analysis included the determination of central tendency indicators (mean, median) and the evaluation of correlations using the Spearman coefficient (rs). The statistical significance threshold was set at $p < 0.05$.

Results. PNI was identified in 65 cases (92.9%). Correlation analysis revealed positive statistical associations between the presence of PNI and lymphovascular invasion (rs=0.21, p=0.04), as well as lymphocytic infiltrate (rs=0.21, p=0.04). Also, the incidence of PNI increased with the pathological tumor stage (rs = 0.27; p = 0.01) and Gleason score (rs = 0.54; p = 0.001), the latter correlation indicating a moderate association in intensity. The presence of signs of chronic prostatitis correlated negatively with PNI (rs = - 0.21; p = 0.04). No statistically significant associations were identified between PNI and patient age (rs = 0.11; p = 0.19), number of affected lobes (rs = - 0.10; p = 0.29), capsule invasion (rs = 0.14; p = 0.12), cellular atypia (rs = 0.11; p = 0.19), lymph node metastases (rs = 0.11; p = 0.20), as well as the development of hyalinosis (rs = 0.13, p = 0.14), lipid degeneration (rs = - 0.17, p = 0.07) and sinus histiocytosis (rs = -0.01, p = 0.47) in lymph nodes. **Conclusions.** Prostate cancer has a significant metastatic potential, and perineural invasion contributes to loco-regional disease progression by facilitating tumor extension along neural structures. This tendency becomes more pronounced as tumor aggressiveness increases and is frequently correlated with the presence of lymphocytic infiltrate, as well as lymphovascular invasion.

Keywords: prostate cancer, acinar adenocarcinoma, perineural invasion.

PROGNOSTIC SIGNIFICANCE OF LYMPHOVASCULAR INVASION IN ASSESSING METASTATIC POTENTIAL IN PROSTATE CANCER

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Introduction. Prostate cancer (PC) is one of the most common malignant neoplasms in the male population and exhibits marked biological heterogeneity, ranging from indolent forms to aggressive variants characterised by an invasive tumour phenotype and increased metastatic potential. In this context, the identification of histopathological markers with prognostic value is essential. Lymphovascular invasion (LVI) is considered an important morphological parameter, as it has been associated with an increased risk of tumour progression and disease recurrence.

Materials and Methods. The study included 70 patients diagnosed with acinar adenocarcinoma of the prostate, who were investigated at the IMSP Institute of Oncology between 2022 and 2025. The mean age of the patients was 67 ± 6.8 years (median: 68 years). Histopathological evaluation was performed on haematoxylin–eosin (H&E)-stained sections. Statistical analysis included the calculation of the mean and median, as well as Spearman's correlation analysis, with the threshold for statistical significance set at $p < 0.05$. **Results.** The presence of lymphovascular invasion was histopathologically confirmed in 25 patients (35.7%). Correlation analysis revealed statistically significant positive associations between LVI and perineural invasion ($r_s = 0.21$, $p = 0.04$). In addition, the incidence of LVI increased proportionally with pathological pTNM staging ($r_s = 0.27$, $p = 0.01$) and total Gleason score ($r_s = 0.54$, $p = 0.001$). Significant correlations were identified between LVI and the presence of lymph node metastases on both the right side ($r_s = 0.42$, $p = 0.001$) and the left side ($r_s = 0.52$, $p = 0.001$). At the nodal level, LVI showed a significant correlation with the presence of hyalinosis ($r_s = 0.49$, $p = 0.001$). In contrast, chronic prostatitis did not demonstrate a statistically significant association with LVI ($r_s = 0.13$, $p = 0.14$). Furthermore, no significant correlations were observed between LVI and patient age, number of involved lobes, prostatic capsular invasion, lymphocytic infiltrate, cellular atypia, lipid degeneration, or sinus histiocytosis ($p > 0.05$). **Conclusions.** Lymphovascular invasion, observed in more than one-third of the patients included in this study, constitutes a histopathological marker linked to an aggressive tumour phenotype in prostate cancer. Statistically significant associations with perineural infiltration, advanced pathological stage, elevated Gleason scores and bilateral lymph node involvement reinforce its prognostic relevance. Moreover, the relationship with nodal stromal changes, including hyalinosis, indicates a possible role of lymphovascular invasion in the processes governing metastatic spread. Accordingly, this parameter may serve as a meaningful indicator of metastatic propensity and tumour biological severity, with practical implications for risk stratification and clinical decision-making in prostate cancer management.

Keywords: acinar adenocarcinoma; lymphovascular invasion; prognostic factors; lymph node metastases.

PARTICULARITIES OF DIAGNOSIS AND SURGICAL MANAGEMENT OF RADICULAR CYSTS

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Introduction: Atypical molar extraction may be complicated by infection, periodontal disease, root resorption, caries of adjacent teeth, cysts, and other issues. Radicular cysts can develop from chronic periapical infection due to pulp necrosis, which stimulates the epithelial rests of Malassez, leading to odontogenic cyst formation. **Case presentation:** In a patient, a radicular cyst of tooth 15 persisted as a residual lesion after extraction and incomplete removal, subsequently involving the mesiovestibular root of tooth 16 in the vicinity of the maxillary sinus. The shape, dimensions, radiographic margins and topographical relationships with the surrounding anatomical structures were analyzed by Cone Beam Computed Tomography-CBCT. Considering that the cyst was located in the vicinity of the maxillary sinus floor, an individualized approach was needed with detailed planning of the cystectomy. To prevent spillage of the cyst's content, the surgical enucleation of the cyst was performed using Lindemann bur mounted on a surgical handpiece. After cystectomy, the cystic cavity was thoroughly checked for the presence of debris, in order to avoid postoperative complications. For hemostasis and facilitation of tissue regeneration, a collagen-based dressing was applied. The histological examination did not reveal any malignancy. The healing process proceeded without any complications. The follow-up of the patient after cystectomy at an interval of 3 to 6 months, showed normal resorptive activity of the cortical bone and good regeneration capacity of the soft tissues. **Discussion:** The most complex cysts are those near the maxillary sinus or mandibular canal, often asymptomatic. Upper molar apical radicular cysts may extend into the maxillary sinus, pterygopalatine and infratemporal fossae, spreading to adjacent head and neck spaces, while lower molar cysts can affect the inferior alveolar neurovascular bundle. **Conclusions:** Due to three-dimensional visualization of the anatomical structures, CBCT is a reliable method of diagnosis and treatment planning, ensuring a high level of safety and diagnostic accuracy, required for programming individualized surgical techniques, decreasing the risk of iatrogenic injuries and ensuring a high quality of life after surgery.

Keywords: maxillary sinus, radicular cyst, surgical management

THE ROLE OF COPPER IN ANGIOGENESIS

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Background. In disease conditions, the goal of therapeutic targeting of the angiogenic process is to normalize vasculature in target tissues by enhancing angiogenesis, where reduced vascularity and blood flow occur, such as in tissue ischemia and wound repair; or to inhibit angiogenesis, as in the case of excessive and abnormal angiogenesis originating from cancer. Copper (Cu) is a trace element and vital cofactor of more than 60 enzymes implicated in blood clotting, hormone maturation, energy metabolism, oxidative detoxification, mitochondrial respiration, DNA synthesis, cell division, antioxidant processes and angiogenesis. The objective of the study was to elucidate the role of Cu in angiogenesis in order to be used in wound healing and in transplanted graft. **Materials and methods**. Literature review from 2016-2026 was performed, using 11 articles, including data from ScienceDirect, PubMed Central, Biomed Central, MedScape, and others. **Results**. Cu homeostasis is regulated by *Copper Transporter 1* (CTR1), *Adenosine Triphosphatase* (ATPase) *copper-transporting alpha* (ATP7A) and Cu chaperones. Intracellular Cu can stabilize the biochemical structure of transcription *hypoxia-inducible factor 1α* (HIF-1α) and promote the expression of angiogenic mediators: basic fibroblast growth factor (*FGF-Basic)*, vascular endothelial growth factor (VEGF), tumor necrosis factor-alpha (TNF-α) and angiogenin. As a result these mediators promote proliferation of *endothelial cells* (ECs) and migration of *vascular smooth muscle cells* (VSMCs). Also Cu as an coenzyme modulates angiogenin's affinity towards ECs and VSMCs and modulates *amine oxidase Cu-containing 3* (AOC3) which involve IL-1β-driven M2 macrophage infiltration. Furthermore, Cu ions mediate the activity of endothelial nitric oxide synthase and increase the production of the vasodilator nitric oxide, thereby promoting angiogenesis. Also, Cu has been extensively studied for its antibacterial activities through *mismetalation* (a process in which a metal-binding site in a protein is occupied by the wrong metal ion). Proteins containing iron, manganese, cobalt, nickel, and zinc as cofactors are all potential targets of mismetalation by Cu. Moreover, Cu is a cofactor of *Superoxide dismutase 1* (SOD1) exerting anti-inflammatory activities. **Conclusions:** In conclusion angiogenic, antibacterial and anti-inflammatory Cu properties demonstrate that Cu derived compounds may be used in wound healing and stimulating angiogenesis in transplanted graft.
Keywords: Copper, angiogenesis, ECs, VSMCs.

THE ROLE OF ANGIOGENESIS IN ISCHEMIC DISEASE

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Background. Ischemic heart disease, myocardial infarction, ischemic stroke, and peripheral arterial disease are non-communicable, highly disabling conditions with high incidence and mortality rates. It is well recognized that elderly patients may exhibit a relative tolerance to acute ischemic events due to long-standing chronic ischemia and the development of collateral vascular circulation, which provides a biological rationale for exploring therapeutic angiogenesis as a targeted strategy to restore perfusion and improve functional outcomes. Both physiological and pathological angiogenesis use similar mechanisms, but pathological angiogenesis continues after adequate perfusion, hindering the development of new anti-angiogenic agents. **Objective of the study**. To elucidate the mechanisms of therapeutic angiogenesis in ischemic disease, in order to elaborate methods of treating and preventing ischemic diseases. **Materials and methods**. A review of the literature from 2014-2024 was performed, using 11 articles, including data from ScienceDirect, PubMed Central, Biomed Central, MedScape, and others. **Results**. Angiogenesis is the process of new blood vessel formation from pre-existing network through endothelial cell migration and proliferation. It occurs during wound healing, foreign body encapsulation, tumor growth, collateral vessel development, and organ transplantation. In reviewed literature have been mentioned the next methods of therapeutic angiogenesis: recombinant *vascular endothelial growth factor* (VEGF), *angiopoietin-2* (Ang-2), VEGF-encoding plasmid *deoxyribonucleic acid* (DNA), platelet-rich plasma transplantation, mesenchymal stem cells (MSCs) transplantation and mitochondrial transplantation. Transplantation strategies rely on hypoxic, pharmacological or genetic preconditioning to enhance ischemic tolerance and activation of pro-angiogenic pathways like *hypoxia-inducible factor 1 alpha* (HIF-1α)/*vascular endothelial growth factor* (VEGF), *phosphoinositide 3-kinase*/*protein kinase B* (PI3K/Akt), *mitogen-activated protein kinase* (MAPK), *extracellular signal-regulated kinase* (ERK) and *wingless-related integration site* (Wnt)/*beta-catenin* (β-catenin). Current challenges in angiogenesis treatments include difficulties in targeted delivery and precise dosage control. For example, excessive concentrations of VEGF lead to the formation of angiomas and aberrant vessels and may promote carcinogenesis, but suboptimal levels trigger insufficient angiogenesis for restoring perfusion, and the newly formed vessels fail to mature and rapidly regress. **Conclusions.** To conclude, pharmacological and transplantation-based angiogenesis therapies hold promise for treating and preventing ischemic diseases; however, optimizing delivery methods, dosing, and pathway activation is critical to ensure effective and mature vascular growth without adverse effects.
Keywords: neoangiogenesis, ischemic disease, VEGF, MSCs.

ANATOMICAL CLINICAL ASPECT IN THE ETIOLOGY OF INGUINAL HERNIA

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Background. Decreased tone of the anterolateral abdominal wall muscles, actually is considered the main etiological factor in the appearance of inguinal hernia. Taking into consideration that the spinal nerves have the primary role in maintaining the muscle tone (in this case the lower thoracic nerves Th 5 - Th 12 and the ileoinginal and ileohypogastric nerves), it seems reasonable to go back and to study their origin, that is, to turn our attention to the intervertebral orifices, as their exit points from the spine, and to evaluate their function of innervating of paravertebral muscles. **Objective of the study.** Studying the correlation between the condition of paravertebral muscles, as a criterion that reflects the functionality of the spinal nerves and the appearance of inguinal hernia in children. **Material and Methods**. 25 patients, age 11-176 months, boys/girls ratio 1.5:1, hospitalized with the diagnosis of inguinal hernia. Data collected: disease history, life history (perinatal period, physiological and pathological history, hereditary-collateral history, etc), objective and physical examination of the patient, in addition intervertebral, lumbar and sacral region were photographed.
Results. The hernia is diagnosed more frequently in male (60% vs 40%). The most affected age groups were 1-24 months and 50-74 months, and the least affected age group – 175-200 months. The surgery was performed at 0-24 months and 25- 49 months (28% and 24%, respectively), less frequently at 150-200 months and 100-124 months. **Conclusion.** Taking into consideration those mentioned above, we can conclude that the pathology of the spinal nerves responsible for tone of antero-lateral abdominal wall muscle should not be underestimated as a predisposing factor in appearance of external abdominal hernias.
Keywords: inguinal hernia, spinal nerves, muscular tone, spinal cord.

SPECTRAL ANALYSIS OF THE SUBMANDIBULAR GLAND SIALOLITHS

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Introduction. Sialoliths are intraductal or intraparenchymal calculi of the large salivary glands. They consist of organic and inorganic mater, with a nucleus and plastic peripheral structures. The sialoliths predominantly are composed of calcium phosphate, with a low content of carbonates and insignificant content of magnesium, potassium and ammonia. Our aim was to study the composition of the submandibular glands calculi in order to assess the mechanisms of their mineralization in sialolithiasis.
Materials and methods. The spectral analysis of the sialoliths, extracted from the submandibular gland of 7 patients (4 males and 3 females) with a mean age of 37.3 ± 6.2 years, who were treated in the Institute of Emergency Medicine, was carried out. To achieve the proposed goal, scanning electron microscopy with VEGA TESCAN TS 5130MM equipment and radio-spectral microanalysis of the concrements by energy-dispersive X-ray spectroscopy, using the EDX (Oxford Instruments energy-dispersive X-ray system) materials detector, was performed. Identification of different crystalloid forms of calcium phosphate was based on at least 3 measurements of the Ca/P ratio: for brushite within range of 0.85-1.0; whitlockite – 1.1-1.5; Ca-deficient hydroxyapatite – 1.5-1.63; hydroxyapatite ≈ 1.67.
Results. Energy-dispersive X-ray spectroscopy revealed the following mean ratios at the interface peripheral part/core of the sialoliths chemical elements (atom%): Carbon (C) – 65.54 ± 1.67/50.16 ± 3.1 ($p < 0.001$); Oxygen (O2) – 30.49 ± 0.76/34.19 ± 2.1 ($p = 0.171$); Calcium (Ca) – 0.77 ± 0.20/2.56 ± 0.9 ($p = 0.029$); Phosphorus (P) – 0.63 ± 0.15/2.2 ± 0.7 ($p = 0.02$); Sulfur (S) – 0.3 ± 0.05/0.2 ± 0.02 ($p = 0.058$); Sodium (Na) – 0.19 ± 0.01/0.28 ± 0.03 ($p = 0.225$); Chlorine (Cl) – 0.09 ± 0.01/0.08 ± 0.01 ($p = 0.141$). **Conclusions.** In the core of the sialoliths, the atomic concentration of calcium ($p<0.05$) and phosphorus ($p<0.05$) was higher, compared to the peripheral part of the sialoliths. The mean value of the calcium/phosphorus ratio (Ca/P) at the interface peripheral part/core of the sialoliths was – 1.1 ± 0.2/1.2 ± 0.1. The reduced concentration of Ca and P contributes to the formation of apatite, while the increased concentration leads to the formation of whitlockite.

Keywords: sialoliths, spectral analysis, submandibular gland

EVALUATION OF BCL-2 EXPRESSION IN 33 CONSECUTIVE CASES OF SEROUS OVARIAN CARCINOMA

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Introduction: Serous ovarian carcinoma, the most frequent subtype, exhibits aggressive behavior and late diagnosis. The BCL-2 protein, with its anti-apoptotic role, promotes tumor cell survival. BCL-2 expression is heterogeneous and, although clinicopathological correlations are not consistent, it remains a potential therapeutic target. Materials and Methods: The study had a retrospective, cross-sectional design, including 33 consecutive cases of serous ovarian carcinoma diagnosed between 2021–2025 at the Oncology Institute. BCL-2 expression was evaluated immunohistochemically on paraffin-embedded sections, with antigen retrieval by boiling at elevated pH for 20 minutes and incubation for 25 minutes with monoclonal BCL-2 antibody, clone 124. Detection was performed using the BioSB, highlighting a brown cytoplasmic reaction. Expression was quantified using the immunoreactive score (IRS), determined according to staining intensity (score 0–3) and the proportion of positive tumor cells, with emphasis on intratumoral heterogeneity. Statistical analysis included descriptive methods and inferential tests (Spearman, Chi-square), with a significance threshold of $p<0.05$ Results: Of the 33 analyzed cases, 78.8% were high-grade serous ovarian carcinoma, while 21.2% were low-grade. Advanced stages predominated, with stage III identified in 63.6% of cases. Immunohistochemical expression of BCL-2 was heterogeneous: absence of expression (score 0) was observed in 36.4% of cases, weak expression (score 1) in 15.2%, moderate expression (score 2) in 27.3%, and strong expression (score 3) in 21.2%. The proportion of positive tumor cells ranged from 0% to 80%, with a mean of 26% and a median of 20%. Analysis of the immunoreactive score (IRS) revealed a median of 2, with values ranging from 0 to 12. Most cases (79%) showed low BCL-2 expression, while high expression was observed in 21%. Statistical analysis did not reveal significant associations between IRS score and tumor stage (Spearman $r = –0.33$; $p = 0.063$) or between BCL-2 expression level (low/high) and disease stage (χ^2, $p = 0.55$). Conclusions: In the analyzed cohort, BCL-2 expression did not demonstrate statistically significant associations with the evaluated clinicopathological parameters. However, the presence of high expression in a subgroup of cases may reflect activation of anti-apoptotic mechanisms, with possible implications for tumor biological behavior Keywords: serous ovarian carcinoma; BCL-2; apoptosis; tumor grade.

THE IMMEDIATE AND DELAYED LOADING OF DENTAL IMPLANTS

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Introduction: Implant supported restorations for partially edentulous patients are a well-accepted and predictable treatment modality. Provisional restorations may be used at the time of implant placement or after an appropriate healing period.
Purpose of the paper: comparative study on treatment of prosthetic implants in different loading times. **Materials and methods.** We applied the retrospective, cohort prognosis. Between 21 January 2021 and 25 Iune 2025, according to the protocols of loading were examined 20 patients (10 women, 10 men) age between 22-60 years, who were divides in 2 groups: study and control). Dental implants in the study group were solved by temporary crowns with occlusal contact at the same day and in the control group was applied a temporary crowns in the occlusal contact by delayed protocol (6 month), after that were changed with porcelain fused to metal crowns. **Results.** All dental implants were succesfully osseointegrated. After the statistical analysis it was revealed a negative correlation between the gingiva thickness and mucosal recession. Mann Whitney test and t-Student test showed no statistical difference between groups. **Discussion and conclusions.** Implant supported-prosthesis treatment restoring the integrity of dental arches and masticatory activity in a short time; the teeth bordering the gap are not preparated; stopped dental migration in vertical and in horizontal plane, and mantaining initial prosthetic space; provisional restoration evaluate the position and contours of the planned definitive restoration, which has immediate comfort and aesthetics. After this treatment we received: a well-defined interdental papillae, healthy looking and well-defined aesthetic.
Key words: dental implants, immediate and delayed loading, primary stability of dental implants, implant restorations, Periotest values®.

ANTITUMOR POTENTIAL OF SANGUINARINE: MOLECULAR MECHANISMS AND EMERGING ROLE IN TARGETED CANCER THERAPY

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Intoduction. Conventional chemotherapy is often limited by primary and secondary tumor resistance, systemic toxicity, and reduced efficacy in advanced disease stages. These limitations have increased interest in natural compounds with antitumor activity. Sanguinarine (SAN), a plant-derived benzophenanthridine alkaloid, has emerged as a promising anticancer agent, demonstrating significant efficacy in multiple preclinical cancer models. **Material and methods.** This review analyzed 30 scientific articles published after 2015 from PubMed and Google Scholar, focusing on the anticancer potential and molecular mechanisms of natural compounds, particularly SAN. **Results.** SAN modulates key intracellular signaling axes, including phosphoinositide-3-kinase/protein kinase B/mammalian target of rapamycin (PI3K/AKT/mTOR), mitogen-activated protein kinase (MAPK), and nuclear factor κB (NF-κB), leading to inhibition of cell proliferation and reduction of tumor invasive potential. Suppression of these pathways results in cell-cycle arrest and inhibition of epithelial–mesenchymal transition (EMT), a process essential for metastasis and tumor progression. SAN can induce apoptosis by regulating the expression of pro- and anti-apoptotic proteins and activating caspases, while also stimulating autophagy, thereby promoting the elimination of resistant tumor cells. In addition, it enhances intracellular oxidative stress by increasing reactive oxygen species (ROS) beyond the tolerance threshold of malignant cells, amplifying selective cytotoxic effects. SAN also exhibits immunomodulatory activity through regulation of inflammatory mediators and transcription factors involved in cancer-associated chronic inflammation. It demonstrates synergistic potential when combined with conventional cytostatic agents, potentially enhancing antitumor efficacy while reducing required doses and systemic toxicity. Furthermore, SAN may increase tumor sensitivity to chemotherapy by interfering with molecular mechanisms of treatment resistance and by influencing epigenetic regulation processes such as DNA methylation/demethylation and histone deacetylation.
Conclussions. In conclusion, SAN exerts multimodal antitumor effects through induction of oxidative stress, inhibition of proliferative signaling pathways, interference with DNA repair, and activation of multiple programmed cell death pathways. These findings highlight its potential integration into innovative targeted cancer therapy strategies.**Keywords:** antitumor, alkaloids, cancer, natural compounds, sanguinarine.

IN VITRO MODULATION OF PSEUDOCHOLINESTERASE ACTIVITY BY Cu-THIOSEMICARBAZONE COMPOUNDS IN RAT C6 GLIOMA CELLS

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Introduction. Glioma represents one of the most aggressive forms of primary tumors of the central nervous system, characterized by rapid proliferation, high invasiveness, and resistance to conventional therapies. The C6 glioma cell line is a well-established experimental model for investigating molecular mechanisms involved in tumor progression and for testing compounds with potential antineoplastic activity. Pseudocholinesterase (PChE) is a plasma enzyme involved in choline ester metabolism and serves as a biomarker of hepatic function and cellular metabolic status. Cu-thiosemicarbazones are heterocyclic compounds with complex biological activity, including antioxidant and cytotoxic effects. However, their impact on PChE activity in C6 glioma cells has not been fully elucidated. **The aim.** The study aimed to evaluate the effects of Cu-thiosemicarbazone compounds on PChE activity in C6 glioma cells *in vitro* and to analyze the concentration-dependent response (10.0 µmol/L and 1.0 µmol/L), using doxorubicin (DOXO) as a reference compound. **Materials and Methods.** C6 cells were exposed to Cu-thiosemicarbazone compounds (CMA-18, CMD-8, MG-22, CMC-34, CMJ-33, CMT-67, CMG-41, TIA-123, and TIA-160) and to DOXO. PChE activity was measured spectrophotometrically and expressed in µmol/s·L, with statistical descriptors reported as median and interquartile range (IQR). Results were expressed as percentage changes relative to the control group. **Results.**Data analysis demonstrated a concentration-dependent effect. At 10.0 µmol/L, most compounds produced significant enhancec in PChE activity, the most pronounced being TIA-123 (20%), MG-22, CMT-67, and TIA-160 (17%), followed by CMA-18 and CMJ-33 (12%). At 1.0 µmol/L, the predominant effect was inhibitory, with marked decreases observed for CMT-67 (42%), CMC-34 (35%), and CMJ-33 (31%). DOXO showed a biphasic behavior, with stimulation at the higher concentration and inhibition at the lower concentration.**Conclusions.**The obtained data indicate significant *in vitro* modulation of PChE activity by Cu-thiosemicarbazone compounds in rat C6 glioma cells in a concentration-dependent manner, with predominant stimulation at 10.0 µmol/L and inhibition at 1.0 µmol/L. These findings suggest potential interactions with plasma esterase metabolism and point toward an anabolic-type effect of the investigated compounds, supporting further studies to elucidate the detailed molecular mechanisms involved.

Keywords: rat C6 glioma, Cu-thiosemicarbazone compounds, supernatant, pseudocholinesterase.

HYPERGLYCEMIC MODULATION OF HUMAN RETINAL PERICYTES: MORPHOLOGICAL RESPONSES AND OSMOTIC CONTROLS IN AN *IN VITRO* MODEL OF MICROVASCULAR STRESS

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Introduction. Retinal pericytes play an emphasizing role in maintaining microvascular integrity and are among the earliest cells affected during diabetic microangiopathy. Robust experimental hyperglycemia models are needed for understanding the cellular responses to metabolic stress. The aim of the study was to evaluate the effects of graded glucose concentrations on cultured human retinal pericytes and to differentiate metabolic from osmotic influences. **Materials and methods**. Human retinal pericytes (Innoprot, Spain) at passage 3 were cultured under controlled *in vitro* conditions. Five experimental groups were formed: physiological glucose (5.5 mM); moderate hyperglycemia (25 mM); severe hyperglycemia (50 mM); osmotic control for moderate hyperglicemia (5.5 mM glucose + 19.5 mM mannitol); and osmotic control for severe hyperglycemia (5.5 mM glucose + 44.5 mM mannitol). Cells were maintained in culture flasks and evaluated microscopically (ELTA'90 MR, Nikon) at baseline and after 24 h of exposure. Morphological assessment focused on cellular confluence, structural integrity, and visible stress-related changes using semi-quantitative visual estimation. **Results.** After 24 h, physiological glucose conditions maintained typical spindle-shaped morphology and showed an estimated 15-25% increase in apparent cell density, consistent with normal proliferation. The 19.5 mMol mannitol osmotic control demonstrated minimal alterations, with an approximate 5-10% increase compared with baseline, suggesting limited osmotic influence. In contract, exposure to higher osmotic load (44.5 mMol mannitol) resulted in slight reduction of spreading and an estimated 5-10% decrease in apparent cell density. Moderate hyperglycemia (25 mMol glucose) was associated with early morphological stress features, including reduced alignment and increased refractile bodies, corresponding to an estimated 10-20% reduction in proliferation relative to control cultures. Severe hyperglycemia (50 mMol glucose) induced more pronounced changes, such as diminished spreading, enhanced intercellular gaps, and scattered rounded cells, with an estimated 25-35% reduction in apparent cell density. These findings imply a dose-dependent inhibitory effect of glucose beyond osmotic stress alone.
Conclusions. Short-term exposure to elevated glucose concentrations created progressive morphological alterations and diminished apparent proliferation in retinal pericytes, highlighting the role of hyperglycemia in microvascular disfunction. The inclusion of mannitol osmotic controls strengthens the interpretation of glucose-specific metabolic effects.
Keywords. retinal pericytes, hyperglycemia, microvascular pathology, osmotic control, diabetic retinopathy model, cell culture, oxidative stress, *in vitro* study

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PAX5 EXPRESSION IN BREAST CARCINOMA

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Introduction. PAX5 is a transcription factor essential for B-cell lineage differentiation, but recent studies suggest its involvement in other types of neoplasms, including breast carcinoma. Understanding PAX5 expression in this context may contribute to elucidating mechanisms of tumor progression and identifying novel prognostic markers.

Materials and Methods. The study included 15 breast carcinoma cases selected from the archive of the Oncology Institute. PAX5 expression was evaluated by immunohistochemistry, and the density of positive cells was quantified separately in the intratumoral and peritumoral stromal compartments. Histopathological parameters analyzed included histological grade and the Nottingham score. Descriptive statistical analysis was complemented by Pearson correlation analysis, with statistical significance defined as $p \leq 0.05$. **Results.** The intratumoral density of PAX5-positive cells showed a mean value of 1.73 (median 0.5; range 0–11; SD 2.87), indicating low and heterogeneous expression. In the peritumoral compartment, values were significantly higher (mean 41.45; median 25; range 15–100; SD 27.45). Histological grade ranged from 1 to 3 (mean 2.36), the Nottingham score ranged from 5 to 9 (mean 7.0), and patient age ranged from 54 to 70 years (mean 63.6). Pearson correlation analysis revealed a positive association between peritumoral density and histological grade ($r = 0.42$, $p = 0.03$), as well as between intratumoral density and the Nottingham score ($r = 0.38$, $p = 0.04$). No significant correlations were identified with patient age ($p > 0.05$). **Conclusions.** PAX5 expression is more pronounced in the peritumoral stromal compartment compared with the intratumoral stroma and correlates with histological tumor parameters. These findings suggest a potential role of PAX5 in stromal remodeling and breast carcinoma progression, warranting further investigation to validate its prognostic value.

Keywords: PAX5, breast carcinoma, immunohistochemistry, intratumoral stroma, peritumoral stroma, Pearson correlation, Nottingham score, histological grade

TUMOR-INFILTRATING CD79α POSITIVE LYMPHOCYTES IN BREAST CANCER

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Introduction. Tumor-infiltrating lymphocytes (TILs) represent a critical component of the immune microenvironment in breast cancer, influencing tumor progression and patient prognosis. Among B-cell markers, CD79α is a reliable indicator of mature B lymphocytes. However, its role in breast carcinoma, particularly in relation to histopathological parameters, remains insufficiently explored. This study aimed to evaluate the density and distribution of CD79α-positive lymphocytes in breast carcinoma and to assess their correlation with histological grade and the Nottingham score.

Materials and Methods. A total of 19 cases of breast carcinoma were retrospectively selected from the archive of the Oncology Institute. Immunohistochemical staining for CD79α was performed, and positive lymphocytes were quantified separately in the intratumoral and peritumoral stromal compartments. Histological grade and the Nottingham score were recorded for each case. Descriptive statistical analysis was performed, and Pearson correlation coefficients were calculated to evaluate associations between CD79α expression and histopathological parameters. Statistical significance was defined as $p \leq 0.05$. **Results.** The density of CD79α-positive lymphocytes varied across compartments, with higher values observed in the peritumoral stroma compared with intratumoral regions. Intratumoral CD79a expression showed a moderate positive correlation with peritumoral density ($r = 0.41$, $p = 0.04$). Peritumoral CD79α infiltration correlated significantly with histological grade ($r = 0.52$, $p = 0.01$), suggesting a link between B-cell presence in the tumor microenvironment and tumor aggressiveness. No significant associations were found between CD79α expression and patient age. The Nottingham score demonstrated a strong correlation with histological grade ($r = 0.73$, $p < 0.001$), confirming its robustness as a prognostic tool.

Conclusions. Our findings indicate that CD79α-positive lymphocytes are more abundant in the peritumoral stroma of breast carcinoma and that their density correlates with histological grade. These results suggest that peritumoral B-cell infiltration may reflect tumor aggressiveness and could serve as a potential biomarker in breast cancer. Further studies with larger cohorts are warranted to validate the prognostic significance of CD79α -positive TILs and to explore their role in shaping the immune response within the tumor microenvironment.

Keywords: breast carcinoma, CD79 α, tumor-infiltrating lymphocytes, histological grade, Nottingham score

ANTIBIOTIC TIME-OUT AS AN EFFECTIVE ANTIMICROBIAL STEWARDSHIP STRATEGY: REDUCED DURATION, PRESERVED CLINICAL OUTCOMES

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Background. Prolonged antibiotic therapy remains common, despite shorter guideline durations. Overexposure to antibiotics has reported negative impacts in patients, such as an increase in resistant, invasive fungal infections and mortality. Given the issue, the WHO has recommended the implementation of antimicrobial stewardship programs (ASPs) that provide for re-evaluation of the efficacy, routes of administration, and spectrum of action after 48-72 hours. We evaluated antibiotic time-out intervention impact on antibiotic use and clinical outcomes. **Materials and Methods. Conducted a pre-poststudy including 4236 antibiotic courses.** The primary outcome: median days of therapy (DOT) per course. Secondary outcomes: proportion of guideline-exceeding courses, rates of de-escalation/ discontinuation, broad-spectrum antibiotic use, *C.difficile* incidence, and clinical outcomes. **Results**. Median DOT decreased by 25%, from 8.0 to 6.0 days (95% CI −2.3 to −1.7; P<0.001). Guideline-exceeding courses declined from 42% to 26% (RR 0.62; P<0.001), driven by reductions in community-acquired pneumonia (47% to 28%) and urinary tract infections (39% to 24%). Time-out implementation increased de-escalation/ discontinuation (37% vs 18%; OR 2.6; P<0.001), preventing an average of 2.1 excess antibiotic days per patient across 1,892 reviewed courses. Broad-spectrum DOT/ 1,000 patient-days declined by 22%, and *C. difficile* incidence decreased by 15% (1.2 to 1.0/ 10,000 patient-days). Clinical outcomes were unchanged: 30-day readmission (8.5% vs 9.0%), in-hospital mortality (3.4% vs 3.2%), and length of stay (6.9 vs 7.1 days). Hospitals integrating the time-out into electronic health record duration-default order sets achieved greater DOT reductions (32% vs 18%; P=0.02). In multivariable analysis, the intervention independently predicted shorter DOT (HR 0.73; 95% CI 0.68–0.79; P<0.001). **Conclusions**. Implementation of an antibiotic time-out significantly reduced antibiotic duration and broad-spectrum use without adversely affecting clinical outcomes. Integration into electronic health record order sets enhanced effectiveness, supporting time-out strategies as scalable ASPs intervention. **Keywords:** Antibiotic time-out, antimicrobial stewardship, DOT, AMR.

A CASE OF ARTERIOVENOUS MALFORMATION

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Introduction. Arteriovenous malformations (AVM) are part of the group of cerebral vascular malformations that represent congenital defects of the circulatory system formed by a cluster of blood vessels through which arterial blood flows directly into the drainage veins without the normal interposition of the cerebral capillary bed. AVMs are considered to develop during the intrauterine period, however, the form in which they are discovered at an older age does not correspond to the size and shape in intrauterine life. Smaller AVMs are associated with higher intranidal pressure. In 1986 Robert Spetzler (an American neurosurgeon renowned in cerebral vascular surgery) and Neil Martin (an American neurosurgeon specialized in cerebrovascular pathology) proposed a grading scale to estimate the surgical risk of AVMs. **Materials and methods:** The patient presented with complaints of headaches and convulsive attacks. The onset of the disease date back to 2020 when the patient marks a tonic-clonic convulsive attack for the first time. He was consulted by the neurosurgeon with the performance of cerebral CT, cerebral MRI, Angiography. **Results:** Cerebral CT revealed hyperdense intraparenchymal focus with mass effect on the right lateral ventricle. Cerebral MRI showed right paramedian serpinginos vascular nidus, heterogeneous area around the nidus with the involvement of deep venous drainage and the right lateral ventricle. Cerebral angiography by digital subtraction confirmed a right fronto-parietal AVM, Martin-Spetzler 2. Surgical tactics are combined with the application of endovascular surgery and microsurgery. Intranidal embolization and feeding branches, preoperative treatment to reduce deep supply with facilitating surgical intervention, pre-radiosurgery necessary to reduce volume not only blood flow. Postoperative MRI with angiography sequence shows complete removal of the nidus. No more abnormal vessels are evident in the vicinity of the malformation bed. Normal cerebral parenchyma. The patient returns to the territory following anticonvulsant treatment. **Conclusions:** AVM rupture represents a medical surgical emergency that requires prompt and immediate intervention. Thus, complete resection is a method to avoid rebleeding, but also the sequelae induced by this pathology.

Keywords: Arteriovenous malformation (AVM), nidus, interventional surgery, embolization.

METABOLIC EFFECTS AND USE OF GLUCOCORTICOIDS IN ATHLETES

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Introduction. Glucocorticoids are hormones secreted by the adrenal cortex, playing an essential role in regulating basal metabolism and the inflammatory response. Due to their metabolic effects, glucocorticoids are frequently misused by athletes with the aim of enhancing and improving performance during competitions, which constitutes a violation of anti-doping regulations. The World Anti-Doping Agency (WADA) strictly monitors the administration of pharmaceutical substances, allowing their use only for therapeutic purposes through the granting of a Therapeutic Use Exemption (TUE). **Aim of the study.** To analyze and synthesize current scientific data on the metabolic effects and impact of glucocorticoid use on the athlete's body, from physiological, biochemical, pharmacological, and ethical perspectives. **Materials and methods.** The paper presents a critical analysis of scientific articles (clinical studies, meta-analyses) published in the last 10 years in electronic databases such as PubMed, ScienceDirect, and Scopus, as well as official reports issued by WADA, to define the medical conditions and real-life situations related to glucocorticoid use in athletes. **Results.** Prolonged and/or uncontrolled administration of glucocorticoids, especially in high doses, activates hepatic gluconeogenesis, reduces peripheral glucose utilization, induces insulin resistance, and consequently, due to persistent long-term hyperglycemia, may lead to steroid- induced diabetes mellitus. At the same time, glucocorticoids increase lipolysis and the redistribution of adipose tissue, promoting the development of dyslipidemia and central obesity. Protein metabolism is characterized by accelerated muscle protein degradation, resulting in the loss of muscle mass and strength. The abusive and uncontrolled use of glucocorticoids causes arterial hypertension, hormonal dysfunction, and osteoporosis. From an ethical point of view, the misuse of pharmaceutical substances, including glucocorticoids, by athletes represents a violation of anti-doping regulations and may result in disqualification. **Conclusions.** Although glucocorticoids are indispensable in the treatment of many diseases, their uncontrolled use poses a high risk of adverse metabolic effects. Their therapeutic administration must be strictly justified, in compliance with official WADA regulations and with regular metabolic monitoring. Education of athletes and medical staff regarding the risks of glucocorticoid misuse is essential for maintaining both health and the integrity of sports competition. **Keywords:** glucocorticoids, metabolism, athletes, adverse effects, doping

FEATURES OF MICROSURGICAL TREATMENT IN PATIENTS WITH PTERYGIUM STAGE III

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Introduction: 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 III. **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.
Key words: recurrent pterygium, free conjunctival flap, recurrence, postoperative period, 5-FU (fluoruracil)

MICROSURGICAL REPLANTATION OF THE FIRST DIGIT FOLLOWING TRAUMATIC METACARPAL-LEVEL AMPUTATION

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Introduction. Replantation of the first digit is one of the most complex and functionally significant procedures in hand microsurgery, due to its essential role in thumb opposition, grasp, and overall upper limb performance. The thumb contributes substantially to hand dexterity, and its loss severely impacts patient autonomy and quality of life. The success of replantation depends on multiple factors, including the mechanism and level of injury, duration of warm and cold ischemia, as well as the conditions of preservation and transport of the amputated segment. Early surgical intervention and strict adherence to microsurgical principles are crucial for maximizing tissue survival and functional recovery.
Case Presentation. A 59-year-old patient presented to the emergency department approximately two hours after sustaining a sharp traumatic amputation of the first digit at the metacarpal level, caused by an axe injury. The amputated segment was properly preserved and transported in a cold environment without direct contact with ice. Clinical and imaging evaluations confirmed the indication for emergency replantation, with no systemic or local contraindications. The patient was immediately transferred to the operating room. The surgical procedure lasted two hours and thirty minutes, and revascularization of the amputated segment was achieved approximately four hours after injury, which is considered favorable for tissue viability. Surgical management included meticulous debridement, skeletal stabilization, repair of flexor and extensor tendons, microsurgical arterial and venous anastomoses under an operating microscope, and fascicular neurorrhaphy. Careful layered closure was performed to prevent tension and vascular compromise. **Discussion.** The first 7 postoperative days represent a crucial period for the survival of the replanted segment, with vascular thrombosis being the primary early complication. Continuous monitoring of tissue perfusion and appropriate anticoagulant therapy are essential to prevent failure. In this case, the postoperative evolution was favorable, with no vascular or infectious complications, and the patient was discharged after 7 days of hospitalization.
Conclusions. Replantation of the first digit performed within an optimal timeframe and in accordance with microsurgical principles can ensure survival of the amputated segment and satisfactory functional outcomes. Prompt trauma management, proper preservation, and intervention in a specialized center are key determinants of success. This case highlights the importance of multidisciplinary collaboration and microsurgical expertise in restoring hand function and improving long-term prognosis.
Keywords: microsurgery, digit replantation, thumb amputation, ischemia time, vascular anastomosis, functional recovery

A CASE OF EXCESSIVE TORTUOSITY OF THE LIENAL ARTERY

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Introduction: The lienal artery is characterized by a wide range of variations including variants of origin, topography, course and branching pattern. In over 90% of cases, it derives from the coeliac trunk, but it may also arise directly from the abdominal aorta and other arteries. Preponderantly, this artery runs along the superior margin of the pancreas, but also an intra-parenchymatous, a retro- or antero-pancreatic course has been reported in the literature. The lienal artery is one of the most tortuous branches of the coeliac trunk. Its excessive tortuosity might cause aneurysms formation, vascular wall dissection, stenosis, thrombosis and lienal infraction. **Material and methods:** Anatomical dissection of a formalized cadaveric sample was performed at the Anatomy and Clinical Anatomy Department. The origin, topography, course, branching pattern, shape and length of the lienal artery loops were determined. **Results:** During routine anatomical dissection an excessive tortuosity of the lienal artery, originating from the coeliac trunk, with a zigzag arterial course, arranged into six loops, was observed. Each loop consisted of a descending and ascending limbs, with sharp angulations of similar shape and size. The inferior angulations of the first and second loops were sharper, surrounded by dilations and narrowing. The length of the loops varied between 44-56 mm. The first loop was the shortest one and the last two loops were the longest. The length of the first loop was 44 mm with equal ascending and descending limbs. The second loop had a length of 50 mm, its ascending limb (AL) – 22 mm and descending limb (DL) – 28 mm; the third loop – 55 mm (AL – 28 mm, DL – 27 mm); the fourth loop – 53 mm (AL – 27 mm, DL – 26 mm); the fifth loop – 56 mm (AL – 26 mm, DL – 30 mm); the sixth loop – 56 mm (AL – 30 mm, DL – 26 mm). Within the first three loops, atheromas were revealed. Before entering the lienal parenchyma, the lienal artery divided into 4 terminal branches. **Conclusion:** The excessive tortuosity of the lienal artery might be the cause of surgical errors and iatrogenic injures. It is also dangerous in terms of aneurisms formation with arterial wall ruptures and abdominal bleeding, or thrombus formation and lienal infarction.

Keywords: splenic artery, tortuosity, variability

THREE-DIMENSIONAL RIGHT-VENTRICULAR EJECTION FRACTION FOR PRAGMATIC TRIAGE AFTER PULMONARY EMBOLISM

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Background: Persistent symptoms after acute pulmonary embolism (PE) are frequent, while access to advanced chronic thromboembolic disease work-up is limited. Three-dimensional echocardiography (3DE) provides a direct quantification of right-ventricular (RV) systolic performance and may support post-PE triage. **Purpose:** To describe 3DE-derived RV ejection fraction (3D-RVEF) at ≥3–6 months after PE and its association with functional status and NT-proBNP. **Methods:** In 104 PE survivors evaluated ≥3–6 months after the index event, 3D-RVEF was measured when feasible and categorised as impaired (<45%) and severely reduced (<35%). Functional limitation was assessed using NYHA class and Post-VTE Functional Status (PVT). NT-proBNP was analysed using non-parametric comparisons and clinically relevant thresholds. **Results:** 3D-RVEF showed wide dispersion (mean 35.5±12.2%; median 36.25 [IQR 25.75–44.0]; range 11.6–58.0). Impaired 3D-RVEF (<45%) was present in 80 (72.7%) and severe reduction (<35%) in 47 (42.7%). Patients meeting a severe RV dysfunction profile dominated by 3D-RVEF <35% exhibited higher NT-proBNP (median 149 [IQR 50–436.5] vs 89.5 [50–146.8] pg/mL; p=0.031), with more frequent elevations >125 pg/mL (58.3% vs 29.0%; p=0.003) and >300 pg/mL (33.3% vs 12.9%; p=0.019). Differences in functional indices were directionally unfavourable but not statistically significant (PVT≥3: 61.4% vs 51.9%, p=0.415; NYHA≥III: 35.6% vs 23.7%, p=0.199). **Conclusion:** 3D-RVEF is feasible in routine follow-up and identifies a high prevalence of residual RV systolic impairment after PE. Severe 3D-RVEF reduction enriches for higher biomarker burden despite only modest separation by functional class. 3DE-based thresholds may provide a pragmatic first-line triage step to prioritise patients for intensified follow-up and advanced investigation. **Keywords:**Pulmonary embolism; 3D right-ventricular ejection fraction (3D-RVEF); Right-ventricular dysfunction; NT-proBNP; Functional capacity; NYHA class; Post-VTE Functional Status (PVT); Risk stratification; Clinical triage
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PARANEOPLASTIC SENSORY NEUROPATHY: CLINICAL FEATURES, DIAGNOSIS, AND TREATMENT

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Introduction. Paraneoplastic sensory neuropathy (PSN) is a phenotype within the spectrum of paraneoplastic neurological syndromes, characterized by the destruction of sensory neurons located in the dorsal root ganglia. The most common underlying cause is small-cell lung cancer (SCLC), which is associated with PSN in approximately 85% of cases, frequently in the presence of anti-Hu antibodies. **Materials and Methods.** This study consists of a descriptive analysis of the scientific literature published between 2013 and 2024. The sources reviewed included databases such as PubMed, Google Scholar, ScienceDirect, and relevant review articles. **Results.** The clinical course of PSN is typically subacute and rapidly progressive over several weeks. The main symptoms include asymmetric numbness affecting the upper or lower limbs. All types of sensory modalities may be impaired, including vibration sense and proprioception. Deep osteotendinous reflexes are usually absent. Patients may also present with severe pain, allodynia, paresthesia, and signs of sensory ataxia. The diagnosis of PSN includes three levels of certainty based on the "**PNS-Care Score"**, which takes into account the clinical phenotype, the presence or absence of neuronal antibodies, and the presence or absence of an underlying malignancy. Detection of serum antibodies such as anti-Hu, CV2/CRMP-5, and amphiphysin-IgG may support the diagnosis; however, approximately 16% of cases are seronegative. In seronegative forms, mitochondrial apoptosis associated with oxidative stress may contribute to the pathogenesis, resulting in the release of autotoxins and subsequent demyelination of peripheral nerves. Immunomodulatory therapy may be beneficial in both seropositive and seronegative forms, as well as in the management of the underlying malignancy. **Conclusions.** PSN represents a severe neurological disorder in which early recognition is essential for identifying an underlying neoplasm and initiating appropriate treatment. Further studies are required to validate new therapeutic strategies. **Keywords:** paraneoplastic sensory neuropathy, antibodies, sensory neurons, sensitivity.

MORPHOLOGICAL SPECIFIC FEATURES OF THE BUCCAL NERVE

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Introduction. Variability of the buccal nerve is of high clinical importance in dental practice, maxillofacial, reconstructive and esthetic surgery. In some cases due to anatomical variation of this nerve, impairments of the neighboring nerves, specifically of the buccal branches of the facial nerve can occur. **The aim** of our study was to identify the morphological peculiarities of the buccal nerve, its connections and their clinical significance. **Material and methods.** The study was carried out at the Department of Anatomy and Clinical Anatomy of *Nicolae Testemitanu* State University of Medicine and Pharmacy. For our purpose, the anatomical dissection of 10 formalized hemiheads was done. The course, connections and peculiarities of the buccal nerve terminal ramifications were highlighted. **Results.** In the majority of cases, the buccal nerve had a straight, or oblique descending course, branching into multiple twigs within the skin and mucosa of the cheeks. In 8 of 10 cases, the buccal nerve was connected with the buccal branches of the facial nerve. On a right female hemiface, the buccal nerve derived from the mandibular nerve with two roots, connecting to each other through an irregular loop. From the upper margin of that loop aroused two branches connecting the buccal nerve with the pterygopalatine ganglion and maxillary nerve. Distally to the loop, the buccal nerve had a tortuous zigzag course until the alveolar juga of the upper third molar, and then it continued its trajectory in an oblique and descending way, branching into multiple twigs within the cheek. **Conclusion.** The tortuous buccal nerve is highly susceptible to iatrogenic injures and due to its connections with the buccal branches of the facial nerve, those iatrogenic injures can lead to facial nerve impairments. Specific features of the buccal nerve should be considered in dental practice when performing anesthesia, as well as in esthetic and reconstructive surgery of the facial region.
Keywords: buccal nerve, connections, specific features

POTENTIAL MOLECULAR TARGETS FOR PREVENTION AND TREATMENT OF PERSISTENT POSTOPERATIVE PAIN

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Introduction. Persistent postoperative pain is a clinically important complication of surgery that develops when acute nociceptive signaling fails to resolve and progresses toward sustained peripheral and central sensitization. Experimental evidence suggests that this transition is driven by coordinated changes in primary afferent excitability, spinal excitatory signaling, neuroimmune activation, and maladaptive synaptic plasticity. Study aims to summarize the main molecular targets involved in the development and persistence of postoperative pain and to highlight mechanism-based strategies for its prevention and treatment. **Materials and Methods.** This narrative analytical review summarizes primary mechanistic and translational studies on molecular pathways involved in postoperative pain persistence. Priority was given to studies investigating ion channels, glutamatergic signaling, spinal glial activation, inflammatory mediators, and neurotrophic factors in validated postoperative pain models. **Results.** The reviewed evidence supports a multifactorial model of persistent postoperative pain. At the peripheral level, increased nociceptor excitability is associated with transient receptor potential vanilloid 1-mediated heat hyperalgesia and upregulation of voltage-gated sodium channels, particularly NaV1.7, while selective sodium-channel blockade has shown analgesic potential in postoperative settings. At the spinal level, persistent sensitization is promoted by glutamatergic signaling through NMDA receptor subunits, enhanced NMDA receptor GluN2B/NR2B phosphorylation, and downstream activation of calcium/calmodulin-dependent protein kinase II and p38 mitogen-activated protein kinase pathways. Neuroimmune mechanisms are also central: activation of microglia and astrocytes, together with Toll-like receptor 4 and NF-kB signaling, increases the release of IL-1 beta, IL-6, TNF-α, further amplifying nociceptive transmission. In addition, elevated BDNF expression contributes to maladaptive synaptic plasticity and maintenance of pain hypersensitivity. **Conclusions.** Persistent postoperative pain results from the interaction of peripheral sensitization, spinal hyperexcitability, neuroinflammation, and pathological neuroplasticity. A mechanism-based therapeutic approach targeting these pathways may help prevent the transition from acute to chronic postoperative pain and support the development of more effective non-opioid perioperative analgesic strategies.

Keywords: persistent postoperative pain, molecular targets, central sensitization, neuroinflammation, ion channels, non-opioid analgesia.

THE ANATOMY OF INTERMUSCULAR CELLULAR SPACES IN THE CONTEXT OF *ERRECTOR SPINAE* FASCIAL PLANE ANESTHESIA: A LITERATURE REVIEW

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Background. Cellular spaces, also referred to as interfascial planes, represent anatomical compartments formed by loose connective tissue and delimited by fasciae, muscles, bones, and other structural elements. These spaces may contain blood vessels, nerves, and lymph nodes and play an important role in facilitating the mobility and interaction of anatomical structures. In pathological conditions, particularly infectious processes, they can also serve as pathways for the spread of purulent collections. Recent anatomical and imaging studies have redefined the cellular space as the plane between two layers of the deep fascia, composed primarily of adipose tissue, elastin, and reticular fibers. In recent years, these interfascial planes have gained increasing importance in regional anesthesia, particularly in the development of fascial plane blocks, which are widely used due to their safety and technical simplicity. **Aim of the study**. The aim of this study was to highlight the anatomical and clinical significance of interfascial cellular spaces, with particular emphasis on the erector spinae plane, and to underline their relevance in the performance of fascial plane blocks used for postoperative and chronic pain management. **Results**. The analysis of the anatomical characteristics of the erector spinae interfascial plane demonstrates that this space is located between the erector spinae muscle and the transverse processes of the vertebrae. Within this plane run the dorsal and ventral rami of the spinal nerves, which can be effectively anesthetized following the administration of local anesthetic. The spread of the anesthetic solution occurs both cranially (approximately 1–3 vertebral levels) and caudally from the injection site, allowing the blockade of multiple dermatomes. This anatomical distribution explains the effectiveness of the erector spinae plane block in providing analgesia for a variety of surgical procedures as well as for the treatment of acute and chronic pain conditions. **Conclusion**. A thorough understanding of topographic anatomy and interfascial cellular spaces is essential for performing medico-surgical procedures with minimal complications. The evolution of fascial plane blocks from landmark-based techniques to ultrasound-guided approaches has significantly increased their safety and accuracy. Consequently, locoregional anesthesia techniques, particularly fascial plane blocks such as the erector spinae plane block, are expected to gain wider applicability across both surgical and therapeutic medical specialties.

MAGNETIC NANOEMULSIONS LOADED WITH DEXAMETHASONE AND ASCORBIC ACID DEMONSTRATE THERAPEUTIC EFFICACY IN RATS WITH COLLAGENASE-INDUCED OSTEOARTHRITIS

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Introduction. Osteoarthritis (OA) is a growing global health concern, significantly impacting patients' quality of life and placing increasing pressure on healthcare systems. Innovative drug delivery approaches may enhance treatment precision and improve therapeutic outcomes. We present a hybrid intra-articular platform that combines magnetic nanoparticles (MNPs) with nano-emulsions (NEs) engineered to deliver dexamethasone (Dex) and ascorbic acid (AA) as a local therapy for OA. **Materials and Methods.** The NE–MNP formulations were characterized using DLS, TEM, VSM, and FTIR to evaluate their size, morphology, magnetic properties, and stability. Cytocompatibility was assessed in vitro using MTT and LIVE/DEAD assays. Effects on cellular senescence, wound healing, and chondrogenesis were studied in adipose-derived stem cells (ADSCs) through SA-β-galactosidase activity, Western blotting, immunocytochemistry, scratch assays, and chondrogenic markers. Safety and biodistribution were examined in mice after intraperitoneal administration, while therapeutic efficacy was evaluated in a collagenase-induced OA rat model following a single intra-articular injection. Animals were monitored using blood tests, CRP levels, organ histology, MRI, and joint histology for up to five months. **Results.** The Dex/AA-loaded NE–MNP carriers were nanosized (20–60 nm), stable, and non-aggregating. In vitro, they reduced senescence markers and promoted ADSC chondrogenesis. In mice, systemic administration showed no significant inflammatory or hematologic effects and no organ damage, aside from mild transient activation of liver Kupffer cells. In the rat OA model, a single injection reduced synovial inflammation and improved cartilage thickness over several months compared with controls. **Conclusions.** Overall, these findings demonstrate the safety and therapeutic potential of Dex- and AA-loaded magnetic nano-emulsions for targeted OA treatment. The platform combines magnetic targeting with multi-drug delivery and shows anti-inflammatory and pro-chondrogenic effects. Further studies in larger animal models are needed to support clinical translation.

Keywords: osteoarthritis, magnetic nanoemulsions, drug-delivery, chondrogenesis, senescence, wound healing

THE VULNERABILITY OF THE HUMAN BODY TO CHEMICALS

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Introduction. The human body is exposed daily to a wide range of chemicals from the environment or occupational environment. Tissues and cells are the first biological levels that come into contact with chemical agents, and their vulnerability largely determines the systemic toxic effects. Chemicals can induce: oxidative damage, mitochondrial dysfunction, changes in cell membranes and can affect intra- and extra-cellular signaling processes. Rapidly proliferating tissues, such as liver, dermal or lung, show increased vulnerability to chemicals. Children, the elderly and those with chronic diseases are more susceptible to the harmful effects of chemical exposures.
Material and methods. Review of national and international scientific literature on the management and exposures to chemicals, toxicology and public health. PubMed articles were analyzed that reflected the mechanisms of chemical toxicity at the cellular and tissue level, oxidative effects, biological, epidemiological and regulatory aspects related to the vulnerability of the human body to chemicals.
Results. Exposure to chemicals can cause various health problems, from minor irritations to serious conditions, affecting the immune system and increasing susceptibility to infections depending on individual vulnerability. The issues related to the safe use of chemicals and reducing potential side effects on health, concern specialists around the world. The results of some studies note that cumulative exposure to various chemicals can worsen liver functions. According to some EU guidelines, around 144,000 synthetic chemicals are registered. Some chemicals can lead to lipid oxidation and oxidative stress, the latter considered to be a central mechanism in cellular toxicity. Analysis of statistical data on the general morbidity of the population of the Republic of Moldova over a period of 10 years (2014-2023) indicates an average annual increase in the number of cases per 100 thousand populations. In particular, the overall prevalence has increased: from 9607,7 $^{0}/_{000}$ in 2014 to 11904,6 $^{0}/_{000}$ in 2023.
Conclusions. The vulnerability of the human body to chemicals is a complex phenomenon. In order to protect the health of the population, it is important to be aware of the potential dangers of chemicals, take appropriate measures, and manage and handle chemicals responsibly.
Keywords: chemicals, risk, toxicology, human body, cells, vulnerability

VESTIBULAR MIGRAINE vs MENIERE'S DISEASE. DIFFERENTIAL DIAGNOSIS

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Introduction. Differential diagnosis (DD) between Vestibular migraine (VM) and Meniere's disease (MD) is challenging because both conditions present with recurrent episodes of vertigo. Correct differentiation is essential due to differences in pathophysiology, prognosis, and treatment strategies. **Materials and Methods.** A systematic literature review (2020–2026) was performed using PubMed, Scopus, and Web of Science, including original studies, reviews, and clinical guidelines on diagnostic criteria, pathophysiology, and treatment of VM and MD. **Results.** MD is a peripheral vestibular disorder associated with endolymphatic hydrops, characterized by excessive accumulation of endolymph in the membranous labyrinth. Clinically, MD presents with recurrent rotational vertigo accompanied by progressive sensorineural hearing loss, tinnitus, and aural fullness. Episodes usually last from 20 minutes to several hours and are often associated with nausea and vomiting. Hearing loss fluctuates at the early stage, mainly affecting low frequencies, and gradually progresses. The disease often begins unilaterally and may later involve the opposite ear. VM is the most common cause of recurrent spontaneous vertigo of central origin. Attacks last from minutes to hours and are often associated with migraine features such as headache, photophobia, phonophobia, or visual aura, although headache may be absent. Persistent hearing loss is uncommon, and audiometry is usually normal. Vestibular symptoms may be positional and triggered by stress, sleep deprivation, or dietary factors. Progressive cochlear symptoms favor MD, whereas migraine features without auditory deficit suggest VM. Acute MD attacks are treated with vestibular suppressants and antiemetics, while long-term therapy includes salt restriction, betahistine, and diuretics; refractory cases may require surgery. VM treatment follows migraine therapy principles: NSAIDs, triptans, benzodiazepines, or dihydroergotamine are used during attacks, while prophylaxis includes beta-blockers, antidepressants, calcium channel blockers, acetazolamide, and antiepileptic drugs. **Conclusions.** DD should be based on clinical characteristics of vertigo, presence of progressive hearing loss, and audiometric findings. Repeated audiometry and modern diagnostic criteria improve accuracy and allow appropriate treatment selection. **Keywords.** Vestibular migraine, Endolymphatic hydrops, Meniere's disease, Headache

TRIGGER POINT THERAPY IN MYOFASCIAL PAIN SYNDROME

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Introduction: Chronic myalgia has a significant impact on health, affecting millions of people worldwide. It is well known that trigger points (TP) when they become active or are in a latent state usually appear in the same areas of muscles, conditioning creation of TP maps. These maps indicate the affected areas of the muscles identified as TP and the radiation of pain to the neighboring or distant areas. In recent decades, the advancements in understanding the pathophysiology of myofascial pain have led to innovative approach and modernization of treatment methods, focused not only on reduction of symptoms, but also, on deactivating trigger points and adjusting factors that contribute to pain maintenance. As a goal of this research was to study the modern treatment methods of TP in myofascial pain syndrome (MPS). **Materials and methods:** Sixty-four bibliographic sources from Google Scholar, PubMed, Hinari, Cambridge Core, Web of Science databases, which offered details about the morphology, topography, etiopathogenesis and treatment methods of TP were studied. **Results:** The contemporary approach of MPS treatment is integrated and multimodal, combining manual therapy, minimally invasive techniques, advanced physical methods, therapeutic exercise, and patient education. The therapeutic mechanism of the dry needling method involves breaking the pain-spasm-pain cycle by producing a local contractile response, normalizing the dysfunction of the terminal motor plate, releasing algogenic substances accumulated in the TP area, and improving local circulation and tissue oxygenation. The method of local infiltration with anesthetics is based on the rapid deactivation of the trigger point by the direct injection of an anesthetic substance into the hypersensitive area of the affected muscle. Ischemic compression is a manual therapy method that involves the application of direct, constant, and progressive pressure on the trigger point, aiming to reduce hypersensitivity and normalize muscle tone. Shockwave therapy is based on increasing the permeability of cell membranes, thereby facilitating the release of anti-inflammatory mediators and endorphins, which activate the descending pain inhibition systems. Spray and stretch are used as therapeutic methods for the rapid relaxation of the TP in an affected muscle and for increasing the amplitude of muscle movement. **Conclusions:** Contemporary management of MPS is multimodal, individualized, combining minimally invasive treatment methods with non-invasive techniques to contribute to the recovery of muscle function and the quality of life of patients affected by chronic myofascial pain.

Keywords: trigger points, myofascial pain syndrome

ANATOMO-TOPOGRAPHIC ASPECTS OF THE BRACHIAL ARTERY AND ITS BRANCHES VARIABILITY

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Introduction. Variation anatomy is a fundamental and highly significant field of morphology, in which every detail has an applicative value, particularly when referring to the cardiovascular system. In medical practice, due to unknown arterial variability, errors with fatal consequences can occur.
Purpose of the work: Determining the peculiarities of the brachial artery (BA) and its branches variability depending on gender and laterality, according to their origin, course, number, and branching pattern. **Material and methods.** Brachial artery variability was studied on 70 upper limbs, collected from adult embalmed cadavers, of both genders (equal number), dissected at the Department of anatomy and clinical anatomy of the Nicolae Testemitanu SUMPh. By anatomical dissection, the BA topography, origin of its branches, and relationship with the neighboring structures were highlighted. **Results.** Variants of the brachial artery were established in 28.6%: 18.6% in males – 7.2% left side (LS) and 11.4% right side (RS); 10.0% in females – 4.3% LS and 5.7% RS. Identified variants: bilaterally – 11.4% (8.6% in males, 2.8% in females), unilaterally – 8.6%: 7.2% in males (2.9% LS, 4.3% RS); 1.4% in females (LS). Single variants: 14.3% – 10% in males (5.7% LS, 4.3% RS); 4.3% in females (2.9% LS, 1.4% RS). Multiple variants: 14.3% – 8.6% in males (1.4% LS, 7.2% RS); 5.7% in females (1.4% LS, 4.3% RS). Variants of origin – 12.9% (7.2% in males, 5.7% in females); variants of branching pattern – 2.9% (in the same proportion); numerical variants – 11.4% (8.6% in males, 2.8% in females), common trunks – 5.7% (1.4% in males, 4.3% in females); Variants of brachial artery bifurcation – 7.2% (4.3% in males, 2.9% in females); BA trifurcation – 4.3% (2.9% in males, 1.4% in females). **Conclusions.** The brachial artery and its branches are subjected to variations, presenting diverse types of variants, more frequently in males and on the right side. Numerical prevalence of the bilateral variants over the unilateral ones, while single and multiple variants were determined in the same proportion. **Keywords:** brachial artery, variability, morphology

ARTERIOVENOUS MALFORMATION: CASE STUDY

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Introduction: Arteriovenous malformations (AVM's) represent abnormal connections between arteries and veins, consisting of a cluster of blood vessels though which arterial blood flows under high-pressure, draining directly into veins, bypassing the normal capillary bed and thus, conditioning a high risk of hemorrhage. Although AVMs may develop in various regions of the body, the cerebral ones can have severe consequences and become symptomatic when the lesion reaches a critical level. Our aim was to present a case study of a right frontoparietal cerebral arteriovenous malformation, of grade II according to Spetzler-Martin grading scale. **Materials and Methods:** A 32-year-old male patient complaining on headache and seizure episodes was hospitalized in October 2025 to the Institute of Neurology and Neurosurgery *Diomid Gherman* Chisinau, Republic of Moldova. The diagnosis of AVM's was confirmed by CT, MRI, and cerebral angiography. The medical history revealed that the onset of that condition occurred in 2020 and was marked by generalized tonic-clonic seizure. **Results:** Brain CT revealed a hyperdense intraparenchymal focus (hematoma) with mass effect on the right lateral ventricle. Brain MRI identified a serpiginous paramedian vascular nidus on the right, surrounded by a heterogeneous area, with involvement of deep venous drainage. Angiographically a right paramedian frontoparietal cerebral AVM with rapid blood flow was determined. Venous drainage occurred through the cortical veins into the frontal part of the superior sagittal sinus, two of which were dilated and tortuous (paranidal aneurysm). A combined interventional strategy was applied. Initially, intranidal and adjacent branch endovascular embolization was performed using detachable coils, which obliterated the fistula and corrected the abnormal blood flow. This was followed by surgical resection of the central portion of the AVM. Postoperative MRI with angiographic sequence confirmed complete removal of the nidus with preservation of the normal brain parenchyma. No abnormal blood vessels were identified adjacent to the malformation site. The patient was discharged from the hospital with ongoing anticonvulsant therapy. **Conclusion:** Rupture and hemorrhage of cerebral AVM's represent a medical emergency requiring prompt intervention. A combined interventional strategy (embolization and resection) is an appropriate method to prevent hemorrhage and long-term complications associated with this pathology. **Keywords:** Arteriovenous malformation, nidus, embolization, resection.

OCCUPATIONAL RISK AWARENESS AND STANDARD PRECAUTION PRACTICES REGARDING HEPATITIS C AMONG HEALTHCARE WORKERS IN THE REPUBLIC OF MOLDOVA

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Introduction. Healthcare workers (HCW) face elevated occupational exposure to hepatitis C virus (HCV). In the Republic of Moldova, HCV prevalence is estimated at 3.8%, yet HCW-specific knowledge, attitudes, and practices (KAP) remain scarce. This study compared KAP scores among physicians, nurses, and the general population, focusing on standard precaution compliance.
Materials and methods. A cross-sectional study (2024-2025) enrolled 567 adults (18-65 years) from four Moldovan regions by random sampling: 151 physicians, 280 nurses, and 136 general-population representatives. Participants completed a structured questionnaire administered via EpiInfo, scored using a 30-point KAP scale (knowledge 0–10, attitudes 0–10, practices 0–10). Kruskal-Wallis and Mann-Whitney U tests compared subgroups; Spearman rho assessed inter-component correlations ($p<0.05$). **Results.** KAP total scores differed significantly ($H=220.10$, $p<0.001$): physicians 19.85±2.95 (66.2%), nurses 18.76±2.91 (62.5%), general population 13.62±3.07 (45.4%). Knowledge was higher in physicians (5.65±0.85) than nurses (5.40±0.95; $p=0.037$) and the general population (3.67±1.55; $p<0.001$). Attitudes were comparable across groups (71–73%; $p=0.617$), with no statistically significant differences. Practice scores diverged most ($H=183.08$, $p<0.001$): physicians 69.3%, nurses 60.4%, general population 28.5%. Risky occupational behaviors persisted: needle recapping was reported by 24.4% of physicians and 37.2% of nurses; glove change per patient by only 52.3% and 39.3%, respectively. Needlestick injuries affected 15.9% of physicians and 18.2% of nurses. HCV testing rates were higher in HCW (physicians 89.4%, nurses 86.8%) than in the general population (46.3%). Knowledge correlated positively with practices ($rho=0.336$, $p<0.001$); attitudes did not correlate with either component. **Conclusions**. Despite superior overall KAP profiles, HCW exhibit critical gaps in standard precaution adherence. The attitude-practice disconnect confirms that positive beliefs alone do not guarantee safe behavior. Competency-based infection-prevention training and reinforced post-exposure protocols are warranted. Longitudinal research should assess whether targeted interventions reduce occupational HCV transmission in Moldovan healthcare settings.
Keywords: hepatitis C virus; healthcare workers; knowledge, attitudes and practices; standard precautions; needlestick injury; occupational exposure; KAP; infection prevention

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