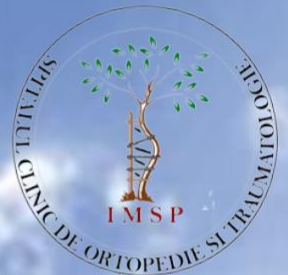


**MINISTRY OF HEALTH OF THE REPUBLIC OF MOLDOVA
NICOLAE TESTEMITANU STATE UNIVERSITY
OF MEDICINE AND PHARMACY**

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



**The Materials of the National Scientific Conference
with International Participation**

**„CELLS AND TISSUES TRANSPLANTATION.
ACTUALITIES AND PERSPECTIVES”**

**Dedicated to the 10th anniversary of the founding of the Human Tissue and Cells
Bank and to the 15th anniversary of the founding of the Laboratory of Tissue
Engineering and Cells Culture of *Nicolae Testemitanu* State University of Medicine
and Pharmacy of the Republic of Moldova**

Chisinau, March 17-18th 2023

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AGENDA

Registration

March, 17, 2023

Opening ceremony 15:00 - 15:20

Emil Ceban, Rector of SUMPh Nicolae Testemitanu, Academician, MD, PhD, Professor.

Ștepa Serghei, Head of Clinical Hospital of Orthopedics and Traumatology, MD, PhD, Associate Professor.

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

DAY ONE – 17 March 2023

Session 1

Plenary meeting

Oral presentations

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

- 1. 15:20-15:40. Nacu Viorel, Cociug Adrian, Ignatov Olga, Cobzac Vitalie.** Tissue and cells transplantation from research to clinical use. *Chisinau, Republic of Moldova.*
- 2. 15:40-15:50. Buga Diana, Țimbădari Tatiana, Bolocan Vladimir, Ciubotaru Ludmila, Visterniceanu Dorian, Farima Marc, Cornea Cornelia, Nacu Viorel.** Management of human tissue donation and transplantation in the Republic of Moldova for the past 10 years. *Chisinau, Republic of Moldova.*
- 3. 15:50-16:00. Cociug Adrian, Macagonova Olga, Țimbădari Tatiana, Valeriu Cușnir, Nacu Viorel.** 10 years of activity of the human tissue bank in the field of cornea harvesting and processing in the Republic of Moldova. *Chisinau, Republic of Moldova.*
- 4. 16:00-16:10. Chornopyschuk Roman, Sidorenko Ludmila, Chepliaka Oleksii, Capcelea Svetlana, Nagaichuk Vasiliu.** Topical application of sorption hydrophilic/ hydrophobic composition based on nanosilica in the treatment of patients with burns. *Vinnitsya, Ukraine. Chisinau, Republic of Moldova.*
- 5. 16:10-16:20. Madan Vadim, Croitor Gheorghe, Caproș Nicolae, Glavan Alina, Hancota Dumitru, Vacula Ion.** The use of bone allografts in the surgical treatment of tibial plateau fractures. *Chisinau, Republic of Moldova.*

16:20-16:50 Coffe Break

Poster session I

- 1. Calistru Anatol, Țărălungă Tatiana, Nacu Viorel.** Treatment of unicameral calcaneus cyst by introducing demineralized allogeneic bone paste: a case report. *Chisinau, Republic of Moldova.*
- 2. Berejanschi Anghelina, Nacu Viorel.** Post Covid-19 respiratory complications treatment by stem cells. *Chisinau, Republic of Moldova.*

3. **Cenușa Alexandrina, Șaptefrați Lilian.** Induced pluripotent stem cells and organoids: advancement and challenges in neurosciences, drug screening and regenerative medicine. *Chisinau, Republic of Moldova.*
4. **Harabari Ștefan, Ojovanu Vitalie.** Stem cell therapy in type 2 diabetes mellitus. *Chisinau, Republic of Moldova.*
6. **Ignatov Olga, Mihaluța Viorica, Nacu Viorel.** Analysis of amniotic membrane processing in the human tissue and cell bank. *Chisinau, Republic of Moldova.*
7. **Mihaluta Viorica, Stoian Alina, Verega Grigore, Nacu Viorel.** Amniotic membrane as a source of treatment in the trophic ulcer of the lower limb. *Chisinau, Republic of Moldova.*
8. **Paduca Ala, Corduneanu Angela, Iacubitchii Maria, Bendelic Eugeniu, Moscalciuc Alina, Bucinscaia Larisa, Magla Tatiana.** Surgical experience in corneal transplantation. *Chisinau, Republic of Moldova.*
9. **Ungurean Elena, Șaptefrați Lilian.** Biological therapies in regenerative medicine. *Chisinau, Republic of Moldova.*

SESSION nr. 2

16:50-18:00

Moderators: **Ficai Anton**, PhD, professor (*Romania*). **Caproș Nicolae**, MD, PhD professor, (Republic of Moldova). **Macagonova Olga**, MD, PhD, researcher (Republic of Moldova).

1. **16:50-17:15. Motelica Ludmila, Ficai Denisa, Oprea Ovidiu, Ficai Anton, Andronescu Ecaterina.** The potential of use of the mesoporous materials in medicine. *Bucharest, Romania.*
2. **17:15-17:25. Iacubitchii Vitalie, Vacarciuc Ion, Caproș Nicolae, Cobzac Vitalie, Cociug Adrian, Nacu Viorel.** The use of stem cells in the wrist arthrodesis. Experimental study. *Chisinau, Republic of Moldova.*
3. **17:25-17:35. Evsiucova Maria, Cirimpei Octavian, Cociug Adrian, Nacu Viorel.** The use of skin allografts in the treatment of burns. *Chisinau, Republic of Moldova.*
4. **17:35-17:45. Macagonova Olga, Cociug Adrian, Braniște Tudor, Nacu Viorel.** Structural and physical characteristics of the dermal decellularized structures evaluation. *Chisinau, Republic of Moldova.*
5. **17:45-18:00. Feghiu Leonid, Feghiu Iuliana, Graur Sorin, Nacu Viorel.** Effective method for treatment of atrophic pseudarthrosis with leg shortening, associated with chronic osteomyelitis. *Chisinau, Republic of Moldova.*

DAY TWO – 18 March 2023

Session 1, 09:00 – 10:20

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

1. **09:00-09:10. Labusca Luminița, Danceanu Camelia, Minuti Anca, Ivanov Iuliu, Zugun-Elloe Florin, Plamadeala Petru, Chiriac Horia, Lupu Nicoleta.** Models for testing regenerative therapies – focus on explants as models for osteoarthritis. *Iasi, Romania.*
2. **09:10-09:20. Stavila Cristina, Minuti A, Herea D, Labusca L, Stoian G, Lupu N, Chiriac H.** Reliable protocol for sample preparation to observe nanomaterial adherence to the surface of biological cells by using scanning electron microscopy. *Iasi, Romania.*

3. **09:20-09:30. Stoian Alina, Pavlovschi Elena, Verega Grigore, Birgit Andrée, Hilfiker Andres, Nacu Viorel.** Experimental study in obtaining of a Vascularized Composite Bone Extracellular Matrix. *Chisinau, Republic of Moldova. Hannover, Germany.*
4. **09:30-09:40. Palarie Natalia, Palii Natalia, Palarie Victor.** Platelet Rich Growth Factor in the treatment of complex corneal disorders. *Chisinau, Republic of Moldova.*
5. **Verdes Irina, Capcelea Svetlana.** Novel treatment strategies for autism spectrum disorder based on cellular therapy and genomics. *Chisinau, Republic of Moldova.*
6. **09:50-10:00. Lupan Valentina, Dumbrăveanu Lilia, Cusnir Valeriu, Storoja Ana-Maria, Cociug Adrian, Nacu Viorel.** Cornea and amniotic membrane transplantation in the No.2 clinic of oftalmology during the SARS COV-19 pandemic. *Chisinau, Republic of Moldova.*
7. **10:00-10:10. Jian Mariana, Cobzac Vitalie, Verestiuc Liliana, Butnaru Maria, Nacu Viorel.** Scaffolds for bone tissue regeneration. *Iasi, Romania. Chisinau, Republic of Moldova.*
8. **10:10-10:20. Procopciuc Vitalie, Cociug Adrian, Nacu Viorel.** Impact of differently processed amniotic membrane grafts on the outcome of corneal ulcers in rabbit models. *Chisinau, Republic of Moldova.*

10:20-10:50.

Cofee Break

Poster session II

1. **Nacu Ana-Maria, Vartic Victoria.** The right to life. Legal status of the human embryo. *Gaesti, Romania.*
2. **Cataraga Tatiana, Nacu Viorel.** Stem cells therapy in infertility. *Chisinau, Republic of Moldova.*
3. **Abu Anem Abd Alaziz, Hacina Tamara.** Variability of the venous drainage of brain. *Chisinau, Republic of Moldova.*
4. **Ashkar Laila, Babuci Angela, Zorina Zinovia.** Anatomical peculiarities of the stylomastoid foramen and mastoid segment of the facial canal. *Chisinau, Republic of Moldova.*
5. **Berlinschi Grigore, Zorina Zinovia, Botnaru Doina, Botnari Tatiana.** The morpho-clinical features of multiple sclerosis. *Chisinau, Republic of Moldova.*
6. **Bobutac Mihail, Babuci Angela.** Variants of the renal pedicle. *Chisinau, Republic of Moldova.*
7. **Chicu Gabriela, Hacina Tamara.** Variability of the human brain and its meninges. *Chisinau, Republic of Moldova.*
8. **Cobileanschii Eugeniu, Cobileanscaia Liubov.** Hepatic volumetric blood flow in patients with duodenal ulcer. *Chisinau, Republic of Moldova.*
9. **Cobileanschii Eugeniu, Cobileanscaia Liubov.** Status of arterial hepatic flow in patients with acute duodenal ulcer. *Chisinau, Republic of Moldova.*
10. **Cojocar-Toma Maria, Toma Maria Mirabela, Jian Mariana, Cociug Adrian, Nacu Viorel.** Histopatological evaluation extracts of *agrimoniae herba* and *cichorii herba* in experimental. *Chisinau, Republic of Moldova.*
11. **Lisnic L., Spinei A.** Correlation between dental caries and quality of life in children. *Chisinau, Republic of Moldova.*
12. **Haim Lital, Sidorenko Ludmila.** Principles of elaboration and usage of mRNA-based vaccines. *Chisinau, Republic of Moldova.*
13. **Malai Ina, Hacina Tamara.** Age peculiarities of the human body and their consideration in medical practice. *Chisinau, Republic of Moldova.*
14. **Pîrvu Victor, Hotineanu Adrian, Peltec Angela, Pîrvu Cristina.** Evaluation of MELD score in liver transplant allocation. *Chisinau, Republic of Moldova.*

15. **Stolearenco Catalina, Popa Serghei.** The new approaches in the treatment of systemic lupus erythematosus. *Chisinau, Republic of Moldova.*
16. **Popusoi Diana, Smisnoi Mariana.** The influence of periodontitis in cardiovascular diseases. *Chisinau, Republic of Moldova.*
17. **Postolaki Alexandr, Bodean Sergiu, Belik Olga.** Anatomico-morphological particulars of the pendant from human molar from eposit component at carbuna. *Chisinau, Republic of Moldova.*
18. **Rusu–Radzichevici Natalia, Radzichevici Mihail.** Facial skin grafting for tissue defects as a result of various injuries. *Chisinau, Republic of Moldova.*
19. **Secrieru Felicia, Bendelic Anastasia.** The hepatic portal vein-normal and variant anatomy. *Chisinau, Republic of Moldova.*
20. **Tocarjevschi Iurie, Stratu Ecaterina, Catcov Carolina, Rakovskaia Tatiana.** Treatment of neurological complications of arterial hypertension. *Chisinau, Republic of Moldova.*
21. **Zorina Zinovia, Babuci Angela, Botnaru Doina, Botnari Tatiana, Cotone Tatiana.** Topographic and morphometric aspects of the internal jugular vein. *Chisinau, Republic of Moldova.*
22. **Cornea Cornelia, Ceban Emil, Tanase Adrian, Groppa Liliana, Sasu Boris, Rotaru Larisa.** “Brain death” donor. Sampling of organs and tissues with their subsequent transplantation. *Chisinau, Republic of Moldova.*
23. **Pavlovschi Elena, Stoian Alina, Gardikiotis Ioannis, Verega Grigore, Nacu Viorel, Cernei Gherman.** The vascularized bone allotransplantation after decellularized process. *Chisinau, Republic of Moldova, Iasi, Romania.*

SESSION nr. 2

10:50-12:00

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

1. **10:50-11:00. Jian Mariana, Cobzac Vitalie, Globa Tatiana, Pălarie Victor, Mostovei Andrei, Ficai Anton, Nacu Viorel.** Bone tissue regeneration using different 3D matrices. *Chisinau, Republic of Moldova. Bucharest, Romania.*
2. **11:10-11:20. Valic Eugeniu, Mereuta Ion.** The role of 3D-printing technologies in the management of breast cancer patients. *Chisinau, Republic of Moldova.*
3. **11:20-11:30. Goreacii Ana, Nacu Viorel.** Is menstrual blood a possible sustainable source of stem cells for regenerative medicine? *Chisinau, Republic of Moldova.*
4. **11:30-11:40. Padurar Luminita, Ignatov Olga, Nacu Viorel.** 3D printing in tissue engineering. *Chisinau, Republic of Moldova.*
5. **11:40-11:50. Fandofan Victoria, Jeru Ion, Bozul Uliana-Ariadna.** Features of microsurgical treatment in patients with recurrent pterygium. *Chisinau, Republic of Moldova.*

12.00

CONFERENCE CLOSING CEREMONY

Keynote lectures

Tissue and cells transplantation from research to clinical use.

Nacu Viorel^{1*}, Cociug Adrian¹, Ignatov Olga¹, Cobzac Vitalie²

¹Human Tissue Bank, Traumatology and Orthopedics Clinical Hospital, Republic of Moldova.

²Laboratory of Tissue Engineering and Cell Cultures, SUMPh *Nicolae Testemițanu*, Republic of Moldova.

In the Republic of Moldova, frozen or freeze-dried bone transplants, for the replacement of bone defects following various dysplastic, tumoral or post-traumatic processes, were imported from the laboratories of the Orthopedic - Traumatology Centers in Kiev, Kharkiv and Moscow, and have been practiced since 1960.

In 1962, at the initiative of Prof. L. Gladârevaschii and Prof. N. Testemițanu, the Tissue Preservation Laboratory was founded within the Republican Blood Transfusion Station in accordance with the order of the Ministry of Health of the Republic of Moldova, no. 46 of 28.02.1962, later, in 1966, this Laboratory was transferred to the Traumatology and Orthopedics Clinical Hospital. During the period 1962-1992 as the head of the laboratory Mr. Igor Ivanenco worked, and during the period 1993-2011 as the head of the Tissue Preservation Laboratory Mr. Dr. in medical sciences Ion Baciuc worked.

From November First, 2011, with the request of the Ministry of Health (directive of 06.10.2011), the process of creating the Human Tissue and Cell Bank within the IMSP SCTO was started, Viorel Nacu, Ph.D., university professor. The bank was placed in the premises of the Republican Combustion Center by designing and placing it in rooms adapted for this type of activity (input filter, reception, processing sector, clean room (sterile processing), storage sector, distribution sector, etc.), being equipped with equipment that allows the diversification of conservation methods and the broadening of the spectrum of grafts taken, processed and preserved (skeletal tissues, corneas, skin, amniotic membrane, auto cells from bone marrow, etc.). It is the only Bank of Human Tissues and Cells in the Republic of Moldova and is intended to provide IMSPs with transplants necessary for the treatment of patients with tissue deficiencies.

Within the Department of Operative Surgery and Topographic Anatomy of *Nicolae Testemițanu* SUMPh (V. Parfentieva, D. Razvodovschii, V. Dmitrienco) a method of preserving tissues in 0.5% formaldehyde with pH 7.3 was proposed. The scientific argumentation of the use of formalinized grafts for different regions of the locomotor system was elucidated in multiple doctoral theses and doctoral habilitation theses completed within the Department of Operative Surgery and Topographic Anatomy: I. Brus, doctoral thesis (1972), O. Bedencov doctoral thesis (1980), B. Topor, doctoral thesis and doctoral habilitation thesis (1980, 1992), L. Chiroșca, doctoral habilitation thesis (1989)

V. Remizov, doctoral habilitation thesis (1979), V. Nacu, doctoral thesis and doctoral habilitation thesis (2001, 2010), and within the Department of Orthopedics and Traumatology: I. Marin, doctoral habilitation thesis (1984), L. Iacunina doctoral habilitation thesis (1983).

During 10 years of activity of the HTCB in the Clinical Hospital of Orthopedics and Traumatology, diverse types of grafts from various tissues have been implemented and prepared:

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Numar total		180	145	243	327	431	582	551	648/649	551	462	700	558
Os cortical	53	137/119	165/144	225/173	384/234	91/201	285/173	149/188	122	130	50	116	96
Os prosopt congelat	0	0	0	0	0	0	0	135/104	646/524	203	134	327	306
Autogrefe osoase	0	0	0	0	0	0	1	3/2	44	0	0	0	0
Tendon		14/6	19/1	16/2	18/5	7/12	10/11	31/11	18/7	2	0	6	1
Cornee	0	0	0	63/40	45/44	40/19	42/28	35/36	27/25	45	14	6	20
Piele	0	0	0	27/2550 14/950	82/6763 87/7293	138/1665 9 78/9355	238/3318 3 133/1602 0	183/2601 7 143/2201 1	118/129	69	118/ 17128 cm2	77/ 8393cm2	0
Aznon	0	0	0	0	33/0	107/1377 3 84/6633	114/9757 114/1393 6	150/8399 69/3324cm2	102/74	101	129 (4110cm2)	147 9186cm2	115 (5255 cm2)
Maduva osoasă autologă	0	0	0	0	0	3/3	5/5	19/18	35/35	32	17	21	8
Fibroblaste autologă	0	0	0	0	0	3/0	0/0	2/0	1/1	0	0	0	0

The tissue bank is a component part of Orthopedic Hospital, but its purpose is not only the storage of bone grafts intended for transplantation, but also the collection, processing and preservation and distribution to National Medical Institutions the other types of grafts that were not accessible until 2011. In 2013, on March 22, the first allogeneic corneas were taken at the IMSP "St. Trinity", and on March 27, the first corneal transplant taken from HTCBB was performed. On March 28, 2013, the Human Tissue and Cell Bank was officially opened. Also, this year, on September 4, the first allogeneic skin sampling was performed, which was processed and preserved in 80% glycerin solution. On October 3, 2013, in the National Combustion Center in Orthopedic Hospital, to a 58-year-old patient underwent the first allogeneic skin transplant, covering 10% of the skin defects.

Conclusion. The modern tissue bank must be an adequately financed unit, equipped with modern equipment for harvesting, preservation and storage of tissue grafts that meet the requirements put forward by the profile structures of the European Union and the National Public Health services.

Key Words: Human Tissue and Cells Bank, Allogeneous Grafts, Tissue Bankin

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The potential of use of the mesoporous materials in medicine.

Motelica Ludmila¹⁻³, Ficai Denisa²⁻⁴, Oprea Ovidiu²⁻⁵, Ficai Anton^{1-3,5}, Andronescu Ecaterina^{1,3,5}

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The development of porous materials is strongly correlated with the development of the type MCM-41 mesoporous materials and firstly reported in 1992. As a consequence of the porous nature, of the very large specific surface area, the chemical properties are strongly changed, the materials based on mesoporous silica becoming active and reactive (at least if we compare them to other non-porous silica-based materials). The increase in activity and the storage potential of these materials in the pores, made these materials to be tested as systems with controlled release, including for medical applications. Additionally, mesoporous silica is sufficiently reactive and transforms into wollastonite and later into apatite, if introduced into bone tissue. The properties of these materials are controlled by the characteristics of the pores (size and arrangement) but also by the chemistry of the surface, by chemical modification of the surface, especially by silanization with appropriate functional groups, with an adequate hydrophilic:hydrophobic ratio can ensure release kinetics suitable for the intended applications. Thus, the analysis of the literature shows that there are numerous mesoporous materials, with varied morpho-structural characteristics and surface chemistry adapted for the release of a wide range of biologically active substances such as cytostatics, antibiotics, vitamins, polyphenols, ions, etc. Mesoporous materials have been tested as regenerative or medicinal supports in hard tissue engineering, in the treatment of infections, cancer, osteoporosis, but also as food supplement having the ability to additionally protect medicinal substances, including the extreme conditions from the stomach.

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Models for testing regenerative therapies – focus on explants as models for osteoarthritis.

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¹ Orthopedics and Traumatology Clinic Emergency County Hospital Saint Spiridon, Iasi, Romania.

² National Institute of Research and Development in Technical Physics, Iasi, Romania.

³ Faculty of Physics, *Alexandru Iona Cuza* University, Iasi, Romania.

⁴ Transcend Centre, Regional Oncologic Institute, Iasi, Romania.

⁵ Pathology Department Saint Mary Emergency County Children Hospital, Iasi, Romania.

Background. Osteoarthritis (OA) is a degenerative disease that progressively involves all joint compartments leading to destruction and loss of function. Regenerative medicine (RM) aims to introduce revolutionary therapies dedicated to drastically improve the way we treat degenerative diseases including OA. Explanted cartilage tissue has been proposed as a modality to study cartilage ontogeny and to understand cartilage repair as well as modality to screen new drug/therapies for the treatment of OA.

Objectives. To establish a working protocol for obtaining human osteochondral tissue explants in co

-culture with synovial tissue to be used as ex vivo models for OA and to demonstrate explant reactivity to conditioned media (CM) from adipose mesenchymal cells (ADSC) tested as a modality for bone and cartilage rescue.

Methods. Human osteochondral samples were collected from patients undergoing total knee replacement were kept in incomplete chondrogenic media (ICM) or in serum free DMEM. Explant-released cytokines were quantified by ELISA for Human tumor necrosis factor alpha (TNF α) and interleukin -6 (IL-6) and qPCR-based immunoassay for Human IL-17A and Human IL-1 β (ProquantumTM immunoassay kit Invitrogen). Histology, Western blot and Immunohistochemistry studies to detect Collagen type II (Col II) matrix metalloprotease 1 and 13 (MMP I, MMP-13), Perlecan and beta galactosidase (BGAL) are going on.

Results. We found that culture media as well as synovial tissue presence influences the level of detectable IL-6, IL-17A CM increased IL-6 presence up to 29 days in culture; TNF α and IL1B levels decrease after 7 days in culture; CM treatment significantly decrease TNF α in both synovium containing DMEM and ICM cultured explants Histology revealed presence of active chondrocyte with enlarged hyperchromatic nuclei in CM treated explants.

Conclusion. Time in culture, type of culture media and synovial presence influence explant reactivity. Presence of synovial tissue increase explant reactivity especially for situation when an anti-

inflammatory effect is expected. Histology and immunohistochemistry can detect markers of tissue regeneration. Explant culture can serve as a reliable ex vivo model for testing both anti-inflammatory

as well as tissue remodeling intervention for articular joint repair.

Keywords: osteoarthritis, regenerative medicine, explant culture, adipose derived mesenchymal cells

Abstracts

Post Covid-19 respiratory complications treatment by stem cells.

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¹ Department of Anatomy and Clinical Anatomy SPhU *Nicolae Testemitanu*, Chisinau, Republic of Moldova.

Background. Covid-19 is a new type of coronavirus that manifests itself with acute respiratory failure and acute respiratory distress syndrome that can progress to multiple organ failure. Despite the therapeutic advances, there are challenges in the treatment of this disease, thus directing attention to stem cells.

Objective of the study. Presentation of the role of treatment, in patients with post Covid-19 respiratory complications with stem cells.

Material and Methods. Review of 25 articles from Pubmed.gov; StemCells journals; The Regenerative Stem Cells Institute; BMC; ERS; Journal of Translational Medicine; American Lung Association.

Results. The primary disorder in the pathogenesis of Covid-19 is at the level of the immune system, by acting on the ACE2 receptor in pneumocytes and the production of the cytokine storm, the increase of C-reactive protein levels and the inability to transform pneumocytes type II into type I while maintaining the transition phase of pneumocytes type II. The role of stem cells in the treatment of covid-19 is represented by: Immunomodulatory role - inhibiting the activity and proliferation of B cells, T cells and natural killer, inhibiting the maturation and antigenic presentation of dendritic cells, activating macrophages. Anti-inflammatory role - release of chemokines (CCL5, CXCL9,10,11), secretion of lipoxin A4, TGF- beta, nitric oxide, prostaglandin E2, secretion of IL-10, reduction of IL6, reduction of TNF- alpha, decrease of neutrophils-secretion of repair factors of vascular endothelial growth, platelet-derived growth factor, IGF1 and HGF - activation of angiogenesis. Antifibrotic role- reducing the expression of pro-fibrotic ligate TGF-p1.

Conclusions. Stem cells with their significant immunomodulatory functionality can suppress the predominant cytokine storm in the acute phase of the disease. At the same time, stem cell transplantation has been shown to be effective in activating endogenous mechanisms of repair, tissue regeneration and decreased pulmonary fibrosis with increasing pulmonary vascularization and improving oxygen saturation. It has been proven that stem cells do not have receptors for ACE2 and thus they cannot be infected by the SARS-Cov-2 virus.

Keywords: Covid-19, cytokine storm, pneumocytes, immunomodulation, anti-inflammatory, repair, fibrosis.

Management of human tissue donation and transplantation in the Republic of Moldova for the past 10 years.

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Introduction: The transplantation of human tissues in recent years has seen a significant increase in the expansion of medical indications as well as an increase in the number of transplanted grafts. The main purpose of the study was to evaluate human tissue donation and transplantation activities in the Republic of Moldova for the past 10 years.

Materials and methods: Prospective study, annual reports of the Human Tissue Bank, and the medical-sanitary institutions authorized for procurement and transplantation activities.

Results: During the study period, 690 actual tissue donors were identified. Cadaveric tissue donors constituted 34.8%/240, of them DBD-22.9%/53, DCD-77.9%/187, and living tissue donors constituted 65.2%/450. In the dynamic there is an increase in actual tissue donors to 11.5 per million population (PMP) in 2022, even though during the pandemic period we had a dramatic decrease in the number of actual tissue donors from 10.8 PMP in 2019 to 3.5 PMP in 2021, the European standard being ≈ 40 deceased donors PMP. The family refusal rate decreased from 40.0% in 2018 to 20.0% in 2021, the European standard being $<10\%$. During the reference period 396 corneas, 180843 cm² of skin, 727 units of musculoskeletal tissues, and 104 units of placenta were procured. The waiting list for corneal transplants is growing steadily. From 2013 to 2022, 487 patients had been included in the waiting list for corneal transplantation. The rate of transplanted patients with 217 corneal grafts compared to patients on the waiting list averaged 44.5%, that is, only 1 cornea available for almost 2 patients in need of a transplant. During the research period, 846 skin grafts, 2851 musculoskeletal tissue grafts and 830 amniotic membrane grafts were transplanted, following the surgeons' requests. **Conclusions:** In the Republic of Moldova, there is an increase in actual tissue donors to 11.5 per million population in 2022. Nevertheless, in order to achieve 100% coverage of corneal transplant services in relation to needs, it would be necessary to increase almost double the number of actual tissue donors. Musculoskeletal tissue and amniotic membrane transplant activity meets the needs of practical medicine.

Keywords: transplantation, human tissue, tissue donors

Treatment of unicameral calcaneus cyst by introducing demineralized allogeneic bone paste: a case report.

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Background. The calcaneus is an uncommon site for unicameral bone cysts. Little is known about the etiology of these lesions. Such cysts are usually symptomatic, because of the concentration of forces through the heel and require surgical treatment in most of the cases.

Material and methods. The purpose of this paper is to present a case of a 25-year-old athlete who was admitted to the Department of Microsurgery and Reconstructive Surgery with pain in the region of the right calcaneus during walking, which appeared 2 months ago. The patient underwent plain chest X-ray, general blood and urine test, all of them came normal beside the X-ray of the foot which showed a 4,0x2,0x2.0 cm cystic lesion of the right calcaneus. The patient underwent surgical treatment, which consisted of extended curettage of the cyst followed by filling of the bone defect with 10 cm³ demineralized allogeneic bone paste mixed with 10 ml of patient blood. The demineralized allogeneic bone paste was prepared by the Human Tissue Bank. An intraoperative X-ray was performed and showed that the bone defect was filled with demineralized allogeneic bone paste. There were no early or late postoperative complications encountered. The patient was discharged from the hospital the second day after the operation.

Conclusions. Imaging data are required when a cystic mass is suspected. Surgical treatment in combination with using of demineralized bone paste should be considered as an effective treatment for bone cysts. Further evaluation is required.

Keywords. bone cyst, demineralized bone paste, reconstructive surgery.

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Stem cells therapy in infertility

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Foreword. Worldwide, infertility affects 8-12% of couples of reproductive ages. In recent years, stem-cell therapy raised new hope in the field of reproductive disability management. Infertility is a major health problem, and the data presented in this review suggest that the treatment of infertility with stem cells seems to be plausible, because some types of treatments have already been tested in humans, achieving live births, while others show great potential only in animal studies.

Material and methods. Was provided scientific research of the preclinical and clinical studies for the last 15 years in order to determine the effects of stem cell-based therapy in the treatment of infertility. Articles were selected from the PubMed, Scopus, and ScienceDirect databases.

Results. Studies using the experimental model have shown that stem cell therapy for infertility treatment gives positive results. The main types of used stem cells are embryonic stem cells (ESCs), mesenchymal stem cells (MSCs), spermatogonia stem cells (SSCs), and induced-pluripotent stem cells (iPSCs).

ESCs can produce germ cells and thereby treat infertility. ESC-derived PGCs are susceptible to ethical controversy because the process involves the destruction of human embryo. Sperm/oocyte-like cells can now be produced from embryonic stem cells. SSC transplantation is presented as a novel and promising strategy, based on the premise of spermatogenesis and stem cell self-renewal. SSCs are responsible for the continuous production of male sperm. This technology can also be used to treat human infertility and does not cause ethical or immune problems. These results strongly suggest that SSC transplantation can be a successful treatment for male infertility caused by premature chemotherapy. Some studies have recently reported that both human iPSCs can differentiate into male germ cells. Functional tests showed that sperm produced by iPSCs were able to fertilize oocytes after intra-cytoplasmic injection and generate fertile offspring after embryo transfer. Ovarian failure is inevitable with age. In addition, injecting BM stem cells can stimulate ovarian function, restore normal ovaries and hormone levels, and possibly allow pregnancy.

Conclusion. Several aspects of stem cell therapy remain unexplored. Thus, vast untapped potential still exists regarding applications in treating diseases such as infertility. We are confident that science will be able to cure infertility once the right approach is found. The reason for great promise is that stem cell treatment can be utilized on many different levels, from direct transplantation of stem cells, or their paracrine factors into reproductive organs, to in vitro differentiation into germ cells or gametes.

Keyword: Infertility; stem cells; fertilization; infertility treatment.

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Induced pluripotent stem cells and organoids: advancements and challenges in neurosciences, drug screening and regenerative medicine.

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Background: Induced pluripotent stem cells (iPSCs) and organoids are powerful technologies that have revolutionized the field of biomedical research. These have tremendous potential in neurosciences, drug screening, and regenerative medicine.

Material and Methods: The goals are to provide an overview of the current state of iPSCs and organoids, their applications in neurosciences, drug screening, and regenerative medicine, and highlight their advantages and limitations as research tools.

Results: iPSCs are generated from adult cells reprogrammed to a pluripotent state, meaning they can differentiate into any cell type in the body. This technology has allowed researchers to generate patient-specific cell models for studying diseases with a genetic basis. Organoids, on the other hand, are three-dimensional structures generated from stem cells that mimic the architecture and function of organs, having tremendous potential for studying diseases, drug screening and regenerative medicine.

In neurosciences, iPSCs are used to study the mechanisms underlying neurological diseases, such as Alzheimer's and Parkinson's disease. The ability to generate patient-specific cell models has allowed researchers to gain insight into the genetic basis of these diseases and to develop novel treatments. iPSCs have been used to test the efficacy and toxicity of new drugs before they are tested in humans, reducing the number of clinical trials and speeding up the drug development process. In regenerative medicine, iPSCs and organoids are used to generate functional tissues and organs for transplantation. This has the potential to revolutionize this field by reducing the need for donor organs.

There are also challenges associated with their use, as iPSCs require extensive quality control to ensure they accurately represent the genetic and epigenetic features of donor cells. Organoids are limited by their reproducibility and variability, which can make it difficult to generate results across different experiments. Additionally, iPSCs and organoids are still relatively expensive and time-consuming to maintain.

Conclusion: Despite the challenges, organoids remain powerful tools for studying human biology and disease. Their ability to generate patient-specific models and reproduce the structural and functional features of organs holds great promise for advancing the fields of neurosciences, drug screening, and regenerative medicine. As these technologies continue to evolve and improve, we can expect to see more widespread use of them in research and clinical applications.

Keywords: iPSCs, regenerative medicine, neurosciences

Topical application of sorption hydrophilic/hydrophobic composition based on nanosilica in the treatment of patients with burns.

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Introduction. One of the promising methods of treatment of patients with burns is the local use of sorption agents with antimicrobial properties.

Objective of the study. Studying the antimicrobial properties and clinical effectiveness evaluation of the local use of a new sorption composition based on nanosilica in the complex treatment of patients with burns.

Material and Methods. The suggested sorption nanocomposition included highly dispersed silicon dioxide, polymethylsiloxane, decamethoxine, metronidazole. The experimental study evaluated the antimicrobial properties of the sorption nanocomposition and antimicrobial agents which are part of it. 42 patients with IIab-III degree burns with an area of 10-30% of the body surface were examined. Depending on the tactics of local treatment, patients were divided into 2 groups: after early necrectomy, xenodermoplasty, the wound surface of the patients in the main group (n = 20) was treated with a solution of decamethoxine in combination with the same sorption powder. Treatment in the control group (n = 22) was similar except the use of sorption drugs. The examination included visual inspection of the injured area in combination with microbiological monitoring of the wound contents on the 3rd, 7th, 14th day.

Results. The obtained results confirmed the sufficient antimicrobial potential of the studied sorption nanocomposition, the properties of which are on the equal foot with the existing antiseptics applied for museum and clinical strains of microorganisms and fungi. Signs of a more favorable wound healing process of the patients in the main group were observed: faster wound cleaning, less inflammatory reactions and much shorter preparation of wounds for grafting.

Conclusion. The obtained results convincingly show the effectiveness of a multicomponent composite based on nanosilica with antimicrobial components in a comprehensive treatment of patients with burns.

Key words: burns, wound healing process, infection, antiseptics, sorbents.

10 years of activity of the human tissue bank in the field of cornea sampling and processing from the Republic of Moldova

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Introduction. The cornea is the window of the eye, allowing light to reach the sensory cells that allow us to see the world around us. In the TUB from the Republic of Moldova, the corneas with a long storage period are the lyophilized ones, with a period of 2 years, and those with a short period are kept in culture media (Tissu „C”), dehydration (Carry „C”) and transport (Eusol „C”) [1].

Material and methods. The conducted study presents the evaluation of cornea sampling, processing and validation in TUB over the 10-year period 2013 - 2022 for 395 corneas, from 202 donors (69.8% men, 30.2% women), with an average 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 death were cardiovascular disease, trauma, and cerebrovascular disease. Invalidation of the cornea was in 25.4% of cases, of which they were determined by serological infections (HBsAg-positive, HCV-positive, HIV/AIDS) - 15%, and biological contamination occurred in 7.8% of the total donor cornea. In total (294 corneas), 74.6% of the processed corneal tissue was used for 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 [2].

Results. The corneas from TUB, during the period 2013-2022, were evaluated in a macro and microscopic study that determined 3 important groups: the first group (160 donors) up to 10 hours of sampling from death - the anterior surface of the cornea was most frequently determined cornea with edema of the epithelium, stroma absolutely "transparent, not thickened, rare short folds, very thin Descemetov membrane, endothelial layer is completely transparent, intact on the entire surface[5]. Areas with uniform redistribution of cells, preferentially at the edge of the cornea and the middle area. Density of endothelial cells being greater than 2800 cells / mm², with moderate signs of polymegetism, cellular pleomorphism, being considered as indications for transfixing keratoplasty. The corneas from the second group (30 donors) - with the sampling period from 10 to 15 hours - the surface of the epithelium is slightly edematous, its integrity is not compromised (exception may be a minor mechanical desquamation). Stroma with initial signs of edema in the lower layers, not thickened, transparent. Descemet's membrane has a single smooth plica, located centro-radially; the endothelial layer is intact. The endothelial layer is arranged uniformly, with the persistence of the mosaic, slightly tumified, which counts 26 cells in a square that forms an average of 2600 cells per mm². The corneas from group III (12 donors) with the sampling period after 15 hours - edematous anterior epithelium, in some areas exfoliated with detachment of Bowman's membrane, sometimes mosaic desquamation is observed. The stroma is edematous throughout the layer, dull in color. Descemetov membrane has pronounced folds, the folds directed in different directions like "parquet floor" or "checkerboard". The endothelial layer is matte, interrupted along the contour of the envelopes that appear transparent. Microscopically, endothelial cells reach the figure of 2000 per mm²[3].

Conclusions. 1. The analysis of the clinical and socio-demographic factors of the donation process associated with the quality of the corneal tissue showed the importance of implementing TUB quality control programs, to promote the selection of good quality corneal tissues and guarantee a donation process with donor identification mechanisms, extraction, preservation and distribution of corneal tissue guided by best practices that aim to minimize the risk of compromising tissue quality. 2. The quality of the corneal tissue is a fundamental factor for the success of transplantation and to guarantee good quality tissues, it is important that the time limits between death and enucleation, death and preservation, and enucleation and preservation are established by the TUB, in order to minimize the risks to which tissues are exposed due to chronological factors related to the sampling process. 3. The best quality of the cornea is that of group I, which had a sampling time of up to 10 hours, which defined the density of endothelial cells as 2800 cells / mm², with moderate signs of polymegetism, cellular pleomorphism, being considered as indications for transfixing keratoplasty.

Key words: evaluation, validation, cornea, quality.

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„Brain death” donor. Sampling of organs and tissues with their subsequent transplantation

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Introduction. Organ and tissue transplantation can save lives or significantly improve the quality of life. In order to organize the activity of taking and transplanting organs and tissues from the donor to the recipient on the territory of the Republic of Moldova, the Law no. 42 of 03.06.2008 "Regarding the transplantation of organs, tissues and human cells" was adopted (published on 25.04.2008 in the Official Gazette, no. 81, art. no. 273, date of entry into force 25.10.2008) and revised Law No. 42 on the transplantation of human organs, tissues and cells of 06.03.2020.

Objectives. Steps in sampling of organs and tissues from a "brain death" donor based on the clinical case.

Materials and methods. Description of a clinical case about a patient hospitalized in the Municipal Clinical Hospital "Saint Trinity", Intensive Care department, 2022.

Results. A man, 67 years old, was hospitalized in extremely serious condition, from the anamnesis (collected from relatives) - the patient had several comorbidities, including hypertension. The clinical diagnosis: Ischemic stroke. Arterial hypertension grade III very high additional risk. Mixed cardiomyopathy (hypertensive, ischemic, dysmetabolic). Heart failure III NYHA. Despite the complex treatment administered, "brain death" was found, which was confirmed according to the Standardized Clinical Protocol. Following the discussion with the relatives, consent was received for the removal of organs and tissues. The kidney transplant recipient was selected based on HLA typing, Cross-match, pre-existing antibody titer, general condition and lack of contraindications for surgery. 2 kidneys, liver, 2 corneas, 4 vessels were taken from the donor, but one kidney was not transplanted due to the presence of suspicious lesions, after histopathological examination it was established: Atherosclerotic nephropathy. Multiple renal infarcts. Atherosclerosis of the renal artery st. IV, degree II.

Conclusions. 1. In the given case, organ removal was possible after the consent of the donor's relatives; 2. Organs, tissues and cells can be taken from the deceased person only if the death has been confirmed according to the criteria established by the Standardized Clinical Protocol (which were confirmed in this case); 3. Following investigations and complex compatibility tests, a patient with liver failure and another with end-stage renal failure were transplanted, other tissues taken (cornea-no.2, vessels-no.4) were processed and stored at the Bank of tissues.

Keywords. Donor, recipient, "brain death", transplant

The use of skin allografts in the treatment of burns

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Background. Burn disease continues to attract the attention of pathophysiologists and clinicians, due to the high level of this pathology in the trauma structure, the severity of the medical and social consequences. The total number of burns registered in the Republic of Moldova is 3,000-3,500 per year. The general lethality is 6.5-8%, and in STI 17.8-25%.

Materials and methods. A retrospective study was conducted, based on the medical documentation of patients treated with skin allografts in the period 2019-2022. Data processing was carried out using Microsoft EXCEL 2010 (Analysis ToolPak), Xlstat 2018 and SPSS 11.0 for Windows, statistical methods and quantitative and qualitative data analysis. The study of the observation sheets was carried out in accordance with the requirements of the Research Ethics Committee of the *Nicolae Testemitanu* State University of Medicine and Pharmacy.

Results. The analysis of the group of patients included in the present study demonstrates a significantly higher incidence of severe burns among male patients and those aged between 40-49 years; 40.68% of patients were aged ≥ 60 years; according to the area of residence, we obtained 2.82% more patients from the rural area. In our study, grafting with preserved allografts was performed in 50 patients (group 1) during the years 2019-2022, patients with severe burns. Group 2 (control) did not receive allograft treatment of the burn and different methods of repair of the tissue defect were used. During the study we established that the duration of hospitalization and discharge of group 1 that benefited from allografts was shorter compared to control group 2, they also presented a more significant rate of postoperative complications.

Conclusions. Early excision and grafting of post-burn lesions has probably been the single greatest development in the treatment of severely burned patients in the last two decades, leading to a significant decrease in basal energy requirements and thus a subsequent improvement in the mortality rate.

Keywords: deep burns, allografts, surgical burn treatment.

Effective method for treatment of atrophic pseudoarthrosis with leg shortening, associated with chronic osteomyelitis. Clinical case

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Background. Even if nowadays there are described many techniques for treatment of chronic osteomyelitis, pseudoarthrosis and defects of the tibial bone, this combination of pathologies till now represents a challenge for orthopedics surgeons. Every surgical techniques, which will allow shortening of the length recovery period and providing bone consolidation, will be recommended.

Aim. to obtain a new technique for treatment of septic pseudoarthrosis of the tibial bone with severe leg shortening associated with hematogenous osteomyelitis.

Material and methods. This surgical technique was realized in a 29 years old patient. The patient is considered ill from the 18 months old, when was identified acute hematogenous osteomyelitis localized at the level of proximal epimethaphysis of the left tibial bone, with involvement of the bone growth region. During childhood, the patient supported a few surgical interventions for removal of the septic foci. At 10 years old was performed correction osteotomy of the tibial bone with plate and screws. At adulthood there was detected a shortening of the left leg with 7 cm when comparing with right leg. At 29 years old, the patient supported a tibial osteotomy at the level of distal metaphysis, osteotomy of the fibula at the level of diaphysis. With extra focal fixator bone fragments were distracted 10 mm daily. After 7 days, the extra focal fixator was removed and the tibial bone defect was filled with fibular auto-graft and alo-ransplantation, fixation with plate and k-wires. Four months after surgery there was detected degradation of the material of osteosynthesis. Re-osteosynthesis was performed with plate. After 6 months clinical evolution was complicated with septic process and again there was detected degradation of material of osteosynthesis. The treatment used by us comprises removal of material of osteosynthesis, removal of grafts, sanitation of septic foci, adaptation of bone fragments and fixation with extra focal Ilizarov device. After 3 weeks at the level of the bone defects were introduced stem cells, which were harvested from posterior-superior spina iliaca. After this, daily bone fragments distraction was performed with 0,5 mm. During a period of 4 months after this procedure, the left leg was 65 mm longer. Percutaneously, in the region of regenerate there was injected a second dose of stem cells harvested from posterior-superior spina iliaca. Bone consolidation was confirmed after 9 months.

Results. Using this technique of treatment there was obtained an elongation of the left leg with 65 mm. Total period of lengthening and bone consolidation was 14 months.

Conclusion. The method of bone distraction associated with injection of stem cells is an effective method for obtaining bone elongation in condition of osteosclerosis and vascular disorders at the level of bone fragments subjected to distraction.

Keywords. stem cells, leg shortening, acute osteomyelitis.

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Is menstrual blood a possible sustainable source of stem cells for regenerative medicine?

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Introduction: The discoveries of the late 20th century in molecular, cellular and biotechnological biology have made it possible to separate and cultivate cells from various tissues and organs. In recent years, the information obtained about stem cells, which have plastic capacities in cultivation, differentiation and survival in vitro, attract the attention of medical practitioners due to the possibility of treating a series of pathologies, currently difficult to cure.

Aim of the study: Evaluation of the latest research progresses in menstrual blood-derived stem cells (MenSC) and their application potential. Clinical indications of the use of MenSCs for various regenerative medicine utilization.

Materials and methods: This study is a review of the literature, based on the synthesis of clinical studies published in the period between 2007-2022, 21 scientific sources were researched. This article includes publications identified through Google Search Engines, PubMed Databases, etc. The information has been systematized, highlighting the most important aspects of the detection and use of stem cells derived from menstrual blood (MenSC).

Results: Menstrual blood secretion has been identified as a valuable source of stem cells (Haining Lv 2018), which are called menstrual blood-derived stem cells (MenSC). Compared to stem cells from bone marrow and adipose tissues, MenSCs originate from body secretions and obtaining them is non-invasive to the body, easy to collect, and there are no ethical concerns. There is therefore a growing interest in the functions of MenSCs and their potential applications in regenerative medicine.

Conclusions: Menstrual blood appears to be a continuous source of stem cells that is easily collected by non-invasive methods and without causing discomfort to the donor. Menstrual blood collecting and processing protocols need to be evaluated and refined and adapted to the conditions of the Laboratory of Tissue Engineering and Cells Culture.

Keywords: Menstrual blood, Regenerative medicine, Stem cells derived from menstrual blood, Stem cell therapy.

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Stem cell therapy in the type 2 diabetes mellitus.

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Introduction. In 2021 it was estimated that there are 537 million adults with diabetes, which is approximately 1 in 10 adults worldwide. There are many arguments in favor of stem cell therapy in type 2 diabetes (T2DM). The purpose of this study was to evaluate the scientific publications in order to elucidate the results of this therapy in patients with T2DM.

Material and methods. A systematic review of the literature on stem cell therapy in type 2 diabetes mellitus has been performed, using NCBI database.

Results. Stem cell therapy in type 2 diabetes results in improved glycemic control and decreased glycated hemoglobin levels. These are associated with clinical improvement and decreased chronic complications of diabetes. It also led to improvement of insulin sensitivity with decreased Peptide level C in patients with T2DM. 20 types of adverse reactions were observed in this therapy, the most common was fever, observed in 0.14% of patients. Also, muscle strain, contusion, viral gastroenteritis, hematuria, and folliculitis complications were the lowest reported adverse effects, with an incidence rate of 0.02%. Stem cell therapy is also possible to use to relieve diabetes complications. Most often it is used for vascular complications such as diabetic nephropathy, diabetic retinopathy. In both cases there are promising studies showing clinical and subjective improvement in these patients.

Conclusions. Stem cells have the ability to be self-renew and differentiate into a variety of cells, including blood, heart, nervous and cartilage cells. Diabetes is one of the areas where the effectiveness of this treatment can be of the maximum/greatest importance, with significant improvement of clinical parameters and the quality of life of these patients.

Key words. Stem cell, diabetes mellitus, T2DM.

The use of stem cells in the wrist arthrodesis. Experimental study

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Introduction. Wrist arthrodesis is a procedure performed in advanced arthritis with painful movement in wrist joint. In the result of the wrist arthrodesis appear intercarpal ankylosis. This surgery is a rescue one, and is made in order to remove the pain syndrome and increase the strength of the hand. Unfortunately, wrist arthrodesis is performed with the cost of losing of range of movement. Aim of study was evaluation of stem cells using in wrist arthrodesis.

Material and Method. Our study was based on experimental research on New Zealand rabbits. As methods of implementation of the study included: preparation of allogeneic demineralized bone grafts, bone marrow sampling and isolation of autologous stem cells. In the first study group, on 7 laboratory animals was performed arthrodesis of wrist joint with allograft. In the second study group, on other 7 laboratory animals, was performed arthrodesis using the allograft with stem cells.

Results. For the initial stage, it was prepared 28 demineralized allografts, then by tissue engineering was obtained 14 osteo-cellular grafts. In all 14 cases, an immediate postoperative radiograph was performed. The clinical and radiological evaluation, performed at 4, 8 and 12 weeks after the surgery. Computer tomography was done 12 weeks postoperatively. Imagistic results showed us, that the group were performed arthrodesis using combined graft with stem cells, the ankylosis were achieved faster. Histological examinations indicate more active involvement in the process of osteogenesis in the use of combined stem cell transplantation.

Conclusion. Our study showed that the arthrodesis of the wrist using the allograft with stem cells have a positive impact in the process of osteogenesis.

Keywords. Demineralized allograft, stem cells, experimental study, wrist arthrodesis.

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Analysis of amniotic membrane processing in the Human Tissue and Cell Bank

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Introduction. Since 2014, the amniotic membrane has been collected and preserved at the Human Tissue Bank (HTB) for use by ophthalmologists and combustologists. In recent years, the need for amniotic membrane grafts increased [1,2]. This has multiple applications in regenerative medicine. Its epithelial and mesenchymal cells are widely used in several components of modern medicine [3]. The amniotic membrane is a rich source of biologically active factors, promotes healing and acts as an effective wound dressing [4].

Materials and methods. The placenta is taken by caesarean section only after the informed consent has been signed by the donor. Serological tests for placenta sampling include human immunodeficiency virus, hepatitis B and C viruses, and syphilis, which must be negative. The amniotic membrane is prepared under sterile conditions, in the clean room. The primary method of processing the amniotic membrane (disinfection stage) includes washing with physiological solution, after which, for 24 hours, the amniotic membrane is kept in an antibiotic environment. In the second processing stage, the amniotic membrane is cut into pieces, depending on the purpose of use, and placed in culture medium and glycerol in a ratio of 1:1. The code, date, dimensions, and area of the graft are indicated on each kit. Amniotic membrane can be stored in a freezer at -80 degrees C for 5 years.

Results. Starting from 2014, 102 placentas were taken for HTB, of which 3 were unvalidated (positive tests of the donor's serum). In total, 928 amniotic membrane grafts were obtained and preserved, of which 639 grafts for ophthalmological use and 289 for use in burn patients. In total, 855 amniotic grafts were released and used, of which 578 with an ophthalmological score and 277 with a combustiological purpose.

Conclusions. The amniotic membrane can be preserved in different conditions, the cryopreservation method in glycerol or dimethyl sulfoxide or their mixture with culture medium is most often used. In the future, it is planned to manufacture and use decellularized and freeze-dried amniotic membrane, which will be processed and stored at HTB.

Key words: amniotic membrane, graft, conservation methods, ophthalmology, combustiology.

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Bone tissue regeneration using different 3D matrices

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Introduction. There are several types of grafts used in the treatment of bone defects [1]. During the research, was tested the regeneration capacity of critical bone defects with several types of materials.

Materials and methods. To 18 New Zealand rabbits, under general anesthesia in both parietal bones, 8 mm in diameter critical defects were made. In the defects made in the right parietal bones were transplanted (n=3): collagen sponges cross-linked with 25% glutaraldehyde (GA) vapours, collagen sponges cross-linked with 25 mM riboflavin under UV-A [3], lamellas of demineralised bone matrix (DBM), shredded DBM [2], and 3D printed PLA discs; the control materials were transplanted in defects made in the left parietal bones: minced autologous iliac bone and Colapan. The rabbits were removed from the experiment at 12 weeks, the calvarias were fixed in 10% buffered formaldehyde. The regenerated defects were examined histologically by Hematoxylin-Eosin staining, and scanning electron microscopy (SEM) [4].

Results. The histological examination of defects treated with minced autologous bone showed an inflammatory process with necrosis and resorption of transplanted bone trabeculae. In defects treated with Colapan formation of bone trabeculae in the areas of contact with the native bone was determined. The defects treated with cross-linked collagen sponges showed a dense and regularly distributed collagen fibers when using GA and degenerated, loose with thin fibrillar structure for riboflavin. When DBM lamellas were used, debris of DBM matrix and disorganized fibrous connective tissue with an infiltrative character were found. The shredded DBM fragments were consolidated with fibrous tissue and at the periphery of the fragments, trabecular extensions of newly formed bone were determined. In spaces between filaments of PLA discs were found thick collagen fibers forming bundles and newly formed trabeculae of reticular fibrous bone. SEM showed that transplanted materials changed significant their structure except the PLA discs.

Conclusions. The difference between the obtained results showed that not all materials can be used for an efficient regeneration of critical bone tissue defects. Compared to the control and the other experimental groups, shredded DBM at 12 weeks filled the defect with bone-like tissue.

Keywords: critical defects, bone regeneration, 3D matrices.

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Scaffolds for bone tissue regeneration

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Introduction. There are many types of scaffolds prepared in order to regenerate bone tissue defects [2]. In performed research were tested matrices of natural origin.

Materials and methods. Collagen sponges were obtained from collagen extracted from the bovine Achilles tendon [3], which were cross-linked with 25% Glutaraldehyde (GA) vapors, and with 25 mM Riboflavin solution under the action of UV-A rays during one hour. Rabbit femoral and iliac wing bones were demineralized in 0.6 M HCl solution. Bone cells (BC) and mesenchymal stem cells (MSC) were isolated from rabbit [4, 5], to perform the MTT assay and to evaluate cellular adhesion on scaffolds with DAPI. The ultrastructure of the scaffolds was analyzed by scanning electron microscopy (SEM).

Results. The MTT assay on BC and MSC showed a high cellular activity. Also, seeded cells had a good adhesion and proliferation on the prepared scaffolds at 7 and 14 days of culture. At SEM examination was determined a high porosity of both cross-linked sponges, and thin walls (2-4 μm) with many small cavities in them, through which the pores communicate. However, it is determined that the pores of sponges cross-linked with riboflavin generally have larger sizes (70-220 μm) compared to those cross-linked with GA (50-150 μm) ($p < 0.01$). Also semnificative difference ($p < 0.01$) between pore size was determined in demineralised femoral (25-80 μm) and iliac wing bones (140-520 μm), and with different wall thickness ($p < 0.01$).

Conclusions. The obtained scaffolds had a good biocompatibility and a very nonhomogeneous structure.

Keywords: collagen, demineralised bone, scaffolds.

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Cornea and amniotic membrane transplantation in ophthalmological clinic No.2 during the SARS COV-19 pandemic

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The actuality of the subject. With the advent of new tissue preservation methods, cornea and amniotic membrane transplantation have become more accessible and more often used.

The purpose of the study. This study aims to analyze the surgical activity of cornea and amniotic membrane transplantation during the period of 2019-2022 within IMSP SCM Sfînta Treime, in order to identify how their use has evolved depending on their need and accessibility.

Methods. The source of the researched material is represented by the medical files of the patients who needed corneal transplantation (60 patients) or amniotic membrane transplantation (297 patients). 483 of them had corneal inflammatory processes, and 60 patients – corneal leukoma.

Year	Corneal transplants	Amniotic membrane transplants
2019	32 (42,10 %)	44 (57,89%)
2020	12 (12,5%)	84 (87,5%)
2021	8 (8,33%)	88 (91,66%)
2022	8 (9,09%)	81 (91,01%)

Results and discussion. As a result of this study, an obvious increase in hospitalized patients with corneal ulcer as a post-covid complication during the years 2020-2021 was found. Thus, we have seen an increase in membrane transplants and a decrease in corneal transplants caused by stopping the collection of biological material (cornea). And the increase in the number of inflammatory pathologies of the cornea caused by SARS-CoV-19 conditioned the decrease in corneal transplants for patients on the waiting lists.

Structural and physical characteristics of the dermal decellularized structures evaluation

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Introduction. Decellularized biomaterials derived from the biological tissues are ideal for tissue engineering applications because they mimic the biochemical composition of the native tissue. The physical and structural properties of the scaffold are important in the fields of tissue engineering and regenerative medicine [1-11].

Material and methods. Study material was 20 decellularized dermal grafts. 10 samples were obtained from piglets slaughtered in the slaughterhouse. Other tissues (n=10) were received from the donor from the Human Tissue and Cell Bank of the Republic of Moldova following the recommendations of the university ethics committee. Extracellular matrices were obtained by decellularization with 0.5% sodium dodecyl sulfate/0.1% EDTA solution [12, 13, 15]. The evaluation of the structural characteristics was carried out by the histological examination with hematoxylin and eosin, scanning electron microscopy (SEM) and the quantification of the amount of deoxyribonucleic acids (DNA). Assessment of the physical characteristics included analysis of extracellular matrix (ECM) volume porosity [13-16], density [17-20], and swelling rate [16, 17].

Results. By histological examination we revealed fewer cells in decellularized tissues compared to non-decellularized ones. More than 80.5% of nucleic acids were removed from porcine matrix and 82.5% of genetic material - from decellularized human dermal structures. A mean correlation and inverse dependence of -0.43 was shown between porosity and swelling rate of decellularized dermis.

Conclusions. The decellularization process significantly ($P < 0.05$) removed the cellular components while preserving the connective three-dimensional structure of the dermal matrices clearly shown by quantification of the amount of DNA and microscopic examination of the structures

Keywords: evaluation, structure, dermis, decellularization.

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The use of bone allografts in the surgical treatment of tibial plateau fractures

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Background. Tibial plateau fractures represent according to literature data approximately 1% of the total fractures in the general population and 8% among the senile age population which are mainly treated surgically. The aim of our study was to analyze the results of using bone allografts in surgical treatment of patients with tibial plateau fractures treated in Orthopedics and Traumatology Clinic *Vitalie Betisor* during period 2017-2021.

Materials and methods. We analyzed 10 clinical cases: 2 men and 8 women, mean age 59,4 years. By Schatzker classification of fractures type II was met in 3 cases, III – 3, V – 3, VI – 1, all the fractures were close. Surgical management consisted of open reduction, internal fixation with angular stability plates. Freshly frozen structural cancellous bone allografts were used to perform bone grafting of the bone defect formed after the reduction of fragments, which consisted at least 8 cm³.

Results. Postoperative follow-up was performed at 6, 12, 16, 24 weeks. Patients were evaluated clinically and radiographically, according to the Lysholm Knee Scoring Scale it was obtained an average score of 90 points. Bone healing was achieved to all patients in a period of between 12 to 16 weeks. No postoperative complications were noted. Results were depending on the the quality of reduction, stability of osteosynthesis, rightness of functional recovery and patient compliance.

Conclusion. Freshly frozen structural cancellous bone allografts are a good and safe option for grafting of large bone defects that may occur after the reduction during the surgical treatment of tibial plateau fractures.

Keywords. bone allografts, tibial plateau fractures

Amniotic membrane as a source of treatment in trophic ulcer of the lower limb.

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Introduction. Prolonged healing of lower extremity ulcers leads to their superinfection, followed by subsequent amputation of the limb. It is often seen in large chronic wounds with considerable tissue loss, which become senescent in the inflammatory process. In this case, the amniotic membrane is used as a biological dressing with a re-epithelialization effect.

Material and methods. For this research activity, the information was obtained by searching PubMed, using the following keywords: amniotic membrane, diabetic ulcer. The selected articles are in English and refer exclusively to the use of human amniotic membrane only in trophic ulcers of the lower limb. It includes an overview of the biologically active factors that induce the clinical effects that can be seen in amniotic membrane ulcers.

Results. Amniotic membrane allografts have been shown to be beneficial in the treatment of difficult to heal ulcers when was combined with standard therapy. Only through a meticulous initial evaluation of the wound is it possible to identify the factors contributing to its complexity.

Conclusions. The amniotic membrane, by its properties, can promote the formation of granulation tissue, with the suppression of excessive fibrosis, thus inducing the re-epithelialization of the chronic ulcer bed.

Keywords. amniotic membrane, diabetes, lower limb, ulcer.

The right to life. Legal status of the human embryo

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Introduction. This paper aims to review the controversial issues in the field of human rights: the status of the human embryo. Since the moment the creation of human embryos in laboratory condition became available, ethical questions continued to arise and emphasize it's irascible status. During pregnancy the embryo is part of another human being's body lacking a legal status distinct from that of his mother's. Defining the right to life and its prime beneficiaries is an important step in gaining a unitary position on a special status of the human embryo. This special legal status derives from the embryo's recognized potential to become a human being.

Aim of the study. Evaluation of the legal, medical, ethical and philosophical approaches of defining life and the right to life.

Materials and methods. This study is a review of the literature, based on the synthesis of articles published in the period 1977-2021, 31 scientific sources were researched. This article includes publications identified through Google Search Engines, PubMed Databases, etc. The information has been systematized, highlighting the most important aspects of the detection and use of stem cells derived from menstrual blood (MenSC).

Results. The new reproductive technologies allows interference in the whole process of human creation, from conception to the establishment of characters such as the choice of sex which, in a world ruled by good faith would only bring benefits, but in reality can be used as a discriminatory tool. Despite the undeniable importance of this right, none of the international documents that value the right to life have come to define it. Moreover, there is no unanimous definition of the term "person" or "human being", the direct beneficiaries of the right to life.

Conclusions. Human embryos, through their potential to become human beings, are a powerful symbol of human life, but it is not possible to grant it an equivalent status to individuals, or any direct collision with the interests of already born human beings would deprive it of any legal protection. **Key words:** the right to life, reproductive rights, embryo

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Surgical experience in corneal transplantation

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Background. The most common and popular type of allograft in the world is represented by corneal transplantation. It is the most successful operation among human tissue transplants, as the cornea is avascular structure which minimize the risk of graft rejection. Aim of the research is to determine the most frequent indication of the corneal transplant and the clinical profile of patients undergoing penetrating keratoplasty at Republican Clinical Hospital *Timofei Mosneaga*.

Methods. It was evaluated the medical records of all the patients undergoing a keratoplasty at Republican Clinical Hospital, between the January 1, 2020 and February 1, 2023.

Results. It was available data from 31 grafts in the study period, including 21 penetrating keratoplasty (PKP) for optical indication, 10 tectonic PKP. 67.74% were performed in male patients with an average of age 40.45 years. The main indication for optical PKP were bullous keratopathy (28.57%), followed by inherited corneal dystrophies (19.04%) and ulcers (19.04%), leukoma (14.29%) and corneal opacifications (14.29%), keratoconus (4.77%). Tectonic corneal transplantation indication was represented by perforated corneal ulcer (100%) with an average of hospital admission of 8.11 days. Postoperative complications allografts rejection occurred in 6.45% being the most common.

Conclusions. The goals of corneal transplantation are to improve vision that has been harmed by trauma, chronic disorders, or infection that are the main causes of corneal blindness. The primary ocular diagnostics that point to the performance of corneal transplantation as a treatment option can be identified by recognizing the clinical profile of patients undergoing penetrating keratoplasties.

Keywords: corneal transplantation, penetrating keratoplasty, corneal pathologies

3D printing in tissue engineering.

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Background. 3D bioprinting is an additive technology that uses bio-inks and biocompatible materials for three-dimensional tissue engineering. Bioprinting is an interdisciplinary field that combines medicine, engineering and materials science. Bioprinting can provide an alternative to autologous and allogeneic tissue implants, as well as replace animal testing for the study of diseases and the development of personalized treatments.

Materials and methods. For the bioprinter, the frame from a Computer Numerical Control (CNC) machine was used, made of metal, for the axes there are trapezoidal screws T8 and linear guide MGN 12, as motors 42HSC4416-235N8-120 are used, DVR8825 drivers are used to control the motors, Arduino Mega and RAMPS 1.4 expansion board are used as control board, the user interface was made through LCD 2004 model, we used S-300-12 as power supply. The extrusion system is based on the piston action principle, we used 28H30H0604A2 stepper motor, with DVR8825 driver, the motor is connected to a T8 trapezoidal screw and MGN12 linear guide, some interconnection parts of the extrusion system were printed on the 3D printer Ultimaker 2+ extended, made of PLA plastic, they support the syringe and tubing from an infusion system, a G20 i/v cannula is used as a nozzle.

Results. During the creation of the printer, some problems arose such as setting the extrusion speed depending on the density of the material used, the size of the nozzle and the diameter of the microperfusion system. This parameter is of great importance to achieve the desired accuracy. Also the precision of the axial movement of the extruder and the printing surface are important for creating the correct geometry.

Conclusions. 3D printing and the great diversity of materials used in this process has revolutionized the medical field, especially in the manufacture of patient-specific implants and prostheses. Bioprinting has great potential in tissue engineering applications in the research phase and current *in vitro* and *in vivo* experiments and represents a near-future solution to the needs of modern transplant medicine.

Keywords: 3D bioprinting, tissue engineering, personalized treatment, *in vitro*, *in vivo*.

Platelet rich growth factor in the treatment of complex corneal disorders.

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Background. Platelet rich growth factor (PRGF) is an autologous blood product rich in proteins and growth factors which can be rapidly obtained from patient blood. Clinically, it is an affordable treatment with potentially broad spectrum of applications in ophthalmology especially in the treatment of complex or refractory corneal wounds. The aim of this study was to evaluate the efficiency of autologous platelet-rich factor in the treatment of complex corneal disorders.

The study was performed at the Ophthalmology Department of International Clinic, Orhei, Moldova in January - December 2022.

Materials and Methods. There were 28 patients with corneal surface disorders, among which 7 patients with chemical burns, 4 patients with corneal ulcers, 5 patients with corneal dystrophies, 8 with advanced pterygium and 4 with neurotrophic keratopathy. Visual acuity varied from hand motion to 0.7. Solid PRGF was either just placed on the corneal surface or sutured with 2 nodes of 10-00 nylon suture at conjunctiva. If necessary, the procedure was repeated. All patients had corneal OCT scan before and after the treatment.

Results. Improved visual acuity and less subjective symptoms were observed in all patients. Complete healing of cornea was observed in all patients with chemical burns and corneal dystrophies. As well considerable improvement experienced 3 of 4 patients with corneal ulcers (reduced size and depth of the ulceration, improved visual acuity, smaller conjunctival injection). Also an improvement was seen in 2 of 4 patients with neurotrophic keratopathy. All patients after pterygium surgery had clear cornea and no recurrences over 6-month period after treatment. None of the patients reported general or local side effects of the treatment.

Conclusions: PRGF is a reliable and effective therapeutic tool to promote wound healing in complex corneal disorders.

Keywords. Platelet rich growth factor, corneal disorders, wound healing

The vascularized bone allotransplantation after decellularization process, *in vivo* testing.

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Background. Massive bone defects require a multidisciplinary therapeutic tactic [1]. Bone transplantation is a successful approach, but insufficient in this case [2]. Decellularized vascular bone allograft included in the host circuit may be the solution [3].

Objective of the study. To test the *in vivo* intraoperative phase of the allografting of the vascularized femoral segment with the internal iliac artery in the domestic rabbit.

Material and Methods. The 5 New Zealand White Rabbit were used, weighing 2.6-3.0 kg. We have studied the possibility of bone allograft osteosynthesis and microsurgical anastomosis of the decellularized pedicle in the host circuit with the vascular pedicle (internal iliac artery). Being located between the upper part of the great trochanter and the distal 1/3 of the femoral shaft. The surgical technique was staged and recorded respecting vascular continuity. The procedure was divided into 2 stages: 1. Performing segmental osteotomy (2.5 cm long) of the femur and his osteosynthesis. 2 The preparation of the vascular pedicle to the internal iliac artery by medial approach for the microsurgical anastomosis of the decellularized pedicle.

Results. We documented and described the successful result of the double approach of the thigh, to repair the massive bone defects by the vascularized bone allotransplant after the decellularization mixt process.

Conclusion. The allografting of the vascularized femoral segment with the femoral and internal iliac artery after the decellularization process can be done by the lateral and medial approach of the thigh. It is a convenient one in the procedure of vascularized bone transplantation of the femur to a laboratory animal-New Zealand White Rabbit domestic rabbit.

Keywords: vascularized bone allograft, combined decellularization

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Impact of differently processed amniotic membrane grafts on the outcome of corneal ulcers in rabbit models.

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Introduction. Thanks to its regenerative properties, the human amniotic membrane (AM) is extensively used in ophthalmology to treat a wide range of eye surface conditions. Despite the vast amount of studies justifying its ophthalmic use, there is lacking scientific data on the effectiveness of differently processed AM in the treatment of corneal ulcers. In this paper, we aim to compare the effectiveness of cryopreserved, lyophilized and decellularized amniotic membrane transplantation (AMT) in the management of corneal ulcers in a rabbit model.

Material and methods. Corneal ulcers were surgically induced in the left eyes of 28 rabbits. Four groups, each containing 7 specimens, were formed: group A (control) – rabbits treated conservatively, with no AMT; group B – rabbits operated with cryopreserved AM; group C – rabbits operated with decellularized AM; and group D – rabbits operated with lyophilized AM. The rabbits were clinically observed for a 3-month period, with the assessment of objective signs, the evolution of the corneal lesion and/or complications. After the follow-up period, the rabbits were euthanized; the left corneas were excised, fixed in 10% formaldehyde and then embedded in paraffin, cut into thin sections, stained with hematoxylin-eosin, and studied by light microscopy.

Results. The cornea regenerated the slowest in the control group (28 days), the fastest in group B (15 days), followed by group D (18 days) and then group C (21 days). The highest rate of infectious complications was found in rabbits from group A (57%, n=4), and the lowest – in the group operated with cryopreserved AM (14%, n=1). Corneal neovascularization and opacification were most intense in the control group. In the groups operated with AM, corneal transparency was relatively uniformly recovered, with a slightly poorer outcome in the group C. In conservatively treated corneas (A), histological examination revealed a thickened and deformed epithelium, patchy connective tissue and epithelial cell depletion; in corneas treated with cryopreserved AM (B), fibroblast proliferation and solitary lymphocytic infiltrate below Bowman's membrane were revealed; in corneas treated with decellularized (C) and lyophilized (D) AM, polymorphic and atrophied epitheliocytes were found.

Conclusion. While there were significant differences between the control group and the eyes treated with AMT, the clinical signs did not differ significantly between groups operated with cryopreserved, decellularized and lyophilized AM. Still, the cryopreserved AM showed the best results in terms of post-operative complications, regenerative capacities and restoration of corneal transparency.

Keywords: amniotic membrane transplantation, corneal ulcer, rabbit model.

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Reliable protocol for sample preparation to observe nanomaterial adherence to the surface of biological cells by using scanning electron microscopy.

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Background. When assessing the interaction between nanomaterials and cells, an important step is to image the effects induced by the material to the cell membrane. In order to evaluate the results of the interaction process, scanning electron microscopy (SEM) is typically used. Commonly, an important step during the preparation of biological cell samples for SEM is represented by the critical point drying, which involves the replacement of the alcohol used for dehydration with an inert gas. This conventional drying method is not only hard to accomplish, but it can lead to sample destruction if specific parameters are not met. On the other hand, when assessing nanomaterials adhered to the cell membrane, the integrity of the cell is not necessarily important, so a little cell deflation doesn't affect the intended purpose of the evaluation. Here, we describe a simple and more cost efficient method to prepare biological samples for SEM imaging that preserves cell integrity and can be used to describe nanomaterials interaction with cell surface.

Methods. Cells were grown on sterilized silica chips, after which the evaluated nanomaterial was added to the cell culture media at least 24h for incubation. Afterwards, the samples were washed to eliminate non-adhered nanomaterials, fixed with glutaraldehyde and osmium tetroxide, and dehydrated with increasing concentrations of alcohol. The silica chips were then air dried in the biological safety hood and in vacuum, followed by a sputter coat film of 5 nm of gold. The samples were imaged with a scanning electron microscope.

Results. We were able to obtain well preserved biological cell samples, both with and without nanomaterials adhered to the cell membrane surface. Nanomaterials such as magnetic nanoparticles and magnetic nanowires were easily traceable on cell surface. Furthermore, the nanomaterials were clearly observed in the images obtained, while the cell surface was not affected by the drying process applied. Although the samples obtained using our method were characterized by a slight deflation of the cells, the morphology of the cells is well preserved and the method is suitable for the evaluation of the interaction between nanomaterials and cell surfaces.

Conclusions: We have described a novel cost efficient and easy to perform method for processing biological samples for SEM imaging that preserves cell morphology and can be used for analyzing nanoparticle and nanowires interaction with cell surface.

Keywords. SEM imaging, nanoparticles, nanowires, cell samples

Experimental study in obtaining of a vascularised composite bone extracellular matrix.

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Introduction. One of the final products of tissue engineering is the extracellular matrix (ECM), a non-cellular component of tissues that can be obtained using different methods of decellularization. Most decellularization protocols are divided into those for soft tissues and those for hard tissues [1-4]. Our study aims to develop and test the universal protocol for decellularization of the composite vascularized bone graft (soft and hard tissue) in order to obtain the vascularized extracellular bone matrix that can be used in reconstruction of the massive bone defects.

Material and Methods. The same protocol was used for the decellularization of different diameters vascular grafts, and different structures of bone tissue (soft and hard tissue) porcine origin. Like large diameter vessel, was taken from the tibial bone. The efficacy of the protocol was demonstrated by histological examinations, DNA quantification and the biocompatibility test.

Results. The used protocol has been effective even for small diameter vascular grafts and on cortical and spongy bone blocks. Histological examination (H&E staining) showed cell death after processing. DNA quantification has shown a decrease in the amount of DNA, especially for spongy bone grafts and the biocompatibility test has demonstrated the biocompatibility of vascular and bone grafts after processing.

Conclusions: We can obtain an effective decellularization for both soft and hard tissues using the same protocol.

Keywords: extracellular bone matrix, decellularization, composite graft.

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Biological therapies in regenerative medicine.

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Background. Regenerative medicine is a relatively new field of medicine that aims to repair or replace damaged tissues and organs using advanced techniques such as stem cell therapy, tissue engineering and biomaterials/scaffolds.

Objective of the study. Highlighting the main biological therapies in regenerative medicine and their applicability.

Material and Methods. This summary is based on the analysis of international bibliographic sources published in electronic databases such as PubMed, Frontiers and ACS.

Results. The potential therapeutic strategies of tissue engineering and regenerative medicine can be divided in three broad categories: (1) recapitulating organ and tissue structure via scaffold fabrication (that mimics the extracellular matrix of the target tissue), 3D bioprinting (using bioinks mixed with living cells), and self-assembly (with special cues for guiding cells to organize themselves into the desired tissue); (2) integrating grafts into the host via vascularization and innervation either through the use of growth factors or by creating microchannels within the scaffold and using co-culture models; and (3) altering the host environment to induce therapeutic responses through cell infusion and modulating the immune system by suppressing it to prevent rejection of a graft, engineering the responses of immune cells or changing the properties of the implanted scaffolds. Most of these methods have successfully passed the preclinical stage of studies and currently are in clinical testing.

Conclusions. All of these techniques have the potential to revolutionize the field of regenerative medicine by providing replacement tissues and organs for patients with tissue damage or organ failure. They are justly considered cost-efficient personalized strategies of treatment with quick palpable results. However more research is needed to fully understand all the possibilities and limitations of these techniques in order to ensure their safety and efficacy in clinical applications.

Keywords: Regenerative medicine, tissue engineering, scaffold, 3D bioprinting, growth factors.

The role of 3D-printing technologies in the management of breast cancer patients.

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Introduction. Breast cancer represents a current problem due to high morbidity, mortality and disability. About 685,000 women worldwide die from breast cancer annually. Only 1.3% are detected in the early stages, while 24% in the late stages. Although mastectomy is an important and definitive treatment option for some patients, it is often associated with substantial psychological, social, and sexual sequelae, as well as a significant distortion of body image. Along with the development of personalized medicine, the principles and methods of diagnosis and treatment, 3D printing technologies have a promising role, aimed at improving the management of breast cancer patients by creating anatomical models of tumors for explanatory and operational purposes, as well as of safe, compatible and easily tolerated breast implants.

Materials and methods. A literature review was performed using scientific articles from PubMed, NCBI, Frontiersin, 3D Printing in Medicine, databases for a period of 5 years. Keywords used in the search: breast cancer, bioprinting, 3D printing, 3D implants, personalized medicine.

Results. This review of scientific articles highlights the main achievements in the field of 3D printing in the management of breast cancer patients. Scanning and subsequent three-dimensional printing of tumors allows the detailed explanation of the tumor process to patients. Also, it facilitates the choice of an appropriate and personalized therapeutic tactic. New printing technologies, including bioprinting, allow the modeling and creation of mammary gland implants using hypoallergenic, durable and compatible materials with the formation of patient-specific bio-absorbable matrices (scaffolds). Different types of stem cells and growth factors can be seeded on the scaffolds, similar to the extracellular matrix, ensuring the processes of cell growth and angiogenesis. These scaffolds, which are later resorbed by the body, keep the injected adipose tissue safe and minimize the significant volume loss of breast adipose tissue typically seen in the lipofilling technique.

Conclusion. Although 3D printing technologies are in development and testing stages yet, they represent an important chain in the appropriate future of personalized medicine in the management of breast cancer patients.

Keywords: Breast cancer, bioprinting, 3D printing, 3D implants, personalized medicine

Novel treatment strategies for autism spectrum disorder based on cellular therapy and genomics.

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Background. Autism spectrum disorder (ASD) is a highly heterogeneous neurodevelopmental and behavioral disorder, that still does not have a known treatment for core behavioral disorders. However, there is an increasing amount of ongoing clinical trials, set out to discover novel psychopharmacological mechanisms, cell transplantation methods, epigenetic regulation, and agents affecting the immune system that show promise in the treatment of ASD.

Methods. The current publication is based on narrative review, synthesizing the insight of clinical trials in determining the efficacy of novel ASD treatments from the fields of genomics, cellular therapy, and systems biology. The studies were selected from Science Direct, Springer Link, Oxford Academic, the National Library of Medicine, Nature, MDPI, PubMed, and Genome Medicine. In the study were included only publications with approved clinical trial design methodology, published in the years 2015-2022.

Results. Cell-based therapies have been found efficacious and recommended for ASD to address the neurobiological changes and core behavioral disorders stemming from such changes. The most promising one is stem cell transplantation from autologous umbilical cord blood (AUCB), being proven to be safe and effective in developing social and communication abilities by increasing white matter connectivity in the brains structure, the mechanism is presumed to decrease neural inflammation through the paracrine effect of the stem cells. Another effective novel molecular treatment is the transcriptional regulation targeting agent *tideglusib* which has the potential to alleviate core symptoms. Furthermore, numerous agents targeting synaptic networks, and immune system cells (astrocytes and microglia) have been trialed for ASD and correlated with improvement of symptomatology in clinical trials.

Conclusions. The current research of cellular therapy in ASD treatment shows promising positive outcomes, but there is an ongoing necessity for placebo-controlled double-blind trials to achieve definitive results, likewise, it requires collaboration and access to progressive genetic testing in genomics and measurement methods to further progress toward identifying the genetic pathogenesis and novel therapeutics in ASD.

Keywords: behavioral disorders, ASD, cellular therapy, autologous umbilical blood, genomics

Varia

Variability of the venous drainage of brain.

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Background. Chronic venous dyscirculation of the brain is one of the most common forms of cerebrovascular pathology, while the numerous scientific papers on the cerebral vessels are more concerned with the arterial system.

Materials and methods. The 121 scientific sources were searched in databases: PubMed, Elsevier, Hinari. Ten formalin-fixed anatomical specimens of the human head from the muzeum, as well as, from dissecting room were analyzed.

Results. According to numerous studies, only three dural sinuses are relatively constant - the superior sagittal, straight and cavernous. Thus, the presence of the superior sagittal, straight and cavernous sinuses was in 100% of cases, while others may be aberrant, hypoplastic, asimetric, bifid, double, triple, septated or absent. The main variations of the venous anatomy of the dural sinuses are: a- the bifid superior sagittal sinus connects to one transverse sinus and the straight sinus to the other; b-the superior sagittal sinus and straight sinus are forked with the connection to the left and the right transverse sinuses; c) torculum variations. Only three anastomotic veins are relatively constant: a - Superior anastomotic vein of Trolard; b - Superficial middle cerebral vein; c - Inferior anastomotic vein of Labbé. With the exception of wide variations of basal vein, the deep system is rather constant compared to the superficial venous system. There is no constancy in the formation of venous circles of the brain. There is a number of researches indicating differences in the venous circles of the base of brain in individuals of various constitutional types. There are variants of diploic veins, with regard to their sizes and anastomoses.

Conclusion. Considering the frequency of chronic venous circulation of the brain and the role of venous bed in the development of this pathology, more attention should be paid to the study of all links of the venous bed of head.

Keywords. veins of skull, veins of brain, venous variants of head, venous anastomoses.

Anatomical peculiarities of the stylomastoid foramen and mastoid segment of the facial canal

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Background. The facial canal comprises three segments and each of them has some specific features. The labyrinthic segment is the narrowest one, and it extends from the bottom of the internal acoustic meatus up to the geniculum canalis facialis, from which starts the tympanic (horizontal) segment and at the level of the second bending of the facial canal, it continues with the mastoid (vertical) segment.

Materials and methods. The study was carried out at the Department of anatomy and clinical anatomy of *Nicolae Testemitanu* State University of Medicine and Pharmacy, Republic of Moldova. The structural peculiarities of the stylomastoid foramen (SMF) and of the mastoid segment of the facial canal (MSFC) and their morphometric parameters were examined on 55 temporal bones. The feasibility of two bony landmarks used in facial nerve surgery was analyzed. One of the landmarks was represented by the distance between the apex of the mastoid process and the posterior margin of the SMF, and the second one was equal to the distance between the anterior margin of the SMF and base of the styloid process (SP).

Results. Out of the total number of samples, 25 temporal bones were from the right side and 30 bones from the left side. The shape of the SMF was variable: round shape, transverse and longitudinal oval shapes, semilunar and irregular shapes. Double SMF and double MSFC were revealed in two cases. The transverse diameter of the SMF had a mean value of 2.6 mm \pm 0.78 (1.5-5 mm); the right/left mean value was 2.7/2.6 mm ($p=0.823$). The mean value of the longitudinal diameter of the SMF was 3.0 mm \pm 0.99; the right/left – 2.8/3.1 mm ($p=0.318$). The minimal value of the MSFC length was 5 mm and the maximal length was 25 mm, with a mean value of 15.3 \pm 3.98; the right/left mean was 15.2/15.6 ($p=0.718$). The angle formed between the course of the MSFC and vertical line traced along the posterior margin of the external acoustic meatus had a minimum value of 10° and a maximum value of 168°, with a mean equal to 111.6° \pm 26.73; the right/left mean was 113.3°/108.7° ($p=0.548$). The mean distance between the apex of the mastoid process and posterior margin of the SMF was 13.2 mm \pm 3.54 (2-19 mm); the right/left mean was 12.7/14.0 ($p=0.208$). The distance between the anterior margin of the SMF and base of the SP had a mean of 2.4 mm \pm 1.28 (1-6 mm); the right/left mean was 2.4/2.6 mm ($p=0.504$).

Conclusions. The shape of the SMF is variable, its transverse diameter was higher on the right side, but the longitudinal one – on the left side. The angle between the MSFC had a wide range of variation and its mean value was higher than 90°. The mean value of the both landmarks were higher on the left side bones.

Keywords: stylomastoid foramen, mastoid segment of the facial canal, landmarks

The morpho-clinical features of multiple sclerosis.

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Background. Multiple sclerosis (MS) is a chronic non-traumatic disease of the central nervous system, heterogeneous, affecting young people. The forms of evolution and clinical manifestation of MS were estimated according to gender and age.

Materials and methods. The studied group consisted of 39 patients with MS, hospitalized in the "Diomid Gherman" Institute of Neurology and Neurosurgery. The study was based on the research and analysis of the medical observation charts taken from the archive of the nominated institution. Descriptive statistical methods were used to process the obtained data.

Results. It was found: that 35.9% were men aged between 24-42 years, the average age being 29.3 ± 1.6 years, and 64.1% were women - aged between 18-47 years, and the average age being $26, 4 \pm 2.1$ years. The male: female ratio was 1:1.8. According to age categories: under 20 years – 20.5% (7.7% men, 12.8% women); 21-30 years – 41% (12.8% men, 28.2% women); 31-40 years – 25.6% (10.2% men and 15.4% women); 41-50 years – 12.8% (5.1% men and 7.7% women). Clinical manifestations: sensitivity disorders: in 64.1% of patients; visual disturbances – at 59%; cerebellar disorders – at 51.3%; motor disorders – at 30.8%. Clinical forms of disease evolution: relapsing-remitting multiple sclerosis (RRMS) – in 59% (18% men and 41% women); primary-progressive multiple sclerosis (PPMS) – in 18% (7.7% men and 10.3% women); secondary-progressive multiple sclerosis (SPMS) – in 12.8% (2.6% men and 10.2% women); progressive relapsing multiple sclerosis (PRMS) – in 10.3% (7.7% men and 2.6% women). Patients with RRMS endured from 1 to 5 flares, the average being 3.5 flares; those with PPMS – from 1 to 7 flares, an average of 4.8; those with SPMS and PRMS – 2-3 flares, which are maintained for quite a long time.

Conclusions. The average age of patients with MS was 26.4 ± 2.1 years, the most numerous being from the 21-30 age category, with a male: female ratio of 1:1.8. The majority of patients with MS showed a polymorphous clinical picture, more frequently showing sensory, visual and cerebellar disorders.

Keywords: multiple sclerosis, morpho-clinical features

Variants of the renal pedicle.

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Background. The renal pedicle includes a wide range of number, topography and relationships variations of its constituents. Taking into consideration the high demand for renal surgery and clinical significance of the data related to the components of the renal pedicle, the aim of our study was to determine the number and topographical variants of the renal pedicle elements.

Materials and methods. The study was carried out at the Department of anatomy and clinical anatomy of *Nicolae Testemitanu* State University of Medicine and Pharmacy, Republic of Moldova. Thirty kidneys (14 right and 16 left), collected from formalized cadavers were examined.

Results. The variants of the renal pedicle were established in 19 (63.3%) of cases. Six types of topographical relationships of the renal pedicle elements were revealed. The most common type was AVU (artery-vein-ureter) – 12 (40%) of cases; followed by the classical type VAU (vein-artery-ureter) – 11 (36.7%); and each of the following types: UAV (ureter-artery-vein), UVA (ureter-vein-artery) and VUA (vein-ureter-artery) were marked out in 2 (6.7%) cases; type AUV (artery-ureter-vein) was present in a single case (3.3%). The renal artery divisions varied from 1 up to 7 branches. A single renal artery was present in 6 (20%) of cases; 2 branches in 15(50%) cases; 3 branches in 3 (10%); 4 branches in 4 (13,4%), and in single cases were determined 5 (3,3%) and respectively 7 (3.3%) arterial branches. The number of the renal vein tributaries varied from 1 up to 3. In 21 (70%) of cases the renal vein did not had any tributaries outside the renal parenchyma; 2 tributaries were present in 7 (23,3%), and in 2 cases (6,7%) were present 3 tributaries. There were not identified any number variants of the ureter.

Conclusions. Six topographic types of the renal pedicle elements were established. The most common type revealed by us was type AUV. The number of the renal artery divisions were twice higher than the number of the venous tributaries. Three positions of the ureter towards the renal vessels were determined: anterior, intermediate and posterior one.

Keywords: renal pedicle, variability, renal artery, renal vein, ureter

Variability of the human brain and its meninges.

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Background. Over the past decade, neurology, and other disciplines have begun to demand more detailed information regarding the normal and pathological individual anatomical variability of the brain due to the rapid development of neurosurgery.

Materials and methods. Fifty-five formalin-fixed anatomical specimens of the human brain, as well as, searches of the following Database: Medline; Embassies; Web of Science; Google search were used in this study.

Results. The study of the relief of cerebral cortex showed a variety in the number of gyri, their sizes and the depth of the sulci. There are many small variations in the secondary and tertiary gyri. For instance, the number of insular gyri constituencies is not constant, it varies from four to six. A number of morphometric variants of the hippocampus have been found, and the variety of the hippocampus head. All types of white substance fibers are characterized by size diversity. The authors note the greater thickness of the corpus callosum in women than in men. Variations of corpus callosum are: complete agenesis, partial agenesis, hypoplasia of corpus callosum, it can have the appearance of a stripe, being uniformly thinned, or atypical curves. The ventricular system likewise does not differ by permanence. Bilateral symmetrical development of the lateral ventricles is found in only 10% of subjects. Other variants are: underdevelopment, aplasia or hypoplasia of the posterior horn, cavum septum pellucidum. The dural sinuses show considerable anatomical variation. Transverse sinuses are often unequal in size, one sinus is usually larger than the other, they can be hypoplastic or atretic.

Conclusion. For the most complete data on the morphological study of the brain, an integrated approach is required, including the methods of automated computer image analysis, immunohistochemistry, and statistical analysis.

Keywords. gray substance, white substance, brain, dural sinuses, callosal body, brain ventricles, insula, hippocampus, grooves for dural sinuses.

Hepatic volumetric blood flow in patients with duodenal ulcer.

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Background. In patients with duodenal ulcer, the disorder of hepatic hemodynamics was confirmed by the retrograde propulsion of the blood through the veins of the liver, the decrease of the gradient of the arterial circuit during systole, compared to the venous reflux during diastole; reducing the elasticity and tone of the large arteries, reducing the filling of small and medium caliber arteries of the liver.

The purpose of the investigation. Assessment of the quantitative index – the average volume velocity of hepatic hemodynamics with the identification of reversal of blood flow (from hepatopet to hepatofug) by Doppler ultrasound in duodenal ulcer.

Material and method. The study included 46 patients with acute duodenal ulcer - 32 men, 14 women, average age - 39 ± 0.21 years. Changes in the lining and structure of the duodenal wall confirmed by video endoscopy. Linear parameters studied by color Doppler, were calculated in the portal vein, spleen vein, superior mesenteric vein and hepatic artery.

Result. The volumetric flow in the portal vein varied between 578 ± 312 ml / min and 324 ± 15.6 ml / min and was approximately 1000-1200 ml / min. In the spleen vein, the volume velocity ranged from -157 ± 0.4 to 366 ± 12 ml / min. There was a linear increase in blood flow of 70%. Upper mesenteric vein: the volume of normal flow is approximately 194 ± 25 ml / min. As the pathology progressed, the volume of the flow also increased: from 785 ± 0.5 ml / min to -979 ± 138 ml / min. The volume of the blood flow rate in the hepatic artery was 269 ± 115 ml / min.

Conclusions. 1. Volumetric flow - the index that characterizes the predominant blood flow - hepatopet or hepatofug (to the liver or from the liver). 2. Received results showed us the reciprocal relationship between gastro-duodenal and hepatic hemodynamics in duodenal ulcer.

Keywords: volumetric flow, average volume velocity, hepatopet, hepatofug.

Status of arterial hepatic flow in patients with acute duodenal ulcer.

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Background. Disorder of the hepatic arterial circuit is particularly characteristic for complicated evolutionary forms of ulcer. There has been a reduction in the elasticity and tone of the arteries, an acceleration of hemodynamics in the large caliber arterial networks of the liver and a decrease in the filling of small and medium caliber arteries.

Material and method. The study included 46 patients with acute UD - 32 men, 14 women; the average age is 39 ± 0.21 years. The hemodynamic indices were studied by means of color Doppler that allows us to direct the beam to the desired point of the visualized vessel and to calculate the flow rate in the area of the interest. -amplitude in the hepatic artery.

Result. Normally, the linear velocity of blood flow in the hepatic artery is 59 ± 15 cm / s, diastolic - 21 ± 5 cm / s, the volume of the velocity of blood flow - 269 ± 115 ml / min, the resistance index (IR) - 0.64 ± 0.02 , pulsation index (IP) - 1.25 ± 0.16 . The linear velocity of the blood flow ranged from 76.8 ± 0.8 cm / s to 85.5 ± 0.5 cm / s. The volume rate of portal blood flow in duodenal ulcer was 990 ± 69 ml / min. In the diagnosis of duodenal ulcer, the most significant specificity and sensitivity had a diastolic speed of blood flow, the index of resistance of the hepatic artery. The peripheral resistance index (IR) and the pulsation index (IP) in the hepatic artery were 25% and 30% higher, respectively, than these indices in the spleen vein.

Conclusions. 1. Acceleration of blood flow in the hepatic artery (HA) is the informative hemodynamic parameter that invoke the secondary process of ulceration and ulcer cicatrization.

2. The most pronounced changes in hepatic blood flow occurred in severe duodenal ulcer, when against the background of stagnant blood flow in the portal system, an increase in arterial vascularization was established.

Keywords: hepatic artery, linear velocity of blood flow, resistance index, pulsation index.

Histopatological evaluation extracts of *agrimoniae herba* and *cichorii herba* in experimental induced hepatotoxicity.

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Background. *Agrimonia eupatoria* L. (Rosaceae) and *Cichorium intybus* L. (Asteraceae) are medicinal plants with a long tradition of use for a variety of therapeutic purposes: anti-inflammatory, astringent, antioxidant, being rich in phenolic compounds (flavonoids, phenolic acids and tannins). There is limited data available on their hepatoprotective effects, particularly in relation to extracts obtained from their aerial parts.

Material and methods. The plant products derived from the two species were collected throughout the flowering period and dried extracts of the aerial parts were obtained with 60% (w/w) ethanol. Toxic hepatitis was induced an *in vivo* model with CCl₄ (0,4 g/100 g) in rats and the protective effects of the two extracts, in doses of 100, 200, 400 mg of (*Agrimonia herba* and *Cichorii herba*) were evaluated by biochemical and histological investigations. For histological analysis of the samples, hematoxylin-euzine staining was performed and the samples were visualized by light microscopy (type Olympus).

Results. The histological analysis (H-Ex90) of the samples determined that in the liver we have swelling of the hepatocyte cytoplasm with granular inclusions, dilated centrilobular vein, dilated dysse spaces and interstitial oedema in all groups treated with CCl₄; for the maximum dose of *Agrimonia herba* extracts (400 mg)- cytoplasmic swelling of hepatocytes with granular inclusions, dilated centrilobular vein, dilated dysse spaces, interstitial oedema and perilobular vesicular and hydropic dystrophy were observed, indicating an aggressive process on the liver parenchyma.

Conclusions. The *Cichorii herba extract* in doses: 100, 200, 400 mg and *Agrimoniae herba extract* (100, 200 mg) can be used in further studies for the development of new pharmaceutical forms.

Keywords: *Agrimonia eupatoria*, *Cichorium intybus* extracts, histopatology.

Features of microsurgical treatment in patients with recurrent pterygium.

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Introduction. Recurrent pterygium is clinically manifested by a triangular fold of the bulbar conjunctiva with the base towards the semilunar fold and the tip towards the cornea. The etiology and pathogenesis of recurrent pterygium is unknown. It would result from a corneo-conjunctival epithelial alteration, associated with a proliferation of fibrinogen tissue, progressing between the epithelium reduced to a few layers of cells and the perforated Bowman's membrane.

Aim. To assess the effectiveness of a modified method in the treatment of recurrent pterygium.

Objectives:

1. To determine the effectiveness of the modified method using the free conjunctival flap in the treatment of recurrent pterygium.
2. To appreciate the benefits of the modified method depending on the addressability of patients with recurrent pterygium.

Materials and methods. The study included 10 patients (5 men and 5 women) with recurrent pterygium aged 20-71 years who underwent pterygium removal according to a modified method. Thus, during the surgical intervention, a movable, free, rectangular flap with sides 5 x 3 mm was prepared inferiorly paralimbally, which was fixed conjunctivally paralimbally, nasally in the area of the body of the pterygium translocated to the superior or inferior fornix. It is important to position the formed conjunctival flap with a limbal orientation.

Discussions. The postoperative recovery was fast, but for several days after the operation the globe was hyperemic, irritating the suture fibers used to fix the conjunctival autograft. Antibiotic and anti-inflammatory in the form of eye drops are needed. Thus, in all patients, 3 months after the microsurgical intervention, no signs of recurrence of the operated pterygium were detected. In 2 late-presenting patients, the pterygium was extended onto the cornea, resulting in deep scarring. As a consequence, the radius of corneal curvature was changed with the decrease in visual acuity in the postoperative period. This is why surgery for recurrent pterygium should not have been delayed.

Conclusions:

1. The microsurgical method proposed for the treatment of recurrent pterygium is safe and effective, determining the lack of recurrence in the postoperative period.
2. Microsurgical intervention based on recurrent pterygium should be performed as early as possible.

Keywords: recurrent pterygium, free conjunctival flap, recurrence, postoperative period.

Acute toxicity studies of extracts from *Lavandula angustifolia mill.*

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Introduction. Fine lavender (*Lavandula angustifolia* Mill., LA) is a valuable plant, broadly cultivated for essential oil production. LA extracts display a broad spectrum of pharmacological activities, including antioxidant, sedative, anti-inflammatory and antimicrobial properties. The use of LA extracts as food additives requires a thorough investigation of their toxicity profile. We report in the current communication preclinical acute toxicity studies of a LA ethanolic extract.

Material și methods. Wistar rats (n=42) of both sexes, with a body weight of 200 - 400 g, aged approximately 3 months, were used for the acute toxicity study. Acute toxicity was modeled by intragastric administration of LA extract solution by gavage to outbred rats. The LA extract was administered in doses of: control group, group I - 500 mg/kg; II - 1000 mg/kg; III - 1500 mg/kg; IV - 3000 mg/kg; V - 4000mg/kg; VI – 5000 mg/kg. After 14 days, the animals were euthanized and blood was collected with the study of biochemical indices (total protein, albumin, urea, creatinine, AST, ALT).

Results. Acute toxicity studies demonstrated that after internal administration of LA extract to rats in doses of 500 mg/kg, 1000 mg/kg; 1500 mg/kg, 3000 mg/kg, 4000 mg/kg, 5000 mg/kg no death of animals. LA extract was established as a relatively harmless biologically active substance (LD50 being >5000 mg/kg). The harmlessness of the LA extract was confirmed by the study of the peripheral blood picture in the animals of the group treated with the LA extract with the administrable dose of 500 mg/kg and 5000 mg/kg in which the level of biochemical indices did not change.

Conclusion. LA extracts in doses of 500 mg/kg - 5000 mg/kg do not produce changes in biochemical parameters and can be considered harmless.

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Correlation between dental caries and quality of life in children.

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Introduction. Measuring quality of life at an individual level can provide important data on health status and the effects of healthcare services. The aim of this study was to assess the impact of caries and its treatment on quality of life (QoL) in school-aged children.

Materials and methods. A cross-sectional prospective study was carried out within the Department of Pediatric Oral-Maxillo-Facial Surgery and Pedodontics *Ion Lupan* of the *Nicolae Testemițanu* SUMPh. The research group (L1) consisted of 70 children with dental caries. In the control group (L0) 70 children free of dental caries were included. For QoL assessment, the Child-Oral Impacts on Daily Performances (Child-OIDP) questionnaire was applied. The study was conducted in accordance with ethical requirements with the written consent of the children's parents. The Spearman ρ (rho) coefficient, calculated via nonparametric rank correlation test, was used to determine the correlation between tooth decay degree and its impact on children's QoL. The Child-OIDP self-administered questionnaire was used to collect data and data was analyzed using Epi-Info.

Results. A total of 140 students responded, of whom 49.2% experienced at least one impact. The most affected performances were eating (22.3%), followed by smiling (18.5%) and emotional state (6.5%), and the least affected daily activities were playing (0.8%) and schoolwork (1.1%). The main causes were bleeding gums (39.3%), injury (26.8%) and sensitivity (33.7%), and adolescents reported an average of 1.5 pathologies as perceived causes of impact.

Conclusion. A significant positive association of very high, high and moderate intensity was established between the indicators of dental caries and the impact of the oral health status on QoL. The high prevalence of dental caries' impact on children's QoL indicates their increased treatment needs and insufficient access to dental care. Estimating the impact of oral health status on daily performance is important for the creation of health policies that address the needs of the population.

Keywords: *oral health, quality of life, dental caries, surveys and questionnaires*

Principles of elaboration and usage of mRNA-based vaccines.

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Introduction. The COVID-19 pandemic and the mRNA vaccines that were developed for it catapulted the topic of mRNA vaccines to the forefront and brought them to the attention of the scientific community and the general public. Hundreds of millions of people have received the COVID-19 mRNA vaccine and they were considered a great success. **Objective of the study.** Providing an overview of the articles available on mRNA vaccines, a description of the method of its development, its mechanism of action, its applications and to discuss of the benefits and limitations of the vaccine.

Material and Methods. This is a systematic review study. The databases PubMed and Google Scholar were searched for studies reporting on mRNA vaccine elaboration, mechanism of action, and applications by searching keywords. Studies that were peer-reviewed, and were published in platforms with higher impact factors were preferred. Also were included relevant publications in the time period of 2012-2023.

Results. The mRNA vaccine development includes- the isolation of a pathogenic genetic material, synthesis of mRNA using a template, mRNA purification, and addition of a delivery system. mRNA vaccine mechanism of action involves the introduction of the vaccine to a recipient, mRNA uptake by targeted cells, mRNA-mediated protein expression, and immunogenicity development. Potential applications of the vaccine are as a protein replacement therapy, cancer immunotherapy, vaccines against various pathogens, and treatment of autoimmune diseases and allergies. The benefits of the technique are-rapid production which is useful in emerging infections, high efficacy, high adaptability to different antigen designs, possible titration, and high safety profile. Challenges and limitations of mRNA vaccines include the requirement of colder conditions in comparison to traditional vaccines, there is need of understanding the role of adjuvant addition to the vaccine, and the formulation of a vaccine in case of rapidly changing targeted antigens (breakthrough infections and immune escapes of cancers).

Conclusion. mRNA vaccine technology has many benefits over traditional vaccines, which makes them a good possible alternative. These vaccines have various potential applications in different fields of medicine, further research should be performed in order to integrate them in the future in clinical practice.

Keywords: vaccine, mRNA, COVID-19, pandemic, elaboration, mechanism of action, applications.

Age peculiarities of the human body and their consideration in medical practice.

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Background. Nowadays, the modern textbooks are abundant with materials on general anatomy and physiology, while the age-related aspects of the body's various organ systems are covered rather briefly.

Materials and methods. The study was carried out based on 30 bibliographic sources from the databases: NCBI, PubMed, EMRO.

Results. The bone mass and volume decreases in the third decade of life in both sexes and people of all ethnic backgrounds, as this fact manifests itself in osteoporosis and increased risk of fracture. Another process that begins around the age of 30 and progresses throughout life is sarcopenia - a gradual loss of muscle mass and muscle strength. This slight loss of muscle strength puts increased stress on certain joints and can predispose a person to conditions such as arthritis. It was found that with advancing age there is an increase in size airspace. From the age of 50 reduction in supporting tissue results in premature closure of the small airways during normal breathing and can cause air trapping and hyperinflation. The cardiovascular system undergoes changes such as thickening and stiffening of the large arteries even in apparently healthy but older individuals. This process occurs due to the deposition of collagen and calcium, as well as the loss of elastic fibers in the structure of the vessels. The digestive system shows some age-related peculiarities related to the structure of the walls of the organs: the walls of the large intestine atrophy with age, resulting in diverticulosis. Another change is the thinning of the stomach mucus membrane with age, leading to lower levels of mucus, hydrochloric acid and digestive enzymes. This reduces protein digestion and can lead to chronic atrophic gastritis.

Conclusions. Taking into account the age peculiarities of organ systems is mandatory both in the prevention of diseases and in the adequate treatment of patients.

Keywords: body aging, structural peculiarities, locomotor system, cardiovascular system, respiratory system, digestive system, body aging.

Evaluation of MELD score in liver transplant allocation.

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Background. The increase in the number of patients with liver cirrhosis has necessitated the revision of the widely used Model for End-stage Liver Disease (MELD), which predicts short-term mortality and determines priority on the waiting list for liver transplantation. Later, sodium levels were shown to be an independent predictor of mortality in cirrhosis and were then incorporated into the MELD score, further enhancing its ability to predict mortality. Thus, revision of the MELD score is needed to increase equity, reduce deaths and optimise outcomes on the liver transplant waiting list.

Materials and methods. We evaluated 265 patients with chronic liver disease, age ≥ 18 years, included on the liver transplant waiting list between February 2013 and January 2022. MELD, MESO Index, MELD-Na, UKELD, iMELD, reFitMELD, reFitMELD-Na, upMELD, MELD 3.0 scores were used. Prognostic abilities for predicting 90-day mortality were investigated by applying receiver-operator-characteristic-curve analysis.

Results: 39 patients (34%) died of whom (male 28, female 21, mean age 48 years) on the liver transplant waiting list within 90 days of listing. However MELD score 3.0, had the best acceptable prognostic performance with areas below Roc-curve (AUROC = 0.836). All scores achieved an average quality score of 75.1%. In 51.66% of patients, however, there was an increase in the prognostic score than the MELD score.

Conclusions. Thus, the MELD 3.0 score effectively predicts short-term mortality among patients with liver cirrhosis and specifically addresses gender disparities on the liver transplant waiting list while maintaining post-transplant survival.

Keywords. waiting list, MELD 3.0, liver transplant

The new approaches in the treatment of systemic lupus erythematosus.

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Introduction. In recent years, the incidence of SLE has increased. The variety of clinical manifestations have an undulating course with alternating remissions and exacerbations, which make this disease one of the most difficult to diagnose, treat and evaluate the effectiveness of therapy. Despite the fact that half of patients starts with low SLE activity, the disease progresses in the future is affecting many organs and systems.

The purpose This article presents the new approaches and recommendations in the treatment of Lupus the peculiarities of the evolution and activity of the disease.

Material and methods: When carrying out this study, we analyzed a group of patients diagnosed with systemic lupus erythematosus, which includes the years 2020-2022, patients admitted to the rheumatology and arthralgia department, within the Republican Hospital of the Republic of Moldova.

Results. Considering that the treatment must be guided according to the activity and severity of the disease, with a moderate activity index were detected 17,4 %patients, with high activity 82,6% patients. We have established that the first-line therapy in patients with non-life-threatening SLE are glucocorticosteroids, hydroxychloroquine, NSAID.

In case of vitally dangerous organic damage with high activity of the disease in treatment se use immunosuppressants (CYC, Azathioprine, MMF, Methotrexate and/or drugs biological (Belimumab, Rituximab).

Conclusions. in the care of systemic lupus erythematosus:

the manifestation of the disease evolves depending on the activity of the disease, the developed lesions, which will define the treatment strategies for the sick.

Keywords: management, activity of the disease, immunosuppressive treatment, treatment guidelines.

The influence of periodontitis in cardiovascular diseases.

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Background. Currently, the relationship between periodontal disease and general health is deeply studied, which refers to the multiple and complex interrelationship between periodontal diseases and general health. There are three ways of interaction between the affected periodontium and non-oral organs: bacteremia, systemic inflammation (interleukins, etc.) and endotoxemia caused by swallowed bacteria.

Aim of the study. Assessment of the correlation between the clinical signs of the chronic periodontitis and the preclinical ischemic myocardial signs.

Material and methods. 92 patients with chronic periodontitis (age between 25–58 years) without clinical manifestations of cardiovascular disease and pathological classical ECG signs were selected for this study. Periodontitis was diagnosed following the clinical and radiological exam. ECG dispersion mapping was used to identify preclinical ischemic myocardial signs.

Results. We have determined that in 85% cases of patients with chronic periodontitis, preclinical ischemic myocardial disorders. The correlation analysis has shown that with the increase in the severity of the periodontitis, the value of the Myocardial Index (ischemic signs) will be higher.

Conclusions. Myocardial Index (ECG dispersion mapping) positively correlates with the severity and duration of the periodontal disease, patient's age and the systolic blood pressure level. Around 85% of patients with chronic periodontitis had preclinical ischemic signs. Researches has revealed the existence of common toxic factors in chronic periodontitis and cardiovascular diseases.

Keywords. periodontitis, cardiovascular diseases, bacteraemia, ECG.

Anatomo-morphological particulars of the pendant from human molar from deposit component at carbuna.

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Background. The Eneolithic deposit at Carbuna (Republic of Moldova) (5th millennium BC) was accidentally pointed out in the fall of 1961 by local school students. Although the repository has benefited from several publications, the piece we are referring to has only been briefly addressed. Our approach consists in its anatomical-morphological study.

Materials and methods. Analysis of literature data and the use of non-invasive research methods (odontoscopy, odontometry, radiovision, digital microscopy) of the pendant from a human molar.

Results. After the analysis, we determined that the tooth is the lower second molar with four cusps of the gracile odontological type. The enamel of the crown along the perimeter is missing, but on the occlusal side visible traces of pronounced functional abrasion are present. The molar was extracted, in all probability, post-mortem. A few perforations can be seen on the upper and middle third of the root. As a result of measuring the diameter of the holes with a digital ruler on the X-ray image, the following values were established: at the cervical level, vestibular – 8,0 mm, lingual – 3,0 mm and lower (blind) from the lingual side - 4.0 mm. At the same time, by direct measurements of the height and width of the tooth with a caliper, the following parameters of the crown were obtained: medio-distal – 10,0 mm, vestibulo-lingual – 7,8 mm, cervical – 8,0 mm, as well as of the tooth, which has a medial height – 19,0 mm and a distal height – 16,0 mm.

Conclusions. As a result of the visual analysis and the use of non-invasive methods, certain anatomical-morphological peculiarities of the pendant from a human molar were highlighted. This piece is of particular scientific interest both from the point of view of dental evolution and the influence of feeding on hard dental tissues.

Keywords. human molar, pendant, Eneolithic age, Carbuna deposit, anatomy

Facial skin grafting for tissue defects as a result of various injuries.

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Background. Various traumas in the facial area can lead to defects in the skin tissues in the facial area. These injuries include burns of various etiologies (burns with acid, liquid nitrogen, manganese, thermal burns), various injuries. In each case, there is a need to restore the skin. In these cases, we use the transplantation of a skin flap from the behind-the-ear area (if the defect is not large), in the case of a lack of tissue, we use skin flaps from other areas. The closure of skin defects in the facial area is an urgent problem, since the skin reserve in the occipital area is small and in many cases the graft is insufficient, and skin flap sampling from other areas has the least disadvantage in that it differs in color from the facial skin (more yellow tint).

Materials and methods. A skin graft was transplanted into four patients: two women and two men aged 20-50 years. Each of them had a skin defect as a result of various traumas.

Results. In all the cases studied, the skin defect in the facial area was of varying size: from two to ten centimeters. The cause was manganese or acid burns; the patient was unable to state the exact cause because she was brought to the maxillofacial surgery department under the influence of alcohol seven days after the injury with a festering wound, in this case a transplant was performed distinguished skin flaps thin – 0,2-0,3mm, after the inflammatory process is removed. In another clinical case, there was an upper lip defect after a traffic accident. In this case we used skin flaps cleft – 0,3-0,6mm, in all thickness, the same flap was also used for a skin defect in the chin area after a burn with liquid nitrogen as a result of cosmetic procedures. One of the cases was a nasal tissue defect, in the formation of an arterialized flap from the temporal-frontal area, was used distinguished skin flaps thin – 0,2-0,3mm from the abdominal region to close the defect in the forehead area, after forming and rotating the flap to the nasal area.

Conclusions. Depending on the location of the defect, taking into account the mobility of the muscles, flaps of different thickness are used.

Keywords. distinguished skin flaps thin – 0,2-0,3mm, skin flaps cleft–0,3-0,6mm, in all thickness, facial area.

The hepatic portal vein- normal and variant anatomy.

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Background. According to Terminologia Anatomica (2019) the hepatic portal vein bifurcates into left and right branches; the left branch supplies segments II, III and IV and the right branch divides secondarily into two branches – the anterior branch supplying segments V and VIII and the posterior branch supplying segments VI and VII. Variants are frequent and account for 20 to 35% of the population.

The purpose of this abstract is to review normal and variant portal vein anatomy and their implications for liver surgery.

Material and methods. A primary review was performed in PubMed and Google Scholar databases for a period of 10 years: from 2012 to 2022. The following key words were searched: hepatic portal vein, origin, branching, variant anatomy. Included articles were cadaver studies, imaging examinations, case reports, full articles studied without restrictions.

Results. The normal anatomy of the hepatic portal vein branching was found in 67 - 89% of cases and its variations in 11 - 33% of cases. The most frequent variant was the portal vein trifurcation with division into left, right anterior and right posterior branches occurred in 3.6 - 10% of cases, and the early origin of the right posterior branch directly from the hepatic portal vein with an incidence of 4

- 10.8%. The right branch trifurcation, in which a separate branch for segment VII is present, was observed in 1 - 7%, and the other type of trifurcation, in which a branch for segment VI is a separate branch, was revealed in 1 - 8%. The other rare forms of the hepatic portal vein branching were found with the incidence of 1 - 8%.

The hepatic portal vein trifurcation and the early origin of the right posterior branch are very relevant in liver transplant surgery; the segmental variations are important for right or left hepatectomy.

Conclusions. These variants must be diagnosed before hepatectomy, living donor transplantation, and before complex interventional procedures.

Keywords: hepatic portal vein, variant anatomy.

Treatment of neurological complications of arterial hypertension.

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Introduction. According to WHO (2021), it is estimated that 1.28 billion adults worldwide have hypertension and its frequency increases with age, with a prevalence of >60% in people with age >60 year. Hypertension provoke acute and chronic injuries of the brain, accelerates its atrophy and induces neuroinflammatory processes, each from these contributing to the impairment cognition and in major neurocognitive syndromes. The purpose of the study is to highlight the drugs or groups of drugs used in different specific neurological complications of hypertension.

Materials and methods. A retrospective study, were taken 82 patient reports admitted to the NNI *Diodim Gherman* in period 2019-2022, with various neurological pathologies. An important inclusion criteria was arterial hypertension. The data from the patient reports were statistically processed with SPSS and Microsoft Excel in depending on: gender, age, neurological complications, comorbidities, level of the blood pressure.

Results. The batch of studied patients had an average age of 67.92 years (56-81 years). Female patients from rural areas predominate. All patients were diagnosed with hypertension, the value varies between 180 mmHg and 250 mmHg, and diastolic 100–120 mmHg. Incidence of neurological complications of hypertension that was present along with others comorbidities was: stroke 78 cases, hypertensive encephalopathy 76, atherosclerosis 32, dementia 3 cases. Of the 78 stroke patients, 48 were determined to be ischemic, and only 2 received Alteplase, because they were transported immediatly, within the first hour after the accident. In 46 patients with acute ischemic stroke were administered Acetylsalicylic acid 150 mg or Clopidogrel 75 mg and Urapidil 10 mg in bolus. In 37 cases were administered metoprolol i/v 2.5 mg with Enalaprilat. Its use is argued by pre-existing cardiac comorbidities. In 34 cases used Enalapril 1.25 mg, repeated after 6 hours. For hypertensive encephalopathy, in 3 cases, was administered Nifedipine 10 mg sublingual.

Conclusions. Hypertension was not decreased suddenly in no patient, but gradually up to 24 hours; Alteplase recanalizes the blocked vessel, but has major risks, such as brain hemorrhages; Antiplatelet agents are administered from the first hours if a cerebral hemorrhage is excluded.

Keywords: stroke, arterial hypertension, neurological complications.

Topographic and morphometric aspects of the internal jugular vein.

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Background. Lately, due to the increasing number of intravascular manipulations, the internal jugular vein (IJV) is more frequently punctured and catheterized, and success of that procedure very much depends on IJV relationship with the common carotid artery (CCA), especially when are known its atypical positions. The topographical and morphometric peculiarities of the IJV were studied according to gender and laterality in patients undergoing Doppler sonographic examination.

Materials and methods. The blood vessels of the neck of 134 patients, without vascular pathology, were examined by Doppler sonography. The examination protocols and Doppler images were taken from the electronic database of the MSPI Republican Center of Medical Diagnostics, Chisinau, Republic of Moldova. The obtained data were statistically processed and the arithmetic mean and standard deviation were calculated.

Results. Five types of the IJV position towards CCA were identified: anterolateral position – 38.0% (14.2%/23.8% – male/female); lateral position – 35.0% (20.9%/14.1% – male/female); posterolateral position – 20.9% (17.2%/3.7% – male/female); posterior position – 5.2% (4.3%/0.9% – male/female) and medial position – 0.7%, established only in males. IJV described a straight trajectory in 77.6% (43.3%/34.3% – male/female), and in 22.4% (14.2%/8.2% – male/female) – it was tortuous. The average length of the IJV constituted 14.8 ± 0.56 cm; in male – 15.0 ± 0.62 cm, and in female – 14.2 ± 0.44 cm; on the right side it was 14.9 ± 0.6 cm, and on the left one – 14.4 ± 0.52 cm. The diameter of the IJV, in its middle portion, was 15.1 ± 0.49 mm; in male – 15.5 ± 0.53 mm, and in female – 14.7 ± 0.33 mm; on the right side in 66.4% the length was 15.7 ± 0.56 mm, and for the remaining 33.6% it was 13.8 ± 0.29 mm, similar with that of the left IJV. The thickness of IJV wall was 0.35 ± 0.08 mm; in male – 0.45 ± 0.09 mm, and in female – 0.3 ± 0.09 mm.

Conclusions. The most frequent position of the IJV towards CCA in female was the anterolateral one, and in male was the lateral position. The morphometric parameters of the right IJV had higher values.

Keywords: internal jugular vein, vein catheterization, Doppler sonography

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