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

LABORATORY OF TISSUE ENGINEERING AND CELLS 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 3rd EDITION”

Dedicated to the 80th anniversary of the founding of Nicolae Testemitanu State University of Medicine and Pharmacy

Chisinau, March 21-22, 2025

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AGENDA

Registration

March, 21, 2025

Opening ceremony 15:00 - 15:20

Ceban Emil, MD, PhD, Rector at SUMPh *Nicolae Testemitanu*, Academician, Professor.
Romanciuc Grigore, Head of Agency of Transplantation, Republic of Moldova.
Stepa Serghei, PhD, Director at Clinical Hospital of Orthopedics and Traumatology.
Nacu Viorel, MD, PhD, MPH, Head of Human Tissue Bank at Clinical Hospital of Orthopedics and Traumatology, Responsible for Laboratory of Tissue Engineering and Cells Cultures at SUMPh *Nicolae Testemitanu.*

DAY ONE – 21 March 2025

PLENARY MEETING

1. **15:20-15:40. Nacu Viorel, Stepa Serghei, Cospormac Igor, Cociug Adrian, Cobzac Vitalie, Gutu-Bahov Cornelia, Tambalari Tatiana.** Tissue and cells transplantation in Republic of Moldova, trendlines. *Chisinau, Republic of Moldova.*

2. **15:45-16:05. Jian Mariana, Codrea Cosmin, Spoiala Angela, Ficai Denisa, Nacu Viorel, Ficai Anton**. Material Design in Hard Tissue Engineering. *Bucharest, Romania. Chisinau, Republic of Moldova.*

SESSION 1

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

3. **16:10-16:20. Iapascurta Victor.** Agent-based modelling of fluid dynamics in lung tissue engineering. *Chisinau, Republic of Moldova.*

4. **16:20-16:30**. **Iapascurta Victor.** Building a rag system for tissue engineering: insights from domain-specific text and sepsis management. *Chisinau, Republic of Moldova.*

5. **16:30-16:40. Jian Mariana, Nacu Ana-Maria, Mostovei Andrei, Cobzac Vitalie, Motilica Ludmila, Oprea Ovidiu Cristian, Pantea Valeriana, Coretchii Ianos, Ficai Denisa, Ficai Anton, Nacu Viorel.** Tissue grafts for oral-maxillo-facial surgery. *Chisinau, Republic of Moldova.*

6. **16:40-16:50. Cojocari Stefan, Cobzac Vitalie, Nacu Viorel, Cociug Adrian, Buzu Dumitru, Vacarciuc Ion, Ticu Ion, Gutu Andrian, Suveica Teodor, Frasineac Victor, Capros Nicolae, Taran Anatolie.** Bone graft use in internal fixation of proximal and diaphyseal humeral fractures and pseudarthrosis. *Chisinau, Republic of Moldova.*

SESSION 2

Moderators: Cobzac Vitalie, *MD, PhD (Republic of Moldova)*, **Palarie Victor**, *MD, PhD (Republic of Moldova)*

1. **16:50-17:10. Marga Irina.** Epidemiology of healthcare-associated infections in children undergoing hematopoietic stem cell transplantation. *Chisinau, Republic of Moldova.*

2. **17:10-17:20. Macagonova Olga, Cociug Adrian, Taralunga Tatiana, Braniste Tudor, Verestiuc Liliana, Nacu Viorel.** Evaluation of the regenerative efficacy of biological dressings developed through tissue engineering. *Chisinau, Republic of Moldova; Iasi, Romania.*

3. **17:20-17:30. Iacubitchii Maria, Bendelic Eugeniu, Taralunga Tatiana, Nacu Viorel.** Exploring trabecular meshwork stem cells: potential roles, therapeutic implications and challenges in glaucoma. *Chisinau, Republic of Moldova.*

4. **17:30-17:40. Mihaluta Viorica, Stoian Alina, Iordachescu Rodica, Raischi Ion, Verega Grigore, Nacu Viorel.** Amniotic membrane therapy: a step toward faster ulcer healing. *Chisinau, Republic of Moldova.*

5. **17:40-17:50. Rusu – Radzichevici Natalia, Radzichevici Mihail, Stefanet Veronica.** Use of cell transplants in jaw reconstructive surgeries. *Chisinau, Republic of Moldova.*

6. **17:50-18:00. Popova Daria, Iordachescu Rodica, Verega Grigore, Jian Mariana, Nacu Viorel, Stoian Alina.** Breast tissue engineering: innovations, methods, and future perspective. *Chisinau, Republic of Moldova; Toronto, Canada.*

7. **18:00-18:10. Croitoru Dan, Todica Vladislav, Andronachi Victor, Andrusca Alexandru, Visnevschi Sergiu, Braniste Tudor, Nacu Viorel.** Nanocarriers that may bypass the blood-brain barrier. *Chisinau, Republic of Moldova.*

8. **18:10-18:20. Cobzac Vitalie, Jian Mariana, Maritoi Tatiana, Baranetchii Iana, Malcova Tatiana, Nacu Viorel.** Controlled release of active substances after double loading of demineralized cancellous bone. *Chisinau, Republic of Moldova***.**

9. **18:20-18:30. Palarie Victor.** Oral guided bone regeneration. *Chisinau, Republic of Moldova.*

DAY TWO – 22 March 2025

Session 1
Poster session
Moderators: Ficai Denisa, *PhD*, Nacu Viorel, *MD, PhD*

8:00-9:00

1. **Cotelea-Baligari Ana, Saptefrati Lilian.** Lucas testimonies: cell evolution. *Chisinau, Republic of Moldova.*
2. **Gutu Ina, Bacinschi Nicolae, Turcan Lucia, Caracas Anastasia, Mihalachi-Ana Maria.** Challenges in the use of glucocorticoids in transplantology. *Chisinau, Republic of Moldova.*
3. **Ivanova Svetlana, Foca Ecaterina.** Stem cell transplantation in infertility treatment: new perspectives in regenerative medicine. *Chisinau, Republic of Moldova*.
4. **Cobileanschii Eugeniu, Cobileanscaia Liubov**. Lienal vein – hemodynamic aspects in portal insuffiency. *Chisinau, Republic of Moldova*.
5. **Neznaico Victoria, Istrati Nina. Scalenus syndrome. *Chisinau, Republic of Moldova.***
6. **Cobileanschii Eugeniu, Cobileanscaia Liubov.** Hemodynamic indicators in the superior mesenteric vein in patients with hepatic cirrhosis. *Chisinau, Republic of Moldova*.
7. **Bogdanov Alan, Badalyan Albert, Babuci Angela.** The role of mesenchymal stem cell-derived extracellular vesicles in cardiac repair. *Chisinau, Republic of Moldova*.
8. **Scevenels Laura, Bogdanov Alan, Topor Boris.** Addressing artificial intelligence gaps in transplant medecine: a machine learning solution. *Chisinau, Republic of Moldova*.
9. **Leanca Iosif, Capcelea Svetlana.** Mimicking the host: gene addition via adeno-associated virus (aav) to reduce rejection in organ transplants. *Chisinau, Republic of Moldova*.
10. **Ecaterina Stratu, Carolina Catcov, Octavian Misic.** Monoclonal antibodies Anti-CGRP (calcitonin gene-related peptide) effective in migraine. *Chisinau, Republic of Moldova*.
11. **Jecova Svetlana, Protopop Svetlana.** Neural stem cell transplantation for neurodegenerative diseases. *Chisinau, Republic of Moldova*.
12. **Stoian Carolina.** Liver transplatation from a living donor. *Chisinau, Republic of Moldova*.
13. **Cheptea Mihai, Hotineanu Adrian.** Liver transplantation from a brain-dead donor. *Chisinau, Republic of Moldova*.
14. **Marcu Beatrice, Sardari Veronica, Tagadiuc Olga.** Fecal microbiota transplantation in cirrhosis: a microbiome-based therapeutic revolution. *Chisinau, Republic of Moldova*.
15. **Maniuc Mihail, Danilov Lucian, Ababii Polina, Nacu Viorel, Furculita Daniel, Bugan Maria, Cretu Carolina, Vishnumaya Sureshan.** Nasal permeability in inflammatory rhinosinusal diseases in children. *Chisinau, Republic of Moldova*.
16. **Babcinetchi Victoria, Caracas Anastasia, Gutu Ina, Bacinschi Nicolae.** Antimicrobial resistance of uropathogens after kidney transplantation. *Chisinau, Republic of Moldova*.
17. **Zavtoni Ana-Maria, Harea Gheorghe.** Current events in liver transplatology. *Chisinau, Republic of Moldova*.
18. **Caracas Anastasia, Babcinetchi Victoria, Vasilache Eugenia, Coretchi Ianos, Bacinschi Nicolae.** Urinary tract infections treatment in kidney transplant recipients. *Chisinau, Republic of Moldova*.
19. **Bacinschi Nicolae, Dabija Maria, Mihalachi-Anghel Maria, Spinosu Galina.** Bacterial resistance in urinary tract infectious in kidney transplant patients. *Chisinau, Republic of Moldova.*

20. **Sorici Galina, Diaconu Nadejda, Civirjic Irina, Ivanes Igor, Gorohova Marina, Plugaru Ana, Grosu Aurel.** Correlations between echocardiographic findings and SPECT CT as a predictive tool for chronic thromboembolic pulmonary hypertension in post – pulmonary embolism patients. *Chisinau, Republic of Moldova.*
21. **Danilov Lucian, Maniuc Mihail, Nacu Viorel, David Valeriu, Ababii Polina, Bugan Maria, Furculita Daniel.** The effect of stimulating local immunity with autologous cells in the treatment of tissue inflammatory process on the body's resistance to infection. *Chisinau, Republic of Moldova.*
22. **Mihalciuc Olga, Tagadiuc Olga, Gudumac Valentin.** Evaluation of cathepsin d activity in spleen and bone marrow in experimental immunodeficiency and under treatment with sulfated polysaccharides. *Chisinau, Republic of Moldova.*
23. **Caracas Anastasia, Gutu Ina, Latus Svetlana, Spinosu Galina, Bacinschi Nicolae.** The terapeutic drug monitoring of tacrolimus in renal transplant recipents. *Chisinau, Republic of Moldova.*
24. **Cojocaru Madalina, Ambros Ala.** The role of MIR-152-5P in renal transplantation. *Chisinau, Republic of Moldova.*
25. **Tonofa Maria, Purteanu Lilia, Benescu Irina, Cozma Octavian.** Cardiorenal syndrome and cellular therapeutic perspectives: risk factor identification for targeted interventions. *Chisinau, Republic of Moldova.*
26. **Brinza Ion, Guliev Corina A., Oresanya Ibukun Oluwabukola, Gok Hasya Nazli, Iorhan Ilkay Erdogan, Hritcu Lucian.** Neuroprotective effects of ethanolic extracts from *solanum macrocarpon* in a zebrafish model of scopolamine-induced Alzheimer's disease-related dementia. *Sibiu, Romania, Ankara, Türkiye, Iasi,Romania.*
27. **Bulicanu Adelia, Cemortan Igor.** Regenerative approaches for epidermolysis bullosa: tissue engineering and gene therapy. *Chisinau, Republic of Moldova.*
28. **Craciun Ana, Zorina Zinovia, Babuci Angela, Bendelic Anastasia.** Peculiarities of the perineum in morphoclinical aspect. *Chisinau, Republic of Moldova*.
29. **Babuci Angela, Paz Eli, Zorina Zinovia, Stratulat Silvia, Lehtman Sofia, Calancea Sergiu.** Biomaterials and nanotechnology in dental osseointegration. *Chisinau, Republic of Moldova.*
30. **Botnaru Doina, Zorina Zinovia, Babuci Angela, Catereniuc Ilia, Botnari Tatiana.** Anatomical variability of the deep femoral artery. *Chisinau, Republic of Moldova.*
31. **Botnari Tatiana, Babuci Angela, Zorina Zinovia, Catereniuc Ilia, Botnaru Doina, Ostahi Nadia.** Variability of the paired visceral branches of the abdominal aorta. *Chisinau, Republic of Moldova.*
32. **Zorina Zinovia, Babuci Angela, Calancea Sergiu, Bendelic Anastasia, Botnari Tatiana, Botnaru Doina, Ostahi Nadia.** Anatomical variants of the deep brachial artery. *Chisinau, Republic of Moldova.*
33. **Goras Valeria, Tanase Adrian.** Regenerative approaches for managing percutaneous nephrostomy complications: stem cell and tissue engineering strategies. *Chisinau, Republic of Moldova.*
34. **Sirbu Mariana, Bologan Alina.** Stem cell transplantation in bipolar disorder: exploring regenerative treatment approaches. *Chisinau, Republic of Moldova*.
35. **Purteanu Lilia, Pîntea Dumitrita, Grejdieru Alexandra, Tonofa Marina, Slonovschi Tamara, Ciobanu Gabriela, Matcovschi Laur.** Renal transplant to a patient with type 2 cardiorenal syndrome who is on hemodialysis: clinical and prognostic factors to think about. *Chisinau, Republic of Moldova.*
36. **Andreea Casian, Veronica Sardari, Stratulat Silvia, Roman Munteanu, Cojoc Daniela, Tagadiuc Olga.** Telomere shortening as a mechanism for the induction of neurodegenetative diseases. *Chisinau, Republic of Moldova.*
37. **Cojoc Daniela, Sardari Veronica, Munteanu Roman, Stratulat Silvia, Pantea Valeriana, Tagadiuc Olga.** The influence of calcitriol on the Warburg effect in cancer. *Chisinau, Republic of Moldova.*

38. **Condrea Daniela, Protopop Svetlana.** The influence of vitamin D on metabolic syndrome. *Chisinau, Republic of Moldova.*
39. **Zavtoni Mariana, Miron Inga, Bernic Vladimir, Coretchi Roman.** Endocrine disruptors-a current problem for the human body. *Chisinau, Republic of Moldova*.
40. **Hotineanu Adriana, Burgoci Sergiu.** Liver transplantation for hepatocellular carcinoma. *Chisinau, Republic of Moldova.*
41. **Cojoc Daniela, Sardari Veronica, Tagadiuc Olga.** Role of vitamin d in the wnt/β-catenin signaling pathway. *Chisinau, Republic of Moldova.*
42. **Marcu Beatrice, Sardari Veronica, Tagadiuc Olga.** Regenerative medicine in liver diseases and cellular mechanisms of liver regeneration and cell-based therapies. *Chisinau, Republic of Moldova.*
43. **Capros Hristiana, Dondiuc Iurie, Surguci Mihai, Bologan Ion, Potacevschi Oleg. Isolation of mesenchymal stem cells from Wharton's Jelly. *Chisinau, Republic of Moldova.***
44. **Casian Andreea, Sardari Veronica.** Mitochondrial calcium regulation in Alzheimer`s disease. *Chisinau, Republic of Moldova.*
45. **Ciobanu Gabriela, Grib Livi.** Human-induced pluripotent stem cell-derived atrial cardiomyocytes: a model for atrial fibrillation research and therapy. *Chisinau, Republic of Moldova.*
46. **Colibaba Vasile, Sardari Veronica, Munteanu Roman, Ciprian Rudic.** Cancer stem cells and tumor microenvironment: implications for therapy resistance and novel strategies. *Chisinau, Republic of Moldova.*
47. **Repciuc Ana, Constantin Taralunga, Sardari Veronica.** Obesity in postmenopausal osteoporosis. *Chisinau, Republic of Moldova.*
48. **Constantin Taralunga, Roman Munteanu, Ana Repciuc, Sardari Veronica.** The implications of autophagy in Crohn's disease. *Chisinau, Republic of Moldova.*
49. **Grusac Evgheni, Tagadiuc Olga, Munteanu Roman, Pantea Valeriana, Sardari Veronica.** The role of glycation on transplantology methods in cancer treatment. *Chisinau, Republic of Moldova.*
50. **Ghinda Daniela, Sardari Veronica, Cojoc Daniela.** The role of glycation processes in aging. *Chisinau, Republic of Moldova.*
51. **Cozma Octavian, Tonofa Maria, Timercan Tatiana.** The prospects of selective JAK inhibitors in hematopoietic stem cells transplantation. *Chisinau, Republic of Moldova*.
52. **Cobileanschii Eugeniu, Cobileanscaia Liubov.** The capacity of hepatic henodynamics in the nutritional assurance of hepatocytes in the elderly. *Chisinau, Republic of Moldova.*

Session 2
Oral presentations

Moderators: Labusca Luminita, *MD, PhD (Romania);* Babuci Angela, *MD, PhD (Republic of Moldova).*

1. 09:00-09:30. Labusca Luminita. Novel therapies in osteoarthritis current status and perspectives. *Iasi, Romania.*

2. 09:45-10:00. Babuci Angela, Zorina Zinovia, Bendelic Anastasia, Ostahi Nadia, Botnari Tatiana, Botnaru Doina, Lehtman Sofia, Motelica Gabriela, Nastas Liliana, Calancea Sergiu. Specific features of the facial nerve trunk. *Chisinau, Republic of Moldova.*

3. 10:00-10:15. Braniste Tudor, Vlad Ciobanu, Ion Tighineanu, Three-dimensional nanoarchitectures based on semiconductor compounds for biomedical applications. *Tehnical University, Chisinau, Republic of Moldova.*

4. 10:15-10:30. Cusnir Valeriu, Dumbraveanu Lilia, Lupan Valentina, Cociug Adrian, Procopciuc Vitalie, Cusnir Valeriu V., Balba Rodica, Bostan Mihaela, Nacu Viorel. Deficiency in the treatment of ocular surface diseases. *Chisinau, Republic of Moldova.*

5. 10:30-10:45. Ostahi Nadia, Catereniuc Ilia, Babuci Angela, Bendelic Anastasia, Zorina Zinovia. Anatomical variants of the common carotid artery. *Chisinau, Republic of Moldova.*

6. 10:45-11:00. Brinza Dumitru. Correlation between CD45 expression and clinical-pathological variables in invasive ductal breast carcinoma associated with type 2 diabetes mellitus. *Chisinau, Republic of Moldova.*

7. 11:15-11:30. Cociug Adrian, Macagonova Olga, Dumbraveanu Lilia, Cusnir Valeriu, Viorel Nacu. Regarding corneal preparation in the Human Tissue Bank of the Republic of Moldova, during 11 years of activity. *Chisinau, Republic of Moldova.*

8. 11:30-11:45. Cornea Cornelia, Ceban Emil, Rotaru Larisa, Groppa Liliana, Sasu Boris, Tagadiuc Olga, Romanciuc Grigore, Timbalari Tatiana, Buga Diana, Nacu Viorel. The impact of renal transplantation in the patient with renal pathology and gout. *Chisinau, Republic of Moldova*

11:20 CONFERENCE CLOSING CEREMONY

Abstracts

NOVEL THERAPIES IN OSTEOARTHRITIS CURRENT STATUS AND PERSPECTIVES

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[2]National Institute of Research and development in Technical Physics, Iasi, Romania.

Osteoarthritis (OA) remains a major contributor to disability worldwide, placing a significant burden on healthcare systems. Current treatment strategies predominantly focus on symptom management rather than halting or reversing disease progression, highlighting an urgent need for disease-modifying interventions. Recent advancements in drug discovery and regenerative medicine have increasingly shifted toward targeted OA therapies aimed at preventing, mitigating, and even reversing degenerative structural changes within the joint.

Among emerging regenerative approaches, orthobiologics such as platelet-rich plasma (PRP), bone marrow concentrate (BMC), and micro/nano-fractionated adipose tissue have demonstrated potential in enhancing joint repair and improving clinical outcomes. Additionally, several advanced therapy medicinal products (ATMPs) addressing cartilage defects have received regulatory approval in Europe, offering novel therapeutic avenues for OA management.

This presentation provides a critical analysis of the evolving OA treatment landscape, emphasizing the role of orthobiologics and ATMPs in disease prevention and structural repair. Furthermore, it explores the regulatory status, economic impact, and accessibility challenges associated with these advanced therapies within the European healthcare framework, highlighting opportunities for optimizing their clinical integration.

TISSUE AND CELLS TRANSPLANTATION IN THE REPUBLIC OF MOLDOVA, TRENDLINES

Nacu Viorel[1], Stepa Serghei[2], Cospormac Igor[2], Cociug Adrian[1], Cobzac Vitalie[1], Gutu-Bahov Cornelia[3], Tambalari Tatiana[4]

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The development of tissue transplantation in the Republic of Moldova began in the 1960s with the use of bone grafts. This laid the foundation for the establishment of national infrastructure for tissue preservation and transplantation. In 1962, a significant milestone was reached with the founding of the Tissue Preservation Laboratory. Over the following decades, Moldova advanced in the field through local innovation, scientific research, and institutional development. The creation of the Human Tissue and Cell Bank (HTCB) in 2011 marked a new era in the country's capacity to collect, process, preserve, and distribute various types of human tissues and cells. This article reviews the historical background, scientific contributions, and medical milestones that shaped the evolution of tissue banking in Moldova.

1. Introduction

Tissue transplantation is a critical component of modern medicine, aiding in the treatment of various degenerative, traumatic, and pathological conditions. In the Republic of Moldova, this field has undergone substantial development since the 1960s. The following article aims to present a chronological and thematic analysis of this evolution, focusing on key institutional developments and scientific contributions that led to the establishment of the Human Tissue and Cell Bank.

2. Historical Background

Bone grafts were initially imported from orthopedic centers in Kiev, Kharkiv, and Moscow, and were primarily used for the reconstruction of bone defects caused by dysplastic, tumoral, or post-traumatic conditions. The domestic preservation and preparation of such grafts began in 1962, with the founding of the Tissue Preservation Laboratory within the Republican Blood Transfusion Station, initiated by Professors L. Gladârevaschii and N. Testemițanu. This establishment operated under Ministry of Health Order no. 46 from 28.02.1962 and was relocated in 1966 to the Clinical Hospital of Traumatology and Orthopedics.

3. Institutional Leadership and Development

The Tissue Preservation Laboratory was led by *Igor Ivanenco* from 1962 to 1992, followed by Dr. Ion Baciu from 1993 to 2011. During this period, the lab contributed significantly to the field of tissue grafting and preservation.

The evolution of tissue banking reached a new level in 2011 with the directive from the Ministry of Health to establish the Human Tissue and Cell Bank (HTCB) within IMSP SCTO. The project was led by Professor Viorel Nacu, Ph.D. The HTCB was housed in the Republican Combustion Center and designed to include specialized units such as reception, processing, clean rooms, storage, and distribution. The facility was equipped to handle a wide array of graft types, including skeletal tissues, corneas, skin, amniotic membrane, and autologous bone marrow cells.

4. Milestones and Achievements

Since its formal establishment, the HTCB has achieved several significant milestones:

March 22, 2013: First allogeneic cornea harvesting at IMSP „St. Trinity".

March 27, 2013: First corneal transplant using HTCB-sourced tissue.

March 28, 2013: Official inauguration of the Human Tissue and Cell Bank.

September 4, 2013: First allogeneic skin harvesting, preserved in 80%

Glycerin.

October 3, 2013: First allogeneic skin transplant, treating a 58-year-old patient with 10% skin defects.

Conclusion

The Human Tissue and Cell Bank in Moldova represents a significant advancement in national healthcare infrastructure. It not only serves as a storage facility but also plays a crucial role in the processing, preservation, and distribution of various human tissues. Moving forward, it is essential to maintain adequate funding, state-of-the-art equipment, and alignment with European Union and national public health standards to ensure its continued success and expansion.

Keywords: Human Tissue and Cell Bank, Allogeneic Grafts, Tissue Preservation, Moldova, Medical Innovation

BIOMATERIALS AND NANOTECHNOLOGY IN DENTAL OSSEOINTEGRATION

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[1]Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.
[2]Light Dental Clinic, Bucharest, Romania.

Introduction: The osseointegration is a process of bone ingrowth into the surface of a load-carrying implant. Due to its low elastic modulus, excellent biocompatibility and resistance to corrosion, titanium is the most applicable material in dental implantology. The dental tissue is characterized by continuous demineralization and remineralization processes. As a bone-specific non-collagen, modular extracellular matrix protein, the osteonectin has selective properties to bind to insolubilized type I collagen and hydroxyapatite, initiating bone mineralization. It also influences the osteoblasts differentiation, maturation and survival, regulating cells behavior and new bone formation. Our goal was to identify the most suitable materials for a successful osseointegration.
Materials and Methods: A systematic review of 57 articles, published in the past 10 years within PubMed, Web of Science, Scopus and Google Scholar databases, supplying information about morphology of dental implants osseointegration, was conducted.
Results: According to the reported data, for a better osseointegration the implants are coated with various bioactive molecules and inorganic elements such as: nanodots, nanorods and nanotubes, which increase the cell adhesion and osteogenic differentiation. It was determined that microtopography of the implant leads to induction of the extracellular mechanical signals and their transformation into intracellular biochemical signals. The Wnt/β catenin signaling pathway plays an important role in osteogenic differentiation, induced by ordered-micro and disordered-nano patterned structures. The micro-patterned structures influence on geometry, aspect ratio, alignment morphology and behavior of the mesenchymal stem cell (MSCs). Variation of cell morphology can be a trigger mechanism in rearrangement of cytoskeleton, inducing its mechanical stimulation. Mechanotransduction has an important role in micromorphology of the induced osteogenesis, with a remodeling action on actin cytoskeleton, caused by microtopography signal, though the mechanotransductive pathways, determining the osteogenic differentiation of the (MSCs) into osteoblasts and osteocytes, ensuring deposition of the collagen matrix and formation of a new bone.
Conclusion: The osseointegration process can be influenced by external coating of the implant surface with nanoparticles, the microtopography of the implant playing a significant role in osseointegration. The micromorphology and remodeling action on the actin cytoskeleton, can be influenced by mechanotransduction, triggering the osteogenic differentiation of the (MSCs).
Keywords: osseointegration, new bone, dental implant, nanoparticles, mesenchymal stem cells

ANTIMICROBIAL RESISTANCE OF UROPATHOGENS AFTER KIDNEY TRANSPLANTATION

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[1]*Timofei Mosneaga* Republican Clinical Hospital, Chisinau, Republic of Moldova.
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Introduction. Antibiotic resistance, particularly among gram-negative pathogens, has become a growing challenge in clinical practice. In kidney transplant recipients, the management of infections is particularly complex due to immunosuppression, increased morbidity and mortality, and the necessity of using nephrotoxic antibiotics. The concomitant administration of calcineurin inhibitors further heightens the risk of nephrotoxicity, limiting therapeutic options. This study aims to assess the antimicrobial resistance patterns of bacterial uropathogens isolated from kidney transplant recipients, providing evidence to guide the rational selection of antibacterial therapy in this vulnerable population.
Materials and methods. This retrospective study was performed based on reviewing electronic medical records of renal transplant recipients from Republican Clinical Hospital *T. Mosneaga*, between January 1, 2020 and January 1, 2025. Urine bacteriologic examination data on the sensitivity of urinary bacteria to antibiotics were analyzed. Antimicrobial susceptibility testing was performed using the disk diffusion method according to the EUCAST guidelines.
Results. According to electronic databases (SIA AMS) 71 hospital admissions among patients who receive kidney transplant were identified, with 59 episodes of culture-proven urinary tract infection. The uropathogens were *Klebsiella pneumoniae (25)*, *Escherichia coli (15)*, followed by *Enterococcus* sp. (6), *Enterobacter cloacae* (6), *Acinetobacter* sp. (3) *Proteus* sp. (3), and *Pseudomonas aeruginosa (1).* Among the 59 isolates, extended-spectrum β-lactamase (ESBL) *K. pneumoniae* and, *E.coli* showed a high resistance to third-generation cephalosporins, extended-spectrum penicillins, and fluoroquinolones. Most bacteria were sensitive to amikacin (44), meropenem (40), imipenem (36), nitrofurantoin (28), piperacillin/tazobactam (21) fosfomycin (15).
Conclusions. The rising prevalence of multidrug-resistant uropathogens, particularly ESBL-producing *Enterobacterales*, underscores the urgent need for tailored antibiotic selection in kidney transplant recipients. While aminoglycosides, carbapenems, piperacillin/tazobactam, and nitrofurantoin remain viable therapeutic options, their nephrotoxic potential requires close monitoring, especially in the context of concurrent immunosuppressive therapy. Regular monitoring of antibiotic susceptibility patterns and a focused approach to antimicrobial stewardship are key to mitigating the risk of antibiotic resistance in this vulnerable patient population. **Keywords**. Antimicrobial resistance, kidney transplant, nephrotoxicity

BACTERIAL RESISTANCE IN URINARY TRACT INFECTIONS IN KIDNEY TRANSPLANT PATIENTS: LITERATURE REVIEW

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Introduction. Urinary tract infections are the most common complication in renal transplant patients and a major cause of morbidity, hospitalization and mortality. The incidence of urinary tract infections varies widely (7-80%) with a more frequent ratio of 42%-75% depending on the length of patient surveillance. The problem of treating UTIs in kidney transplant patients is becoming more challenging due to the increasing incidence of antibiotic resistance, including the detection of multi-drug resistant (MDR) and extensively drug resistant (XDR) strains: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*. The aim of the present study was to determine effective management strategies according to antimicrobial susceptibility pattern of causative agents among renal transplant recipients.
Materials and methods. A narrative literature search was performed in the Hinari database with source selection for the last 5 years. Keywords used for the search were: Kidney transplantation, Urinary tract infection, Drug resistance, gram-negative bacteria, antibiotics, β-Lactamase inhibitors. Inclusion criteria were: clinical trials, literature reviews accessible in full-text, articles published in English. Exclusion criteria were: articles without full-text version, studies with irrelevant results, case reports, letters to the editor or articles in languages other than English.
Results. In renal transplant patients several studies have reported an increasing detection of gram-negative bacteria (*E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumanni*) producing extended-spectrum β-lactamases (ESBLs) with resistance to almost all penicillins and cephalosporins of I-III generation. Cases of resistance (10-25%) to combinations of penicillins with β-lactamase inhibitors (ampicillin+sulbactam, amoxicillin+clavulanic acid, piperacillin+tazobactam) are currently also reported. The introduction of the new β-lactam/β-lactamase inhibitors (ceftazidime/avibactam, cefepime/taniborbactam, ceftolozane/tazobactam meropenem/vaborbactam, imipenem/relebactam, etc.), carbapenems (doripenem, ertapenem, razupenem etc.), new cephalosporin antibiotic - siderophore (cefiderocol), aminoglycosides (plazomicin), polymyxins (colistin), phosphonic antibiotic (fosfomycin) opens new perspectives in the treatment of urinary tract infections in kidney transplant patients.
Conclusions. The empiric selection of antibiotics in urinary tract infections in renal transplant patients should be based on local resistance data, the degree of manifestation of the infection, individual patient characteristics, type of immunosuppressive therapy and post-transplant period. For a rational antibiotic selection is necessary to study their pharmacokinetic properties (metabolization, elimination pathways) and possible adverse reactions (probability of nephrotoxicity).
Keywords: kidney transplantation, urinary tract infection, drug resistance, gram-negative bacteria, antibiotics, β-lactamase inhibitors.

THE ROLE OF MESENCHYMAL STEM CELL-DERIVED EXTRACELLULAR VESICLES IN CARDIAC REPAIR

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Introduction: Cardiovascular diseases remain the predominant cause of global morbidity and mortality. Traditional treatments, including therapeutical and surgical approaches, primarily address symptoms rather than myocardial tissue regeneration. Mesenchymal stem cells (MSCs) with extracellular vesicles (EVs) emerging as key mediators of their therapeutic effects, are widely used in regenerative medicine. This review aims to comprehensively synthesize existing systematic reviews and meta-analyses on MSC-EVs for cardiac repair.
Materials and Methods: A comprehensive search of PubMed, Scopus, Web of Science, and Embase identified systematic reviews and meta-analyses (2015–2024) evaluating MSC-EV efficacy in preclinical and clinical cardiac repair. A total of 25 references were included in this umbrella review.
Results: Findings show that MSC-EVs exert cardioprotective effects through multiple mechanisms. For instance, they have anti-apoptotic effects by modulating pro-survival signaling pathways, such as PI3K/Akt and ERK. An increased expression of VEGF and other pro-angiogenic factors improved vascularization in infarcted tissue. Furthermore, MSC-EVs regulate inflammatory responses by reducing pro-inflammatory cytokines like TNF-α and IL-6, while promoting anti-inflammatory mediators such as IL-10 and TGF-β. Additionally, MSC-EVs downregulate fibrotic markers, limiting pathological scar formation after myocardial infarction (MI). Despite promising preclinical findings, several limitations must be addressed before clinical application. The standardization of MSC-EV production is crucial, as variability in isolation methods and dosing can impact reproducibility affecting results. Furthermore, the optimal delivery methods, including intravenous, intracoronary, or direct myocardial injection, require further investigation. Lastly, long-term safety remains a concern, as potential risks like immune reactions and off-target effects necessitate additional clinical evaluation.
Conclusion: MSC-EVs represent a prospective area in regenerative medicine, offering a cell-free therapeutic strategy for myocardial repair. Current evidence supports their efficacy in preclinical models, yet clinical translation requires standardized protocols, larger trials, and long-term safety assessments. Future research focused on optimizing biomanufacturing techniques and conducting well-controlled human studies will bring MSC-EV therapy closer to clinical reality.
Keywords: mesenchymal stem cells, extracellular vesicles, cardiovascular diseases, myocardial infarction, regenerative medicine, angiogenesis, immunomodulation.

AUTOTRANSPLANTATION OF THE THYROID GLAND

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Introduction: Thyroid autotransplantation, where thyroid tissue is relocated within the same individual, is utilized in both human and animal models to preserve thyroid function following thyroidectomy, which aims to prevent permanent hypothyroidism by re-establishing thyroid hormone production. While human studies have focused on clinical outcomes, animal models offer insights into the biological mechanisms and optimal conditions for successful graft survival and function.
Materials and Methods: A comprehensive review was performed using studies from PubMed, and Google Scholar. Both human clinical studies and animal research, particularly on rats, were included. Studies were selected based on criteria that assessed the outcomes of thyroid autotransplantation, including thyroid function preservation, graft survival, histological findings, and complication rates. Animal models provided additional data on experimental techniques, while human studies contributed clinical insights into the effectiveness of the procedure.
Results: In a cohort of 180 patients who underwent thyroid autotransplantation, 82% showed preserved thyroid function post-surgery, with normal TSH and thyroid hormone levels. Follow-up at 1 year showed that 75% of patients remained free of hypothyroid symptoms. In animal studies involving 50 rats, thyroid function was successfully preserved in 85% of autotransplantation cases, with serum T3 and T4 levels within normal range after 12 weeks. TSH levels normalized in 90% of the animals. Histological examination of the transplanted tissue revealed that 70% of grafts in humans maintained structural integrity, with intact thyroid follicles and normal cellular architecture. Histological analysis in rats showed that thyroid follicles in autotransplanted tissue retained normal architecture, with active proliferation. The complication rate was relatively low, with graft failure occurring in 5% of patients. There was a 3% incidence of recurrence of goiter. In rats, complications included graft failure (8%) and tissue hyperplasia in 5% of cases, indicating potential long-term risks.
Conclusion: Thyroid autotransplantation has shown promising results in both human and animal models for preserving thyroid function after thyroidectomy. While animal studies indicate high rates of thyroid function preservation and graft survival, human studies confirm these findings but also emphasize the importance of surgical technique, graft vascularization, and patient selection. The integration of animal model data into clinical practice may improve surgical outcomes, although further research, especially long-term studies, is needed to refine techniques and better predict outcomes in humans.

Keywords: thyroid autotransplantation, thyroid function preservation, postoperative.

HUMAN TISSUE DONATION AND TRANSPLANTATION IN THE REPUBLIC OF MOLDOVA

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Introduction: In recent years, human tissue transplantation has gained increasing importance in modern medicine, expanding both in scope and medical applications. Advances in surgical techniques, improvements in tissue preservation, and growing awareness of donation have contributed to a rise in transplant procedures. However, the availability of tissue grafts remains a critical challenge, particularly in countries with developing transplant infrastructures. This study evaluates the progress, trends, and existing barriers in human tissue donation and transplantation in the Republic of Moldova over the past decade (2015–2024), providing insight into the current situation and potential areas for improvement.
Materials and Methods: This prospective study is based on annual reports from the Human Tissue Bank and medical institutions authorized for tissue procurement and transplantation activities.
Results During the reference period, a total of 838 actual tissue donors were identified. Among them, cadaveric tissue donors accounted for 26% (218), with 26% (56) classified as DBD and 74% (162) as DCD, while living donors constituted 74% (620). The donation rate demonstrated a positive trend, reaching 8.8 donors per million population (PMP) in 2024, despite a sharp decline during the COVID-19 pandemic, when the rate dropped to 3.03 donors PMP in 2020. However, this figure remains well below the European benchmark of approximately 40 deceased donors PMP. The family refusal rate has remained high, reaching 62% in recent years.
Throughout the study period, the following tissues were procured: 376 corneas, 188,679 cm^2 of skin, 787 musculoskeletal tissue units, and 128 amniotic membrane grafts. The waiting list for corneal transplantation continues to expand, with an insufficient number of available grafts to meet the growing demand. By the end of 2024, the corneal transplant rate stood at 19.6%, with only one corneal graft available for every two patients in need.
Conclusions: The Republic of Moldova has made progress in human tissue transplantation, with an increasing number of donors, but the donation rate remains below the European benchmark. The shortage of corneal and skin grafts persists, with only one cornea available for every two patients in need. To further improve transplant activity, efforts should focus on raising donor awareness, optimizing procurement processes, and enhancing institutional capacities.
Key words: transplantation, human tissue, tissue donors.

THE EFFECT OF STIMULATING LOCAL IMMUNITY WITH AUTOLOGOUS CELLS IN THE TREATMENT OF TISSUE INFLAMMATORY PROCESS ON THE BODY'S RESISTANCE TO INFECTION

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Introduction. The application of autologous mononuclear cells to the area of inflammatory affected tissue produces the stimulation of certain cytokines with anti-inflammatory properties, the proliferation of cells involved in repair and reconstructive processes, and accelerates the normalization of local and systemic immune status.
Materials and methods. Standard conservative treatment with local application (peritonsillar space) of autologous cells was applied to 32 children with chronic tonsillitis.
Results. Immunohistochemical studies of tonsils (12 children) showed that in the dynamics of treatment the number of preimmune resistance cells CD56+ CD68+ in the germinal center (GC), the peripheral part of the tonsillar lymphoid node, in the crypt and taping epithelium increased significantly. The amount of e-RNA and RLO decreased significantly in the GC. Posttreatment, there was an increase in cellular immunity, which was evidenced by high levels of CD3+ CD4+ CD8+ density in the studied areas. Humoral immunity (lymphocytes CD20 cy+, plasma cells) did not undergo a normalization process, the levels of density of these lymphocytes being low.
Evaluation of the bacteriological profile on the tonsils determined the following bacterial flora: *Staphylococcus aureus* – 56.2%, *β-hemolytic streptococcus* group A – 12.5%, *β-hemolytic streptococcus* group C – 6.5%, *Streptococcus pneumoniae* – 6.3%. After treatment, after 2 months, the predominated flora: *Staphylococcus aureus* – 72.2% of cases, *Streptococcus pneumoniae* – 11%, *β-hemolytic streptococcus* group F – 5%.
After treatment, the levels of allergic and autoimmune reaction indices in general immunity (eosinophils (%), IgE (IU/ml), ANA-combi decreased significantly, a tendency to decrease in ASL-O, PCR and RF was detected, the levels of T-lymphocyte sensitization to streptococcal, staphylococcal, pneumococcal antigens decreased significantly.
Over the course of 2 years, a positive clinical evolution was observed in most children, characterized by a decrease in the number of ARIs and the use of antibiotic therapy.
Conclusions: Local therapy with autologous mononuclear cells has a strong immunostimulatory effect that has a beneficial effect on the elimination of local pathogenic flora and, as a result, normalizes the indices of allergic and autoimmune reactions in the general immune system.
Keywords: immune status, immunohistochemistry, humoral immunity, lymphocytes, autoimmune, autologous mononuclear cells.

REGENERATIVE APPROACHES FOR EPIDERMOLYSIS BULLOSA: TISSUE ENGINEERING AND GENE THERAPY

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Introduction: Epidermolysis bullosa (EB) is a group of rare genetic disorders characterized by skin fragility and blister formation. The current management of EB is mainly symptomatic, with no definitive cure. Recent advancements in tissue engineering and cell therapy have provided promising alternatives: gene-edited keratinocyte transplantation, fibroblast therapy, mesenchymal stem cell (MSC) transplantation, revertant mosaicism-based therapy (RMBT), and induced pluripotent stem cell (iPSC)-based therapy.
Materials and Methods: A literature review of recent preclinical and clinical studies was conducted. The focus was on therapeutic efficacy, safety, and clinical feasibility.
Results: Gene-edited keratinocyte transplantation has shown long-term epidermal regeneration and reduced blister formation, particularly in EB junctional and dystrophic subtypes. These transplants, created through *ex vivo* gene correction, have demonstrated engraftment success rates exceeding 80%, with no major immune rejection reported. Fibroblast therapy improves collagen production and enhances dermal stability, though it doesn't address the genetic cause of EB. MSC therapy demonstrates immunomodulatory effects, promoting tissue repair. Clinical trials report improvements in patient-reported pain and skin elasticity. RMBT utilizes naturally corrected keratinocytes, offering a genetically stable and patient-specific treatment option. iPSC-based therapy presents a novel strategy by reprogramming patient-derived fibroblasts into pluripotent cells, genetically corrected using CRISPR-Cas9 and differentiated into keratinocytes, facilitating autologous grafts with long-term stability. Vyjuvek, the first FDA-approved topical gene therapy for dystrophic EB, delivers functional COL7A1 via a herpes simplex virus (HSV-1) vector, significantly improving wound healing in patients with dystrophic EB. Despite these advances, challenges such as immune compatibility, tumorigenicity, and cost remain key barriers to widespread implementation.
Conclusion: Cellular therapies represent a significant advancement in the management of EB, with gene-edited keratinocytes and iPSC-based approaches holding the most potential for long-term disease correction. Fibroblast and MSC therapies provide supportive benefits in wound healing and inflammation control. Further clinical trials and optimization of these strategies are required to enhance accessibility and long-term safety.
Keywords: Epidermolysis bullosa, gene therapy, cell therapy, keratinocyte transplantation, MSC, iPSC, Vyjuvek.

ISOLATION OF MESENCHYMAL STEM CELLS FROM WHARTON'S JELLY

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Introduction: Mesenchymal stem cells (MSCs) derived from Wharton's jelly of the umbilical cord are increasingly recognized for their potential in regenerative medicine. These cells offer significant advantages, including high proliferative capacity, multipotent differentiation, and immunomodulatory properties. Due to their accessibility and low risk of immunological rejection, they are considered a valuable resource for various therapeutic applications.
Methods: The collection of umbilical cords is performed under sterile conditions, followed by the isolation of MSCs using two primary techniques. The first, the direct explantation method, involves sectioning the umbilical cord into small fragments, removing the blood vessels, and placing them in culture plates with a medium (DMEM/F-12) supplemented with fetal bovine serum (FBS). The fragments are incubated at 37°C in a 5% CO_2 atmosphere for 7-14 days, allowing the cells to migrate from the tissue and adhere to the culture surface. The second technique, enzymatic digestion, involves incubating Wharton's jelly fragments with collagenase type I and/or trypsin for 30-60 minutes at 37°C with gentle agitation. After digestion, fetal bovine serum is added to stop the enzymatic process, and the cell suspension is centrifuged. The cells are then resuspended in DMEM/F-12 medium with FBS and growth factors and cultured under standard conditions. **Results:** The MSCs obtained from Wharton's jelly exhibit high proliferative potential and the ability to differentiate into osteoblasts, chondrocytes, and adipocytes. These cells also display immunomodulatory properties, making them suitable candidates for applications in autoimmune disease treatment, tissue regeneration, and advanced cell therapy. **Conclusion:** Wharton's jelly-derived MSCs present a promising alternative for regenerative medicine, offering a favorable safety profile and versatile therapeutic applications. The optimization of isolation and characterization protocols is crucial for their successful integration into clinical protocols, advancing the field of regenerative therapies.

URINARY TRACT INFECTIONS TREATMENT IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction. Kidney transplantation remains the treatment of choice for patients with end-stage renal disease. Urinary tract infection in kidney transplant recipients is the most frequent and considered a potential cause of bacteremia, sepsis, and graft rejection. The purpose of this study was to determine its causative agents, and antimicrobial resistance pattern among renal transplant recipients in a transplant center, to appreciate the rational selection of antibacterial treatment.
Materials and Methods: Using the information system (SIA AMS), patients undergoing renal transplant surgery in the Hemodialysis and Renal Transplant Center of the *Timofei Mosneaga* Republican Clinical Hospital during 2017-2024 were identified. Data on hospitalization due to urinary tract infection were selected with subsequent evaluation from the observation records of bacteriologic investigations and antibacterial treatment**.**
Results: According to the data obtained, 32 patients underwent renal transplantation and 13 were readmitted with urinary tract infection. The pathogens identified in the urine were gram-negative and antibacterial treatment was selected according to sensitivity: *E. Coli* (8)-amoxicillin/clavulanic acid (1), piperacillin/tazobactam (2), ceftazidim (1), cefoperazone/sulbactam (1), meropenem (3); *E. Faecalis* (1)-amoxicillin/clavulanic acid (1), *K. Pneumoniae* (4)-cefotaxime (1), sulfametho-xazole/trimethoprim (1), imipenem/cilastatin (2). The dosing regimen was adjusted according to renal function and the duration of administration ranged from 7 to 14 days.
Conclusions: The high resistance of Enterobacteriaceae bacteria has led to the use of antibiotics from the WHO watch group-carbapenems (imipenem, meropenem), generation III cephalosporins (cefotaxime, ceftazidim), antipseudomonas penicillins with beta-lactamase inhibitors (piperacillin/tazobactam). Drug selection and dosing regimen requires assessment of bacterial sensitivity, renal function, associated pathologies of the patient to provide clinical and bacteriologic improvement, considering the role of urinary tract infections in graft failure and rejection.
Key words: urinary tract infection, kidney transplant, antibacterial medication, bacterial resistance.

THERAPEUTIC DRUG MONITORING OF TACROLIMUS IN RENAL TRANSPLANT RECIPIENTS

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Introduction. Tacrolimus, the calcineurin inhibitor has been the cornerstone of immunosuppression following renal transplantation for the last 10–15 years. The narrow therapeutic index and large pharmacokinetic interindividual and intraindividual variability makes therapeutic drug monitoring (TDM) of tacrolimus mandatory. The purpose of the study was to focus on tacrolimus pharmacokinetics, pharmacodynamics, and toxicity profiles to highlight the importance of TDM for post-transplant management.
Material and methods. A narrative literature search was performed in the Hinari database with source selection for the last 5 years. Keywords used for the search were: *tacrolimus pharmacokinetics, TDM of tacrolimus, tacrolimus in renal transplantation*. Inclusion criteria were: clinical trials, literature reviews accessible in full-text, articles published in English. Exclusion criteria were: articles without full-text version, studies with irrelevant results, case reports, letters to the editor or articles in languages other than English. Out of 129 articles found, 39 articles were included in the study after reviewing the title, abstract, inclusion and exclusion criteria.
Results: Therapeutic doses of tacrolimus are adjusted by monitoring the morning whole blood trough concentrations. Achieving trough levels of 7–12 ng/mL (preferably to > 7 ng/ml, following the second consensus report in 2019) early post-transplant reduces the risk of acute rejection compared to trough levels of 4–7 ng/mL (2009 European consensus conference), while levels between 5.35 and 7.15 ng/mL manage to balance acute rejection prevention and infection risk. These data highlight the importance of personalized therapeutic drug monitoring (TDM) for optimal transplant outcomes. Pharmacokinetic variability of tacrolimus may be caused by variable absorption, low bioavailability, increased risk of drug interactions, liver and renal function, genetic polymorphisms. The side effects of tacrolimus-nephrotoxicity, neurotoxicity, cardiotoxicity, metabolic disturbances, infections can be prevented by monitoring and adjusting the dose as needed.
Conclusion. Tacrolimus is essential immunosuppressive agents for preventing organ rejection in kidney transplant patients, but its use is associated with significant variability in response that requires careful management, including TDM and pharmacogenomics, avoiding drug interactions, proper dosage regimen. Therapeutic drug monitoring guides healthcare providers to achieve therapeutic efficacy (prevention of graft rejection), and limit potential dose-dependent toxicities.
Key words. tacrolimus pharmacokinetics, TDM of tacrolimus, tacrolimus in renal transplantation.

LIVER TRANSPLANTATION FROM A BRAIN-DEAD DONOR

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Introduction: Liver transplantation from a brain-dead donor is a vital procedure, often the only solution for patients with terminal liver diseases. Evaluating its outcomes will involve analyzing demographic data, postoperative results, and medical indications for transplantation.

Material and Methods. A retrospective analysis was conducted on 21 medical records of patients aged 38–61 years who underwent liver transplantation in the Republic of Moldova between August 2017 and February 2024. Data on medical indications, postoperative outcomes, and complications were collected, using standard selection criteria. Descriptive statistical analysis was applied.

Results. Of the 21 patients, 12 were men (57.1%) and 9 were women (42.9%), with ages ranging from 38 to 61 years. The indications for transplant were: viral hepatitis B and D-related cirrhosis—10 patients (47.6%), hepatocellular carcinoma—6 patients (28.6%), chronic liver graft rejection—2 patients (9.5%), mi
xed viral hepatitis C and metabolic cirrhosis—1 patient (4.8%), and viral hepatitis B-related cirrhosis—1 patient (4.8%). Postoperative recovery was achieved in 17 patients (81%), of whom 11 were men (64.7%) and 6 were women (35.3%). Postoperative complications included chronic rejection (1 case, resolved through reintervention) and postoperative mortality, recorded in 4 patients (19%)—3 women and 1 man. Mortality was associated with severe complications, including sepsis and multiple organ dysfunction syndrome.

Conclusions. Liver transplantation from brain-dead donors has an 81% success rate but a 19% mortality rate, highlighting the need for better patient selection and postoperative care.

Keywords.liver transplant, brain death, donor, complications.

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN MYASTHENIA GRAVIS

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Background. Myasthenia gravis (MG) is a rare neurological disease, autoimmune-mediated, which targets the neuromuscular junction, involving the acetylcholine receptors on the motor endplate. We aimed to evaluate the safety, efficacy of autologous hematopoietic cell transplantation (HCT) in patients with severe, refractory myasthenia gravis who are resistant to conventional therapies.
Material and Methods. Have been selected and analyzed 16 articles from PubMed, NCBI, Google Scholar, as well as medical books, scientific journals published in the 2018-2024 period. **Results**. Some patients with myasthenia gravis do not respond to standard treatments and experience severe or life-threatening symptoms. Autologous hematopoietic stem cell transplant has shown promise in treating other serious autoimmune neurological disorders and may offer similar benefits for MG. The procedure of autologous HCT includes intensive conditioning chemotherapy regimens to destroy the autoreactive immune system followed by graft reinfusion for blood and immune reconstitution. A retrospective cohort study at The Ottawa Hospital, reports the results of 7 cases of severe MG treated with autologous HCT. Five patients (71%) were diagnosed with concomitant autoimmune or lymphoproliferative diseases related to immune dysregulation. All patients achieved complete stable remission with no residual MG symptoms and freedom from any ongoing MG therapy. Three patients (43%) experienced transient viral reactivations and 1 (14%) developed a secondary autoimmune disease after autologous HCT, all of which resolved or stabilized with treatment. Improvement was first noted within days after autologous HCT and the patients status progressively improved in subsequent months. Abnormal decremental response on repetitive nerve stimulation testing resolved 30 days after transplant. There were no treatment- or MG-related deaths.
Conclusion. Autologous hematopoietic stem cell transplantation shows potential as an effective treatment for patients with MG, it may bring significant improvements in disease control and may reduce the need for long-term immunosuppressive medications.
Keywords: myasthenia gravis, autoimmune neurological disorders, stem cell transplant.

HUMAN-INDUCED PLURIPOTENT STEM CELL-DERIVED ATRIAL CARDIOMYOCYTES: A MODEL FOR ATRIAL FIBRILLATION RESEARCH AND THERAPY

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Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting over 33 million individuals worldwide. Despite extensive research, current AF treatment options are limited by high recurrence rates, adverse effects, and variability in pathophysiology. Human-induced pluripotent stem cell-derived atrial cardiomyocytes (hiPSC-aCMs) offer a promising in vitro model for studying AF, drug screening, and personalized therapy.
Materials and Methods: The differentiation of hiPSCs into atrial cardiomyocytes involves the manipulation of signaling pathways such as Wnt, retinoic acid, and bone morphogenetic proteins. Techniques including electrical stimulation, metabolic modifications, and three-dimensional (3D) tissue engineering have been employed to enhance hiPSC-aCM maturation. Additionally, CRISPR/Cas9 gene editing and electrophysiological assessments have been utilized to refine AF models and investigate patient-specific mutations.
Results: Studies have demonstrated that hiPSC-aCMs recapitulate key electrophysiological and structural characteristics of atrial cardiomyocytes. Patient-specific hiPSC-aCMs have been used to model familial AF and investigate the impact of ion channel mutations. Furthermore, pharmacological assessments using atrial-selective drugs, such as IKur and If channel inhibitors, have validated hiPSC-aCMs as a robust platform for drug screening. In disease modeling, optogenetic pacing has been used to induce AF-like remodeling, revealing novel insights into AF pathophysiology.
Conclusions: The development of hiPSC-aCMs represents a significant advancement in AF research, providing a scalable and patient-specific model for studying disease mechanisms, drug efficacy, and toxicity. Despite the challenges of achieving full cellular maturation, continued optimization of culture conditions and gene-editing technologies holds promise for refining AF models. Ultimately, hiPSC-aCMs offer a transformative approach to personalized medicine, enabling the development of targeted therapies and regenerative strategies for AF treatment.
Keywords: Atrial fibrillation, human-induced pluripotent stem cells, atrial cardiomyocytes, disease modeling, pharmacological testing, personalized medicine.

CONTROLLED RELEASE OF ACTIVE SUBSTANCE AFTER DOUBLE LOADING OF DEMINERALIZED CANCELLOUS BONE

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Introduction. Demineralized bone graft (DBG) preparation involves substantial growth factor loss due to prolonged liquid exposure during demineralization, marrow and fat removal, and pH restoration. Albumins bind various endogenous substances and drugs in blood, and their incorporation into demineralized bone enhances regeneration. This study investigates the controlled release of biologically active substances from primary DBM loading after secondary bovine serum albumin (BSA) impregnation.
Materials and methods: Demineralized cancellous bone was obtained from bovine iliac bone using 0.5 M HCl and processed per Human Tissue Bank protocols. To assess controlled release, primary coating was performed using Methylene Blue (MB) 10X solution (BioGnost, Croatia). Thirteen DBG samples were vacuumed at 400 mBar, then immersed in 150 ml of 325 µg/ml MB. Four groups were established based on secondary loading: (1) Positive control (MB+dH2O), (2) MB+10%BSA, (3) MB+20%BSA, and (4) Negative control (MB only). DBG weights did not significantly differ across groups ($p > 0.2$). After secondary vacuum loading with BSA, samples were frozen at -80°C and freeze-dried. MB release was assessed during 33 days by spectrophotometry at 570 nm (BioTek Instruments, USA).
Results and Conclusions. The MB release differed significantly ($p<0.05$) between control groups from 4 hours to day 8, with higher release in the negative control. After this period, no significant difference was observed ($p>0.05$). Compared to the positive control, MB release in experimental groups did not differ within the first 6 hours (MB+10%BSA) or 21 hours (MB+20%BSA) ($p>0.05$). However, from this point until day 6, MB release was significantly higher in the positive control ($p<0.05$) before declining ($p>0.05$). MB release in the negative control was significantly higher than in experimental groups for the first 11 days ($p<0.05$), with no significant differences observed across groups from day 11 to day 33 ($p>0.05$) (Fig. 1).
Keywords: controlled release, active substance, double loading, demineralized cancellous bone.
Acknowledgements: research founded by young researchers project #24.80012.8007.02TC.

REGARDING CORNEAL PREPARATION IN THE HUMAN TISSUE BANK OF THE REPUBLIC OF MOLDOVA, DURING 11 YEARS OF ACTIVITY

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Introduction. The cornea is the tissue of the human eye that improves the quality of the image formed on the retina. The quality of corneal tissue can be influenced by several factors inherent to the recipient, the donor, the donation and transplantation process. Donated corneal tissue can be classified according to its quality as for transplantation with optical and tectonic purposes evaluated macro and microscopically. The corneal quality classification, assigned by the Human Tissue Bank following the assessments, took into account 13 criteria: senile arcade, scars, epithelial defect, epithelial exposure, stromal infiltrate, subepithelial opacity, pterygium, Descemet folds, stromal edema, stromal reflex, stromal, stromal and gutstrial reflex. cell loss. The ophthalmological criteria used were chosen by the Pan American Association of Eye Banks, the Association of American and European Eye Banks. Purpose of the work. The study conducted presents the challenges in evaluating the sampling, processing and validation of corneas in the Human Tissue and Cell Bank for the 12-year period 2013 - 2024 on 470 corneas.
Material and Methods. We examined 264 donors (69.8% male, 30.2% female), with a mean donor age of 59.4 years (SD 18.3 years) and between 18 and 91 years. Donors were from forensic medicine (23.5%), public hospitals (67.6%), and multi-organ donors (7.1%). The most common causes of donor deaths were cardiovascular disease, trauma, and cerebrovascular disease.
Results. Corneal failure was in 25.4% of cases, of which serological infections (HBsAg-positive, HCV-positive, HIV/AIDS) - 15%, and biological contamination occurred in 6.8% of all donor corneas and 1% cases with hemolysis. In total (470 corneas), 74.6% of the processed corneal tissue was used for optical corneal transplantation (74.8% for penetrating keratoplasty, 2.1% for lamellar keratoplasty and 1.3% for unspecified transplants) and 25.4% (101 corneas) were destroyed as waste.
Conclusion. The best quality of the cornea is that taken up to 10 hours that defined the endothelial cell density being 2800 cells / mm2, with moderate signs of polymegetism, cellular pleomorphism, being considered as indications for transfixing keratoplasty with optical purpose.
Keywords: transfixing keratoplasty, polymegetism, cellular pleomorphism.

BONE GRAFT USE IN INTERNAL FIXATION OF PROXIMAL AND DIAPHYSEAL HUMERAL FRACTURES AND PSEUDOARTHROSIS

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Introduction: This study explores the use of bone graft in combination with internal fixation for treating fractures and pseudarthrosis of the proximal and diaphyseal humerus.
Materials and Methods: We retrospectively analyzed data collected for proximal and diaphyseal humerus fractures between 2020-2024. The analysis focused on cases treated with open reduction and internal fixation (ORIF), with or without bone graft utilization.
Results: Out of 584 cases analyzed, 65 (8.9%) were diagnosed with pseudarthrosis. In 12 cases post ORIF treatment with implant stability of diaphyseal segment were applied mononuclear stem cell apheresis (1.6%), and ORIF with T-plates or LCP for Neer 3-4 part fractures in 5 cases (0.6%) and humeral diaphysis fractures in 13 cases (1.8%). Bone graft(alo-auto) was used in 35 (4.8%) pseudarthrosis cases. 349 cases (47.6%) were extremity superior humerus fractures treated with ORIF using T-plates or LCP for Neer 2-parts fractures in 92 cases (12.5%), Neer 3-4 parts fractures in 229 cases (31.2%), and Neer 3-4 parts fractures with diaphyseal extension in 22 cases (3.0%). Bone graft was used in 6 (0.8%) of these cases. 170 cases (23.2%) were diaphysis humerus fractures treated with ORIF using T-plates or LCP in the proximal 1/3 in 5 cases (0.7%), the middle 1/3 in 157 cases (21.4%), and the distal 1/3 in 7 cases (1%). Bone graft was used in 1 (0.1%) of these cases.
Conclusions: The use of bone graft is frequent in the treatment of proximal and diaphyseal humerus pseudarthrosis. Internal fixation with plates remains an essential method in managing these fracture types. This has implications for future research in bone healing and fracture management.
Keywords: humeral fracture, pseudarthrosis, bone graft, internal fixation.

THE ROLE OF miR-152-5p IN RENAL TRANSPLANTATION

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Introduction. miR-152-5p is a microRNA involved in the regulation of gene expression at the post-transcriptional level, primarily expressed in hematopoietic cells. It impacts the regulation of genes involved in T cells and macrophage activation, making it an important biomarker for monitoring transplant rejection. In the context of kidney transplantation, it plays a significant role in modulating the immune response, preventing allograft rejection, and slowing the progression of chronic lesions such as fibrosis or chronic allograft nephropathy.
Materials and Methods. A literature review was conducted using PubMed, BioMed Central and the Cochrane Library, alongside the analysis of international publications.
Results. Recent studies have demonstrated that by inhibiting DNMT1 (DNA methyltransferase 1), miR-152-5p blocks T cell activation and reduces the production of pro-inflammatory cytokines associated with acute allograft rejection (IL-6, TNF-α). Additionally, by inhibiting pro-apoptotic genes (BIM, CASP3), it protects renal cells from apoptosis. miR-152-5p has also been shown to provide protection against fibrosis and chronic renal lesions by suppressing the expression of TGF-β1, a key mediator of tubulointerstitial fibrosis and chronic allograft nephropathy. Low levels of miR-152-5p in blood, urine, or renal biopsies have been identified in patients with progressive renal fibrosis and impaired kidney function, and it has ben associated with a high risk of chronic allograft rejection. Furthermore, miR-152 mitigates oxidative stress and inflammation by inhibiting reactive oxygen species and reducing NF-kB expression, providing protection against ischemia-reperfusion injury. Moreover, the use of miR-152-5p mimetics can reduce inflammation and fibrosis in the renal allograft, while combined therapies with immunosuppressants such as tacrolimus or mycophenolate allow for dose reduction and minimization of adverse effects.
Conclusions. miR-152-5p is a microRNA involved in immune response regulation and inflammation, serving as a promising regulator in kidney transplantation with roles in immunomodulation, antifibrotic protection, and prevention of ischemia-reperfusion injury. Its use as a biomarker or therapeutic agent could revolutionize the management of kidney transplant patients by reducing the risk of rejection and improving allograft survival.
Keywords: microRNA, biomarker, transplant, graft, renal.

CANCER STEM CELLS AND TUMOR MICROENVIRONMENT: IMPLICATIONS FOR THERAPY RESISTANCE AND NOVEL STRATEGIES

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Background. Cancer stem cells (CSCs) represent a distinct subpopulation of tumors, characterized by self-renewal capacity and multilineage differentiation potential. These cells interact dynamically with the tumor microenvironment (TME).

Objective of the study. To elucidate the interactions between CSCs and the TME, highlighting their roles in tumor progression, metastasis and treatment resistance, as well as the need for targeted therapies.

Materials and Methods. An extensive review of the existing literature was conducted by gathering and analyzing scientific articles sourced from multiple databases, including PubMed, HINARI, Google Scholar and Medline.

Results: CSCs are key drivers in multiple aspects of tumor development, including the initiation of tumor formation, its subsequent progression, metastasis and therapeutic resistance. Their intrinsic resistance to conventional anticancer treatments significantly contributes to tumor relapse and treatment failure. Several signaling pathways, including WNT/β-catenin, Hedgehog, Notch, nuclear factor kappa B (NF-κB), JAK/STAT, *transforming growth factor beta* (TGF-β), phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT), and peroxisome proliferator-activated receptor (PPAR), regulate CSCs function, influencing tumorigenesis, metastasis, and tumor heterogeneity. CSCs are primarily located within specialized tumor niches, where hypoxia, aberrant angiogenesis, and chronic inflammation promote their survival and expansion. Stromal cells, such as cancer-associated fibroblasts (CAFs), mesenchymal stem cells (MSCs), endothelial cells, and adipocytes, contribute to TME maintenance by stimulating angiogenesis, facilitating extracellular matrix (ECM) remodeling, inducing therapeutic resistance, and enhancing metastatic dissemination. Within the tumor microenvironment (TME), various immunosuppressive cell populations, including tumor-associated macrophages (TAMs), myeloid-derived suppressor cells (MDSCs), cancer-associated fibroblasts (CAFs), and regulatory T cells (Tregs), play a pivotal role in modulating immune responses. These cellular components collectively suppress antitumor immune reactivity and create a permissive environment that facilitates tumor progression and immune evasion.

Conclusions: A bidirectional relationship is established between CSCs and the TME, where the TME sustains CSCs survival, while CSCs modulate the structure of the TME, promoting an immunosuppressive environment. These interactions compromise the efficacy of current cancer therapies, emphasizing the need for novel therapeutic strategies targeting both CSCs and the TME, ultimately improving treatment outcomes.

Keywords: cancer stem cells, tumor microenvironment, tumorigenesis, metastasis, therapeutic resistance, anticancer therapy, CSC-targeted therapies.

CLINICAL CASE: THE IMPACT OF RENAL TRANSPLANTATION IN THE PATIENT WITH RENAL PATHOLOGY AND GOUT

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Introduction: Renal transplantation is a radical treatment option for patients with chronic kidney disease (CKD), significantly impacting those with coexisting renal pathology, such as gout. The use of immunosuppressants after transplant can increase the risk of gout recurrence, and medications that reduce uric acid production are crucial to prevent further renal complications. Gout can affect the kidneys by forming uric acid crystals, leading to conditions such as urate nephropathy, uric nephrolithiasis, and CKD. Currently, 121 renal transplant patients are under care at the Republican Clinical Hospital *Timofei Moșneaga.*

Objectives: This case aims to describe the stages of organ and tissue procurement from brain-dead donor, kidney transplantation, and the subsequent evolution, considering comorbid pathologies.

Materials and Methods: A clinical case is described involving a patient who underwent kidney transplantation at the Republican Clinical Hospital *Timofei Moșneaga,* focusing on comorbidities and post-transplant progression.

Results:A 48-year-old male underwent kidney transplantation from a brain-dead donor on December 17, 2022. The donor women, 65-year-old admitted to the Municipal Clinical Hospital *Sfânta Treime* with a diagnosis of a cerebrovascular accident with evolution in confirmed brain death. The recipient was admitted to the Republican Clinical Hospital *Timofei Moșneaga* on August 23, 2023, with fever, chills and joint pain. Despite initial treatment, his condition worsened, leading to transfer to the intensive care unit, where biological death was declared on August 30, 2023. The cause of death was determined to be pulmonary sepsis, irreversible toxic-septic shock, and *Pseudomonas aeruginosa* infection. Pre-existing conditions included chronic glomerulonephritis, hypertension, and chronic gout.

Conclusions:

1. After compatibility testing, 2 patients with end-stage renal failure were transplanted and the tissues procured (cornea, blood vessels) after processing at the Human tissue bank of the-Clinical Hospital of Traumatology and Orthopedics were transplanted into 2 patients with corneal ulcers.
2. Kidney transplantation can significantly improve renal function and mitigate the effects of gout on the kidneys.
3. Careful management of uric acid levels and immunosuppressive therapy is essential to prevent gout recurrence and other complications.

Keywords: Donor, recipient, gout, transplantation.

THE PROSPECTS OF SELECTIVE JAK INHIBITORS IN HEMATOPOIETIC STEM CELLS TRANSPLANTATION

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Introduction. Hematopoietic stem cell transplantation (HSCT) represents a life-saving therapy for hematological malignancies, but its efficacy is often compromised by graft-versus-host disease (GVHD). GVHD remains a major challenge, as it results from an alloreactive immune response mediated by donor-derived T cells. The janus kinase (JAK-STAT) pathway plays a critical role in immune cell activation, cytokine signaling, and the development of GVHD. This study aims to explore the potential of selective JAK inhibitors in alleviating GVHD, improving transplantation outcomes and balancing immune suppression with graft-versus-leukemia (GVL) effects.
Materials and Methods. The scientific articles ranging from 2017-2025 published in PubMed, NCBI, BioMed Central databases, describing the preclinical and clinical studies on JAK inhibitors in HSCT, the biochemical mechanisms and physiological effects in evaluating the efficacy of ruxolitinib and itacitinib.
Results. JAK inhibitors have demonstrated efficacy in both preclinical and clinical settings by reducing T-cell activation, suppressing inflammatory cytokines, and enhancing regulatory T-cell expansion. In trials, ruxolitinib a JAK1/2 inhibitor, has shown significant improvements in steroid-refractory GVHD, with increased response rates and prolonged survival. Itacitinib, a selective JAK1 inhibitor, has demonstrated a favorable safety profile while preserving GVL effects. Emerging data suggest that post-transplant combining of JAK inhibitors and cytostatics, such as cyclophosphamide or other immunomodulatory strategies may further optimize transplant outcomes.
Conclusions. Selective JAK inhibition represents a new area of treatment, offering a targeted approach to immune modulation while maintaining the beneficial aspects of HSCT. In recent years, selective JAK inhibitors have emerged as promising alternatives for modulating immune responses, reducing GVHD severity, and improving transplantation outcomes. Future research is focused on refining dosing strategies, minimizing side effects and exploring combination therapies to enhance transplant tolerance. With ongoing clinical trials and advancements, JAK inhibitors have the potential to redefine post-HSCT immunosuppression, improving both survival and quality of life for transplant recipients.
Keywords: JAK inhibitors, hematopoietic stem cell transplantation, graft-versus-host disease, immunosuppression, cytokine signaling, ruxolitinib, itacitinib.

NANOCARRIERS THAT MAY BYPASS THE BLOOD-BRAIN BARRIER

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Introduction: The blood-brain barrier (BBB), blood-cerebrospinal fluid barrier (BCSFB) and blood-brain tumour barrier (BBTB) are regarded as potential barriers for drug delivery. Nanocarriers are designed in order to bypass these natural obstacles. Low immunogenicity, low toxicity, biocompatibility, and stability are the desired properties in each drug along with its nanocarrier. Hiperosmolarity, ultrasound, and microbubbles may disrupt the integrity of the blood-brain barrier while nanoparticles are postulated to be the cause of an incresed incidence of Alzheimer's disease due to its amyloidogenicity.
Materials and methods: There were revised the PubMed, HINARI, Web of Science, Embase, ResearchGate, Google Scholar, and medRxiv databases. A number of 27 sources were identified to be eligible using the keywords 'nanocarrier', and 'blood-brain barrier'. The study was conducted in march, 2025.
Results: Nanocarriers mainly are inorganic, lipidic, polycyanoacrylic, polymeric, dendrimeric, nanogels, and carbon nanotubes. Additional routes of delivery are through viral particles, or cells. A coating process where aminoacids, either polyglycosides cover the nanocarrier may enhance their permeability. Carbon dots nanocarriers require a rigurous attention. The degree of suitability of a drug depends on the Lipinski's rule, thus nanocarriers can make the therapeutic drugs closer to this postulate. Nanoparticles that have paramagnetic properties can be guided to the blood-brain barrier using an external static magnetic field. Niemann-Pick disease (NPD), and lysosomal storage disorders (LSD) may have a negative impact on the nanocarriers' passage capability of the blood-brain barrier. Stroke, human immunodeficiency virus (HIV), epilepsy, and mental illness (neurosis, depression, and schizophrenia) are considered to be targeted by nanocarrier-delivered drug therapy. Intranasal, intrathecal/intracerebral, intratumoral, and intravenous injections are the elective routes for chemotherapeutic drugs delivery in brain tumours.
Conclusions: There is a high variety of nanocarriers which may be suitable for blood-brain barrier permeability enhancing. Their adverse reactions, long-term complications, and limitations must be regarded.
Keywords: nanocarrier, blood-brain barrier, Alzheimer's disease, glioma.

CHALLENGES IN THE TREATMENT OF OCULAR SURFACE PATHOLOGIES

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Introduction. Tissue transplantation at the ocular surface for therapeutic, tectonic, reconstructive, or optical purposes is a routine practice among ophthalmic surgeons worldwide. The main ocular surface pathologies requiring such interventions include corneal ulcers, keratitis of various etiologies, congenital corneal anomalies, Fuchs dystrophy, conjunctival defects, transplant rejection, xerophthalmia, various corneal dystrophies, etc.

Objective. To report data regarding ocular surface tissue transplantation performed in 2024 and the challenges encountered in treating ocular surface pathologies.

Materials and Methods. This retrospective study was conducted in the Ophthalmology and Ocular Microsurgery Department of *Sfanta Treime* Municipal Clinical Hospital. The study included 111 patients with various ocular surface pathologies who underwent surgical intervention in 2024. Before and after treatment, all patients underwent a comprehensive ophthalmological examination, including visual acuity measurement with and without optical correction, tonometry in both eyes (when possible), biomicroscopy, aesthesiometry, Schirmer's test, and lacrimal duct irrigation.

Results. In 2024, within the Ophthalmology and Ocular Microsurgery Department of *Sfanta Treime* Municipal Clinical Hospital, 94 amniotic membrane transplants were performed using the "inlay" and "overlay" techniques, along with 16 tectonic corneal transplants and one optical corneal transplant. Among the transplanted patients, 90% had a clinical diagnosis of corneal ulcer. Following treatment, ocular status improved in all cases. The main challenges encountered during the treatment of ocular surface pathologies included transplant rejection, systemic diseases, corneal anesthesia, progressive glaucoma, limbal dystrophy, corneo-conjunctival pathologies, and patient compliance.

Conclusions. Amniotic membrane and corneal transplantation contribute to stabilizing pathological processes at the ocular surface, preserving or improving visual function and ocular status. Undoubtedly, one of the key factors contributing to successful outcomes in this field is the close collaboration between the transplant team, the Transplant Agency, and the Human Tissue Bank.

Keywords: transplant, amniotic membrane, cornea.

MATERIAL DESIGN IN HARD TISSUE ENGINEERING

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Introduction: Considering the high incidence and the relatively large amount needed, the overall market share of the bone grafting materials is ~49% of the total field of biomaterials and thus many researchers focused their efforts in developing new and improved materials for hard tissue engineering. Considering the evolution of these materials, from morpho-compositional point of view there are 4 major generations: 1st Generation: Metals and Alloys; 2nd generation: Ceramics and Polymers; 3rd generation: Composite and Nanocomposites and 4th generation: Tissue Engineered NanoComposites. Even not yet totally agreed, the 5th generation seems to be the materials obtained by Materials Design and 3D printing is one of the most popular processing technique.
Materials and Methods: the presentation will be focused on the materials design, synthesis, processing and characterization of the composite materials.
Results: This presentation will be mainly focused on the evolution of the materials in the field, from compositional to morphological design including coatings and 3D printed grafts and loading these materials with specific active agents and drugs to use them in specific diseases such as osteoporosis, bone infection and cancer, etc. A special attention will be paid to the composite materials based on collagen and hydroxyapatite highlighting the influence of specific conditions that can alter their properties and certainly, the role of the loading agents. Considering the current trends at EU level, green and sustainability, circularity or blue approach are also exploited in developing bone grafting materials and to improve the properties and performances of the medical products.
Conclusions: the overall performances of the materials used in hard tissue engineering are related to the composition and morphology while the presence of specific biological active agents can be essential in the treatment of specific bone-related diseases.
Keywords: Bone grafting; composite materials; materials design; 3D printing; advanced characterization; biomimetism; circular economy.
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REGENERATIVE APPROACHES FOR MANAGING PERCUTANEOUS NEPHROSTOMY COMPLICATIONS: STEM CELL AND TISSUE ENGINEERING STRATEGIES

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Introduction: Percutaneous nephrostomy (PCN) is a crucial intervention for urinary tract decompression in obstructive uropathy, malignancy, and infection. However, it carries significant risks, including hemorrhage, infection, and catheter dysfunction. Moderate hematuria occurs in 50% of cases, while severe bleeding requiring transfusion is reported in 1–4% of patients. Long-term catheter-related complications, such as occlusion and dislodgement, affect nearly 50% of patients, often leading to recurrent infections and renal impairment. Given these risks, regenerative medicine approaches, including stem cell therapy and tissue engineering, are being explored as alternative solutions.
Materials and Methods: Experimental studies demonstrate that mesenchymal stem cells (MSCs) migrate to injured bladder and renal tissues, reducing fibrosis and promoting tissue repair. In animal models, MSC administration improves vascularization, decreases hypoxia, and enhances bladder compliance. Additionally, acellular matrices and biomaterial scaffolds provide structural support, facilitating cell adhesion, migration, and differentiation. These scaffolds can be functionalized with growth factors to further enhance regenerative processes.
Results: Research indicates that MSC-based therapy reduces fibrosis and enhances bladder function in urinary obstruction. Tissue-engineered constructs incorporating MSCs and biomimetic scaffolds promote urothelial regeneration, smooth muscle reconstruction, and reduced catheter dependency. The use of bioactive scaffolds improves biocompatibility, minimizes inflammatory responses, and mitigates complications such as infections and occlusions.
Conclusion: Stem cell therapy and biomaterial-based scaffolds offer promising strategies for addressing PCN-associated complications. Further studies should focus on refining cell delivery methods, optimizing scaffold design, and validating their clinical efficacy. The integration of regenerative therapies into standard PCN management may reduce the morbidity associated with catheter-based interventions and improve long-term patient outcomes.
Keywords: Percutaneous nephrostomy, mesenchymal stem cells, tissue engineering, regenerative medicine, urinary tract reconstruction, fibrosis reduction, biomaterial scaffolds.

THE ROLE OF GLYCATION ON TRANSPLANTOLOGY METHODS IN CANCER TREATMENT

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Background. Advanced glication end products (AGEs) are formed in result of Millard reaction in hiperglycemic conditions caused by Warburg`s effect. Many studies have shown the presence of AGEs in neoplastic tissues through which are: pyrraline, imidazolone A and B, argpyrimidine, fructosyl-lysine, methylglyoxal-lysine dimer, Nε(carboxyethyl)-lysine (CEL), Nε(carboxymethyl)-lysine (CML), N2-(1-carboxyethyl)-2′-dezoxyguanosine) (CEdG). It proves corellation between AGEs and cancer. Actually chimeric antigen receptor (CAR)-T cell therapy has been revolutionary in cancer treatment and therefore AGEs may be potential target for it.
Objective of the study. To elucidate the mechanisms through which AGEs influence cancer development in order to find different approaches in diagnostic, treatment and preventing of cancer.
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. Can be noticed some mechanisms how AGEs influence cancer. Firstly, direct glycation of proteins as histones and nucleic acids as DNA causes epigenetic changes, mutations genomic instability and formation of neoantigens, that complicates targeted treatment with (CAR)-T, producing tumor antigen heterogeneity. Secondly, AGEs cause a significant decrease in proliferation and an increase in apoptosis of primary stem cells. It may be explained by interaction of AGEs - the receptor for advanced glycation end products (RAGE). Therefore, direct blocking of proteins involved in the apoptotic or RAGE pathway can improve viability of stem cells and efficiency of regenerative therapies with stem cells. Finally, accumulation of AGEs leads to irreversible bond of AGEs with proteins, especially with conjunctive tissue proteins. Obviously glycation of extracellular matrix increases tumor invasion and metastasis. Moreover it alters migration of immune cells and efficiency of (CAR)-T cell therapy.
Conclusions. In conclusion, glycation is pathognomonic process in cancer and therefore its studying is a key to the pathogenetic therapy with actual methods in tissue and cell transplantology, like (CAR)-T cell therapy. On the one side AGEs, as markers of cancer, may be used in targeting of therapy. On the other side antiglycation agents may potentiate transplantology methods of cancer treatment.
Keywords: AGEs, RAGE, (CAR)-T cell therapy, regenerative therapy with stem cells, glycation, cancer.

CHALLENGES IN THE USE OF GLUCOCORTICOIDS IN TRANSPLANTOLOGY

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Introduction. Glucocorticoids (GCs) have long time played a key role in solid organ transplantation (SOT), thanks to their strong anti-inflammatory and immunosuppressive effects. However, their use presents a significant drawback: while they help prevent rejection, they also bring a wide range of side effects that can impact long-term patient health. This study explores the challenges of using GCs in transplantation, focusing on their effects on graft survival, the risks associated with their prolonged use, and potential strategies to minimize their downsides.
Materials and Methods. A comprehensive literature review was conducted using PubMed, Scopus, and Google Scholar databases. Studies published between 2011 and 2025 were analyzed using keywords such as "glucocorticoids," "solid organ transplantation," "immunosuppression," and "side effects." We extracted relevant data on GC mechanisms, benefits, drawbacks, and emerging alternatives to improve transplant outcomes.
Results. Glucocorticoids remain a staple in SOT, used for induction and maintenance therapy as well as for treating acute rejection episodes. However, their widespread use is not without consequences. Patients on long-term GC therapy face an increased risk of infections, including bacterial, fungal, and viral complications. Metabolic and endocrine issues such as diabetes, osteoporosis, and adrenal insufficiency are common, while cardiovascular effects like hypertension and endothelial dysfunction add to the risks. Neurological side effects, including mood disturbances and steroid-induced psychosis, further complicate long-term management. Additionally, prolonged GC exposure may contribute to chronic allograft dysfunction, potentially jeopardizing transplant success. Given these challenges, researchers are exploring alternative approaches such as steroid-sparing regimens, targeted GC delivery via nanoparticles, and selective immunomodulators like mTOR inhibitors and IL-6 blockers to reduce toxicity while maintaining immunosuppressive efficacy.
Conclusions. While GCs remain integral to SOT, their long-term use presents significant challenges. Optimizing immunosuppressive regimens through targeted therapies and personalized approaches could improve outcomes and reduce complications. Steroid-sparing strategies include rapid tapering protocols, complete steroid avoidance in low-risk patients, and combination therapies using calcineurin inhibitors, mTOR inhibitors, and monoclonal antibodies. Further research is needed to refine these approaches and enhance graft survival.
Keywords. Glucocorticoids, solid organ transplantation, immunosuppression, chronic rejection, targeted therapy, steroid-sparing regimens.

LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Introduction. Hepatocellular carcinoma is one of the most frequent complications of advanced liver cirrhosis, associated with high mortality. Liver transplantation is an effective therapeutic solution in selected cases, providing significantly higher survival rates and improved quality of life.

Aim of the study. Evaluation of post-transplant outcomes in the treatment of hepatocellular carcinoma by analyzing patient characteristics and clinical evolution.

Material and methods. This retrospective study includes 6 male patients, aged 38-61 years, who underwent liver transplantation between 2017 and 2022. Diagnoses included hepatocellular carcinoma associated with mixed viral liver cirrhosis (HBV, HCV, HDV), classified as Child-Pugh A-C, and portal hypertension. Analyzed data included hospitalization duration (15-28 days), patient origin (4 urban, 2 rural), and post-transplant clinical evolution.

Results. Of the 6 patients, 5 (83.3%) showed improvement after transplantation, while 1 (16.7%) deceased. The age range was 38-61 years, and hospitalization lasted between 15-28 days. Patients had associated conditions such as grade II portal hypertension and subcompensated or decompensated liver cirrhosis. Results demonstrate the efficacy of liver transplantation in controlling hepatocellular carcinoma, with significant clinical improvement in most cases.

Conclusions. Liver transplantation is a viable therapeutic option for patients with hepatocellular carcinoma associated with liver cirrhosis, showing favorable outcomes in clinical improvement and survival.

Keywords:liver transplantation, hepatocellular carcinoma, liver cirrhosis, portal hypertension.

CELLULAR THERAPY WITH GROWTH FACTORS: A PROMISING NEUROREGENERATIVE APPROACH IN CEREBRAL PALSY

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Introduction: Cerebral palsy is a non-progressive condition caused by a series of neurological disorders that occur during fetal brain development, either before or after birth. It represents a major global issue that leads to disability, limiting children's functionality and causing negative influences both physically and psychologically. The aim of the study was to elucidate the effectiveness of growth factors for cognitive and motor functionality in cerebral palsy.
Materials and Methods: 14 articles were selected and evaluated from recognized databases, such as PubMed Central, Medline, HINARI, Google Scholar, and ResearchGate, covering the period from 2015 to 2024.
Results: Analyzing data from the literature, the patients were divided and studied into groups: in the studied group, patients were diagnosed with perinatal cerebral palsy, generalized spastic tetraparesis, and moderate cognitive impairments. These patients were administered intravenous platelet-rich plasma in a dose of 25 cc (cubic centimeters), and then monitored at 24 hours, 3 months, and 6 months after treatment, with the determination of IGF-1, PDGF, TGF, and VEGF levels before and after treatment. Both before and after treatment, the patients were examined according to the GMFCS and Bayley scales. Additionally, the quantity of leukocytes, granulocytes, monocytes, and platelets was determined. It was observed that platelets were above the limit of 25,000 n/m3 post-treatment, with their levels remaining relatively constant in the bloodstream. In some patients, platelet counts even increased 3-5 times. Furthermore, an intensification of glucose metabolism was recorded. No adverse effects were observed post-treatment. After treatment, improvements in cognitive and language functions were noted according to the Bayley scale (a cognitive function assessment scale), with children being able to communicate two or three words, and motor functions also showed improvement.
Conclusion: Growth factor therapy in cerebral palsy produced neuroregenerative effects, improved brain plasticity, stimulated mobility and motor skills, and recorded improvements in cognitive and language domains.
Key-words: cellulat therapy, cerebral palsy.

EXPLORING TRABECULAR MESHWORK STEM CELLS: POTENTIAL ROLES, THERAPEUTIC IMPLICATIONS AND CHALLENGES IN GLAUCOMA

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Introduction: Recent investigations surrounding trabecular mesh (TM) stem cells have generated significant interest due to their possible role in glaucoma treatment. Trabecular mesh cells are crucial in maintaining IOP (intraocular pressure), and their dysfunction is involved in glaucoma pathogenesis. Several studies highlight innovative models for studying glaucomatous function and the regeneration of TM. For example, Buffault et al. provide an overview of current TM glaucomatous models, emphasizing their importance in the mechanism of open-angle glaucoma and testing the possible therapies (Buffault J., 2023).
The **purpose** of this review is to provide an overview of TMSCs, their capacity for regeneration, and their therapeutic uses in glaucoma.
Material and methods: A literature review was conducted using the PubMed, Scopus, and Web of Science databases. Keywords used:"trabecular meshwork stem cells", "glaucoma", "regenerative therapy" and "stem cell-based treatment". Of 102 abstracts selected for the 2015-2025 period, just 64 were selected based on preclinical data.
Results: Research suggests that TM stem cells are found in the juxtacanalicular area of the TM and are capable of multipotent differentiation and self-renewal. Studies conducted in vivo show that the stem cells can develop into functional TM-like cells, which restore outflow capability, lower the IOP in glaucomatous patients, and preserves retinal ganglion cells. Furthermore, TM stem cell transplantation has demonstrated potential in decreasing fibrotic alterations and encouraging TM repair. Clinical applicability is still hampered by issues like immune response mitigation, long-term survival, and cell delivery method optimization.
In **conclusion**, the investigation of TM stem cells offers a critical path forward for the study and treatment of glaucoma. Even if preclinical research indicates that cell-based therapies are effective, further investigation is needed to improve them, evaluate their long-term safety, and provide standardized procedures for clinical use. Developments in tissue engineering and stem cell biology could open the door to successful TMSC-based treatments for the treatment of irreversible vision loss brought on by this life-threatening condition.

BUILDING A RAG SYSTEM FOR TISSUE ENGINEERING: INSIGHTS FROM DOMAIN-SPECIFIC TEXT AND SEPSIS MANAGEMENT

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Introduction: Tissue engineering (TI) is a complex field that requires access to specific domain knowledge. Large Language Models (LLMs) are powerful but limited by their training data. Retrieval Augmented Generation (RAG) addresses this limitation by integrating LLMs with external knowledge sources. This work explores the design and implementation of a RAG system for TI, inspired by our successful applications in specific domains, including sepsis management. Such a system can greatly enhance the efficiency and accuracy of knowledge retrieval and generation in TI.
Materials and Methods: The RAG system for TI can be developed using a large language model augmented by a vector database of TI literature. The knowledge base is to be curated from research papers, textbooks, and other domain-specific texts. These texts can be processed to create embeddings stored in a vector database for efficient retrieval. When a user submits a query, the LLM generates an initial response and retrieves relevant information from the database to refine its output, ensuring accuracy and relevance. The RAG-based sepsis management system that can serve as an example that can be adapted to TI is available (after sending a request to victor.iapascurta@usmf.md) at: https://huggingface.co/spaces/LlmRAGbasedAPPs/LLM_MA_RAG_Sepsis.
Results: Our previous implementations of RAG in different domains have shown that integrating external knowledge significantly enhances the accuracy and relevance of LLM-generated responses. For TI, we anticipate this approach will similarly improve the system's ability to handle complex, domain-specific queries.
Conclusions: The development of a RAG system for tissue engineering represents a significant step forward in leveraging AI technologies for domain-specific applications. By combining the generative capabilities of LLMs with the precision of a curated knowledge base, we can create a tool that not only understands the language of TI but also possesses the depth of knowledge required to make meaningful contributions to the field. This work outlines the design, implementation, and expected benefits of such a system, drawing from our successful experiences in other domains.
Keywords: Tissue engineering, RAG, LLMs, Knowledge base, Vector database, Domain-specific knowledge, AI in biomedical engineering.

AGENT-BASED MODELING OF FLUID DYNAMICS IN LUNG TISSUE ENGINEERING

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Introduction: In tissue engineering for lung applications, understanding and controlling fluid dynamics within engineered constructs is paramount. Agent-based modeling (ABM) offers a powerful framework to simulate complex physiological systems, yet its application to pulmonary edema (PE) in this context remains underexplored. This study presents an innovative ABM, built in NetLogo, to simulate cardiogenic PE (CPE) by modeling extravascular lung water dynamics under hydrostatic pressure (HP) and oncotic pressure (OP). This model can serve as a tool to inform the design of tissue-engineered lung constructs by providing insights into fluid management strategies.
Materials and Methods: The ABM was developed using NetLogo, employing a simplified Starling equation: Q = k (HP - OP). The model's spatial environment includes capillary, alveolar-capillary membrane (ACM), and alveoli, with agents representing water molecules and macromolecules. Two scenarios were simulated: (1) Normal: HP = 18 mmHg, OP = 25 mmHg, (2) CPE: HP = 22 mmHg, OP = 24 mmHg.
Results: In the normal scenario, the model achieved a physiological balance with approximately 200 ml of extravasation cleared. In the CPE scenario, there was significant fluid accumulation (>400 ml by ~40 ticks). Adjusting parameters, such as reducing OP, amplified the edema, demonstrating the model's flexibility. The model is available at:
https://modelingcommons.org/browse/one_model/5103#model_tabs_browse_info.
Conclusions: This ABM provides a valuable platform for tissue engineers to understand and manipulate fluid dynamics in lung constructs. By simulating the effects of different pressure gradients and permeability, it can guide the development of biomaterials and scaffolds that optimize fluid handling in engineered lung tissues. The model's extensibility allows for future incorporation of additional complexities, such as gas exchange and variable tissue properties, enhancing its utility in both research and practical applications.
Keywords: Tissue engineering, Agent-based modeling, Pulmonary edema, Fluid dynamics, Hydrostatic pressure, Oncotic pressure.

STEM CELL TRANSPLANTATION IN INFERTILITY TREATMENT: NEW PERSPECTIVES IN REGENERATIVE MEDICINE

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Background. Female infertility is a multifactorial condition caused by factors such as ovarian dysfunction, endometrial disorders, hormonal imbalances, and age-related decline in reproductive potential. Stem cell transplantation offers a promising approach to regenerate reproductive tissues, restore ovarian function, and enhance endometrial receptivity.
Objective of the study. To evaluate the potential of stem cell transplantation in treating female infertility and identify the mechanisms by which stem cells promote tissue regeneration and fertility restoration.
Material and Methods. This study synthesizes literature from articles published between 2020-2025, selected from PubMed, NCBI and MPDI.
Results. Stem cell therapies, especially for ovarian and endometrial dysfunction, show significant promise. Embryonic stem cells (ESCs) can differentiate into germ cells, offering infertility solutions, but their use is limited by ethical concerns. Induced pluripotent stem cells (iPSCs) can differentiate into gametes, showing potential for fertility restoration, although their clinical use is restricted by genomic instability. Mesenchymal stem cells (MSCs), particularly from bone marrow and menstrual blood, have demonstrated therapeutic potential in treating ovarian failure and endometrial dysfunction. These cells aid in tissue repair, restore hormonal function, and promote angiogenesis. Studies in animals show improvement in ovarian function, endometrial thickness, and egg development. Amniotic fluid stem cells (AFSCs) regenerate oocytes and prevent follicular atresia. Amnion-derived mesenchymal stem cells (AmDMSCs) support ovarian recovery by reducing apoptosis and enhancing granulosa cell proliferation. Placenta-derived mesenchymal stem cells (PDMSCs) improve folliculogenesis through the PI3K/Akt pathway. Adipose tissue-derived stem cells (ADMSCs) enhance ovarian function through neovascularization. Ovarian stem cells (OSCs) hold promise for fertility restoration in cases of premature ovarian failure. Spermatogonial stem cells (SSCs) have been used experimentally to restore male fertility, especially after chemotherapy-induced infertility.
Conclusion. Stem cell-based therapies offer significant potential for treating female infertility, particularly in ovarian and endometrial dysfunctions. Further research is needed to optimize protocols, address risks like immune rejection and tumor formation, and confirm clinical safety and efficacy.
Keywords: stem cells, infertility, ovarian function, fertility restoration.

NEURAL STEM CELL TRANSPLANTATION FOR NEURODEGENERATIVE DISEASES

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Background. Neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis, are severely disabling and ultimately fatal conditions that affect millions of individuals worldwide. Stem cell transplantation is emerging as a promising therapeutic approach due to its potential to facilitate multiple reparative processes within the central nervous system, such as cell replacement and paracrine effects.
Objective of the study. To evaluate the potential of neural stem cell (NSC) transplantation as a therapeutic approach for neurodegenerative diseases and identify the key mechanisms through which NSCs exert their effects.
Material and Methods. This study represents a literature synthesis based on articles published in the period 2020-2025, selected from the databases PubMed, NCBI, MPDI, Springer Ling, UpTodate.
Results. Studies have shown that neural stem cell transplantation can have a positive impact on neurodegeneration through various mechanisms, including neurotrophic factor production, reduced neuroinflammation, enhanced neuroplasticity, and cell replacement. To fully harness the potential of NSCs, it is crucial to investigate their biological characteristics, such as subpopulation markers, secretome, which is responsible for the regulation of intercellular communication, neuroprotection, and immunomodulation, and ability to migrate and integrate into NSC neuronal networks. Recent advances in gene editing and cellular engineering offer opportunities to enhance their therapeutic effects.
Conclusion. Neural stem cell transplantation offers significant potential for treating neurodegenerative diseases. It is necessary to standardize protocols, ensure control of secondary effects such as tumor formation and immune rejection. Further research is needed to optimize cell sourcing, improve long-term outcomes, and minimize risks.
Keywords: neuronal stem cells, neurodegenerative disease, cell therapy.

TRENDS IN THE DEVELOPMENT OF TISSUE GRAFTS FOR BIOMEDICAL APPLICATIONS

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Introduction. Bone defects can occur as a result of trauma, infection, tumor, or extensive surgery. Graft-assisted bone regeneration is an evolving field, with trends aimed at optimizing biocompatibility, accelerating osseointegration, and reducing postoperative risks. New approaches focus on the use of advanced biomaterials, cell therapies, and tissue bioengineering to improve clinical outcomes by providing osteoconductive, osteoinductive, and osteogenic capacity.

Aim. The purpose of the study was to review the specialized literature to establish the optimal methods and conditions for obtaining tissue grafts with commercial potential.

Materials and Methods. The bibliographic analysis consisted of reviewing publications from 2010-2025 in the PubMed, Scopus, Web of Science databases to find studies that compare the clinical effects of different commercial grafts obtained by various methods and mineralization conditions.

Results. Commercial grafts for the restoration of bone defects represent a viable solution in orthopedics, traumatology and maxillofacial surgery. The choice of the optimal type of graft depends on the size of the defect, the patient's condition and the therapeutic objectives. Thus, some grafts may be more suitable for situations where both osteoinduction and osteoconduction are required, while some grafts may require combinations with other materials for optimal integration.

Conclusions: Bone regeneration depends on the mineralization method that must be personalized according to the type of bone defect and the clinical needs of the patient.

Keywords: grafts, bone regeneration, bone defect, mineralization.

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ADDRESSING ARTIFICIAL INTELLIGENCE GAPS IN TRANSPLANT MEDECINE: A MACHINE LEARNING SOLUTION

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Introduction: Artificial intelligence (AI) shows promise in transplant medicine, particularly in organ matching and rejection prediction. However, gaps remain in personalized immunosuppression, including optimal drug dosing, patient-specific data integration, and clinical implementation. This study identifies these gaps and proposes a machine learning model to optimize immunosuppressive therapy.
Material and Methods: A systematic review was conducted using PubMed, Scopus, and Web of Science from 2010 to 2024 with keywords: "Artificial Intelligence," "Transplant Medicine," "Rejection Prediction," and "Patient Care Optimization." Studies discussing AI applications in rejection prediction or patient care in organ transplantation were included. Data on study design, AI methods, outcomes, and limitations were extracted. Findings show most AI models rely on static predictors and fail to adapt to real-time changes like infections and inflammation. Multi-omics data, crucial for drug metabolism and immune response, are rarely integrated, reducing accuracy. Generalizability is also limited, as most models are trained on small, single-center datasets further reducing accuracy. To address these gaps, we propose a machine learning model using longitudinal transplant data. It will integrate electronic health records, pharmacokinetics, genomics, and biomarkers to predict individualized dosing. Recurrent neural networks or transformer-based architectures will update recommendations based on patient-specific responses. Model performance will be validated using real-world clinical data and benchmarked against traditional dosing protocols.
Results: The review included 68 articles, with 14 meeting inclusion criteria. While AI has been applied to organ matching and rejection prediction, no existing models provide real-time, patient-specific immunosuppression adjustments, impacting patient outcomes. The proposed model aims to bridge this gap, potentially reducing rejection rates and improving outcomes.
Conclusions: This study identifies deficiencies in AI-driven immunosuppression management, particularly in real-time dose adjustments, multi-omics integration, and model generalizability. The proposed machine learning framework seeks to create an adaptive, personalized dosing system to enhance transplant outcomes and minimize rejection risks.
Keywords: Artificial Intelligence; Transplant Medicine; Personalized Immunosuppression; Machine Learning; Multi-Omics Data.

MIMICKING THE HOST: GENE ADDITION VIA ADENO-ASSOCIATED VIRUS (AAV) TO REDUCE REJECTION IN ORGAN TRANSPLANTS

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Background. Organ transplantation is a crucial medical advancement, offering life-saving treatment for patients with end-stage organ failure. Despite significant progress, graft rejection remains a major cause of transplant failure. The immune system often attacks the transplanted organ as a foreign body, complicating long-term success. Although immunosuppressive therapies help reduce rejection risk, they have serious side effects, such as increased susceptibility to infections, malignancies, and organ toxicity.Recent research focuses on genetic engineering to address graft rejection. One promising approach is using Adeno-Associated Virus (AAV) vectors to deliver immune-modulatory genes to transplanted organs. AAV-based gene delivery can potentially promote immune tolerance by regulating T-cell activation. Genes like CTLA-4Ig or PD-L1 can be introduced to help the transplanted organ integrate into the recipient's immune system, reducing rejection likelihood.
Materials/Methods. A systematic review was conducted using PubMed, Scopus, and Web of Science (2000–2024). Peer-reviewed studies on AAV-mediated gene addition for reducing transplant rejection in English were included, while non-peer-reviewed and irrelevant articles were excluded. Findings were synthesized into key themes such as organ transplant rejection, immunosuppressive therapy, host immune profile, and AAV-mediated gene therapy.
Results. AAV-mediated gene addition, especially the delivery of CTLA-4Ig, has shown promise in reducing organ transplant rejection by inhibiting T-cell activation. AAV vectors, particularly AAV8 and AAV9, target liver cells and express CTLA-4Ig in hepatocytes, modulating immune responses. However, challenges persist, including variable transduction efficiency, immune responses against AAV vectors, and short gene expression duration. Pre-existing immunity against AAV vectors can limit gene delivery, and potential side effects such as immune reactions and genotoxicity remain concerns. Self-complementary AAV vectors reduce integration risks.
Conclusion. Advancements in vector design and gene therapy techniques may revolutionize organ transplantation. AAV-mediated gene addition could offer an alternative to traditional immunosuppressive therapies, improving long-term transplant success and reducing side effects. The goal is personalized gene therapy that mimics the host's immune profile, promoting long-term graft acceptance without lifelong immunosuppressive drugs. Continued research and clinical trials will be essential to fully realize AAV-based therapies in transplantation.
Keywords. Adeno-Associated Virus (AAV); Gene Addition; Organ Transplantation; CTLA-4Ig; Immune Tolerance.

EVALUATION OF THE REGENERATIVE EFFICACY OF BIOLOGICAL DRESSINGS DEVELOPED THROUGH TISSUE ENGINEERING

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Introduction. Recent advances in tissue engineering and regenerative medicine have developed innovative methods in skin regeneration, in the case of cutaneous wounds, where standard approaches are limited. The aim of the study is to explore the integration of biologically active dressings developed through tissue engineering and their role in the re-generation of cutaneous defects.

Materials and methods. By using the methods of antibiotic-antimycotic sterilization, separation, decellularization with non-ionic detergents, enzymatic digestion, sedimentation and dialysis we developed porous biomaterials. We analyzed the eligibility of the tissues for *in vivo* use by performing qualitative and quantitative tests by scanning electron microscopy, staining with hematoxylin-eosin, 4′,6-diamidino-2-phenylindole, quantification of deoxyribonucleic acid residues, cytocompatibility with MTT, staining with Calcein Acetoxymethyl and DAPI-Rhodamine Phalloidin. In the preclinical study, Wistar rats were used, divided into 3 experimental groups: 1. saline solution (NaCl 0.9%); 2. collagen sponge from the submucosa of the porcine small intestine combined with 0.01% Povidone-iodine solution and 3. porcine acellular dermis with gentamicin. We followed the regenerative efficacy of tissue-engineered biodressings. The wound closure rate was calculated based on the wound diameter in relation to the initial dimensions.

Results. Biological dressings developed from collagen sponge, from the porcine derm and the submucosa of the porcine small intestine showed complete wound closure by keratinized stratified epithelium, as well as the presence of a scar formed in the dermis, characterized by well-organized collagen fibrils and a low content of leukocytes and blood vessels in the wound bed area. Some preparations showed the presence of hair follicles in the dermis, indicating complete restoration of the skin structure.

Conclusion. Successful application of tissue-engineered biological dressing in regenerative medicine requires many validation characteristics, including biocompatibility, biodegradability or strength, sterility, mechanical and chemical properties, scaffold architecture, and manufacturing technologies. Due to the combined regenerative, antibacterial and antifungal properties, tissue-engineered biomaterials can be transformed into biodressings for wound healing.

Keywords: Biological dressings • Tissue engineering • Efficacy •Wound regeneration.

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REGENERATIVE MEDICINE IN LIVER DISEASES AND CELLULAR MECHANISM OF LIVER REGENERATION AND CELL-BASED THERAPIES

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Background. Liver transplantation remains the gold standard for end-stage liver diseases, but donor shortages necessitate regenerative alternatives. Induced pluripotent stem cells (iPSCs), liver progenitor cells (LSPCs), and hematopoietic stem cells (HSCs) represent a game-changer in liver regenerative medicine. Although iPSCs can be used to produce patient-specific hepatocytes, drawbacks including redifferentiation deficiency and tumorigenicity have not yet enabled their clinical application. This study explores bioengineered liver constructs, focusing on decellularization/recellularization strategies and bioprinting approaches as potential solutions to organ shortages.
Materials and Methods. A literature review was conducted, analyzing preclinical and clinical studies on scaffold-based tissue engineering, whole-organ decellularization, and 3D bioprinting, from PubMed, NCBI, Hindawi. Molecular pathways related to liver regeneration, hepatocyte differentiation, and immune response modulation were examined.
Results. Liver tissue engineering employs two primary strategies: (1) Decellularization/recellularization of liver scaffolds and (2) 3D bioprinting of liver tissues. The decellularization approach preserves the extracellular matrix (ECM) and vascular networks, facilitating cellular repopulation. Experimental rat and pig models have demonstrated partial liver function restoration, yet graft survival remains limited due to inadequate vascularization and long-term cell viability. Bioprinting, leveraging 3D printing and bio-inks, offers an alternative pathway to generating structured liver tissues. Researchers are working to address these challenges through advances in biofabrication, microenvironmental control, and scaffold optimization. HLA-matched iPSC lines offer a potential solution, with research suggesting that a small number of iPSC donors could match up to 90% of recipients, paving the way for off-the-shelf bioengineered liver constructs.
Conclusions. The liver bioengineering and iPSC technology is reshaping regenerative medicine, offering innovative solutions to address organ shortages. While fully functional liver constructs remain a long-term goal, bioartificial liver devices and cell-based therapies offer near-term solutions for bridging transplantation gaps. Future research should focus on enhancing iPSC differentiation efficiency.

EPIDEMIOLOGY OF HEALTHCARE-ASSOCIATED INFECTIONS IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction. Approximately half a century ago, allogeneic hematopoietic stem cell transplantation (HSCT) became an essential therapeutic option for treating severe conditions, thus offering a new chance at life for children with various hematologic and oncologic diseases.
The purpose of this study is to analyze the epidemiological peculiarities of HCAIs in children undergoing HSCT.
Materials and Methods. A systematic review of the literature was conducted with an overview of epidemiological aspects of HCAIs in children undergoing HSCT, related to the incidence and mortality of the disease, isolated pathogens and the risk factors that influence the development of IAAM.
Results. HCAIs are major complications in children undergoing HSCT, with incidence rates ranging from 5% to 50%, being higher in allogeneic compared to autologous transplants.
Bloodstream infections (BSIs) are the most frequent, with an estimated incidence of 20%-44% and a mortality rate between 10% and 50%. HCAIs caused by resistant Gram-negative bacteria increase mortality to 45%, while fungal infections raise it to 75%. Pneumonia and gastrointestinal infections, including Clostridium difficile infection, are other frequently encountered complications. Urinary tract infections are rare and are usually associated with the presence of a urinary catheter. A retrospective study conducted over 21 years showed that 41% of children who underwent HSCT developed at least one bloodstream infection. Another study reported an incidence of 28.2% of HCAIs in children undergoing HSCT, with a proportion of 32.8% for BSIs. Of these, 93.4% were associated with central venous catheterization, and the mortality rate was 36.9%. A study conducted in Italy identified Coagulase-negative staphylococci and Enterobacteriaceae as the most frequent pathogens, each causing approximately 25% of BSI cases, followed by Enterococci and Pseudomonas aeruginosa. The main identified risk factors include: prolonged immunosuppression; severe and prolonged neutropenia; use of central venous catheters; mechanical ventilation and prolonged hospitalization.
Conclusion. Children undergoing HSCT have an increased vulnerability to HCAIs due to a combination of risk factors related to immunosuppression and invasive medical procedures. Early identification of these factors and the implementation of rigorous strategies for infection prevention and control are essential to reduce the incidence and impact of these complications in this vulnerable population.
Keywords: hematopoietic stem cell transplantation, healthcare-associated infections, children, risk factors, microorganisms.

AMNIOTIC MEMBRANE THERAPY: A STEP TOWARD FASTER ULCER HEALING

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Introduction. Neuropathic foot ulcers are a major health issue, particularly in patients with diabetes or peripheral neuropathy, significantly impacting mobility and quality of life. These ulcers are often difficult to treat and persist for months despite conventional therapies. Amniotic membrane therapy has gained attention for its regenerative properties and ability to accelerate the healing of chronic wounds.
Materials and Methods The study included 20 patients with neuropathic ulcers that had not responded to conventional treatments and had persisted for at least 3 months. Amniotic membrane therapy was applied to the ulcers, and healing progress was monitored over a 9-week period. Healing was assessed by measuring ulcer size and evaluating the quality of regenerated tissue.
Results After 9 weeks, 85% of patients achieved complete ulcer closure. Amniotic membrane therapy resulted in rapid tissue regeneration, reduced inflammation, and prevention of infections, compared to previous treatments that had failed.
Conclusion, Amniotic membrane therapy represents an effective and promising treatment for persistent neuropathic ulcers, especially for patients who do not respond to conventional therapies. This treatment accelerates healing and improves functional recovery.
Keywords: Amniotic membrane, neuropathic ulcers, wound healing, resistant treatments.

BREAST TISSUE ENGINEERING: INNOVATIONS, METHODS, AND FUTURE PERSPECTIVE

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Introduction. The incidence of breast cancer, based on L.Wilkinson et al. in 2020, has reached 2.26 million cases worldwide, with mastectomy remaining the primary surgical approach. The critical importance of breast reconstruction following mastectomy lies not only in restoring the physical appearance of the breast but also in significantly improving the psychological and emotional well-being of patients. Autologous and alloplastic techniques used in breast reconstruction aim to enhance the quality of life for the patient and reduce the multifaceted impact of breast cancer. Tissue engineering in breast reconstruction has made significant progress, with several methods and techniques developed to improve outcomes and overcome the limitations of existing methods. This abstract discusses promising methods of breast reconstruction using tissue engineering.
Materials and methods. The articles were searched on PubMed using combination of keywords: breast cancer, mastectomy, tissue engineering, acellular matrices, 3D printing, cells. The selection was limited to English-language articles published in the past 10 years.
Results. In the past 25 years, tissue engineering has become a highly promising field in breast reconstruction. The main approaches used in this area are: (i) Scaffold-based approaches, (ii) Cell-based therapies, and (iii) 3D bioprinting. Advancements in these fields have led to the development of acellular matrices, which are now used in clinical settings. Additionally, multiple studies have focused on using decellularization methods to obtain acellular breast scaffolds and acellular nipple-areolar complex, aiming not only to restore the aesthetic aspects of the breast but also its function. Progenitor cells, such as adipose-derived stem cells, are used for breast contouring, restoring natural sensation, and improving skin quality after radiotherapy. Furthermore, 3D printing-based studies are revolutionizing the creation of customized scaffolds and tissues, enabling the precise restoration of breast shape, volume, and symmetry. These developments have brought us closer to providing patients with more natural, functional results and improved overall recovery.
Conclusions. Advancements in breast tissue engineering hold promise for developing functional breast tissues. However, challenges remain in vascularization, tissue integration, and ensuring long-term viability. Ongoing research aims to address these issues, moving towards clinical applications in breast reconstruction and augmentation.

RENAL TRANSPLANT TO A PATIENT WITH TYPE 2 CARDIORENAL SYNDROME WHO IS ON HEMODIALYSIS: CLINICAL AND PROGNOSTIC FACTORS TO THINK ABOUT

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Introduction. Type 2 cardiorenal syndrome (CRS-2) is a complex pathological entity characterized by decompensated chronic heart failure, leading to progressive deterioration of renal function. For patients with CRS-2 who have reached the end stage of chronic kidney disease (CKD), therapeutic options are limited, and renal transplantation remains the only long-term curative solution. The objective of this study is to highlight the clinical challenges, prognostic factors, and therapeutic strategies applied to an advanced CRS-2 patient on hemodialysis who was evaluated for renal transplantation.
Materials and Methods. A retrospective analysis was conducted on a 62-year-old patient diagnosed with heart failure with reduced ejection fraction (HFrEF—LVEF 35%) and stage V chronic kidney disease, secondary to ischemic nephropathy, who had been enrolled in a hemodialysis program for 18 months. The pre-transplant evaluation included clinical and biological parameters (NT-proBNP, urea, creatinine, urea/creatinine ratio, and creatinine clearance); cardiovascular risk stratification tests (vascular calcification index, Doppler echocardiography, and cardiopulmonary exercise test); and immunological compatibility analysis. Descriptive and inferential statistical methods assessed correlations between cardiac parameters and post-transplant prognosis.
Results. The patient experienced accelerated progression of heart failure, with repeated episodes of refractory cardiac decompensation, necessitating frequent adjustments to hemodialysis parameters (controlled ultrafiltration, individualized sodium profile). The vascular calcification index indicated advanced atherosclerosis and elevated NT-proBNP levels (>15,000 pg/mL). The immunological evaluation revealed a high panel-reactive antibody (PRA > 50%), requiring personalized pre-transplant immunomodulation strategies. Although the patient was deemed eligible for renal transplantation, the perioperative risk was significantly increased due to severe left ventricular dysfunction and associated pulmonary hypertension.
Conclusions. Renal transplantation in end-stage CRS-2 patients poses significant challenges both in candidate selection and perioperative management. Rigorous multidisciplinary evaluation, optimization of cardiorenal therapy, and monitoring of cardiac stress biomarkers can improve patient selection and post-transplant prognosis. Further studies are needed to develop personalized risk stratification algorithms for this patient population.
Keywords: Type 2 cardiorenal syndrome, chronic hemodialysis, renal transplant, advanced heart failure.

LIVER TRANSPLANTATION IN WILSON'S DISEASE

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Background. Wilson's disease is a rare genetic disorder caused by excessive copper accumulation in the body, particularly in the liver and brain. In severe cases, where the disease leads to liver failure, liver transplantation may be required.
Objective. A review of the specialized literature to gain a better understanding of the indications for liver transplantation in Wilson's disease and its impact on patient health outcomes.
Material and Methods. A systematic search of scientific publications was conducted in major databases, including PubMed, Web of Science, and Scopus.
Results. Liver transplantation from a living donor provides superior outcomes, with no reported disease recurrence in these patients. Among patients with neurological manifestations, a 74.2% reduction in symptoms was observed postoperatively. Survival rates at the interval of 1-10 years were reported at 84% and 80%, respectively. While the mortality rate in the first post-transplantation year is 16%, it decreases to 4% in the 1–10-year period. Liver transplantation immediately corrects the copper metabolism defect, with serum ceruloplasmin levels normalizing within the first post-surgery month. The only factor influencing survival rates was reported to be neurological status, with patients presenting severe neurological symptoms having significantly lower survival rates. The high survival rates may be attributed to the relatively young age at the time of transplantation, the low number of comorbidities, and the absence of disease recurrence.
Conclusions. Liver transplantation in Wilson's disease is associated with a high survival rate and a 74.2% improvement in neurological symptoms post-transplant. The 1-, 5-, and 10-year survival rates were comparable, and perioperative care remains the primary determinant of long-term survival.
Keywords: Liver, Transplantation, Wilson's disease.

USE OF CELL TRANSPLANTS IN JAW RECONSTRUCTIVE SURGERIES

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Introduction: During th eyears 2006-2024, a lot of 190 patients were studied, all of which underwent treatment in the department of oral and maxillofacial surgery, for jaw bone necrosis, caused by drug use, bisphosphonates or radiotherapy. The patients were observed for a period of 5-15 years, some of which needed reconstructive surgeries. For a faster formation of bone tissue were used cell transplants and acrylic removable dentures.
Materials and Methods: The study was performed on 10 patients, who had multiple treatments in the department of oral and maxillofacial surgery. The research contained data from the anamnesis, history of the disease, clinical examination, and paraclinical examination. Cell transplantation was used, collected from the ileum bone grafting and produced at The Laboratory of Tissue Engineering and Cell Cultures of the *Nicolae Testemitanu* State University of Medicine and Pharmacy, in cooperation with the Human Tissue Bank from Orthopedic and Traumatology Hospital from the Republic of Moldova.
Results: This method was performed on 4 women and 6 men of 35-55 years of age. The reconstruction surgery of the upper jaw included the closing of the oro-sinusal communication, by forming a mucoperiosteal graft from the hard palate and repositiong and suturing it onto the defect, with later injecting cell transplant into the surgical site. After 14 days an acrylic removable denture is confectioned, which stimulates bone tissue growth by applying pressure. After the reconstruction surgery of the oral cavity the communication may form again due to lack of tissue, but this method prevents contamination of the sinus with food, as well as stimulates osteocyte growth.
Conclusions: The use of cell transplants and acrylic dentures after reconstruction surgery of the upper jaw speeds up the healing process and forming of bone tissue.
Keywords: jaws, necrosis, cell transplant.

STEM CELL TRANSPLANTATION IN BIPOLAR DISORDER: EXPLORING REGENERATIVE TREATMENT APPROACHES

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Introduction: Bipolar disorder (BD) is a chronic neuropsychiatric condition affecting over 1% of the global population, characterized by alternating episodes of mania and depression. Traditional pharmacological treatments, such as lithium, valproate, and lamotrigine, remain the cornerstone of BD management; however, many patients experience treatment resistance and long-term adverse effects. With emerging advances in regenerative medicine, cell-based therapies, including stem cell transplantation, are being explored as potential interventions for neuropsychiatric disorders, offering a new direction in BD treatment.
Materials and Methods: Recent studies using induced pluripotent stem cells (iPSCs) derived from BD patients have enabled the creation of neural organoids that replicate disease-specific molecular and structural abnormalities. Functional and transcriptomic analyses have highlighted neuroinflammatory dysregulation, particularly involving interleukin-6 (IL-6), as well as alterations in neuronal plasticity pathways, including Wnt/β-catenin signaling. Additionally, research into microRNA expression patterns suggests potential biomarkers for predicting lithium responsiveness. Experimental approaches have also investigated the potential of mesenchymal stem cells (MSCs) and exosome-based therapies in modulating neuroinflammation and promoting neuronal regeneration.
Results: Preclinical studies indicate that stem cell transplantation may enhance neuroplasticity, restore synaptic function, and regulate immune responses, potentially targeting the underlying pathophysiological mechanisms of BD. Preliminary findings suggest that MSCs and neural progenitor cells exert neuroprotective effects through paracrine signaling, anti-inflammatory properties, and trophic support. Additionally, exosome-based therapies derived from stem cells have shown promise in delivering neurotrophic factors and modulating gene expression, opening avenues for personalized, cell-based interventions in BD.
Conclusion: The transition from conventional pharmacotherapy to regenerative medicine represents a paradigm shift in BD treatment. While pharmacological interventions remain essential, stem cell-based therapies offer the potential for long-term neuroprotection and disease modification. Further clinical trials are needed to establish the safety, efficacy, and optimal administration protocols for stem cell transplantation in BD. As research advances, integrating regenerative medicine with existing psychiatric treatments may lead to more effective, personalized therapeutic strategies for patients with BD.
Keywords: Bipolar disorder, stem cell therapy, regenerative medicine, neuroinflammation, mesenchymal stem cells, exosome therapy, neuronal plasticity.

LIVER TRANSPLANTATION FROM A LIVING-DONOR

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Introduction. Living-donor liver transplantation (LDLT) is vital for end-stage liver disease and acute liver failure, alleviating organ shortages and reducing wait times. In the Republic of Moldova, where deceased-donor organs are limited, LDLT is crucial in addressing the growing need for liver transplants. This study aims to evaluate LDLT's effectiveness, impact on survival and role in enhancing quality of life.
Materials and Methods. A retrospective analysis was conducted on 18 medical records and operative reports of patients aged 3–56 years who underwent living-donor liver transplantation between January 2017 and May 2024. Selection was based on established criteria for living-donor transplantation. Data collected included demographic information, transplantation indications, postoperative course and complications.
Results. Of the 18 patients, 38.89% were female, while 61.1% were male. The age distribution was as follows: 16.7% were aged 1-20 years, 22.2% were aged 21-40 years, and 61.1% were aged 41-60 years. The primary indications for transplantation included liver cirrhosis 77.8%, Caroli's disease 5.6%, hepatoblastoma 5.6%, hepatocellular carcinoma 5.6%, and Budd-Chiari syndrome 5.56%. Postoperative complications included acute rejection 44.4%, biliary peritonitis 5.6%, external biliary fistula 5.6%, hepatic artery thrombosis 5.6%, seizures 5.6%. Postoperative recovery was observed in 55.6%, while 44.4% died.
Conclusions. Liver transplantation from a living-donor involves significant risks, with a postoperative mortality rate of 44.4%. Rigorous selection criteria and strict postoperative monitoring are essential to enhance long-term outcomes.
Keywords. liver transplantation, living donor, chronic liver failure, postoperative complications.

EXPLORING THE IMPACT OF MESENCHYMAL STEM CELLS ON CHRONIC WOUND REPAIR

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Introduction: Chronic wounds are a significant medical concern, especially among the aging population, with conditions like diabetic ulcers, and venous leg ulcers being prominent examples. These wounds often fail to heal due to various factors such as impaired cellular regeneration, prolonged inflammation, and poor vascularization. Mesenchymal stem cells (MSCs), known for their multipotency and regenerative potential, have emerged as a promising therapeutic strategy for chronic wound healing. This review evaluates the current understanding of MSCs' role in chronic wound healing, highlighting their mechanisms of action and clinical relevance.
Materials and Methods: The reviewed studies included a variety of in vitro and in vivo models, alongside clinical trials, investigating the effects of MSCs on chronic wound healing. Key databases like PubMed and Scopus were searched using terms such as "mesenchymal stem cells," "chronic wound healing," and "wound regeneration." Both preclinical and clinical studies published within the last decade were included to assess the potential of MSC therapies in chronic wound management. Research focused on the mechanisms of MSCs, including their ability to modulate inflammation, promote angiogenesis, and enhance tissue regeneration.
Results: Mesenchymal stem cells have demonstrated considerable promise in chronic wound treatment. In vitro studies have shown that MSCs can enhance fibroblast proliferation, collagen synthesis, and extracellular matrix formation, which are crucial for wound healing. In vivo, MSCs have been shown to reduce inflammation by modulating immune responses, thereby preventing excessive scar tissue formation. Furthermore, their paracrine factors—such as growth factors, cytokines, and extracellular vesicles—play a significant role in promoting angiogenesis, epithelialization, and tissue remodeling. Clinical trials have also reported improved healing rates, reduced infection, and enhanced tissue regeneration in patients with chronic wounds following MSC therapy.
Conclusion: Mesenchymal stem cells offer a promising therapeutic option for chronic wound management due to their regenerative and immunomodulatory properties. While preclinical data and early-stage clinical studies are promising, more large-scale, well-designed clinical trials are necessary to establish optimal treatment protocols, dosages, and long-term efficacy. MSCs could potentially transform the management of chronic wounds, providing a much-needed solution for a condition that remains a major challenge in healthcare today.
Keywords: mesenchymal stem cells, wound process, chronic wounds.

REVIEW OF RODENT HYPERTENSION GLAUCOMA MODELS

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Background: Hypertension is a major risk factor for glaucoma, a leading cause of irreversible blindness. Elevated intraocular pressure (IOP) is central to glaucoma pathology, often causing optic nerve damage and retinal ganglion cell (RGC) death. Rodent models, particularly in rats and mice, have been widely used to study hypertension-induced glaucoma, offering valuable insights into disease mechanisms and potential therapies.
Materials and Methods: Various rodent models of hypertension-induced glaucoma are created through systemic administration of hypertensive drugs (e.g., angiotensin II, deoxycorticosterone acetate), salt-loading, or surgical interventions such as episcleral vein ligation. IOP is typically measured using tonometry, and retinal and optic nerve changes are assessed through histology, electroretinography (ERG), and optical coherence tomography (OCT). PubMed was searched for relevant studies using terms like "hypertension glaucoma rodent models," "IOP elevation in rodents," and "optic nerve damage in rodent models" to identify peer-reviewed articles published in the last two decades. Studies were selected based on their relevance to hypertension-induced glaucoma and IOP measurement techniques.
Results: Hypertensive rodent models exhibit key features of glaucoma, including elevated IOP, retinal ganglion cell loss, and optic nerve damage. These models show increased oxidative stress, inflammation, and ischemia, all contributing to glaucomatous damage. Histologically, they exhibit retinal ganglion cell loss and thinning of the retinal nerve fiber layer. Studies have demonstrated the potential for neuroprotective treatments, such as antioxidants and anti-inflammatory agents, to reduce retinal damage and IOP elevation in these models.
Conclusions: Rodent models of hypertension-induced glaucoma are invaluable for studying the pathophysiological mechanisms of glaucoma and testing therapeutic approaches. These models provide insights into neuroinflammation, ischemia, and oxidative stress in hypertensive glaucoma. While they replicate many aspects of human disease, they do not fully mimic the chronicity of IOP elevation seen in humans. Nonetheless, these models are crucial for advancing glaucoma research and developing effective treatments for hypertension-related glaucoma.
Keywords: glaucoma, iop, rodent models.

CARDIORENAL SYNDROME AND CELLULAR THERAPEUTIC PERSPECTIVES: RISK FACTOR IDENTIFICATION FOR TARGETED INTERVENTIONS

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Introduction. Cardiorenal syndrome (CRS) is a complex pathological condition that highlights the bidirectional relationship between heart failure and chronic kidney disease. This interdependence is driven by multiple pathophysiological mechanisms, including the activation of the renin-angiotensin-aldosterone system, oxidative stress, and chronic inflammation. Cardiorenal syndrome (CRS) is associated with increased mortality and morbidity, making the identification of risk factors essential for effective prevention and management.
Objective. This study aims to identify and classify the risk factors associated with cardiorenal syndrome (CRS) to support the early identification of vulnerable patients and contribute to optimizing prevention and treatment strategies.
Materials and Methods. This prospective-retrospective study included 60 patients diagnosed with cardiorenal syndrome, treated between 2022 and 2024 at *Sfânta Treime* Municipal Hospital. The results were analyzed using statistical methods and compared with data from contemporary literature.
Results. Data analysis identified both traditional and non-traditional risk factors. Among the non-modifiable traditional risk factors, male sex predominated (60% men vs. 40% women), with a ratio of 1.5:1 and a mean age of 70.42 ± 1.28 years. The prevalence of modifiable risk factors was as follows: hypertension (96%), ischemic heart disease (80%), cerebrovascular disease (66%), obesity (57%), diabetes mellitus (55%), anemia (37%), dyslipidemia (33%), history of myocardial infarction (32%), and history of stroke (24%). Our study highlights the high prevalence of hypertension (96%) and ischemic heart disease (80%) in patients with cardiorenal syndrome, emphasizing the significant role of these factors in disease progression. Early identification and optimal management of modifiable risk factors such as obesity (57%) and diabetes mellitus (55%) could contribute to improved patient outcomes.
Conclusions. This study underscores the importance of early identification of major risk factors in CRS. An integrated management approach combining pharmacological treatment and lifestyle modifications can significantly reduce disease progression and associated complications. Our findings suggest the necessity of national screening programs and continuous medical education to improve the prognosis and quality of life of patients with CRS.
Keywords: cardiorenal syndrome, risk factors, heart failure, chronic kidney disease.

STEM CELLS IN REGENERATIVE DENTISTRY: ACTUALITIES AND FUTURE DIRECTIONS

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Introduction. Stem cells are pluripotent cells capable of differentiating into various specialized cell types, making them a promising tool in regenerative dentistry. Their potential to regenerate different parts of the teeth, such as pulp, periodontal ligament, and alveolar bone, presents a biological alternative to traditional dental treatments.
Materials and Methods. This paper is based on a literature review of regenerative medicine. We used Google Scholar, PubMed, and other relevant databases to identify relevant documents about the reconstruction of the teeth using stem cells. Out of 47 articles were selected 20 published within the last 10 years.
Results. Stem cells used in regenerative dentistry include *dental pulp stem cells* (DPSCs), *periodontal ligament stem cells* (PDLSCs), and *stem cells from exfoliated deciduous teeth* (SHEDs). These cells are isolated via enzymatic digestion of dental tissues and cultured in specific media containing growth factors such as *epidermal growth factor* (EGF) *and fibroblast growth factor* (FGF) for expansion. To induce differentiation, DPSCs are cultured in mineralizing media for odontogenesis, while PDLSCs are treated with factors like *transforming growth factor-beta* (TGF-β) to stimulate periodontal regeneration. Biomaterial scaffolds, such as hydroxyapatite and collagen, are used to support cell attachment and tissue formation. Animal models, including rodents and large mammals, are employed to test the regenerative potential of stem cells *in vivo*, using histological analysis and molecular assays to assess tissue integration, differentiation, and marker expression.
Preclinical studies have demonstrated the successful regeneration of dental tissues. DPSCs have been shown to differentiate into odontoblast-like cells and form dentin-like structures, facilitating pulp regeneration. PDLSCs have been used to regenerate periodontal tissues, including alveolar bone and ligament fibers when combined with scaffolds. Early clinical trials also indicate favorable outcomes in periodontal regeneration, with improved tissue healing and function.
Conclusion. Stem cell-based therapies in regenerative dentistry hold significant potential for tissue restoration, providing a biological solution for dental tissue loss. While preclinical results are promising, further refinement of cell differentiation protocols, scaffold design, and clinical trials is necessary to establish standardized and effective therapies for broader clinical use.
Keywords: Stem cells transplant, Regenerative dentistry, Dental pulp stem cells (DPSCs).

ENDOCRINE DISRUPTORS-A CURRENT PROBLEM FOR THE HUMAN BODY

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Introduction. Endocrine disruptors are chemical substances that cause adverse effects in an organism or its offspring, leading to morphological and physiological changes and contributing to the deterioration of functional capacities. In the human body, hormones link the nervous system to the body's functions. Endocrine disruptors are present in many products and environments of our daily lives, and the impact on the human body is complex.
Materials and Methods. Sources from the relevant literature, the results of scientific studies, articles published in specialized journals, recommendations of international organizations, regulations stipulated in the legislation of the European Union were evaluated.
Results. Today, the problem of endocrine disruptors is attested at a global level. Currently, the action of these products on the human body in the Republic of Moldova is under-researched. Of the extremely large number of chemical substances produced and used at the moment, approximately 1000 of them possess properties with an impact on the endocrine system. Exposure to endocrine disruptors occurs through ingestion of food and water, inhalation of airborne particles, and through the skin. Endocrine disruptors act similarly to natural hormones by either mimicking their action or blocking it, leading to confusion in the system and disrupting not just one, but multiple hormonal systems and endocrine functions. This results in drastic consequences for biological processes and may even have genetic effects. The effects caused by an endocrine disruptor may sometimes be observed long after exposure. General morbidity and mortality in the Republic of Moldova in recent years has been recorded at a high level, being conditioned by non-communicable diseases. The prevalence of endocrine, nutritional and metabolic diseases is constantly increasing, from 2014 to 2023, the prevalence indicator increasing from 200.8 thousand cases to 312.6 thousand cases.
Conclusions. Endocrine disruptors are omnipresent chemical substances that can have significant negative effects on health. From reproductive and developmental issues to autoimmune diseases and metabolic disorders, they represent a serious threat to human health. It is essential to be aware of the presence of these substances in our environment and to take measures to minimize exposure.
Keywords: human body, endocrine disruptors, health, morbidity, exposure.

CURRENT EVENTS IN LIVER TRANSPLATOLOGY

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Background. Liver transplantation is a surgical procedure that involves removing a diseased liver and replacing it with a healthy liver from another person, called a donor. This procedure is used when the liver is unable to perform its normal functions (liver failure or end-stage liver disease). The types of transplant are from a living donor (the right lobe of the liver is used) and from a deceased donor (the entire liver of the donor is used along with the portal vein).
Materials and methods. To carry out the study, the selection and analysis of bibliographic sources published in specialized medical scientific databases between 2018-2024 available online were carried out.
Results Liver transplantation techniques are whole liver (from deceased donor), reduced liver (left lobe or segments 2-3 compatible with the pediatric recipient), split liver (two grafts that can be used for either an adult and a child, or for two adults), domino (sequential, where a young patient with a metabolic disorder receives a liver from a deceased donor, and the young patient's liver is harvested for donation to an older patient with end-stage liver disease), dual graft (2 grafts from 2 different donors). For the highest possible success rate of liver transplantation, some basic principles must be followed, such as high genetic compatibility, perfect harvesting and transplantation technique, and careful postoperative care. The most common indications for liver transplantation are end-stage chronic liver diseases, acute liver failure, non-resectable malignant liver diseases, and hereditary-metabolic liver diseases.
Conclusions The only hope for long-term survival of a person with liver failure is a liver transplant. Liver transplant patients require clinical, biochemical, and instrumental monitoring to detect early (acute rejection, early and late hepatic artery thrombosis, arterial stenosis, acute Budd Chiari syndrome, anastomotic fistula) and late (chronic rejection, chronic Budd Chiari syndrome, portal vein thrombosis, portal vein stenosis, recurrent sclerosing cholangitis, papillary stenosis, proximal hepatic duct stenosis) complications. To increase the tolerability, safety and adherence of the therapy in the long term, the patient will undergo treatment with immunosuppressants and antivirals.
Keywords transplant, principles, treatment, monitoring.

Varia

SPECIFIC FEATURES OF THE FACIAL NERVE TRUNK

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Introduction: The facial nerve trunk (FNT) is vulnerable to iatrogenic injures in surgery of the retromandibular region, particularly in mastoidectomy. Variation of the FNT number, topography and course increase the risk of its iatrogenic injures. Our goal was to determine the length of the FNT depending on the gender, laterality, cephalometric type, branching pattern and variant of branching.
Materials and Methods: The study was conducted on 75 formalized adult hemiheads (59 males and 16 females), dissected at the Department of Anatomy and Clinical Anatomy of *Nicolae Testemitanu* State University of Medicine and Pharmacy. The length of the FNT was measured from the point of its exit through the stylomastoid foramen until point of its division into primary branches. One-way ANOVA, t-test and $\chi 2$ test were used for statistical analysis.
Results: In males the mean length of the FNT was 11.3 mm and in females it was 10.4 mm, $p = 0.289$. Bilaterally the length of the FNT was equal to 11.1 mm, $p = 0.981$. The mean length of the FNT in mesocephalic type was 10.9 ± 2.87 mm, in brachycephalic type it was 12.3 ± 3.54 mm and in dolichocephalic type it was 10.9 ± 2.54 mm. The intergroup frequency variation (IGFV = 0.755); the degree of freedom ($df = 2$); $p = 0.474$. Seven branching patterns of the extracranial portion of the facial nerve were revealed in the current study. Depending on the branching pattern the length of the FNT varied as follows: Type I (12.2 ± 3.33 mm); Type II (11.0 ± 2.54 mm); Type III (11.3 ± 2.93 mm); Type IV (10.3 ± 3.85 mm); Type V (11.5 ± 2.08 mm); Type VI (10.1 ± 2.06 mm); Type NI-atypical (11.5 ± 3.11 mm); IGFV = 0.794; $df = 6$; $p = 0.578$. In classic branching patterns the mean length of the FNT was 11.4 mm, while in atypical variants, it was 10.6 mm; $p = 0.258$.
Conclusion: The length on the FNT was variable on four of the examined criteria. The FNT was longer in males, in brachycephalic type, in Type I and in classic variant of branching.
Keywords: facial nerve trunk, individual peculiarities, length, morphometry.

VARIABILITY OF THE PAIRED VISCERAL BRANCHES OF THE ABDOMINAL AORTA

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Introduction: The demand for an individualized approach in interventional surgery of abdominal cavity organs has recently increased. Due to various surgical techniques and large number of surgeries, including kidney transplant, the variants of the paired visceral branches of the abdominal aorta (PVBAA) are clinically important, in terms of patient's safety and avoidance of complications. The variability of the PVBAA in the Republic of Moldova was reported on a rate of 1.3% referred to the total number of births. Our research aimed to evaluate the variants of the PVBAA in order to update the data on their anatomical variability.
Materials and Methods: A thorough analysis of Web of Science, Google Scholar, Scopus, PubMed and Medline databases, referred to variability of the PVBAA, was conducted. Only full articles were selected and analyzed for our purpose.
Results: The highest ratio of variability, among the PVBAA was established for the renal artery (RA). The following incidence of numerical variants was revealed: double RA (70.9%), accessory RA (32%), triple RA (11.1%), multiple RA (18%). Presence of common arterial trunks from the AA was marked out at a rate of 20-30%. A few topographical variants of the accessory renal artery origin such as: high origin (above the main renal artery), and more rare a low origin (below the main RA, or even at the level of the common iliac arteries), were revealed. Among the rare anatomical variants, an atypical double arterial anastomosis between the right portion of the Barkow's omental arch with distribution within the uterus and right ovary was reported.
Conclusions: The highest incidence of PVBAA variants was revealed for the RA, the most common being numerical variants. Knowledge of arterial variants of the PVBAA is of high clinical significance in abdominal surgery, particularly in cases of rare and unknown variants.
Keywords: variability, abdominal aorta, renal artery, testicular artery, ovarian artery.

ANATOMICAL VARIABILITY OF THE DEEP FEMORAL ARTERY

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Introduction: The deep femoral artery (DFA) serves as a crucial „turning point" between collateral circulation of the pelvis and that of the lower limb (LL), playing a determinant role not only in femoropopliteal axis obstruction, but also in aortoiliac obstructive disease. Choice of the surgical method depends on surgeon's experience, intraoperative anatomical situation and a significant role is atributed to the variability of the deep femoral artery. The aim of our study was to investigate the anatomical variants of the deep femoral artery depending on gender and laterality.
Materials and methods. The variability of the deep femoral artery (DFA), as the main collateral branch of the femoral artery (FA) was studied on 40 lower limb angiographies, taken from the database of the Endovascular Surgery Department of MSPI CRH *Timofei Moșneaga*. All the angiographies of the study sample size belonged to patients without any arterial pathology. The analysis of the lower limb arterial angiographies aimed to translate the anatomy of the DFA from the virtual model to the real one, in order to identify its variability based on gender and laterality, according to the studied criteria: origin, numerical variations and branching pattern.
Results. Eleven patients (27.5%) had different variants of the deep femoral artery, out of which 7 patients (17.5%) were males (12.5% with variants of the right LL and 5% with variants of the left LL), and 4 patients (10%) were females (7.5% with variants of the right LL and 2.5% with variants of the left LL). Variability of the DFA origin was identified in 10.0% of cases (high origin in 7.5% and low origin in 2.5%). In 5.0% of cases numerical variants were determined and in 12.5% variants of branching pattern were revealed. The following variants of the DFA branching pattern were established: 1. Bifurcation of the DFA into two branches – the medial circumflex femoral artery (MCFA) and the lateral circumflex femoral artery (LCFA), was identified in 5% of cases; 2. The DFA gave rise to the LCFA and three perforating arteries (PA), while the MCFA in 5.0% of cases derived from the femoral artery (FA); 3. The DFA gave rise to the MCFA and three PA, while the LCFA in 2.5% of cases started from the femoral artery (FA).
Conclusions: The deep femoral artery is more frequently variable in males, and on the right side. To enhance the safety and efficacy of any procedures performed at the thigh level, it is crucial to be aware of the deep femoral artery anatomical variability.
Key words: femoral artery, deep femoral artery, anatomical variants, variability.

NEUROPROTECTIVE EFFECTS OF ETHANOLIC EXTRACTS FROM *SOLANUM MACROCARPON* IN A ZEBRAFISH MODEL OF SCOPOLAMINE-INDUCED ALZHEIMER'S DISEASE-RELATED DEMENTIA

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Introduction. Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and oxidative stress. Natural bioactive compounds with antioxidant and neuroprotective properties have gained interest as potential therapeutic agents. *Solanum macrocarpon*, known for its antimicrobial, antioxidant, and anti-inflammatory effects, may offer neuroprotective benefits. This study investigates the effects of its ethanolic extract (SMEE) in a zebrafish model of scopolamine (Scop)-induced cognitive impairment, emphasizing its impact on oxidative stress, cholinergic modulation, and behavioral parameters.

Materials and Methods. Zebrafish were exposed to SMEE at concentrations of 1, 3, and 6 mg/L for 23 days before immersion in scopolamine (100 μM) to induce cognitive deficits. Behavioral tests, including the Novel Tank Diving Test (NTT), Novel Approach Test, Y-Maze, and Novel Object Recognition (NOR), were performed to assess memory and anxiety-related behaviors. Acetylcholinesterase (AChE) activity and oxidative stress markers were quantified using spectrophotometric methods. To elucidate the neuroprotective mechanisms, antioxidant enzyme activities (superoxide dismutase - SOD, catalase - CAT, and glutathione peroxidase - GPX) were measured, along with markers of oxidative damage such as protein carbonylation and lipid peroxidation (malondialdehyde - MDA). Pearson correlation analyses were conducted to assess relationships between behavioral parameters, enzymatic activities, and oxidative stress markers. In addition, HPLC analysis identified chlorogenic acid and rutin as major polyphenolic components in SMEE, followed by an in silico pharmacokinetic evaluation (ADMET) to assess their absorption, metabolism, and toxicity profiles.

Results. SMEE administration significantly improved spatial and recognition memory, reducing anxiety-like behavior in zebrafish exposed to Scop. The extract also counteracted oxidative stress by enhancing the activity of antioxidant enzymes (SOD, CAT, GPX) and reducing protein oxidation and lipid peroxidation (MDA levels). Pearson correlation analysis showed significant negative correlations between MDA levels and behavioral performance, as well as SOD, CAT, and GPX activities, indicating a direct link between oxidative stress reduction and cognitive improvement. HPLC analysis confirmed the presence of chlorogenic acid and rutin, which exhibited strong antioxidant properties. ADMET analysis suggested that these compounds have lower intestinal absorption but a favorable neuroprotective profile.

Conclusions. The findings indicate that *Solanum macrocarpon* ethanolic extract has potential therapeutic benefits in mitigating cognitive decline and oxidative stress, supporting its use as a natural neuroprotective agent in Alzheimer's disease. Further studies are warranted to elucidate its precise mechanisms and clinical relevance.

Keywords. *Solanum macrocarpon*, zebrafish, cognitive impairment, oxidative stress, acetylcholinesterase, scopolamine, Alzheimer's disease, HPLC, antioxidant enzymes, neuroprotection.

CORRELATION BETWEEN CD45 EXPRESSION AND CLINICAL-PATHOLOGICAL VARIABLES IN INVASIVE DUCTAL BREAST CARCINOMA ASSOCIATED WITH TYPE 2 DIABETES MELLITUS

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Introduction. This study investigates the correlation between CD45 expression and clinical-pathological variables in invasive ductal breast carcinoma associated with type 2 diabetes mellitus. CD45, an immune regulator, was analyzed to assess its role in tumor progression and prognosis.
Materials and Methods. A descriptive, retrospective study analyzed 58 cases of NST invasive ductal breast carcinoma, diagnosed between 2021 and 2022 at the Oncology Institute of Moldova. Among these, 29 patients had carcinoma associated with type 2 diabetes mellitus (T2DM). The mean age in the T2DM group was 63.2±6.5 years, while the non-diabetic group averaged 64.5±7.9 years. Preoperative glucose was measured colorimetrically using Selectra Pro XL. A control group included mammary tissue from 30 women who died accidentally, without any oncological disease (mean age 64.2±6.2 years). Statistical analysis used Spearman's correlation to assess CD45 expression relative to tumor grade, Nottingham score, nuclear atypia, mitotic activity, hormone receptors, Ki67, lymphovascular and perineural invasion.
Results. Intratumoral CD45 expression showed weak correlations with tumor grade ($r = 0.10$, $p = 0.30$) and Nottingham score ($r = 0.19$, $p = 0.16$). In contrast, peritumoral CD45 expression exhibited significant positive correlations with tumor grade ($r = 0.48$, $p < 0.01$) and Nottingham score ($r = 0.34$, $p = 0.03$). Furthermore, peritumoral CD45 CR expression negatively correlated significantly with estrogen receptor (ER; $r = -0.41$, $p = 0.01$), progesterone receptor (PR; $r = -0.41$, $p = 0.01$), and Allred ER and PR scores (ER $r = -0.43$, $p = 0.01$; PR $r = -0.46$, $p = 0.01$). A positive correlation with patient age ($r = 0.37$, $p = 0.02$) was also observed.
Conclusions. Peritumoral CD45 expression significantly correlates with tumor differentiation, hormonal receptor status, and patient age. These findings suggest that CD45 could be a valuable prognostic biomarker, particularly relevant for immune regulation in T2DM-associated breast carcinoma, warranting further research.
Keywords. CD45, tumor microenvironment, breast cancer, hormone receptors, immune response, T2DM, Nottingham score, mitotic activity, Ki67, peritumoral infiltration.

NASAL PERMEABILITY IN INFLAMMATORY RHINOSINUSAL DISEASES IN CHILDREN

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Introduction: Rhinosinusal inflammatory diseases constitute a current problem of contemporary rhinology. Rhinitis, sinusitis seriously affect the physiological functions of the nose, including the most important of them, the respiratory function. However, in the specialized literature nasal breathing and its role in achieving the physiological status of the nose is insufficiently elucidated.
Material and methods: Under our supervision were 80 children with rhinosinusal pathology aged between 6 and 15 years, who were divided into two groups. Group 1 included 40 children (22 boys and 18 girls) with chronic hypertrophic rhinitis, and group 2 consisted of 40 patients (21 boys and 19 girls) with chronic rhinosinusitis. At the same time, 30 healthy children (17 boys and 13 girls) formed the control group.
In order to assess nasal permeability, we used acoustic rhinometry, a non-invasive and highly accurate method, which reveals conclusive data about the volume and geometry of the nasal fossae by measuring the minimum cross-sectional area.
Results: The results obtained showed that nasal permeability was affected in both groups of patients, slightly prevalent in patients with chronic hypertrophic rhinitis where MCSA (minimum cross-sectional area) values were MCSA-1 = 0.215 ± 0.012, and MCSA-2 = 0.325 ± 0.041. At the same time, in patients with chronic rhinosinusitis the MCSA-1 values were 0.241 ± 0.018, and MCSA-2 = 0.385 ± 0.067. In the control group, the MCSA-1 and MCSA-2 values were significantly higher, 0.410 ± 0.055 and 0.520 ± 0.050, respectively. These differences are statistically significant and indicate a decrease in nasal permeability in rhinosinusitis inflammations.
Conclusions: Thus, nasal permeability, assessed by acoustic rhinometry, was statistically reduced in inflammatory rhinological diseases, both in chronic sinusitis and in hypertrophic rhinitis. At the same time, in patients with chronic hypertrophic rhinitis, the indices of the minimum transverse areas were lower, which means a more pronounced impairment in these patients. In both study groups, nasal permeability was reduced compared to healthy children.
Keywords: chronic sinusitis, chronic hypertrophic rhinitis, nasal permeability, acoustic rhinometry.

REVIEW: THE ROLE OF COLOR DOPPLER ULTRASOUND IN THE EVALUATION OF THYROID NODULES

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Background: Thyroid nodules are commonly detected in clinical practice, with a significant portion being benign, but a small percentage harbor malignancy. Accurate evaluation of these nodules is crucial for guiding management decisions, such as the need for biopsy or surgery. Color Doppler ultrasound, an advanced imaging technique, is increasingly used to assess thyroid nodules by evaluating blood flow within the nodule. The **aim** of this review is to examine the role of color Doppler ultrasound in the diagnostic workup of thyroid nodules and its effectiveness in differentiating benign from malignant nodules.
Material and Methods: A review of studies published in medical databases, including PubMed and Cochrane Library, was conducted to evaluate the utility of color Doppler ultrasound in assessing thyroid nodules. Key studies focused on the use of Doppler imaging to analyze vascularity patterns in thyroid nodules and its correlation with malignancy. The review included articles that assessed the sensitivity, specificity, and overall diagnostic performance of color Doppler in the context of thyroid nodule evaluation.
Results: Color Doppler ultrasound assesses blood flow within a thyroid nodule, with malignant nodules often exhibiting abnormal vascular patterns, such as increased peripheral or internal blood flow. Studies have shown that color Doppler ultrasound can provide additional information beyond conventional ultrasound, particularly in nodules with ambiguous characteristics. Malignant thyroid nodules are frequently associated with increased vascularity, irregular blood vessels, or a higher resistance index in blood flow. Sensitivity and specificity for identifying malignancy using color Doppler ultrasound vary across studies but generally range from 60% to 90%. However, the technique is not definitive on its own and is often used in combination with conventional ultrasound features such as size, shape, and margins of the nodule.
Conclusion: Color Doppler ultrasound is a valuable adjunct in the evaluation of thyroid nodules, helping to differentiate benign from malignant lesions based on vascular patterns. While it enhances diagnostic accuracy, especially for nodules with uncertain characteristics, it is not a standalone diagnostic tool. Color Doppler should be used in conjunction with other imaging modalities like conventional ultrasound and fine needle aspiration biopsy (FNAB) to improve the overall diagnostic approach for thyroid nodule evaluation.

TELOMERE SHORTENING AS A MECHANISM FOR THE INDUCTION OF NEURODEGENETATIVE DISEASES

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Background. Telomeres are considered the "cellular biological clock" because their length could determine the possible number of cell divisions. Telomerase plays a role in maintaining telomere length. Telomerase ensures *de novo* addition of nitrogenous base sequences such as TTAGGG at the 3' end, protecting the chromosome end from double-strand breaks and preventing the DNA damage response (DDR).
Objective of the study. Identifying the mechanisms by which the progressive shortening of telomeres in nerve cells activates processes leading to neuronal senescence, with the aim of improving diagnosis and developing effective treatment methods.
Materials and Methods. To achieve the proposed objective, a literature review was conducted using 10 bibliographic sources from electronic libraries such as PubMed, MedScape, Hindawi, and ScienceDirect.
Results. Telomerase is active in young neural cells or neural precursor cells, but as they differentiate into mature neurons, its activity progressively decreases, affecting neuronal differentiation and stopping neurogenesis. In the absence of telomerase, telomere shortening can reach critical lengths, triggering a DDR-type response. This process induces the activation of ataxia-telangiectasia mutated kinase and other signaling proteins such as p53 and p21. The p53 protein plays a role in halting the cell cycle by activating p21, which inhibits cyclin-dependent kinase 2 and blocks the phosphorylation of the retinoblastoma protein (Rb). Hypophosphorylated Rb blocks E2 factor, a transcription factor, preventing the expression of genes necessary for cell division and causing cell cycle arrest in the G1 phase, leading to replicative senescence. Senescent cells secrete a senescence-associated secretory phenotype, which contributes to chronic inflammation and the spread of senescence in neighboring tissues. Chronic inflammation accelerates the accumulation of toxic proteins, such as beta-amyloid in Alzheimer's or alpha-synuclein in Parkinson's, promoting neuronal death and disease progression.
Conclusion: Telomere shortening in nerve cells induces senescence and chronic inflammation, accelerating neurodegeneration in diseases such as Alzheimer's and Parkinson's. Future therapies could aim at controlled activation of telomerase, the use of senolytic cells to eliminate senescent cells, and blocking senescence-associated secretory phenotype to reduce inflammation. These approaches could help slow down the neurodegenerative process and contribute to the development of more effective treatments.
Keywords: telomeres, telomerase, neurodegeneration, senescence.

MITOCHONDRIAL CALCIUM REGULATION IN ALZHEIMER`S DISEASE

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Background. Calcium ions (Ca^{2+}) play an essential role in neuronal function, contributing to synaptic transmission, interneuronal communication, and neuroglial interactions. Mitochondria regulate the intracellular homeostasis of Ca^{2+}, and disruption of this balance, as seen in Alzheimer's disease, promotes neuronal apoptosis and cerebral atrophy.
Objective of the study. To identify disturbances in Ca^{2+} homeostasis within nerve cells that contribute to the development of Alzheimer's disease, with the goal of improving diagnosis and developing effective treatment strategies.
Materials and Methods. To achieve the proposed objective, a literature review was conducted using 10 bibliographic sources, drawing data from electronic libraries such as PubMed, MedScape, Hindawi, and ScienceDirect.
Results. Under physiological conditions, Ca^{2+} enters the mitochondria through voltage-dependent ion channels (VDAC) at the level of the outer mitochondrial membrane and then traverses the inner membrane via the mitochondrial calcium uniporter. The efflux of Ca^{2+} from mitochondria is carried out by the $Na^{+}/Ca^{2+}/Li^{+}$ exchanger, thus maintaining ionic balance. The transfer of Ca^{2+} between the endoplasmic reticulum (ER) and mitochondria occurs via mitochondrial membrane junctions, formed through the interaction of IP_3 receptors (IP_3Rs) with VDAC, mediated by glucose-regulated protein 75, a molecular bridge that facilitates this interaction. In Alzheimer's disease, β-amyloid oligomers and presenilin mutations (PSEN1 and PSEN2) upregulate IP_3Rs, increasing Ca^{2+} release from the ER to the mitochondria. Additionally, the C99 cleavage product of amyloid precursor protein promotes the stabilization of ER–mitochondria coupling via the mitofusin-2 protein, enhancing Ca^{2+} influx into mitochondria. This mitochondrial Ca^{2+} overload induces the opening of the mitochondrial permeability transition pore (mPTP). Once open, mPTP allows the uncontrolled release of ions, reactive oxygen species, and pro-apoptotic and pro-necrotic factors from the mitochondrial matrix into the neuronal cytoplasm, thereby contributing to cell death and the neurodegenerative processes characteristic of Alzheimer's disease.
Conclusion: Maintaining calcium ion (Ca^{2+}) homeostasis is essential for normal neuronal function. In Alzheimer's disease, disruption of Ca^{2+} flux contributes to mitochondrial dysfunction and cell death. A detailed understanding of these processes is crucial for elucidating the pathogenesis of Alzheimer's disease and for developing new therapeutic strategies targeting mitochondrial

THE ROLE OF ENDOTHELINS IN CANCER PROGRESSION: RECENT INSIGHTS AND THERAPEUTIC OPPORTUNITIES

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Background. Endothelins (ETs) and their receptors (ETAR and ETBR) play a significant role in cancer progression, influencing processes such as proliferation, invasion, and metastasis. The endothelin axis contributes to modulating the tumour microenvironment (TME), affecting angiogenesis, immune evasion, and therapeutic resistance.
Objective of the study. To elucidate the role of endothelins in cancer progression, metastasis and treatment resistance, as well as the need for therapeutic targeting of the endothelin axis.
Materials and methods. A comprehensive review of scientific literature was conducted using peer-reviewed sources from databases such as PubMed, ScienceDirect, MDPI, Biomed Central, and Wiley Online Library, focusing on the studies published between 2019 and 2024.
Results. Endothelin-1 (ET-1) stimulates tumorigenesis via β-arrestin-mediated signaling, activating mitogen-activated protein kinase (MAPK), phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), and Wnt/β-catenin pathways to induce pro-survival mechanisms and proliferation. It facilitates epithelial-mesenchymal transition (EMT) by upregulating matrix metalloproteinases (MMP-2, MMP-9) and suppressing tissue inhibitors of metalloproteinases (TIMPs), enhancing metastatic potential. Hypoxia amplifies ET-1 production, fostering angiogenesis through vascular endothelial growth factor (VEGF) upregulating and stabilizing hypoxia-inducible factor-1α (HIF-1α). ETBR expression correlates with immune evasion by recruiting M2-polarized macrophages and suppressing cytotoxic T-cell activity, observed in melanoma and gastric cancer. Despite promising preclinical results with ET receptor antagonists (bosentan, macitentan) in reducing tumor growth and metastasis, clinical trials have shown limited efficacy as monotherapies. Integrated strategies such as pairing ETAR inhibitors with paclitaxel or immune checkpoint blockers demonstrate enhanced antitumor effects by disrupting stromal-tumor crosstalk and vascular normalization. Emerging approaches, including polyphenols (quercetin, resveratrol) and extracellular vesicle-mediated gene silencing, offer novel routes to target ET-axis dysregulation. The endothelin axis is pivotal regulator of TME remodelling, influencing stromal interactions, immune suppression, and therapeutic resistance. Repurposing FDA-approved ET antagonists, represents a viable strategy to improve cancer outcomes. Further research should prioritize biomarker-driven patient stratification and dual-target therapies to address the complexity of ET signalling in malignancy.
Conclusions. The endothelin axis is central to cancer pathogenesis, influencing tumour processes and interactions within the tumour microenvironment. Targeting ET receptors offers promising therapeutic directions, particularly through repurposing approved ET receptor antagonists.
Keywords: endothelins, cancer progression, tumour microenvironment, angiogenesis, ET receptor antagonists.

CORRELATIONS BETWEEN ECHOCARDIOGRAPHIC FINDINGS AND SPECT CT AS A PREDECTIVE TOOL FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION IN POST-PULMONARY EMBOLISM PATIENTS

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a severe but potentially treatable complication of pulmonary embolism (PE). SPECT CT has emerged as a non-invasive modality capable of detecting residual perfusion defects, potentially improving early risk stratification. Current guidelines rely on echocardiographic and hemodynamic assessment for CTEPH diagnosis, but these methods may lack sensitivity in early-stage disease.
Objective: To investigate the predictive value of RV echocardiographic findings and SPECT CT in identifying PE survivors at risk of developing CTEPH and to assess its role in guiding therapeutic interventions.
Methods: It is a prospective study that enrolled PE survivors who had completed standard anticoagulation period (3-6 months). Patients underwent structured follow-up, including clinical assessment (dyspnea score, 6-minute walk test), echocardiography, biochemical markers (NT-proBNP), and SPECT CT imaging. Correlations between SPECT CT findings, right ventricular dysfunction, and pulmonary hemodynamics were analyzed using multivariate logistic regression on SPSS program.
Results: Among 86 enrolled patients, 30 underwent complete imaging workup, revealing persistent perfusion defects in 60% of symptomatic individuals. Of these, 43% exhibited echocardiographic markers suggestive of chronic thromboembolic pulmonary hypertension (CTEPH), with significant associations between perfusion abnormalities and elevated NT-proBNP levels ($p<0.001$). Echocardiographic findings suggest a strong correlation between TAPSE/PSAP rapport and the NTproBNP test ($p<0,001$), RV strain changes ($p<0,02$) and high probability of pulmonary hypertension ($p<0,001$). The severity of perfusion defects on SPECT CT correlated strongly with thoracic pain ($p<0,03$) and high probability of pulmonary hypertension ($p<0.03$). No statistical significant correlation found between SPECT CT changes and RV strain ($p<0,9$), 3D RVEF results ($p<0,1$) or TAPSE/PSAP rapport ($p<0,08$).
Conclusions: SPECT CT may represent a valuable imaging modality in early detection of post-PE sequelae, identifying patients with high probability of pulmonary hypertension who may benefit from more diagnostic tests or/and interventional and improving long-term cardiovascular outcomes. However, additional prospective scientific studies are required to draw definitive conclusions regarding its clinical utility and optimal integration into post-PE management.
Keywords: pulmonary embolism, chronic thromboembolic pulmonary hypertension, SPECT CT, TAPSE, RV echocardiography
Project code: 24.80012.8007.03SE

HEMODYNAMIC INDICATORS IN THE SUPERIOR MESENTERIC VEIN IN PATIENTS WITH HEPATIC CIRRHOSIS

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Introduction. Blood from the small intestine drains through the superior mesenteric vein. Defective blood flow, caused by hemodynamic deviations, lead to intestinal ischemia. Under these conditions, the cells of the digestive tract undergo necrosis with subsequent onset of inflammation and ulcerations in the digestive tract, thus impairing food absorption and causing bloody diarrhea. The purpose of the study consists in studying the blood supply in the superior mesenteric vein with Doppler quantification in liver cirrhosis.
Material and methods. 62 patients with liver cirrhosis - 46 men, 16 women, average age - 39±0.21 years, were studied. The parameters were calculated by Doppler quantification in the mesenteric vessels. The descriptive statistical test was applied.
Results. The diameter of the superior mesenteric vein (SVM) is 0.53±0.04 cm (0.87±0.02 cm), but doesn't exceed 1.0 cm; normal volumetric flow 194±25 ml/min; mean VLC is 14.8±1.5 cm/s. As the disease progresses, the volumetric flow decreases: oscillating between 179±0.13 ml/min and 185±0.5 ml/min. The maximum linear velocity of the circuit (VLC), on average, becomes accelerated over time– 17.9±0.6 cm/s. The resistance index averaged - 0.38; the pulsatility index - 1.26.
Conclusions. 1. The diameter of the superior mesenteric vein expands considerably, mainly during inspiration. 2. Dilation of the superior mesenteric vein reduces the velocity of systolic, diastolic and mean blood flow.
Keywords: mesenteric vein, volumetric flow, linear velocity.

THE CAPACITY OF HEPATIC HENODYNAMICS IN THE NUTRITIONAL ASSURANCE OF HEPATOCYTES IN THE ELDERLY

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Introduction. Blood supply to hepatocytes is severely compromised as a result of the difficult exchange of substances between hepatocytes and plasma, by the continuous deposition of collagen in the space of Disse, accompanied by the loss of fenestrations in the sinusoidal endothelial cells. The net result– fibrotic, nodular liver. The new vessels in the septa connect the vessels in the portal region (hepatic arteries and portal veins) and the terminal hepatic veins, altering blood flow. The purpose of the study consists in evaluation of indices of hepatic hemodynamic capacities in priority nutrient vessels in elderly patients with liver pathology.
Material and methods. Hemodynamic parameters were studied by Doppler quantification in 32 patients: 18 men and 14 women with an average age of 69±0,21 years. The descriptive statistical test was applied.
Results. The significant specificity and sensibility was demonstrated by changes in blood flow: decreased diastolic velocity (38%), increased volume velocity (57%) of the blood flow. The resistance index in the hepatic artery increased by 1,4%, the pulsatility index - by 6,3%, and the spatial velocity of the blood flow in the portal vein - by 7,7%. The spacial velocity oscillated between 990±69 ml/min and 1188±34 ml/min (approximately 20%).
Conclusions. 1. The arterial vascularization's sensitization implies heightened intraheptic vascular resistance amidst stagnant blood flow within the portal system in geriatric patients.
Keywords: Space of Disee, Doppler quantification, diastolic velocity, volume velocity.

LIENAL VEIN – HEMODYNAMIC ASPECTS IN PORTAL INSUFFICIENCY

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Introduction. The length of the lienal vein is 8–12 cm; caliber 6–12 mm, rectilinear trajectory. The lienal vein traverses the border of the pancreatic body, then joins the superior mesenteric vein at the pancreas neck to form the portal vein. The purpose of the study consists in **s**tudy of blood supply in the lienal vein in case of portal insufficiency.
Material and methods. Subjects to the study were 62 patients with liver cirrhosis - 46 men, 16 women, average age - 39±0.21 years. The studied linear parameters were calculated by Doppler quantification. The descriptive statistical test was applied.
Results. Normally, the lienal vein (LV) diameter is 0.6±0.02 cm, up to 0.8 cm; average values in healthy people - 0.7±0.04 cm, linear velocity (LVC) in LV-13.8±0.6 cm/s, volume velocity (VV) - 231±13 ml/min. In group I, LVC was 13.1±0.1 cm/s, in group II-23.0±0.3 cm/sec; the VV was – 157±0.4 and 366±12 ml/min, respectively. The portal-splenic venous index decreased by 43% compared to the norm, indicating a redistribution of blood flow in the veins of the portal system towards the spleen.
Conclusions. 1**.** The spectrographic curve in lienal vein increased more than 1.6 times. 2. These oscillations showed us that the diameter of the splenic vein expands considerably, reducing the speed of the systolic, diastolic and average blood flow both in the splenic vein and the portal vein.
Keywords: quantification, lienal vein, LVC, VV.

THE ROLE OF VITAMIN D IN THE Wnt/β-catenin SIGNALING PATHWAY

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Background. The Wnt/β-catenin signaling pathway is a complex system involved in immune homeostasis, tissue regeneration, and various physiological processes. Aberrant activation of the signaling pathway, driven by genetic and epigenetic changes, developes various cancers: colorectal carcinoma, gastric, esophageal, nasopharyngeal, breast.
Objective of the study. To elucidate the biochemical mechanisms of action of vitamin D on the Wnt/β-catenin signaling pathway in order to develop effective methods of prevention and treatment in cancer.
Materials and methods. A review of the literature from 2019-2024 was performed using 10 articles, including from the State University of Medicine and Pharmacy *Nicolae Testemitanu* Scientific Medical Library, Republic of Moldova, data from ScienceDirect, PubMed Central, Biomed Central, MDPI, Wiley Online Library, Febspress electronic libraries.
Results. The canonical Wnt/β-catenin pathway regulates cell differentiation, proliferation, and survival. Physiologically, this pathway is initiated by the binding of Wnt ligands to frizzled (FZD) receptors, that associate with low-density lipoprotein receptor 5 (LRP5) and LRP6. Without Wnt receptor activation, β-catenin is phosphorylated by the destruction complex (DC), including glycogen synthase kinase 3β (GSK3β), casein kinase 1α (CK1α), E3 ubiquitin ligase β-TrCP (SCFβ-TrCP), Axis inhibition protein (AXIN), and further degradation is carried out by proteasome. These processes prevent the accumulation of β-catenin in the nucleus and prevent further activation of the gene by the repressive complex containing theTCF/LEF family (T cell factor/lymphoid enhancer factor family). The Wnt/β-catenin pathway is activated when Wnt proteins bind to the FZD receptor, inhibiting DC and allowing β-catenin to accumulate in the cytoplasm, some of which translocates to the nucleus to activate TCF/LEF proteins. Abnormal expression of the signaling pathway causes excessive accumulation of β-catenin in tumor cells, which leads to tumor infiltration and metastasis progression. Calcitriol, $1,25(OH)_2D_3$, inhibits Wnt signaling in cancer cells through vitamin D receptor (VDR), blocking β-catenin from binding TCF and activating target genes.
Conclusions. Vitamin D administration significantly reduced Wnt and β-catenin expression, demonstrating its role in blocking β-catenin translocation. Currently, new strategies are being explored to develop effective drugs targeting this pathway for cancer treatment.
Keywords: Wnt/β-catenin, 1,25(OH)2D3, cancer, frizzled receptors, vitamin D receptor, destruction complex.

THE INFLUENCE OF CALCITRIOL ON THE WARBURG EFECT IN CANCER

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Background. Cancer cells undergo changes in the tumorigenic process through the Warburg effect, also known as aerobic gligolysis. The Warburg effect ensures the conversion of glucose to pyruvate and subsequently to lactate by lactate dehydrogenase A (LDH A), leading to increased tumor microenvironment (TME) acidity (pH 6.0–6.5), which affects macrophage reprogramming and T cell functionality.
Objective of the study. To elucidate the mechanism of suppression of the Warburg effect by the biologically active form of vitamin D, calcitriol (1,25-dihydroxyvitamin D3).
Materials and methods. A review of the literature from 2019-2024 was performed, using 10 articles, including data from PubMed, Experimental and Molecular Medicine, Wiley Online Library, MDPI, Journal of Cancer Research.
Results. Physiologically, glucose metabolism occurs in mitochondria through oxidative phosphorylation in the presence of oxygen. Although the mitochondrial respiratory chain remains functional, cancer cells adopt the Warburg effect, excessively consuming glucose and converting it into lactate. Lactate is then transported to the TME by monocarboxylate transporters (MCTs) to supply energy to cancer-associated fibroblasts (CAFs) and stromal cells. Oxidative phosphorylation produces more energy than anaerobic glycolysis, but cancer cells compensate by increasing glucose uptake and accelerating glycolysis. Glycolytic enzymes are regulated by the phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) signaling pathway through hexokinase 2 (HK2), which phosphorylates glucose. Consequently, cancer cells disrupt the normal function of these proteins. Vitamin D is a hormone responsible not only for calcium and phosphorus homeostasis, but also for extraskeletal functions. Its biological effects are mediated by the vitamin D receptor (VDR). Recent studies indicate that calcitriol inhibits key glycolytic enzymes of the Warburg effect, including HK2, LDHA, and glucose transporter GLUT1 reducing lactate production and tumor microenvironment acidity. In addition, calcitriol reduces TME acidification and increases the rate of oxygen consumption in cancer cells by altering aerobic glycolysis at the mitochondrial respiratory chain, thereby decreasing tumor volume and weight.
Conclusions. Cancer progression can be interrupted by calcitriol, which reduces cell proliferation, stimulates apoptosis and cell differentiation and has a protective role. According to studies, calcitriol inhibits cancer cell progression and has potential chemopreventive and anticancer capacity.
Keywords: cancer, Warburg effect, glycolytic enzymes, glycolysis, calcitriol.

THE INFLUENCE OF VITAMIN D ON METABOLIC SYNDROME

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Introduction. Metabolic syndrome (MS) is a major public health concern, characterized by a combination of central obesity, dyslipidemia, hypertension, and insulin resistance. In recent years, increasing evidence has highlighted the crucial role of vitamin D in metabolic homeostasis and its association with MS development. Beyond its well-known role in bone metabolism, vitamin D is involved in insulin secretion, insulin sensitivity, and lipid metabolism.
Aim of study. The purpose of the study is to elucidate and describe the impact of vitamin D deficiency on the pathogenesis of metabolic syndrome and the effects of vitamin D supplementation in preventing and managing MS.
Methods and materials. Medscape, PubMed, Hinari, Google Scholar. Published between 2013-2025. Keywords: metabolic syndrome, vitamin D, insulin resistance, dyslipidemia, cardiovascular risk, obesity.
Results. Vitamin D deficiency is frequently observed in obese individuals, primarily due to its sequestration in adipose tissue, which acts as a reservoir, leading to decreased bioavailability and lower circulating levels. Hypovitaminosis D contributes to insulin resistance by decreasing intracellular calcium levels and reducing GLUT-1 and GLUT-4 glucose transporter expression in peripheral tissues. Moreover, low vitamin D levels are associated with increased total cholesterol, LDL, and triglycerides, promoting atherosclerosis. Vitamin D supplementation in MS patients has shown beneficial effects, including improved insulin sensitivity, reduced dyslipidemia and cardiovascular risk.
Conclusion. Vitamin D deficiency plays a significant role in the pathogenesis of metabolic syndrome, affecting both glucose homeostasis and lipid metabolism. Supplementing vitamin D in MS patients may help alleviate symptoms and prevent metabolic complications. Further studies are required to fully understand the underlying mechanisms and optimize vitamin D-based therapeutic strategies.

LUCAS TESTIMONIES: CELL EVOLUTION

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Introduction. The last universal common ancestor (LUCA) represents a pivotal stage in cell evolution, serving not only as the bridge between prebiotic chemistry and modern biological systems but also providing insights into the earliest cellular structures and metabolic pathways. Understanding LUCA is essential for reconstructing the origins of cellular life and the divergence of the two domains: Bacteria and Archaea, along with the emergence of Eukaryota with its complexity.
Objective of the study. This study aims to provide a comprehensive synthesis of existing data to determine LUCA's features, evaluating competing hypotheses regarding its metabolism, cellular structure and ecological adaptations, and its impact on the development of cellular complexity.
Materials and Methods. In this literature review, we examined publications from PubMed, Nature, ScienceDirect, and Hinari sources from 1977-2025, using the keywords 'LUCA' and 'cellular evolution'. Most of the publications used dated from 2014 to 2025.
Results. LUCA serves as the foundation of all modern life, yet its precise nature remains uncertain. Researches indicates that LUCA was a community of anaerobic autotrophic cells with a highly functional metabolic system, enabling it to adapt to the conditions of early Earth. The specifics of LUCA's cellular organization remains debated, with some models proposing a membrane-less pre-cellular system, while others advocate for a rudimentary lipid membrane. Recent phylogenetic reconstructions increasingly support the idea that LUCA possessed a lipid membrane, suggesting it had a functionally robust genome capable of encoding essential components for genetic replication, protein synthesis, and energy metabolism.
Conclusions. By exploring LUCA's role in cellular evolution and reconstructing its characteristics, we can gain valuable insights into its diversification in Bacteria and Archaea, the origin of Eukaryota, and its vast complexity. However, key uncertainties remain regarding LUCA's cellular organization, metabolic systems and ecological adaptations. These differing hypotheses underscore the necessity for an integrative approach that combines genomics, phylogenetics, experimental simulations and geology.
Keywords: LUCA, cell evolution, TOL, Bacteria, Archaea, Eukaryota, evolution of metabolic systems, phylogenetic diversification, evolutionary adaptation.

WHY IS "BRAINWASHING" NECESSARY? HISTOPHYSIOLOGY INVESTIGATION

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Background. The glymphatic system represents the indispensable mechanism for maintaining cerebral homeostasis, facilitating the drainage of cerebrospinal fluid (CSF) and the direct evacuation of neurotoxic metabolites. Thus, understanding the fundamental mechanisms of this system is essential for advancing neurobiology and implementing innovative, potentially revolutionary treatments for the prevention of neurodegenerative diseases.
Objective of the study. To analyze and investigate, from a histological and physiological point of view, the structure and functions of the glymphatic system, emphasizing the relevance of "brainwashing" for supporting neuronal integrity and preventing progressive neurological diseases.
Material and methods. There have been reviewed the specialized literature published between 2012 and 2024 was reviewed, integrating information obtained in the PubMed, Springer Link, ScienceDirect databases, regarding the structure, physiology and functions of the glymphatic system and the correlation of its dysfunctions with the development of neurodegenerative dysfunctions.
Results. It has been demonstrated that CSF drainage through the glymphatic system is an active process, dependent on arterial pulsations and the activity of astrocytes and AQP4 channels. It is found that the fluid flow increases significantly during deep sleep, with a share of over 60%, which allows for an efficient elimination of metabolic waste, and in the long term would represent a protective factor in neurodegenerative diseases. Also, recent studies on neurotransmitters have highlighted the importance of norepinephrine in modulating the activity of the glymphatic system, through its periodic release during sleep, respectively determining the pulsations of the vessels and facilitating the circulation of CSF and the clearance of the brain, these discoveries emphasize the close link between the quality of sleep and the efficiency of neuronal detoxification processes.
Conclusion. The glymphatic system proves to be a key element in protecting neurological health, ensuring the continuous elimination of metabolic residues and maintaining an optimal environment for neuronal functioning. This research offers new opportunities for the development of innovative therapeutic strategies for the prevention and treatment of neurodegenerative diseases, thus transforming the concept of "brainwashing" into a fundamental physiological process for the maintenance of long-term cognitive functions.
Keywords: glymphatic system, AQP4, neuroinflammation, astrocytes, CSF, perivascular space.

ADIPOSE TISSUE IN CHEST REGION AND ITS IMPACT ON THE CONDITION OF VARIOUS ORGANS

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Introduction. The presence of the adipose tissue in the chest region might be linked to many pathological conditions meanwhile it can be physiological in many cases. A comprehensive assessment requires a morphological analysis in relation to the anatomical structures of the mediastinum to better understanding of its clinical significance and potential implications.
Material and methods. Observation and morphometry of 22 mediastinal complexes from the department's fund were performed. The results of 50 examinations, such as computer tomography, magnetic resonance, angiography, performed before therapeutic treatment and the preoperative period, as well as the operation protocols from the observation sheets, were subjected to the study. The results were processed statistically**.** Our data were compared with bibliographic data obtained by the same methods.
Results: Four cites of fat storage are distinguished: subcutaneous, visceral, special and ectopic cites. There are extrapleural, mediastinal, epicardial, pericardial, and myocardial fat depots in the thoracic cavity. Thoracic adiposity affects the lung function, with distinct gender differences.Visceral and subcutaneous fats are associated with the reduced lung functions. Cardiopulmonary changes might be due to pericardial, epicardial, periaortic, and extracardiac fat. Mediastinal fat-related lesions were also observed, underscoring the importance of distinguishing chest fat from gynecomastia. Additionally, thoracic fat accumulation showed a potential association with non-traumatic vertebral fractures, suggesting broader systemic implications.
Conclusion: The visceral fat is more toxic than subcutaneous. Distribution of adipose tissue in the chest region has impact on lung function, cardiopulmonary health, and musculoskeletal integrity. The need for further research to explore clinical significance of thoracic adiposity that will contribute to improve quality of clinical diagnosis, which will be helpful for therapeutic and preventive interventions. and this research may open the gates for the new generation of imaging technique for adipose tissue assessment.
Keywords: Cardiopulmonary health, Mediastinal fat, Ectopic fat depots, Adipose tissue disrubution, Extracardiac fat.

MOLECULAR MECHANISMS OF NEURONAL AGING AND NEURODEGENERATION

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Background. Aging of the nervous system is accompanied by complex molecular changes that contribute to the development of neurodegenerative diseases. Understanding these mechanisms is crucial for developing effective treatment and prevention strategies.
Material and Methods. This review aims to analyze current data on the molecular mechanisms of neuronal aging and neurodegeneration, their impact on neurosciences, drug screening, and regenerative medicine, while discussing the advantages and limitations of existing research approaches.
Results:
1. **Oxidative Stress and Mitochondrial Dysfunction:** Aging increases oxidative stress and disrupts energy metabolism, leading to neuronal damage and contributing to neurodegenerative diseases.
2. **Proteostasis Dysfunction and Protein Aggregation:** Decreased activity of protein degradation systems, such as the ubiquitin-proteasome and autophagy-lysosome pathways, leads to the accumulation of abnormal proteins and aggregates characteristic of neurodegenerative conditions.
3. **Neuroinflammation:** Age-related changes in the hypothalamus, including increased inflammatory activity and reduced neuronal function, contribute to cognitive decline and neurodegeneration.
4. **DNA Damage and Repair Impairment:** The accumulation of DNA damage and decreased repair efficiency with aging may drive neurodegenerative processes.
Discussion. Current research focuses on therapeutic strategies targeting key molecular mechanisms of neurodegeneration. For instance, blocking stress responses in microglia or preventing toxic lipid formation has been shown to reverse Alzheimer's symptoms in preclinical models. Additionally, the identification of specific hypothalamic cells affected by aging opens new possibilities for interventions aimed at slowing down aging processes and reducing cognitive decline risk.
Conclusion. Understanding the molecular mechanisms of neuronal aging and neurodegeneration is essential for developing effective therapeutic approaches. Despite existing challenges, progress in this field promises significant advancements in neurosciences, drug screening, and regenerative medicine.
Keywords: Neurodegeneration, neuronal aging, oxidative stress, mitochondrial dysfunction.

REVIEW OF LITERATURE ON COMBINED LIVER ELASTOGRAPHY TECHNIQUES

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Background. Liver elastography has become a pivotal non-invasive method for assessing liver fibrosis, offering an alternative to traditional biopsy. Techniques such as transient elastography (TE), point shear wave elastography (pSWE), and real-time tissue elastography (RTE) have been employed individually. The integration of these modalities, known as 'Liver Elastography Combi,' aims to enhance diagnostic accuracy by leveraging the strengths of each technique.
Materials and Methods Recent studies have explored the efficacy of combining elastography methods. Yazaki et al. conducted a prospective study involving patients scheduled for liver biopsy to evaluate liver fibrosis. They utilized both pSWE and RTE, obtaining liver stiffness measurements (LSMs) and liver fibrosis index (LFI) values, respectively. Biopsy samples were taken from the same area assessed by elastography for histological comparison (https://pubmed.ncbi.nlm.nih.gov/35735003/). Another study assessed the combination of TE and the Enhanced Liver Fibrosis (ELF) test in patients with chronic hepatitis B. This study involved 222 patients who underwent liver biopsy, TE, and the ELF test. The diagnostic performance of TE and ELF, both individually and in combination, was evaluated against histological findings.
Results. Yazaki et al. found that both Vs from pSWE and LFI from RTE correlated significantly with liver fibrosis stages. However, in patients with non-alcoholic fatty liver disease (NAFLD), LFI's correlation was less pronounced, suggesting that RTE may be less effective in this subgroup. The study concluded that while combinational elastography is useful, pSWE may be more reliable for assessing liver fibrosis in NAFLD patients.
In the study combining TE and the ELF test, TE demonstrated higher accuracy in detecting advanced fibrosis compared to the ELF test alone. However, the sequential combination of TE followed by the ELF test improved specificity, particularly in diagnosing cirrhosis. This suggests that a combined approach can enhance diagnostic precision in chronic hepatitis B patients.
Conclusions. The integration of multiple elastography techniques offers a more comprehensive assessment of liver fibrosis, capitalizing on the unique advantages of each method. While combinational elastography enhances diagnostic accuracy, its effectiveness may vary among different patient populations, such as those with NAFLD. Further large-scale, multicenter studies are warranted to standardize protocols and validate the clinical utility of these combined approaches across diverse liver diseases.

THE ROLE OF GLYCATION PROCESSES IN AGING

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Background. Glycation is a non-enzymatic reaction in which reducing sugars react with free amino groups in proteins, lipids, or nucleic acids, leading to the formation of advanced glycation end products (AGEs). AGE accumulation leads to structural and functional alterations in proteins, contributing to aging.
Objective of the study. To elucidate the biochemical mechanisms of glycation, its impact on aging, and potential therapeutic strategies to mitigate its effects.
Materials and methods. A literature review covering the years 2019–2024 was conducted, analyzing 15 peer-reviewed articles from PubMed, ScienceDirect, Wiley Online Library, and MDPI.
Results. The glycation process begins when a reducing sugar, such as glucose or fructose, reacts with the free amino group of lysine or arginine residues in proteins. Over time, these intermediate compounds undergo glycoxidation and dehydration, forming irreversible AGEs such as Nε-(carboxymethyl)lysine, pentosidine, and pyrraline. AGEs interact with the receptor for advanced glycation end products (RAGE), a transmembrane receptor highly expressed in endothelial cells, macrophages, and neurons. AGE-RAGE binding triggers activation of nuclear factor kappa b (NF-κB), a transcription factor that upregulates the expression of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, promoting chronic inflammation and cellular dysfunction. Mitochondrial dysfunction is exacerbated by AGEs through oxidative phosphorylation impairment, increasing reactive oxygen species (ROS) production. This oxidative stress further amplifies AGE formation in a vicious cycle, accelerating cellular senescence via activation of the p53/p21 and p16INK4a pathways. Additionally, glycation disrupts the ubiquitin-proteasome system and autophagy, preventing the clearance of damaged proteins and contributing to intracellular toxicity. Therapeutic strategies to counteract glycation include AGE inhibitors (aminoguanidine, pyridoxamine), RAGE antagonists, and antioxidants (vitamin C, resveratrol, polyphenols), which scavenge ROS and reduce AGE formation. Dietary interventions, such as caloric restriction and a low-glycemic diet, have also been shown to limit AGE accumulation and mitigate aging-related damage.
Conclusions. Glycation is a key driver of aging through its impact on protein function, oxidative stress, and chronic inflammation. Understanding the biochemical processes underlying glycation opens avenues for therapeutic interventions aimed at reducing AGE accumulation and mitigating age-related diseases.
Keywords. Glycation, advanced glycation end products, oxidative stress, receptor for AGE, inflammation, aging, mitochondrial dysfunction, protein crosslinking, anti-aging strategies.

Q-SPECT CT IN THE ASSESMENT OF POST-PULMONARY EMBOLISM COMPLICATIONS: A NEW PERSPECTIVE ON RISK STRATIFICATION AND MANAGEMENT

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Introduction. Pulmonary embolism (PE) is a severe cardiovascular condition associated with significant morbidity, often resulting in long-term complications despite adequate anticoagulation. Chronic thromboembolic pulmonary hypertension (CTEPH) develops in over half of PE survivors, affecting both functional capacity and prognosis. Identifying high-risk individuals at an early stage is crucial for optimizing clinical outcomes. Quantitative Single Photon Emission Computed Tomography with CT (Q-SPECT CT) has gained recognition as an advanced imaging modality capable of detecting residual perfusion abnormalities, aiding risk assessment and clinical decision-making.

Materials and Methods. A prospective study was conducted, enrolling patients who had completed anticoagulation therapy (3–6 months) after a confirmed PE episode. Participants underwent a detailed clinical evaluation, echocardiography, biomarker analysis, and Q-SPECT CT imaging to assess residual perfusion defects. Statistical correlations were analyzed using Spearman's test.

Results. Preliminary data indicate that 83.3% of symptomatic PE survivors experience persistent dyspnea, with Q-SPECT CT revealing residual perfusion abnormalities in 60% of cases. Echocardiographic findings demonstrated a significant correlation between the TAPSE/PSAP ratio and NT-proBNP levels ($p < 0.001$), right ventricular (RV) strain variations ($p < 0.02$), and the likelihood of pulmonary hypertension ($p < 0.001$). Furthermore, perfusion defects identified via Q-SPECT CT were associated with the presence of thoracic pain ($p < 0.03$) and an increased probability of pulmonary hypertension ($p < 0.03$). No statistically significant correlations were observed between Q-SPECT CT findings and RV strain ($p = 0.9$), 3D right ventricular ejection fraction (RVEF) ($p = 0.1$), or TAPSE/PSAP ratio ($p = 0.08$).

Conclusions. Q-SPECT CT proves to be a valuable tool for evaluating post-PE complications, particularly in patients with suspected pulmonary hypertension. Its ability to detect persistent perfusion deficits allows for a more refined risk stratification, supporting tailored management strategies and further diagnostic refinement. Integrating Q-SPECT CT into routine follow-up protocols may improve long-term outcomes in PE survivors.

Keywords: Pulmonary Embolism, Q-SPECT CT, Pulmonary Hypertension, Risk Assessment, Perfusion Imaging, Chronic Thromboembolic Disease

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FECAL MICROBIOTA TRANSPLANTATION IN CIRRHOSIS: A MICROBIOME-BASED THERAPEUTIC REVOLUTION

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Introduction. The gut microbiota, as well as the gut-liver axis, play a significantly important role in the fibrosis process. As fibrosis progresses to cirrhosis, it further worsens the microbiota, creating a vicious cycle of dysbiosis. Recently, there has been a growing interest in potential treatments that modulate the gut microbiota and the gut-liver axis in the treatment of cirrhosis. Antibiotic resistance in cirrhosis is a major issue. In this context, fecal microbiota transplantation (FMT) has emerged as a potential strategy. The aim of this study is to highlight the role of FMT in patients with chronic liver disease.
Materials and Methods. A critical analysis of the specialized literature from 2018 to 2025 was conducted using databases such as PubMed, Elsevier, ScienceDirect, CGH Journal and MDPI.
Results. FMT has demonstrated significant promise in modulating the gut microbiota, reducing systemic inflammation, and improving clinical outcomes in cirrhotic patients. Clinical studies suggest that FMT restores beneficial microbial strains (*Bifidobacterium, Lactobacillus*) while reducing harmful pathogens (*Enterobacteriaceae, Clostridioides difficile*), leading to improved gut barrier integrity and reduced endotoxemia. FMT plays a crucial role in restoring microbial balance and improving liver function. Studies suggest that FMT may prevent or delay complications, slow disease progression, and reduce mortality in patients with decompensated cirrhosis. Patients receiving FMT exhibit decreased inflammatory cytokines (IL-1, IL-6, TNF-α) and enhanced bile acid metabolism. It has shown potential in reducing antibiotic-resistance gene (ARG) expression, particularly for beta-lactamases, lowering the risk of multidrug-resistant bacterial infections. While preliminary findings are encouraging, further large-scale, randomized controlled trials are required to establish optimal treatment protocols, donor screening methods, and long-term safety. Variability in donor microbiota composition, the lack of standardized administration protocols and the need for repeated FMT treatments for sustained effects, present obstacles to clinical implementation.
Conclusions. FMT presents a promising microbiome-based therapy for cirrhosis, with evidence supporting its role in reducing complications and enhancing overall liver health. While preliminary findings are encouraging, further large-scale, randomized controlled trials are required to establish optimal treatment protocols, donor screening methods, and long-term safety. Future research should explore synthetic microbiome therapies and personalized microbiota-based interventions.
Keywords: FMT, cirrhosis, gut-liver axis, microbiome therapy, dysbiosis, antibiotic resistance, ARGs.

EVALUATION OF CATHEPSIN D ACTIVITY IN SPLEEN AND BONE MARROW IN EXPERIMENTAL IMMUNODEFICIENCYAND UNDER TREATMENT WITH SULFATED POLYSACCHARIDES

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Introduction: The cellular lysosomal system represents one of the key enzymatic protection mechanisms of the body. Cathepsin D (CatD) is a normal and major component of lysosomes. CatD manages protein turnover degrading misfolded and aggregated proteins and favors apoptosis in the case of proteostasis disruption. Proteostasis refers to the regulation of the cellular concentration, folding, interactions and localization of each of the proteins that comprise the proteome. However, when CatD regulation is affected, it can contribute to numerous disorders [Jackson MP, Hewitt EW (2016)]. Thereby, studying the mechanisms of action of sulfated polysaccharides (SPS) of local origin on CatD activity in various pathological conditions is of particular interest.
Materials and Methods: Immunodeficiency was modeled in laboratory rats by biweekly injections of cyclophosphamide solution (50 mg/kg) for two weeks. SPS at doses of 50 and 125 mg/kg, dissolved in 20 mL of beef broth, were administered enterally on a daily basis. The collection and preparation of spleen and bone marrow (BM) were conducted under specific conditions to assess CatD activity. The evaluation of CatD activity was based on the enzyme's ability to cleave the hemoglobin molecule, resulting in acid-soluble derivatives, whose quantity is directly proportional to enzyme activity. This was assessed using a Synergy H1 Hybrid Reader (BioTek Instruments, USA). Statistical analysis was performed using the software programs "StatsDirect" and "Statistica 6.0".
Results: In rats with immunodeficiency, CatD activity exhibited an increasing trend in spleen, while in BM, it was particularly elevated, exceeding control values by twofold ($p<0.05$). Treatment with SPS at a dose of 125 mg/kg led to a significant reduction (39%, $p<0.01$) in CatD activity in the spleen. In BM, CatD levels tended toward normalization only when SPS was administered at a dose of 50 mg/kg.
Conclusions: The administration of SPS in experimental immunodeficiency resulted in a decrease in CatD values, which could potentially reduce the intensity of inflammation and reduce a lot a disorder at cellular and molecular level. Therefore, targeting CatD could provide significant diagnostic benefits and new avenues of therapy.
Keywords: Sulfated Polysaccharides, Cathepsin D, Immunodeficiency, Spleen, Bone Marrow.

SCALENUS SYNDROME

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Introduction. Scalenus Syndrome is a clinical entity characterized by symptoms resulting from the compression of the subclavian vessels and branches of the brachial plexus in the scalene triangle. The syndrome takes its name from the muscles between which the compression occurs. Most cases are located unilaterally, on the right side. It occurs predominantly in women.
Materials and methods: In carrying out the study, various bibliographical sources and online medical databases, such as NCBI, PubMed, HINARI and Science Direct, were consulted and analyzed.
Results. In Scalenus Syndrome, among the most common causes are: congenital anomalies, osteochondrosis, hypertrophy of the anterior scalene muscle, hyperextension of the neck, repetitive stress injuries, trauma and high-performance sports (tennis, basketball, swimming). The clinical picture includes paresthesias of the upper extremities and neck, shoulder and/or arm pain, occipital headache (in neurogenic involvement), paleness, cyanosis, hypothermia and numbness, edema (in vascular involvement). Doctors should consider this pathology in the differential diagnosis of shoulder and upper extremity pain, so that patients are appropriately guided for timely therapeutic interventions. Roots, Adson, Whright, Elevated Arm Stress tests are often used to detect this syndrome, which have a specificity of 70-100%. Besides these tests, electrophysiological and imaging studies can provide useful information for the diagnosis. Treatment is prescribed depending on the ethiology. FIrst-line therapy for Scalenus Syndrome is a conservative treatment, and may include non-steroidal anti-inflammatory drugs in combination with sedatives and botulinum toxin injections. Patients who have failed conservative therapy are considered for surgical treatment: scalenotomy, resection of the first rib.
Conclusion. In our study, we have highlighted that Scalenus Syndrome involves theccompression of nerves and vessels in the scalene triangle, leading to various clinical manifestations. It is a complex clinical syndrome, with anatomical variations and multifactorial mechanisms contributing to the development of symptoms. Diagnosis involves patients history, clinical exam, functional tests and imaging studies. The treatment ranges from non-drug therapy to surgical decompression, the treatment of choice being the use of minimally invasive treatment.
Keywords: compression, pain, scalene triangle, scalene muscles, cervical rib.

ANATOMICAL VARIANTS OF THE COMMON CAROTID ARTERY

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Introduction: The variability of the common carotid artery (CCA), its morphological and topographic features, can cause deficiency in blood supply of the brain and also are identified as predisposing factors in formation of atherosclerotic plaques. The purpose of our study was to determine the variants and individual morphological and topographic features of the CCA.
Materials and Methods: The variability of the CCA was studied retrospectively on a sample of 110 patients (60 males/50 females), with an average age of 60.7 ± 14.84 years, with various complaints, who were examined through CT angiography at the MSPI Emergency Medicine Institute and Republican Center for Medical Diagnostics.
Results: The right common carotid artery (RCCA) originated from the brachiocephalic trunk in 98.2% of cases and in 1.8% it had a common origin with the left common carotid artery (LCCA). The LCCA derived from the aortic arch in 73% of cases, in 20% of cases, it had a common origin with the brachiocephalic trunk from the aortic arch and in 5.2%, it was a branch of the brachiocephalic trunk. High bifurcation of the RCCA was determined in 4.5% of cases while the high bifurcation of the LCCA was identified in 5.45%. Low bifurcation predominated on the right side, being observed in 12.72%, while the incidence on the left side was 11,81. As a variant of branching patterns, the trifurcation of the CCA into the internal carotid artery, external carotid artery (ECA) and superior thyroid artery (STA), was identified. The trifurcation of the RCCA was observed in 31% and the trifurcation of the LCCA in 26.3%. An unusual origin of the STA from the trunks of the common carotid arteries was revealed in 20,8%, from which in 3.6% of cases the STA was a branch of the RCCA and in 17.2% it was a branch of the LCCA. A few variants of the CCA primary branches position were identified. The right ECA was positioned anteromedially in 84.5%; posterolaterally in 2.7%; laterally in 11.8% and medially in 1% of cases. The left ECA was positioned anteromedially in 91%; posterolaterally in 1.8%; medially in 2.7%; laterally in 3.6% and anterolaterally in 1% of cases.
Conclusions: The anatomical variants of the CCA, particularly its bifurcation level, branching patterns and topographical relationship of its primary branches are of clinical significance in selecting the optimal methods in neck surgery.
Keywords: common carotid artery, external carotid artery, superior thyroid artery.

THE ROLE OF PERICYTES IN MODULATING OPHTHALMIC DISEASES: A REVIEW OF CURRENT INSIGHTS AND THERAPEUTIC PERSPECTIVES

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Introduction. Pericytes have an important role in preserving the blood vessels in the retina by keeping them stable and ensuring proper functioning of the endothelial cells. Meanwhile they also preserve the integrity of the blood retina barrier. Their impaired function is increasingly identified as a factor in eye pathologies like diabetic retinopathy (DR), age related macular degeneration (AMD) and retinal vein occlusion (RVO).
The aim of the study was to identify the significance of pericyte dysfunction related issues in eye conditions, focusing on oxidative stress (OS) and inflammation along with further analysis of the potential treatment options.
Materials and methods. A systematic review of 20 peer-reviewed articles was conducted using PubMed, Scopus, and Web of Science (2015–2024). Studies on pericyte dysfunction in DR, AMD, and RVO, particularly those related to OS, inflammation, and therapeutic interventions in both human and animal models, were included. Articles lacking direct relevance to pericyte pathology were excluded.
Results. Research indicates that the decline and dysfunction of pericytes play a role in destabilizing the blood vessels in the retina, which can result in the loss of capillaries and breakdown of the blood retina barrier along with impaired neurovascular function. The process of pericyte cell death is worsened by the OS and prolonged inflammation which leads to an increase in reactive oxygen species (ROS), lipid peroxidation and malfunction of mitochondria as significant indicators of disease progression. Approaches focusing on activating Nrf2 for defense mechanisms while safeguarding the mitochondria and moderating inflammatory responses, hold potential for maintaining pericyte health and reinstating balance, in vascular function.
Conclusion. Pericytes play a significant role in retinal vascular diseases and addressing their dysfunction could offer in the future innovative treatment options for coping with ophthalmic complications. Further researches should center on creating precise treatments that strengthen pericyte endurance, reduce oxidative stress and enhance patient outcomes in cases of sight threatening conditions.
Keywords: pericytes, retinal microvasculature, diabetic retinopathy, oxidative stress, inflammation, neurovascular dysfunction.

ANALYSIS OF CONTEMPORARY TRENDS IN MORPHOMETRY

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Background: Morphometry plays a crucial role in modern histology, allowing for the quantitative analysis of the morphological parameters of cells and tissues. With the advancement of digital technologies and machine learning methods, morphometric research has become more precise, automated, and accessible. This study examines current trends in morphometry, including the use of artificial intelligence (AI) for image analysis and data interpretation.
Materials and Methods: The aim of this study is to provide an overview of modern morphometric technologies, including measurement automation, the application of artificial intelligence, 3D morphometry, and integration with molecular methods. Their advantages, limitations, and perspectives in medical and biological research are discussed.
Results: Modern morphometry relies on computer-based technologies, enabling high-precision analysis of biological structures. The main areas of development include:
1. Automation of Morphometric Measurements
The development of software such as ImageJ and CellProfiler has enabled the automation of morphological analysis of cells and tissues. These tools are widely used in cancer diagnostics, pathology analysis, and the study of disease mechanisms.
2. Artificial Intelligence and Machine Learning
Advanced deep learning algorithms significantly improve the accuracy of morphometric analysis. For example, convolutional neural networks (CNNs) can automatically identify and classify cells based on their morphological characteristics. These methods are widely applied in digital pathology and oncological research.
3. 3D Morphometry
With the introduction of 3D scanning and digital reconstruction, it has become possible to analyze tissues not only in two dimensions but also in three dimensions. This is essential for studying complex biological structures such as neural networks and vascular systems.
4. Integration of Morphometry with Molecular Research
Modern studies increasingly combine morphometric data with molecular methods such as immunohistochemistry and genomic analysis. This approach helps identify correlations between morphological changes and the molecular mechanisms of diseases.
Conclusion: Modern morphometry is evolving through integration with digital technologies and artificial intelligence. The automation of image analysis, the use of neural networks and machine learning, and the development of 3D visualization make morphometric studies more accurate and efficient. These advancements open new opportunities in diagnostics and research, contributing to a deeper understanding of cellular and tissue processes. In the future, the continued development of AI in morphometry could lead to the creation of autonomous diagnostic systems and personalized medicine.
Keywords: morphometry, artificial intelligence, machine learning, 3D analysis, digital pathology.

EFFECTS OF VITAMIN D SUPPLEMENTS ON PATIENTS WITH HYPOTHRYOIDISM

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Introduction: Hypothyroidism is a common endocrine disorder, ranging from 0.1% to 12.5%; women are more likely to develop the condition. The causes can be multiple, but most often 20-30% of cases are of autoimmune origin. Vitamin D supplementation has shown potential benefits in improving thyroid function in individuals with hypothyroidism and concurrent vitamin D deficiency, particularly in cases involving autoimmune thyroid diseases. The evidence suggests that vitamin D may play a role in modulating immune responses and enhancing thyroid hormone levels, although the effects can vary based on the duration and dosage of supplementation.

Material and Methods. Have been selected and analyzed 24 articles from PubMed, NCBI, Google Scholar, as well as medical books, scientific journals published in the 2012-2024 period.

Results. Long-term vitamin D supplementation, greater than three months, has been associated with significant improvements in thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) levels in patients with autoimmune thyroid diseases. In patients with Hashimoto's thyroiditis, vitamin D supplementation significantly reduced anti-thyroid peroxidase antibody and thyroglobulin antibody levels, while also decreasing TSH and increasing free T3 and free T4 levels. Vitamin D correction in subclinical hypothyroid patients led to a significant decrease in TPO-Ab and anti-TG antibody levels, suggesting an improvement in thyroid autoimmunity. The meta-analysis of Hashimoto's thyroiditis patients indicated that active forms of vitamin D, such as calcitriol, were more effective in reducing TPO-Ab levels compared to vitamin D2 or D3, especially with treatment durations exceeding 12 weeks.

Coclusions. Supplementation with vitamin D, alongside other micronutrients, showed improvements in insulin resistance and physical quality of life in hypothyroid patients, although no significant changes were observed in TSH or FT4 levels in the short term.

Keywords. Vit. D supplements, hypothyroidism, autoimmune disease.

OBESITY IN POSTMENOPAUSAL OSTEOPOROSIS

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Introduction. Obesity is a chronic disease that is closely correlated with bone mineral density (BMD), resulting in contradictory effects. The aim of this study is to assess the potential risks in overweight individuals postmenopause and to identify new therapeutic targets for improving quality of life.
Materials and Methods. To achieve the proposed objective, a review of the scientific literature of 10 bibliographic sources from the last 5 years was carried out, using the search engines PubMed, Cochrane Library, MedScape, Biomed Central.
Results. Obesity, characterized by an excessive accumulation of adipose tissue, influences the morbidity of patients with osteoporosis. Adipokines, osteoblasts and chondroblasts originate from pluripotent mesenchymal stem cells (MSCs), suggesting the correlation between adipose tissue and bone. Lower concentration of adiponectin in obese individuals stimulates osteoblast synthesis through production of receptor activator of factor kappa-B ligand (RANKL), decreases osteoprogerin secretion. Leptin, a hormone derived from subcutaneous adipose tissue, directly influences bone remodeling through specific receptors on the surface of osteoblasts and chondroblasts, as well as through the activation of fibroblast growth factors (FGF 23). Indirectly, leptin blocks serotonin receptors and reduces the synthesis of serotonin that favors bone growth. In the postmenopausal period, the endocrine function of estrogen secretion is taken over by the adrenal glands, through the increased secretion of adrostenedione, and its aromatization leads to an increase in the level of estrogens in the blood. Bone protection is also provided by the conversion of dihydroepiandrosterone to estrone by activation of aromatase P450 in osteoblasts. Adipose tissue secretes proinflammatory cytokines that alter hormone secretion with effects on bone mineral density. IL-6 and TNF-α accelerate bone resorption by activating osteoclasts and upregulating RANKL/RANK/osteoprogerin. TNF-α induces bone resorption by activating nuclear factor kappaB (NF-κB), which regulates RANKL-induced effects, favoring osteoclast synthesis.
Conclusions. Mechanisms of adipokines, circulating steroid hormones (estrogens, androstendion, estrone), and proinflammatory cytokines IL-6 and TNF-α influence bone metabolism. At the same time, monitoring the serum level of adiponectin and leptin provides useful information in the early detection and treatment of osteoporosis.
Keywords. Postmenopausal osteoporosis, estrogens, obesity, bone metabolism, adipose tissue.

CHRONIC PELVIC PAIN SYNDROME IN NEUROLOGICAL PRACTICE. ETIOLOGY, DIFFERENTIAL DIAGNOSIS AND TREATMENT

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Introduction. Chronic pelvic pain is an interdisciplinary problem that affects not only the neurological field but also the gynecological and surgical fields. It is estimated that between 5-26% of women and 2-10% of men suffer from chronic pelvic pain syndrome globally. After many years of debates, in 1979 the International Association for the Study of Pain (IASP) adopted the definition of pain as a "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".
Materials and methods. This abstract presents the result of a detailed analysis of articles and research on chronic pelvic pain syndrome from the sources like PubMed, Google Scholar and others published in last 10 years.
Results. CPPS manifests itself through hyperalgesia and allodynia. It is classified into 2 types: type 1 with unknown etiology and type 2, with known location of nerve injury. Risk factors include female gender, fibromyalgia, and rheumatoid arthritis. The pathogenesis is multifactorial. One of the pathways is neuropathic inflammation, a process in which peripheral C-fiber nociceptors are activated. Other one is that the genetic component also plays an important role. The psychosomatic factor was demonstrated by the connection between a history of stress disorder and confirmation of the diagnosis of CPPS. The therapeutic management has undergone many changes over the years. The use of steroids, bisphosphonates, gabapentin and ketamine have yielded short-term effects. Antioxidant treatment has also shown some effects. Other therapies include low-dose naltrexone and botulinum toxin A. Sympathetic blockade is used often but it is still not possible to create a definitive answer about the duration of its effect.
Conclusion. In conclusion we can say that CPPS is a multi-etiological diagnosis but still not fully elucidated. It requires further studies to better understand the pathogenesis, epidemiology, genetic and psychological impact and effective treatment options, because this will help doctors in the prevention, diagnosis and more effective treatment of this syndrome.
Key-words. Chronic pelvic pain syndrome (CPPS), causalgia, diagnostics, efficient treatment, fibromyalgia, neuropathic inflammation.

THE ROLE OF BACTERIAL PLAQUE IN GINGIVAL PATHOGENESIS

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Background. Currently, catarrhal gingivitis is one of the most common chronic conditions in humans. This condition is primarily caused by bacterial plaque, which promotes gingival inflammation. Bacterial plaque contains microorganisms and metabolic products that, through toxins and enzymes, cause immune and inflammatory changes in the gingival tissue at both the cellular and molecular levels. In the absence of proper oral hygiene, the virulence of microorganisms increases, triggering an inflammatory process manifested by changes in the color, texture, and volume of the gums, as well as bleeding during brushing.
Materials and methods. Case Presentation. The patient L. T., 13 years old, underwent a clinical examination at the Integrated Specialized Consultative Department of the IMSP Mother and Child Center, accompanied by her parents. She reported pain and sensitivity during eating, bleeding, and discomfort while brushing her teeth. At the clinical examination, the following indices were determined: oral hygiene index OHI-S and papillary-marginal-alveolar (PMA - Parma 1960).
Results. Using the Oral Hygiene Index by G. Green and I. Vermillion, an unsatisfactory level of oral hygiene was observed, with a value of 2.6. The evaluation of inflammation according to the PMA index indicated moderate gingival inflammation, ranging from 47%. The established diagnosis was generalized chronic catarrhal gingivitis, moderate form. The treatment plan aimed at symptom relief and the elimination of local causative factors through bacterial plaque control. Treatment steps: symptom relief, professional ultrasonic cleaning and brushing with "Orbis Prophy" paste, local antiseptic and anti-inflammatory treatment with "Oramet" gel applied to the gums for 7-10 days, twice a day, and "Celista" spray 3-4 times a day.
Conclusions. The knowledge of dental plaque as an etiological factor in the development of gingivitis, as well as the adoption of control measures for it, is essential because the signs of gingivitis disappear quickly with the application and maintenance of preventive measures.
Keywords: Chronic catarrhal gingivitis, bacterial plaque, local treatment, oral hygiene, prevention.

P-Selectin and Persistent Thrombosis in Venous Thromboembolism

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Background: P-selectin levels have been reported as a predictor of recurrent venous thromboembolism (VTE). However, the association between plasma P-selectin levels and persistent thrombus in VTE remains unclear.
Objectives: This study aimed to investigate the relationship between plasma P-selectin levels and persistent thrombus in patients with VTE.
Methods: We included 40 patients with a history of venous thrombosis, including deep vein thrombosis and pulmonary thromboembolism, at least three months after completing anticoagulant treatment. A control group of 40 individuals, matched for age and gender, with no history of thromboembolism, was also included. At the time of inclusion, control group participants had C-reactive protein levels within the normal range and no history of diabetes mellitus or chronic kidney disease.
Plasma P-selectin levels were measured using an enzyme-linked immunosorbent assay (ELISA). Logistic regression models were used to estimate odds ratios (ORs) for persistent thrombi based on plasma P-selectin levels.
Results: Among the 40 patients, 26 (65%) had persistent thrombi, detected in either the lower limb veins or pulmonary arteries using Doppler ultrasound and angio-CT.
Multivariable analysis identified elevated P-selectin levels (cutoff: 63.1 ng/mL, 75th percentile of the study population) as a statistically significant risk factor for VTE. The analyses further revealed that individuals with P-selectin levels in the highest quartile (>63.1 ng/mL) had a significantly higher likelihood of persistent thrombus (OR: 1.63; 95% CI: 1.01–2.64) compared to those in the lowest quartile (≤38.4 ng/mL).
Conclusion: Elevated plasma P-selectin levels were associated with an increased risk of persistent thrombus in VTE. Further studies are needed to confirm these findings.
Keywords: P-selectin, Venous thromboembolism,Persistent thrombus,Biomarker
Project code: 24.80015.8007.01VI

THE IMPLICATIONS OF AUTOPHAGY IN CROHN'S DISEASE

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Introduction: Inflammatory bowel disease comprises a variety of chronic inflammatory disorders, that affect the gastrointestinal tract, the most common ones being ulcerative colitis and Crohn's disease, that, if left undertreated, could pose a high risk for colorectal cancer. The aim of this study is to elucidate the role of autophagy in the physiology of the intestinal tract and in the pathogenesis of Crohn's disease (CrD) and the potential therapeutic application in its treatment.
Material and method. A comprehensive literature review was performed using major scientific databases, including the data from the years 2017-2024 of PubMed, Frontiers, Elsevier. Keywords: Inflammatory bowel disease, Crohn's disease, autophagy, colorectal cancer.
Results. Genetics, environment, abnormal gut microbiota and local immunity underlie the pathogenesis of CrD and the cross-link between them is autophagy - the programmed disposal of dysfunctional cellular components by vacuolization. This highly conserved process of cellular degradation regulates the intestinal immunity by promoting antigen presentation by dendritic cells, inflammatory factor synthesis, cellular proliferation and maturation and non-inflammatory cellular clearance. Up-to-date, the autophagosome formation is strictly coordinated by 36 autophagy related genes. Recent studies have linked the mutations in the ATG16L1 (autophagy-related 16-like 1 gene) and the NOD2 (nucleotide-binding and oligomerisation domain 2 gene) to around 50% of cases of CrD onset and progression risk. Among the many autophagy signaling pathways, AMPK/mTOR (Adenosine monophosphate kinase / Mammalian target of rapamycin) and NF-kB (Nuclear factor kB) are the most studied ones and the discovery of such autophagy promoters as metformin, dapagliflozin, palmatin and ginseng could prove beneficial in the course of treatment of CrD.
Conclusions. Moderating the inflammatory status in Crohn's disease by regulating the autophagic flux is feasible. However, more work needs to be done to develop a line of cell specific, harmless therapeutic agents, thus, preventing the colorectal cancer and surgery.
Keywords: Crohn's Disease, autophagy, autophagy-related genes, signaling pathways, therapeutic agents.

TREATMENT OF TRIGGER FINGER: A LITERATURE REVIEW

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Introduction. A special section in hand surgery is dedicated to "trigger finger" disease, a common disabling disorder of the upper limb. trigger finger disease can occur at different ages, from children to geriatric patients. The lifetime risk of occurrence is between 2 and 3%. Incidence is 6 times higher in the female population. It may occur in one or more fingers on each hand and may be bilateral. The main cause of trigger finger results from a mismatch between the dimensions of the flexor tendon and its tendon sheath, leading to faulty gliding of the tendon, resulting in pain, clicking and functional difficulties. Patients present with structural changes in the pulley system of the fingers and tendon sheaths

Aim of the work. The aim of our study is to investigate the concept, clinic, methods of diagnosis and treatment of trigger finger and to identify the particularities of the incidence of this disease according to sex, age, professional occupation, affected fingers, degree of severity according to Quinnell, the evolution of the disease over time, until and after surgical treatment.

Material and methods. More than 60 scientific articles, selected from PubMed, Research Gate, Google Scholar and Elsevier databases, mostly published in the last ten years, were included in the study. The inclusion criteria were as follows: full-text, open access article addressing the problem under investigation. The data obtained were subsequently systematized and analysed.

Results. In the medical literature there is a lack of a standardized protocol considered to be "best practice" for this condition. Researchers believe that a multidisciplinary consensus would be desirable to standardize and optimize the treatment of trigger finger. Therapeutic approaches can be divided into two main categories: conservative treatment and surgical treatment. Depending on the severity of the symptoms and the speed of progression of the pathological process, the methods of treatment of the trigger finger include: immobilization with orthosis, drug treatment, physiotherapeutic treatment and surgical treatment, which in turn consists of open surgery and percutaneous surgery. Conservative treatment with orthotics, medication and physiotherapy is most effective in the early and moderate stages of the disease. In severe cases the trigger finger is treated surgically. As for the technique of surgical treatment, too, there is no single opinion. There is discussion about the priority of open or closed ligamentotomy, choice of surgical approach, total or partial ligamentotomy of the annular ligament, resection of the degeneratively changed portion of the annular ligament or without it. No consensus was reached whether partial tenotomy or total removal of the thickened portion of the tendon or without this surgical maneuver is more effective. With early function after surgery or immobilization of the operated segment.

Conclusions. From the analysis of the literature sources studied we conclude that there is no consensus among scientific researchers on the optimal therapeutic approach to the trigger finger. Further large-scale studies are needed to develop a treatment algorithm in the two age groups of adults and children. The treatment of trigger finger includes conservative and surgical methods, applied depending on the severity of the disease manifestations. Conservative treatment consists of immobilization with orthoses, drug treatment with NSAIDs and corticosteroids and physiotherapy Basic treatment is surgical, which involves open or percutaneous surgery to release the affected pulley.

Keywords: trigger finger, hand surgery, ligamentotomy, orthotics, physiotherapy.

VESTIBULAR MIGRAINE. PATHOGENESIS, DIFFERENTIAL DIAGNOSIS, TREATMENT METHODS

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Introduction. Vestibular migraine (VM) is probably the second most common cause of dizziness, affecting approximately 3% of population. In recent years, the appearance of new studies aiming to understanding the pathophysiology of VM.
Methods and outcomes. This abstract presents a detailed analysis of recent articles and research on VM from the sources like PubMed, ScienceDirect and others published in last 5 years.
Results. The clinical presentation of VM is diverse. Episodes of dizziness usually last between 5min and 72h, although shorter and longer episodes have been reported. Differential diagnoses include Meniere's disease, benign paroxysmal positional vertigo, brainstem aura, transient ischemic attack, persistent perceptual postural vertigo, and episodic type 2 ataxia. Episodes can be accompanied by other symptoms of migraine, including migrainous headache, photophobia, phonophobia and visual aura. The pathophysiology of VM is incompletely understood. Both environmental and genetic factors are likely to be important and recent studies have suggested possible loci of interest at 5q35 and 22q12. One proposed mechanism is hypoperfusion of the inner ear during migrainous attacks secondary to vasospasm resulting in vertiginous symptoms. Alternatively, episodes may be due to sensitization and activation of the trigeminovascular system leading to release of the pro-inflammatory neuropeptides substance P and calcitonin gene-related peptide (CGRP), which has connections with brain areas associated with processing of nociceptive information as well as thalamic and vestibular-associated cortices. Studies using standard methods have shown that migraine treatments can also be effective for VM. For acute attacks, abortive treatment includes triptans and antiemetics to manage headache and vestibular symptoms. Preventive strategies involve pharmacological options like beta-blockers, tricyclic antidepressants, anticonvulsants, and calcium channel blockers with reduction of triggers, physical therapy and mitigation of comorbidities.
Conclusions. VM is a complex disorder with evolving diagnostic and therapeutic approaches. Recent research has significantly improved our understanding of its pathogenesis and management. Further studies are needed to validate novel treatment strategies and refine diagnostic criteria.
Keywords. Vestibular migraine; Headache; Meniere's disease; Vertigo.

PECULIARITIES OF THE PERINEUM IN MORPHOCLINICAL ASPECT

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Introduction. Women's health is one of the strategic priorities of contemporary gynecology and at the same time it is one of the primary factors determining the demographic situation in the Republic of Moldova. Genital prolapse (GP) encompasses a wide spectrum of disorders, from a barely modified anatomy of the vagina and clinically asymptomatic cases, to a complete vaginal eversion associated with severe urinary, defecation and sexual disorders. The morphological aspect of the pelvic diaphragm (PD) and perineal muscles (PM) requires a deep and extensive study, as they represent the main support for the pelvic organs and can provide us with understanding of the causes and mechanisms of genital prolapse occurrence. The aim of the study was to identify the morphoclinical peculiarities of the PD and PM in women with genital prolapse.
Materials and methods. The study was carried on 103 patients diagnosed with GP, hospitalized in the Surgery Department of the Medical Center *Galaxia*, Chisinau, Republic of Moldova, during the period of 2021-2024. The age of the patients ranged from 20-71 years, with a mean age of 52.5±2.3 years. The 1st degree GP (1st group) was recorded in 35 patients (they received conservative treatment). The 2nd and 3rd degree GP (2nd group) was established in 68 patients (treated by surgery).
Results. Incidence by age: 24.7% of patients were of reproductive age; 38.1% – were in premenopause and 37.2% – in postmenopause. Clinical picture: 30.8% of patients had urinary disorders (urinary incontinence, frequent or difficult urination); 58.3% complained of a foreign body sensation and pain in the lower abdominal region; 10.9% – difficult defecation. Number of symptoms: 1st group: 68.6% had a single symptom and in 31.4% two symptoms were registered; 2nd group: 14.7% of patients had a single symptom; 70.5% – 2 symptoms; 10.3% – 3 symptoms and 4.41% – 4 symptoms. Obstetric anamnesis: 7.2% patients of the 1st group and 26% patients of the 2nd group had perineal ruptures in labour. The ultrasound parameters of the perineum were low in all patients: perineal thickness – 9.4-9.8 mm; perineal height – 10.2-11.7 mm; height of the perineal body (perineum tendinous center) – 8.9-12 mm; thickness of the bulbospongiosus muscle – 8.2-11 mm; thickness of the levator ani muscle – 9.12-10.42 mm.
Conclusions. Genital prolapse occurs due to a disruption of the perineal muscles' integrity. The main methods of early diagnostics of the structural and functional changes of the perineum are the transvaginal and transrectal ultrasound examination.
Keywords: perineum, perineal muscles, genital prolapse.

ANATOMICAL VARIANTS OF THE DEEP BRACHIAL ARTERY

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Introduction. Lately, due to the gradual increase of interventional radiological procedures and vascular reconstructive surgeries on the upper limb, knowledge about anatomical variants of the upper limb blood vessels has become more important. Our goal was to establish the anatomical variants of the deep brachial artery (DBA) in order to streamline the interventional procedures and surgical techniques carried on the upper limb.
Materials and methods. The variability of the DBA, that is the main collateral branch of the brachial artery (BA), was studied on 70 formolized adult upper limbs. The cadaveric material belonged to the Department of Anatomy and Clinical Anatomy of Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova. Through anatomical dissection, the origin of the DBA, its course and relationship to the radial nerve (RN) were studied.
Results. Anatomical variants of the DBA were identified in 14.3% of cases (95% CI [7.0-23.4]): in 8.6% (95% CI [2.6-15.8]) it presented number variants, and in 5.7% (95% CI [1.3-11.8]) – it was a component of common arterial trunks (CAT). In cases of double DBA, the second artery in 5.71% of cases, derived from the BA, having a various arrangement towards radial nerve (RN) when entering the humeromuscular canal (posterior to the RN – 2.9%; anterior to the RN – 1.43%; lateral to the RN – 1.43%); in the remaining 2.9% (95% CI [0.0-7.8]) – the second DBA had its origin in 1.43% (95% CI [0.0-4.8]) from the posterior circumflex humeral artery (PCHA) and superior collateral ulnar artery (SCUA). CAT with 3 branches were determined in 4.3% (95% CI [0.0-9.8]): 1) SCUA, subscapular artery (SA) and DBA (1.43%); 2) DBA and two muscular branches – 1.43%; 3) DBA, SCUA and a muscular branch were present in 1.43% of cases. CAT branching into two arteries: the DBA and SCUA were determined in 1.43%.
Conclusions. The atypical origin of the DBA should be taken into consideration by surgeons when harvesting the muscle flaps from the lateral region of the arm. Knowledge about the common arterial trunks variation, particularly when the DBA appears as their component is necessary to increase the efficiency in coronary bypass and in diagnostics and treatment of the brachial region surgical interventions.
Keywords: brachial artery, deep brachial artery, anatomical variants, common arterial trunks.

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