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ABSTRACTS BOOK

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Epigraph of Conference
“All about CoViD-19. Theory, Practice”

MODERN APPROACHES OF LANGUAGE AND SPEECH THERAPY IN GEORGIA

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The basis of any behavior is thinking. Speech therapist and baby Relationships should be based on the desire to transfer knowledge, in simple terms, the speech therapist should not force the child but create a favorable environment for learning and realization of potential. An emotional factor to consider. Motivation stimulates thinking and increases creative potential, Emotional Intelligence EQ is no less important than IQ. The free creative process stimulates the brain to develop, while the pressure and force burn to block it. Modern speech therapy uses neurostimulation techniques and therapy. As a practicing speech therapist, I tailor activities for each child. In personal conversations with patients and their parents, we doactively argue that every child is a separate world. From here, we choose different approaches (though always within the framework of European recommendations and guidelines), with the parent of a particular child being informed. We must test which representation system does the child belong to? visual, auditory or kinesthetic. So we have to give the visualist a chance to see what we are talking about and teaching. I.e. Use different kinds of visualizations. Specialists need to speak clearly and calmly, while allowing kinesthetics to touch and feel the material we use in our work. Thus, it is necessary to choose a comfortable option, though combining all three representational systems provides information, retrieves and activates relevant memories in action. In this way, the skills gained from the experience are combined and new information is added to it, which activates the functioning of the brain. The number of children with developmental disabilities in Georgia

and abroad is catastrophically increasing. There is also an increase in the aggression of various psychopathological phenomena. Speech problems occur amid the damage to the central nervous and peripheral systems. Well-known therapies are neuromodulation, bioenergoplasticity, kinesotherapy, biological feedback method. The development of such a new approach and improvement of existing methods, as well as their coordination was carried out on the base of Association of Language and Speech Therapists. The studies were conducted on the basis of the Tbilisi Kindergarten #103 (previous name Tbilisi speech therapies kindergarten). Our target group is the pupils of this and another kindergarten in Tbilisi. We used the biological feedback method in language disorders, attention deficit disorder, hyperactivity. Also during physiological disorders, when the sound is received, but needs strengthening. When traditional exercises and tasks are less productive, we used a neurostimulation method that involves concurrent movement of speech organs and hand movements. This increased the child's motivation, improved motor function, promoted the synchronous functioning of both hemispheres, which in turn had a positive effect on the development of mental processes. During our activity we used bioenergetics. Her description is: The child is introduced to articulation training and is trained in front of a mirror. The articulation exercise is supplemented by the dominant hand action. Gradually the other hand is attached and articulation exercises are completed with both hands. Consider the "Swinging" exercise. Explanation to the child: open mouth; touch the upper teeth with the front part of the tongue; then lower teeth, with the hands moving. Extend the hand clusters upwards, then let down. We use music therapy along with bio-elasticity. Children sing and do exercise. Using this method increases motivation for speech therapy activities. In turn, music therapy promotes hearing, rhythm, movement coordination, speech stimulation, and communication skills. We choose exercises based on age and individual characteristics. At the same center we use articulation and mimicry exercises,

log massage, breathing exercises, general and fine motor development, self-training, tactile and sensory paths, balance boards. During phonological disorders, rhinolysis, dysarthria, expressive and impressionistic speech disorders. The list of traditional therapies available to us, in particular, silage therapy, art therapy, bibliotherapy, aromatherapy, vocal therapy, occupational therapy, speech therapy, and the above-mentioned innovative methods in the complex often gives us positive results in the shortest time. However, all practitioners of speech therapists should bear in mind that, regardless of the results, no less important process sustainability. This is achieved through maximum involvement of the speech therapist, patient personification, the addition of a creative component from the specialist. *Acknowledgment: Multidisciplinary High School of Society of Rheology.*

SODIUM GLUCOSE COTRANSPORTER 2 INHIBITORS - LOOKING BACK TO THE FUTURE

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The sodium glucose cotransporter 2 inhibitors (SGLT2 inhibitors) have been around for over 180 years. In 1835, French chemists extracted an ingredient from an apple tree bark called Phlorizin, and in 1886 a German diabetes research pioneer, Joseph von Mering, demonstrated that Phlorizin could produce glucose from own urine. In 2003, SGLT1 inhibitors were tested on humans, and in 2012 the FDA approved its use in patients with type 2 diabetes mellitus. The positive effects of SGLT2 inhibitors on cardiovascular disease can't be explained solely by decrease in systolic and diastolic blood pressure and glycosylated hemoglobin (HbA1c). Improvement in hemodynamic data that leads to a reduction in mortality has not been enough

to explain such benefits. Scientists believe that we have different direct mechanisms of action in addition to hemodynamic shifts. The meta-analysis of SGLT2 inhibitors based on three major studies, including EMPA-REG-OUTCOME, CANVAS, and DECLARE TIMI-58, have got us clue to explain the mechanism of SGLT2 inhibitors on reduction cardiac failure and cardiovascular death. They include: 1. Osmotic diuresis and natriuresis - reduce the left ventricular myocardial wall stretching and loading; 2. Positive Impact of SGLT2 Inhibitors on Cardiac metabolism and bioenergetics. (Heart muscle inflammation, oxidative stress and, heart cell apoptosis reduction, as well as the addition of energy derived from the breakdown of ketone bodies to the basic but weakened glucose metabolism); 3. Increased intracellular Na^+ and Ca^{2+} are known to reduce cardiac output and increase the risk of sudden cardiac death. Inhibition of SGLT2 inhibitors, the Na^+/H^+ pump, results by reducing intracellular Na^+ and Ca^{2+} , decrease in cardiac mortality. Large randomized trials, especially by “CREDENCE”, have shown that SGLT2 inhibitors have a positive effect on the prevention and treatment of renal disease, especially on diabetic nephropathy. The mechanism of action has not been definitively established, but glycosuria, blood pressure, uric acid and intra-glomerular blood pressure reduction, as well as improving metabolism by using ketone bodies are considered as the main reasons of it. However, the action of SGLT2 inhibitors is associated with a number of side effects, including genital infection, hypoglycemia, diabetic ketoacidosis, hypovolemia, temporary impairment of renal function, and most importantly, as the “CANVAS” study has shown increasing rate of ankle and thumb amputation. However, if we compare the SGLT2 inhibitors side effects of its benefits, including heart failure and death prevention, maintaining of kidney function, blood glucose regulation, arterial blood pressure, weight, heart failure patient's hospitalization and death reduction - the advantage is on the benefit's side. Other important studies are ongoing on SGLT2 inhibitors. A study will be

published by the end of 2020 to determine whether these drugs can reduce the number of heart failure-related hospitalizations and cardiovascular deaths in non-diabetic patients with preserved or reduced ejection fraction. From all of the above, it can be said those SGLT2 inhibitors, which originate from the past time - by ability of treat: type 2 diabetes, heart and kidney disease, and obesity at the same time - may have great consequences for future times. So we can say - The Era of SGLT2 inhibitors really begins!

THE IMPACT OF DIFFERENT DOSES OF IONIZING RADIATION ON THE NUMBER OF GLIAL AND NERVE CELLS IN THE HIPPOCAMPUS OF MICE

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The limbic cortex and hippocampus are especially sensitive to ionizing radiation. Disorders caused by radiation, including changes in synaptic activity, reflect in animal behavioral activity and learning and memory processes. Radiation-induced dysfunction of limbic structures is associated with cell damage and death. An important factor in changing number of cells is the direct impact of radiation causing their death through necrosis and apoptosis. Radiation causes dysfunction of glia and consequences in changes in limbic system structures. The aim of this study is to identify changing number of neurons and glial cells in cortical and subcortical structures of limbic system at different stages of postnatal development of adult mice males after different doses of ionizing irradiation. To study morphological changes, the number of pyramidal neurons and glial cells was determined at different stages of the study (48 hours from irradiation, 12th day, 38 day and 2.5 months) for the control and experimental groups. The number of cells was measured in the CA1 and CA3 regions of the hippocampus, on serial paraffin sections (10 μ m)

stained with Cresyl-violet. An analysis of the obtained data on the hippocampus revealed changes in CA1 and CA3 areas after different doses of ionizing irradiation (3,5 and 5 Gray). Irradiation with 5 Gray showed increased number of glial cells after 48 hours. In the case of 3,5 Gray irradiations the amount of cells did not differ from the control indicators. The determination of the number of glial cells in the CA1 and CA3 areas of hippocampus of mouse revealed a significant increased number of cells at three stages after irradiation (12th day, 38 day and 2,5 months) in the case of both doses. Regarding the number of neurons, it did not differ from the control. In conclusion, it should be noted that an increase in the number of glial cells indicates a process of gliosis. As a result, it was shown that the number of nerve cells did not change and they turned out to be less sensitive to radiation.

HIGH INTENSITY CHRONIC WHITE NOISE INDUCES BEHAVIORAL CHANGES IN ULTRASTRUCTURAL ALTERATIONS IN MALE ADULT RATS

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Noise pollution is a severe public health problem as continuous exposure to even moderate noise levels between 55-65 dB can lead to various pathologies, including hearing impairment and neurological states. In the present study, using high-resolution transmission electron microscopy, we assessed the ultrastructural alterations in the hippocampus (CA 1 and CA 3 areas) and central nucleus of amygdala of male rat brain following high intensity white noise exposure. In addition, some behavioral performances,

such as learning, anxiety-like behavior and locomotor activity were assessed. Adult male rats were exposed to 100 dB HIWN, one hour daily for 10 consecutive days. Behavioral and electron microscopic evaluations were performed on day 11. Exposure to HIWN did not affect learning (the components of cognitive parameters in multibranched maze test) or the components of locomotor activity (open field behavior). However, it induced significant anxiety-like behavior as evidenced by time spent in the closed arm of the elevated-plus maze. Concomitantly, ultrastructural changes in the hippocampus and central nucleus of amygdala, considered an integral component of the non-classical auditory pathways were noticed. In particular, in both regions high intensity white noise resulted in chromatolysis (mainly mild), moderate destruction of endoplasmic reticulum and Golgi complex, moderate alterations in mitochondria, as well as astrocyte and microglial activation. In another part of neurons, the accumulation of normal organelles and lysosomes, as well as deep invaginations were observed. The alterations were more pronounced in the hippocampal CA1 area. These results provide further evidence of detrimental consequences (behavioral and ultrastructural) following exposure to high intensity white noise.

IMPACT OF DEPRESSION ON STUDENT'S MENTAL HEALTH

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Depression is affecting more than 264 million people around the globe irrespective of age. We all feel sad, moody, lonely, miserable sometimes and worry about our future, career, family, relationships. Feelings like these are absolutely normal every now and then especially if you are a student studying away from home. There are some factors like not taking proper sleep, either overeating or undereating, along with academic stress including financial

problems, job issues failed relationships is quite enough to make a student depress or even do worse like suicide. Nobody can be prepared for what's coming in their life next specially students who are alone in a new city/country away from friends and family. We did some research on students around 15-30 years of age regarding how they feel most of the times, whether they take proper sleep and food on time, how are their interests in academics and other recreational activities, how much time do they spend in socializing on internet or how often they spend time with friends and family and how do they manage their daily routine and issues through a survey. We have used a survey to study and obtain data of students from India, Georgia, Nairobi, Kyrgyzstan, mainly university going undergraduate medical students. The survey was done online using SurveyMonkey.com. 10 multiple choice questions were asked regarding the feelings, academic status, socializing, eating and sleeping habits with options like always, most of the time, once in a while and never. According to the results from more than 204 participants 54% students have felt 2depressed, sad and lonely once in a while whereas 32% feel it most of the time. The primary and major contributing factor of depression is over thinking and 71% students find it difficult to come out of problems, hence keep on struggling over irrelevant matters. The root cause that we concluded from our survey is that there is no special method to identify that a person is really depressed or living a happy life. After going through the overall study and statistical data it affirms that depression is more prevalent in students especially medical students because the course of the study is so vast and time consuming that it burns out their head and being alone complicates it even more leading to homesickness, feeling helpless and at last opens the door towards depression. *Acknowledgments: Program Support for Young Science and Specialists of Multidisciplinary High School of Society of Rheology and mentor Lali Koptonashvili.*

NEW STEPS IN THE STUDY OF THE FUNCTIONAL STATE OF RESISTIVE ARTERIES THROUGH CHATBOTS

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A successful business must be aware of the preferences of the target audience. Modern medical practice is one of the most serious businesses that requires continuous restructuring. This is the platform which gives satisfaction of population's need on medical care, and on the other hand, it provides support to medical service institutions to develop rapidly. Recently, one of the leading places in world innovations has been the merging of medical trends and the use of chatbot with artificial intelligence. Chatbots are not a threat to the medical industry. They had been created to perform basic and repetitive tasks that can optimize the daily work of medical practice. They are used more in planning meetings. However, our goal was to create a psychological questionnaire to assess the risk of changes in the functional state of resistive arteries as a tool for assessing microcirculation resistance. As we know, resistive arteries are arteries of small diameter located at the anatomical boundary of macro- and microcirculation. Particulate arteries participating in the regulation of blood circulation are a prognostic object and a target of treatment at the same time. From the above it follows that the assessment of the functional state of resistive arteries is very relevant as a practical clinical study. In addition, it is known that the reaction of resistive arteries to ischemia reflects their functional state. Ischemia occurs when the total blood pressure rises by 30-40 mm Hg. higher than diastolic pressure. This is valid for any type of pressure gauge (water, mercury, software, electrical, touch, etc.). Summarizing all these fundamental questions and adding a psychological questionnaire we designed a chatbot with spatial platform (VirtualSpirits,

England). We selected three women patients with arterial hypertension with the same average age and duration of the disease (all women worked as music teachers in one of the art schools in Tbilisi, Georgia). They were issued three standard monometers (Vocse, China). By answering machine have been suggested instructions that are easily followed by the patient on the 'other end of the telephone line'. After a chatbot session, we invited the same patients to the clinic and did an in-depth study of the function state of resistive arteries according to the existing standard. Collecting data in the center, we have evaluated the parameters of the research on chat bot and in reality. It turned out that in all three cases the tendency to change the functional state of resistive arteries is the same. We continue research in this direction in order to so that our chatbot will overgrow with specific psychological allowances that can fully talk about the state of microcirculation resistance. Thus, by creating bots for specific tasks, the patient's stay in the clinic will be optimized, and the stress of expectation will be regulated, the stress of the "doctor-patient relationship" will be minimized. All this will certainly have a positive effect on the conditions of the patient as a whole. *Acknowledgment: Program Support for Young Science and Specialists of Multidisciplinary High School of Society of Rheology.*

PRIMER DESIGNING FOR IDENTIFICATION OF CUTIBACTERIUM ACNES IA1: MAIN CAUSATIVE AGENT OF ACNE VULGARIS

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New researches indicate that Cutibacterium acnes formerly known as Propionibacterium acnes is important in the pathogenesis of Acne. PCR for diagnosis of C. acnes is widely used, however existing primers specific to C. acnes strains give opportunities to identify and differentiate between species

and fails to inform about the phylotype of strains. To solve this problem, we have designed a new set of primers. PCR done by using these primers will give chance to identify not only *C. acne* strains but also phylotype IA1, the main causative agent of Acne Vulgaris. The pathogenic strain IA1 produces porphyrins as it lacks a repressor gene (*deoR*) which is expressed in all other phylotype. This gene is our target which we used as it is actively expressed in all other phylotype except IA1. NCBI data base was used for getting repressor gene (*deoR*) sequence. By using Blast (Basic local Alignment Search Tool) we managed to find all repressor gene (*deoR*) sequences existing in *C. acnes* genome available on NCBI data base. BLAST results showed 25 strains of *C. acnes* with repressor gene (*deoR*) which were very similar to each other, as Query Cover was approx. 100 % and E-value - 0.0. All 25-repressor gene (*deoR*) sequence was used for multiple alignments using ClustalW. Multiple alignments showed that despite 5 strains were considered as separate clusters, all 25 sequences shared a lot of similarity, enough to design primers. For primer designing were used online available tools: primer 3 and Primer-BLAST. After designing forward and reverse primers we checked whether they are universal or not using Primer-BLAST. Our results are manifested in the following: we have designed primers - GTCACGAGGCGGGAGACC and reverse primer CGAGGATGGCGCGTTTCAC, PCR product size - 315bp. Therefore, designing of primer can not only be done for Acne bacteria but also for any other species, because given the fact that our genes are different from each other. Based on our research we can talk about this, that gene manipulation and molecular techniques are very needing and significant as new generation diagnostic and therapeutic methods. *Acknowledgments: Program Support for Young Science and Specialists of Multidisciplinary High School of Society of Rheology and mentor Kasradze Ia.*

QUORUM SENSING AND BIOFILM FORMATION IN ENTEROBACTERIACEAE

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Several bacterial species participate in two confirmable behaviors. Irreversible attachment to the surface (biofilm) and to regulate certain phenotypes expression which will synchronize their behavior (quorum sensing). This sophisticated intercellular communication mechanism called quorum sensing (QS). QS play a major role in the formation of the biofilm & biofilm helps the bacteria in adhesion/ cohesion potentiality, metabolite interchange, cellular connection, defense, nutritious and resistance to medication. Since biofilm is resistant to antibiotics so targeting biofilm is the main therapeutic approach. Biofilm formation is one of the major reasons of catheter associated urinary tract infections (CAUTI). *E. coli* and *K. pneumonia* cause Urinary Tract Infection which cost about \$1.6 billion in medical expenses every year. Both of them have ability to form biofilms. Exopolysaccharide matrix of biofilm is a double barrier for antibiotics and other antimicrobial substances therefore makes bacteria more resistant. In many species QS mediated biofilm formation is present, targeting the QS system (anti-QS) are attracting attention in the drug development field. Another treatment strategy is using of bacteriophages. During the studies were used two *E. coli* (*E. coli*#3 & *E. coli*#5) and four *K. pneumoniae* strains (kp3, kp4, kp19, kp477). *E. coli* and *Klebsiella pneumonia* specific bacteriophages were used to study of the activity of bacteriophages towards formation of biofilms. 96 well plates well were filled with 100µl of 1/100 dilution bacterial culture incubated for 18 hours. After filling 96 well plates were incubated for 18 and 24 hours at 37°C. Incubated plates were emptied out of bacterial culture. Each well first was washed with distilled water and then filled with 1% (V/V) crystal violet and then washed twice with

distilled water. CFU/ml was acquiring from the same wells find out to obtain biofilm formation. Colonies were counted on the plates and the numbers of cells per milliliter (cfu/mL) were calculated. Totally 6 strains were screened for biofilm formation. From the tested strains only E. coli #5 was able to form biofilm. Formation of biofilms, as we already mentioned also depends if they express fimbriae important for bacterial adherence on indwelling systems and also biofilm formation. To study of the activity of phages against biofilms phages were added prior to incubation and also after 18 hours incubation. Phage activity towards E. coli#5 biofilm showed 2log and 3log reduction in bacterial cell count comparing to their control (bacterial strains without phage), prior and after 18 hours' incubation respectively. *Acknowledgments: Program Support for Young Science and Specialists of Multidisciplinary High School of Society of Rheology and mentor Karumidze Natia.*

BACTERIOPHAGE THERAPY AGAINST MULTIRESISTANT ACINETOBACTER BAUMANNII INFECTIONS

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Acinetobacter baumannii is very powerful superbug and ranked 1st among the world deadliest superbugs. These superbugs are killing about 700,000 people per year. All the drug including the last resort drugs is resistant to this type of bacterial strain. The infections which are caused by these superbugs are hard to treat and are too expensive. In the past, we don't have any proper ways to treat Acinetobacter infection but nowadays we found one therapy which can treat such infections and we called it "Phage Therapy". A virus is used to treat the infections caused by bacteria. A bacteriophage is a virus which infects bacteria only and is harmless to the human cell, they also have high therapeutic ratio and they are better than any of the antibiotics because they

can penetrate biofilm easily and are the future for multidrug-resistant bacteria's. Materials/methods: In our study we used *A. baumannii* G7strain, isolated from the wound of a soldier injured during the one of war in Georgia territories. For antibiotic sensitivity were used five different antibiotics – Amikacin (30µg), Norfloxacin (10µg), Imipenem (10µg), Ceftazidime (10µg) and Rifampicin (5ug) by using Kirby-Bauer Disk Diffusion Susceptibility Test for antibiotics sensitivity. Bacteriophage sensitivity was done towards 5 specific *Acinetobacter* monophages and 6 phage lysates by using Spot-test technique. Disk diffusion susceptibility test revealed that *A. baumannii* strain used in our study was sensitive to norfloxacin and amikacin antibiotics, but showed resistance to ceftazidime, rifampicin and also to imipenem. Bacteriophage sensitivity was different: from complete lysis to resistance. Bacteria are becoming immune to all drugs. Alternatives to antibiotics could be considered bacteriophages. They have many characteristics that make phages as potentially attractive therapeutic agents. And in the future, the only solution for all the bacteria is the phage therapy as one day all the bacteria will become resistant to every drug and in this situation phages will work and become our future. In the abstract, medicines were named, but the manufacturers were not named. This gives the right to consider that our abstract has only scientific content without affecting the issues of advertising and marketing. *Acknowledgments: Program Support for Young Science and Specialists of Multidisciplinary High School of Society of Rheology and mentor Karumidze Natia.*

A NOVEL CORONAVIRUS - NEW APPROACHES IN PATHOGENESIS AND EFFECTIVE ANTIVIRAL DRUGS

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An outbreak of “mystery pneumonia” caused by new variant of coronaviruses (CoVs) in Wuhan, China since December 2019 has been under attention around the world. CoVs are important pathogens for human and vertebrates. They can infect respiratory, gastrointestinal, and central nervous system of humans, birds, bats, livestock, mice and many other wild animals. The outbreaks of the severe acute respiratory syndrome (SARS) in 2002/2003 and the Middle East respiratory syndrome (MERS) in 2012 have demonstrated the possibility of animal-to-human and human-to-human transmission of newly emerging CoVs. Different CoVs display diverse host range and tissue tropism. Usually alphacoronaviruses and betacoronaviruses infect mammals. In contrast, gammacoronaviruses and deltacoronaviruses infect birds and fish, but some of them can also infect mammals. The new coronavirus designated by the WHO as 2019 novel coronavirus (2019-nCoV), which belongs to betacoronaviruses based on sequence analysis, can also infect the lower respiratory tract and cause pneumonia in human. Most of the infected patients had a high fever and some had dyspnea, with chest radiographs revealing invasive lesions in both lungs. It more affects older males with comorbidities, and can result in severe and fatal respiratory diseases, for example, acute respiratory distress syndrome. Phylogenetic analysis suggests that bats might be the original hosts of this virus, an animal sold at the seafood market in Wuhan might represent an intermediate host facilitating the emergence of the virus in humans. Importantly, structural analysis suggests that 2019-nCoV

might be able to bind to the angiotensin-converting enzyme 2 receptor in humans. Viral envelope spike (S) protein mediates receptor binding and membrane fusion and is crucial for determining host tropism and transmission capacity. The spike protein of CoVs is functionally divided into the S1 domain, responsible for receptor binding, and the S2 domain, responsible for cell membrane fusion. Similar to other beta coronaviruses, the receptor-binding domain was composed of a core and an external subdomain. The external subdomain of the 2019-nCoV receptor-binding domain was more similar to that of SARS-CoV. This result suggests that 2019-nCoV might also use angiotensin-converting enzyme 2 as a cell receptor. At present, there is no single specific antiviral therapy for 2019-nCoV and the main treatments are supportive. Recombinant interferon with ribavirin has limited effects. After SARS and MERS outbreaks, new antivirals were developed targeting CoVs proteases, polymerases, MTases, and entry proteins, but none of them have shown effectiveness in clinical practice so far. The antiviral compound EIDD - 1931 discovered at Emory University revealed effectiveness against SARS and MERS viruses in the laboratory, and researchers suggest its modified version - EIDD-2801 could potentially be used to treat 2019-nCoV. Also, Plasma and antibodies derived from the convalescent patients have been proposed for use in treatment. In addition, various vaccine strategies have been developed but have only been evaluated in animals so far.

BRAIN BLOOD FLOW CONTROL WITH ARTIFICIAL INTELLIGENCE

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Blood flow in the brain is regulated by neurons. Knowledge of how these cells control blood flow is crucial for understanding how connect neural computation

and electric circuit, for fix disease of eyesight, and for developing treatments for neurological disorders. It is now recognized that implant of artificial intelligence electric processor on skull has a key role in brain blood flow regulation via electric stimulation on blood cells. After creation hybrid of human and artificial intelligence, brain neural network working will not depend on human's autonomous operating system control, but It will be under artificial intelligence operating sytem control, which will be excludes complex of brain desease like Alzheimer's syndrome, Humans will never forget any information anymore. These conceptual shifts in our understanding of artificial intelligence operating system have important implications for the development of new therapeutic approaches.

POLYPRAGMACY AND DRUG INDUCED IATROGENECITY

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Drug induced iatrogenicity is widely common in medical practice, which means several (5 or more), unreasonable prescription of drugs. Most often it develops when a patient is being treated by a variety of physicians for a number of diseases, especially older or polymorbidity patients. Polypragmacy which is more often caused by comorbidity and polytherapy, leads to the development new nosological forms, ie, iatrogenic diseases. According to the data of World Health Organization's pharmaco-epidemiological studies, drug-related deaths are ranked as V-VI place in developed countries after cardiovascular, cancer, trauma, intoxication and respiratory diseases. In general, Polypragmacy is a serious problem for the health care system worldwide because it: decreases the effectiveness of pharmacotherapy; causes the development of serious side

effects; leads to an increased financial cost of healthcare. The following factors contribute to the development of dangerous drug interactions and iatrogenic diseases during polypragmacy: age, concomitant diseases and short therapeutic window of prescribed medicine. Most frequently, polypragmcy is the cause of the development of iatrogenic diseases. Drug induced iatrogenic diseases are the most common causes of hospitalization, its prolongation and mortality of patients, which is a serious challenge for the healthcare sector. A more common cause of drug induced iatrogenesis is self-medication or poor adherence to take the drugs as prescribed by the doctor. The following types of drug-induced diseases are more commonly found, for example, hypoglycemic coma in case of excess insulin intake, mutagenic, oncogenic, teratogenic, embryotoxic, immunosuppressive action, drug allergy reactions, drug addiction; incompatibility, in case of 5 or more than 5 drugs combination (polypragmacy), including pharmacodynamic and pharmacokinetic interactions. Iatrogenic diseases can be avoided by using simple precautions, such as sufficient knowledge of indications to use medication, contraindications, and side effects; Limiting self-medication and reducing drug overuse (polypragmacy); establishment of qualified systematic training programs for physicians and other medical staff; consultation with a clinical pharmacologist at any stage of treatment to help any specialty physician minimizing complications and iatrogenic diseases caused by polypragmacy. The risk/benefit ratio of prescribed medications can be improved by having a proper knowledge of the patient's medical history and the side effects of the medication. Additionally, it is reasonable to evaluate drug administration and dosage regimen of a chronic patient at least twice a year; including pharmaceutical products such as over the counter medicines, phyto drugs and nutritional supplements. Thus, one of the important preventions of drug induced iatrogenesis is the identification of high-risk elderly patients, early diagnosis and treatment of the disease, minimization of

prescribed medication, optimal management of chronic diseases, i.e. rational pharmacotherapy. Good Prescribing, which avoids drug-induced iatrogenicity, implies: selecting the most effective and harmless drug; justification of choice - motivation; knowledge of the basic principles and approaches of clinical pharmacology and rational pharmacotherapy.

EFFECT OF PRACTICE ON VISUAL FUNCTION IN AGING

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Aging is accompanied by changes in many visual functions. Evidences show declines in motion discrimination, visual attention, face recognition and many others including the most prominent declines in visual and contrast acuities in elderly people. Deficiency in visual functions has significant impact on the quality of life. To find implementation for improving visual functions in elderly is very important issue especially now when the world population is aging very fast. Method of perceptual learning is used to improve performance of specific visual tasks with practice. The impact of practice on performance of visual tasks is well investigated in young adults, however, little is known about such practice effect on aging. Here we used perceptual learning method to check whether perceptual learning method can be used for improvement of visual task performance in elderly people. Two groups of participants - elderly (60-75 years old) and control young adults (20-32 years old) participated in our experiments. Participants performed vertical line bisection task - a type of hyperacuity task, where stimulus is comprised of three parallel lines. In each presentation (trial), the central line is closer to one of the two outer border lines and the task of the observers is to indicate the closer line. Practice procedure

lasted for two successive days and included 2 practice sessions of 1600 trials totally. Baseline measurement also were performed before and after practice sessions to check specificity of perceptual learning. Vertical line bisection stimulus, horizontal line bisection stimulus, vertical dot bisection stimulus, horizontal dot bisection stimulus and vertical Vernier stimulus were used as baseline stimuli. The results showed that after practicing performance of bisection task improved significantly for both elderly and young control group subjects. Baseline measurement showed that improvement of performance transferred on practiced stimulus and vertical dot bisection stimulus in both groups, but performance did not change for other baseline stimuli. These results indicate that mechanisms of perceptual learning are not affected by aging and works in the same way as in young population. Specificity of perceptual learning on practiced task restricts use of this method on one specific direction but still can be a good tool for improvement specific visual function in elderly.

PALOSURAN AS THE POTENTIALLY EFFECTIVE ANTIHYPERTENSIVE REMEDY

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According to the World Health Organization, arterial hypertension is the most common cardiovascular disease in the world causing approximately 26% of the population to die each year and 64 million to become disabled. Problems of treatment of hypertensive disease are mainly caused due to: drug side effects, development of tolerance to the antihypertensive drugs, using angiotensin converting enzyme inhibitors at treatment of hypertension of renal genesis and many others. For this reason, search for new targets and

construction of new substances/remedies with principally different mechanisms of action is very topical nowadays. In recent years, interest toward the cyclic vasoactive neuropeptide urotensin-2 (U-II), as a regulator of vascular tone significantly has increased. U-II and UTR-receptor (UTR) are strongly expressed in the CNS, but also widely expressed throughout peripheral tissues including the heart, vasculature (endothelial and smooth muscle), kidney, liver and other sites. Such distribution suggests that U-II is a potential autonomous regulator of cardiovascular function. U-II binds to the Gq-protein (GPR14/SEN1) of UTR causing activation of the inositol triphosphate cycle by activation of phospholipase-C. U-II is a more potent vasoconstrictor than endothelin-1. It acts as an endothelium-independent vasoconstrictor and endothelium-dependent vasodilator. However, in case of pathology, this vasodilatation-vasoconstrictor equilibrium is altered and the aforementioned imbalance has been considered as the potential trigger for the development of pathological processes. Increased U-II secretion and overexpression of UTR have been reported in case of hypertension, heart failure, diabetes, portal hypertension and renal failure, indicating that the U-II/UTR system could be involved in the mechanism of development of these diseases. Thus, use of U-II/UTR system antagonists could be discussed as a prospective way for elaboration of new and effective antihypertensive drug. Recently, the non-peptide UTR antagonist - Palosuran (ACT-058362) has been developed. Palosuran inhibits the accumulation of calcium and phosphorylation of mitogen-activated protein kinase caused by U-II. Investigations, where UTR antagonists has been used for study of the U-II system, mainly refers to the diabetic nephropathy. However, pathogenic mechanism of action is still unknown. The role of the U-II system in the development of essential hypertension is unclear. Indeed, systemic hypertensive responses to U-II were observed in several animal models. However, these effects were not uniform across species. Information about

antihypertensive effects of palosuran in literature is scarce and contradictory as well. Coming from the aforesaid, could be concluded that study of the pharmacological effects and pathogenesis of the UTR antagonist - palosuran may allow us to determine: the role of the U-II/UTR system in the development of hypertension, pharmacological effects, antihypertensive properties and mechanisms of action of palosuran, role of the new target in the regulation of cardiovascular system functioning and modulation of hypertensive disease progression, that supposedly could significantly reduce the incidence of hypertension-associated diseases/complications, improve quality of the life, increase lifespan and reduce mortality rate of patients

MACROVIPERA LEBETINA OBTUSA VENOM AS A TOOL FOR BBB INTEGRITY INVESTIGATION AND HEMORRAGE STROKE MODELLING

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Blood-Brain Barrier integrity plays a crucial role in CNS functioning. Some cerebrovascular lesions such as hemorrhagic strokes are today a difficult medical and social problem due to high rates of morbidity, mortality, and disability. As a tool for inducing an experimental hemorrhage, the Levantine viper venom was used. The metalloproteinases and phospholipase A2 are the main enzymes of *Macrovipera lebetina obtusa* (MLO) venom and play a decisive role in the destructive and toxic effects on the organism of animals. Metalloproteinases cause hemorrhagic damage, destroy the blood vessel's basement membrane and disrupt connections between endothelial cells. In the present study, the *Macrovipera lebetina obtusa* venom vasodestructive action in the rat's brain and BBB integrity was investigated. Particularly, the hemorrhage changes of brain microcirculatory bed and activation of microglial cells (MGCs) under MLO venom high doses (intra peritoneal and intra cerebral

injections) action were studied. Histochemical staining of the micro vessels and microglial cells of the rat brain allows qualitatively and quantitatively study damage to the brain parenchyma during venom-induced hemorrhage. The disruption of capillaries and activation of MGCs up to final, macrophage stage was shown. The MLO venom is assumed to be a very useful tool for investigation of experimentally induced hemorrhage in brain.

SEEKING SUPPORT: FOREIGN MEDICAL STUDENTS „UNDER PRESSURE THAT BURNS A BUILDING DOWN! “

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The present study investigated the stressors associated with students' life, daytime sleepiness, and pre-sleep arousal for assessing causal relationship among sleep disturbance, pre-sleep arousal, and stress in foreign medical students in Georgia. Forty-four foreign volunteer students (21.7 ± 1.7 y) from the European University, Tbilisi, Georgia participated in this study in November 2018. Participants completed Epworth the Sleepiness Scale (ESS), Pre-Sleep Arousal Scale (PSAS), and Student-Life Stress Inventory (SLSI), and the data were statistically analyzed. ESS scores were slightly higher than the normal value in the general population (7.25 ± 3.00). Students revealed high somatic (13.55 ± 4.39) and cognitive PSAS scores (18.05 ± 6.13) and high overall self-rating (1.95 ± 0.57) and total SLSI scores (143.86 ± 40.33). ESS scores were slightly higher in females (7.86 ± 3.00 vs 6.64 ± 2.94). Females showed higher somatic (13.73 ± 3.71 vs 13.36 ± 5.07) and cognitive PSAS scores (18.36 ± 5.34 vs 17.73 ± 6.94). Overall, self-rating and total SLSI scores were slightly higher among males (2.00 ± 0.69 vs 1.91 ± 0.43 and 146.55 ± 42.48 vs 141.18 ± 38.86 , respectively). The differences were not statistically significant. In females, only

the cognitive pre-sleep arousal was significantly correlated with ESS ($p<0.05$), overall self-rating ($p<0.05$), and total SLSI scores ($p<0.05$). In males, ESS showed significant correlation with both somatic and cognitive PSAS scores ($p<0.05$). ESS showed significant association with overall self-rating ($p<0.01$), which in turn was significantly associated with somatic and cognitive arousal ($p<0.05$). Both somatic and cognitive arousal were strongly correlated with total SLSI scores ($p<0.01$). Both Total PSAS score and total SLSI scores significantly predicted ESS total scores in general population ($p<0.001$); Total PSAS score was a significant predictor of ESS total score in both male and female participants ($p<0.05$); Total SLSI scores was not a significant predictor of ESS total scores neither male nor female participants, but total SLSI scores significantly predicted cognitive pre-sleep arousal scores both in male and female groups with more significance for male participants ($p<0.001$ and $p<0.05$, relatively), which in turn was a significant predictor of ESS total scores in both group ($p<0.05$). Medical students are at high risk of developing sleep disturbance and psycho-behavioral difficulties. The preliminary data highlights the importance of studying stress, sleep disturbances and the related adverse consequences the foreign medical students. Additional studies with a large sample size are needed to assess the specific relationship among sleep patterns, stress, and academic performance of foreign medical students.

USING OSL DOSIMETRY FOR CATARACT PREVENTION IN BRACHYTHERAPY PATIENTS

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Cataract is a frequent complication of brachytherapy for melanoma located on the face near the eyes. To protect the eyes many clinics in the world use lead shielding along with in-vivo dosimetry for monitoring. There are several

technologies for in-vivo dosimetry. One of them is OSL (optically stimulated luminescence) dosimetry practiced at Fridon Todua Named Research Institute of Clinical Medicine. For OSL dosimetry we use special nanoDot dosimeters. They are designed for use in single point radiation assessment applications. Due to its small size, it does not affect the quality of the treatment. The nanoDot dosimeters are wireless and radiolucent. The nanoDot dosimeters of have got the following technical specifications: Dose operating range is 10 μ Gy to >100Gy for general applications; Lower Limit of Detection is 0.1 mGy; Useful Energy Range is from 5 keV to 20 MeV; Energy Dependence is follow - Accurate within $\pm 10\%$ over diagnostic energy range 70-140 kVp; within $\pm 5\%$ for photons and electrons from 5 MeV-20MeV; Accuracy (total uncertainty - single measurement) is $\pm 10\%$ with standard nanoDot; $\pm 5.5\%$ with screened nanodot; Precision is $\pm 5\%$, $k=2$ for both standard and screened nanoDot. NanoDot dosimeters have got the following key features and advantages: Nondestructive readout: allows for reanalysis and reuse; Accurate measurement across a wide dose range; No need to anneal every time the dosimeter will be exposed to ionizing radiation; Element correction factors are not required; Minimal fading; Dosimeter archiving is possible; Dosimeters are durable: Shock resistant; moisture resistant; high temperature tolerance. No required heating parameters and gas to maintain; Effective replacement for older radiation measurement technology (e.g., TLD). Brachytherapy in Fridon Todua Named Research Institute of Clinical Medicine has been introduced since 2018. During the period 2018-2019, OSL dosimetry was carried out in patients with melanoma located on the face in 437 fractions of radiation therapy, including 236 in 2018 and 201 in 2019. According to the results of dosimetry monitoring, the risk of cataract occurrence was revealed in only 5 patients in 2018 and 2 patients in 2019. This risk has been minimized by a dose correction within the limits to allow successful treatment.

ELECTRIC-MAGNETIC STIMULATION ENHANCES COGNITIVE FUNCTION OF AUDIOGENIC KINDLING RATS

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Many people with epilepsy have problems with their memory. Antiepileptic drugs also causes subsequent cognitive impairment. The Electric Magnetic Stimulation (EMS) is an powerful method for treating epilepsy. EMS can be used as a separate treatment therapy for epilepsy or together with pharmacological substances. The goal of the recent investigation was to study the effects of EMS on cognitive function in audiogenic kindling rats. The experiments were conducted in an animal model of epilepsy using the genetically determined epileptic prone rats strain (GEPRs) (250-450g) (n=15). After repetitive audiogenic stimulation twice a day for 5 days, Audiogenic kindling were recieved. It result of the spread of seizure discharge to forebrain structures: amygdale hippocampus, neocortex. For studying EMS (10000 - 15000Hz frequency, 1,5m/Tesla, during 15 min, 10 days) effects on the cognitive function of depressed rats, an elivated maze test was used. The process of maze learning itself was evaluated by variations in the number of errors (getting in the deadlock branch) made from trial to trial in search of optimal runway to the housing-box and by the time needed for passing the maze-test. The maze was cleaned with a 30% ethanol. Animals were tested 1 month after learning tests. Data reliability was assessed using parametric and non-parametric techniques. The passage time (300 seconds) of kindling GEPRs after EMS decreased sharply on the third day (7 seconds). In non-stimulated kindling GEPRs, the passage time of the maze gradually decreased to 150 sec. In the performance of the task, a different dynamics of the errors in

stimulated and control GEPRs was revealed. In particular, the stimulated rats did not commit errors from the third day of training. They did not enter in the maze deadlock branches. Whereas non-stimulated kindling rats made mistakes even on the 6th day of the study. Kindling rats were tested in a maze 1 month after learning. Experiments showed that audiogenic kindling rats remembered the trained test on the background of EMS only. Therefore, EMS opens up the potential for new treatment options, for memory impairments in epileptic people. We suggested that basic mechanisms of memory enhancement after EMS are direct modulation of a cortical region or network that leads to a more efficient processing and addition-by-subtraction, which is adisruption of processing which competes or distracts from the task performance; As a result of EMS, the tension and the fear reaction decreased, which is facilitate the study of the maze trajectory.

PREMEDICATION WITH OXYTOCIN HELPS TO NORMALIZE BLOOD QUANTITATIVE INDICES IN DEPRESSED RATS WITH ELECTROMAGNETIC STIMULATION

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Depression is linked to systemic inflammation. Increased white blood cell (WBC) count and red cell distribution width (RDW) is associated with negative clinical outcomes in a wide variety of pathological conditions. WBC is a non-specific inflammatory marker and RDW is also strongly related to other inflammatory markers. There is an association between these hematological inflammatory markers and depression symptoms. Oxytocin reduces the

activity of brain regions that produce anxiety and might involve in the rehabilitation of depressive-like behavior. Repetitive EMS (electromagnetic stimulation), is used in the treatment of moderate depression. So, the goal of this investigation was to study the quantitative characteristics of blood cells after premedication of oxytocin in depressed rats on the background of EMS. In the implementation of the project the depressed rats (250-450g) were used (n=20). For each task two groups of the animal were conducted: experimental group (with EMS) and control group (without EMS). For repetitive (10-days) EMF exposure, the following parameters were used: 10000-15000Hz frequency, 1,5m/Tesla, for 15 min. An animal model of depression was received by subcutaneous injection of Clomipramine from 8 to 21 days of neonatal development. The blood counts were performed 2 months later after clomipramine injection using blood HumaCount 30 TS. This analyzer allows quantifying the number of red blood cells, leukocytes (agranulocytes and granulocytes), platelets, hemoglobin, the hematocrit in 1 ml blood of rats. The hematological analysis was performed 2 weeks later after oxytocin (4 mcg/per animal during 10 days) injection and EMS. On the background of oxytocin injection, the amount of RBC and hemoglobin were increased, RDW was decreased. Additional EMS did not change these data significantly, but in this condition obtained results did not differ from the results of control, non-depressed rats. Increased level of WBC in depressed rats was decreased after oxytocin injection and EMS. Despite the growth of white blood cells, depression decreased lymphocyte content. Oxytocin injection did not change the content of lymphocytes, but in light of the 10 day of EMS, the content of lymphocytes ($P \leq 0.05$) increased. In depressed rats, the oxytocin alone, or together with EMS can restore the blood cell imbalance. Effects of oxytocin enhanced in simultaneous action with EMS. *Acknowledgment: Shota Rustaveli National Science Foundation of Georgia. FR 17_333*

THE OXYTOCIN EFFECT ON THE PASSIVE AVOIDANCE TASK IN ELECTRIC-MAGNETIC STIMULATED DEPRESSED RATS

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Depression linked to memory problems. Antidepressant use also causes subsequent cognitive impairment. For the treatment of depression, it is important use nontraditional treatment methods, such as Electric Magnetic Stimulation (EMS). Besides, the oxytocin has anxiolytic action. So, the goal of the recent investigation was to study the effects of oxytocin and EMS on cognitive function in depressed rats. In experiments, the depressed rats (250-450g) were used (n=20). An animal model of depression was received by subcutaneous injection of Clomipramine from 8 to 21 days of neonatal development. For studying oxytocin (4 mcg/per animal during 10 days) and EMS (10000-15000Hz frequency, 1,5m/Tesla, during 15 min, 10 days) effects on the cognitive function of depressed rats, a passive avoidance test was used. Animals were tested 1, 3, 5, 14 and 30 days after learning tests in the chamber. Data reliability was assessed using parametric and non-parametric techniques. The acoustic range EMS decreases fear and anxiety degree and consequently, increases the locomotor-exploratory activity. It attenuates the retention of passive avoidance task. On the background of Oxytocin, the latency period of entrance in the dark compartment was increased compared to depressed rats. In the dark component, they received electrical impulse - mild foot shock-12 imp/min; 1.5mA. Additional EMS did not change the latency period of entrance compared to depressed treated with oxytocin rats. Depressed rats did not entrance in dark component 1 month later. On the

background of oxytocin, on the 14th day after learning test, depressed rats entered the dark section. In the dark section, they were not given painful irritation. On the 30th day, the latency to enter the dark section was reduced ($P \leq 0.01$). We think that after getting into the dark section without any aversive stimuli, the already remembered conditional reflex is extinguished. The correct behavior of depressed rats can be explained by the decreased locomotor activity of depressed rats. Following simultaneous exposure to oxytocin and EMS, the rats were kept in a dark section for 30 days, with a latent period of 250 ± 4 sec. The Oxytocin together with acoustic range EMS reduces the level of fear and anxiety, and therefore, increases motor activity in depressed rats. It offers clinicians a novel alternative for the treatment of this disorder.
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MOLECULAR MECHANISM OF NA,K-ATPASE SENSITIVITY TO NEUROTRANSMITTER

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Na,K-ATPase is a member of the P-type ATPases and a vital enzyme involved in numerous cellular processes. The enzyme was discovered by Skou in 1957 as an energy transducing ion pump that converts the free energy of ATP into transmembrane ion gradient. It should be acknowledged that Synaptosomal membrane Na,K-ATPase is sensitive to Noradrenaline. This neurotransmitter inhibits enzyme system and changes catalytic cycle from MgATP dependent ($[MgATP] \gg [Mg^{2+}] = [ATP]_i$) to Mg^{2+} dependent ($[Mg^{2+}] \gg [ATP]_i$) cycle. These cycles have different stoichiometry for Na^+ and K^+ . The stoichiometry of MgATP dependent cycle is: $3Na^+ : 2K^+ : 1MgATP$, while the stoichiometry of

Mg²⁺ dependent cycle is the following: 4Na⁺:1K⁺:1MgATP. Kidney microsomal fraction Na,K-ATPase is not sensitive to Noradrenaline. Comparative kinetic analysis of albino rat brain synaptosomal membrane and kidney microsomal fraction Na,K-ATPase was performed for understanding different sensitivity of this fractions to neurotransmitter. To investigate the mechanism, underlying this difference, we have studied the enzyme velocity dependence upon the concentration of Mg²⁺. V=f(Mg²⁺) function has shown different kinetic features for synaptosomal membrane and kidney microsomal fraction Na,K-ATPase. Adding EGTA to the reaction medium, effects the geometric form of V=f(Mg²⁺) function differently. We have measured essential activator and full inhibitor numbers for Na⁺ and K⁺ with the surplus of Mg⁺⁺, which resembles MgATP cycle with the following stoichiometry: 3Na⁺:2K⁺:1MgATP. According to the results of this experiments it can be concluded, that kidney microsomal fraction Na,K-ATPase does not possess Mg²⁺ dependent cycle and thus cannot manifest sensitivity towards Noradrenaline.

EEG PATTERN IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDERS

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Importance of ADHD studies are determined by its significant plenty in the children's population (2%-21%) and by the high extent of social desadaptation developing on this background. ADHD is considered to be the result of a brain dysfunction and EEG assesses brain function; it is natural that this method be examined with respect to study ADHD. To find out the

distinctive topographic EEG profiles of children with ADHD has a prognostic value. This present study investigates EEG peculiarities using qEEG procedure. The EEG of 46 ADHD children aged 6 to 11 years was studied. EEG signals were digitally recorded using a set of 19 scalp electrodes according to the International 10-20 system. For each child, 10 sec artifact-free EEG epochs were selected (at rest, with open and closed eyes), during functional exertion. The topography of delta, theta, alpha and beta frequency bands over the brain convexital brain's surface was also analyzed into. Preliminary analysis of data allows to reveal 4 basic types of EEG alteration children with ADHD: 1. Disorganization of basic EEG' rhythmicity - 84.5%; 2. Increase of indices of absolute power in the low frequency bands - 36.3%; 3. The sharp potentials in alpha/theta ranks - 23.2%; 4. The paroxysmal discharges during hyperventilation - 39.3%. These basic patterns of EEG disturbances in different combination may be found in the same patient. A variety of EEG abnormalities have been described in children with ADHD that is associated with atypical brain wave. The primary analysis allows to suppose that children with ADHD is not homogeneous. It should be related with differences of neurophysiological mechanisms. Based on our results, we suggest further longitudinal research in ADHD patients to investigate the changes of EEG abnormalities with age gender and ADHD subtype.

BACTERIAL INFECTION INDUCED SEPSIS, ITS MOLECULAR MECHANISMS AND WAYS TO SOLVE IT

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Sepsis is recognized as a life-threatening organ dysfunctional disease that is caused by deregulated host responses to infection. Sepsis is the most expensive health-care problem in the USA, with a cost of more than \$20

billion. Sepsis is one of the most prevalent causes of mortality in intensive care units (ICUs), and its incidence increased by more than double over the last 10 years. According to data from the Surviving Sepsis Campaign, mortality rates from sepsis are 41% in Europe and 28.3% in the USA. Sepsis is a word derived from the ancient Greek. The word 'sepsis' was used in Homeric poems. The first step in the initiation of the host response to the pathogen is the activation of innate immune cells, constituted primarily by macrophages, monocytes, neutrophils, and natural killer cells. This occurs via the binding of pathogen-associated molecular patterns (PAMPs), such as bacterial endotoxins and fungal β -glucans to specific pattern recognition receptors, on these cells. Another source of such interaction is damage-associated molecular patterns (DAMPs) that may be intracellular material or molecules released from dead or damaged host cells, such as ATP and mitochondrial DNA. These bind to specific receptors on monocytes and macrophages such as toll-like receptors (TLRs), C-type leptin receptors, NOD-like receptors (nucleotide-binding oligomerization domain) and RIG-1 like receptors (retinoic acid inducible gene 1). This results in the activation of intracellular signal transduction pathways that cause the transcription and release of proinflammatory cytokines like $\text{TNF}\alpha$, IL-1, and IL-6. In addition, some of the pattern recognition receptors, such as the NOD-like receptor group, can aggregate into larger protein complexes called inflammasomes that are involved in the production of crucial cytokines, such as IL-1 β and IL-18 as well as caspases, which are involved in programmed cell death. We report a case of septic shock syndrome caused by *Pseudomonas Aeruginosa* in a patient who had a mediastinitis due to a peritonsillar abscess. The patient received adequate treatment with Antibiotics and Vasopressors, under the treatment the patient could be successfully stabilized.

CHANGE IN THE GROOMING MICROSTRUCTURE AS A MEASURE OF THE STRENGTH OF THE STRESSOR IN RATS

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Grooming changes its pattern in response to the stressor. The comparison of the grooming pattern before and after the exposition to the stressor is useful for the study of behavioral response to the stressor as well as for evaluation of the strength of the stressor as well. We compared the grooming pattern of albino mongrel rats in two stressogenic situations: fur moistening and exposure of animals to the bright light. Rat behavior was registered by the video camera. The number of syntactic chains as well as the number of single grooming bouts as well as a number of rearing and body stretching was calculated before and after the fur moistening as well as before and after the exposure to the bright light. Fur moistening, as a stressor was found to affect grooming pattern much less as compared to the exposition to the bright light - the data confirming the earlier reports of other authors. We conclude, that the change in the grooming pattern may identify the stress in the rats and moreover, may serve as a measure for the evaluation of the strength of the stressor.

HEAVY METALS AND NEUROTOXICITY: ARSENIC, MANGANEZE (EXPERIMENTAL RAT MODEL)

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Heavy metals remain one of a serious environmental problem due to their toxic effects. The effects of arsenic and manganese compounds on rat behavior and neuromorphology were studied. Wistar rats were assigned to four groups: rats in control group were given regular water, while rats in other groups drank water with final manganese concentration of 10 mg/ml (group A), 20 mg/ml (group B) and final arsenic concentration 68 mg/L (group C), respectively, for a month. To study exploratory and anxiety behavior rats were tested in open field, home cage and elevated plus maze. To estimate learning and memory status multi-branched maze was used. Statistically significant increase of motor and oriental-searching activity in experimental groups was revealed by open field test, which was expressed in increase of number of lines crossed, rearing and hole reflexes. Obtained results indicated the suppression of fear in rats exposed to low dose of manganese. Specifically, this was estimated by frequency of getting to the central part of the open field. Experiments revealed that 30-day exposure to 10 mg/ml manganese did not stimulate aggressive behavior in rats, while exposure to the higher dose (20 mg/ml) 37% of initially non aggressive animals manifested aggressive behavior, furthermore 25% of rats were extremely aggressive. Obtained data support the hypothesis that excess manganese in the body is one of the immediate causes of enhancement of interspecific predatory aggressive and violent behavior in rats. It was also discovered that manganese intoxication produces non-reversible severe learning disability and insignificant, reversible

memory disturbances. Studies of rodents exposed to arsenic also revealed changes in learning process. As it is known, the distribution of metal ions differs in various brain regions. The principle manganese accumulation was observed in hippocampus and in the neocortex, while arsenic was predominantly accumulated in nucleus accumbens, striatum and cortex. These brain regions play an important role in cognitive functions. Histopathological analyzes of brain sections illustrated two morphologically distinct altered phenotypes of neurons: (1) shrunk cells with indications of apoptosis - nucleus and cytoplasm were very difficult to be distinguished, integrity of neuronal cytoplasm was not disturbed; and (2) swollen cells - with indications of necrosis. Pyknotic nucleus, plasma membrane disruption and cytoplasmic vacuoles were observed in swollen neurons and they were surrounded by activated gliocytes. It's worth to mention that in the cortex the majority of damaged neurons were apoptotic while in subcortical nuclei -neurons were mainly necrotic. Ultrastructural analyses demonstrated that all cell types in cortex and nucleus caudates represent destructed mitochondria, widened neurons' vacuolar system profiles, increased number of lysosomes and degeneration of axonal endings.

PREDICTORS OF LIFE-THREATENING CRITICAL INFECTIONS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Infectious complications - bloodstream infections (BSI) including sepsis, septic shock remain the prevalent reason of mortality in patients (pts) with hemoblastosis during the intensive cytostatic therapy and in recipients of hemopoietic stem cell transplantation (HSCT). Infectious complications occur

up to half of all HSCT recipients with mortality rate from 24.0 to 43.6%. Prevention of the mortal outcome of system infections requires the novel strategies of preemptive therapy, based on reliable predictors of high informational value. Early use of such predictors would allow timely making optimal decision with regard to patient's treatment including antimicrobial and antiviral treatment. The study was performed to estimate possible risk factors for an adverse outcome in patients with a microbiologically-proven BSI. The study was conducted to assess the risk factors for fatal outcomes in pts., with hematological malignancies: acute myeloid leukemia, acute and chronic lymphoblastic leukemia, myelodysplastic syndromes, multiple myeloma, Hodgkin's and non- Hodgkin's lymphoma. We studied the group of 72 pts., with infectious complications, fulfilled the criteriums of sepsis (by definition of SEPSIS-3 Consensus Panel, 2016). We studied bacterial and viral complications. To detect the genomes of herpes viruses in the blood we used PCR-RT. PCR-RT was performed every 3-5 days before and after HSCT, as well as during the course of antileukemia therapy. For blood culture, the BacT/Alert 3D automatic culture system was used. Blood cultures were taken regularly with an interval of 3-5 days for neutropenia and or in the presence of fever. The rout of infections was investigated by controlling the intestinal microbiome and its changes as well as the flora of central venous catheter. We conclude that Gram-negative bloodstream infections are the predictors of severe complications with high level of mortality. The significant role is played also by viruses, especially the herpes viruses. Using this algorithm allows the rapid diagnosis of the infectious process, establishing its etiology and conducting timely adjustment antibacterial and antiviral therapy.

UBIQUITIN GUIDES PROLIFERATIVE ACTIVITY OF LEUCOCYTES DOSE-DEPENDENTLY

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Extracellular Ubiquitin regulates activity of proliferating cells. Molecular pathways involved in up and down-regulation of hematopoietic proliferating cells by ubiquitin is not clear. Dose dependent effects of chemicals indicate to existence of receptor-ligand relationships. We presumed that ubiquitin might interact with some of membrane proteins to regulate the cellular processes. The very first and simple test for indication on existing protein-protein interaction is the elucidation of the dose dependent of the substance consequences. We studied the influence of three different doses of ubiquitin on blood nucleic cell counts. Nonlinear white mice *Mus Musculus* of 25gr. were used for experiment. Animals were divided into four groups. Intact mice of the first control group were injected by saline. Mice of the second, third and fourth test groups were injected intraperitoneally by ubiquitin doses of 1.5mg/kg, 8mg/kg and 10mg/kg correspondingly. Blood was collected at different hour points. Microscopy and statistical methods have been implicated for calculation of cell counts of peripheral blood. 5000 cells have been counted per sample. Animals were anesthetized by ether before decapitation. Treatment of animals performed in accordance with regulations established by the Centre animal's ethic committee (Protocol N02/02.09.2019). The ubiquitin dose of 1.5mg/kg turned out to be involved efficiently in proliferative processes. Effect of ubiquitin exposes the dose dependent activity. Further investigation is needed for identification of potential receptors orchestrating pathways for outer-cellular ubiquitin actions. *Acknowledgment: Shota Rustaveli National Science Foundation. #217342*

BEHAVIORAL CHANGES INDUCED BY WHOLE BODY HYPERTHERMIA IN EXPERIMENTAL RATS

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It is known that Whole Body Hyperthermia (WBH) can enhance the effects of certain anticancer drugs, which is mutually strengthening and makes healing more likely - the so-called synergistic effect of hyperthermia. The less is known concerning the possible effects of WBH on the processes of learning and memory, and on rheological properties of blood. These issues served as the main purpose of this work. In experiments on laboratory rats (using hyperthermia chamber, behavioral tests in multi-branch maze and exogenous changing of Nitric Oxide production and blood rheological properties) we have revealed: 1. WBH might be used as one of the most effective triggering factor for launching of Hormetic Mechanism, which maintains the normal behavior of experimental animals; 2. In all cases when we use WBH as a trigger for Hormetic mechanisms in cancer or any other clinics, the critical is to make sure that chosen level of temperature does not exceed the hormetic range and that is very critical not just for action of Hormesis mechanisms, but for maintenance of blood rheological properties on the normal levels.

THE IMPROVEMENT OF THE “MARGINAL LIVER” TRANSPLANT SUITABILITY BY PERFECTING THE METHOD OF PERFUSION METHOD OF PERFUSION CONDITIONING IN EXPERIMENT

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One can hardly find a medical field that has advanced immensely in a relatively short period of time other than liver transplantation. There has been the increased number of liver transplantation in the wake of this progress, which in turn has caused a severe shortage of the donated organs. In such cases expansion of the ranges of the existed criteria concerning the usage of the donated organs becomes quite noteworthy. In the recent years the focus has been on the development of the dynamic methods of the preservation. It ensures the optimization of the organ before implantation and thus ameliorates the long-term outcome of transplantation. For this purpose, so called perfusion conditioning of marginal organs is addressed. This comprises complex works that maintain the structural integrity, viability and cellular functional capability of these organs. The method of perfusion conditioning (PC) of the organ transplants makes conservative solution/blood artificial flow within the ex vivo transplant possible and by this way provides ability of its thermal stability, excretion of byproducts and catabolic enzymes, supplying with the energetic substrates and oxygen, maintaining microcirculatory homeostasis.

EXTRACORPOREAL MEMBRANE OXYGATION (ECMO) USE IN ACUTE RESPIRATORY DISTRESS SYNDROME

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Acute respiratory distress syndrome (ARDS) is a non-cardiogenic pulmonary edema and diffuse lung inflammation syndrome that often complicates critical illness. The pathophysiology of ARDS is complex and incompletely understood. Early in the development of ARDS, the primary pathological finding is diffuse alveolar damage, although this is not seen uniformly in all patients. The diffuse alveolar damage leads to injury to the alveolar-capillary membrane, made up of type I and type II alveolar pneumocytes and capillary endothelial cells. The alveolar air spaces are subsequently flooded with proteinaceous edema fluid, inflammatory cells (neutrophils and activated alveolar macrophages), and inflammatory mediators, including pro-inflammatory cytokines, lipid mediators, and oxidants. Epithelial injury may be severe, with necrosis and sloughing of the type I cells exposing the basement membrane. Fibrin deposition occurs along the denuded basement membrane, resulting in the hyaline membranes that are characteristic of diffuse alveolar damage. The incidence of ARDS is estimated at 64 cases per 100,000 people, or 190,000 cases per year in the US. The mortality of ARDS is approximately 40% to 50%. Many different conditions can lead to ARDS, although sepsis is the most common cause, usually with a pulmonary origin (e.g., pneumonia). Other conditions associated with ARDS include aspiration, inhalation injury, acute pancreatitis and trauma. Extracorporeal membrane oxygenation (ECMO) is an increasingly accepted means of supporting those with severe acute respiratory distress syndrome (ARDS). Extracorporeal membrane oxygenation provides temporary

cardiorespiratory support for patient with severe respiratory or cardiac failure refractory to conventional therapy. It can be configured to provide oxygen, remove carbon dioxide, support perfusion, or all of the above. It may provide a bridge to recovery in patients with acute cardiopulmonary failure or to heart or lung transplant. In ECMO, venous blood is shunted through a machine to add oxygen, remove carbon dioxide, and regulate temperature.

C HEPATITIS VIRUS ELIMINATION PROGRAM IN GEORGIA (2010-2019) - POLICY ADVOCACY AND OPPORTUNITIES FOR EXTERNAL FACTORS TO INFLUENCE THE PUBLIC POLICY FORMATION AND IMPLEMENTATION

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The present study is part of a group seminar research conducted within the framework of the Georgian Institute of Public Affairs, Doctoral Program in Social Sciences. Its purpose is to analyze the main tendencies of policy advocacy initiated by external actors, opportunities for success, supporting and challenging factors in the period of Georgian Dream's governance (2012-2019). Implementation of the Hepatitis C virus elimination programmed in Georgia has been selected as one of the most successful advocacy cases. The major goal was to study degree of success in policy advocacy, initiated by external actors, and the policy change as well as its dependence on the structure, resources, strategies and internationalization of the advocacy coalition. Advocacy is defined as a set of targeted actions undertaken by advocacy group to change a specific public policy or maintain the status quo. Kingston's "Policy Window Opportunity Concept" was taken as one of the

theoretical frameworks. The qualitative research methods were used, conducting the secondary literature analysis, in-depth interviews and focus group with experts. Policy change was defined as dependent and policy advocacy as independent variables. The issue is actual due to a global challenge (71 mln.pers. infected, over 400,000 lethal results annually). Also, Georgia had an extremely high rate of infection - 6.7% of adult population infected (Stvilia, 2000). There is high risk factor associated with level of injecting drug-use - 3rd places in the world/50000pers. (Curatio International Foundation, 2015. Policy advocacy started during UNM's governance in 2010 and continued during the Georgian Dream's authority. Three stages of advocacy process were identified: 1. 2010-2014 The coalition is in favor of changing the status quo. Critical policy change: awareness raising, incorporation of policy issues, 60% reduction in market prices for medicines, introduction of a small-scale program in penitentiaries, development of a large-scale implementation strategy and action plan, resulted in incremental change; 2. 2015-2016 The Coalition was still in favor of the status quo change, the large-scale implementation of the program began and a significant policy change was adopted; 3. 2017-2019. The advocacy team works to increase access to program treatment, help with the community, reduce harm and stigma. Here the coalition is already in favor of maintaining the status quo. So called In terms of "removing barriers," the advocacy outcome is seen as incremental change. The composition of the coalition was heterogeneous and included: OSGF as coordinating Institute, GHRN (26 organizations), community entities, MDM, NCDC, MOH, SPS, Public Defender's Office, GPHC. International organizations such as CDC, Gilead Sc.Inc, US Academic-Research Institutes, WHO, GF were actively involved. Coalition used various strategies, i.e.: street activism, media campaign, lobbying and research-based argumentations. In-depth interviews revealed the role of the personality's factor, reflected in active involvement of specific senior officials

having positive impact on the process. The key role of internationalization has been identified. The issue was activated as the GD came to power (2012) when an international commitment came to the force in light of the European Court of Human Rights convictions (>200). Georgia became a Show Case and the CHV program was evaluated as an opportunity to share as the best practice to world. The success was driven by: a heterogeneous advocacy coalition, international actors, well-coordinated (OSGF) process, diverse strategies, well-defined action roles and action plans. Effective media campaigns have played a huge role in the success. Amid internationalization, experts' mobilization, technical and financial resources were nominated as key for success. Technical Advisory Group had important function in monitoring and evaluating, annually producing action plan and recommendations for State. Compliance of international and national interests was key factor. One of the study's assumptions - the use of the "Windows of opportunity" by GD was confirmed. Despite the weaknesses identified while monitoring, CHV Elimination State Program is assessed as very successful 'Show-Case' - 175,000 tested, 82,000 diagnosed, 65,000 treated, over 60,000 (98.7%) cured. Finally, as revealed by study, the UNM's Government had been skeptical about introducing the wide-scale CHV elimination program, whilst the first years of the I election cycle of 'Georgian Dream' is characterized by openness to participatory politics, thus link between success of policy advocacy, initiated by external actors, and application of the "Window of opportunity" has been confirmed.

THE REDOX-DEPENDENT MECHANISM FOR REGULATING THE FUNCTIONING OF A LIVING ORGANISM

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Reactive oxygen species play a key role in cell signaling, act as signaling species, participating in the modification of proteins, lipids, and DNA. Therefore, the regulation of oxidative homeostasis is very important for maintaining the health conditions in the living body. Redox regulatory system in the integrated biological system reacts to alterations of the production oxidants from their steady-state rate to eliminate the disorders and prevent damage. Determination of the mechanism of regulation redox-system in a living organism in health and disease state is of fundamental interest. We investigated the activity of total antioxidant system (TAA) in blood plasma during different pathological conditions - the chronic influence of ecological contaminants (dust) of different intensity (in the population of the Upper Imereti villages placed on the different distance from manganese ore deposit), ionizing radiation (X- and gamma radiated animals; human after course of radiotherapy of tumors) and chronic inflammatory diseases (atherosclerosis, diabetes), eating habits). It was revealed the correlation between TAA stress parameters and inflammatory and genomic instability markers of the living body. The mechanisms of these correlations and their prognostic role and impact for planning preventing activity and future treatment will be discussed.

ERYTHROCYTES DISTRIBUTION ACCORDING TO THEIR SPHERULATION DEGREE AND VOLUME AND ITS CLINICAL SIGNIFICANCE

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Changes in the population of peripheral red blood cells (RBC) is considered the earliest and most sensitive indices, significantly associated with increased risk of morbidity and mortality of heart disease, pulmonary disease, sepsis, and cancer, chronic obstructive pulmonary disease, stroke, anemia, and many more. This explains that a routine blood test is a necessary step in any diagnostic procedures, however, there is still much unclear in the mechanisms of regulation of the population spectrum of RBC - in time-dependent changes in the properties of cells that cause their aging and elimination from the circulatory bed. This article presents the results of an analysis of the distribution of red blood cells according to their degree of spherulation (Q) and volume (V) in humans and laboratory animals.

$$Q = \frac{V}{V_{SF}} = 6 * \pi^{1/2} * \frac{V}{S^{3/2}}$$

This parameter characterizes cell deformability and can be considered as the biological age of cells. In these coordinates the regions of minimal and maximal values of degree of spherulation corresponds to distribution by volumes young and old fractions of erythrocytes. Population spectra of RBC were determined using the specially developed method. The materials on the method and some examples of its application are published in a number of

scientific papers. It was revealed that in the region of the fraction of young red blood cells ($Q \approx 0.45 \div 0.55$), an increase in Q occurs mainly due to an increase in the volume of cells. In the region of cells of intermediate age ($Q \approx 0.55 \div 0.65$), the volume of cells changes little. At this stage of the RBC Life Cycle (60-80% of the total RBC mass), an increase in Q (aging) mainly occurs due to a decrease in the surface area of the cells (fragmentation). At the final stage of the life cycle ($Q \approx 0.65 \div 0.7$), the fragmentation intensity increases, and a decrease in the average volume of this fraction of red blood cells is also observed, however, this is due only to the disappearance of macrocytes and normocytes from the circulatory bed. This pattern with a high degree of probability indicates the leading role of morphometric characteristics (sizes and shapes) of cells in their selective elimination. It should be especially noted that the distribution by volumes of the young fraction of RBC is approximated by the Gaussian (symmetric) distribution, whereas the RBC integral distribution is characterized by significant asymmetry. In the light of the data obtained by us, it can be argued that the asymmetry of the RBC integral distribution is entirely determined by the specifics of the aging and elimination of cells and, therefore, in a good approximation can serve as their characteristic. In light of the foregoing, it seems that the study of the asymmetry of the distribution of RBC by volumes in combination with the standard characteristics of RBC (MCV, RDW-CV and RDW-SD) under physiological conditions and under various pathological conditions of the body, is a perspective way to increase specificity and, therefore, clinical significance of blood routine test.

MODELING AND REAL FOOD SYSTEMS FOR THE STUDY OF COMPLEX INTERACTIONS OF SALIVA WITH SURFACES

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We using biomedical laws, concretely theoretic and practical rheology for the development of knowledge for enabling rational food structure design, as well as generally for defining micromechanical models in soft systems. Sciences - Multi-scale rheology, soft-tribology, and soft matter physics as well as colloid, surface and bio interface sciences help us make better food product. Our science work bases on new approaches to improve quantification of relevant structure property - processing (SPP) relationships of soft food materials for situations spanning manufacturing processes to oral processing and digestion. This includes highlighting recent progress and new multiscale techniques in rheology and tribology for quantifying how oral processing transforms food during consumption, where the aim is to determine the physical basis for texture and mouth feel in various multicomponent foods (beverages, semi- fluids/soft solids, solid snacks). Our key challenge has been to capture the highly complex interactions that occur with saliva and surfaces. The combination of studies conducted using both model and real food systems are providing superior ability to evaluate new tribological/rheological-based techniques and develop causal SPP relationships. Well - characterized polysaccharides and densely packed microgel suspensions are proving reasonable models for liquid and soft foods, and recent studies indicate an important role of micromechanical and interfacial properties of individual dietary components and whole food

systems. The outcomes are being used for the design of next generation foods and beverages that are both nutritionally beneficial and acceptable to consumers. We also consider the development of nano indentation, which is very important for creating new mechanical multimodels. Our collaboration with rheologist from Georgia, who are working in nanonutritionology will be increase researcher area in this direction in the World, that is very significant.

THE ULTRASTRUCTURE OF THE HIPPOCAMPUS AND MEDIAL PREFRONTAL CORTEX IN ADOLESCENT, ADULT AND SENESCENT RATS

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Aging, the time-related decline of physiological functions necessary for survival, affects all the individuals of species. The brain is especially vulnerable to the aging. Many neurological and neurodegenerative disorders, including alterations in cognition are associated with aging. Even normal aging, which is not accompanied with age-related pathological states, is often characterized with the changes in cognition. One of the key directions in neurobiology of aging is the evaluation of aging-related structural changes in brain regions, associated with cognition, for the purpose to distinguish what types of alterations are related with normal aging and what types of changes reflects the onset of age-associated brain disease. In this research, we elucidate the ultrastructure of the hippocampus and medial prefrontal cortex in adult male rats. The results revealed almost the same morphology of both regions in adolescent and adult rats. The difference was observed only in

senescent rats. Thus, in some neurons, glial cells and synapses of the hippocampus and medial prefrontal cortex moderate and significant alterations synapses were detected. The alterations include the concentrations of the granules of lipofuscin in neurons, focal chromatolysis of cells, rarely - total chromatolysis, mild (rarely significant) alterations of cytoplasmic organelles, the appearance of small pathological inclusions in the cytoplasm of neurons, moderate alteration of a number of synapses, and glial activation. Such alterations were more numerous in the medial prefrontal cortex. *Acknowledgment: Shota Rustaveli National Science Foundation. #PHD 18-1146.*

AMPULLAR COLON CANCER AND ANTITROMBOLOTIC QUESTIONS

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Periampullary cancers include pancreatic, ampullary, biliary and duodenal cancers. At presentation, the majority of periampullary tumours have grown to involve the pancreas, bile duct, ampulla and duodenum. Patients with resected (22-54 mo) compared to pancreatic cancer (13-19 mo). Ampullary cancers can be subdivided into intestinal or pancreatobiliary subtype cancers with histomolecular staining. Patients (men and women, mean age 57 ± 3.2 years) had a verified ampullar colon cancer and did not have a thrombotic complication. Operations front low resection of the colon with anastomosis operations abdominal rectum extirpation was carried out under spinal anesthesia with bupivacaine 15-20mg and sedation in medozalamom. General criteria for inclusion in the study were the following signs: the absence of localized and systemic inflammation, diabetes, lack of taking drugs that affect blood clotting. Our study starts 2016 and continues now. In this

moment the control group included 38 patients. The study group included 67 patients who in the course of surgery correct hemostasis. Fencing material produced just before skin incision, at the time of surgical exposure on the fabric and immediately after the closure of the wound. The lack of significant differences in terms of the data confirms their insensitivity, and thus not informative in the diagnosis of disease and hypercoagulable fibrinolysis. Investigation of concentration of plasminogen activator produced only in the control group, and was designed to determine the presence or absence of the ejection of fibrinolysis activator during handling on the rectum. TAT complex is a marker of activation of the hemostatic system and is the reaction product of thrombin and antithrombin. A statistically significant increase in the concentration of TAT in to study the fibrinolytic system to determine the level of the complex plasmin-a- 2-antiplasmin. This active complex is not formed in the inhibition of plasmin by binding it to a-2-antiplasmin. It should be noted that the concentration of the complex in these patients higher than those in healthy individuals. This may indicate the presence of both reactive (secondary in response to hypercoagulability) and strengthen primary fibrinolysis. The presence of the latter suggests a higher initial level of urokinase plasminogen activator. The sharp increase in the complex in the postoperative period, most likely due to the release of i-RA, the level of which increased significantly in the postoperative period. The mechanism of receipt of the enzyme in blood is as follows and includes a lasting effect on the tumor tissue directly with possible permanent contact yawning blood vessels and possible entry into the blood released from malignant cells plasminogen activator. D-dimer is a product lysis cross linked fibrin by plasmin, and thus is a measure that reflects the state of both the coagulation and fibrinolytic link, in the study group was lower, which testifies to the state of the system compensirvannom homeostasis background of the treatment. Patients with ampullary cancer of the large intestine are an increase in the capacity of the

blood coagulation syste. Based this, we have initiative: these results needing add to questions for discussion about antithrombotic therapeutically treatment after and before surgery treatment of ampullar colon cancer. We are thinking BIOMED2020 will be very good place for this.

STATISTICAL ASSESSMENT OF CONCENTRATION CHANGES OF ALBUMIN AND EXTRACELLULAR UBIQUITIN LEVELS IN BLOOD SERUM OF ONCOLOGY PATIENTS

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The investigation of protein dysfunction can play the major role in understanding and prediction of the development of many diseases. Modern medicine has already studied a lot of proteins and their features, which can be successfully used as biomarkers of various types of diseases. Albumin level (hypoalbuminemia) in blood serum found the application as a biomarker of oncology diseases and systemic inflammatory response; that is why it is very intriguing to understand the molecular mechanism of this fact. Ubiquitin is a protein that plays the major role in protein degradation via ubiquitin-proteasome system; also, ubiquitin is responsible for posttranslational modification of proteins, DNA repair and other regulatory processes in cell. There is a lot of information that, along with other proteins, ubiquitin can be used as a biomarker in disease formation. In this work, we studied serum proteins of 82 oncology patients, and compared albumin and ubiquitin levels in the blood serum of diseased people to a group of healthy volunteers. Research involving human patients was performed in accordance with the requirements of the Council of Europe Convention on Human Rights and Biomedicine, Biomedical Research, as well as the UNESCO Declaration of

Bioethics and Human Rights. SDS PAGE and densitometry of Serum albumin level was used for assessment. Ubiquitin level was obtained by enzyme-linked immunosorbent assay (ELISA). Statistical methods OriginPro, ImageJ and ANOVA were used for quantitative analysis. According to our studies, there is no statistically confirmed confidence for the correlation between albumin and ubiquitin levels in blood serum, but tendency to negative correlation is evident. Obtained results may reveal the unique information about changes in molecular interaction between extracellular ubiquitin and albumin in blood serum during the development of oncology diseases. The results are significant for further investigation of the regulation of cellular processes by extracellular ubiquitin significant for cancer research. *Acknowledgment: Shota Rustaveli National Science Foundation. #217342*

QUANTITATIVE ANALYSIS OF PET ACQUISITION PERFORMED BY VARYING THE ACQUISITION/RECONSTRUCTION SETTINGS: A CORRECTIVE POST-PROCESSING METHOD

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The limited spatial resolution in positron emission tomography (PET) images leads to difficulties to measure correct uptake in tumors. In particular, this is the cause of the partial volume effects (PVE) and can lead to serious bias, especially for small tumors. Correct uptake values are essential for the correct quantification of a parameter widely used in clinical practice, i.e. the standardized-uptake-value (SUV). The aim of this research is to theoretically elaborate and experimentally evaluate a corrective method for PVE, alternative to the Recovery Coefficient (RC). In order to obtain the PSF of the PET system, we had to acquire the activity distribution from a point-like source. The acquisition was performed by GE MEDICAL SYSTEMS,

DISCOVER 710. In the study, acquisition was performed using NON TOF and TOF correction, in order to analyze the effect of a change in the reconstruction algorithm on the PVE. For acquisition NEMA IEC Body Phantom, has been used. The counts C of the six spheres has been evaluated inside spherical ROI with radius R equal to the real one using an ideal segmentation criteria. We obtained the x and y coordinates of the six spheres centers from the CT. After determining the center, we construct binary masks in which the voxels inside the ROI have value 1 while the voxels on the background have a value of 0. In order to be more precise in the application of the spherical mask on the acquired image we have done a rebinning. This procedure has been implemented in the MATLAB program and it Works. We did a voxel by voxel product between the finer image matrix and the binary mask, selecting only voxel in the ROI. We made the sum of these voxel obtaining the counts inside the spheres, which are representative of the activity in the ROI. From the different acquisition mode and time, we took the maximum value of counts, the mean value over a 1 cc inside each sphere and the average value on the total volume of each sphere. In order to recover the concentration values, we multiply the counts by the calibration factor normalizing to the volume. With this procedure, we obtain the respective SUV_{max}, SUV_{peak} and SUV_{mean}. If the tracer is distributed uniformly throughout the VOI, then the SUV would be 1 everywhere. Any departure from 1 indicates a different distribution of the tracer in the VOI in comparison to that the rest of the body. There is no single way to assess the tumor uptake. SUV therefore does not refer to a unique and standard definition. The ways the numerator and denominator are calculated can significantly affect the SUV estimate. We obtain the ratio between lesion SUV on the background SUV for theoretical and experimental (measurement) one. Thanks to data analysis, as it is visible from LBR_{mean}, PVE effect is present for small dimension of ROI. In this paper a method for the correction of the PVE in PET exams is presented. The method is based on the use of

mathematical formula that describes the effect of the limited resolution of the system under reference conditions (homogeneous lesion on a constant background). We tested the effectiveness of the method by acquiring an IEC NEMA Phantom (6 spheres of different diameters) by varying acquisition time (noise) and reconstruction algorithms (TOF and NON-TOF iterative OSEM algorithm) at a fixed value of lesion-to-background ratio (LBR=4). The results obtained are very good: SUV_{mean} corrected differs from the theoretical value less than 10% for all the spheres within the time of acquisition is longer than 2 min (standard acquisition time of a PET exam). The limits and the applicability of this work to the clinical routine depend on the fact that our method was developed from reference conditions, different from those of acquisition of a patient. *Acknowledgment: Grant of ICTP (The Abdus Salam International Centre for Theoretical Physics), Fellowship Application #106583, #GEO6010*

DEVELOP A GENETIC PREDICTION VECTORS FOR IDENTIFICATION INDIVIDUAL SENSITIVITY OF CHILDREN WITH ACUTE LEUKEMIA TO GENOTOXICITY OF THERAPY

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Thanks to the achievements of medicine, today, children with leukemia have the opportunity to not only receive long-term remission, but also to completely recover. However, the disease can proceed in different ways and the chances of recovery in different patients with approximately the same indicators are different, i.e. the prognosis of the course of the disease is individual. It

depends on the individual characteristics of the body and the various sensitivity to current therapy. Recently, much attention has been paid to genomic instability, considering that it determines the development of both early and late complications. We conducted a set of genetic studies, including chromosome analysis, counting the frequencies of micronuclei in buccal cells and in bone marrow erythrocytes (Jolly body), as well as DNA comets. Studies were conducted in children with acute lymphoblastic leukemia in dynamics (upon admission, on the 15th and 33rd day, as is customary in the guide-line to determine the severity of the course and achieve remission). Despite the fact that all the patients showed the increase in frequencies of MN and DNA-comets during treatment, using cluster analysis, 2 groups of patients were identified that differed in the intensity of the increase in frequencies of MN and comets. The factorial analysis of variance revealed a statistically significant relationship between the rate of increase in frequencies of MN and their initial level. These data illustrate differences in the sensitivity of individual patients to the genotoxic effects of chemotherapy.

APPLICATION OF 3R PRINCIPLES IN BIOMEDICAL EXPERIMENTS

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Just a year ago the scientific society celebrated the 60th anniversary of William Russell's and Rex Burch's "The Principles of Humane Experimental Technique" - the work that triggered the development and adoption of 3Rs (Replacement, Reduction and Refinement) in biomedical research around the world. Since the "Directive 2010/63/ EU on the protection of animals used for scientific purposes" has been adopted by the EU Parliament, became a

leading guiding principal for those involved in biomedical experiments and resulted in significant decrease in the amount of used animal, but the total numbers still remain very high - 9.3 mln were used for research and testing only in the EU in 2017. Among important 3R-contributing factors there are rapidly developing technologies, such as predictive computational tools and robotic high-throughput screening in drug design and development; artificial intelligence in-vivo imaging systems in cancer research; organ-on-a-chip systems and 3D printed organoids with multiple cell types in toxicological studies, etc. As well, the 3Rs Principles are increasingly being incorporated into both national and international legislation, guidelines, and animal experimentation practices to ensure animal welfare. Commitment to 3R management is strongly recommended to candidates seeking participation in innovation, validation and implementation biomedical projects. 3R principles are emphasized on achieving the reduction in animal numbers used in basic, translational and applied research studies in vivo. As well, the synergy between in silico-, in vitro and in vivo methods within the project definitely increases its 3R potential and is highly appreciated. But despite growing number of scientific questions solved through alternative methods, the use of animals for scientific purposes, including biomedical studies, is still irreplaceable (and this year's COVID-19 outbreak is one more proof). Therefore, use of animals is necessary and, probably, will remain necessary in the foreseeable future. In this context, the application of 3R principles will be of top priority for both protecting animal welfare and increasing the quality of scientific research.

THE EFFECT OF RADON INHALATIONS OF AGGRESSIVE RATS

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Radon is a radioactive element that basically has radiation. Here we consider Tskaltubo waters where radon radiation is about 1Nk/l. American scientist Lac and Russian scientist A.G. Kozin proposed a theory of radon hormesis. The word hormesis comes from the word hormone and denotes stimulation. This is a universal phenomenon when small doses cause activation of the body's protective processes and have a healing effect. Therefore, we decided to study radon therapy (radon hormesis) in the diseases associated with aggression and determine unhealthy lifestyle impact on their development in order to understand the mechanisms of the treatment with radon gas. Consequently, we studied biogenic amines (noradrenaline, serotonin) and amino acids participating in excitation (glutamine and asparaginic acid) and retention processes (glycine and gaba) in the brain. Aggression is a motivated behavior which has a certain direction. On the other hand, it can be regarded as the cause of social degradation. There are different types of aggression: maternal, fear and irritation-induced aggression, male aggression and others. In our case we have studied such behavioral aggression as "The rat as a mouse killer". It can be considered as an interesting aggression because the rat does not consider victims as food. In this case rats are not hungry but still kill mice. These rats differ from the same kind of rats by their behavior in the open field. We carried out radon inhalations within 7 days, then measured the amount of amino acids and studied their behavior in the open field and endurance on the treadmill on the 14th and 30th days from the inhalation. These experiments showed that aggressive rats move fast in the open field spent less time, the number of stands and grooming were more long-lasting

what shows their dominance. And, as a result of radon impact, the processes caused by anxiety were reduced.

THE EFFECT OF ELECTROMAGNETIC FIELD ON PLACENTAL GROWTH HORMONE (GH2) IN PREGNANT RATS

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Nowadays, most human environments are immersed large amounts of electromagnetic waves. These electromagnetic waves have two principal roots, natural sources and man-made sources. Mobile phones and base stations, video and radio broadcasting facilities, radar, medical equipment, microwave ovens and radio frequency heaters as well as a diverse variety of other electronic devices, are just a few examples within our living and shaping environments that generates Electromagnetic fields (EMF). EMF might have various biological effects on the developing embryo. Researchers found that mobile phone radiation exposure during the incubation period of chicken eggs leads to some detrimental effects on growth development. Placental growth hormone (PGH) is the product of the GH-V gene, predominantly expressed in the syncytiotrophoblast layer of the mammalian placenta. PGH is one example of a trophoblast hormone, which allows maternal metabolic adaptation to pregnancy. GH2 act in mother's body to stimulate insulin-like growth factor (IGF) production and modulate intermediary metabolism, resulting in an increase in the availability of glucose and amino acids to the fetus. Our aim was study impact of EMF on growth hormone concentration (GH2) in pregnant rats, the quantitative change of their offspring weight and number. Presence of vaginal plug and sperms in the vaginal smear used as indicator of day one of pregnancy. Pregnant rats were divided into 3 groups (n=10 in each group). It's control and experimental groups. Experimental groups will be exposed to EMF

effect with frequency of (1800 MG/H). EMF Exposure System: The electromagnetic field was generated only day time 10 hours per day during 15 days, while animals of group 2 stayed exposed during the whole period of pregnancy. The control group's rats were placed under the same conditions, but the control group did not expose to EMF and they were placed in the other room. Determination of GH-2 occurred in experimental groups on 15th days and the last week of pregnancy, in control group determination of GH-2 occurred on 15th days and last week of pregnancy. GH-2 hormone change was determined by ELISA kits. In our research under EMF action GH2 hormone is change. Concentration changes of GH2 affect changes in weight and number of offspring in rats. Mobile phone exposure induced significant hormonal changes. Therefore, the public should be aware and limit their exposure as much as possible.

THE STUDY OF THE DURATION OF EXPOSURE TO ELECTROMAGNETIC FIELDS OF FREQUENCY ON ADOLESCENTS REGARDING THE CHARACTERISTICS OF ORAL HYGIENE

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Over the past two decades, more than 20,000 articles have been published on various aspects of the biological effects of EMF of a wide frequency range, but we had not found detail information about effect of EMF on the young generation. Therefore, the main goal of our research is to study the stress caused by the use of the electromagnetic field in adolescents (18-25 years

old) in the context of periodontal development. The problem is relevant, given that the electromagnetic field of the communication frequency (frequency 1800/900 MHz) causes a number of diseases. There has been little research on this subject. There have been no studies of adolescents included in the risk group of periodontitis development. Of course, we cannot resist civilization development, but it is necessary to introduce the practice of “smart evasion” from the prolonged exposure of adolescents to EMF. To solve these problems, 135 adolescents aged from 18 to 25 were examined. They were divided into three groups according to the duration of exposure to EMF. For complex processing-generalization of the experimental materials and results we used multidimensional and multi-parameter methods of modern statistics, such as analysis of variance (ANOVA), calculations were performed using the STATISTICA-6 and MATLAB-7 mathematical datasets with standard and original programs. Our data show that the electromagnetic field has a negative effect on people and especially on the facial part, since this part of the body experiences the greatest stress when interacting with EMF. This is reflected in changes in the hygienic characteristics of the oral cavity, such as: determination of the hygiene index; papillary-marginal index and the study of periodontal index.

CHATBOTHS IN MONITORING COMPLICATION OF DIABETES MELLITUS

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Manifestations and complications of diabetes mellitus belong to those diseases that result disability and premature mortality. Such as microangiopathy, nephropathy, hypertension, heart attacks, strokes, etc. are very hard disease, which developments during diabetes mellitus. Any kind of

studies, findings and conclusions, which will help us to investigate previously unknown reasons of diabetes and its complications, avoid complications or their management, early detection of diabetes, planning/implementation of preventive measures, that very important to reduce the number of sick people and increase of quality of life of diabetics. Modeling Health Business will help reduce the percentage of patients with diabetes mellitus. We identify the problems of building a healthcare organization model, we specifically aim to determine and describe typical business processes for designing a healthcare organization management information system. We propose the requirements to the methodology of business process modeling. We offer new methods in business of care. We are going to introduce new methods of research. From our point of view, it is very important to divide the types of diabetes. It turned out that with intensive monitoring the cost of patient care will be reduced by early identifying microangiopathies and their treatment. One of the most original innovations is electronic chatbots, which will allow you to diagnose complications of diabetes at an early stage. One of these has already been introduced and is being tested by volunteers.

**DYNAMICS OF DENTAL PLAQUE HYGIENIC INDEX MODIFIED
BY TURESKY, ALPHA-DEFENSIN AND RHEOLOGICAL STATUS
ESTIMATION IN PATIENTS UNDERGOING ORTHODONTIC TREATMENT**

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Thus, the index of dental plaque was reliably low in patients undergoing the treatment by aligners as compared with the patients with fixed bracket-systems. Non-removable orthodontic equipment affects marginal periodontal

tissues and mouth hygienic condition more than removable one. In spite of observed considerable data spread, when comparing the initial level of antimicrobial peptide measured before the placing the bracket systems, statistically significant differences were obtained. In mixed saliva in patients of basic group the content level of alpha-defensin was higher than in the control group. 3 months after carrying bracket systems value index significantly changed: in the group with inflammatory processes the content of alpha defensin decreases in periodontal tissues whilst in comparison group it increases. The changes in basic group after three months were significant. Thus data evaluation suggests that orthopedic problems are accompanied by blood rheological changes that lead to the increase in plasma viscosity red blood cells aggregability and decrease in red blood cells deformation. That is, (blood rheology) and coagulation changes are notable while dysfunction of vascular endothelium is present. These patients might be considered as risk groups for cardiovascular problems. Thus, data evaluation suggests that orthopedic problems are accompanied by blood rheological changes that lead to the increase in plasma viscosity and red blood cells aggregability. That is, blood rheology and coagulation changes are notable while there is dysfunction of vascular endothelium. And this is a very significant problem. These patients might be considered as risk-groups for cardiovascular problems. Study measures of rheological parameters have not been implemented in dental clinics of Georgia yet. With this work we would like to show how important theological changes are. At the time we would like to show that aligners are very convenient, they are also very beautiful, although non-removable brackets have their strong side, when it is necessary to straighten teeth and their insertion in appropriate place and stretching becomes necessary in certain conditions.

UNDERSTANDING AND TAILORING THE VISCOELASTIC RESPONSE OF POLYMER MELTS

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The time marching algorithm represents the key ingredient of our approach to study of tailoring the viscoelastic response of polymer melts or concentrated solutions, we have developed a general coarse-grained approach based on the tube model, that we are now using as a predictive tool in order to investigate the viscoelastic properties of complex, entangled polymer architectures. We have been elucidating the molecular origin of their relaxation processes and in particular, their constraint release mechanisms. We are extending this approach to describe the complex rheology of entangled macromolecular self- assemblies built from sticky polymers, and use our model as a new tool for an in-depth analysis of their viscoelastic properties. In particular, we investigate the dynamics of a series of model telechelic linear and star polymers which create a reversible network through metal-ligand association, and study the effect of blending different architectures on the network relaxation. We also investigate the behavior of entangled polymers bearing stickers along their backbone. Our studies show that the dynamics of these associating polymers strongly depends on the ratio between entanglements and stickers density, as well as on the ratio between their association and disentanglement times, leading to a large variety of viscoelastic responses. Understanding and tailoring the viscoelastic response of polymer melts or concentrated solutions from the knowledge of their molecular structure (architecture) represents a formidable challenge and remains a prime field of soft matter research. These researches and our approaches are very significant of polymer rheology.

ISCHEMIC STROKE IN NEUROSYPHILIS POSITIVE PATIENT: CASE REPORT

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In recent years neurosyphilis (NS) has undergone pathomorphosis, meningovascular, asymptomatic and atypical difficult-to-diagnose forms of the disease, which indicates the relevance the actual and medico-social significance of the problem. Up to four to 10 percentage of patients with untreated syphilis can develop NS. The objective of the present study is to investigate of functional state of hemostasis system and hemorheological status of meningovascular NS patient associated to ischemic stroke (IS) before, during and after specific therapy. We describe the Caucasian 50-years old female presented to Emergency Department, who had the right middle cerebral artery territory infarct, verified by magnetic-resonance angiography (MRA). This patient had no other cardiovascular risk factors. The disease severity was evaluated according to MMSE and NIHSS. Serologic and cerebrospinal fluid (CSF) treponemal tests (VDRL, TPHA) before and after beginning therapy were performed. The following hemostatic (HS) and hemorheological (HR) markers were studied: activated partial thromboplastin time (APTT); antithrombin III (AT III) activity; plasmin- α_2 plasmin inhibitor complex (PIC) by immunoferrmental (ELISA) method; fibrinogen concentration by M.Machabeli method; erythrocyte aggregability (EA) index by "Georgian method"; plasma viscosity (V) (capillary viscometer); systemic hematocrit (Hct) (blood centrifugation). Based on clinical-MRA findings, positive serologic and CSF treponemal tests (VDRL, TPHA) NS, associated to neurosyphilitic vasculitis leading to IS, was diagnosed. In addition to the early management of acute IS she was started on intravenous bentsylpenicillin 4 million units 4

hourly (24 million units per day) for a total 14 days. In this patient before specific therapy the tendency to APTT elongation was revealed. A multidirectional change in APTT was noted against the background of the treatment, which can be explained by the presence of antiphospholipid antibodies (AA) in NS patient's blood. AA introduces an imbalance in the coagulative hemostasis system. AT III activity was reduced before, during and after specific therapy. The decrease of AT III activity indicates its consumption during the first 14 days of antisyphilitic treatment. AT III activity reduces is the specific and highly sensitive marker of thrombin generation in vivo and activation of coagulative processes. The concentration of PIC was slightly increased on the first day of hospitalization, whereas two weeks later the significant increase in the level of this marker was revealed. Cross-linked fibrin degradation is known to be catalyzed by plasmin. This process is regulated by plasminogen, a plasmin precursor, and α_2 -plasmin inhibitor, which is reacted with plasmin, forms an enzymatically inactive PIC, that undergoes degradation in the reticuloendothelial system. Therefore, the PIC is a direct indicator in vivo plasmin generation. Our data on the dynamics of PIC levels indicate that endogenous fibrinolysis is always secondary. F plasma concentration was increased on the first day of hospitalization. Two weeks after the start of specific therapy the level of F remained elevated, which may indicate incomplete resolution of inflammatory processes in NS. The EA index was elevated before specific therapy and was still high after 14 days of the therapy. The direct correlation was found with development of the microcirculatory stasis, caused by erythrocyte hyperaggregability in cerebral microvessels. Recent studies have proved the role of microcirculatory stasis as a critical hemorheological disorder in the microcirculation system of the brain, which plays an important pathogenetic role in the development of IS. The enhanced EA index was correlated with hemostasis system activation, in particular, with F plasma concentration. The EA index and F

concentration where not connected with Hct and blood V levels. Blood plasma V remained almost within normal limits throughout the investigation period. No noticeable dependence of the EA index and F level on a low or high systemic Hct was found. IS as manifestations of NS have been reported quite rarely. It is to be noted that IS can be an initial presentation of meningovascular NS and requires combined specific pathogenetic therapy of NS and IS. The obtained data indicate: (a) the enhanced erythrocyte hyperaggregability and hyperfibrinogenemia are the main risk-factors in the development of microhemorheological disorders and activation hemocoagulative processes in meningovascular NS associated to IS; (b) the lack of full normalization of the studied HR and HS indicators against the background of specific therapy allows us to attribute our patient to the risk group for the occurrence of repeated cerebral infarction.

GENETIC BASIS OF ANTIBIOTIC RESISTANCE IN CLINICAL ISOLATES OF ENTEROBACTERIACEAE

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The prevalence of the beta-lactam resistant enterobacteriaceae, specifically the 3rd generation cephalosporins and carbapenems, is steadily increasing and spreading globally. Antibiotic resistance is supported by various molecular mechanisms, including intrinsic and acquired resistance genes. Here, we examined an antibiotic resistance phenotype and beta-lactam gene content of MDR clinical isolates of enterobacteriaceae, recovered from patients atintensive care units of multi-profile hospitals in the Country of Georgia. Bacterial isolates were collected between July 2017 and May 2019 from four clinical sites in Georgia. Bacterial identity and antimicrobial susceptibility were

determined by the Vitek 2 automated system according to CLSI standards. Antimicrobial resistance gene content was examined by multiplex PCR (Streck Inc.), targeting plasmid-mediated AmpC and beta-lactamases, representing fifteen gene families. 168 specimens, consisting of *Klebsiella pneumoniae* (n=72), *Pseudomonas aeruginosa* (n=35), *Escherichia coli* (n=51) and *Serratia marcescens* (n=10) were selected for this study. It was found that 100%, 97%, 94% and 78% of *S. marcescens*, *P. aeruginosa*, *K. pneumoniae* and *E. coli* isolates, respectively, were multi-drug (MDR) resistant. CTX-M-15 or CTX-M-14 extended spectrum beta-lactamase genes were detected in 100% of MDR *K. pneumoniae* and *E. coli* strains, followed by 78% and 13% found among MDR *S. marcescens* and *P. aeruginosa*. In addition to CTX-M-15 gene, subset of *K. pneumoniae* co-harbor OXA-48 (n=15) or NDM (n=8) carbapenem resistance genes, whereas single *E. coli* isolates were found to also carry OXA-48 (n=1), NDM (n=1), VIM (n=2) and IMP (n=2) carbapenem resistance genes. In addition, only two strains of *S. marcescens* demonstrated the presence of OXA-48. VIM and IMP were found in 11 and 2 strains of *P. aeruginosa*, respectively. DHA and EBC were co-harbored together by one isolate of *E. coli*, and CMY-2 was found in single isolate. MOX ACC and FOX genes were not detected in any of presented isolates. Multi-drug resistance has been observed in bacterial isolates recovered in the country of Georgia. Detection of highly transmissible plasmid associated resistance genes indicates the high potential for horizontal spread of resistance that in combination with already existing multi-drug resistance could lead to the emergence of a novel “superbug” in Georgia.

A COMPREHENSIVE STUDY OF THE INFLUENCE OF THE THERAPEUTIC PROPERTIES OF TSKHALTUBO WATER ON PATIENTS WITH PARODONTITIS AND RESTORATION OF ORAL FLUID MINERALIZATION

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In the process of preserving homeostasis of the oral cavity, the alpha radiation of radon, which is abundantly contained in the Tskhaltubo waters, plays a huge role. Therefore, the goal of the study is to determine the mechanism of action of radon hormesis and its use to preserve the mineral metabolism of the oral cavity. The use of Tskhaltubo water in the form of inhalations and rinses in case of parodontitis causes the reduction or elimination of the inflammatory process that has developed in the case of parodontitis. It is these unique properties that have become an important component in the treatment of the initial stage of parodontitis, in particular, the treatment was based on an individual approach to each patient, taking into account the general condition and development of dental status. The treatment was performed with the help of inhalations and rinses with radon-containing waters of Tskhaltubo for 10 days. Patients suffering from parodontitis were divided into two groups, depending on the degree of severity of parodontitis. 60 patients with a periodontal pocket depth of 1.3 mm were conditionally allocated in the group with a mild severity of parodontitis. Another 60 patients with a periodontal pocket depth of 4 mm were conditionally allocated in the group with an average severity of parodontitis. After that, each group was further divided into two groups of 30 patients in each. In two groups consisting of 30 patients in each, the inhalations with the waters of Tskhaltubo were applied, and in the

other two groups of 30 patients in each, the inhalations and rinse with the waters of Tskhaltubo were applied twice a day after meals.

**PARALLEL STUDY OF HEMORHEOLOGICAL, INFLAMMATION
AND ANEMIA PARAMETERS BEFORE, DURING
AND AFTER SURGERY IN PATIENTS WITH STOMACH CANCER**

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The aim of our work was to study the biomechanical markers of blood flow in patients with stomach cancer. Therefore, we paid attention to the parameters of hemorheology, rheology, inflammation and anemia in the group of patients with stomach cancer and in the control group; with the help of a new surgical technique, we simultaneously examined the flow parameters in the central blood and locally at the site of tumor growth during the operation. As a result of the matrix analysis and statistical data processing, it turned out that in the group of patients the average values of hemorheological parameters went beyond the limits of the clinical norm and significantly differed from the parameters in the control group. Moreover, the parameters of inflammation and anemia also differed in the group of patients from the values of the control group, but with a little difference. Consequently, the parameters of hemorheology, inflammation, and the parameters that determine the presence of anemia are variable in the local circulation as compared to the central one, mainly due to the hemorheological component.

**OLD GEORGIAN MEDICAL MANUSCRIPTS AND EXPERIMENTAL
STUDY OF THE PRESERVED MEDICAL PRESCRIPTIONS
(THE STUDY OF THE EXAMPLE OF A BEETROOT-CONTAINING
MEDICAL PRESCRIPTION IN THE CASE OF EXPERIMENTAL PEPTIC
ULCER INDUCED BY ETHANOL AND NSAD)**

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The project “Medical and Veterinary Manuscripts from the Depositories of Georgia and Abroad” (Grant project №HE17-54; 2017-2020), funded by the Shota Rustaveli National Science Foundation is implemented at the Korneli Kekelidze Georgian National Center of Manuscripts. One of the main aims of the project is creation of the new agent (prototype) based on the prescriptions preserved in the manuscripts and study of its pharmacological efficacy and safety. This goal defined not only the interdisciplinary nature of the project what was always customary for the projects of the National Center of Manuscripts, but at the same time turned it to the multidisciplinary project, as it demanded connection of such distant fields of sciences as pharmacology and philology (textology). Consequently, there appeared necessity of using of bioscience research, in particular, experimental-laboratory methods. This paper discusses the methodology of preparation of the pharmaceutical product from herbal raw materials (beet root, beet leaves, beet water) based on the medical prescriptions preserved in the old Georgian medicinal manuscripts (Q 877. Zaza Panaskerteli, Medicinal Book, XV century; Q 270. Yadigar Daud, Medical collection, XVII century; etc.), as well as study of the efficiency of the abovementioned pharmaceutical product (prototype) BVLP in case of

experimental peptic ulcer induced by ethanol and NSAD. Experimental studies of specific pharmacological activity of BVLP on lab animals have shown well-defined gastro protective effect at gastric mucosal injury induced by a local irritant – ethanol and for systemic agents such as steroids, NSADs, BVLP was ineffective in preventing the characteristic pathological changes. BVLP, neither in single nor multiple (14 days) oral administration, did not cause any toxic effects in laboratory mice and rats. Animal behavior, weight changes, body weight ratios do not differ from the control (intact) animal data. These results reiterate the importance and perspectives of multidisciplinary projects. *Acknowledgment: Shota Rustaveli National Science Foundation of Georgia. #HE17-54*

INHERITED THROMBOPHILIA AND PERSONALIZED MEDICINE

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Personalized/precision genomic medicine provides opportunities for new approaches to healthcare delivery and comprehensive population health management. For example, it will identify individuals at risk for many diseases and significantly reduce the incidence of these diseases. This will fuel a drive towards personal health optimization, with enormous benefits for individuals, the healthcare system and the national economy. The medical and scientific communities around the world are just starting to seize the opportunities that personalized genomic medicine offer. Inherited thrombophilia is a genetic disorder of blood coagulation resulting in a hypercoagulable state, which has been suggested as a possible cause of recurrent thromboembolism. Family and twin studies have established a heritable component to venous and

arterial thrombosis. For the vast majority of patients, thrombosis is a complex, multifactorial disease caused by a combination of numerous, often unknown, environmental and genetic factors. 1340 unrelated Georgians with thromboembolism and pregnancy complications and 100 controls were genotyped by PCR analyses for detection of inherited thrombophilia (Factor V Leiden (FVL), Prothrombin (PTH G20210A) and Methylenetetrahydrofolate-reductase (MTHFR C677T) gene mutations). Statistical analysis was performed on SPSS v.21 statistical software. Fisher's exact test and Pearson's chi-squared (χ^2) test were used to assess inter-group difference, Odds ratio (OR) and 95% confidence interval were used to evaluate the strength of the association between the inherited thrombophilia and the risk of developing thromboembolism and pregnancy complications. The difference between the groups and the risk of pregnancy complications were considered to be significant when $p < 0.05$. Relationships between thromboembolism or pregnancy complications and FVL (7.1% in patients and 0% in control; $\chi^2(1, N=1440)=7.59$, $p=0.006$) and MTHFR (7% in patients and 1% in control; $\chi^2(1, N=1440)=5.382$, $p=0.02$) mutations were significant. Relationship between thromboembolism or pregnancy complications and Prothrombin mutation (6.25% in patients and 1% in control; $\chi^2(1, N=1440)=2.325$, $p=0.127$) was weak. The combined double and triple mutations were seen only in patients and no one case was seen in control group. As a result of our study it is possible to consider Leiden, Prothrombin and MTHFR mutations, especially its homozygous form and double heterozygous carriage as an independent high risk factors for development of thromboembolism, pregnancy loss and pregnancy complications in the Georgian population patients. Distribution of studied mutations in Georgian general population is high and resembles upper data of Caucasians. This is the first study in our population and shows that inherited thrombophilia has significant impact on development of blood coagulation disorders in Georgian population. Understanding importance of

these results will help clinicians and healthcare professionals to manage thrombosis and develop prevention program.

RBC ADHESION AND ENDOTHELIAL CELLS DURING DISEASES

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RBC adhesion to endothelium can be studied in static and flow conditions. Increased RBC adhesion was first described in sickle cell disease. Several molecules were shown to be involved in this phenomenon: VCAM-1, $\alpha 4\beta 1$, Lu/BCAM, ICAM-4. In malaria, Plasmodium falciparum erythrocyte membrane protein 1 binds to ICAM-1, PECAM-1 and facilitates the parasite dissemination. In diabetes mellitus augmented RBC adhesion is correlated to the severity of vascular complications. Glycated RBC band3 reacts with the endothelial receptor for Advanced Glycation End Products (RAGE) RAGE engagement induced endothelial cell dysfunction. In patients with Polycythemia Vera (PV), the most frequent myeloproliferative disorder, constitutive phosphorylation of RBC Lu/BCAM responsible for an increased adhesion to endothelial cell laminin. Retinal vein occlusion (RVO) is a common cause of permanent visual loss. Spontaneous growth of erythroid precursors was observed in more than 25% of patients. RBC adhesion was enhanced and correlated to phosphatidy1 serine (PS) expression on RBC. Anti-PS Receptor blocked RVO RBC adhesion indicating that the counterpart of RBC PS is PS endothelial cell receptor. Erythrocyte adhesion is mediated by different molecule abnormalities in different diseases but is associated to a higher risk of thrombosis and vascular complications.

THE DEVELOPMENT LEADING TO THE CONCEPT OF THE CIRCULATION OF THE BLOOD

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The seminal event in the history of Hemorheology must surely be Harvey's discovery of the circulation of the blood. Until that happened, the ideas concerning the movement of blood were based, in Europe and Middle East, largely on the principles laid down by Galen which had been, in effect, dogma for something like a millennium and a half. The essential concept here was that the blood is formed in the liver, thence it travels to the periphery and is consumed - hence there is no circulation at all. Harvey's revolutionary idea that blood circulates repeatedly around the cardiovascular system laid the foundation for hemorheology in that once the idea of a circulation was accepted, then the fluidity of the blood immediately became potentially of crucial importance - and the prime aspect of hemorheology was born.

UNDERSTANDING THE BEHAVIOUR OF BLOOD FLOW AT THE MICROSCALE IN THE PRESENCE OF AGGREGATIONS

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Microvascular blood flows are characterized by complex bifurcating geometries and distinct hemodynamic phenomena such as phase separation, which affects the hematocrit, viscosity and the wall shear stress experienced by the endothelium. These phenomena are further exaggerated in the presence of aggregation. Understanding the properties of blood at the

microscale is thus of both fundamental and practical importance. Advances in microfluidics and microscopic imaging techniques allow detailed characterization of microscale blood flow in vitro. In the present study, a micro-PIV technique is employed to obtain information on the velocity characteristics of blood in the parent and daughter branches of a T-junction PDMS microchannel and in the presence of aggregation. Human blood samples at 25% hematocrit were used in the study and Dextran 200 was employed to promote aggregation. RBCs were used as tracers; strobe and brightfield illuminated images were acquired for various flow ratios through the bifurcation and processed further to obtain both the velocity field as well as the local cell distribution. The estimated hematocrit profiles were used in conjunction with an established empirical viscosity model to obtain relative viscosity distributions. The approach was validated by comparing the measured velocity profiles with predicted ones based on the estimated relative viscosities.

A STUDY OF BLOOD RHEOLOGY IN PREGNANT WOMEN WITH PLACENTAL CHRONIC INSUFFICIENCY

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Placental insufficiency is one of the common pathologies of pregnant women. As part of our work, 12 women with chronic placental insufficiency were examined. The study was conducted in accordance with legislative norms. In each case, informed consent was obtained from the pregnant woman. During a consultation with a doctor for patients to perform standard (mandatory) tests, patients underwent a test to assess blood rheology (the amount of blood sampling did not increase for those included in the study compared to those not participating in the study). Rheology was assessed by evaluating the aggregation of red blood cells and the deformability of red blood cells. The

control group consisted of 15 women with a physiological course of pregnancy. Rheological parameters of blood. Evaluation of red blood cell aggregation was carried out using the "Georgian technology". Erythrocyte deformability was assessed using the Raid principle. The results of the study found that there was a violation of the processes of aggregation and deformability of red blood cells in patients with chronic placental insufficiency. It was revealed that rheology is impaired due to changes in the aggregation of red blood cells and changes in the deformability of red blood cells. Our research is ongoing. Our preliminary results showed that timely diagnosis of rheological parameters in pregnant women is necessary, which will lead to correction of blood rheology parameters. It is necessary to develop a scheme for the diagnosis and treatment of such pregnant women in order to improve the gas transport function of red blood cells in the area of the microcirculatory bed of the fetoplacental complex. This will have a positive effect on perinatal outcomes. *Acknowledgment: Medical Clinic Baiebi*

ANTIDEPRESSIVE EFFECTS OF ICV OREXIN-A IN ANIMAL MODELS OF MAJOR DEPRESSIVE DISORDER

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Orexin/Hypocretin-producing neurons are believed as involved in the strengthening of arousal and wakefulness state. Despite the multiplicity of systems involved in retention of wakefulness this condition becomes unstable if brain Orexinergic system is deficient. Suppression of wakefulness is considered as one of the main reasons for sleep disorders and depression. Data from preclinical and clinical studies allow us to assume that Orexins may be involved in pathophysiology of depression. It was shown by us that early

postnatal dysfunction of brain muscarinic cholinergic system (MChS) has lasting effects on general behavior and sleep-wakefulness cycle (SWC) in adult age rats and disturbances produced by this procedure are similar to sleep disorders in patients with major depressive disease. Present study was aimed to assess whether the increase in the CSF content of orexin-A can have an antidepressant effect on sleep disorders and behavioral disturbances in animal model of depression. Animal model of depression was developed by early postnatal dysfunctioning of MChS that was produced by subcutaneous injection of Scopolamine (30 mg/kg,) two times daily, in rat pups (n=10) from postnatal day 7 to 28. Control rat pups (n=5) received the same volume of saline from postnatal day 7 to 28. Experiments were started in adult age, 2-3 month after discontinuation of drugs receipt. Surgery with implantations of stainless-steel screws, for epidural EEG registration and microinjection cannulas (Plastics one) were made under general anesthesia. Two doses of Orexins (10µg/µl and/or 25µg/µl) were injected in lateral ventricle (ICV) by special cannulas and Hamilton Syringe. After post-surgery recovery EEG registration of SWC was started immediately after microinjection of Orexin-A lasted continuously during 5 h daily for three consecutive days. Statistical processing was made by ANOVA, $P < 0.05$ was considered as statistically significant. Direct ICV Microinjections of Orexin-A produces in animal models of depression: sharp increase of locomotor activity; significant diminution of searching or exploratory behavior; rise up in the rate of food intake and does not influence on the drinking motivation. Research has shown that animal models of depression are characterized by significant disturbances of sleep-wakefulness cycle in comparison with control animals. Namely the incidence and total time of active wakefulness are reduced, the incidence and total time of passive wakefulness and light slow wave sleep are increased, incidence of deep slow wave sleep episodes is also raised but its total time is reduced that indicates to the deterioration of sleep quality. The incidence and total time of

REM sleep are sharply increased. These changes are very similar with sleep disorders, characteristic of the major depressive disorder and so they can be an indicator of the validity for this type of animal model of depression. ICV microinjection of Orexin-A at the doses of 10 and 25µg/µl significantly ameliorates disturbances in sleep-wakefulness cycle ultradian structure. Under the action of orexin-A, in animal models of depression, subjected in early ontogenesis to the dysfunction of brain muscarinic cholinergic system, sleep onset latency, incidence and total time of active wakefulness became significantly increased, incidence of REM decreases and the latency of REM sleep becomes significantly longer. Elevation of the level of Orexin-A in CSF has an anti-depressive effect in animal models of depression. It is manifested in the enhancement and stabilization of wakefulness, which is suppressed during depressive-like state, in an increase in the latency of REM sleep, which is sharply reduced in these models and removal of REM sleep that develops very frequently during depression and requires to be deprived.
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THE EFFECT OF RIVAROXABAN ON BLOOD RHEOLOGY IN CASES OF RENAL IMPAIRMENT WITH AND WITHOUT ATRIAL FIBRILLATION

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Over the past 20 years, atrial fibrillation has become one of the most serious public health problems. Atrial fibrillation is often accompanied by pathological changes in the heart and concomitant diseases such as impaired renal function. There is a close relationship between kidney function and thromboembolic complications in patients with non-valvular atrial fibrillation.

Rivaroxaban is a widely used direct oral anticoagulant that is not a member of the vitamin K antagonist group. The drug is marketed under the trade name Xarelto™. Xarelto is registered and has a favorable profile for the prevention of venous and arterial thromboembolism. RELOADED studies have shown that one fourth of patients who received Xarelto had kidney disease. There is a very large number of studies that Xarelto is an effective and safe medicine. But our goal was to study in vitro the effect of Xarelto on the blood of patients with impaired renal function on the background of atrial fibrillation and without it. We investigated the effect of Xarelto in vitro. In 10 test tubes was the blood of patients with atrial fibrillation and in 10 test tubes was the blood of patients with impaired renal arrhythmia. We investigated the aggregation of red blood cells using the modern aggregometry method. We added Xarelto solution in equal proportions in all 20 cases. It turned out that Xarelto had a uniform in vitro effect on the blood of patients with atrial fibrillation with and without renal dysfunction. With this small experiment, it can be shown that Xarelto has a positive effect on blood rheology, regardless of whether atrial fibrillation is isolated or complicated.

EFFECT OF DOXORUBICIN TO RHEOLOGICAL ASPECTS

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Doxorubicin, known by brand name Adriamycin, is a chemotherapy medicine for cancer treatment. It is a 14-hydroxylated version of daunorubicin and is mostly used for breast cancer, bladder cancer, lymphoma and acute lymphocytic leukemia. Doxorubicin may give a reddish color to urine, tears, and sweat; because of that and red color of itself, doxorubicin earned the nickname “red devil”. Doxorubicin is in the antitumor antibiotic family of

medications, they are not really antibiotics but, they interact directly with DNA of the cancerous cells by intercalation. Doxorubicin forms a complex by DNA strands through G bases in both sides of the strands and it inhibits topoisomerase activity and the process of DNA synthesis in S PHASE of the cell cycle, it also elevates free radicals and it contributes to cytotoxicity. Doxorubicin may cause many side effects such as: hair loss, bone marrow suppression, vomiting, rash, and inflammation of the mouth, and allergic reactions might be present like anaphylaxis, heart damage, tissue damage at the site of injection, radiation recall, and treatment-related leukemia. Doxorubicin interact directly with DNA of the cancerous cells by intercalation and forms a complex by DNA strands through G bases in both sides of the strands and it inhibits topoisomerase activity and the process of DNA synthesis in S PHASE of the cell cycle, it also elevates free radicals and contributes to cytotoxicity. As indicated earlier, doxorubicin may cause many side effects in body such as: hair loss, bone marrow suppression, vomiting, rash, and inflammation of the mouth, and allergic reactions might be present like: anaphylaxis, heart damage, tissue damage at the site of injection, radiation recall, and treatment-related leukemia. Doxorubicin may give a reddish color to urine, tears, and sweat. This led us to a think and form our aim. Maybe the reddish color of the biological systems of the body depends on the violation of the rheological properties of the blood. One of the new properties that describe blood rheology is the aggregation of red blood cells. This is a very influential variable. Disruption of red blood cell aggregation can lead the body to heart attacks, strokes and other complex diseases. Our goal was to study Adriamycin on red blood cell aggregation in vitro. Despite the fact that the drug has long been used in practice, there are no large-scale studies of the direct effect of Adriamycin on the rheological properties of blood. We examined the effect of the drug on blood samples from healthy white rats weighing approximately 220 g to 240 g. Blood sampling was proceeded by

special surgery with sedation and anesthesia. For the entire study, permission was received from the Ethics Committee of the International Society of Rheology. Due to the fact that the name of the drug is mentioned in this scientific work, the issue was considered by the financial, marketing and legal departments of the International Society of Rheology. We received a conclusion from them, that our study is not pharmaceutical advertising. We took 1.5 ml blood from each rat and divided into three tubes. In all samples, erythrocyte aggregation was studied using a texture analysis method. A statistical analysis was done. Our study shows that doxorubicin can have significant impacts on rheological factor and increase the red blood cell aggregation. Subsequently, doxorubicin can increase the risk of medical difficulties caused by red blood cell aggregation. Doxorubicin is a chemotherapy medicine that frequently used for patients that suffer from breast cancer, bladder cancer, lymphoma and acute lymphocytic leukemia; and embrace a large population of patients. Doxorubicin may cause many side effects including rheological problems that can cause serious problems such as increment in red blood cell aggregation that can cause stroke. Doxorubicin, known by brand name Adriamycin, is a chemotherapy medicine and mostly used for breast cancer, bladder cancer, lymphoma and acute lymphocytic leukemia. It interacts directly with DNA of the cancerous cells by intercalation and inhibits topoisomerase activity and the process of DNA synthesis in S PHASE of the cell cycle, it also elevates free radicals and it contributes to cytotoxicity. Studies shows that doxorubicin may have serious side effect including our study which shows that doxorubicin increases red blood cell aggregation and blockage of vessels in body that may cause stroke.

THEORETICAL PREREQUISITES FOR MEASURING THE FUNCTIONAL STATE OF RESISTIVE ARTERIES

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Research of resistive vessels, assessment of their functional state is one of the key issues of multidisciplinary approach of biomedicine. Intravascular changes in pathological and physiological processes provide adequate blood supply. Compensatory mechanisms in pathological situations and the normal functioning of tissues and organs under physiological conditions depend on intravascular changes. Intravascular variability is important for regulating blood circulation. Resistive vessels, located at the anatomical boundary of macro- and microcirculation, like cranes, which regulate of blood flow and allow organs and tissues to consume the amount of oxygen that is currently needed by the situation, thereby ensuring the trophic property of the blood. The walls of the resistive arteries consist of three layers: hyperechoic outer and inner layers (adventitia and intima), which are separated by a hypoechoic medial layer. Normally, the thickness of the inter-medial layer in the distal sections of the resistive arteries does not exceed 1 mm, however, during pathological conditions and various diseases, the thickness of the inter-media layer changes irreversibly. Ultrasound test shows to identify pathological changes in the vascular reaction already in the early stages of the disease by determining the thickness of the vascular wall, its echo structure, echogenicity, and surface shape. In addition to changes in the thickness of this layer, the reactivity of resistive arteries is very important. It is the reaction of the walls of resistive

arteries on blood flow regulates blood circulation at the turn of macro- and microcirculation. This reaction causes compression pressure in the transverse direction with respect to blood flow, that regulates blood circulation at the turn of macro- and microcirculation. The functional state of resistive vessels is characterized by a reaction of vessels to reactive hyperemia. For this, we measured the coefficient of resistance of resistive vessels. The functional state of resistive arteries also depends on the Young's modulus, which displays the ability of the material to resist stretching, compression during elastic deformation. In the case of resistive arteries, Young's modulus characterizes the dilatational ability of resistive vessels and reflects changes in elastic properties that are directly proportional to the amount of collagen in the wall and inversely proportional to stiffness. Given that resistive arteries are the main regulators of blood circulation, it becomes clear how important their detailed description is from the point of view of diagnosis and prevention of diseases. In our project we examined some physical quantities that describe the functional state of resistive arteries. Our interest and purpose of the study was to develop a method for studying the functional state of resistive arteries by comprehensively measuring the thickness of the intima-medial layer, resistance of resistive arteries and Young's modulus in young people to determine normative clinical values in the control group. In carrying out research, it became necessary to expand the research protocol in order to deepen the study of the issue. According to the results of our study, such physical components as the thickness of the intimal medial layer, the coefficient of resistance of the resistive arteries and Young's module turned out to be interesting pathophysiological markers that can reflect the change in the vascular wall at earliest stages, when there are no yet other precursors of the disease. The study of the functional state of resistive arteries by determining the thickness of the intima-medial layer, the resistance coefficient of resistive arteries and Young's modulus, standardization of the data will

reveal early signs of changes in the vascular wall, causing its stiffness and contributing to a decrease in elasticity. Even small remodeling of the vascular wall can be detected with a full comprehensive assessment of the resistive arteries proposed by this study. Apparently, the list of tests described in the article can be used as early markers of changes in the state of arteries in all population categories. *Acknowledgment: European University GR/EU/001/01-08-2019.*

THE UNIVERSITY STUDY PROGRAMS INVOLVEMENT IN PHARMACOVIGILANCE IN GEORGIA

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Nowadays, when we are talking about global education and global health, Academia must be in the forefront for socio-economic, cultural and healthcare developing of the country. We have several biggest global challenges among them most important is improving of healthcare. For improving healthcare system in developing and developed countries we need professionals with deep theoretical knowledge, practical and clinical skills based on Ethic and Moral Principles and Codes. We have very big positive results of medication of many serious acute and chronic diseases, but also adverse drug reactions (ADRs) cause serious health problems. National Center for Health Statistics USA indicate that ADRs account for approximately 5% of all acute hospitalization. Among medical errors medication errors are the fifth cause of death of patients. According to bulletin of the WHO 2018 in high-income countries, clinical pharmacy services have been shown to improve quality use of medicines and reduce drug-related problems, hospital readmissions and health-care expenditures. Meaningful role of clinical pharmacy is to provide rational pharmacotherapy, which includes: effectiveness, safety, suitability

and cost of medication. That is reason why we have seen very deep link between Clinical Pharmacy and Pharmacovigilance. Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. In 2019 Uppsala Monitoring Centre united 136 full members and 29 associate members. In 2018 Georgia has become a member of Uppsala Monitoring Centre. It gives us more possibility to participate and be more active in this direction, to involve our healthcare professionals and patients as well. In Georgia Clinical Pharmacy, Pharmacovigilance and clinical Pharmacology education faces own/specific challenges. As representatives of Universities, we understand the importance of pharmacovigilance in the context of Pharmacotherapy. No standard exists for teaching PV at universities for medical, pharmacy, dentistry and nursing students, so a core curriculum needs to be developed to teach important aspects of PV to students. Clinical Pharmacology, Toxicology and Pharmacotherapy curricula should give a higher priority to the study of the safety of medicines. The results of the study “Barriers of development of Clinical Pharmacy among the healthcare professionals in Georgia” what was conducted at the University of Georgia through the Bachelor qualification thesis were identified lack of knowledge in Pharmacovigilance among of students, pharmacists and physicians as well. Medical and pharmacy students may recognize the importance of ADR reporting and express the intention to report ADRs, they are insufficiently prepared to handle ADRs. Information of safety of medication is scattered throughout the basic and clinical pharmacology, but is not complete and systematic. In 2016 Pharmacy Department of The UG created new Master program in Pharmacy and got National accreditation. This curriculum was first in Georgian academic area in which was included pharmacovigilance and pharmacoepidemiology as independent subjects. As professionals of medicine and pharmacy spheres we are aware of need for

pharmacovigilance in Georgia. At the SEU - Georgian National University, MD program includes Pharmacovigilance as an obligatory elective subject. PV education of students at university level will improve knowledge about safety of medicines and skills for a safer use of medicines at an early stage of their career. The proposed key aspects, formulated as learning outcomes of undergraduate PV education, are as follows: understanding the importance of PV in the context of pharmacotherapy; preventing ADRs, recognizing ADRs when they occur, managing ADRs, reporting ADRs. It is very important that competency-based educational models are becoming more dominant. In the context of pharmacotherapy competencies in pharmacovigilance are timely recognition, prevention and management of ADRs. We agree with description of WHO PV core Curriculum for University Teaching. We are Aware of the impact of ADRs on individual patients and at on population level and we understand importance teaching of medication safety issues. The moral responsibility for the Thalidomide tragedy still haunts us to this day. We need to teach future generations the important thing is "not to harm". Through study programs and activities, which include seminars, workshops and public lectures, helps to raise awareness about the importance of safe medication for students and healthcare specialists and patients as well in Georgia.

NEW RHEOLOGICAL APPROACH IN CRAZING

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Polymer crazing is a relatively new, efficient, and high-tech approach to creating nanocomposite polymer materials. Crazing helps incorporate targeted additives into polymer films and fibers. This provides the fiber or film with new useful properties: incombustibility, bactericidal activity, etc. Using crazing, we can continuously give polymer films and fibers a transverse relief, which is

fundamentally impossible to create with the traditional method of manufacturing synthetic fibers (using the traditional method, you can create only a longitudinal relief). Crazing technology is fully linked to rheology issues. Theoretical rheology helps for numbering this process. The making new and the newest profile need rheological algorithms. At the moment, we are forming surface micro- and nano reliefs in polymer films and fibers in a continuous mode to improve their optical characteristics with used rheological laws.

ISSUES OF THE APPEARANCE OF STRUCTURES CAUSED BY THE SHIFTS

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Question about polymer are very actuality during last 20-30yaers. In recent years, various tools have been developed to probe locally the flow properties and to provide a two-dimensional description of the flow. In this context, we will discuss the different time scales involved in the kinetics of formation of the shear banding flow following step shear rate and step shear stress. At long times, we will show that the coupling between the flow and the shear-induced structures leads to additional complexity in the flow dynamics due to the emergence of elastic instabilities on top of the shear banding flow. Such a phenomenology is not restricted to simple shear flow but can also be observed using other experimental protocols such as LAOS. Now, such as early the polymer liquids fluids been model systems for rheological research. Like most if not all soft matter systems, living polymers have mesoscopic structure that can be readily reorganized by a flow. This is base for rheological actuality. The structural reorganization of polymer feeds back on the flow itself. Such interplay between microscopic kinetics and macroscopic kinematics often leads to the emergence of shear-induced structures

associated with highly nonlinear rheological behaviors as well as new organization of the flow field. The shear banding phenomenon where the flow splits into domains bearing different shear rates is the prototypical example of such a flow/structure coupling. It has been observed in a wide range of complex systems but has been very specific in wormlike micelles.

TREATMENT AND PREVENTION OF POST-CHEMOTHERAPY THROAT DRYING IN ONCOLOGY PATIENTS WITH NATURAL DRUG ISLA MINT

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Isla Mint is a natural drug, which has been used to treat the inflammation and dryness of oral mucosa, is extracted from the plant Iceland moss. It contains substances that are characterized by its protective mucous membrane effects and its anti-irritant effect. The dose and therapeutic effectiveness has been analyzed in this clinical study. The goal of this study is to check the effectiveness in dryness of mouth caused by the chemotherapy in cancer patients, and determine its rate based on the subjective and objective data. A study of 60 patients (including 30 in the study group, 30 in the control group) has been conducted in the overall study duration of 6 months. These patients suffer from dryness of the oral cavity due to post chemotherapy treatment. The patients treated with drug Isla Mint with a dose of 1 tablet 6 times in a period of 24 hours with additional dietary recommendations. The subjective and objective were collected on a clinician derived scale which recorded the subjective discomfort sensation from 1 to 10. The treatment with Isla Mint has shown a significant reduction in the severity of dryness of mouth. The drug was found to have a significant effect on lowering the severity of xerostomia in the intervention group compared with the control group. Isla Mint a natural

drug presents a therapeutic opportunity for the treatment of xerostomia without drug interactions and adverse effects.

NITRIC OXIDE AS A HEMORHEOLOGICAL FACTOR

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Blood viscosity (BV) depends on plasma viscosity, hematocrit, erythrocyte aggregation, erythrocyte deformability (ED) and fibrinogen values. Erythrocyte deformability is a complex hemorheological parameter that depends on the surface-volume ratio, mean cell hemoglobin concentration, membrane lipid fluidity and cytoskeleton proteins phosphorylation degree. Red blood cell (RBCs) protein kinase is a second messenger that influences the protein tyrosine kinase (ptk) and protein tyrosine phosphates (PTP) enzymes activities. PTK and PTP are implicated in protein band 3 phosphorylation degrees and are both influenced by peroxynitrite levels. Nitric oxide (NO) produced by endothelial cells interacts with RBCs via protein band 3, being scavenged by either hemoglobin originating S-nitrosohemoglobin or nitrosylhemoglobin and by glutathione forming S-nitrosoglutathione (GSNO). Beyond the NO presentation inside the erythrocyte's derivative molecules such as nitrite, nitrate and peroxynitrites are also present. RBCs Membrane protein band 3 when phosphorylated favors NO efflux without ED changes. Binding of acetylcholine to RBCs membrane acetylcholinesterase originates a signal transduction mechanism involving protein Gi and protein band 3 that stimulates NO efflux and ED. RBCs receive NO from spermine- NONOate with their deformability improvement. Among the hemostatic and the inflammatory functions attributed to plasma fibrinogen it is also a hemorheological parameter that influences plasma viscosity, contributes for the ability of RBCs to aggregate with repercussion on BV. Fibrinogen decreases the RBCs NO

efflux and enhances the GSNO formation, preserving the erythrocyte NO scavenger property letting Ed unchanged. However RBCs in presence of high fibrinogen concentration and (i) when protein band 3 is dephosphorylated ED increases at low shear rate without NO efflux modifications (ii) when protein band 3 is phosphorylated the NO efflux increased and EEI maintained the normal level. Hypercholerolemia, hypertension and erectile dysfunction are vascular dysfunction pathologies with impaired ED and enhanced RBCs ability to liberate NO.

METHODS IN BLOOD RHEOLOGY - FROM THEORETICAL AND EXPERIMENTAL APPROACH TO CLINICAL APPLICATIONS

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The purpose of the work is to overview existing and introduce new methods and instruments for assessing mechanical properties of blood and red blood cells. A great variety of instruments and methods to study hemorheological parameters under conditions close to physiological are currently used: viscometers, different techniques for assessment of RBC deformability and aggregation. More of these methods allow determining the average characteristics measuring erythrocyte deformability and their ability to change their shape under force acting on the cell as a whole. A new method, based on dielectric properties of dispersed system in Couette viscometric blood flow, applied to investigate the kinetics of RBC aggregation and break-up of the aggregates has been introduced. The experimental relationships between the blood conductivity, apparent blood viscosity, shear rates and time at rectangular changes of shear rates from 94.5 s^{-1} to 0.945 s^{-1} at $T=37^\circ\text{C}$ show that the human blood conductivity is time and shear rate dependent under transient flow. It is established that the blood conductivity is dependent on the

regime and time of the applied shear rates in the Couette viscometric flow. The results show that valuable information could be received about the mechanical properties of blood, in particular about the kinetics of “rouleaux formation” and that the technique may be used to clarify the mechanism of dynamics of RBC aggregates. Thus, a method, based on the dielectric properties of dispersed systems in Couette viscometric blood flow could be applied to investigate the kinetics of RBC aggregation and the break-up of the aggregates. The best fit functions of blood conductivity during aggregation - disaggregation process is provided. Their parameters have been determined from the experimental data and can be used to characterize the transient organization of RBCs. Atomic force microscopy (AFM) permits to investigate living cells and cellular structures per high resolution visualization and to assess local mechanical properties index and surface topography of the membrane various cellular processes, such as elasticity and mobility of the surface layers, adhesion, molecular bonding and electrical charge can be studied more deeply through AFM measurements of the mechanical properties. AFM allows measuring the adhesion forces which take place during the interaction of the probe with the surface and gives an opportunity to determine the localization of receptors or other structures on the membrane surface in the case of the modified probe. These studies of structural and mechanical property of blood and blood cells which arise as a result of the initiation and development of certain diseases allow to improve their diagnostic and therapeutic approaches.

PROBLEM OF PHOTOGRAPHING

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The problem of photographing in biomedicine is very acute. A photograph of statistical preparations and a dynamic system is considered by telemedicists and is a direction of telemedicine. Photographing has gained particular importance now during the pandemic. This was due to the fact that it became necessary to photograph the tissues both for a diagnostic tool and for monitoring the onset of pneumonia against the background of CoViD19. In addition, infrared photography (wavelength 760-1000 nm) on special photographs is successfully used to study saphenous veins, pupil reaction in complete darkness, as well as to determine the structure of the eyesore and determine the condition of the sections of the anterior part of the eye located behind the clouded cornea. Photographing in infrared rays is based on the use of electron-optical converters that transform infrared radiation into a visible image. The goal of our study is to crop and frame photography. For this, we processed photographs of the lung on which the inflammatory process was clearly visible. We have processed more than 100 images of the right lung of sick men from different countries. The obtained storyboards made it possible to write special research protocols.

THE NEED FOR TIMELY DETECTION OF THE LATENT FORM OF ARTERIAL HYPERTENSION

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Hypertension is one of the most common cardiological diagnoses. Our goal was to study the structural and functional changes in the myocardium, interpreted as signs of hypertension of the heart, arterial hypertension. We conducted an instant cohort study. The examination accompanied the main clinical study of pentoxifylline. Women and men with normotonic and arterial hypertension (approximately 1: 1) mean age 54.2 ± 7.6 years, were examined. In addition to the standard examination and measurement of total blood pressure, daily monitoring and echocardiography were performed. The criteria for left ventricular hypertrophy were the left ventricular myocardial mass index $> 115 \text{ g/m}^2$ in men and $> 95 \text{ g/m}^2$ in women. Among people with normal total blood pressure, twisted arterial hypertension as a disease was detected in 50% of people; latent treatment failure of arterial hypertension in 24.8%. According to the results of echocardiography, signs of an increase in the thickness of the interventricular septum, posterior wall were recorded. There is a degree of severity of latent arterial hypertension and an undisclosed form. Due to the high prevalence of latent arterial hypertension established during periodic preventive medical examinations, especially in people with risk factors for arterial hypertension, it is necessary to use an echocardiographic study. This will increase case detection and the effectiveness of their treatment.

STUDY OF VESSELS, RHEOLOGY AND COAGULATION IN PATIENTS WITH COVID TOES

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Coronavirus infection is an acute viral disease with upper respiratory tract infection caused by a virus of the genus Beta coronavirus of the Coronaviridae family. Coronaviruses (Official names have been announced for the virus responsible for CoViD-19 (previously known as “2019 novel coronavirus”) and the disease it causes. The official names are: Disease coronavirus disease (CoViD-19); Virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) One of the widespread but poorly studied manifestations of CoVid-19 was “CoViD toes”. By manifestation, it is very similar to the feet of patients with Raynaud's phenomenon. This is an angiospastic manifestation. We know that with such disorders, three factors mainly play a role: vascular, coagulation and rheological. Our goal was to investigate how the characteristics of these factors change with CoViD toes and the Raynaud phenomenon. For this, we examined 12 patients with CoViD-19 and compared with the data of patients with Raynaud (without CoVid-19). It turned out that the trends in the recognition of the vascular wall and the rheological and coagulation properties are absolutely uniform. This is the beginning of a large collaboration intercontinental work. *Acknowledgment: Organizing Committee of World Pandemic Prevention Platform.*

HIGHLIGHTS OF FUTURE TREATMENT STRATEGIES OF THE CYSTIC FIBROSIS

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Cystic Fibrosis is a very complex genetic disease, which leads to buildup of thick, sticky mucus. It usually affects lungs, digestive system and in certain cases reproductive system of humans. As we already know it is hereditary disease, inherited in autosomal recessive pattern. Since the very first discovery of the underlying gene defect, our knowledge of how the genetic mutations in cystic fibrosis cause lung damage has substantially increased, but we obviously still lack certain information. Nevertheless, the information gained so far has led to new therapeutic approaches that address key factors of cystic fibrosis pathophysiology. Previous therapeutic successes were mostly based on targeting the consequences of the cystic fibrosis transmembrane regulator dysfunction, such as phlegm retention, infection, and inflammation, but new therapies may be able to address the underlying abnormality rather than its downstream effects. The efficacy of these treatments still needs to be established, but early studies look quite promising. This review summarizes our current understanding of the pathophysiology and treatment of cystic fibrosis lung disease and its future. Promising treatments are being developed that have the potential to treat the causes, rather than just the symptoms, of CF lung disease. There is continuing progress on treating the downstream aspects of CF, such as sputum retention, airway infection, and inflammation, but improving understanding of the underlying pathophysiology will serve as helper to target the early abnormalities in CF, and early results from studies of several compounds look promising. Treating the early and root causes of CF will improve outcomes and hopefully also reduce the considerable burdens of

treatment. It would be ideal to develop a “single hit” cure and thus obviate other treatments.

ASPECTS OF MODERN MANAGEMENT OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Heart failure with preserved ejection fraction (HF-PEF), previously known as diastolic heart failure, refers to the clinical syndrome of heart failure (HF) which is associated with normal or near-normal systolic function. Its prevalence has been increasing lately and is responsible for around half the cases of Heart Failure. Heart failure with preserved ejection fraction increases with age and especially affects those older than 70 years. A review of the ADHERE (Acute Decompensated Heart Failure National Registry) database demonstrated that, compared with patients who have HF with systolic dysfunction, patients with HF-PEF are usually older, more expected to be female, and more likely to have hypertension (HTN) likely to have had a myocardial infarction. Different other cardiovascular comorbidities also present in these patients, including obesity, coronary artery disease (CAD), diabetes mellitus, atrial fibrillation, chronic obstructive pulmonary disease, chronic kidney disease, and dyslipidemia. Despite the initial prognosis, according to which HF-PEF were previously assumed to have better prognosis than patients with depressed systolic function. Recent data suggest that mortality rates and rates of hospitalization are not significantly different between the 2 groups. Nevertheless, in contrast to the improvements in survival with systolic HF, mortality from HF-PEF has remained similar to initial number. This dissociation may in large part be due to the clinical and pathophysiologic heterogeneity of HF-PEF and the consequent varied cardiovascular and

noncardiovascular causes of death. The recognition of the magnitude of the problem of heart failure with preserved ejection fraction in the past two decades has spurred an explosion of clinical investigation and growing intensity of informative outcome trials. The given scientific review addresses the historic development of this type of the heart failure syndrome, reviews present treatment strategies and plans for the future.

SOME BIOMARKERS OF ARTERIAL THROMBOSIS

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Cardiovascular diseases are the leading cause of death in worldwide. The study of the cells and molecules involved in the pathogenesis of cardiovascular disease cause by arterial thrombosis is very important for early diagnosis and treatment of these diseases. Especially if they will be used as an early marker and it will be helpful in disease prevention. The aim of our research was to study level of homocysteine and antiphospholipid (anti-cardiolipins and anti- β 2GPI) antibodies in some cardiovascular diseases, such is myocardium infarction and stroke. For this purpose, we studied plasma samples of 59 patients and 53 healthy control group. According to our study results, we found that levels of homocysteine and antiphospholipid IgG were higher in the samples of diseased patient than in healthy people. Homocysteine level was especially higher in patients with arterial thrombosis. In addition, we found some correlations with gender, age and smoking. Based on the results of study, homocysteine may be used in combination with antiphospholipid IgG as a marker for early diagnosis of these diseases.

PREVALENCE OF RHESUS SYSTEM PHENOTYPES COMBINATION IN BLOOD DONORS

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Our goal was to study the Rh group system antigens in the donors. Due to the fact, that the only D antigen has been investigated in donor-recipient throughout the region (Adjara, Georgia Republic), it was interesting to see the frequency of other Rh antigens and estimate the theoretical risk of alloimmunization. The blood of 852 donors has been investigated on Rh group antigens. The research was carried out within 2016-2019 years. The sample has been provided from the diagnostic laboratory of Medina Ltd Health Centre of Batumi. Blood typing of the sample has been carried out on the basis of the immunogenetics laboratory of Batumi Shota Rustaveli State University. The following specific test-systems were used during the research: anti -AB, -B, -A, A1, -A2 (H), -C, -c, - D, -E, -e. For identification Rh group antigens ABO/D + Reverse Grouping cards were also used. The prevalence e antigen is 94,6%, c antigen - 85%, C-68,03%, E antigen - 38,07%. Majority (84%) of donors are Rh positive, 133 (16%) donors are Rh negative. C antigen most common is present in the combination with D antigen. 65, 8 % case donors had CD+ combination. E antigen in most cases is presented with a combination of D antigen. 36, 9% of the donors had ED+ combination. A miserable number of studied donors had CD - (2,23%;) and ED - (1,17%) combinations. We allocated 17 Rh phenotypes among studied donors. CdE phenotype was not present in donors. Other 17 phenotypes showed different frequency.

EPIDEMIOLOGY OF EPILEPSY IN ADJARA REGION

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Epilepsy is a chronic disease of the brain. Statistical data on the prevalence of epilepsy in the world is 1%. The main problem associated with epilepsy is also a treatment gap which is very important for planning healthcare delivery for people with epilepsy. The prevalence of active epilepsy in Georgia was estimated several times in the 1990s and results - 5.7 per 1000 and in 2012 8.8 per 1000. The same research identified that the treatment gap in East Georgia was 62 % (Under medical care are only 1/3; 15% never visited a doctor; 62% take inadequate anticonvulsants; 12.5% do not have epilepsy but take anticonvulsants). All the studies were conducted in the East part of Georgia. In the Adjara Region no single research was performed. More than 10 years ago the Institute of Neurology and Neuropsychology in Tbilisi implemented a program of the Georgian Ministry of Health, Labor and Social Affairs for identification and monitoring of epilepsy in the population of Georgia. From 2019 by the INN program started to act in Batumi too. Since last year from 24.04. 2019 to 1.02.2020 in Batumi more than 500 patients went through the screening program, 223 of them went through all steps of the examination, like screening, Neurological Examination, Electroencephalography, Neuropsychological examination, and consultation of Epileptologists. Some of the diagnosis and drugs were replaced.

STUDY OF PREVALENCE OF E. COLI IN SOME RIVERS OF ADJARA REGION

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Shiga toxin-producing *E. coli* (STEC) strains are foodborne pathogens that can cause high mortality in humans by the hemolytic uremic syndrome and thrombotic thrombocytopenic purpura. Ruminants' gastrointestinal tracts are the reservoir for it, that is why diseases primarily developed through the undercooked particular beef products. Although products can be easily contaminated at any point where pathogens are present in the production line, surface water, such as rivers or lakes, as a starting source of contamination in the pre-harvest environment, is responsible for the spread of the various food borne pathogens, including STEC, to produce through irrigation. Because of the global warming process environment changing may allow some bacteria to occupy new areal. According to the statistics of the local health care, office outbreak of gastrointestinal infection during the summer season might be caused by *E.coli* (STEC) but is it impossible to be sure without laboratory confirmation. The aim of our study was to investigate of Adjara region rivers for detecting STEC *E.coli*. A total of 10 samples were collected during the Summer-Autumn season from rivers and were sowed on MacConkey, CHROMagar. Tree *E.coli* isolates were selected from them for further characterization. Two O:H serotypes were identified, and none of them belonged to the O:157 serotype. For confirmation of STEC was used latex agglutination test. We are going to continue investigation in some other river and see too.

DATABASE OF ANTIMICROBIAL ACTIVITIES AND STRUCTURE OF PEPTIDES - DBAASP

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Nature was aiming to develop the innate immune defense relying on the antimicrobial peptides (AMPs). To reach the aim nature had to take into account the possibility of the development of resistance by the microbes. To avoid the problem, it was forming the defense system constituted by many different players with distinct modes of actions. It should be emphasized, that each player has to have such an original mode of action, that it's hard to microbe to develop resistance. AMPs, as players of innate immunity satisfy the last request, that is, have the ability to provide the hindrances to the development of resistance. This is a reason why at the raising of the problem of resistance, AMPs become an attractive subject of investigation. Publications concerning AMPs are permanently increased. Research interest and the promise of practical applications of AMPs resulted in the creation of several web-based AMP databases. Nowadays, there are more than 30 AMP databases. DBAASP (<https://dbaasp.org/>) is the manually curated database of AMPs created in the laboratory of Bioinformatics of the Ivane Beritashvili Center of Experimental Biomedicine. The database provides users with comprehensive information to develop effective tools for the AMP-prediction. Offered by the DBAASP prediction tools allow conducting the design of new antibiotics. The vast majority of existing antimicrobial peptide predictors are not strain-specific, i.e., they can predict whether a given peptide sequence is antimicrobial, but they are unable to predict whether the sequence can target a particular microbial species. The current version of DBAASP offers

possibilities to generate new amino acid sequences having potency against particular species.

FRAILITY IN OLDER COMMUNITY-DWELLING POPULATION OF ADJARA (GEORGIA)

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The aim of our research was to study frailty prevalence in the old persons living in Adjara region of Georgia. The target group randomly selected from community-dwelling individuals aged 60 years and older, In total 112 samples (69 female and 43 male). The target population was divided in two aging group: the first were 60-80 years old individuals and second up to 80. Frailty phenotypes were assessed within five criteria: weight loss, self-reported exhaustion, weakness, slowness and low physical activity. The existence of three and more criteria from these listed criteria were assessed as frail phenotype; the existence of one or two criteria - prefrail, and if a person did not have any criteria, was assessed as robust. In our research we used a survey, which was approved in the study of Portuguese centenarian population. The survey was adapted to the Georgian reality. Identification of phenotypes of frailty syndrome was conducted according to the following criteria and procedures: socio-demographic characteristics (age, sex, education, marital status and ADL); for determining the cognitive status we applied MMSE (Mini Mental State Examination). According to obtained results, in the first group frail phenotype comprised 21,8%; prefrail - 9% and robust - 69,2%; In the second group frail phenotype is 33,3%; prefrail is 31,6% and robust 35,1%. In total frailty was found out in 31 individuals (19female and 12male). Among the frailty phenotype the most spread was: low physical

activity, weakness and slowness. In the group of 80+, the frailty was frequent than in the first age group (60-80). There was no significant difference according to sex. As we see, in the population as much is the chronological age frail phenotype is more frequent. Several researches concluded that the frailty is a predictor for the onset of disability. Hence, the individuals over 80 years of the population are a particularly vulnerable group in this regard. Frailty is a dynamic process and timely identification of prefrailty phenotypes can be used for right health care policy.

CORONAVIRUS AS A RISK FACTOR FOR CARDIOLOGICAL PATIENTS

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2019 is a disease caused by a specific virus called SARS-CoV-2. World Health Organization (WHO) assigned it a new name COVID-19. The disease first appeared at the end of 2019 in the city of Wuhan in China. It quickly spread to a large number of countries, so WHO declared it a pandemic. Georgia has small number of patients with COVID-19, but this number is growing and is likely to increase further. Symptoms usually begin a few days after a person is infected with the virus and may include: High body temperature, Cough, Shortness of breath or shortness of breath, Muscle pain, Sensation of fatigue. Most people have a mild form, some have no symptoms at all. However, in others, infection can lead to serious complications, such as pneumonia, lack of oxygen, or even death. This is more common in older people and those who have other health problems, including heart disease,

lung disease, diabetes, and a weakened immune system. According to cardiologists and rheologists, people with coronary heart disease and heart failure have an increased risk of destabilizing these conditions against the background of acute respiratory viral infections (ARVI), and other concomitant diseases (diabetes, obesity, arterial hypertension, chronic obstructive pulmonary disease [COPD], kidney disease) further increase the risk. Acute viral infections can contribute to the development of arrhythmias, decompensation of heart failure, or even the occurrence of a heart attack in such patients. A study based on more than 100 cases of COVID-19 in Georgia. Our study showed that men and those with heart disease are at greater risk of contracting coronavirus. According to our analytical studies, the percentage ratio in our studies is equivalent to the WHO data. In our study 13.2% of infected patients were patients with cardiovascular nosology's and 8.4% were patients with hypertension. This is a very high percentage. From this it follows that people with heart disease should take measures to reduce the chances of becoming infected with coronavirus. The recommendations developed for the prevention of coronavirus infection (COVID-19) are important for everyone, but especially for people over the age of 65 and for those who have cardiac problems. *Acknowledgment: Organizing Committee of World Pandemic Prevention Platform.*

USING AFFINITY CHROMATOGRAPHY FOR ISOLATION OF PROTEASE FROM UREA EXTRACT OF VIBRIO CHOLERAE

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The well-known affinity sorbent Blue Sepharose CL-6B, which includes the dye Cibacron blue F3GA, covalently crosslinked with sepharose, is widely used for the purpose of isolating proteins and enzymes of microorganisms. We have previously shown that subcellular fractions of *Vibrio cholerae* obtained by extraction with urea solution contain a number of proteases with different molecular weights. The aim of this work was to isolate protease from the urea extract of *V. cholerae* El Tor M-878 by affinity chromatography on Blue Sepharose CL-6B. We used a specifically sterile preparation of urea extract (ue) *V. cholerae* M-878, obtained by treating live cells of *Vibrio cholerae* with 9 M urea solution. Ue, suspended in 0.05 M Tris-HCl buffer pH 8.3 and clarified by centrifugation, was applied cold to a column with Blue Sepharose CL-6B ("Pharmacia", Sweden), washed with a starting buffer from unbound material, and the material sorbed on the ligand was eluted with 0.05 M Tris-HCl buffer pH 8.3 with 40 mM NaCl. Next, the eluate was collected, dialyzed for a day against distilled water, concentrated on a rotary evaporator, and lyophilized. Electrophoresis of the resulting preparation was performed under denaturing conditions according to Laemmle with the staining of proteins on gels with silver nitric acid. Determination of the presence of protease activity in the resulting preparation was carried out in the reaction of radial enzyme diffusion in 1% agarose gel containing 0,1% gelatin as a substrate and daily incubation in a "wet" chamber at 37°C. Electrophoretic analysis of the resulting preparation using affinity chromatography showed the presence of one major

polypeptide with a relative molecular weight of 35 kDa. In the enzyme diffusion test, the presence of protease activity was determined, and a gelatin hydrolysis zone was formed around the well with the drug, the size of which was (5.0 ± 0.2) mm. The thermal stability of the protease was established, since the hydrolysis zone was halved at 56 °C for 7 minutes compared to the initial one, and it disappeared completely at 97 °C for 7 minutes. Judging by the inhibition of proteolytic activity by phenyl methionine sulfonyl fluoride (PMSF), the detected protease should be attributed to serine peptidases. Thus, the suitability of affinity chromatography on Blue Sepharose CL-6B for isolation of urea-extracted thermolabile serine protease of *Vibrio cholerae* with relative molecular masses of 35 kDa (according to SDS electrophoresis under denaturing conditions).

| | |
|------------------------|--------------|
| Abuladze Tamar | 72 |
| Advadze Maia | 24, 32 |
| Akhobadze Nino | 35 |
| Akhvlediani Leila | 99, 100, 102 |
| Aloeva Manana | 66 |
| Andronikashvili George | 35 |
| Antia Natia | 16 |
| Antonyan Marina | 23 |
| Antonova Nadia | 92 |
| Avdian Vadim | 66 |
| Arutinova Nana | 31 |
| Ayushi Verma | 8 |
| Babilodze Mariam | 78 |
| Bagashvili Tamila | 35 |
| Bakradze Tamar | 61 |
| Balabani Stavroula | 76 |
| Beriashvili Sesili | 70 |
| Bessmeltsev Stanislav | 37 |
| Bikashvili Tamar | 36 |
| Brun Jean-Frederic | 96 |
| Bukia Nato | 27,28,30 |
| Butskhrikidze Marina | 27,28,30 |
| Chebotkevich Vitali | 37 |
| Chikobava Mamuka | 63 |
| Chipurupalli Alikya | 11, 84 |
| Chkadua Gvantsa | 31 |
| Chkhartishvili Eka | 78 |

| | |
|----------------------|----------------|
| Chkheidze Tamta | 105 |
| Dalakishvili Mariam | 97 |
| Dalakishvili Tamar | 97, 98 |
| Darbaidze Mariam | 40 |
| Darbinyan Anna | 23 |
| Davlianidze Lena | 40 |
| Delibashvili David | 21 |
| Devdariani Marina | 40 |
| Didbaridze Tamar | 68 |
| Dolidze Ketevan | 99 |
| Dondoladze Khatuna | 59, 60 |
| Dusting Jonathan | 76 |
| Dzneladze Sofio | 31 |
| Esvanjia Nino | 54 |
| Gabashvili Nino | 2 |
| Gabaidze Shorena | 99 |
| Gabunia Luiza | 16, 18, 21, 72 |
| Gagua Giorgi | 33 |
| Galogre Ana | 61 |
| Gamkrelidze Natia | 16, 18 |
| Gegenava Lali | 6 |
| Gelazonia Lia | 36 |
| Ghambashidze Ketevan | 21 |
| Ghvinadze Nino | 6 |
| Gogeshvili Ketevan | 35 |
| Gogiberidze Sopio | 63 |
| Gogiberidze Mariam | 98 |
| Gognadze Tinatin | 90 |

| | |
|-------------------------|---------|
| Gogokhia Nina | 7 |
| Gogonaia Irina | 72 |
| Gotsadze Maia | 80 |
| Gotsiridze Irina | 25 |
| Grigolava Maia | 103 |
| Gugushvili Manana | 32 |
| Gurashvili Tea | 35 |
| Inasaridze Ketevan | 32 |
| Ioramashvili Irina | 39, 53 |
| Jabanashvili Sopiko | 97 |
| Japaridze Nadezhda | 7, 50 |
| Jashiashvili Soppio | 56 |
| Jikia Gogi | 59, 60 |
| Joju Natia | 28, 30 |
| Juke Nati | 88 |
| Kajaia Albina | 21 |
| Kalandadze Giorgi | 102 |
| Kaliviotis Efstathios | 76 |
| Kalmakhelidze Sophio | 6 |
| Kartvelishvili Ketevan | 73 |
| Kasradze Sofio | 101 |
| Khachidze Irma | 32 |
| Kharati Natia | 101 |
| Khelashvili Ana | 62 |
| Khetsuriani Shorena | 16, 18 |
| Khukhunaishvili Rusudan | 99, 104 |
| Kiriakidi Rima | 99 |
| Koiava Tea | 102 |

| | |
|---------------------|--|
| Kochiashvili Nino | 73 |
| Koridze Marina | 99, 104 |
| Kotaria Tamar | 96 |
| Kozlov Stanislav | 107 |
| Kuchava Giorgi | 17 |
| Kuleshova Alena | 37 |
| Kumar Nikhil | 91 |
| Labadze Ekaterine | 71 |
| Leladze Marine | 31 |
| Lerouge Sandra | 89 |
| Lomadze Elene | 46, 56 |
| Lomidze Nino | 50 |
| Lordkipanidze Tamar | 36 |
| Machavariani Lamara | 27, 28,30 |
| Maglakelidze Neli | 78 |
| Makashvili Malkhaz | 35 |
| Makharadze Kristine | 104 |
| Malidze David | 4 |
| Manivannan Hemanth | 84 |
| Mantskava Maia | 10, 17, 47, 62, 66, 71, 77, 80, 81, 84, 95, 96, 105 |
| Margishvili Davit | 98 |
| Markov Evgeni | 107 |
| Mchedlidze Olga | 78 |
| Mikaberidze Manana | 43 |
| Mirianashvili Iamze | 105 |
| Mironova Lilia | 107 |
| Modebadze Irakli | 42 |

| | |
|-----------------------|-----------------------------|
| Momtselidze Nana | 66, 71, 80, 84, 95, 96, 105 |
| Mosemghvdlshvili Nino | 63 |
| Mulkijanyan Karen | 57, 72 |
| Museliani Tea | 59, 60 |
| Museridze Diana | 6 |
| Nachkebia Nargiz | 78 |
| Nagervadze Marina | 99, 100, 104 |
| Nakashidze Irina | 99, 104 |
| Namchevadze Emma | 56 |
| Namoradze Manana | 21 |
| Narsia Nugzar | 71 |
| Nikolaev Valeri | 107 |
| Nikolaishvili Marine | 59, 60, 61, 63, 70 |
| Nikoleishvili Elza | 86 |
| Nozadze Eka | 31 |
| Okujava Michael | 35 |
| Omiadze Salome | 70 |
| Ormotsadze Giorgi | 46, 47, 56 |
| Parkosadze Khatuna | 20 |
| Parseghyan Lilya | 23 |
| Pilishvili Otar | 41 |
| Pirtskhalava Malaqia | 103 |
| Pirtskhelani Nino | 73 |
| Pitskhelauri Ana | 25 |
| Pkhaladze Maia | 21 |
| Pkhaladze Neli | 21 |
| Pochkhidze Nino | 7, 36, 50 |
| Porchkhidze Khatuna | 46 |

| | |
|--------------------------------|--------|
| Rabiee Amirreza | 81 |
| Ragini | 90 |
| Rampling Michael | 76 |
| Rahul | 90 |
| Rathore Rohit | 13,14 |
| Ratiani Levan | 47 |
| Rathiman Rahul Kannan | 84 |
| Rukhadze Londa | 18 |
| Ruymbeke Evelyne | 65 |
| Sabaru Venkata Naga Meghana | 84 |
| Sakhelashvili Irine | 24 |
| Sakvarelidze Natela | 61 |
| Saldanha Carlota | 91, 96 |
| Samkurashvili Liana | 72 |
| Sanikidze Tamar | 46, |
| Sashan Gursimran Kaur | 84 |
| Shahrul Khan | 8 |
| Shatirishvili Lela | 72 |
| Shekiladze Ekaterine | 46 |
| Shengelaya Asmat | 56 |
| Shengelia Lolita | 10 |
| Shervood Joseph | 76 |
| Shioshvili Lia | 31 |
| Sikharulidze Nino | 40 |
| Skoblo Michail | 51 |
| Songulia Akaki | 84, 94 |
| Songulia Barbare | 94 |

| | |
|----------------------------|------------|
| Stokes Jason | 49 |
| Sujashvili Rusudan | 39, 53 |
| Svanidze Militsa | 27, 28, 30 |
| Tamasidze Archil | 63 |
| Tamasidze Nino | 63 |
| Tavadze Viktoria | 102 |
| Tsakadze Leila | 31 |
| Tsalugelashvili Aleksandre | 71 |
| Tsiklauri Shorena | 90 |
| Tsintsadze Irina | 100 |
| Tskvitinidze Sophiko | 99, 104 |
| Urbanovich Lyudmila | 107 |
| Urdulashvili Tamar | 95 |
| Varazi Elena | 16, 18 |
| Vishnepolsky Boris | 103 |
| Voskanyan Armen | 23 |
| Zardoshtian Afshin | 81 |
| Zedginidze Alla | 56 |
| Zenaisvili Salome | 61 |
| Zeragia Nana | 77 |
| Zhvania Mzia | 7, 50 |
| Wautier Jean-luc | 75 |
| Wautier Marie-Paule | 75 |

CONTENTS

| | |
|--|----|
| Nino Gabashvili MODERN APPROACHES OF LANGUAGE AND SPEECH THERAPY IN GEORGIA | 2 |
| David Malidze SODIUM GLUCOSE COTRANSPORTER 2 INHIBITORS - LOOKING BACK TO THE FUTURE | 4 |
| Sophio Kalmakhelidze, Lali Gegenava, Nino Ghvinadze, Diana Museridze THE IMPACT OF DIFFERENT DOSES OF IONIZING RADIATION ON THE NUMBER OF GLIAL AND NERVE CELLS IN THE HIPPOCAMPUS OF MICE | 6 |
| Nina Gogokhia, Nino Pochkhidze, Nadezhda Japaridze, Mzia Zhvania HIGH INTENSITY CHRONIC WHITE NOISE INDUCES BEHAVIORAL CHANGES IN ULTRASTRUCTURAL ALTERATIONS IN MALE ADULT RATS | 7 |
| Verma Ayushi, Khan Shahrul IMPACT OF DEPRESSION ON STUDENT'S MENTAL HEALTH | 8 |
| Maia Mantskava, Lolita Shengelia NEW STEPS IN THE STUDY OF THE FUNCTIONAL STATE OF RESISTIVE ARTERIES THROUGH CHATBOTS | 10 |
| Alikya Chipurupalli PRIMER DESIGNING FOR IDENTIFICATION OF CUTIBACTERIUM ACNES IA1: MAIN CAUSATIVE AGENT OF ACNE VULGARIS | 11 |
| Rohit Rathore QUORUM SENSING AND BIOFILM FORMATION IN | 13 |

| | |
|--|----|
| ENTEROBACTERIACEAE | |
| Rohit Rathore BACTERIOPHAGE THERAPY AGAINST MULTIRESTANT ACINETOBACTER BAUMANNII INFECTIONS | 14 |
| Shorena Khetsuriani, Luiza Gabunia, Natia Gamkrelidze, Elena Varazi, Natia Antia A NOVEL CORONAVIRUS - NEW APPROACHES IN PATHOGENESIS AND EFFECTIVE ANTIVIRAL DRUGS | 16 |
| Giorgi Kuchava, Maia Mantskava BRAIN BLOOD FLOW CONTROL WITH ARTIFICIAL INTELLIGENCE | 17 |
| Luiza Gabunia, Shorena Khetsuriani, Natia Gamkrelidze, Elena Varazi, Londa Rukhadze POLYPRAGMACY AND DRUG INDUCED IATROGENECITY | 18 |
| Khatuna Parkosadze EFFECT OF PRACTICE ON VISUAL FUNCTION IN AGING | 20 |
| Albina Kajaia, Ketevan Ghambashidze, Luiza Gabunia, Maia Pkhaldze, David Delibashvili, Manana Namoradze, Neli Pkhaldze PALOSURAN AS THE POTENTIALLY EFFECTIVE ANTIHYPERTENSIVE REMEDY | 21 |
| Armen Voskanyan, Marina Antonyan, Anna Darbinyan, Lilya Parseghyan MACROVIPERA LEBETINA OBTUSA VENOM AS A TOOL FOR BBB INTEGRITY INVESTIGATION AND HEMORRAGE STROKE MODELLING | 23 |
| Irine Sakhelashvili, Maia Advadze SEEKING SUPPORT: FOREIGN MEDICAL STUDENTS „UNDER PRESSURE THAT BURNS A BUILDING DOWN!“ | 24 |

| | |
|---|-----------|
| <p>Irina Gotsiridze, Ana Pitskhelauri</p> <p>USING OSL DOSIMETRY FOR CATARACT PREVENTION IN BRACHYTHERAPY PATIENTS</p> | <p>25</p> |
| <p>Militsa Svanidze, Nato Bukia, Marina Butskhrikidze, Lamara Machavariani</p> <p>ELECTRIC-MAGNETIC STIMULATION ENHANCES COGNITIVE FUNCTION OF AUDIOGENIC KINDLING RATS</p> | <p>27</p> |
| <p>Marina Butskhrikidze, Nato Bukia, Natia Jojua, Lamara Machavariani, Militsa Svanidze</p> <p>PREMEDICATION WITH OXYTOCIN HELPS TO NORMALIZE BLOOD QUANTITATIVE INDICES IN DEPRESSED RATS WITH ELECTROMAGNETIC STIMULATION</p> | <p>28</p> |
| <p>Nato Bukia, Marina Butskhrikidze, Lamara Machavariani, Militsa Svanidze, Natia Jojua</p> <p>THE OXYTOCIN EFFECT ON THE PASSIVE AVOIDANCE TASK IN ELECTRIC-MAGNETIC STIMULATED DEPRESSED RATS</p> | <p>30</p> |
| <p>Gvantsa Chkadua, Eka Nozadze, Leila Tsakadze, Lia Shiohvili, Marine Leladze, Nana Arutinova, Sofio Dzneladze</p> <p>MOLECULAR MECHANISM OF NA,K⁺A-TPASE SENSITIVITY TO NEUROTRANSMITTER</p> | <p>31</p> |
| <p>Irma Khachidze, Manana Gugushvili, Ketevan Inasaridze, Maia Advadze</p> <p>EEG PATTERN IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDERS</p> | <p>32</p> |
| <p>Giorgi Gagua</p> <p>BACTERIAL INFECTION INDUCED SEPSIS, ITS MOLECULAR MECHANISMS AND WAYS TO SOLVE IT</p> | <p>33</p> |
| <p>Malkhaz Makashvili, George Andronikashvili, Tamila Bagashvili, Tea</p> | <p>35</p> |

| | |
|--|----|
| Gurashvili, Ketevan Gogeshvili, Nino Akhobadze, Michael Okujava CHANGE IN THE GROOMING MICROSTRUCTURE AS A MEASURE OF THE STRENGTH OF THE STRESSOR IN RATS | |
| Tamar Bikashvili, Tamar Lordkipanidze, Lia Gelazonia, Nino Pochkhidze HEAVY METALS AND NEUROTOXICITY: ARSENIC, MANGANEZE (EXPERIMENTAL RAT MODEL) | 36 |
| Vitaly Chebotkevich, Alena Kuleshova, Stanislav Bessmeltsev PREDICTORS OF LIFE-THREATENING CRITICAL INFECTIONS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES | 37 |
| Rusudan Sujashvili, Irina Ioramashvili UBIQUITIN GUIDES PROLIFERATIVE ACTIVITY OF LEUCOCYTES DOSE-DEPENDENTLY | 39 |
| Mariam Darbaidze, Marina Devdariani, Lena Davlianidze, Nino Sikharulidze BEHAVIORAL CHANGES INDUCED BY WHOLE BODY HYPERTHERMIA IN EXPERIMENTAL RATS | 40 |
| Otar Pilishvili THE IMPROVEMENT OF THE “MARGINAL LIVER” TRANSPLANT SUITABILITY BY PERFECTING THE METHOD OF PERFUSIONMETHOD OF PERFUSION CONDITIONING IN EXPERIMENT | 41 |
| Irakli Modebadze EXTRACORPOREAL MEMBRANE OXYGATION (ECMO) USE IN ACUTE RESPIRATORY DISTRESS SYNDROME | 42 |
| Manana Mikaberidze C HEPATITIS VIRUS ELIMINATION PROGRAM IN GEORGIA | 43 |

| | |
|---|----|
| (2010-2019) - POLICY ADVOCACY AND OPPORTUNITIES FOR EXTERNAL FACTORS TO INFLUENCE THE PUBLIC POLICY FORMATION AND IMPLEMENTATION | |
| Tamar Sanikidze, Giorgi Ormotsadze, Ekaterine Shekiladze, Khatuna Porchkhidze, Elene Lomadze THE REDOX-DEPENDENT MECHANISM FOR REGULATING THE FUNCTIONING OF A LIVING ORGANISM | 46 |
| Giorgi Ormotsadze, Maia Mantskava, Levan Ratiani ERYTHROCYTES DISTRIBUTION ACCORDING TO THEIR SPHERULATION DEGREE AND VOLUME AND ITS CLINICAL SIGNIFICANCE | 47 |
| Jason Stokes MODELING AND REAL FOOD SYSTEMS FOR THE STUDY OF COMPLEX INTERACTIONS OF SALIVA WITH SURFACES | 49 |
| Nino Lomidze, Nino Pochkhidze, Mzia Zhvania, Nadezhda Japaridze THE ULTRASTRUCTURE OF THE HIPPOCAMPUS AND MEDIAL PREFRONTAL CORTEX IN ADOLESCENT, ADULT AND SENESCENT | 50 |
| Michail Skoblo AMPULAR COLON CANCER AND ANTITROMBOLOTIC QUESTIONS | 51 |
| Irina Ioramashvili, Rusudan Sujashvili STATISTICAL ASSESSMENT OF CONCENTRATION CHANGES OF ALBUMIN AND EXTRACELLULAR UBIQUITIN LEVELS IN BLOOD SERUM OF ONCOLOGY PATIENTS | 53 |
| Nino Esvanjia QUANTITATIVE ANALYSIS OF PET ACQUISITION PERFORMED | 54 |

| | |
|---|----|
| BY VARYING THE ACQUISITION/RECONSTRUCTION SETTINGS: A CORRECTIVE POST-PROCESSING METHOD | |
| Alla Zedginidze, Asmat Shengelaya, Giorgi Ormotsadze, Emma Namchevadze, Sopio Jashiashvili, Elene Lomadze DEVELOP A GENETIC PREDICTION VECTORS FOR IDENTIFICATION INDIVIDUAL SENSITIVITY OF CHILDREN WITH ACUTE LEUKEMIA TO GENOTOXICITY OF THERAPY | 56 |
| Karen Mulkijanyan APPLICATION OF 3R PRINCIPLES IN BIOMEDICAL EXPERIMENTS | 57 |
| Marine Nikolaishvili, Tea Museliani, Gogi Jikia, Khatuna Dondoladze THE EFFECT OF RADON INHALATIONS OF AGGRESSIVE RATS | 59 |
| Tea Museliani, Gogi Jikia, Marine Nikolaishvili, Khatuna Dondoladze THE EFFECT OF ELECTROMAGNETIC FIELD ON PLACENTAL GROWTH HORMONE (GH2) IN PREGNANT RATS | 60 |
| Tamar Bakradze, Marine Nikolaishvili, Ana Galogre, Natela Sakvarelidze, Salome Zenaisvili THE STUDY OF THE DURATION OF EXPOSURE TO ELECTROMAGNETIC FIELDS OF FREQUENCY ON ADOLESCENTS REGARDING THE CHARACTERISTICS OF ORAL HYGIENE | 61 |
| Maia Mantskava, Ana Khelashvili CHATBOTHs IN MONITORING COMPLICATION OF DIABETES MELLITUS | 62 |
| NinoTamasidze, Marine Nikolaishvili, Nino Mosemghvdlishvili, Sopio Gogiberidze, Archil Tamasidze, Mamuka Chikobava | 63 |

| | |
|--|----|
| DYNAMICS OF DENTAL PLAQUE HYGIENIC INDEX MODIFIED BY TURESKY, ALPHA-DEFENSIN AND RHEOLOGICAL STATUS ESTIMATION IN PATIENTS UNDERGOING ORTHODONTIC TREATMENT | |
| Evelyne van Ruymbeke UNDERSTANDING AND TAILORING THE VISCOELASTIC RESPONSE OF POLYMER MELTS | 65 |
| Manana Aloeva, Vadim Avdian, Maia Mantskava, Nana Momtselidze ISHEMIC STROKE IN NEUROSYPHILIS POSITIVE PATIENT: CASE REPORT | 66 |
| Tamar Didbaridze GENETIC BASIS OF ANTIBIOTIC RESISTANCE IN CLINICAL ISOLATES OF ENTEROBACTERIACEAE | 68 |
| Marine Nikolaishvili, Salome Omiadze, Sesili Beriashvili A COMPREHENSIVE STUDY OF THE INFLUENCE OF THE THERAPEUTIC PROPERTIES OF TSKHALTUBO WATER ON PATIENTS WITH PARODONTITIS AND RESTORATION OF ORAL FLUID MINERALIZATION | 70 |
| Ekaterine Labadze, Aleksandre Tsalugelashvili, Maia Mantskava, Nana Momtselidze, Nugzar Narsia PARALLEL STUDY OF HEMORHEOLOGICAL, INFLAMMATION AND ANEMIA PARAMETERS BEFORE, DURING AND AFTER SURGERY IN PATIENTS WITH STOMACH CANCER | 71 |
| Liana Samkurashvili, Irina Gogonaia, Tamar Abuladze, Lela Shatirishvili, Luiza Gabunia, Karen Mulkijanian OLD GEORGIAN MEDICAL MANUSCRIPTS AND EXPERIMENTAL STUDY OF THE PRESERVED MEDICAL PRESCRIPTIONS | 72 |

| | |
|--|----|
| (THE STUDY OF THE EXAMPLE OF A BEETROOT-CONTAINING MEDICAL PRESCRIPTION IN THE CASE OF EXPERIMENTAL PEPTIC ULCER INDUCED BY ETHANOL AND NSAD) | |
| Nino Pirtskhelani, Nino Kochiashvili, Ketevan Kartvelishvili INHERITED THROMBOPHILIA AND PERSONALIZED MEDICINE | 73 |
| Jean-luc Wautier, Marie-Paule Wautier RBC ADHESION AND ENDOTHELIAL CELLS DURING DISEASES | 75 |
| Michael W. Rampling THE DEVELOPMENT LEADING TO THE CONCEPT OF THE CIRCULATION OF THE BLOOD | 76 |
| Efstathios Kaliviotis, Joseph Shervood, Jonathan Dusting, Stavroula Balabani UNDERSTANDING THE BEHAVIOUR OF BLOOD FLOW AT THE MICROSCALE IN THE PRESENCE OF AGGREGATIONS | 76 |
| Zeragia Nana, Maia Mantskava A STUDY OF BLOOD RHEOLOGY IN PREGNANT WOMEN WITH PLACENTAL CHRONIC INSUFFICIENCY | 77 |
| Neli Maglakelidze, Olga Mchedlidze, Eka Chkhartishvili, Mariam Babilodze, Nargiz Nachkebia ANTIDEPRESSIVE EFFECTS OF ICV OREXIN-A IN ANIMAL MODELS OF MAJOR DEPRESSIVE DISORDER | 78 |
| Maia Mantskava, Nana Momtselidze, Maia Gotsadze THE EFFECT OF RIVAROXABAN ON BLOOD RHEOLOGY IN CASES OF RENAL IMPAIRMENT WITH AND WITHOUT ATRIAL FIBRILLATION | 80 |
| Maia Mantskava, Afshin Zardoshtian, Amirreza Rabiee EFFECT OF DOXORUBICIN TO RHEOLOGICAL ASPECTS | 81 |
| Maia Mantskava, Alikya Chipurupalli, Venkata Naga Meghana | 84 |

| | |
|--|----|
| Sabaru, Gursimran Kaur Sashan, Hemanth Manivannan, Rahul Kannan Rathiman, Nana Momtselidze, Akaki Songulia THEORETICAL PREREQUISITES FOR MEASURING THE FUNCTIONAL STATE OF RESISTIVE ARTERIES | |
| Elza Nikoleishvili THE UNIVERSITY STUDY PROGRAMS INVOLVEMENT IN PHARMACOVIGILANCE IN GEORGIA | 86 |
| Nati Juke NEW RHEOLOGICAL APPROACH IN CRAZING | 88 |
| Sandra Lerouge ISSUES OF THE APPEARANCE OF STRUCTURES CAUSED BY THE SHIFTS | 89 |
| Tinatini Gognadze, Shorena Tsiklauri, Nikhil Kumar, Rahul, Ragini TREATMENT AND PREVENTION OF POST-CHEMOTHERAPY THROAT DRYING IN ONCOLOGY PATIENTS WITH NATURAL DRUG ISLA MINT | 90 |
| Carlota Saldanha NITRIC OXIDE AS A HEMORHEOLOGICAL FACTOR | 91 |
| Nadia Antovona METHODS IN BLOOD RHEOLOGY – FROM THEORETICAL AND EXPERIMENTAL APPROACH TO CLINICAL APPLICATIONS | 92 |
| Akaki Songulia, Barbare Songulia PROBLEM OF PHOTOGRAPHING | 94 |
| Maia Mantskava, Nana Momtselidze, Tamar Urdulashvili THE NEED FOR TIMELY DETECTION OF THE LATENT FORM OF ARTERIAL HYPERTENSION | 95 |
| Maia Mantskava, Nana Momtselidze, Carlota Saldanha, Jean-Frederic Brun, Tamar Kotaria | 96 |

| | |
|--|-----|
| STUDY OF VESSELS, RHEOLOGY AND COAGULATION IN PATIENTS WITH COVID TOES | |
| Mariam Dalakishvili, Sopiko Jabanashvili, Tamar Dalakishvili HIGHLIGHTS OF FUTURE TREATMENT STRATEGIES OF THE CYSTIC FIBROSIS | 97 |
| Tamar Dalakishvili, Mariam Gogiberidze, Davit Margishvili ASPECTS OF MODERN MANAGEMENT OF HEART FAILURE WITH PRESERVED EJECTION FRACTION | 98 |
| Leila Akhvlediani, Rima Kiriakidi, Marina Koridze, Marina Nagervadze, Rusudan Khukhunaishvili, Ketevan Dolidze, Sophiko Tskvitinidze, Irina Nakashidze, Shorena Gabaidze SOME BIOMARKERS OF ARTERIAL THROMBOSIS | 99 |
| Marina Nagervadze, Leila Akhvlediani, Irina Tsintsadze PREVALENCE OF RHESUS SYSTEM PHENOTYPES COMBINATION IN BLOOD DONORS | 100 |
| Natia Kharati, Sofio Kasradze EPIDEMIOLOGY OF EPILEPSY IN ADJARA REGION | 101 |
| Tea Koiava, Giorgi Kalandadze, Viktoria Tavadze, Leila Akhvlediani STUDY OF PREVALENCE OF E. COLI IN SOME RIVERS OF ADJARA REGION | 102 |
| Malaqia Pirtskhalava, Boris Vishnepolsky, Maia Grigolava DATABASE OF ANTIMICROBIAL ACTIVITIES AND STRUCTURE OF PEPTIDES - DBAASP | 103 |
| Kristine Makharadze, Sophiko Tskvitinidze, Marina Nagervadze, Irina Nakashidze, Marina Koridze, Rusudan Khukhunaishvili FRAILTY IN OLDER COMMUNITY-DWELLING POPULATION OF ADJARA (GEORGIA) | 104 |

| | |
|---|-----|
| Maia Mantskava, Tamta Chkheidze, Iamze Mirianashvili, Nana Momtselidze CORONAVIRUS INFECTION AS RISK FACTOR FOR CARDIOLOGICAL PATIENTS | 105 |
| Stanislav Kozlov, Valeri Nikolaev, Evgeni Markov, Lyudmila Urbanovich, Lilia Mironova USING AFFINITY CHROMATOGRAPHY FOR ISOLATION OF PROTEASE FROM UREA EXTRACT OF VIBRIO CHOLERAE | 107 |