Abstracts of Presentations

XIII GEORGIAN NATIONAL CONGRESS ON ALLERGY, ASTHMA & IMMUNOLOGY

IX EUROPEAN CONGRESS ON ASTHMA,COPD & RESPIRATORY ALLERGY

III INTERNATIONAL CONGRESS "CORONAVIRUS INFECTION (COVID-19): PREVENTION, DIAGNOSIS, TREATMENT AND REHABILITATION

HYBRID CONGRESS

Georgian Association of Allergology and Clinical Immunology (GAACI)
Shota Rustaveli National Science Foundation of Georgia (MG-ISE-23-369)
Tbilisi State Medical University
Washington University
Georgian National Academy of Sciences
World Immunopathology Organization (WIPO)
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Eurpean Respiratory Society (ERS)
National Institute of Allergology, Asthma and Clinical Immunology of the Georgian National Academy of Sciences

Tbilisi, Georgia, May 7–10, 2024

INVITED SPEAKERS

CURRENT APPROACH TO FOOD ALLERGY DIAGNOSIS AND TREATMENT

Mitchell Grayson, ACAAI Past-President, Nation wide Children Hospital,The Ohio State University, Columbus, USA

Food allergy is a major health problem especially in children. Previously skin testing and serum specific IgE testing was used to identify potential food allergies, and patients were instructed to avoid the food. More recent data suggests that most patients with food allergies will be able to tolerate some of the offending food, and that positive skin tests or serum specific IgE is not sufficient to truly prove the diagnosis of food allergy. This presentation will detail the current approach to food allergy diagnosis and treatment. In general, the diagnosis can be made from the history, with testing as a supportive measure. The gold standard of diagnosis is the use of a food challenge, which can also have significant impact on the quality of life of the patient, as many find that they can tolerate more of the offending food than they original thought. We will also discuss treatment options for food allergy, focusing on the use of food ladders and oral immunotherapy. The utility of anti-IgE as a therapeutic tool in introducing foods in food allergic individuals will also be discussed.

ARTIFICIAL INTELLIGENCE IN RESPIRATORY MEDICINE AND ALLERGY: THE FUTURE IS NOW

Kamal Maurice Hanna, MD, PhD, Dr.A.I. Professor Emeritus, Faculty of Medicine, Cairo University, Cairo, Egypt

Artificial intelligence (AI) applications encompass a wide range of software programs designed to perform specific tasks, from simple to complex, often requiring human-like cognitive abilities. These AI technologies primarily rely on machine learning and deep learning techniques. One common AI training model is the artificial neural network, inspired by the structure of the human brain. These networks consist of computational nodes (artificial neurons) used for data classification and analysis.
The development of AI involves interdisciplinary collaboration across fields such as computer science, data analytics, statistics, hardware and software engineering, linguistics, neuroscience, philosophy, and psychology. AI finds applications in diverse domains, including education, healthcare, finance, business, manufacturing, transportation, energy, agriculture, and robotics.

In the field of Medicine, AI plays an increasingly vital role. AI-powered tools are of great help in diagnosis, treatment development, and personalized patient care.
Within Pulmonary medicine, AI has been leveraged for nearly two decades. It assists in diagnosing respiratory conditions by analyzing clinical data, chest imaging, lung pathology, and pulmonary function test results. For instance, AI can predict respiratory diseases using audio recordings from electronic stethoscopes, enabling accurate and early diagnoses.
AI algorithms can also evaluate chest CT scans for lung cancer detection. These algorithms recognize patterns in temporal and spatial changes, as well as features related to nodular and non-nodular lesions. Consequently, they predict lung cancer risk and guide clinical decision-making.
In fibrotic lung disease, high-resolution CT evaluations conducted by deep learning algorithms have demonstrated several advantages. These include low cost, reproducibility, and instantaneous classification of fibrotic lung disease with human-level accuracy.

Research studies have increasingly explored the application of AI and machine learning in chronic airway diseases such as Asthma and COPD. AI offers several proposed benefits including accurate diagnosis, classifying Asthma endotypes for optimal use of biologics, prediction of future Asthma development, exacerbation prediction and assessment of clinician adherence to guidelines.

AI has also found applications in Atopic Dermatitis (AD). Deep learning algorithms analyze photographic images of skin lesions, accurately distinguishing AD from other common skin conditions. Additionally, AI assesses and scores AD severity rapidly and without interobserver variability. Furthermore, it predicts the response to Dupilumab treatment in severe AD cases.

Chronic Rhinosinusitis has been another area of interest for AI strategies. These include classification, image processing, predicting treatment outcomes, and optimizing surgical approaches. AI tools can even differentiate the eosinophilic endotype using clinical biomarkers. Moreover, AI contributes to assessing adverse reactions to drugs and vaccines, food allergies, anaphylaxis, urticaria, and eosinophilic gastrointestinal disorders. In summary, integrating AI into Pulmonology and Allergy care promises improved diagnostic accuracy, personalized therapeutic approaches, and a deeper understanding of disease processes.

BALNEOTHERAPY AND HYDROTHERAPY IN CHRONIC RESPIRATORY DISEASE

Nikolai Khaltaev, WHO Global NCD Platform, Geneva, Switzerland

Balneotherapy and hydrotherapy have a huge potential in the prevention and control of major Noncommunicable Diseases (NCD) and in particular Chronic Respiratory Diseases (CRD).

The use of natural mineral waters, gases and peloids in form of bathing, drinking, inhalation, etc. is now internationally called Balneotherapy. The use of water (regardless its chemical / physical characteristics and its geological origin) for therapy is referred to as Hydrotherapy. While the impact of medical hydrology/balneology on the prevention and management of allergic conditions and bronchial asthma exists, we stress the role of Balneotherapy/Hydrotherapy in the prevention and management of chronic obstructive pulmonary disease (COPD). High-intensity water-based physical training in patients with moderate-to-severe COPD three times per week (45 min per session) for 12 weeks, improved exercise performance and health-related quality of life, compared to a control group without intervention. High intensity physical training once per week for 6 months seemed to be sufficient to avoid respiratory function deterioration compared to baseline, and to reach a significant functional improvement of respiratory muscles performance.

101 patients with mild or moderate COPD registered at South London General Practice were invited to a swimming pool-based Pulmonary Rehabilitation (PR) programme. Two sessions per week over 6 weeks at 29°C pool temperature led to significant improvements in dyspnea score and walking distance. Swimming pool is a feasible and positive alternative venue for PR for COPD patients in Primary Health Care. Exercise in water is interesting from the view point of overcoming patients fears and their socialization, since depression is a major confounding COPD condition.
The heat associated with sauna baths may also have direct effects on the lung tissue by reducing pulmonary congestion and increasing tidal volume, vital capacity, ventilation, and forced expiratory volume in 1 second (FEV1) of the lungs.

On the other hand, repeated cold water stimulations in COPD patients after 10 weeks treatment with 3 cold effusions and 2 cold washings of the upper part of the body (self-treatment) reduced frequency of infections; increased peak expiratory flow, lymphocyte counts, and expression of gamma-interferon; modulated interleukin expression; and improved quality of life in COPD patients.
Inhalation therapy with sulphurus and salsojodic mineral waters improve symptoms as cough and sputum and functional indices as (FEV1) in COPD. SPA therapy of COPD is based on the inhalation of sulphureous and salsojodic mineral water.
Sulphureous mineral waters have vasodilating activity on bronchial mucosa, improving its trophic state, and increase the production of secretory IgA and muco-ciliary clearance; they have fluidificant activity on bronchial secretion. Clinical trials showed improvement of cough, sputum and functional indexes as FEV1 and exhaled carbon monoxide.
Along with high prevalence and mortality, CRD is a cause of increasing pharmaceutical and hospital costs.
In view of this Health Resort Medicine should not be ignored as a potential resource in the WHO NCD strategy for prevention and control of CRD.

CYCLOPHILIN, A NEW, RELEVANT PANALLERGEN FOR POLLEN ALLERGIC PATIENTS

Paolo Matricardi, Sharite Clinic, Berlin,Germany

Background: Cyclophilins are ubiquitous panallergens whose epidemiologic, diagnostic, and clinical relevance is largely unknown and whose sensitization is rarely examined in routine allergy practice.
Objective: We investigated the epidemiologic, diagnostic, and clinical relevance of cyclophilins in seasonal allergic rhinitis and its comorbidities.
Methods: We examined a random sample of 253 (25%) of 1263 Italian children with seasonal allergic rhinitis from the Panallergens in Pediatrics (PAN-PED) cohort with characterized disease phenotypes. Nested studies of sensitization prevalence, correlation, and allergen extract inhibition were performed in patients sensitized to birch pollen extract but lacking IgE to Bet v 1/2/4 (74/1263) or with highest serum level of IgE to Bet v 1 (26/1263); and in patients with sensitization to various extracts (ragweed, mugwort, pellitory, Plantago, and plane tree), but not to their respective major allergenic molecule, profilins, and polcalcins. IgE to cyclophilin was detected with recombinant Bet v 7, and extract inhibition tests were performed with the same rBet v 7.
Results: IgE to rBet v 7 was detected in 43 (17%) of 253 patients. It was associated with asthma ($P < .028$) and oral allergy syndrome ($P < .017$) in univariate but not multivariate analysis adjusted for IgE to profilins (Phl p 12), PR-10s (Bet v 1), and lipid transfer proteins (Pru p 3). IgE to rBet v 7 was also highly prevalent (47/74, 63%) among patients with unexplained sensitization to birch pollen extract. In patients with unexplained sensitization to ragweed, mugwort, pellitory, Plantago and plane tree pollen, the levels of IgE to those extracts correlated with the levels of IgE to rBet v 7, and they were also significantly inhibited by rBet v 7 (inhibition range 45%-74%). Conclusions: IgE sensitization to cyclophilin is frequent in pollen-allergic patients living in temperate areas and can produce ‘‘false’’ positive outcomes in skin prick and IgE tests to pollen extracts. Molecular diagnostic guidelines should include this panallergen family.

ASSESSMENT THE EFFECTIVENESS OF BIOLOGIC TREATMENT IN ASTHMA PATIENTS WITH DIFFERENT T2 TYPE BIOMARKERS

Todor A. Popov, MD, PhD, University Hospital Sv. Ivan Rilski, Sofia, Bulgaria

Evaluation and effective management of asthma, and of severe asthma in particular, remains as the ultimate goal of physicians dealing with this diseases. Over the last decades, there has been increasing understanding that severe asthma encompasses multiple different phenotypes, each with differing presentations, and endotypes with prevailing molecular mechanisms. Type-2 (T2-high or –low) severe asthma variants are now easily identified. Serum immunoglobulin E, fractional exhaled nitric oxide and blood eosinophil counts can be routinely applied in different clinical settings to identify these pheno- and endotypes, helping to predict responses to specific treatments, thus complying with the principles of precision medicine. Since the end of the last century, different biologic formulations have been designed and licensed that have improved the control of severe asthma and the quality of life of those suffering.

The effectiveness of the different biologic therapies, monoclonal antibodies targeting key molecules of the T2-high inflammatory pathway, have been subjected to classical double-blind randomized trials involving thousands of patients, leading to the licensing of well-established now products: omalizumab, mepolizumab, reslizumab, benralizumab, dupilumab, and the most recent arrival tezepelumab. Each of these has characteristics that give ground to suggest it as more suitable for one asthma phenotype / endotype or another. However, there are no classical prospective studies making direct head-to-head comparisons between the separate biologics. An alternative approach to comparatively study their effectiveness is to design real-life database studies. Most existing databases are confined to the countries where such registries exist. An International Severe Asthma Registry (ISAR) has been set up involving more than 17000 patients form 28 countries, detailing a plethora of variable. ISAR offers a rich source of real-life data for scientific research to understand and improve symptoms, treatments, and patient outcomes for severe asthma with 14 articles and 40 accepted abstract published so far.

TREATABLE TRAITS: AN EMERGING INTERDISCIPLINARY APPROACH IN ALLERGY AND ASTHMA

Todor A. Popov, MD, PhD, University Hospital Sv. Ivan Rilski, Sofia, Bulgaria

The concept “Treatable traits” has been proposed in 2019 as a new approach for the management of airway diseases with complex characteristics and comorbidities. The rationale behind it is to apply personalised medicine on the basis of the contemporary understanding of phenotypes and endotypes. The core of the Treatable Traits approach is the recognition that not all people are the same, and that asthma and COPD are expressed differently from individual to individual and treatment should be tailored individually to obtain optimal outcomes.

The Treatable Traits approach looks beyond problems associated with the lungs and includes the management of other common chronic illnesses and behavioral or risk factors. This allows for the application of the most appropriate treatments to the most appropriate people. It has been demonstrated that this leads to improvements in quality of life and disease control for people with asthma and COPD. The Treatable Traits approach looks beyond problems associated with the lungs and includes the management of other common chronic illnesses and also the modification of behavioral or risk factors.

Airway diseases are typically paired with comorbidities with similar endotypic layout: allergic asthma & rhinitis; local allergic rhinitis & non-allergic asthma; non-allergic rhinitis & eosinophilic syndrome; non-allergic eosinophilic asthma & chronic rhinosinusitis; chronic obstructive pulmonary disease & chronic rhinosinusitis. Common mechanisms interplay between the components of these paired conditions: treating them in parallel achieves best results for the individual patients.

As simple as this may sound, the Treatable Traits approach requires special organization of healthcare provision, multidisciplinary management and is associated with considerable resources. The future will tell if it will impose itself as a viable management option.

INTERACTION OF RESPIRATORY VIRUSES AND ASTHMA

Mitchell Grayson, ACAAI Past-President, Nation wide Children Hospital,The Ohio State University, Columbus, USA

Wheezing in childhood is common, being present in up to a third of children within the first few years of life. Nearly all of these wheezing episodes are associated with a respiratory viral infection. In fact, many of these children will go on to develop asthma. In children (and adults) with asthma, exacerbations are most often caused by respiratory viral infections. The interaction between respiratory viral infections and atopic disease is a complicated one, and this presentation will discuss these relationships. Single stranded RNA viruses, like respiratory syncytial virus, infection early in life has been associated with a significantly increased risk of recurrent wheeze and possibly even asthma – especially in those children who do not have pre-existing atopy at the time of the infection. Based on mouse and human data, it appears that IgE is important in both the antiviral immune response and atopic disease. The development of IgE against respiratory viruses may be important in driving wheezing and asthma, especially in those without pre-existing atopy, while having atopic disease may lessen morbidity and even mortality to respiratory viral infections. The presentation will conclude with a discussion of potential mechanisms that may underlie this bidirectional relationship between respiratory viral infections and atopy (including asthma).

NEW MECHANISTIC INSIGHTS INTO CNS IMMUNE PRIVILEGE

Jonathan Kipnis, Washington University in St Luis, USA

The traditional dogma posited a separation between the immune and nervous systems, an idea referred to as the central nervous system's immune privilege. Yet, contemporary research has brought to light ingenious adaptations occurring at the borders (meninges and perivascular spaces) of the central nervous system, positioning these as key locations for neuroimmune exchanges. Although both systems generally work in tandem to preserve homeostasis, under unusual conditions, they can form detrimental interactions that result in neurological or psychiatric illnesses. We will delve into recent insights that elucidate the crucial anatomical, cellular, and molecular mechanisms that facilitate neuroimmune interactions at the brain and spinal cord's borders, as well as the potential impact of these interactions on central nervous system diseases.

IMMUNOLOGY OF AGING

Maxim Artyomov, Washington University in St Luis, USA

Extensive, large-scale single-cell profiling of healthy human blood at different ages is one of the critical pending tasks required to establish a framework for the systematic understanding of human aging. Here, using single-cell RNA/T cell receptor (TCR)/BCR-seq with protein feature barcoding, we profiled 317 samples from 166 healthy individuals aged 25–85 years old. From this, we generated a dataset from ~2 million cells that described 55 subpopulations of blood immune cells. Twelve subpopulations changed with age, including the accumulation of GZMK+CD8+ T cells and HLA-DR+CD4+ T cells. In contrast to other T cell memory subsets, transcriptionally distinct NKG2C+GZMB−CD8+ T cells counterintuitively decreased with age. Furthermore, we found a concerted age-associated increase in type 2/interleukin (IL)4-expressing memory subpopulations across CD4+ and CD8+ T cell compartments (CCR4+CD8+ Tcm and Th2 CD4+ Tmem), suggesting a systematic functional shift in immune homeostasis with age. Our work provides novel insights into healthy human aging and a comprehensive annotated resource.

NEUROINFLAMMATION IN ISCHEMIC STROKE - PROS AND CONS!

Zaal Kokaia, Lund University, Sweden

Stroke is currently the third leading cause of disability-adjusted life-years and mortality worldwide, with a projected 23 million cases and 7.8 million deaths in 2030. As the risk of stroke increases sharply with age, incidence, and prevalence are expected to rise even further as a result of an aging population. This disease affects about 3.5 million people in the EU, with 700 000 new cases yearly. More than half of the patients suffer significant residual impairments, causing huge economic and societal burdens. Acute clinical intervention, typically surgical removal or dissolution of the clot by administration of tissue plasminogen activator (tPA), aims to restore blood flow in the affected brain areas. Unfortunately, these interventions are only possible within a very short time window after stroke onset, and as a result, 10% of all stroke patients are eligible for this treatment. The spontaneous functional outcomes appear to be consistent with a degree of rewiring of surviving neural networks and recruitment of intact synapses, which tends to occur mainly in the contralateral brain hemisphere but also ipsilateral to the lesion. Ischemic stroke leads to brain tissue lesions triggering inflammation, activation of resident immune cells, i.e., microglia, as well as infiltration of immune cells from the blood, including monocytes. Activated microglia and monocytes produce pro- and anti-inflammatory mediators. Thus, neuroinflammation serves as a double-edged sword in the context of ischemic stroke, exerting both detrimental and beneficial effects on stroke-induced damage as well as post-stroke regeneration and recovery. Understanding the mechanisms underlying neuroinflammation-mediated regeneration is crucial for developing targeted therapeutic strategies aimed at promoting functional recovery in stroke survivors.

AI-GUIDED HISTOPATHOLOGY PREDICTS BRAIN METASTASIS IN NON-SMALL CELL LUNG CANCER PATIENTS

Richard J. Cote, Washington University in St Luis, USA

Brain metastases can occur in nearly half of patients with early and locally advanced (stage I-III) non-small cell lung cancer (NSCLC). There are no reliable histopathologic or molecular means to identify those who are likely to develop brain metastases. We sought to determine if deep learning (DL) could be applied to routine hematoxylin and eosin (H&E) stained primary tumor tissue sections from Stage I-III NSCLC patients to predict the development of brain metastasis. Diagnostic slides

from 158 patients with Stage I to III NSCLC followed for at least 5 years for development of brain metastases (Met+, 65 patients) versus no progression (Met–, 93 patients) were subjected to whole slide imaging. Three separate iterations of DL were performed by first selecting 118 cases (45 Met+, 73 Met–) to train and validate the DL algorithm, while 40 separate cases (20 Met+, 20 Met–) were used as the test set. DL algorithm results were compared to a blinded review by four expert pathologists. The DL-based algorithm was able to distinguish eventual development of brain metastases with an accuracy of 87% ($p<0.0001$) compared to an average of 57.3% by the four pathologists. In patients with Stage I NSCLC, the earliest stage with the best chance of cure, the DL algorithm was particularly useful in predicting which patients did not develop any kind of metastasis; of 47 patients where the algorithm predicted no metastasis, 45 (95.7%) remained metastasis free after over 8 years of average follow-up. This result suggests that AI may be used to specify patients with early (Stage I) NSCLC who could avoid the expense and side effects of systemic therapy.
The DL algorithm appears to focus on the subtle and complex histological features, but these features driving the deep neural network (DNN) predictions are not well understood. For pathology, this lack of DNN "explainability" is problematic as it hinders the broader clinical interpretation of the pathological features that may provide physiological disease insights. Using our DL algorithm and NSCLC cohort, we examined the role of resolution and tissue scale in our DNN's predictive power. At the cellular scale, we found that the DNN's predictive power is progressively increased at higher resolution and is largely lost when the resolvable feature length is > 5 microns. Additionally, we found that the DNN uses more macro-scale features associated with tissue organization/architecture to make its predictions. Altogether, these results suggest that a combination of sub-cellular and macro-cellular features are important in DNN learning, suggesting that tumor architecture and microenvironment are crucial in this learning.
Because we separately interrogated 1000 separate areas (100 micron by 100 micron tiles) in each individual tumor, the DNN was able to show which of these tiles provided information that correlated with the correct prediction (Met+ vs. Met-), which tiles provided no information, and which tiles predicted the incorrect information relative to the actual outcome (e.g. predicted Met+ in a case that was correctly predicted as Met-). When assessing the general histologic features that DNN used in making its determination, a surprising result was observed. The tiles that were most accurately informative of predicting Met+ or Met- nearly always contained tumor and tumor microenvironment (e.g., desmoplastic stroma, lymphocytic infiltration). Review by expert pathologists revealed that these areas showed no discernable, separable characteristic; that is, they are histologically indistinguishable from each other by the human eye. On the other hand, those areas that were not informative, or that predicted an outcome the opposite from the actual outcome (e.g., areas that predicted for Met+ in a tumor that was correctly predicted as Met-) almost always showed no tumor or tumor microenvironment, rather these areas consisted of normal structures or reactive tissue. This suggests an extra layer of training that could be applied to DNN learning. In the future it will be interesting to dissect the molecular features that underlie the predictive power of DNN.

REGULATION AND DYSREGULATION OF IMMUNE RESPONSES BY HUMAN DENDRITIC CELL SUBSETS

Eynav Klechevsky, Washington University in St Luis, USA

Dendritic cells (DCs) are key antigen-presenting cells that control both immunity and tolerance. Understanding the principles by which DC control these responses have provided a rich basis for studying and improving clinical outcome in treating human diseases. Part of the complexity is due to the existence of distinct DC subsets, each bearing different microbial receptors, surface molecules and cytokine expression. The biological *raison d'être* for separate DC subsets has been the focus of

many studies, including our own. Our research focuses on skin-migrated DC2 lineage cells, specifically on two subtypes differentiated by CD5 expression. The $CD5^+$ DCs are highly efficient at priming cytotoxic $CD8^+$ T cells and induce inflammatory T helper cell responses compared to their $CD5^-$ counterparts. Their elevated levels in inflamed psoriatic skin plaques, where high effector T cell responses are seen, compared to distal cutaneous tissue, suggest they are critical players in the pathogenesis. On the other hand, $CD5^+$ DC numbers are reduced in malignant tissues and correlate with cancer patient survival. Consistent with this notion, we demonstrate, using human patient cells and mouse models, that CD5 functions to trigger an inflammatory pathway of DC maturation and effector T cell activation. Deletion of CD5 on DCs educes tumor rejection and immunotherapy response. During successful immunotherapy, CD5+ DCs increased, which was critical for their interaction with CD5hi T cells. Thus, understanding the function and development of CD5-expressing DCs in immune regulation provides insight into how ICB immunotherapies work and identifies CD5 on DCs as a potential therapeutic target.

PRE AND POSTNATAL IMMUNITY

Roxane Tussiwand, Washington University in Luis, USA

Immunity to pathogens is achieved through the complex interplay between innate and adaptive immune subsets. Each subset is characterized by selective functional properties that reflect and are defined by their transcriptional identity, which is achieved during lineage commitment and subset specification. Our work is focused on understanding how development of immune subsets occurs and how ontogeny translates into specific functions. Both branches of the immune system, innate and adaptive, are generated pre- and postnatally; with myeloid cells and in particular macrophages appearing already a few days after conception. After birth both lymphoid and myeloid cells are either maintained by self-renewal, or are newly generated throughout the life of an individuum. To understand how ontogeny translates into functional features, we recently developed a genetic mouse model that allows to segregate per and post-natal cells at any age, within any tissue and during any immune or non-immune perturbation. While several studies have shown how pre-natal myeloid cells are relevant for tissue homeostasis, the function of pre-natal lymphocytes remains to date unclear. Importantly, prenatal lymphocytes appear to be differently selected as compared to postnatal cells and show different functional properties. We hypothesize that pre-natal cells are likely devoted to preserve tissue homeostasis while postnatal cells to perform immune functions.

HEREDITARY ANGIOEDEMA WITH NORMAL C1 INHIBITOR

Allen P. Kaplan, M.D. The Medical University of South Carolina, USA

There are now 6 types of Hereditary Angioedema in which C1 inhibitor is normal. These include families in which there is a mutation in: 1) factor XII, 2) plasminogen, 3) kininogen, 4) angiopoietin 1, 5) myoferlin, and 6) heparin sulfate-3-0-sulfotransferase 6 (HSSOST). All are autosomal dominant in inheritance, thus only one mutated gene is necessary for the disorder to be expressed. The molecular mechanisms for the common factor XII mutation ($Arg/lys^{309}Thre$) and plasminogen mutation ($glu^{311}lys$) are known, and like C1 inhibitor deficiency result in over-production of bradykinin. The kininogen mutation, being the protein substrate for bradykinin formation may involve bradykinin formation as well. The mutations involving angiopoietin 1 and myoferlin act at the level of the endothelial cell. Both relate to the functioning of vascular endothelial growth factor 2 receptors which may modulate (augment) bradykinin functioning. The mechanism of action of HSSOST is complex, may involve binding of bradykinin-forming proteins to the cell surface, but its effect on the rate of bradykinin formation, is not yet known.

Details will be presented but briefly the factor XII mutation facilitates plasmin cleavage at the mutant site to create a small version of factor XII (δ factor XII) which is then very rapidly activated by kallikrein to initiate the bradykinin-forming cascade and overwhelms the inhibitory action of C1 inhibitor. The plasminogen mutation is such that upon conversion to mutant plasmin, both HK and LK are directly digested to produce bradykinin, thereby bypassing both factor XII and prekallikrein. This is the first known role for LK in bradykinin formation in HAE and it may be more important than HK because its concentration is 2-3 fold greater.

ACTIVATION OF THE BRADYKININ-FORMING CASCADE IN ALZHEIMER'S DISEASE

Allen P. Kaplan, M.D. The Medical University of South Carolina, USA

One major pathogenic factor associated with Alzheimer's Disease is the deposition of "plaque" throughout the brain, and particularly within the area of the hippocampus. It is thought that considerable damage to neurons and neural connections is not just due to space-occupying plaques but to its precursor, which consists of aggregates of the protein β amyloid (Aβ). We have shown that aggregation is dependent on zinc ion and that the rate and extent of aggregation is proportional to the ability of aggregates to activate the plasma bradykinin-forming cascade. β amyloid occurs in varying lengths e.g. 39 to 42 amino acids long, and the slightly larger forms aggregate more rapidly and appear to do more damage. Aggregated Aβ binds factor XII and initiates its autoactivation. Activated factor XII then converts prekallikrein to kallikrein which in turn digests high molecular weight kininogen (HK) to release bradykinin. Plasma of patients has been shown to recapitulate all of these steps previously demonstrated in vitro, including elevated levels of plasma kallikrein, cleaved HK, and bradykinin.

NEW EFFECTORS IN THE RESOLUTION OF INFLAMMATION AND TISSUE FIBROSIS

Amiram Ariel, University of Haifa, Department of Human Biology, Haifa, Israel

Active and temporally aligned termination of immune responses is cardinal for the prevention of chronic inflammation and autoimmunity. During the resolution of inflammation macrophages undergo phenotypic and functional conversions that are essential for the completion of inflammation resolution, and restoration of homeostasis. The engulfment of apoptotic leukocytes (efferocytosis) by macrophages during the resolution of inflammation is essential for tissue homeostasis and results in macrophage reprogramming/immune-silencing. Previously, a distinct subtype of $CD11b^{low}$ resolution-phase macrophages characterized by arrest of efferocytosis (satiation), and enhanced reprogramming into pro-resolving and anti-fibrotic phenotypes was identified. These satiated macrophages display increased production and secretion of the immunomodulatory cytokine IFNβ. Here, we show that satiated macrophages display increased activation of the STING pathway concomitantly with increased expression of IFNβ and ISG15. Consequently, we found IFNβ levels were reduced in peritoneal exudates from $STING^{-/-}$ mice, while activation of the STING-IFNβ pathway, macrophage efferocytosis, and reprogramming were all diminished in $STING^{-/-}$ resolution phase macrophages. Treatment with exogenous IFNβ rescued, at least in part, all the resolution deficiencies observed in $STING^{-/-}$ macrophages. Finally, we show that in vivo treatment with the murine STING agonist DMXAA enhanced macrophage efferocytosis and reprogramming and that a novel biased STING agonist, BiST 2.1, promotes the resolution of inflammation and of liver fibrosis. Thus, our findings indicate that STING is an essential mediator in driving IFNβ expression and

secretion by satiated macrophages and consequently in shaping macrophage function and phenotype changes during resolving inflammation.

ROLE OF EXPOSOME AND MICROBIOTA IN ASTHMA AND ALLERGIC DISEASES

Cevdet Özdemir, M.D.Professor of Pediatrics/Allergy National Allergy Societies Committee Chair of EAACI (European Academy of Allergy and Clinical Immunology). Assistant Editor, ALLERGY, the official journal of EAACI. Istanbul University, Institute of Child Health, Department of Pediatric Basic Sciences, Istanbul, Türkiye. Istanbul University, Istanbul Faculty of Medicine, Department of Pediatrics, Division of Pediatric Allergy and Immunology, Istanbul, Türkiye.

The increased prevalence in allergic diseases has been explained by several hypothesis and theories, including 'Hygiene hypothesis', 'Old-friends hypothesis', 'Microbiota and loss of biodiversity hypothesis' and most recently by the 'Epithelial barrier theory'.

Allergic disorders are multifactorial. For example, asthma is a complex, heterogenous disease with accompanying dysregulated immune response and hypersensitivity, with an ongoing chronic inflammation, which may take course with remittances and exacerbations and in long term may result with airway remodeling and fibrosis. Although several related genes were described, twin studies could not point out a specific gene that covers all allergic disorders. Today we know that atopy is important, however several other diverse factors are also enrolling in the development of allergic disorders. Indoor and outdoor environment, infectious triggers, medications, in addition to several treatments, dietary habits, pollutants, and microbiome are among these key players. This influence acts in a dynamic manner. For example, microbiota of a newborn changes with age, due to factors such as diet, antibiotic usage and environmental influences throughout adulthood. It has been proposed in the 'Biodiversity hypothesis' that contact with natural environments enriches the human microbiome, induces immune balance and prevents from allergy and inflammatory disorders.

Exposome is abiotic or biotic environmental, ecological or eco factors that are affecting living organisms. General and specific external and host-related internal exposomes play roles in shaping the course of existing diseases or may induce new developments. Pollution, chemicals, microplastics, and alterations in microbial compositions have detrimental effects on both health of living organisms and planetary health. The importance of exposome is more pronounced nowadays as we all notice the impact of global warming and climate change that we generally used to blame for all negativities.

Today in the concept of One Health, with human beings, we recognize that animals, plants and their shared environment are in close connection. Thus, to achieve the best health outcomes in a global level we need to apply multi-sectorial and interdisciplinary approach (20). In order to better understand and manage chronic diseases including allergic disorders, we need to evaluate and approach our patients as a whole, together with their surroundings.

A PLATFORM FOR PROBING CELL-ENTRY AND NEUTRALIZATION OF EMERGING ENVELOPED VIRUSES.

Sean P. J. Whelan Ph.D, Department of Molecular Microbiology, Washington University in St. Louis. St. Louis, MO. USA.

Vesicular stomatitis virus (VSV), a prototype of negative-strand RNA viruses, contains a single surface attachment and fusion glycoprotein (G) that mediates all of the steps of viral entry into cells. The virus is endemic in Central America, where it is transmitted by blackflies to livestock causing lesions in the mouth and on the coronary band of the hoof. VSV replicates in virtually all eukaryotic cells, yielding up to 10,000 infectious particles from a single cell in 8 hours. The ease of propagation of the virus in the laboratory has resulted in a deep mechanistic understanding of the structure of all components of the virus, and robust forward and reverse genetic systems for generation of viral mutants. We generated chimeric viruses that replace the single surface glycoprotein (G), with the attachment and fusion proteins of other enveloped viruses including those that are highly pathogenic for humans such as Ebola and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Those chimeric viruses serve as safe and effective mimics of the entry of the pathogenic virus, and in the case of VSV-Ebola provide the basis of a licensed vaccine in use in humans. We have used such chimeric viruses to understand how they enter into cells, and to understand mechanisms of inhibition of viral infection mediated by envelope protein targeted inhibitors. Using such chimeric viruses we have identified host cell requirements for infection mediated by the heterologous envelope protein including the identification of viral receptors, as well as pathways of entry and exit from cells.

We have also profiled the genetic barriers to resistance for multiple envelope protein targeted inhibitors including monoclonal antibodies that have been used clinically, multivalent minibinders and soluble receptor decoys. This versatile platform can be deployed to study the envelope proteins of virtually all enveloped viruses, providing a laboratory tool for safe and rapid studies of emerging enveloped viruses.

Oral and Poster Presentations

THE ROLE OF ANTI-CCP ANTIBODIES IN RHEUMATOID ARTHRITIS (RA) AND ANKYLOSING SPONDYLITIS (AS)

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Unveiling the exact causes of autoimmune diseases remains a challenge, but ongoing research ignites hope for future advancements.

It's important to note that Rheumatoid Arthritis (RA) and Ankylosing Spondylitis (AS), are a complex and multifactorial diseases. Triggers and experiences with these diseases can vary greatly from person to person. Certain factors may increase the risk of developing or worsening symptoms, but they are not deterministic. Both genetic, environmental, and lifestyle factors interact in complex ways to influence the development and progression of these diseases. More research is crucial to understand the intricate interplay between these factors.

The aim of our research was to study the level of anti-CCP antibodies in the blood serum of patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) by the ELISA method in the Adjara

region. A total of 140 patients were examined, of which 42 had a confirmed diagnosis of RA and 19% had elevated anti-CCP antibodies, and 41 had a suspected diagnosis and 24% had elevated anti-CCP antibodies.
Regarding AS, only 13 had a confirmed diagnosis, and an increase in anti-CCP antibodies was observed in 15%, while 22% of the 18 patients with a suspected diagnosis had high antibody levels.
As it known anti-CCP antibody are the diagnostic marker of RA. The precise reason for the occasional presence of anti-CCP in AS remains unclear. It might be associated with peripheral arthritis, meaning inflammation in joints outside the spine, which occurs in about 30% of AS patients. However, it's not a reliable predictor of this complication. It's possible that presence of anti-CCP in patients with AS reflects overlapping mechanisms between AS and RA, or simply individual variations in immune response.
Our findings highlight the surprising high level presence of anti-CCP antibodies in a significant proportion of both confirmed and suspected AS patients, suggesting these antibodies might play a more complex role in AS than previously understood.
This research was funded by the grant of Shota Rustaveli State University ("Study of factors influencing the development of some autoimmune diseases"), and conducted in the laboratories of both BSU and BAU.
Key words: Rheumatoid Arthritis (RA); Ankylosing Spondylitis (AS), anti-CCP antibodies

ABO SYSTEM ANTIGEN-ANTIBODIES IN NEWBORNS AND BLOOD DONORS ON THE EXAMPLE OF ADJARA REGION

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Introduction. Erythrocyte blood group antigens are on the surface of the red blood cell (RBC). ABO blood group is determined by presence or absence of A and B antigens on the surface of RBC and of anti-A and anti-B antibodies in the serum. Their erythrocyte natural antibodies are IgM type, and usually not present in newborns, but appear in the first year of life**.**
Research materials and methods. A total of 208 newborn biological materials (blood samples) were studied in the current study. The immunoserological standard blood typing procedures were used with monoclonal anti-A, anti-B, anti-AB, anti-A1, and anti-H antibodies. The mentioned method is based on specific antigen-antibodies agglutination reactions.
Result. In the majority case of the studied newborns, the natural origin anti-erythrocyte antibodies were not detected, in the same case of O(I) blood group individuals, it was partially synthesized. 41.92± 3.5% of our studied newborns were expressed natural anti-A and anti - B antibodies like as adults. Blood donor population the frequency of the A2 subgroup is much less; while in the studied newborn it is equal to 85.41±3.5%.
Conclusion. Our research shows that in the majority of cases of newborns, ABO antibodies are not expressed and also we found the predominance of the A2 and A2B phenotypes in the newborns. The postnatal period of development is required for the full expression of ABO system antigens.
Keywords: anti-erythrocyte antibodies; ABO antigens; A1 and A2 subgroup**.**

DEVELOPMENT OF CYTOKINE STORM DURING INFECTION WITH COVID-19

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Objective: To describe clinical features, diagnostic findings, treatments, and outcomes in patients with new-onset postural orthostatic tachycardia syndrome (POTS) and other autonomic disorders following SARS-CoV-2 infection (COVID-19).
Methods: We retrospectively reviewed medical records for patients who presented

with persistent neurologic and cardiovascular complaints between April and December 2020 following COVID-19 infection.
Results: Twenty patients (70% female) were included in this study.Fifteen had POTS, 3 had neurocardiogenic syncope, and 2 had orthostatic hypotension. Six patients had abnormalities on cardiac or pulmonary testing, and 4 had elevated autoimmune or inflammatory markers. All patients were treated with non-pharmacologic therapies, and most required pharmacologic therapies. Six to 8 months after COVID-19, 17 (85%) patients had residual autonomic symptoms, with 12 (60%) unable to return to work.
Conclusions: POTS can follow COVID-19 in previously healthy patients. Appropriate diagnostic investigations and therapies are necessary to identify and treat autonomic dysfunction after COVID-19.

INFECTIOUS DISEASES OF ANIMALS: A FUTURE TREND

Ana Kamkamidze, Georgian Agricultural University

The topic that I will be presenting is RNA vaccines for infectious diseases of animals: a future trend. In my presentation i will discuss the following topics: what are RNA vaccines, how they are developed and what types of RNA vaccines are available. Presentation also includes the topic of the advantages of RNA vaccines as well as the difference between DNA and RNA vaccines.
RNA vaccines differ from traditional vaccines, unlocking a new era of veterinary medicine. My topic includes how mRNA vaccine works and how it induces immune responses This approach can allow for faster, cheaper development of vaccines. I will speak about mRNA vaccine trials for diseases of importance in veterinary medicine, for example: rabies virus and influenza virus. All issues are accompanied by photos and diagrams which will make the information easy to grasp. There will be a discussion on why RNA vaccine production is so important for veterinary medicine.

HYALURONIC ACID – IRREPLACEABLE PRODUCT IN DERMATO-COSMETOLOGY

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Hyaluronic acid is a naturally occurring glycosaminoglycan that composes the extracellular matrix of connective tissue, synovial fluid, and other vital tissues. The popularity of hyaluronic acid specifically stems from its effectiveness, ease of administration, and safety profile (low potential for allergic reactions and requires no skin testing). Hyaluronic acid is widely used in Dermato-cosmetology because participates in the healing process, tissue renewal, skin hydration, and growth factor stimulation. Depending on the concentration, molecular weight, and stabilization of hyaluronic acid, it is used in mesotherapy cocktails, revitalization, and dermal fillers.

BOVINE MUCOSAL VACCINES: CHALLENGES AND PERSPECTIVES

Salome Badiashvili, Agricultural University of Georgia

Mucosal vaccines have been used in cattle for almost five decades, primarily via intranasal and oral delivery routes. There is an increasing interest in the use of mucosal vaccination in cattle for several reasons. In newborn calves, Intranasal mucosal vaccination provides a strategy to reduce vaccine interference by maternal antibodies and enhance disease protection as maternal antibodies diminish. Additionally, mucosal vaccines offer advantages in controlling both clinical disease and reducing transmission of mucosal pathogens. Mucosal vaccines may offer opportunities to activate both innate and adaptive mucosal effector cells and improve control of mucosal infections while preserving mucosal barrier integrity and vital mucosal functions.
Greater understanding of host-microbiome interactions may inform vaccine strategies to control

opportunistic pathogens residing within the commensal microbiome. Comprehension of the unique aspects of the bovine mucosal immune system are crucial in optimizing vaccination approaches. The potential for new vaccine delivery vehicles and vaccination strategies to improve mucosa vaccine efficacy are discussed, considering limitations and opportunities. Refinement of mucosal vaccination aims to address current infectious disease challenges in cattle, ultimately bolstering herd health and productivity.

FIRST APPROVED CRISPR/CAS9-BASED TREATMENT FOR SICKLE CELL DISEASE

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Background: Sickle Cell Disease is an inherited red blood cell disorder that causes anemia, severe pain and other complications. People with SCD have decreased quality of life. So it is crucial to create treatment for this disorder. Over decades scientists have tried to create a drug that can solve this problem and now by unifying old knowledge with modern technologies they created a revolutionary therapy for SCD treatment.
Objectives: Since the discovery of the CRISPR-Cas system in bacteria, it has become a major field of study. It is a very promising tool that gives us the opportunity to discover new therapeutics. After years of hard work, in December 2023 FDA approved the first drug.
Methods: Scientists used the CRISPR-Cas9 system to "knock out" a gene called BCL11A. This is a transcription factor that is located on the second chromosome and silences γ-globin gene after the birth of a person. When BCL11A is deactivated, the organism produces fetal hemoglobin instead of mutated sickle-shaped cells. HbF can take over the supply of oxygen to the body. The process consists of few steps: Firstly, the doctor collects patients' blood stem cells, then cells will undergo genetic editing in the laboratory. The next step is to remove existing blood stem cells from the bone marrow to make room for newly edited cells, for this patient goes under chemotherapy and finally receives an IV infusion of the drug.
Results: Firstly, 44 people were enrolled in the study, but only 31 remained long enough to collect data. 29 out of 31 did not have severe Vaso-occlusive crises. None of the patients needed hospitalisation. After the treatment patients can have low levels of platelets and white blood cells, which can cause bleeding and high risk of infections. Also, treatment can cause mucositis and febrile neutropenia.
Conclusions: Despite all side effects and high price, this revolutionary discovery can change peoples lives. Based on results, it can be said that after some time the CRISPR-Cas9 system will be used to treat many other diseases too.
Keywords: CRISPR/Cas9; Sickle Cell Disease; Genome Editing; Treatment.

IMMUNODEFICIENCY IN PATIENT WITH KEGG DISEASE (X-LINKED CREATINE DEFICIENCY SYNDROME) - A RARE CLINICAL CASE REPORT

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Background - The creatine deficiency disorders (CDDs), inborn errors of creatine metabolism and transport, comprise three disorders: the creatine biosynthesis disorders guanidinoacetate methyltransferase (GAMT) deficiency and L-arginine:glycine amidinotransferase (AGAT) deficiency; and creatine transporter (CRTR) deficiency.

Creatine transporter deficiency is an X-linked genetic disorder caused by a variant in the SLC6A8 gene located on the X chromosome (Xq28). This condition varies in severity with features often including intellectual disabilities, speech delay, autistic features, attention deficit hyperactivity, gastrointestinal issues and immunodeficiency.

Case report - On August 20,2021, a 5-month old male was admitted to Ingorokva High Medical Technology University Clinic with a significant birth history. The main complaints during this admission were T-36.8 C ; P-164; R-68; T/A - 80/49mm.Hg; SaO_2-89%. Tachypnoe , dyspnoea, desaturation, excessive bronchial mucus production - hard to evacuate. The patient has a history of recurrent hospital admissions for the same presenting complaint.

On physical examination the patient exhibited pallor of the skin and circumoral cyanosis. Capillary refill time-2. Turgor and elasticity were reduced.Auscultation revealed a systolic murmur at the heart's apex, although the heart's tones were unclear. shallow, rhythmic breathing accompanied by retraction and wheezing. Palpation reveals a smooth and painless abdomen. spleen and liver at normal size. normal diuresis combined with normal intestinal function. Patient was on an enteral tube feeding.

Based on this condition genetic disorder was suspected and performed testing for mucoviscidosis, which was negative. CT scan excluded congenital tracheal abnormalities.

Immunological indicators were studied and In blood serum was detected low range of immunoglobulins: IgM - 0,43g/l (0,55-2,2g/l); IgA - 0,36g/l (0,8-2,2g/l). It demonstrated a malfunction in humoral immunity, which led to the diagnosis of congenital primary immunodeficiency. After that, the patient was administered intravenous immunoglobulins.

Blood tests also showed low creatinine level (normal - 0.39mg/dl) , genetic testing for SLC6A8 gene (which is located on the X chromosome. This gene encodes the creatine transporter protein responsible for transporting creatine into cells, particularly in the brain and muscles) was performed. genetic analysis revealed KEGG Disease (X-linked Creatine deficiency syndrome). SLC6A8 gene inactivation impairs CD8+T cell survival, Slc6a8 or Ckb ablation compromises CD8+ T cell expansion in response to infection and Slc6a8 or Ckb deletion weakens TCR-mediated activation of mTORC1 signaling.

Conclusion - Our case particularly highlighted creatine transporter deficiency (CRTR) as an X-linked genetic disorder. CRTR deficiency affects the transport of creatine, leading to creatine deficiency. While it primarily impacts neurological functions, it's not linked to immunodeficiency. Due to absent of neurological symptoms and presence of immunodeficiency was revealed, which gave us suspicion that patient has SLC6A8 gene mutation.In the context of the patient's lack of neurological symptoms alongside the presence of immunodeficiency, the possibility that the patient had an SLC6A8 gene mutation was raised.

LIVER TRANSPLANTATION IMMUNOLOGY: IMMUNOSUPPRESSION AND REJECTION

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Liver transplantation (LT) represents a life-saving intervention for patients facing end-stage liver disease, where conventional medical therapies have proven ineffective. The primary goal of treatment is to optimize efficacy while minimizing adverse effects associated with immunosuppressive therapy, thereby aiming for enhanced graft longevity and patient survival. Immunosuppressive agents are typically initiated during the an hepatic phase of transplantation and continued long-term for maintenance therapy. The specific immunosuppressive regimen varies across transplant centers. During the early post-transplant period, particularly within the initial three months

when the risk of rejection is highest, maintaining optimal immunosuppression levels is crucial.
Acute liver allograft rejection represents a significant cause of graft dysfunction and can impact long-term graft survival. The administration of potent immunosuppressive agents for both induction and maintenance therapy has substantially decreased the incidence of acute rejection, characterized by liver allograft dysfunction accompanied by specific pathological changes in the graft. Acute rejection can be categorized as T cell-mediated rejection (TCMR) or antibody-mediated rejection. TCMR is more frequently observed, occurring in approximately 10 to 30 percent of liver transplantation recipients.
This presentation aims to assess the current scenario, examining rejection rates among patients and delving into the effective management strategies in place, providing valuable insights into our practice based on findings from a retrospective study conducted at Batumi Referral Hospital-Medcenter, Georgia, a liver transplant center operational since 2014, with over 94 procedures performed (with perioperative surveillance at 98% and five-year surveillance at 75%).

SCREENING OF DIAGNOSED AND UNDIAGNOSED PEDIATRIC ASTHMA IN BATUMI, GEORGIA

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Background and Objective. A population-based survey including 3239 urban children (age: 9.0±2.4 y.) in Batum, Georgia showed a low prevalence of asthma in children (1.8%). One potential explanation is underdiagnosis of asthma. To investigate this, we conducted a follow up to the survey with the objective of estimating the level of childhood asthma underdiagnosis and to describe factors related to it.
Methods. Subjects included 437 survey participants who had a history of asthma-like symptoms and no diagnosis of asthma. All children underwent clinical examination (spirometry, skin prick tests, FeNO measurement) to identify new cases of asthma. The distribution of host and environmental factors was compared between the group with newly identified asthma and a group of 59 children with previously known asthma (diagnosed asthma).
Results. Clinical investigation identified 107 cases of undiagnosed asthma. The corrected asthma prevalence estimate was 5.1% (95%CI: 4.4%-5.9%) suggesting that 65% of asthma cases were undiagnosed. Compared to children with diagnosed asthma, children with undiagnosed asthma were younger (8.2±1.6 vs 9.3±2.1; p=0.0005), had less frequent history of allergic disorders (38.3% vs 64.4%; p=0.001), and a lower prevalence of parental asthma (1.8% vs 8.4%; p=0.04). The groups did not differ in terms of environmental characteristics except for more exposure to passive smoking in the undiagnosed asthma group (p=0.01). Multivariate analysis confirmed results of simple analyses.
Conclusion. In Batumi, 65% of children with asthma remain undiagnosed. Older age of a child, coexisting allergic disorders, and parental asthma seem to facilitate diagnosis. Implementation of current diagnostic guidelines should improve diagnostic accuracy of pediatric asthma in Batumi

A 12-YEAR-OLD BOY WITH MACROCEPHALY AND PIGMENTED MACULES ON THE PENIS

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Pathogenic variants in *PTEN* are linked with a group of inherited disorders termed *PTEN* hamartoma tumor syndrome (PHTS). Conditions falling under PHTS, like Cowden syndrome and Bannayan-Riley-Ruvalcaba syndrome, can affect numerous body systems, including the skin. Individuals with PHTS have elevated risks of various cancers over their lifetimes, including melanoma, although skin manifestations are generally non-cancerous. Examples of mucocutaneous manifestations associated with PHTS include trichilemmomas, oral papillomas, penile freckling, acral keratoses, and arteriovenous malformations. Due to the wide array of possible clinical presentations and the varying degrees of symptom severity, many individuals with PHTS might remain undiagnosed for an extended period. We describe a case of a male child who received the PHTS diagnosis at the age of 12. His clinical features included macrocephaly, hypertrophy in the left arm, thyroid nodules, penile freckles, developmental delay, and an autism spectrum disorder. Whole exome sequencing revealed a *de novo* heterozygous variant in the *PTEN*. The case highlights the diverse and complex nature of PHTS, emphasizing the necessity for early diagnosis, multidisciplinary care, and surveillance protocols, offering the potential for improved prognostic outcomes and enhanced quality of life for affected individuals.

Keywords Macrocephaly, PTEN, *PHTS*, pigmented macules

CURRENT TREATMENT OF PEMPHIGUS VULGARIS

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Pemphigus vulgaris is a rare autoimmune disease characterized by the formation of blisters and erosions on the skin and mucous membranes. Historically, treatment of pemphigus vulgaris has been challenging, relying heavily on high-dose systemic corticosteroids and immunosuppressive agents, which can lead to significant side effects. In recent years, advances in understanding the pathogenesis of pemphigus vulgaris have led to the development of new, targeted therapies that aim to improve disease control while minimizing treatment-related toxicity.

We discuss the current standards of treatment for pemphigus vulgaris, focusing on the emerging therapeutic options that have shown promise in clinical trials and real-world practice. These new treatments include rituximab, an anti-CD20 monoclonal antibody that selectively targets B cells, as well as other biologic agents and novel small molecules that modulate key pathways involved in pemphigus vulgaris pathogenesis.

The efficacy and safety of these new treatment modalities are compared with traditional therapies, highlighting the potential benefits of personalized and targeted approaches to managing pemphigus vulgaris. Additionally, the importance of multidisciplinary care involving dermatologists, immunologists, and other specialists is underscored to optimize patient outcomes and quality of life.

Overall, new treatment options for pemphigus vulgaris offers new hope for patients with this challenging autoimmune condition, emphasizing the need for ongoing research and collaboration to further improve disease management.

IDIOPATHIC THROMBOCYTOPENIC PURPURA AND ROLE OF THROMBOPOIETIN-RECEPTOR AGONISTS IN THE PEDIATRIC PRACTICE OF HEMATOLOGISTS

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Background: Idiopathic thrombocytopenic purpura (ITP, also called immune thrombocytopenic purpura) is an acquired disorder in which there is immune-mediated destruction of platelets and possibly inhibition of platelet release from the megakaryocyte. Treatments of ITP continue to challenge medical doctors because of a lack of well-tolerated and effective drugs. Children who develop chronic ITP may benefit from splenectomy. Immunosuppressive therapy with glucocorticoid drugs and intravenous immunoglobulin is the classical initial treatment for ITP. A novel class of thrombopoietin agonists has recently been developed. Eltrombopag is an oral thrombopoietin-receptor agonist that stimulates thrombopoiesis, increasing platelet production. Eltrombopag produced a very outstanding response in adult and pediatric patients with severe chronic ITP.

Methods: From M. Iashvili Central Pediatric Clinic (Tbilisi, Georgia) with the hematology and oncology department, we analyze 5 patients, suitable according to the study criteria. The study aims to evaluate the clinical and laboratory manifestations. Additionally, we discuss the best way of treatment.

Results: We built charts showing that the median age of our five patients is 11 years. They all have chronic idiopathic thrombocytopenic purpura and platelet counts of less than 30,000 per microliter of blood. All patients have been hospitalized several times in Iashvili Central Pediatric Clinic and have received standard treatments. Two of them have had splenectomy. However, after reducing the dose or stopping the treatment, the relapse occurred soon. In three of them COVID-19, Helicobacter, and Staphylococcus exacerbated ITP. Along with other basic drugs, they were prescribed Eltrombopag 50 mg per day. In 4 patients, the number of platelets increased after taking the drug. Only one patient is resistant to this medication. It responds only to intravenous immunoglobulin. Side effects of Eltrombopag were not detected in the patients studied by us.

Conclusion: The results of our study show that Eltrombopag is well tolerated in raising platelet counts in patients. Additionally, Eltombopag is an effective treatment option for pediatric patients with chronic ITP and who have an increased risk of bleeding.

STEVENS-JOHNSONS SYNDROME: A CASE STUDY

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Background: Stevens-Johnson syndrome is an acute, rare, immune-complex-mediated disease involving the skin and the mucous membranes. It is considered a minor form of toxic epidermal necrolysis, with less than 10% of the body surface area evidencing detachment. Various etiologic factors such as infections and drugs have been implicated in the etiology. Physicians must therefore consider Stevens-Johnson syndrome as a potential complication of treatment, especially when the use of medication is questionable. Diagnosis relies mainly on clinical signs together with the histological analysis of a skin biopsy. The differential diagnosis includes drug hypersensitivity reactions, staphylococcal scalded skin syndrome, acute generalized exanthematous pustulosis, and autoimmune bullous dermatoses. Immunosuppressive medications have been used with some success in patients. Our case report underscores the imperative of teamwork, vigilance, and thorough patient examination to prevent any unfortunate oversights.

Case report:
A 6-month-old boy was hospitalized at M. Iashvili Central Pediatric Clinic in Tbilisi, Georgia. According to the parents, nasal obstruction, rhinorrhea, and restlessness started two days before hospitalization. The pediatrician assessed it as a respiratory infection and prescribed an antiviral spray and nasal drops. On examination in the hospital, there was a diffuse maculopapular rash on the neck and face, Swelling of the soft tissues of the face, large painful erosions, and blistering rash on the face, trunk, limbs, and mucosal surface. He also had Blepharoconjunctivitis. The patient was diagnosed with Stevens-Johnson syndrome. A council was held, where the patient's condition was assessed as critical, and the patient was managed with supportive care. The patient was prescribed dexamethasone, atarax, and sodium chloride. He was consulted by an ophthalmologist and was prescribed Tobrex and Ophtaquix. Despite the treatment, on the third day after hospitalization, the general condition of the patient worsened. Hyperemia and desquamation of the skin expanded and spread to the dorsal surface, the groin area became swollen and hyperemic. The patient had adynamia, vomiting, and widespread skin pain, which is why Infulgan was prescribed. Under active observation, the treatment continued unchanged, and from the seventh day, the patient's condition gradually improved. On the ninth day, the desquamation of the necrotic areas of the patient's skin was completed, and the picture of blepharoconjunctivitis was not expressed. Paraclinical studies showed positive dynamics. Due to the positive dynamics, the patient was discharged with the appropriate prescription on the tenth day.
Discussion: Our case shows that Stevens-Johnson syndrome is a rare disease, especially, at this age. It remains a significant challenge for pediatricians, as it requires accurate anamnesis collection, rapid and accurate differential diagnosis, adequate management, and active monitoring during treatment.

EPIDEMIOLOGY AND RISK FACTORS OF HOSPITAL-ACQUIRED PNEUMONIA IN TERTIARY PEDIATRIC HOSPITAL, TBILISI, GEORGIA

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Introduction - Hospital-acquired pneumonia (HAP) is one of the most common complications among hospitalized children. This study aimed to determine the epidemiology and risk factors of HAP in the tertiary pediatric hospital in Tbilisi, Georgia.

Methods - The study included pediatric patients admitted to the Iashvili Central Children's Hospital from March 2023 to January 2024. The following data were recorded: age, sex, hospital ward, and risk factors, including comorbid disease, Hb<10 g/dL, pH<7.35, invasive techniques, surgery, hospital admission in the previous month, and interval from admission to presentation of HAP.

Results - The study was performed on 36 patients with a median age of 36 months. Most of the patients (58%) were males. The most common causes of the admission were upper respiratory tract infection (9 patients, 25%), fever (7 patients, 19%), and bronchitis (5 patients, 14%). Seventeen patients (47%) had histories of hospitalizations within the last 30 days. Most cases (20 out of 36) were late-onset HAP. The median time of HAP onset was 8 days. The median length of the hospital stay was 17 days. Twenty-two out of 36 patients experienced a prolonged length of hospital stay of more than ten days. Most of the patients (24 patients, 67%) had comorbidities. The most frequent comorbidities were developmental delay (6 patients) and epilepsy (5 patients). Logistic regression showed a significant relationship between HAP and the presence of comorbidities, prior hospitalization, prolonged hospitalization, and anemia.

Conclusions - Early identification of risk factors may be useful in identifying patients at high risk of HAP development.

INFLAMMATORY INDICES ROLE IN PREDICTING THE SEVERITY OF COVID-19

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The severity of COVID-19 patients can be predicted by evaluating various clinical parameters, however, the identification of time-consuming and cost-effective biomarkers is still relevant. Inflammatory indices (neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), eosinophil and neutrophil ratio (ENR), Systemic inflammatory index (SII, platelet X neutrophil count/lymphocyte count), due to their reflection of the body's inflammatory response and potential prognostic value are among the potential indicator. Previous studies have provided conflicting findings about the validity of these coefficients, with some studies indicating a significant association and others indicating the opposite. Our study aims to gain a deeper understanding of the significance of inflammatory indices (NLR, PLR, ELR, SII) in the assessment of disease severity in patients with various severities of covid-19.

Methods: Our study included 100 COVID-19 patients who were divided according to clinical classification into: mild (n=60, CT score <8), moderate (n=19, CT score>8 and <12) and severe (n=21, CT score >12) categories. Inflammatory indices were calculated in all patients. Through statistical analysis, including logistic regression and ANOVA, the relationship between these hematological ratios and the clinical severity of COVID-19 was examined.

Results: Our analysis revealed statistically significant differences in the studied parameters in patients with severe and mild form ($p<0.05$). In severe patients, the SII index is especially elevated after hospitalization, while this index does not change in mild and/or moderate patients. Also, CRP and ferritin were statistically higher in patients with severe disease compared to patients with mild or moderate disease.

Conclusion: SII was found to be an important marker of severity progression in COVID-19 patients and could be used as an independent prognostic factor. At the same time, SII is low-cost and time-consuming blood test for COVID-19 patients. Additionally, this study contributes to a growing body of evidence that calls for a holistic approach to patient evaluation that includes clinical and laboratory parameters to accurately predict COVID-19 prognosis.

Keywords: COVID-19, SARS-CoV-2, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, disease severity, SII

THE ROLE OF VITAMIN A SUPPLEMENTATION ON WEIGHT IN OBESE CHILDREN AND ADOLESCENTS

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Introduction: The prevalence of overweight children and adolescents in Georgia has raised concerns regarding their health. Evidence shows that vitamin A has been found to reduce concentrations of adipocytokines, such as leptin and resistin and have great impact on obesity. This study aimed to investigate the association between vitamin A supplementation and weight loss in Georgian population.

Methods: We conducted a cross-sectional study involving 40 obese children and adolescents. It was a prospective research. BMI >90 percentile. Age range was 5-17. All participants received dietary guidance, and those with insulin resistance were treated with metformin. We used therapeutic dose of vitamin A. Additionally, 20 patients received daily vitamin A supplementation for three months.

Results: The results indicated a significant reduction in weight for all participants, with those who

received vitamin A supplementation experiencing nearly twofold greater weight loss compared to those who did not.

Conclusion: These findings suggest that vitamin A consumption may be an effective strategy for facilitating weight loss in overweight children and adolescents. This research contributes valuable insights that can inform future interventions and public health strategies in Georgia. The study was small, and the conclusions can't be very clear, but this small study shows that expanded research is required in this direction, as vitamin A supplementation can be promising when dealing with children and adolescents with obesity

Key words: Vitamin A, Obesity, Weight loss

AUTOIMMUNE SKIN DISEASES IN DOMESTIC ANIMALS

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Immune-mediated skin diseases driven by either autoantibodies or self-reactive T cells are commonly encountered by veterinarians. Origin of some of these diseases are identified while others have unknown pathogenesis. Major groups of immune-mediated skin diseases are Blistering Diseases, Melanocyte Diseases and Hair Follicle Diseases. They have commonalities and differences in clinical signs, pathological mechanism and tropism. Participants in immune-mediated skin diseases are autoantibodies such as IgG, IgA, together with complement and other inflammatory molecules as well as white blood cells: neutrophils, macrophages, mast cells, T and b cells, plasma cells, and NK killers. Their target is amongst 50 different skin proteins, such as Desmoglein, Desmcollin and others. Major symptoms include lesions of epidermal and dermal layers, blisters, vesicles, pustules, alopecia, pruritus. Treatment is combination of immunosuppressive therapy.

TOPICAL ANTIANDROGENETIC THERAPY IN THE MANAGEMENT OF ACNE

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Introduction: Prevalence of acne vulgaris is estimated to affect 9.4% of the global population making it the 8th most prevalent disease worldwide.

Treatment scheme based on the acne pathogenesis (Gollnick H. et al. JAAD.2003;49 (suppl 1) S1-37) is actual even for today. But not each pathway of acne development has an appropriate active ingredients for topical therapy, especially for regulations of sebaceous glands abnormalities.

The goal of our study was to analyze the results of "Multicenter, randomized, double-Blind, vehicle-controlled study to evaluate the safety and efficacy of clascoterone1 (CB-03-01) Cream, 1% applied twice daily for 12 weeks in subjects with facial acne vulgaris".

Materials and methods: There were involved 708 subjects (age 12 year and older) with mild to moderate acne (24 from our site); During 6 months 353 patients used clascoterone, 355 - only placebo. IGA (International of Global assessment), inflammatory lesion count (ILC), non-inflammatory lesion count (NILC) and total lesion count (TLC) were assessed in every scheduled visit.

Study results: 2 Point Reduction in IGA & IGA - score of 0 (clear) or 1 (almost clear) was significant and P = 0.0006. Absolute change from baseline in non-inflammatory lesion count (NILC) - P = 0.0009. Absolute change from baseline in inflammatory lesion count (ILC) - P = 0.0027. Treatment emergent adverse events were similar between clascoterone and vehicle and were mostly mild.

Discussion: Clascoterone cream 1% demonstrated statistically significant efficacy in primary endpoints with side effects similar to vehicle—IGA Success & Absolute Reduction.

Conclusion: Based on the clinical research clascoterone cream 1% is approved for use as a topical androgen receptor inhibitor indicated for the treatment of acne vulgaris in patients 12 years of age

and older. And for nowadays it's indicated as one of the alternative topical medication for mild acne.

IMPACT OF CLIMATE CHANGE ON HUMAN IMMUNE RESPONSE: A COMPREHENSIVE REVIEW

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Abstract: Climate change is not only jeopardizing the health of our planet but is also increasingly affecting our immune health. This comprehensive review investigates the potential impacts of climate change on human immunity, focusing on a broad range of climate-related exposures such as air pollution, heatwaves, wildfires, extreme weather events, and biodiversity loss. These exposures disrupt the functioning of the human immune system by affecting the physical integrity and functional efficacy of the epithelial barrier.

Additionally, they can hyperstimulate the innate immune system and influence adaptive immunity, leading to the development of noncommunicable diseases such as autoimmune conditions, allergies, respiratory illnesses, and metabolic disorders. The loss or failure of immune tolerance can instigate a wide spectrum of health issues.

There is an urgent need for additional research in climate change and immunology, spanning diverse environments and utilizing modern biologic and epidemiologic tools. Understanding the complex interactions between climate change and human immunology is crucial for developing effective strategies to enhance human immune resilience and mitigate adverse health impacts.

Keywords: Climate change, human immune response, environmental exposures, epithelial barrier, noncommunicable diseases, immune tolerance, interdisciplinary research.

MEASURING LDL-C LEVELS: COMPARING DIFFERENT METHODS

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Introduction

In modern medical practice, there are many routinely done tests. Based on these test results, patients are diagnosed and appropriate treatments are chosen. For the measurement of LDL-C levels, the most commonly used methods are- centrifugation (Direct Method) and Friedewald formula. The aim of the study is to determine the accuracy of the Friedewald equation compared to centrifugation.

Material and Methods

The study was retrospective. Data was taken from Medcapital Laboratory. The laboratory used centrifugation and directly measured LDL-C. We manually calculated LDL-C levels with the Friedewald equation. Those two results after-centrifugation and Friedewald equation-were compared. Patient data was taken from 2019-2021. Patients whose lipid profile lacked any component of lipid profile were excluded from the research.

Results

In total 500 patients were included. Their date of birth ranged from 1930 to 2008. Analyzing data showed that the Friedewald equation overestimates data compared to centrifugation. It displayed underestimation only in two cases.

Conclusions

Although there is controversy about LDL-C measuring techniques, it **is** acknowledged that the Friedewald formula cannot estimate LDL-C levels correctly when TG≥400 mg/dl and LDL-C levels are <70 mg/dl (10). In the data we reviewed only a minority of patients displayed these changes in lipid profile. We also compared the number of patients who had abnormal LDL-C levels. After centrifugation 160 patients had elevated LDL-C, but when reevaluating the same patients with Friedewald equation 238 showed elevated LDL-C. In these 78 patients, LDL-C levels

were overestimated, which could be a reason for unnecessary pharmacological intervention and other medical complications (11)
Limitations
1. No background and follow up information about patients
2. No information how standartized the laboratory work was
Keywords: Lipid spectrum; LDL-C; Friedewald equation; Centrifugation; Laboratory tests

ONYCHOPAPILLOMA – CLINICAL CASE

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Onychopapilloma is a rare, benign nail tumor of unknown etiology. It mainly occurs in middle and advanced aged population of all races. For the first time, based on several clinical cases, in 2001, the term "Onychopapilloma" was presented by scientists Baran and Perrin. Onychopapilloma is mainly manifested in the form of Erythronychia, leukonychia and Melanonychia, and in the distal part of the nail there is Onycholysis and subungual warty growth - subcutaneous keratosis. The diagnosis is based on the micromorphological study of the biopsy material, and after formulating diagnosis surgical treatment is recommended.
The clinical case is about a 37-year-old female patient, who came to the clinic because of these following complaints: 3-year history, pain of the nail area of the right thumb, a linear brown spot and a warty growth of the nail area. The patient was not consulted by a dermatologist, and neither systemic nor local treatment was performed. As a result of clinical examination: there was a linear hyperpigmented spot in the central part of the nail area of the first finger of the right hand, on the distal part, a whitish-colored hyperkeratosis with a warty surface was expressed in the area under the nail. According to digital dermoscopy and clinical-laboratory studies, the clinical decision was – Onychopapilloma, and a treatment recommendation was surgery. The performed surgical method included excision of the formation by the curettage method, based on the conclusion of the subsequent pathomorphological study of the material, the diagnosis of Onychopapilloma was confirmed. The patient's condition is stable and there is no relapse.

IMMUNOLOGICAL BIOMARKERS IN OPHTHALMOLOGY - RECENT ADVANCES AND THEIR APPLICATION IN DISEASE DIAGNOSIS, PROGNOSIS AND PERSONALIZED TREATMENT

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Recently, immunological biomarkers have been particularly effective and useful in elucidating the pathogenesis of ophthalmic diseases, assessing progression and appropriate management. Recent advances in immunological research have revealed the utility of such biomarkers as cytokines, chemokines, and autoantibodies.
For example, cytokine profiling in aqueous humor and tear samples has made it possible to differentiate between infectious and non-infectious uveitis, thus facilitating the choice between antimicrobial treatment and immunosuppressive therapy. Antibodies to retinal antigens are useful as diagnostic markers of autoimmune retinopathy, which is very useful for timely identification and classification of the disease. New diagnostic tools such as high-throughput multiplex assays and point-of-care testing especially contribute to fast and accurate diagnosis by means of immunomarkers.
Regarding prognostic value, for example, elevated levels of inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) are associated with poorer outcomes and increased risk of relapse in diseases including diabetic retinopathy and age-

related macular degeneration. Chemokine gradient in neovascular age-related macular degeneration correlates with disease severity and response to anti-VEGF therapy.
Obviously, immune biomarkers alone are insufficient to draw conclusions, but integrating data with clinical parameters and other laboratory-instrumental research results is useful.
Current research is focused on exploring the importance of new biomarkers, including micro-RNAs, extracellular vesicles, and immune cells, which will greatly refine the understanding of disease phenotypes and thus contribute to better diagnosis, treatment, and prognosis.
Thus, the development of a precision medicine approach, such as the management of ophthalmic diseases using immunological markers, offers unprecedented opportunities and has great potential to revolutionize clinical practice.

EXPERIMENTAL AUTOIMMUNE DISEASE MODELS

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Autoimmune diseases in veterinary medicine pose significant challenges for diagnosis and treatment. This abstract provides an overview of experimental models used in veterinary research to understand autoimmune diseases, their mechanisms, and potential therapeutic interventions.
These models, adapted for veterinary medicine, replicate autoimmune conditions seen in animals, such as autoimmune hemolytic anemia (AIHA) or immune-mediated polyarthritis (IMPA). They involve inducing immune responses against self-antigens or tissues, often through immunization or genetic manipulation.
Studying these models has shed light on the underlying mechanisms of autoimmune diseases in animals, including the roles of autoantibodies, immune cell dysregulation, and tissue inflammation. Additionally, they have served as platforms for testing novel treatments, such as immunosuppressive drugs or biologics, tailored for veterinary patients.
Advancements in experimental techniques, including the use of genetically modified animals and advanced imaging technologies, have improved the accuracy and relevance of these models in veterinary research. By leveraging these models, veterinarians aim to develop better diagnostic tools and more effective treatments for autoimmune diseases in companion animals, ultimately improving their quality of life.

ELIMINATION OF DEPENDENCE ON THE NASAL VASOCONSTRICTION AGENTS

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Introduction, significance of the issue: Rhinosinusitis is a global problem, its prevalence is quite high, occurring in 28% of the population. Therefore, consumption of the nasal vasoconstriction medicines is high as well, every third individual all over the world (68%) consumes the nasal vasoconstriction agents and hence, it is the most sold medicine. Its wide consumption is caused by both, local nasal pathologies and various general diseases, including consumption of certain medicines and global air pollution. It is widely known that the patient can consume nasal vasoconstriction medicines for 7 days but no more than 10 days and people do not comply with this requirement. Hence, dependence on the nasal vasoconstriction sprays is quite high. The mentioned medicines have both, local and general side effects. Thus, the issue of their reasonable consumption is of significance.
Research design: open controlled research data processing was provided by SPS V/12 method.
Goal of the work: elimination of dependence on nasal vasoconstriction medicines by means of the nasal steroids. Two groups were compared, for the main group was used two-

component combined medicine Fluticasone propionate and Azelastine nasal spray, for the control group there was used single-component nasal steroid Fluricasole furoate. Effectiveness of these two nasal sprays was compared, with respect of elimination of dependence on vasoconstriction agent.
Research result: the patients selected for the research were the individuals with pure nasal vasoconstriction agents' dependence, i.e. the patients, whose nasal vessel dependence was caused not but the other pathologies, among them, the patients with allergic rhinitis were not involved in the research. The sample included 186 patients aged from 18 to 54, it was divided into two groups: in the main group there were 96 patients and they were treated with two-component combined nasal steroid – Fluticasone propionate and Azelastine. The control group included 90 patients treated with single-component nasal spray Fluticasole furuate. As a result of six-month observations, high effectiveness of the combined medicine was revealed, in comparison with the single-component Fluticasone furuate, with respect of elimination of the dependence on nasal vasoconstriction agents. After use of the combined medicine, in maximum 30 minutes, the breathing through nose improved, in 80% of cases, in 10% cases, symptoms disappeared in 3 days and in the remained 10% of cases, treatment did not yield any results. For the single-component nasal spray, breathing through nose improved in 12 hours, in 40% of cases, in 20% of cases, the symptoms disappeared in 48 hours and in 40% of cases no result was yielded (dependence was not eliminated).
Conclusion: effectiveness of two-component nasal steroid is much higher than that of single-component nasal steroid, with respect of elimination of nasal vasoconstriction dependence, as the combined preparation eliminates more rapidly and it is much more effective, compared with the control group, P>0.05; also, combined preparation has less side effects (drying of mucous tunic, bleeding in case of medicine consumption).

COMPLETE BLOOD COUNT DERIVED BIOMARKERS OF METHOTREXATE RESPONSE IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent inflammation of the synovium, leading to joint damage and systemic complications. Methotrexate (MTX) is commonly used as a first-line treatment for RA due to its immunosuppressive properties. However, a significant proportion of patients exhibit resistance to MTX therapy. Lately, certain complete blood count (CBC) derived biomarkers such as RDW, HGB/PLT, and HGB/MON ratios have emerged as promising indicators in various inflammatory conditions, providing insights into disease prognosis and therapeutic response. However, there is currently limited data available on the effectiveness of the abovementioned biomarkers as prognostic ones to predict treatment outcomes in newly diagnosed RA patients who are initiating MTX treatment.
Objective: This study aimed to determine the potential of RDW, HGB/PLT, and HGB/MON as prognostic biomarkers in newly diagnosed RA patients commencing MTX therapy. Additionally, to investigate their possible correlation with the Disease Activity Score of 28 joints (DAS-28), which is a widely accepted tool to monitor and assess disease activity and treatment response in RA patients.
Methods: We conducted a comprehensive analysis involving 64 RA patients categorized into Methotrexate-resistant (MTXR) and Methotrexate-sensitive (MTXS) groups and 28 age- and sex-matched healthy individuals. ANOVA analyses were employed to assess differences in hematological biomarkers between groups. Standard T-tests were used to compare specific biomarkers between MTXR, MTXS, and control groups. For the comparison of categorical variables between the groups Chi-square test was employed. Furthermore, we examined correlations with Pearson's correlation test between RDW, HGB/PLT, HGB/MON ratios, and DAS28 in both groups. To determine the predictive capabilities of these biomarkers, Receiver Operating

Characteristic (ROC) curve analysis was performed.
Results: No statistically significant difference was observed between the biomarkers of interest in MTXR and MTXS groups, according to an unpaired t-test. No significant positive correlations were identified between CBC-derived biomarkers and DAS-28 in either the MTXR or MTXS groups. Additionally, The ROC curve analysis showed that their predictive capability was insignificant.
Conclusion: Based on our findings, we cannot support the use of RDW and HGB/PLT and HGB/MON ratios as predictors of methotrexate response in newly diagnosed RA patients. Also, our study cohort has shown that they cannot replace DAS-28 for assessing disease activity in RA patients.

HOW WE BATTLE CANCER EVERYDAY

Beka Jalabadze, 7th grade student at QSI Tbilisi, Georgia

Healthy cells turning into tumor cells is quite common when it comes to humans. It can happen any time as long as the needed circumstances are met. People are developing cancer all the time; however, the immune system is doing a great job keeping an eye over it. Without cancer immunosurveillance these malignant cells would pose an even bigger risk to our health. In this presentation we will expand about immunosurveillance; the damage that leads to cancer; and how the immune system, precisely the natural killer and cytotoxic T-cells take care of cancer cells. Furthermore, we go over how tumors can develop strategies to evade detection from such cells, leading to immune escape and progression. The concept of immunosurveillance is now well established and has a solid foundation. To sum up everything that has been stated so far, learning about immunosurveillance is crucial so we can understand cancer development better.

CORONA VIRUS INFECTION AND HEALTHCARE WORKERS

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Maintaining thehealth state of the employed population is a priority of the state's policy in the direction of labor relations, creation of safe work practices for employees and prevention of occupational diseases, because the economic prosperity of the state depends on the state of health of the employed population.

WHO, ILO, EU have discussed in detail the harmful working conditions of employees in the health care system, which have become extreme during the pandemic of infections and COVID-19.

The purpose of the work is to review various literary and statistical data on the health status of the staff infected with Covid-19 working in medical institutions. Diagnosing an occupational infectious disease used to be a difficult expert issue, and during a pandemic, high mortality rates make this process even more difficult. In order to determine the occupational nature of the disease in the case of COVID-19, it is necessary to have clear and transparent criteria.

The examination establishes a cause-and-effect relationship between the developed disease and professional activity. Working conditions are one of the main reasons that affect the employee's health. Based on a special assessment, it was found that 56,7% of people are employed in harmful and dangerous conditions in the healthcare system, and 43,3% are employed in optimal acceptable conditions.

Conclusion: based on the analyzed data, it was determined that a multidisciplinary approach to the diagnosis, treatment, and complications of COVID-19 is needed, and it is necessary to involve various specialists, such as a neuropathologist, a rheumatologist, and other medical specialists when necessary, so that pathology can be detected early; It is also relevant to create scientifically based programs for patients after the transfer of COVID-19, which includes the detection of

the effectiveness of preventive methods, and then to perfect the expert issues that will be related to the connection of the profession of COVID-19 and the admission of medical personnel to high-risk work.

AUTOINFLAMMATORY DISEASES IN ANIMALS

Lizi Kaishauri, Agricultural University of Georgia

Immune-mediated diseases usually involve a mixture of both dysfunctional innate and adaptive immune responses. The importance of these responses varies among diseases. Thus, there is a continuum from purely autoinflammatory disease at one extreme and purely autoimmune at the other. Innate autoimmunity or autoinflammation at one point was believed to be a set of monogenic human diseases marked by recurrent episodes of systemic and organ-specific inflammation caused by dysregulation of the innate immune system. While initially encompassing only innate immunity, it is apparent that many such systemic diseases play an important role in both autoimmune and even immunosuppressive disorders.

Many autoinflammatory disorders have complex genotypes and phenotypes, and overproduction of proinflammatory cytokines is the most characteristic feature.

Such diseases that will be discussed are: Shar-Pei fever syndrome, canine hypertrophic osteodystrophy, sweet syndrome, sterile nodular panniculitis, type 1 and type 2 autoimmune pancreatitis.

We will talk about specific immune factors involved in the development of these disorders as well as clinical signs, and existing diagnostic methods and treatment plans.

IMPACT OF THE BOTULINUM NEUROTOXIN INJECTIONS ON PATIENTS WITH DEPRESSION: IMMUNOGENICITY, THERAPEUTIC MECHANISMS AND POSSIBLE FUTURE PERSPECTIVE

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Background: Despite the fact that today's medicine is constantly developing in all directions, there are still some diseases that burden humanity and interfere with daily life. Depression is one of them. Existing treatment tactics are often ineffective, and Botox injections in such cases are an experimental method.

Objectives: Our goal is to review previous researches and make this information available on a larger scale so that clinicians can access similar therapies for use in unconventional cases. The purpose of the study was not to directly cure depression, but to evaluate the positive impact that manipulations carried out for aesthetic purposes would have on their general mood and condition. Our attention was especially drawn to the fact that research on this topic has not been conducted in our country yet.

Methods: The study involved 15 participants and it lasted on average two months. The Beck Depression Inventory (BDI) Questionnaire, in total 21 question, was used for assessment, just like our predecessors.

Results: The results, to our delight, gave us very interesting feedback, based on which we can assume the positive contribution of Botox in the management of patients with depression. BoNT/A injections led to significant improvement of self-rated depression score by using Beck Depression Inventory (BDI). The response rates of BoNT/A were 34%. From the literature, we know that positive results in previous studies ranged from 13% to 52%.

Conclusion: Botulinum Neurotoxin therapy shows promise as a novel approach to treating depression. While further research is needed to establish its effectiveness, Botox may offer a unique and potentially valuable option for individuals struggling with depression.
Keywords: depression, botulinum neurotoxin, therapy, facial feedback, Beck Depression Inventory (BDI).

BRONCHIAL ASTHMA AND THE ROLE OF VITAMIN D IN THE IMMUNE SYSTEM IN A PEDIATRIC POPULATION

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INTRODUCTION: Although we can name genetic predisposition as the cause of the development of bronchial asthma in children, its complex interaction with environmental factors is noteworthy.
OBJECTIVES:The main goal of the study is to describe the role of vitamin D in the immune system of the children's population, whether the amount of maternal vitamin D and the lifestyle are important for the development of the children.
METHODS:This was a series of observations and cohort studies based on which we can discuss the specific numbers of disease formation and their prevalence. Reliable data provides research such as The Vitamin D Antenatal Asthma Reduction Trial (VDAART) and The Copenhagen Prospective Studies on Asthma in Childhood (COPSAC2010).
RESULTS:While the results of the above trials did not meet statistical significance, the effect of prenatal vitamin D3 supplementation was of similar magnitude and direction in both trials (HR of 0.8 for VDAART and 0.76 for COPSAC2010), suggesting a true effect. One possible explanation is that baseline vitamin D status may affect the response to vitamin D supplementation, and since baseline vitamin D level was not a criterion for entry in either trial, this may have biased the results toward the null.
CONCLUSION:Accumulating evidence suggests a relationship between maternal vitamin D deficiency and the risk of childhood asthma. High-dose vitamin D supplementation during pregnancy appears to reduce the risk of early life wheeze/asthma, but not long-term asthma, in the offspring.
Key Words: bronchial asthma, vitamin D, genetic, children, population.

CHRONIC ASTHMA

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Introduction: childhood bronchial asthma is an important public health problem worldwide. it is one of the most common chronic diseases in childhood, which affects the quality of life not only of the child, but of the entire family. despite effective and safe treatment, bronchial asthma imposes a significant burden on a child's health-related quality of life. asthma symptoms and lung function tests are very important for the diagnosis of the disease, however, determining the health-related quality of life (hrqol) can lead to an important and more comprehensive assessment of the impact of asthma on the child's quality of life.
Objective: to improve the quality of management of a child with bronchial asthma by introducing quality of life assessment questionnaires into clinical practice.
methods: the study was observational, cross-sectional. data were collected from 2017 to 2020 from 3 clinics of the evex hospital network: - m.iashvili central children's hospital, batumi mother and child center and zugdidi referral hospital.

The research tool was a collection of questionnaires, which consisted of the following questionnaires: 1) general questionnaire - a basic, general questionnaire that included information about the participants' asthma; 2) pediatric quality of life inventory (pedsql), asthma module (version 3.0, short form. pediatric quality of life inventory (pedsql), asthma module (version 3.0, short form); 3) pedsql multidimensional fatigue scale. pedsql multidimensional fatigue scale; 4) pedsql family impact module. pedsql family impact module; 5) asthma control test (act) and the childhood asthma control tests (cact).
the pedsql asthma module and the multidimensional fatigue scale were completed independently by parents and children from 5 years of age. age-appropriate versions of the questionnaires were used (2-4; 5-7; 8-11; 12 and 13-18 years). the younger children were interviewed, and the older children filled out the questionnaires independently. visual aids were used for 5- to 7-year-old children.
the form and severity of asthma were determined by a pediatrician and an allergist using the british thoracic society (bts) asthma management step approach, with stage 4–5 asthma being classified as severe asthma.
in addition, children over 6 years of age were assessed for external breathing by computer spirometry, determining the following parameters: fev1, fvc, fev1/fvc, fef 25-75.
Results: 507 children aged 2 to 18 and their parents were included in the study. the quality of life was evaluated both by children with asthma and by their parents. as a result of the research, it was revealed that bronchial asthma affects the quality of life not only of the child, but also of the whole family. assessments of qol by children and their parents are correlated; the mean score for both children's and parents' qol assessment was 43.6. severe asthma, poor asthma control, smoking, presence of dampness, child overweight and obesity were associated with lower qol scores. the qol score was also related to socioeconomic status and family education level. qol was not related to the age and gender of the study participants, spirometry results, pet ownership and concomitant allergies. qol assessment revealed that asthma limits the child's daily activities.
this was the first study in georgia that examined bronchial asthma symptoms, severity, and control using currently used childhood asthma qol instruments and questionnaires in clinical practice. "asthma-related quality of life" refers to the perceived impact (perception) of asthma on the patient's quality of life. qol assessment will help us understand the subjective impact of the disease on the patient's daily life. this type of analysis is very important for a comprehensive and complete assessment of bronchial asthma, for planning the correct management of the disease and for prognosis. properly managed asthma provides symptom control, treatment efficacy, reduced risk of adverse outcomes and complications, eliminates the need for hospitalization, all of which significantly reduces health care costs.

SOCIO-ECONOMIC FEATURES OF SEXUALLY TRANSMITTED INFECTIONS AMONG MSM IN GEORGIA

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Objectives. The aim of our study was to investigate correlation between socio-Economic conditions and prevalence of Sexually Transmitted Infections among MSM in Georgia.
Methods. The study was conducted in 5 main cities in different regions of Georgia (Tbilisi, Batumi, Kutaisi, Zugdidi, and Telavi). During 2015-2019, social workers, LGBT community and non-governmental organizations (NGOs), conducted screening of MSM for STI, which was achieved by disseminating required information through electronic and print media, resulting in maximum involvement of MSM in screening programs for STI disseminating. A specially designed questionnaire/survey has been used to investigate the correlations between the following parameters: age, education, income, awareness of STI, sources of information, residence,

frequency of safe sex, number of sexual partners and etc.
Results. The results of current study indicated that low income and educational attainment are the key socio-economic risk factors leading to high rates of STI prevalence among MSM. On the contrary, STI rates were inversely associated with the level of education.
Conclusion. Consideration of Socio-economic risk-factors and using of informational data together, screening and prevention programs should be planned, which will lead to a decrease in the number of STIs among MSM in Georgia
Keywords: MSM, STD, Syphilis, Gonorrhea, Chlamydiosis.

CELLULAR AND HUMORAL IMMUNE RESPONSES TO COVID-19

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At the Sachkheri Medical Center in 2021, for the first time in Georgia, a evaluation of immunity in Covid-19 patients was conducted on Elispot. The EliSpot analysis was used for the assessment of T-cell immunity in persons exposed to the Covid-19 or SARS-CoV-2 virus vaccinated individuals. To assess the stability of the immune response against SARS-CoV-2, especially those who have no antibodies against the virus. Elispot is an imaging technology to measure the active effects of the immune response to infection. In order to use venous blood to isolate T-lymphocytes, we added the SARS-CoV-2 antigen mixture to the gel. If the lymphocytes and the virus met each other earlier, then the lymphocytes release cells, visually this is expressed in the so-called varnish.
In the central clinic, 24 patients were examined for both humoral immunity (IgM & IgG) and cellular immunity in the form of interferon gamma and interleukin-2.
Research has found a proportional position between immunities, namely in those organisms with high antibodies, low cellular immunity and resistance;
It was noteworthy that in 2 patients with lethal interferon gamma and interleukin-2, the dynamics decreased sharply, while the level of antibodies increased.
Answers To conclude that the presence of T-cell immunity against Covid-19 is not difficult, the immunity is solid from 6 months to 1 year.

MODERN APPROCEHES TO ATOPIC DERMATITIS. BYOND THE SKIN

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Atopic dermatitis (AD) is a common chronic inflammatory skin disorder, with periods of exacerbation and remissions , that is affetcing approximatly 7 to 20% of children and 5–8% adults. AD clinical presentation with severe pruritus and recurrent eczematous lesions often result sleeplessness, stress, poor self-esteem and school achivement, that has a great impact on chaild's and family's quality of life and psychological and social well-being. AD is a complex and multifactorial disorder that combains skin barrier dysfunction, increased transepidermal water loss, changed skin microbiome, environmental factrs and immune dysregulation with prevalence of the T2-mediated immune pathway. The exact mechanisms of the pathogenesis of AD are still unclear, but recent research shows that AD can be considered as an infammatory skin disease with a systemic component. The main goal of treatment of AD include relief of symptoms, improvement of quality of life and reduction of relapses. The classical treatment include nonpharmacological emoliants and use of topical corticosteroids and calcineurin inhibitors, with antihistamines, antibiotics, adding of phototherapy, and immunosuppressant drugs in severe cases. Recent understanding of the pathogenesis of AD has allowed the development of new drugs targeting different mechanisms and cytokines that have changed the treatment approach. A lot of new agents are aproved by FDA for tratement of pediatric AD, including topical crisaborole (PDE4 inhibitor), topical ruxolitinib (JAK 1/2 inhibitor), oral upadacitinib (JAK 1 selective inhibitor), and injected dupilumab

(anti-IL-4/13 monoclonal antibody). The resent studies showed effect of topical PDE4 inhibitors, topical and oral JAK inhibitors, and the injectable biologic treatments as well as using the bacteriophages for modulation of the skin microbiome and specific nanoparticle skin delivery systems, but more reaserch is needed to prove the efficiency and safety of new approches.

ASSOCIATION OF ALLERGIC RHINITIS AND ATOPIC DERMATITIS WITH BRONCHIAL ASTHMA IN A PEDIATRIC POPULATION

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Introduction: Allergic rhinitis, atopic dermatitis (AD) and asthma constitute the triad of atopic diseases, which are common in infants and children and represent a major concern because of leading to a heavy economic burden as well as poor quality of life. More specifically, childhood allergic diseases cause sleep disorders, impede growth, disrupt education and etc.

Aim: The aim of our current research is to study and specify how frequent the coexistence of the mentioned three diseases or any two of them is in population of students of a Georgian public school. In addition, through a specially designed questionnaire, we have the opportunity to study in the case of each patient at what age and which allergic disease was diagnosed for the first time and whether it caused later the development of any other disease with an allergic mechanism, in order to asset the prevalence of the association of AR, AD and BA in the study cohort. Because our research is still in process, to date, our study group includes 109 children, from them there are 65 boys and 44 girls.

Results: Because the prevalence of allergic diseases is closely related to age and dependent on the type of these ailments, the symptoms manifest at different ages. On average, the rate of atopic dermatitis is highest in children under 5 years of age, asthma symptoms are highest in children between 2 and 9 years of age and allergic rhinitis – in those between 6 and 11 years of age.

According to the results of our current study, with 109 participants to date, we can highlight that the prevalence of rhinitis in patients with previous AD (42%) is about 22% more than in the individuals without AD (20%). The co-existence of Asthma and allergic rhinitis (AR) is found in 39% of patients, but the prevalence of having both rhinitis and asthma is about 9-10% in patients with AD.

Discussion: When it comes to the association of allergic rhinitis and atopic dermatitis with bronchial asthma in a pediatric population, some studies appear to support the atopic course, according to which allergic diseases occur following a time-based order from atopic dermatitis and food allergy to asthma and allergic rhinitis. But, meanwhile, there are several other researches, the results of which seem to support that the atopic march is less frequent than classically considered. According to our current data, we can say, that there is an association between AD and allergic rhinitis, but as our results show, less than 10% of children with atopic dermatitis or eczema follow the trajectory of the classic atopic march, while Asthma and AR co-exist more often.

Conclusion: At the end of our study, the obtained data will allow us to more accurately assess the relationship between the manifestations of allergic rhinitis, atopic dermatitis and bronchial asthma and their frequency in the study population.

Key Words: allergic rhinitis, atopic dermatitis, bronchial asthma, atopic march.

BRONCHIAL ASTHMA IN THE PEDIATRIC POPULATION AND ITS GENETIC PREDISPOSITION

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Introduction: Bronchial asthma is the most common chronic disease in children and affects 14.2% of the world's child population. The disease is characterized by reversible airway obstruction and chronic inflammation. Asthma exacerbations are a significant cause of morbidity and hospitalization in children, with a mortality rate of 0-0.7 per 100,000 children. Consequently, it represents a large financial burden for both the family and the healthcare system. 1-2% of the health budget of developed countries is spent on disease management.

Research material: the importance of genetic predisposition in bronchial asthma patients in the children's population, we made a map - a questionnaire based on which we had to determine the genetic factor of allergic diseases in the children's population, we took as a research contingent 150 children aged 6 to 17 years, where how many of the 150 children had bronchial asthma, the children were positive They answered, the questionnaire included: - family anamnesis, tobacco use in the family, pets, dust collectors, food allergens, the period of the year was focused on - the season, environmental conditions, sports, overweight in girls and boys, age.

Research Discussion: The pathogenesis of asthma is based on the interaction of genetic and environmental factors. In recent years, for the development of appropriate preventive or therapeutic measures, special attention has been paid to determining the influence of genetic factors, which, although observed in adult patients, significantly prevails in pediatric age. The genetic and epigenetic mechanisms underlying bronchial asthma in children are not fully understood. To date, more than 100 genes have been associated with asthma, related to the immune system, airway mucosa and lung structure and function, including specific cytokines, Toll-like receptors, sphingolipid biosynthesis regulator 3, gasdermin B, filaggrin protein , genes encoding the major histocompatibility complex and the cysteine-leukotriene metabolism pathway.

Conclusion: the expression of some genes depends on environmental factors based on epigenetic mechanisms. Histone modification at certain loci, DNA methylation, and micro-RNA production regulated by environmental factors (tobacco and alcohol consumption, obesity, stress, etc.) have been reported in pediatric patients with asthma.

Key words: bronchial asthma; child population; Genetic and epigenetic factors.

CONDITIONS MIMICKING ANDROGENETIC ALOPECIA

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Androgenetic alopecia (AGA) is the most common form of hair loss in both men and women. Its prevalence varies among different populations and the frequency increases with age. It is most commonly observed in the Caucasian population, affecting up to 80% of men and 42% of women.

AGA is characterized by gradual hair loss in androgen-dependent areas of the scalp. To differentiate between the specific models of alopecia, the terms "female pattern hair loss" (FPHL) and "male pattern hair loss" (MPHL) are used. FPHL is characterized by a diffuse thinning of the centro-parietal area with preservation of the frontal hairline. MPHL presents with a recession of the frontal hair line, mainly in a triangular pattern, later followed by a vertex thinning. Women usually present with FPHL while men are affected by MPHL. However, in some cases, male pattern hair loss can affect women and vice versa.

For diagnosing AGA, detailed medical history and clinical examination are not enough because there are several conditions mimicking this disease.

Disorders that may be difficult to distinguish from FPHL include: telogen effluvium, lichen planopilaris, fibrosing alopecia in pattern distribution and central centrifugal cicatricial alopecia. Disorders that can be challenging to differentiate from MPHL include: frontal fibrosing alopecia and traction alopecia. Additionally, there are several hair conditions that may mimic both female and male pattern hair loss. These are: trichotillomania, diffuse alopecia areata and alopecia areata incognita.

Trichoscopy can be considered an important, non-invasive tool for diagnosing hair and scalp disorders that may have similar clinical signs to AGA. With the help of trichoscopy it is possible to evaluate the whole research area. If a diagnosis is unspecified, trichoscopy helps us identify the specific area for biopsy.

SURFACE EXPRESSION OF CD180, MD-1, IGM AND IGD AND THEIR TURNOVER AT VARIOUS TIME POINTS AND CELLULAR CYCLE PHASES IN CLL-DERIVED MEC1 CELL LINE

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Introduction: Chronic lymphocytic leukemia (CLL) is the most common leukaemia in the Western world and represents expansion of CD19+CD5+CD23+ cells. CLL cell proliferation and expansion is driven by B cell receptor ligation with (auto)antigens and by interaction with the microenvironment through a variety of receptors. One of these receptors is the CD180 toll-like receptor. Our team has shown, that it is expressed on about 60% of CLL cells, is involved in the regulation of CLL cell proliferation and apoptosis and correlates with overall patients survival. Since all normal B cells express CD180, its absence from 30% of the CLL samples is puzzling. The MD-1 satellite molecule, which is essential for CD180 expression on the cell surface, may play a role in this heterogeneity. We have shown high CD180 expression is associated with a favorable disease outcome and superior overall survival [7] emphasizing the importance of understanding the modulation of CD180 expression in CLL. We therefore characterized the surface expression of of CD180, MD-1, IgM and IgD by the MEC1 cells over 72-hours.

Methods: For this purpose MEC1 CLL-based cell line was used, which was grown in special cell culture RPMI-1640 medium, which consisted of inactivated bovine serum, L-Glutamine and Pen strep in 37°C. Synchronised MEC1 cells were assessed for surface expression of CD180, MD-1, IgM and IgD -24h, 48h, and 72h using flow cytometry. The viable cells were selected through a parallel identification of cell-cycle phases using propidium iodide [8]. To assess the effect of MD-1 on the expression of CD180, after stimulating MEC1 24-72 hour culture cells with IgM and IgD CD19+/MD1+//CD180+ expression alteration was measured.

Results: In MEC1 the increase in expression of MD1 correlated with increasing of expression of CD180 positively. As we can see at 48hrs, CD180 expression dropped, but regained its level of expression after 72hrs. After 24hrs, MD1 expression significantly increased, but then dropped in 48h cell culture, but regained its expression level in $CD180^+$ 72h cell culture (Figure 1, 2). After 72hrs the expression of IgD drastically dropped compared to $CD180^+$ 24h and 48h cell cultures. After 48-72hrs the expression of IgM decreased compared to $CD180^+$ 24 cell culture (Figure 3, 4).

As we can see, MD1 and CD180 expression level drastically dropped in 48hr cell culture. We were inquisitive about the reason and factors that caused such decreasement in the expression of following proteins. We decided to assess the effect of MD-1 on the expression of CD180, after 24 hours stimulating MEC1 24-72 hour culture cells with IgM and IgD CD19+/MD1+//CD180+ expression alteration was measured.

The stimulation of MEC1 24-hour culture by bindings with IgM or/and IgD decreased $CD19^{+}CD180^{+}$ expression, but $CD180^{+}MD1^{+}$ remained the same level by binding with IgD as in unstimulated 24-hour cell culture, unlike by binding with other antibodies (Figure 5, 6).
The stimulation of MEC1 48-hour culture by bindings with IgM or/and IgD increased $CD180^{+}MD1^{+}$ expression, but $CD180^{+}$ population decreased compared to unstimulated and stimulated 24-hours cells. The stimulation of MEC1 72-hour culture by bindings with IgM or IgD didn't cause any alterations in the immunophenotype of cells (Figure 7).
Conclusion: As a result of our research, it was concluded that MD1 in MEC1 cell culture is a positive regulator of CD180 receptor; MEC1 72-hour cell culture is anergic to IgM, IgD and joint binding of B cell receptor. In result, the impact of MD1 expression was determined on the expression of CD180 and its functions, which modulation is followed by leukemic cell apoptosis. This research will allow us to determine new approaches to CLL immunotherapy.
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EFFECTS OF EPICYN, FLOSTERON AND CONTRATUBEX ON IL-1 AN IL-6 CYTOKINES DURING THE SKIN WOUND HEALING PROCESS.

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Skin wounds, ranging from minor cuts to severe injuries, are common occurrences in everyday life. The problem of wound healing is multifaceted, involving scar formation, infection risk, and cosmetic outcomes. The wound healing is a complex, dynamic and highly regulated process involving a cascade of cellular and molecular events. Interleukin-6 and interleukin-1 emerge as critical mediators in orchestrating inflammation and tissue repair during wound healing. Understanding the roles of these cytokines provides valuable insights into the mechanisms underlying wound healing and may offer potential therapeutic targets for enhancing the healing process in various pathological conditions. Our investigation carried out on lab. rats was designed to study effects of Flosteron, Contratubex and Epicyn on IL-1 an IL-6 cytokines during the skin wound healing process. Excisional of the full-thickness skin wounds were aseptically made on the dorsal skin of lab. rats. Contractubex and Epicin creams were applied to the wound surface as a thin layer 2-3 times a day for 4 weeks, Flosteron (0.2 ml) was injected subcutaneously in the wound area 3 times for 4 weeks. Proinflammatory cytokines (IL-1, IL-6) were studied by ELISA.
Results showed that IL-1 on the 7^{th} day of wound healing was increased significantly in all experimental group animals compared to the data of healthy group animals. In subsequent days the IL-1 gradual decrease was detected only in the epycin-treated group animals and by the 21^{st} day of wound healing it was within the normal range. IL-1 in flosteron-treated animals was normalized by 28^{th} day of wound healing, while in control and contratubex-treated animals it was still increased by 35% and 24% respectively. Increase in IL-6 was detected later, on the 14^{th} day of wound healing. Its gradual decrease and normalization was obvious in epicyn- and flosteron-treated animals on 28^{th} day. There was no significant difference in data of control and contratubex-treated animals and by the 28^{th} day of healing process IL-6 was still increased by 17% and 14% respectively compared to normal value. **Conclusion**: IL-1 and IL-6 are pivotal in skin wound healing, with implications for inflammation modulation and tissue repair. During wound healing, IL-1 and IL-6 exhibit distinct temporal patterns, reflecting their roles in different phases. As wounds progress, IL-1 and IL-6 decline, signaling resolution of inflammation and tissue remodeling. Although, epicyn revealed better wound healing properties, further research is warranted to elucidate the precise mechanisms underlying the effects of Flosteron, Contratubex, and Epicyn on IL-1 and IL-6 dynamics during wound healing. Therapeutic interventions targeting these cytokines may offer

promising avenues for enhancing wound healing outcomes.

Key words: Epicyn, Flosteron, Contratubex, IL-1, IL-6, skin wound healing.

DISCOVERER AND EXPLORER OF SUBTERRANEAN MARVELS

Shorena Kitsmarishvili

Jumber Jishkariani was a Georgian geographer and journalist, renowned for being one of the early explorers of Prometheus Cave. He held the esteemed title of honorary member of the Geographical Society of Georgia and was recognized as a distinguished journalist, earning the honor of being a laureate of the Sergey Meskhi Prize. Additionally, he was a member of the Phasis Secular Academy and was granted the status of honorary citizen of Tskaltubo.

Since his student years, Jumber actively engaged in various expeditions, dedicating his entire life to the underground investigation. From 1959 until the end of his life, he served in the karstology-speleology department of the Vakhushti Bagrationi Institute of Geography. In 1986, he assumed the role of scientific researcher, and from 1997 to 1999, he held the position of the head of the department. His involvement led to the exploration of over 400 caves and abysses, including the New Athos Cave, for which he created the initial plan. In 1984, Jumber led a team of speleologists from the institute in discovering a cave in the village of Kumistavi, Tskaltubo district, which stands out as one of the unique caves in Europe. He played an active role in advancing speleotherapy. Mr. Revaz Sepiashvili, the director of the Scientific Research Institute of Allergology, Asthma, and Clinical Immunology of the Georgian Academy of Sciences, made significant contributions to studying the healing properties of the cave's microclimate.

In addition to his dedication to speleology, Jumber pursued journalism with great passion, authoring over 1000 publications in various journals and newspapers.

From 1999 to 2008, he embarked on a business trip to the United States of America to gain expertise in cave improvement. This endeavor served as a connecting and unifying bridge for Georgians dispersed across different parts of the world.

Upon returning to his homeland, he fervently continued his pursuits despite facing vision impairment (having lost an eyeball), yet remaining spiritually resilient. With the assistance of generous individuals, he successfully published five books: "Our Otia," "Treachery in the Dal Valley," "Above Envy and Slander," "Fragments from an American Diary & Letters," and "Amazing Subterranean."

Until the end of his life, Jumber upheld the life motto of the great writer Levan Gotua: "I don't desire any happiness if it comes at the expense of my homeland."

ONYCHOMYCOSIS – HOW TO RECOGNIZE IT?

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The term "onychomycosis" is used to describe dermatophytoses (a fungal disease caused by dermatophytes) of the finger- and toenails. The disease is widely distributed worldwide. In addition to dermatophytes, onychomycosis may be caused by other fungi, such as molds and Candida. Despite this, dermatophytes are the most common cause of onychomycosis in all countries.

Factors that contribute to the development of onychomycosis include wearing closed shoes, chronic nail trauma, genetic predisposition, and the presence of diseases such as diabetes mellitus, peripheral circulatory disorders, HIV infection, and other immunosuppressive conditions.

The variety of causes leads to the variety of clinical manifestations, which makes diagnosis difficult. The diagnosis is established, first of all, according to the clinical picture, in addition, following laboratory research methods are used: detection of fungi by direct microscopy with KOH-test, cultural method, molecular (PCR) diagnosis, and in some cases histological

research. The results of the research need to be interpreted correctly. The probability of a false negative result when using any test is high, so a negative test does not rule out the presence of onychomycosis. Differential diagnosis should be carried out with such nosologies that occur with nail damage. Treatment of onychomycosis requires correct mycological identification, selection of the correct method of treatment, that is more appropriate for one or another clinical form of onychomycosis and it's etiological cause (systemic, local or combined therapy).

NAILS – A MESSENGER OF HEALTH

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Changes in the nail plate indicate various diseases of the skin or internal organs which gives it diagnostic value. Sometimes these changes appear before the full manifestation of the disease, sometimes - directly during the course of the disease, or after its resolution. Damage of the nail plate can clinically manifest by changes in its structure or color.

There are various known structural changes of the nail, including: onycholysis, koilonychia, irregular pitting, beau's lines, onychauxis, onychogryphosis, onychomadesis, onychorexis, onychomalacia, median canaliform nail dystrophy. Behind each of above mentioned conditions, another pathology may be hiding, such as the impact of external or internal factors: trauma, contact with chemical substances, nail polish, soap, age (metabolic changes, circulatory disorders), drugs - retinoid or chemotherapy.

It may indicate the pathology of other organ systems, such as anemia, hemochromatosis, hypothyroidism, systemic lupus erythematosus, diabetes, lung, heart and digestive system diseases, eating disorders, obsessive-compulsive disorder; Or it may be a manifestation of the following skin diseases: psoriasis, atopic dermatitis, alopecia areata, ichthyosis, tuberous sclerosis, lichen planus, eczema, pemphigus vulgaris, psoriatic arthritis, scleroderma, fungal and bacterial skin infections.

Nail deformities with color changes may also indicate any pathology of internal organs, for example, blue color can be a sign of oxygen deficiency, white - liver disease and diabetes mellitus, light pink - anemia, half pink and half white - kidney disease, yellow color - lung disease, nail infection and tobacco use, red lunula can be seen in lupus, heart disease, alopecia areata, arthritis and dermatomyositis, blue lunula can indicate intoxication. Collection of complete patient history and clinical evaluation helps us in making the differential diagnosis.

RHEUMATIC ARTRITS CONTROL AND REHABILITATION BALNEOLOGY-RESORT TSKALTUBO"

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Rheumatoid arthritis (RA) is the most common form of inflammatory arthritis in the UK and affects around 1% of the population. Approximately 10,000 people receive a diagnosis of RA every year.

Rheumatoid arthritis is a long-term condition that causes pain, swelling and stiffness in the joints. The condition usually affects the hands, feet and wrists.

Rheumatoid arthritis is an autoimmune disease. This means your immune system (which usually fights infection) attacks the cells that line your joints by mistake, making the joints swollen, stiff and painful. Over time, this can damage the joints, cartilage and nearby bone.

It's not clear what triggers this problem with the immune system, although you're at an increased risk if: you are a woman, you have a family history of rheumatoid arthritis, you smoke.

To combat this problem, balneotherapy with various hydrotherapy is successfully used in the Tskaltubo balneological resort. Today, modern medical and rehabilitation facilities allow us to treat, prevent and raise the tone of the body.
It is generally recognized that in the conditions of modern rehabilitation of patients, a great role is assigned to non-drug treatment methods, and balneology, in particular, radon therapy, plays a leading role in these methods.
It has been proven that radon increases the protective functions of the body, strengthens the immune system, activates blood circulation, regulates blood pressure, promotes cell recovery and regeneration (after wounds and burns), has an analgesic and anti-inflammatory effect, has a pronounced sedative (relaxing) effect, Activates cognitive functions.
Based on the above, the Tskaltubo resort is the best base for highly effective treatment with natural healing factors. Taking radon procedures leads to reduction of inflammatory processes and increase of flexibility in damaged joints and reduction of pain syndrome.

VIRAL INFECTION: COVID-19 IN THE POPULATION OF CHILDREN SUFFERING FROM BRONCHIAL ASTHMA.

Guri Kuprashvili, Tamar Khmaladze, Nino Adamia, Irma Ubiria. TSMU, Faculty of Medicine, M.Iashvili Children's Central Hospital.

A unique clinical approach is required for children with asthma who are susceptible to SARS-CoV-2 infection. This approach should take into account the clinical characteristics of the infection, as well as the safety, effectiveness, and efficiency of the COVID-19 vaccine. The purpose of this study is to evaluate the impact of SARS-CoV-2 and the COVID-19 vaccine on pediatric patients with asthma. Through specific search queries, we conducted a thorough investigation of the major medical databases from March 2023 to early global spread of COVID-19, along with relevant data from significant national and international organizations.
Although there was no statistically significant difference in the incidence and morbidity of SARS-CoV-2 between pediatric asthmatic patients and pediatric non-asthmatic patients, it was found that uncontrolled asthmatic children had a higher risk of experiencing severe illness during SARS-CoV-2 infection. A growing body of research suggests that COVID-19 vaccinations are safe, effective, and useful for children with asthma, regardless of the severity of their illness. Since evidence of novel viral variations driving epidemic waves shows that the existing paradigm is out of date, more cohort-based research is needed..

LIVER TRANSPLANTATION IMMUNOLOGY: IMMUNOSUPPRESSION AND REJECTION

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Background: Liver transplantation (LT) is a critical intervention for patients with end-stage liver disease, offering hope where conventional treatments fail. The key challenge lies in balancing the efficacy of immunosuppressive therapy with its adverse effects to optimize graft longevity and patient survival. Initiated during the anhepatic phase and continued long-term, immunosuppressive therapy varies across centers, with early post-transplantation period vigilance crucial to mitigate rejection risk.
Objective: This study aims to evaluate rejection rates post-liver transplantation and explore management strategies.
Methods: We conducted a retrospective analysis of medical records from liver

transplant recipients at our center. The study subjects were adult liver recipients who underwent liver transplantation at our center (Batumi Referral Hospital-Medcenter, Georgia) since 2014, including December 2023, totaling 95 recipients, with a median age of 49.5 years. Perioperative survival was observed in 98% of cases, and a five-year follow-up demonstrated a survival rate of 75%. Cross-sectional study analysis was employed to examine rejection episodes, focusing on both acute and chronic rejection.
Results: Among the 95 liver transplant recipients, our analysis identified instances of rejection. Specifically, one patient experienced chronic rejection, while acute rejection occurred in another patient. These occurrences led to adverse outcomes, resulting in patient mortality. Our findings highlight the significance of vigilant management of rejection episodes post-transplantation.
Conclusion: In summary, our study emphasizes the importance of effective immunosuppressive strategies. Our findings underscore the need for ongoing research to refine protocols and enhance graft survival. Collaboration and innovation in transplant medicine are essential for addressing the complexities of rejection and improving patient outcomes. Ultimately, our pursuit of excellence in liver transplantation relies on both clinical expertise and scientific advancement.

EXPLORING PHAGE THERAPY AS A SOLUTION TO ANTIMICROBIAL RESISTANCE: CURRENT LANDSCAPE, PROSPECTS, AND HURDLES

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Antimicrobial resistance poses a significant challenge in healthcare, particularly among opportunistic pathogens, which exhibit complex diagnostic hurdles and an escalating prevalence of multiple drug resistance, often leading to mixed and endogenous infections. Obligate pathogens, by contrast, present a milder concern, with early diagnosis facilitated, effective vaccines available, and limited avenues for dissemination, coupled with a lack of antimicrobial resistance.
Addressing antimicrobial resistance necessitates a multifaceted approach, including adherence to rational antimicrobial therapy principles and exploring alternative biological therapeutics such as phages. Phages offer distinct advantages over antibiotics, including lack of adverse effects, ability to penetrate and disrupt bacterial biofilms, function as self-dosing agents, adaptability to resistant strains, environmental safety, and cost-effectiveness.
There is a burgeoning interest in phage therapy globally. Western European nations are observing a steady increase in the establishment of enterprises and laboratories specifically dedicated to producing phage therapeutics.
Phage therapy employs virulent (lytic) phages, typically in cocktail formulations, and offers a broad therapeutic spectrum against various tissue purulent infections and intestinal diseases. Prior to treatment initiation, phage sensitivity testing via phage-gram is essential. Personalized phage preparations (autophages) may be employed in cases of phage resistance.
Phages are administered over 2-3 weeks, with a dosing regimen of 2-3 times daily, typically ranging from 10^5-10^8 phage particles per administration. Additionally, phages exert an indirect immune-modulating effect, augmenting their therapeutic efficacy and showcasing adjuvant and vaccine-like actions.
Large-scale technologies for endotoxin purification, notably tangential filtration, are imperative to facilitate the widespread adoption of phage therapy. Furthermore, future phage formulations should incorporate long-circulating and low-immunogenic variants to mitigate humoral immune responses.
The abundant diversity of phages in the environment ensures the availability of effective options against antimicrobial-resistant bacteria. Formally approving phage therapy and refining treatment protocols are crucial for its ongoing advancement and clinical utility.

EXPLORING THE IMPACT OF PHYSICOCHEMICAL PROPERTIES ON PHAGE IMMUNOGENICITY: A STUDY OF E. COLI PODOVIRIDAE PHAGES AND THEIR DNA

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Introduction & Objectives: Phage therapy holds promise against antimicrobial resistance. However, developing anti-phage neutralizing antibodies poses a challenge for chronic infections, limiting its long-term efficacy. To mitigate this obstacle, it is imperative to formulate phage therapeutics utilizing phages characterized by low immunogenicity. We hypothesize that physicochemical properties like size, charge, and hydrophobicity influence phage immunogenicity, aiding preliminary prediction. During therapy, phage DNA, a ligand for Pattern Recognition Receptors, accompanies phage particles, necessitating the study of its host impact.

Materials & Methods: We analyzed the hydrophobicity, charge, and hydrodynamic diameter of ten E. coli-specific Podoviridae phages. Three bacteriophages (BL-2, ECC, BS) with distinct properties were selected for immunogenicity assessment. Phage preparations underwent endotoxin purification via tangential filtration and EndoTrap. Intraperitoneal administration of each phage type in 5x10^8 PFU to CD1 outbred female mice (n=7/group) ensured endotoxin levels stayed below 0.01 EU. Blood serum collected at intervals (0-100 days) measured anti-phage IgM and IgG class antibodies via ELISA.

The impact of purified phage DNA was evaluated through intravenous injection (5 ng) in plasma samples obtained at 6, 12, 24, and 72 hours. Proinflammatory cytokine (IL-1, IL-6, IL-12, TNF α, IFN γ) levels, lipid profiles, liver enzymes, creatinine, and leukocyte count were assessed. Liver and kidney histological analysis was conducted on days 5, 10, 15, and 30.

Results: Anti-phage IgM antibody levels peaked on day 5, stabilizing thereafter. IgG antibody levels rapidly increased until day 25-30, followed by a slower rise. Notable differences in anti-phage IgG levels were observed until day 25, diminishing thereafter. Further studies should compare phages differing significantly only in each trait to minimize confounding factors. Administration of phage DNA had no impact on the examined parameters.

VITILIGO – PERSPECTIVES IN TREATMENT

Sopiko Liluashvili, Kanveni - S/R National Center of Dermatology and Venereology, head of scientific-research direction, Kutaisi University, Tbilisi, Georgia

Vitiligo is a chronic autoimmune skin disorder caused by lack of pigment melanin. Its etiology is not entirely certain, although there are known contributing factors such as: other autoimmune diseases, worn invasion, intoxication, sun exposure, iron and copper deficiency, chronic inflammatory diseases and endocrinopathies.

Vitiligo is clinically manifested as a single or multiple depigmented areas on the skin, often symmetrically or rarely asymmetrically located on the body, mainly in areas of sun exposure. Segmental, nonsegmental, mixed and unclassified forms are clinically

distinguished. Complications include the presence of other types of autoimmune diseases and severe psychological conditions.
Among the treatment methods, local and systemic treatment are distinguished. Steroids, calcineurin inhibitors and vitamin D analogs are mainly used as a local treatment. In systemic therapy are systemic steroids, cytostatics and cyclosporine. Phototherapy is actively used. Fortunately, recently there has been strong evidence for the use of topical JAK inhibitors and their high efficacy. It should be noted that there are fewer side effects and ease of use, which makes the prognosis of vitiligo much more favorable in the future.

GENETIC FACTORS IN AUTOIMMUNITY

Giorgi Loladze, Agricultural University of Georgia

The development of autoimmune diseases in animals is influenced by both environmental and genetic factors. More commonly, interactions between multiple genes and the environment contribute to autoimmunity. Possessing several common risk gene variants collectively increases susceptibility. Notably, autoimmune diseases often result from MHC gene interactions. MHC molecules play a crucial role in antigen presentation and immune responsiveness.

Genetic predisposition plays a crucial role in autoimmunity. There are numerous loci associated with autoimmune risk. These shared loci may reveal common pathways, but their effects are often small. For instance: In mice, over 25 gene loci contribute to autoimmunity, including those related to cytokines, apoptosis, and antigen clearance. Some diseases result from single gene defects, while others involve complex interactions.

Breed predisposition is one important topic to discuss, as we know dogs are descended from wolves. This process was achived by inbreeding and loss of genetic diversity which caused certain types of autoimmune diseases in animals.

Monogenic Diseases - specific gene mutations encoding crucial regulatory proteins can trigger autoimmune diseases. For example - AIRE mutations leading to autoimmune polysystemic syndrome-1. Sex Hormones and Autoimmunity is an important factor. Estrogen and prolactin promote B-cell proliferation, while testosterone has the opposite effect.

In conclusion, Autoimmunity results from complex interactions between genetic predisposition and environmental factors. Genome-wide studies identify multiple risk loci, often with small effects. Breed predisposition highlights the impact of genetic diversity loss. Monogenic diseases and sex hormone influence play roles, with certain gene mutations triggering specific conditions.

WHOLE BLOOD CELL COUNT DERIVED BIOMARKERS OF THYROID DYSFUNCTIONS ASSOCIATED WITH THE TREATMENT OF NON-SMALL CELL LUNG CANCER AND CERVICAL CANCER WITH IMMUNE CHECKPOINT INHIBITORS

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BACKGROUND: Treatment with immune checkpoint inhibitors (ICIs) for advanced malignancies has been associated with developing immunerelated adverse events (irAEs) severe enough to require the cessation of life-saving tumor immunotherapy.
OBJECTIVES: The present study aimed to identify predictive inflammatory markers of the development of immune-related thyroid dysfunctions
in patients with cervical cancer (CC) and non–small cell lung cancer (NSCLC) treated by ICIs.
METHODS: A retrospective study was conducted on twenty-seven patients with CC and NSCLC treated by ICIs. The data were collected before and 12 weeks after treatment. Complete blood count-derived inflammatory markers: dNLR (derived neutrophil to lymphocyte ratio),

NLR (neutrophil to lymphocyte ratio), SSI (systemic inflammation index), PLR (platelet to lymphocyte ratio), WHR (white blood cells to hemoglobin ratio) were calculated. In addition, thyroid functional tests were collected. Data statistical analysis was performed by STATISTICA (Stat soft, Inc, USA).
RESULTS: Five patients out of twenty-seven with CC treated by PD-1 and CTLA-4 inhibitors who developed hypothyroidism showed significantly high baseline PLR and low WHR compared to patients without clinical symptoms of hypothyroidism and reference levels TSH and FT4. Association between NLR, dNLR, SSI, and thyroid dysfunction was not observed.
CONCLUSIONS: Our findings show a strong correlation between hypothyroidism and WHR and PLR biomarkers. As a result, using these biomarkers for early identification of hypothyroidism helps treat thyroid dysfunction and improves cancer immunotherapy outcomes.
KEYWORDS: Hypothyroidism; immune checkpoint inhibitors; inflammatory markers; platelet/lymphocyte ratio; white blood cell/lymphocyte
ratio.

ALLERGEN-SPECIFIC IMMUNOTHERAPY MECHANISMS, STAGES OF DEVELOPMENT AND FUTURE PERSPECTIVES

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Allergen-specific immunotherapy (AIT) is considered one of the leading directions in its influence on the course of allergic diseases. The main goal of AIT is to reduce the symptoms caused by the allergen and prolong the remission of the disease. It is the only identified disease-modifying intervention for allergic diseases, developing both rapid de(hypo)sensitization and subsequent allergen-specific immune tolerance and suppression of allergic inflammation in damaged tissues. AIT is considered the only treatment option capable of inducing cure and long-term tolerance even after cessation of therapy. It was first used in 1911 and later took a special place in allergy practice as "subcutaneous immunotherapy" (SCIT). AIT has undergone significant changes to address issues of standardization, effectiveness, safety, duration of treatment, and cost.

Although modern research confirms the effectiveness of SCIT for bronchial asthma and rhinitis, an alternative method, sublingual immunotherapy (SLIT), has been increasingly used over the past 20 years.

Safety of SLIT. Original, replicative, and secondary studies conducted in this direction cannot prove the feasibility of routine implementation To date, there is insufficient evidence in the medical literature regarding the effectiveness and of sublingual immunotherapy in medical practice.

We conducted a prospective cohort study to evaluate the efficacy, safety, and cost-effectiveness of SLIT. Patients included in the study (patients with polysensitization to seasonal and non-seasonal allergens, allergic rhinitis, and asthma, aged 6-60 years, both sexes) were divided into two parallel groups (active/test and control). Patients in the active group received SLIT therapy for at least 18 months with three 6-month periods.

The results of our study revealed sufficient arguments to consider SLIT as a promising, albeit non-standard approach to the treatment and prevention of allergic rhinitis and asthma.

EPIDEMIOLOGY, CLINIC AND OUTCOME OF MULTISYSTEM INFLAMMATORY SYNDROME (MIS-C) IN GEORGIA

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Aim of the study was to assess the clinical and lab characteristics and outcomes of MIS-C in Georgia. The study comprised 126 children with MIS-C admitted to Iashvilichildren's central hospital from December 2020 to February2024. Data were obtained from medical record retrospectively.

For today, 126 cases have been diagnosed in our hospital, about 200 throughout Georgia, Concurrently, the most common presenting symptoms include fever (100%), gastrointestinal (GI) symptoms (86%), cardiac symptoms (66%), rash (48.1%), respiratory (39%) and neurological (28%) symptoms.The average duration of fever was observed to be 8,5 days, ranging from 4 to 12 days. Shock and/or hypotension were common occurrences among patients with MIS-C(24%). In total, 38.7% of the patients admitted to pediatric intensive care unit and 19.3% received vasopressor support. 20% of patient had depressed left ventricular ejection fraction. Cardiac symptoms (69%) predominated over respiratory (40%) and neurological (32%) symptoms. Admission lab findings - elevated CRP -99.8%, procalcitonine-97.1%, erythrocyte sedimentation rate-98%, D-dimer-98.8% and ferritin-78%; Lymphopenia-98.9%, neutrophilia - 96% and hypoalbuminemia 40.3%. High level of 38% received IV Intravenous immunoglobulin, 98.2% - corticosteroids; Anakinra was not used in our clinic. Median duration of hospital length of stay was 14.5 days. Comorbidities were present in 1.1% of the patients. No mortality was recorded. While being rare MIS-C has very severe presentation that need early recognition and aggressive treatment. The increasing number of MIS-C cases shows that this phenomenon is more common than was thought at the beginning of pandemic. Here is not enough evidence about the long-term consequences yet and we conduct monitoring and evaluation of patients in dynamics.

Keywords: COVID-19; SARS-CoV2; children; multisystem inflammatory syndrome in children (MIS-C).

DIAGNOSIS AND MANAGEMENT OF COPD EXACERBATIONS IN INPATIENT SETTINGS

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Introduction: In this presentation we discuss COPD exacerbations, explore their prevalence, diagnostic challenges, and the latest treatment strategies that is pressing concern in healthcare today.
Objective: To inform healthcare providers about COPD exacerbation management, covering diagnosis, comorbidities, and treatment options.
Content: We discuss the growing prevalence of COPD and the over and underdiagnoses it often faces, also covers nuances of COPD exacerbations, including their frequency and diagnostic intricacies. We place emphasis on recognizing comorbidities and their impact on exacerbation frequency and management, treatment strategies, incorporating both pharmacological and non-pharmacological interventions to optimize patient care.
Conclusion: By understanding the complexities of COPD exacerbations and implementing tailored treatment approaches, healthcare providers can improve patient outcomes and alleviate the burden of this condition.

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) ASSOCIATED WITH COVID-19: THE CLINICAL AND LAB CHARACTERISTICS AND OUTCOMES OF MIS-C IN GEORGIA

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During pandemic COVID-19 in majority of children presented less severe phenotype, multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2 subsequently evolved as a post-infectious inflammatory condition associated with severe clinical deterioration and multi organ involvement.

Aim of the study was to assess the clinical and lab characteristics and outcomes of MIS-C in Georgia. The study comprised 126 children with MIS-C admitted to Iashvili children's central hospital , from December 2020 to February 2024. Data were obtained from medical record retrospectively. 54.2% of patients were male. Median age of patients was 8.5 (1-17) years. The most common presenting symptoms were - fever (100%), gastrointestinal (GI) (68%), rash (48.1%) and vomiting (46%) were. Average fever duration was 8,5 (4 -12) days. Shock and/or hypotension were common in patients with MIS-C (24%). In total, 38.7% of the patients admitted to pediatric intensive care unit and 19.3% received vasopressor support. 20% of patient had depressed left ventricular ejection fraction. Cardiac symptoms (69%) predominated over respiratory (40%) and neurological (32%) symptoms. Admission lab findings - elevated CRP -99.8%, procalcitonine-97.1%, erythrocyte sedimentation rate-98%, D-dimer-98.8% and ferritin-78%; Lymphopenia-98.9%, neutrophilia - 96% and hypoalbuminemia 40.3%.

All of the MIS-C patients reported in our study have received standardized treatment courses with steroids, intravenous immune globulin (IVIG), or IVIG combined with steroids, each patient's illness has resolved without any sequelae. 38% received IV Intravenous immunoglobulin, 98.2% - corticosteroids. Anakinra was not used in our clinic. Median duration of hospital length of stay was 14.5 days. Comorbidities were present in 1.1% of the patients. No mortality was recorded. While being rare MIS-C has very severe presentation that need early recognition and aggressive treatment. The increasing number of MIS-C cases showed that this phenomenon is more common than was thought at the beginning of pandemic. Here is not enough evidence about the long-term consequences yet and we conduct monitoring and evaluation of patients in dynamics.

Keywords: Kawasaki disease, Pediatrics, Hyperinflammation, Multisystem inflammatory syndrome in children (MIS-C), SARS-CoV2.

ACNE - HOW OUR VIEWS HAVE CHANGED

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Acne is one of the most common chronic skin diseases and affects adolescents of both sexes with equal frequency. However, it is a universal condition and can occur at any age. In the last period, the so-called Late acne has become more frequent, affecting almost 40% of adult women.
In recent years, our knowledge of the pathogenesis of acne has improved significantly due to intensive research. According to the modern concept, acne is an Androgen-dependent disease of the pilosebaceous unit, in which the activation of the immune response and the development of inflammation are caused by hyperseborrhea, changes in the composition of sebum, dysbiosis between skin commensal microbes (and not an increase in the number of C acne, as previously thought). It

turned out that a specific phylotype C-acne (IA1) plays an important role in pathogenesis.
Although the disease is not considered life-threatening, it significantly reduces a person's quality of life, self-esteem, and can leave live long physical or psychological scars.
At a certain age (from 1 year to 7 years), when the level of androgens should be at the lowest, the development of acne can be considered a signal of endocrine disorders with hyperproduction of androgens (early adrenarche, adrenal hyperandrogenism, androgen-secreting tumor), which requires consultation of pediatric endocrinologist. It is important to identify signs in children that predict severe disease in adulthood and require timely and relatively aggressive treatment.
A modern approach to acne treatment involves a combination of local, systemic and procedural methods, the use of appropriate skin care products, restoration of normal skin microbiota, taking into account patient expectations, maximum abstinence from antibiotic therapy, the use of active substances that act on several pathogenic mechanisms simultaneously, prevention and treatment of post-acne scars and spots. In cooperation with the patient all this makes it possible to obtain an ideal result.
This report will outline modern views on the pathogenesis and treatment of acne, as well as own long-term clinical experience in treating acne patients.

IDIOPATHIC THROMBOCYTOPENIC PURPURA AND ROLE OF THROMBOPOIETIN-RECEPTOR AGONISTS IN THE PEDIATRIC PRACTICE OF HEMATOLOGISTS.

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Background: Idiopathic thrombocytopenic purpura (ITP, also called immune thrombocytopenic purpura) is an acquired disorder in which there is immune-mediated destruction of platelets and possibly inhibition of platelet release from the megakaryocyte. Treatments of ITP continue to challenge medical doctors because of a lack of well-tolerated and effective drugs. Children who develop chronic ITP may benefit from splenectomy. Immunosuppressive therapy with glucocorticoid drugs and intravenous immunoglobulin is the classical initial treatment for ITP. A novel class of thrombopoietin agonists has recently been developed. Eltrombopag is an oral thrombopoietin-receptor agonist that stimulates thrombopoiesis, increasing platelet production. Eltrombopag produced a very outstanding response in adult and pediatric patients with severe chronic ITP.
Methods: From M. Iashvili Central Pediatric Clinic (Tbilisi, Georgia) with the hematology and oncology department, we analyze 5 patients, suitable according to the study criteria. The study aims to evaluate the clinical and laboratory manifestations. Additionally, we discuss the best way of treatment.
Results: We built charts showing that the median age of our five patients is 11 years. They all have chronic idiopathic thrombocytopenic purpura and platelet counts of less than 30,000 per microliter of blood. All patients have been hospitalized several times in Iashvili Central Pediatric Clinic and have received standard treatments. Two of them have had splenectomy. However, after reducing the dose or stopping the treatment, the relapse occurred soon. In three of them COVID-19, Helicobacter, and Staphylococcus exacerbated ITP. Along with other basic drugs, they were prescribed Eltrombopag 50 mg per day. In 4 patients, the number of platelets increased after taking the drug. Only one patient is resistant to this medication. It responds only to intravenous immunoglobulin. Side effects of Eltrombopag were not detected in the patients studied by us.
Conclusion: The results of our study show that Eltrombopag is well tolerated in raising platelet counts in patients. Additionally, Eltombopag is an effective treatment option for pediatric patients with chronic ITP and who have an increased risk of bleeding.

ANTIBACTERIAL TREATMENT ALTERNATIVES STUDIES IN CLL PATIENTS

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Introduction: Chronic lymphocytic leukemia (CLL) is an oncohematological disease characterized by accumulation of a large number of lymphocytes in the central and peripheral lymphatic organs and tissues that results in decline of humoral and cellular immunity and development of opportunistic infections, the most common cause of death for CLL patients. The identification of infectious agents and effective methods of their elimination is one of the key aspects of CLL patient's therapy. Antibiotic treatment still remains one of the main approaches, but nowadays, selection of an effective antimicrobial drug is problematic because of increased antibiotic resistance. Phage therapy is considered as a promising, safe alternative to antibiotics, although it's potential for treatment or prevention of bacterial infections in patients with CLL hasn't been investigated.

The aim of the study was to identify opportunistic infectious agents and their antibiotic and phage sensitivity in patients with CLL. Additionally, we aimed to detect anti-phage natural antibodies that could potentially hinder phage effectiveness.

Research methodology: Swabs from the nasopharynx of 20 CLL patients (both-males and females, age 60- 67) were subjected to standard bacteriological analysis, through primary 4 quadrant striking on SBA and TSA plates followed by sub-culturing of developed colonies on a number of selective- differential media. The phenotypic identification was done using API test systems (bioMerieux, France). Antibiotic sensitivity was studied by Kirby-Bauer disc-diffusion method according to the EUCAST standards, and phage susceptibility (6 commercial phages, produced by Eliava Biopreparations) - by Spot-Test technique. The control group comprised 6 healthy donors matched for age and gender parameters with the study group. The presence of anti-phage antibodies in the sera of CLL patients was examined via EIA using Sigma-Aldrich reagents. The control group for this study comprised healthy donors matched for age and gender parameters.

Results: A total of 46 bacterial strains were collected from 40 nasopharyngeal swabs of CLL patients and identified at species level. Among these, 37 strains were classified as opportunistic pathogens such as P.luteola; S.epidermidis; S. salivarius; S. lentus; S. capitis; S. warneri; S. hominis; S. xylosus; S. heamolyticus; S.saprophyticus; S. cohnii spp; Kocuria varians/rosea; A.viridans; B.subtilis, while 9 were identified as pathogens (S.aureus, E.coli). The antibiotic sensitivity testing involved the following antibacterial drug groups: tetracyclines, glycopeptides, oxazolidinones, cephalosporins, fluoroquinolones and aminoglycosides. Our study indicated that the most effective antibiotics against isolated pathogenic agents (S.aureus; E.coli) were tetracyclines, fluoroquinolones, and aminoglycosides (susceptibility range – 89- 100 %). For the isolates of opportunistic flora (P.luteola; S.epidermidis; S. salivarius; S. lentus; S. capitis; S. warneri; S. hominis; S. xylosus; S. heamolyticus; S. saprophyticus; S. cohnii spp; Kocuria varians/rosea; A.viridans; B.subtilis) the promising susceptibility was shown towards all antibiotic groups (≥56% susceptibility), with the higher efficacy of oxazolidinones (86%). However, for pathogenic agents (S.aureus; E.coli), high resistance (up to 100%) to glycopeptides was registered while susceptibility to other antibiotic classes remained high. None of the commercial phages exhibited activity against the isolated strains, prompting an investigation into natural anti-phage antibodies in CLL patients' sera. Our study revealed that the titers of natural anti-phage antibodies were significantly high in CLL patients' sera, rendering phage treatment ineffective with standard commercial phages.

Conclusions: Study results showed the possibility for elimination of bacterial colonization in CLL patients by rational use of antibiotics. At the same time it became clear that in case of need a customized phage treatment of CLL patients, it can be done through selection of active phages (monophages, or mixtures) from the Eliava Institute's collection and preparing

autophages, since the standard commercial phages, cannot replace antibiotic treatment for the effective elimination of infectious agents in CLL patients.

GROUP ANTIGENS AS A PERIPHERAL BIOMARKERS AND THEIR POTENTIAL ROLE IN THE DEVELOPMENT OF INFECTIOUS AND NON-INFECTIOUS DISEASES

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Group antigens are placed on the surface of erythrocytes and determine the phenotypic characteristics of a person. There is a lot of scientific literature, where the possible association of these antigens with various types of diseases is experimentally substantiated. On the basis of the laboratory of immunogenetics of Batumi State University, the characteristics of the distribution of the mentioned antigens throughout the region were studied, which were used as a model option to study their possible association with infectious and non-infectious diseases. We have studied possible associations with such infectious diseases as a viral hepatitis, covid 19 infection, pulmonary tuberculosis. Possible correlations with various types of tumors, diabetes, cardiovascular system and autoimmune diseases are also studied. During the study, the susceptible and resistant phenotypes and the risk factors for disease severity were identified.

BIOLOGICS FOR THE TREATMENT OF PSORIASIS – RECOMMENDATIONS FROM BRITISH ASSOCIATION OF DERMATOLOGISTS

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"Biologics'' are the protein-based drugs derived from living cells, and are designed to target specific areas of the immune system that are over-active in psoriasis, including tumor necrosis factor (TNF) and interleukins (IL) 17 and 23. There are now 11 licensed and NICE-approved biologics for use in psoriasis. This 2020 evidence-based guideline has been developed by a multi-stakeholder guideline group with the British Association of Dermatologists, and provides recommendations on how to use these important drugs effectively and safely to maximize patient benefit.
When deciding which biologic to use, clinicians are asked to consider the person's psoriasis, other medical problems, patient preferences and drug cost. The guideline covers all the new as well as the older biologics, use in children and special groups (history of), and new recommendations on what do when treatment fails, when to increase the dose of biologics and preferred options for conception, pregnancy and breastfeeding. To help ensure guideline recommendations are put into practice, the guideline group have also developed an implementation "tool kit". This includes a decision-aid, which has been designed to help explain the similarities and differences between the different agents and to support clinicians and patients when deciding which biologic is most appropriate and to help minimize problems when taking these drugs.

PRIMARY IMMUNODEFICIENCIES IN GEORGIA. CURRENT SITUATION

Karaman Pagava, Temuri Mikeladze, Tbilisi State Medical University

The lecture presents modern views on primary immunodeficiencies (definition, classification, diagnosis, management). It is emphasized that this group of diseases includes cellular and humoral immunodeficiencies, combined immunodeficiencies with associated syndromes, primarily antibody deficiencies, immune dysregulation syndromes, phagocytosis disorders, innate immune disorders, complement deficiencies and also auto-inflammatory disorders.

Currently, a study is being conducted with the Molecular Medicine Research Center Primax (Tbilisi) and ViennaLabDiagnostics (Vienna, Austria) to create a registry of patients with familial Mediterranean fever (the registry already includes more than 200 patients), a study is also underway to create a registry of patients with other primary immunodeficiencies (so far it includes 11 genetically confirmed cases).
In order to raise the level of awareness of primary immunodeficiencies in Georgia, special conferences are held (6 conferences have already been held) within the framework of the J project. At the international level, the J project publications with the participation of Georgian authors serve the same purpose (Front Immunol. 2022, J Clin Immunol. 2020, 2022).

PSYCHODERMATOLOGY – INTERACTION BETWEEN THE MIND AND THE SKIN

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Psychodermatology is science about interaction between mind and skin. Patients may have many types of mental disorders which are manifested by various, unpleasant sensations on the skin. Although it is a mental illness, patients with a similar diagnosis usually go to a dermatologist because they are convinced that they have a skin problem.
For example, delusional disorder in dermatology is one of those health states where observation, patience and correct management are required not only to treat the patient, but also to assess the behavior of his/her family members, as the "Folie a Deux" phenomenon is not so rare.
Among approximately one third of dermatological patients, effective management of the skin diseases involves taking into account psychological factors related to it. Management of such patients requires caution so that they do not lose trust in doctors (as a rule, such patients have a bad experience of communication with doctors due to the fact that doctors do not take their complaints seriously) and in the future receive the treatment they need without any doubts.
We have to remember that the dermatologist can be the only doctor from whom the patient will receive recommendations and follow them.

TRICHOLOGICAL MANIFESTATIONS OF OBSESSIVE-COMPULSIVE DISORDER

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Trichotillomania is a constant desire of removing hair from the scalp and from different parts of the body. Trichotillomania often begins in childhood, although it can occur in any age group. Different mental disorders, such as depression, multiple types of addictions, and other problems, can aggravate trichotillomania, so it is important to know the conditions in order to be able to properly manage the disease. Trichotillomania is diagnosed mainly as a result of trichoscopic examination. The characteristic signs of trichotillomania are revealed with the help of the above-mentioned research, which allows us to make a differential diagnosis with such alopecia as, for example, Alopecia Areata. In such cases, it is fundamentally important to diagnose trichotillomania in order to carry out the correct treatment and avoid complications. When diagnosed with trichotillomania, it is very important to properly inform the patient/patient's family and explain the role of mental health in this situation. Trichotillomania is a diagnosis that, if left without attention, can lead to such a complicated condition as bezoars and require surgical intervention.

POLYCLONAL IMMUNOGLOBULIN FOR TREATMENT OF COMPLICATED STAPHYLOCOCCAL INFECTION

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The aim of the Project is to obtain a anti-staphylococcal polyclonal immunoglobulin with high therapeutic (healing) properties, and the Laboratory and Experimental study thereof. The works and studies to develop immunoglobulin were including the following: selection of Staphylococci, Immunogens – alpha-anatoxin, receiving of PV-leukocidin, hyaluronidase and determining an activity; Immunization of Producer animals (goats) with immunogens; reception of hyperimmune serum and release of immunoglobulin fraction; enzymatic processing of antibodies to obtain a harmless medicine (preparation); received final product controls. 30 strains having the stable characteristics were selected out of 102 strains gathered from Tbilisi and Kutaisi Clinics. (Staphylococcus aures -24, Staphylococcus epidermidis -6). In order to obtain immune serum, the producer animals, have been vaccinated according to a pre-developed Immunization Schedule, with increasing doses of immunogens, with the addition of adjuvants. In the normal (K), immune serum and immunoglobulin we have determined the protective Antibody Titer. For this purpose, we have used hemolysis reaction (Lh), passive hemagglutination test (using dry diagnostic test systems), Immunoenzymatic analysis ("Sandwich-ELISA" method). Antibody titer in immune preparations in hemolysis reaction to alpha-toxin it was 150 IU/ml, in normal serum -0.5-1.0 IU/ml;

The titer of Antibacterial Antibodies in the passive hemagglutination reaction was found to be as - 1:6400 - 1:12800, of the anti-leukocidin antibodies - 1:640-1:1280, and for hyaluronidase - 1:160-1:320, the titer of the same antibodies in normal serum ranged from 1:10 to 1:40.

These antibodies were determined by immunoenzymatic method in the analysis. Medium values of normal serum against alpha-toxin was 0.081; The index of positivity to the same toxin in immune serum amounted to 10.08; The index of positivity of antibacterial antibodies was equal to 9.2517. PV-leukocidin positivity index -4.3968, and hyaluronidase -0.9214. To remove anaphylactogenic Fc fragments from antibody molecules, we used enzyme (Pepsin) treatment with a special kit ,,PierceTM Fab Preparation Kit, USA".

The medicine (preparation) tested in accordance with the requirements of the European Pharmacopoeia was found to be sterile, non-toxic, reactogenic, stable, non-pyrogenic. Purified immunoglobulin 5 IU/ml -0.5 ml subcutaneous injection protected 91.7% of white mice from an unconditionally lethal (Dcl) dose of pathogenic staphylococcus. Mortality in animals under the control amounted to 100%.

Thus, a harmless medicine (preparation) with high healing properties have been obtained - Antistaphylococcal purified Polyclonal Immunoglobulin.

This work was supported by Shota Rustaveli National Science Foundation of Georgia, Grant #AR-18-306: "Development of Policlonal Immunoglobulin for the Treatment of the Complicated Staphylococcal Infections".

DEFICIENCY OF COMPLETE NUTRITIONAL MICRONUTRIENTS, DISEASE PREVENTION.

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Introduction: The World Health Organization systematically makes recommendations for the need for a complete, balanced diet for children in order to prevent their normal growth, development and disease in children. Considering all age incisions.
The aim of our study is (2019-2021) to strengthen the monitoring of micronutrient deficiencies in the nutrition of 986 children aged 1 day to 16 years of age in children.
Research objectives: We developed the target groups: children from 1 day to 2 years of age (354 children) (145 girls and 209 boys), school children (632 children, 256 girls and 367 boys). 3 nutritional indicators were selected: iron, iodine, and folate.
The results of the study: - It was found that out of 589 children from 1 day to 6 years from whom blood was taken from a vein for ferritin testing - 35.7% were anemic, and 64.3% were without anemia and from 397 children (from 7 to 16 years) from whom blood was taken from a vein For ferritin and folate tests, 43.2% had anemia and 56.8% had no anemia. Based on the results of the research, a recommendation was issued; Improving the promotion of exclusive breastfeeding during the first 6 months of life. Many adequate steps are still needed as it is still a problem to continue breastfeeding after 3 months of age; Getting a product Fe in I and other essential micronutrients and vitamins for children, a study based on medical practice over the last 2 years - on the example of 986 patients. Deficiency of essential nutrients in children - 0-16 years.
Conclusion: Observations have shown that iron deficiency anemia, vitamin D and calcium deficiency are still a significant problem. Especially during the pandemic period.
Key words: Children, Iron, Iodine, Fluoride, D-vitamin

TSKALTUBO RESORT, ITS MINERAL SPRINGS AND OUTSTANDING PEOPLE - OTARI SHAVIANIDZE (1926-1999)

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Tskaltubo is one of the ancient resorts. It is mentioned in 1245 in the charter of the Gelati monastery. Therefore, we must assume that the resort has a 1000-year history.
Tskaltubo located is in the Colchis plain 100 meters above sea level. The resort has a terraced layout. In the center there is a balneological zone where mineral springs are concentrated. Tskaltubo mineral springs do not contain toxic or potent substances, which is, of course, their advantage.
Of the physical properties of water, the most important is high flow rate and natural temperature. Flow rate is 15-18 million liters per day. Because of this, a special treatment method is used in Tskaltubo – a flow bath. The water temperature is 33-34 degrees, the acid-base balance is 7,2, water mineralization is 0,8 g/l. Water contains 6 ions – natrium, calcium, magnesium, bicarbonate, sulfate, and chlorine. Water also contains gases- nitrogen, radon, argon, and helium. In addition, the water contains biologically active microelements iodine, zinc, lithium, bromine, manganese, and silica. Based on the above, the method of treatment with Tskaltubo mineral baths is determined by a 20-day course of treatment, 20 -minute baths, 20-25 baths rep course. Tskaltubo mineral baths have a wide range of effects, they have a beneficial effect on cardiovascular, musculoskeletal, diseases of the peripheral and central nervous system, skin, gynecological and endocrine diseases.
One of the outstanding figures at the Tskaltubo resort was Otari Shavianidze who made a significant contribution to the development of the resort. He was born in 1926. In 1948 he graduated from the Tbilisi state medical institute. Worked as director of the Scientific Research Institute of Balneology and Physiotherapy for 30 years.
Candidate of medical sciences, academic Doctor of Medicine, professor, senior researcher, doctor of the highest category, published more then 180 scientific papers, 10 monographs, numerous articles in magazines and newspapers. His monographs include “Tskaltubo”, “Tskaltubo children resort”, “Tskaltubo – 1000 years” and others.
He was the first in world literature to study the effect of Tskaltubo mineral baths on tumors and

proved the stimulating effect. He was also the first to develop differential treatment for children at the resort.
His works are fundamental in the field of pediatrics. He is considered the founder of children balneology.

BASOSQUAMOUS CARCINOMA – A RARE METATYPICAL VARIANT OF BCC

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Introduction: Basosquamous carcinoma (BSC), also called metatypical basal cell carcinoma, is an uncommon and malignant subtype of non-melanoma skin cancer. It has features that are halfway between basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). BSC currently represents approximately 2% of all non-melanoma skin malignancies and is predominant in men. It generally affects elderly or older adults; some cases may rarely develop in children too. Clinical manifestations may be a plaque, papule, or nodule with an ulcerating potential, especially on the head and neck or in other sun-exposed areas. Probably due to its very rare occurrence, data on pathogenesis, course and treatment are inconsistent. BSC may behave aggressively, with a propensity for local recurrence and a potential risk for distant metastatic spread. Differential diagnosis includes SCC, BCC, Merkel cell carcinoma, amelanotic melanoma, actinic keratosis.
Case description: We present 73 years' male patient with asymptomatic, solitary, scaly, pink papule on his forearm, measuring 0,5X0,4 cm. The skin rash had developed about one year ago, slow growth was observed. Dermoscopic features were arborizing vessels, keratin masses, white structureless areas, superficial scale and blood spots in keratin masses. The patient was referred to an oncologist with a preliminary diagnosis: Basosquamous carcinoma. A wide excision of the tumor was performed. Histological analysis with hematoxylin and eosin (H and E) stained slides revealed multiple islands of atypical keratinocytes throughout the dermis, exhibiting both basaloid and squamous differentiation. Immunohistochemical (IHC) analysis with p63 and CK5/6 confirmed the diagnosis of a basosquamous carcinoma.
Conclusion: In the differential diagnosis of pink lesions on sun-exposed areas of the body, it is important to consider a rare and aggressive variant of BCC, basosquamous carcinoma, which both dermoscopic and histopathological findings exhibit features of both BCC and SCC. It is vital to appreciate the importance of early resection with free margins, a full workup for lymph node and distant metastases, and a regular follow up to detect a disease recurrence.

AUTOIMMUNE EYE DISEASES

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Autoimmune eye diseases are conditions where the body's immune system mistakenly attacks eye tissues, causing inflammation and vision problems. This abstract provides a simplified overview of these diseases, including how they develop, how doctors diagnose them, and the available treatments.
These conditions occur when the immune system malfunctions and targets parts of the eye like the uvea, retina, or cornea. Factors like genetics and environmental triggers can contribute to their onset. Common autoimmune eye diseases include chronic superficial keratitis, uveitis, uveodermatologic syndrome.
Symptoms vary but often include eye pain, redness, sensitivity to light, and blurred vision. Diagnosis involves eye exams and sometimes additional tests like scans or blood work.
Treatment aims to reduce inflammation and protect vision. Options range from eye drops and pills to more specialized therapies like immunomodulatory drugs or surgery in severe cases.
In conclusion, while autoimmune eye diseases present challenges, advancements in understanding and treatment offer hope for better outcomes and improved quality of life for affected individuals.

DIGITAL TRANSFORMATION IN UNDERSTANDING AND MANAGING OF IMMUNE MEDIATED DISORDERS - BENEFITS AND CHALLENGES

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Exploring the pathogenesis of immune diseases is a critical task for their therapeutic management. Effective monitoring of immunopathological mechanisms in an individual patient is crucial for accurate diagnosis and the selection of personalized treatment strategy. In recent years, personalized treatment approaches have been the main focus of pharmaceutical companies and clinics worldwide. However, the experimental research for such investigations requires expensive experimental bases and long research processes, that entails a heavy economic burden on the country. Therefore, an innovative approach is to create the mathematical models of immunopathogenesis and immunotherapy. Such models serve as alternatives to experimental biomedicine and allow for the theoretical determination of disease dynamics and treatment outcomes.
Our interdisciplinary team of immunologists and applied mathematicians developed mathematical models of the immunopathogenesis and treatments of widespread immune mediated disorders. These models are based on non-linear differential equations, with variables reflecting the dynamics of measurable immune parameters over time during the progression of the disease and the course of its treatment. The creation of corresponding computer programs is also addressed by our team. The mathematical and computer models are regularly tested with real patient data and evaluated for their challenges and benefits. As a result, such models, representing a digital transformation in the understanding and managing of immune-mediated disorders, contribute to the creation of new knowledge and technological products in a competitive interdisciplinary direction.

MATHEMATICAL MODELING OF T LYMPHOCYTE CROSS-TALK IN RHEUMATOID ARTHRITIS

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Rheumatoid arthritis is a systemic autoimmune disease characterized by the joint inflammation and the cartilage destruction. Autoreactive B lymphocytes represent integral elements of the pathophysiology of rheumatoid arthritis. Immune balance between the effector and the regulatory T cell subsets guide the production of autoantibodies by B lymphocytes and, therefore, play a cardinal role in disease severity. Mathematical models of immune mediated disorders provide an analytic framework in which we can address specific questions concerning disease immune dynamics to dictate the choice of treatment. Herein, we present a novel mathematical model that describes the immunopathogenesis of rheumatoid arthritis using non-linear differential equations. The model explores the functional dynamics of cartilage destruction during disease progression, in which a system of differential equations deciphers the interactions between autoreactive B lymphocytes and T helper cells. Moreover, immunomodulatory effects of IL-6 that deviates the fate of T cells towards pro-inflammatory vs. regulatory subsets is also solved in these equations. In conclusion, we propose a novel mathematical model that best describes the immunopathogenic cross-talk of T lymphocytes in patients with rheumatoid arthritis and, therefore, may take a rapid pace towards its individualized testing schemes.

MATHEMATICAL MODELING OF TREATMENT OF RHEUMATOID ARTHRITIS WITH METHOTREXATE AND TOCILIZUMAB

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Mathematical models of immune mediated disorders provide a platform in which we can address specific treatment choice in the vast personalized manner. Our interdisciplinary research team has created a mathematical model of rheumatoid arthritis, which determines the level of cartilage damage in the patient and, accordingly, the progression of rheumatoid arthritis over time with a system of equations that calculates the interaction variables between B and T lymphocytes. Inter-relation between different CD4+ T lymphocyte subsets is also solved in this model. The proposed mathematical model is a nonlinear system of ordinary differential equations and describes immunopathogenic dynamics in patients with rheumatoid arthritis. As part of the further tasks, based on the mathematical model of the pathogenesis of the disease, again using non-linear differential equations, we created a mathematical model of disease treatment. In this novel model features of treatment with methotrexate and tocilizumab in a separate or combined scheme are taken into account as variables. In conclusion, we propose a novel mathematical model that best describes the readouts on the treatment outcomes in patients with rheumatoid arthritis and, therefore, may take a rapid pace towards its implementation in biomedical and clinical research.

COMPUTER MODELING OF AUTOIMMUNITY AND ITS TREATMENT

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Computer models of immune mediated disorders provide an analytic framework in which the specific questions concerning the disease immune components and the management strategies are addressed. We have developed the mathematical models of autoimmune diseases using non-linear differential equations which accurately decipher the interactions of immune cells and their soluble mediators in the pathogenic process. Disease management using diverse treatment options is also explained in these models. Herein, we present a novel computer model that describes the dynamics of T helper and T regulatory cells subsets in the pathogenesis and treatments of autoimmune arthritis. The model explores the functional polarization of opposite T cell fates based of IL-6 value. The interaction of T and B lymphocytes is also reflected in the present model. Of importance, our model provides a mechanistic interpretation of a real patient data and the disease intervention options.

ARTIFICIAL INTELLIGENCE IN THE MEDICAL FIELD: DIAGNOSTIC CAPABILITIES OF GPT-4 IN COMPARISON WITH PHYSICIANS

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GPT-4 is an extensive language model designed to understand and generate human-like text, with the ability to accomplish complex tasks such as data analysis and decision-making. This study aimed to evaluate the effectiveness of GPT-4 in making medical diagnoses comparable with those of experienced physicians across various medical specialties.
We conducted a retrospective observational study, which involved preprocessing 340 clinical cases, the contents of which included medical history, physical findings, laboratory, and instrumental data. We provided this information to GPT-4, which was instructed to give us the top five most likely differential diagnoses. The discrepancies between AI's five differentials and the physician's final

diagnosis were analyzed regarding different specialties and laboratory/instrument data inclusion. Before we integrated laboratory data, GPT-4 showed a 60% diagnostic match with physicians on the first differential and 86% in all five. After we integrated the instrumental and laboratory findings, these percentages grew to 72% and 92%, respectively. The integration of laboratory and instrumental data increased GPT-4's diagnostic accuracy, evidenced by an odds ratio factor of 2.1 and McNemar's test chi-squared value of 10.76, highlighting the substantial impact of this data on AI's diagnostic precision.
This study highlighted the potential of using GPT-4 in medical diagnostics, provided a basis for integrating AI tools with clinical judgment, and opened avenues for future research, particularly in developing AI models tailored to the diagnostic needs of different medical fields.

UNG-ABSCESSES-IN-CHILDREN

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Pulmonary infections continue to be a leading cause of morbidity and mortality in children. This was due to the advances in radiological imaging in recent years and the emergence of new lung infections. The clinical picture of diseases and the results of treatment have changed. Thus, we considered it necessary to evaluate the updated results on this topic. In this review article, we will discuss the complicated forms of lung infections in children, in particular, several cases of rare forms of pneumonia with a destructive process. which are caused by new pathogens - coronavirus disease, as well as bacterial and parasitic infections. We will introduce you to the current stages of the abscess process and visualization findings based on the data of our clinic.

Lung abscess is a localized volumetric formation of pus in the lung. It is often difficult to control and treat, and in some cases can be life-threatening

Since the clinical presentation of pulmonary infections in children is often nonspecific, radiological imaging evaluation plays an important role in initial detection, follow-up of disease progression, and assessment of potential complications.

IMMUNE-MEDIATED ENTEROPATHIES IN ANIMALS

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The gastrointestinal tract has a special role to play in the relationship between the body's immune responses, the commensal microbiota, and invading pathogens: The immune system has to be discriminating – it cannot react very strongly to everything foreign that it encounters, especially if it does not pose a threat.
As a result, the gastrointestinal tract is home to many regulatory and tolerance-inducing mechanisms, that ensure that immune-mediated responses to all these antigens are either totally suppressed, as in the responses to foods, or at the very least, are carefully regulated, as in the responses to the microbiota.
Food allergies can be considered as a failure in immune regulation. Autoinflammatory diseases that affect the intestine and other enteropathies, represent another consequence of a loss of peripheral tolerance; In this topic, there will be discussed loss of food tolerance and as a result, induced Gluten-Induced enteropathy.
We will also cover other immune-mediated enteropathies, such as Canine inflammatory bowel disease (IBD), in dogs characterized by chronic inflammation of the gastrointestinal tract. It's thought to be caused by a complex interplay of genetic predisposition, immune system dysregulation, and environmental factors.

Equine Inflammatory Bowel Disease is a condition in horses characterized by chronic inflammation of the gastrointestinal tract, like its equivalent in canines. However, IBD in horses is less commonly diagnosed compared to other species.
In this topic, it will be discussed the causes of such immune-mediated enteropathies, the clinical features, diagnostic methodologies, and therapeutic approaches of those diseases mainly in dogs and horses.

THE ROLE OF THE SCALP BIOPSY IN THE DIAGNOSIS OF ALOPECIA

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Introduction: Alopecia refers to the simultaneous loss of a hair shaft or follicle, or both, on a certain area of the scalp. It is divided into scarring and non-scarring forms, the treatment and outcome of which are different. Correct and timely diagnosis has a great impact on the effectiveness and outcome of treatment.
For diagnosis, biopsy is rarely used. In most cases, Trichoscopy is used to clarify the diagnosis along with the evaluation of the clinical picture. Scalp biopsy is used when it's not clear, what type of alopecia we are dealing with - scarring or non-scarring. It is the diagnostic value of biopsy that will be focused on in these two clinical cases.

Case 1

The patient is a 41-year-old woman with a 20-year history of alopecia, untreated, otherwise healthy.
Clinically: in the forehead area - baldness characteristic of female androgenetic alopecia; In the occipital region- an oval bald area of 3 cm in diameter.
With dermatoscopy: miniaturization of hair strands in the forehead area, variable diameter-anisotrichosis, single yellow dots. There were no miniature strands of hair in the occipital region. Single yellow and black dots, weak exclamation mark-like hair strands, with perifollicular erythema in some places, weak skin atrophy on both sites were observed.
Preliminary diagnoses: androgenetic alopecia and combined variant of alopecia areata. At the first stage, the patient refused to do a biopsy.
After 3 months of treatment with 2% minoxidil and mometasone furoate topical therapy, as well as triamcinolone acetate injections, the patient had multiple new hair growths on the forehead, while the occipital area remained unchanged. To clarify the diagnosis, the patient agreed to perform a biopsy from the occipital region.
Histologically (hematoxylin&eosin) it was revealed: Keratinocyte vacuolization, exocytosis, lymphoid aggregates in the papillary dermis, miniaturization of some hairs and perifollicular lymphoid infiltration in the infundibulum area of the follicle and focal small perifollicular fibroplasia, loss of bordering sebaceous glands, reduction in the number of hair follicles. No significant incorporation of specific antibodies was observed by direct immunofluorescence assay.
Based on the obtained results, a diagnosis of Lichen Planopilaris in the occipital area was made. along with local therapy, Hydroxychloroquine 200 mg tablets 2 times a day, for 6 months, was prescribed. 3 months after the treatment, perifollicular hyperemia was no longer observed in the occipital region, the treatment continues.

Case 2

33-year-old female patient with complaints of hair loss in the frontal-parietal-occipital areas since 2017. In 2021, she consulted a dermatologist and was treated with a diagnosis of Alopecia Areata. She was treated with local corticosteroid ointment (triamcinolone), tacrolimus, castor oil with periodic improvement, however, new lesions appeared, which is why intralesional injections of triamcinolone were performed from March to June 2023, with temporary results, however, an increase in the number of lesions was noted, which is why he referred to our

clinic.
Clinical Features: multiple 2-3 cm round hairless, hyperemic site on the scalp in the frontal-parietal-occipital areas, skin atrophy in the forehead area.
Trichoscopy features: the atrophic area of the skin in the forehead area with a significant capillary network, in the parietal and occipital area, hair follicles are absent in the areas of damage.
Based on clinical and trichoscopic findings, a diagnosis of cicatricial hair loss (L66) was made; to clarify the diagnosis, a skin biopsy was performed from an atrophic area of the skin.
According to histomorphological and direct immunofluorescence studies, a diagnosis of non-scarring alopecia - alopecia areata was established and treatment with Minoxidil 2% 1 ml rubbed once a day, Bepanthen cream once a day rubbed into atrophic areas of the head for 2 weeks was prescribed. In 1 month after the beginning of treatment the condition improved.
During the treatment of the patient, based on atrophic areas of the scalp and trichoscopy findings, cicatricial hair loss was suspected, which was not confirmed by histomorphological examination.
Conclusion: Despite its diagnostic value, scalp biopsy is rarely prescribed to determine the form of alopecia, which is sometimes due to the patient's refusal, the cost of the study, also waiting time for result. These two clinical cases clearly confirm the importance of histomorphological investigation for accurate diagnosis and adequate treatment.

LEUKOENCEPHALOPATHY WITH BRAIN STEM AND SPINAL CORD INVOLVEMENT AND LACTATE ELEVATION

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Background: Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation, (LBSL) according to MR-spectroscopy is a rare, slowly progressive, hereditary neurodegenerative disease. Dystrophic changes in the nervous tissue are observed, which will lead to a decrease in the volume of the white matter of the brain and functional limitation. The disease is related to the mutation of the DARS2 gene, which provides instructions for making an enzyme called mitochondrial aspartyl-tRNA synthetase.
This enzyme is important in the production (synthesis) of proteins in cellular structures called mitochondria, the energy-producing centers in cells. A decrease in the activity of mitochondrial aspartyl-tRNA synthetase leads to the non-inclusion of aspartic acid residue in the structure of all mitochondrial proteins and to the disruption of redox processes in the cell, as well as to the activation of the histotoxic hypoxia mechanism. Clinically, LBSL manifests symptoms of damage to the pyramidal tract, cerebellum, and posterior columns of the spinal cord.
Neurological dysfunction affects the legs more than the upper limbs. It is characterized by slowly progressive cerebral ataxia, and later learning problems, cognitive impairment and deterioration of the general neurological status appear. MRI reveals diffuse damage of cerebral hemispheres, brain stem, and spinal cord white matter. The exact number of people diagnosed with this disease is unknown, but based on reported clinical cases, there are less than 200 cases of LBSL worldwide. The disease is considered a pediatric pathology, adult forms are sporadic. Here we present a clinical case of LBSL.
Clinical case: a man is 56 years old, and currently presents with a typical neuromuscular clinical picture with complaints: weakness in the legs, leg muscle cramps at night, lethargy, and blurred vision. The patient has been under observation since the age of 15.
Keywords: Leukoencephalopathy with brainstem and spinal cord involvement and elevated lactate (LBSL), DARS2, MR spectroscopy, MRI, white matter lesions

COVID-19 AND VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA

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INTRODUCTION:Vaccine-induced immune thrombotic thrombocytopenia (VITT), also known as thrombosis with thrombocytopenia syndrome, is a catastrophic and life-threatening reaction to coronavirus disease 2019 (COVID-19) vaccines, which occurs disproportionately in response to vaccination with non-replicating adenovirus vector (AV) vaccines. The mechanism of VITT is not well defined and it has not been resolved why cases of VITT are predominated by vaccination with AV vaccines. However, a normal platelet count does not exclude the possibility of this syndrome in its early stages, Positive antibodies against platelet factor 4(PF4) identified by enzyme-linked immunosorbent assay (ELISA) assay Significantly elevated D-dimer (> 4 times ULN),
OBJECTIVES: VITT remains a risk for patients after administering AV vaccines. In addition to COVID-19 vaccination, the first clues point to the possibility that not only adenoviral vector-based vaccines can cause VITT-like symptoms. This review article aims to describe the etiology, epidemiology, pathophysiology, clinical features, diagnosis, and management of COVID-19 vaccine-induced thrombotic immune thrombocytopenia based on the latest available published literature.
METHODS: Preceding the approval of these vaccines, the clinical constellation of this new syndrome was not observed in clinical trials of the ChAdOx1 nCoV-19 vaccine, and a single case was observed in the Ad26.COV2. S vaccine trial recipient. Furthermore, the incidence of major adverse effects has remained exceptionally low following the vaccination of more than 400 million people worldwide.
RESULT: Due to the concern of VITT associated with the Ad26.COV2. S vaccine, the FDA modified the EUA and recommends limiting the use of this vaccine only to individuals > 18 years of age who are otherwise ineligible to receive any other FDA-approved vaccines due to anaphylaxis to mRNA vaccines or its components or are unable/unwilling to receive any other vaccine.
CONCLUSION: Fortunately, VITT is very rare. However, it can be life-threatening, especially if the diagnosis and treatment are delayed. Adenovirus vectors provide an affordable framework for highly effective vaccines. Unravelling the mechanisms of the anti-PF4 response in VITT has the potential to provide the basis for a more rational approach to developing safer vaccine delivery systems.
Key Words: COVID-19, vaccine, ELISA, thrombocytopenia, PF4 , FcγRIIa, CD32a.

NUTRITION AND PHYSICAL ACTIVITY OF PREGNANT WOMEN

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A healthy, balanced diet of a pregnant woman is important for the full development of the fetus, mainly pregnant women receive the mentioned recommendations from gynecologists, because consulting a nutritionist is less mandatory at this stage still in our country, so I created a medical booklet that will be available for them, easy to understand and I think will bring results.
In the article, I also talk about bariatric surgeries, that have increased among women who want to get pregnant, but being overweight prevents it. Pregnancy is often achievable, but the important part is how many months later the pregnancy occurred and how her nutrition was going.

For me, as for a pediatrician and nutritionist is important to observe the newborns, that the mother gave birth to after the mentioned operation. I also talk about the research I made in the article.

Keywords: Development, Nutrition, Bariatric, Pediatric

CUTANEOUS HORN (CORNU CUTANEUM)

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Increasing the number of the geriatric population is a big challenge for both the primary care physicians and dermatologists. The old-age dependency ratio (for both sexes 65 years old and above) was increased 1.5 times in Georgia between 1994 and 2023.
The cases of the skin tumors increases and their courses changes in the geriatric age, which significantly affects the quality of life of the patients. The clinical diagnosis - cutaneous horn is more commonly found in the elderly population between 60 to 80 years of age. The causes of the development of cutaneous horn is mainly related to viral wart and seborrheic keratosis in 50% and more cases, in 23-37% cases to actinic keratoses, and only in 20% cases to malignancy.
Histological examination is crucial to determine the cause of the cutaneous horn and is necessary to rule out the malignancy. The knowledge and experience of the clinician is also very important to distinguish the malignant and non-malignant processes on the skin. Treatment and supervision of the old-age dermatological patients should be performed considering the central principles of geriatric science.

GERIATRIC PATIENTS AT THE DERMATOLOGY OUTPATIENT CLINIC

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BACKGROUND: The elderly population is rapidly growing worldwide. The old-age dependency ratio (for both sexes 65 years old and above) increased 1.5 times in Georgia between 1994 and 2023. In the geriatric age, the number of the certain dermatoses respectively increases, there are changes in their courses, and the presence of polypharmacy and comorbid diseases complicates the process of treatment, significantly affecting the quality of life of patients.
MATERIALS AND METHODS: The aim of the study was to determine the prevalence of dermatological diagnoses among geriatric patients during their ambulatory visits to a Dermatology Clinic. This involved a retrospective analysis of the ambulatory patients in 2023, who sought a dermatologist's consultation for their skin disorders for the first time and were aged 65 and older. The study additionally investigated the number of patients in 2023 utilizing the multi-disciplinary ambulatory care services of the Kutaisi Federal Hospital, encompassing both outpatient and inpatient services across all age groups, with a specific focus on geriatric patients.
RESULTS: The total number of ambulatory patients who addressed the dermatologist for the first time at the dermatological clinic was 2,495, of which 219 (8.38%) were aged 65 and older, presenting with various dermatoses. The age distribution of the geriatric patients (219) with dermatoses is as follows: 65-74 years old - 128 (58.4%), 75-84 years old- 77 (35.2%), and over 85 years - 14 (6.4%). Following is the gender distribution: 106 males (48.4%) and 113 females (51.6%), differentiated by residency: urban residents constituted 119 (54%) and rural residents 100 (46%).
Among the six most frequently diagnosed dermatoses in elderly patients, dermatitis was the most prevalent (n=86, 39.27%); including Stasis dermatitis (n=15, 17.44%); lichen simplex chronicus (n=6, 6.97%), seborrheic dermatitis (n=3, 3.49%). The Fungal infections were the second most frequently diagnosed dermatological pathology (n=31, 14.15%); including the numbers of onychomycosis,(n=7, 25.9%) and Cutaneous candidiasis,(n=4, 12.9%).

Xerosis was observed in (n=20, 9. 13%) cases, and pruritus in (n=19, 8.67 %); Zoster was the most frequently diagnosed viral disease (n=17, 7.76%); Psoriasis accounted in (n=9, 4.11 %); and Skin tumors were identified in (n=6, 2.74%), Including basalioma (n=5 83.3%).
The study also included an examination of the number of patient visits across all age groups of the multi-disciplinary ambulatory care services of the Kutaisi Federal Hospital, for the year 2023. The total number of those patients was 22,129, which included 1,218 (5.5%) geriatric patients (aged 65 and above). Comparatively, within the hospital during the same period, there were 8,009 patients from all age groups, of which 1,971 (24.6%) were aged 65 and above.
CONCLUSIONS: The proportion of geriatric patients (aged 65 and above) who visited the dermatology clinic for the first time constituted 8.38%. In the multi-disciplinary ambulatory clinic, the segment of geriatric patients (aged 65 and over) who were consulting for the first time included 1,218 (5.5%) patients. Among the hospitalized patients, geriatric individuals (aged 65 and over) accounted 24.6%.
The main age range of the geriatric patients consulted for the first time at the dermatological clinic was 65-74 years accounting for 128 patients (58.4%). The six most frequently diagnosed dermatoses in these elderly patients and their prevalence were as follows: dermatitis (n=86, 39.27%); fungal infections (n=31, 14.15%); Xerosis (n=20, 9. 13%), pruritus (n=19, 8.67 %); Zoster (n=17, 7.76%); Psoriasis (n=9, 4.11 %); Skin tumors (n=6, 2.74%).
The knowledge and experience of the clinician regarding the most frequent geriatric dermatoses is also very important. Treatment and supervision of the old-age dermatological patients should be performed considering the central principles of the geriatric science. The issue requires further in-depth epidemiological research to reveal the prevalence of the geriatric skin diseases.
KEYWORDS: geriatric dermatology, epidemiology, prevalence.

RESPIRATORY VIRUSES IN THE PRE AND POSTPANDEMIC PERIODS IN AN M. IASHVILI CHILDREN' S HOSPITAL

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Background: The COVID-19 pandemic has had a major impact on healthcare systems throughout the world. The precautions taken to prevent COVID-19 have seemingly had an indirect effect on the seasonal variations of viral diseases and the frequency of relevant viruses . Therefore, the aim of this study is to evaluate the impact of the COVID-19 pandemic on the frequency and seasonal variation of common respiratory viruses in children pre- and post-pandemic.
Methodology: A cross-sectional retrospective cohort study was conducted by analyzing the electronic database of the M. Iashvili Children's Clinic. A total of 3,640 samples were collected from children under the age of 17 who were hospitalized in the M. Iashvili Children's Hospital between January 2018 and December 2023. A study was conducted to assess the impact of the COVID-19 pandemic on the frequency and seasonal variation of common respiratory viruses in children pre- and post-pandemic.
Results : All nasopharyngeal swabs (NPS) for viral Polymerase chain reaction (PCR) multiplex that were done for all admitted children of age up to 17 years were included, and the total samples amounted to 3640 , There were 2270 (62.4%) positive samples for viruses and 1370 (37.6%) negative samples. The number of positive samples pre-COVID-19 pandemic was 493 (60%), and the number of positive samples -COVID-19 pandemic was 797 (35%) and post pandemic period was 980 (57%). The frequency of different viruses has decreased post-COVID-19 and seasonality has changed; Although Rhinovirus, and influenza viruses have no big changes, but HMPV (Human Metapneumovirus) has increased frequency post-COVID-19 (13%), while post-COVID-19 it was (2 %). The seasonal peak for Respiratory Syncytial Virus (RSV) pre-COVID-19 showed mainly in winter (70%), while post-COVID-19 it showed no peak.

Keywords: Respiratory Syncytial Virus (RSV), Rhino virus, COVID-19, nasopharyngeal swabs (NPS)

THE POTENTIAL OF BACTERIOPHAGES IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME (IBS)

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Irritable Bowel Syndrome (IBS), affecting approximately 10-15% of the global population, is a multifactorial gastrointestinal disorder. Its etiology is attributed to various factors including heightened visceral sensitivity, dietary intolerances, ingestion of lipid-rich foods, psychosocial stressors, and alcohol consumption. Emerging evidence underscores a significant correlation between dysbiosis of the gut microbiota and the pathogenesis of IBS, highlighting the critical role of microbial imbalances in its development.

Traditional pharmacotherapy for IBS often involves the administration of antibiotics. Although efficacious in certain contexts, this approach is fraught with numerous adverse effects, including but not limited to, anxiety, vesical discomfort, hematuria, and increased respiratory rate. Moreover, antibiotic treatments precipitate disruptions in the microbiome's equilibrium and foster antibiotic resistance among bacterial populations over time.

In light of these challenges, bacteriophages, or phages, represent a novel therapeutic avenue. These viruses exhibit bactericidal activity with high specificity, targeting select bacterial species while sparing the broader microbiome. This specificity minimizes the collateral damage associated with broad-spectrum antibiotics and mitigates the risk of disrupting the gut's microbial harmony. Consequently, there is a burgeoning interest in the exploration of phage biology and the application of phage therapy in treating IBS. Unlike antibiotics, phage therapy is associated with a markedly lower incidence of adverse effects, rendering it a potentially promising alternative for managing this complex disorder.

POTENTIAL OF BACTERIOPHAGE –BASED STRATEGY TO COMBAT HEALTHCARE ASSOCIATED INFECTIONS IN PEDIATRIC HOSPITALS

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Healthcare associated infections (HAI) represent a big challenge to clinical medicine, including pediatric services, worldwide. Gram negative bacilli (GNB), primarily *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and Enterobacteriaceae species in addition to *Staphylococcus aureus* and coagulase-negative (CoN) staphylococci are important HAI pathogens with high potential for horizontal spread. Their elimination remains difficult because of resistance of infectious agents to many antibiotics. Bacteriophages are considered as effective and safe tool for control of multidrug resistant bacterial infections.

Our long term study was undertaken to identify the dynamics of prevalent bacterial flora in the respiratory department with ICU of a large children's hospital, and to analyze their antibiotic and phage susceptibility profiles. The various samples from patients with respiratory disorders and from fomites were collected during multiple sampling series. The obtained isolates were identified by biochemical profiling and using API systems (Biomereux, France), followed by PCR confirmation. The susceptibility to specific sets of antibiotics was determined by disc diffusion method according to the EUCAST guidelines, phage susceptibility was studied by spot test followed by EOP determination.

Among GNB isolates collected at the children's hospital *P. aeruginosa* was most frequently isolated, followed by *Serratia marcescens, A. baumannii, K. pneumoniae* etc. Among gram-positive bacteria *S. aureus* and CoN staphylococci remained dominant. Majority of GN clinical isolates, primarily *P. aeruginosa , A. baumannii* and other nonfermentes, also *K.pneumoniae* were shown to be multidrug resistant, frequently resistant to carbapenems. *S. aureus* strains showed variable profiles of antibiotic susceptibility with obvious resistance to Beta- lactams and in a few cases- warning signs of vancomycin resistance.

The isolates of prevalent clinical pathogens were screened against 6 commercial phage preparations ("Eliava Biopreparations") and more then 50 individual phages from Eliava collection active to *P. aeruginosa,A. baumannii* , S. *aureus* and CoN staphylococci, *K. pneumoniae*. Up to 90 % of *S. aureus* strains in were lysed by Sau phages. The high cumulative lytic activity (>80%) of phages was demonstrated towards multidrug resistant clinical isolates of *P. aeruginosa, A. baumannii* and *K. pneumoniae*. Based on the obtained results 4 individual phages *P. aeruginosa* with broad host range, also 4 phages of *A. baumannii* and 5 - of *S. aureus* were selected as candidate phages. The developed experimental mixtures showed extended lytic activity against multidrug resistant pediatric hospital strains thus demonstrating obvious potential of bacteriophages to combat HAI in this critical era of antibiotic resistance.

PROBLEMS OF BONE MINERAL DENSITY IN THE PEDIATRIC POPULATION OF ADJARA REGION

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Background: Despite having a low mortality rate, pediatric low bone density has a significant morbidity burden. During pubertal peak growth velocity, approximately 25% of peak bone mass is accumulated. If this peak is not optimal, it will manifest the development of osteoporosis in adulthood. Thirty percent of pediatric population suffers fractures. One of the main risk factors is low bone mass.

Objectives: During clinical practice, attention was paid to the fact that osteopenia was observed in the pediatric population. We decided to investigate the bone density index using ultrasound densitometry in children of Adjara Region. Also, up to date statistical data was not found in reliable scientific sources, which fueled our desire to be more interested in the prevalence of low bone density in pediatric population.

Methods: Research was conducted at JSC „Seamen's Medical Centre – 2010" Batumi, Adjara, Georgia between 2020 to 2023 by utilizing an Ultrasound Bone Densitometer Sonost 2000 in children aged 4-18 years.

Results: Among the 155 evaluated participants included in this study were aged less than 18 years, 52.90% (n=82) were girls, and 47,10% (n=73) were boys. Among them, 94.83% (n=147) demonstrated a bone density index below Normal (Low, Deficient, Critical), and 67% (n=98) of them had a deficiency in the daily consumption of dairy products.

Conclusion: According to our research, 94.83% (n=147) of children in Adjara region had a low bone density index, indicating a significant prevalence of osteopenia. Notably, girls exhibited a more pronounced reduction in bone density than boys (ratio 1.13:1). These results highlight the significance of monitoring and promoting the ideal bone mass in children and adolescents, also the necessity of early interventions to reduce the chance of osteoporosis in later life. There is a probable association with the reduced consumption of dairy products, as a significant proportion of children are found to be using inadequate amounts of these products.

Keywords: Bone Mass Density, Osteopenia, Z score.

TREATING ANKYLOSING SPONDYLITIS IN ADJARA REGION: WHY BIOLOGICAL THERAPY?

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BACKGROUND

Ankylosing Spondylitis is an autoimmune chronic inflammatory disease of the axial/central skeleton of human body that leads to partial or complete fusion and rigidity of spine. As Ankylosing Spondylitis have its onset typically in late adolescents or middle age group, it is quite necessary to have a hold on it. Ankylosing Spondylitis was thought of having a bad prognosis earlier but in recent few years, with help of research advancement techniques a totally new and highly effective treatment known as biological therapy is used.

OBJECTIVE

Our aim was to identify the outcome with biological treatment of 29 patients which got biological medication Simpon (Golimumab). We evaluated the effectiveness of managing Ankylosing Spondylitis with biological therapy in Adjara region. As this is an autoimmunity disorder and it may affect any person especially the young and middle age people, everyone must be educated about getting biologic treatment as soon as possible so that they immediately get control over the disease progression.

MATERIALS AND METHODS

We investigated 29 patients of Ankylosing Spondylitis (22 males and 7 females) from 24 yrs. old to 65 yrs. old age-group. We used the biological therapy with TNF-α inhibitor named Simponi (Golimumab). 50 mg of Golimumab was injected once a month subcutaneously in the beginning of therapy. We identified pain intensity, levels of CRP and ESR in all recruited patients since the first day over a period of 3 months, 6 months, and 12 months.

RESULTS

The effectiveness of biological treatment with Simponi (Golimumab) is appreciated as it has shown a significant reduction in symptoms of Ankylosing Spondylitis such as the pain intensity, levels of CRP and ESR. About Pain intensity – After 3 months, moderate pain intensity was in about 18% of males with 14% of females and severe pain intensity was in about 82% of males with 86% of females. It decreased and after 12 months, now moderate pain intensity was in about 22% of males and severe pain intensity was in none of the males. But in contrast, the female patients had neither severe nor moderate pain intensity rather they all had light pain intensity. About CRP – In the beginning all patients including both males and females had an increased level of CRP. It decreased and after 12 months only 9% of males and 8% of females had an increased CRP. About ESR – In the beginning 95% of males and 85% of females had an increased ESR. It decreased quickly with biological therapy and consequently after 12 months of treatment only 1 patient had increased ESR. After receiving Golimumab, 3 patients had episodes of acute rhinitis within 2 months, 2 patients had minor sneezing for 3 months as side effects, 5 patients had general weakness just after getting injection. 3 patients had urinary tract infection for 1 month as complication. And, no one had any serious complications.

CONCLUSION - According to these studies, it can be said that biologics have improved the life quality of these patients by improving body mobilization .To take care of the youth, use of biological therapy is advised so that the disease do not progress any further. Biological therapy is a present-day superlative method to manage Ankylosing Spondylitis as it reaches a stable remission period and alleviates the symptoms of Ankylosing Spondylitis.

WHY IDENTICAL TWINS AREN'T IDENTICAL: GENETIC TRAITS OF ALLERGIC INHERITANCE.

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Introduction and Objectives: As we know, there are two main theories around allergy inheritance: hygienic theory and genetic theory. Identical twins share not only the same genetic code but also the same environment. That's why it's very interesting for us to learn why twins develop different allergies throughout their lives and why identical genetic codes don't guarantee the same diseases. That's where epigenetics comes in.
Materials and Methods: Through five years of research, we have used questioning as the main resource for our work, as well as longitudinal research. While doing research, we were making blank questions and saying that we were looking after couples. In terms of developing allergies further in life, while researching, we found a correlation between older and younger twins developing allergies. Also looking for correlation between c-sections and allergies.
Results: from 70 pairs of twins, 20.2% of cases developed allergies in both (but it was a different kind of allergy for most cases, 87%); in 12.8% of cases, allergies developed in the A twin; and in 24.2%, twin B was allergic. In other cases (42.8%), both kids were healthy. Also, those born due to c-sections developed allergies more often (68%).
Discussion and Conclusion: In conclusion, we can say that B twins develop allergies more often and have more severe forms, while Twin A is usually less responsive to allergens.

BRONCHOPULMONARY DISPLASIA – ETIOLOGY, CLINICAL AND RADIOLOGIC FEATURES, DIAGNOSIS

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Bronchopulmonary dysplasia (BPD), also known as neonatal chronic lung disease is an important contributing factor in the increased risk of mortality and morbidity in the preterm population.
BPD is a lung disease characterized by disruption of pulmonary development and/or lung injury in the context of preterm birth.
Clinically, BPD is defined as an ongoing need for supplemental oxygen and/or respiratory support at either 28 days postnatal age or 36 weeks postmenstrual age in a preterm neonate with radiographic evidence of parenchymal lung disease (1).
Various criteria are used to define the severity of BPD.
Severity categories in the 2019 definition (Jensen definition) are based primarily on the mode of respiratory support administered at 36 weeks PMA, regardless of whether the infant requires supplemental oxygen and are classificated in three categories: mild, moderate and severe categories (2):
The severity of BPD increases with decreasing gestation age.
The etiology of BPD is multifactorial and involves disruption of lung development and injury due to antenatal (intrauterine growth restriction, maternal smoking) and/or postnatal factors (eg, mechanical ventilation, oxygen toxicity, infection) that cause inflammation and damage to the vulnerable premature lung (3).
Physical examination — The physical examination is variable. Infants with BPD usually are tachypneic. Depending upon the extent of pulmonary edema and/or atelectasis, they may have mild to severe retractions, and scattered rales may be audible. Intermittent expiratory wheezing may be present in infants with airway narrowing from scar formation, constriction, mucus retention, collapse, and/or edema.
Chest radiograph — As BPD evolves, the chest radiograph also changes from clear lung fields to findings that include diffuse haziness and a coarse interstitial pattern, which reflect

atelectasis, inflammation, and/or pulmonary edema. Lung volumes are normal or low. With further evolution of the disease, there may be areas of atelectasis that alternate with areas of gas trapping, related to airway obstruction from secretions or bronchiolar injury.

PATHOPHYSIOLOGY OF PRURITUS IN ELDERLY

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Pruritus represents an unpleasant sensation that may appear at any age and affect the quality of life. Itching developed in elderly represents chronic pruritus in people over 65 years of age. Despite the fact that many different signaling pathways and mediators of both the peripheral and central nervous system in the neuronal sensitivity to pruritus have been identified, the pathophysiology of chronic pruritus is still not fully understood. The neurogenic pathway of pruritus involves a path from the skin to the brain. The transmission of itch signaling is mediated by interactions between histaminergic, nonhistaminergic sensitive C nerve fibers in the skin, keratinocytes, and the immune system. The pathway of itch transmission to the central nervous system includes the dorsal horn of the spinal cord, the spinothalamic tract, and the thalamocortical pathway. In addition, the phenomenon of neuronal sensitization is described, which leads to the initiation of a vicious circle, that affects patient behavior, scratching, and worsens the itch sensation.
The high prevalence of pruritus in elderly is closely related to the changes associated with skin aging, including changes in the structure of the skin, altering its regeneration and barrier functions, declining in its normal immune function and changes in the density of nerve fibers which are determined by intrinsic and photoaging factors.

HEART HEALTH AND IMMUNE CHECKPOINT INHIBITORS (ICIS)-WHAT WE ARE LEARNING AND HOW TO HELP

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Millions worldwide fight two health conditions: Cancer and Cardiovascular diseases. The correlation between these two have been demonstrated, as advances in the treatment of malignancies prolong the lives of patients while posing a threat to their cardiovascular health.
Cancer Therapy Induced cardiotoxicity (CTIC) is an effect of chemotherapies and immunotherapies on the heart. CTIC is defined as an asymptomatic reduction in EF by less than 55% but more than 10% and in the presence of symptoms and signs of heart failure (HF) a decrease in EF by 5 % or more to less than 55%. A rare, but fatal cause of CTIC is Immune checkpoint Inhibitors (ICIs).
ICIs are monoclonal antibodies that non-specifically block immunosuppressive checkpoints on cytotoxic T-cells: CTLA-1, PD-L1, and PD-1. Therefore, they can initiate T-cell-mediated immunity against tumor cells. Unfortunately, with widespread activation of the immune system, ICIs can induce off-target immune-related adverse effects (irAEs) that can manifest as CTIC.
While the mechanism of ICIs induced CTIC is still incompletely understood, it is believed to be caused by several processes: in mouse models, PD-1 plays an important role in cardiac immune tolerance and in human individuals with fulminant myocarditis PD-L1 expression is increased in cardiomyocytes, which is consistent with the increased level of this marker found in human studies and mouse models. This suggest that PD-1 plays part in protecting myocytes against immune attacks. As this immunosuppressive mechanism is inhibited during ICIs treatment, robust T cells attack cardiomyocytes and cause irreversible damage. Activated T- cells also target unknown common antigen shared by cancer cells and cardiomyocytes further augmenting the damage, also they infiltrate the myocytes and directly kill the cells and increase cytokine production. The most common cytokines produced include granzyme B, TNF, IF-gamma.
Based on Pathomorphological analyses of cancer patients' hearts after cancer treatment, cardiotoxic effects were grouped into two categories - irreversible (type I) and reversible (type II).

Type I is usually associated with loss and injury of cardiomyocytes, while in type II there are dysregulation of cardiomyocyte functions without cell death. Anthracyclines cause type I injury by formation of Reactive Oxygen Species (ROS) which damage mitochondria, alter metabolism of the cell and induce apoptosis. Alkylating agents mediate type I toxicity by damaging vasculature and/or thromboembolic ischemia. Tyrosine kinase inhibitors (TKI) or monoclonal antibodies are usually implicated in type II toxicity and their effect stem from damaging signaling pathways of cardioprotective factors such as Neuregulin-1.

Although the rate of occurrence of cardiac irAEs is 1%, the mortality rate can reach up to 50-60%. The most common manifestation is myocarditis (14.1%), followed by pericarditis.
The standard treatment of cardiac irAEs is discontinuation of ICIs and high-dose corticosteroids. If the response to the treatment is adequate, the patient can be switched to 1mg/kg/day corticosteroids and the dose should be tapered over several weeks. With no symptomatic improvement, other immunomodulatory drugs should be started. One serious problem is that T -cells can become resistant to steroids and if this happens other treatments may not be effective.
Considering these complications, researchers suggested: that instead of using corticosteroids to initiate nonspecific immunomodulatory effects, cardiac irAEs should be treated by specifically targeting T-cells. To achieve this, they proposed using two drugs -abatacept which binds costimulatory molecules CD80 and CD86, and Ruxolitinib -an inhibitor of jak 1 and jak 2 proteins. Rutoximib does not provide a long-lasting effect, it commences working immediately, while abatacept has long-lasting effect but takes several weeks to achieve efficacy.
To test this, they enrolled 40 patients with ICIs-induced cardiotoxicity. 10 were treated with standard care, while 30 were with a new treatment plan. The 3-month survival rate for group I was 40% and after 6 months 20%, while in the experimental group, the 3-month survival rate was 77% and 6 months-70 %.
To conclude, ICIs have revolutionized cancer treatment and have prolonged millions of lives, one of the most feared side effects of these drugs is cardiotoxicity, but with new experimental treatment there is hope that not many people will succumb to this complication.

INCREASE IN CASES OF GASTROENTERITIS NOSOLOGY DEPENDING ON THE RESORT SEASON IN CHILDREN (0-10 YEARS OLD)

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This study aims to investigate the rise in cases of gastroenteritis among children aged 0-10 years during the holiday season in Batumi, comparing it with other medical conditions. We analyze the epidemiological situation in Batumi during the holiday season, particularly focusing on the surge in gastroenteritis cases. Methodologically, this research utilizes data from St. Batumi Central Hospital for Mothers and Children and Batumi Republican Clinical Hospital. We employ a quantitative approach to process data related to gastroenteritis and other medical conditions during the holiday season. Specifically, we use correlation analysis and calculate the Pearson correlation coefficient.
The results indicate a significant increase in gastroenteritis cases during the holiday season, primarily attributed to the influx of tourists during this period, resulting in a higher number of children. Additionally, the rising number of infections can be linked to improper food preparation, unhealthy lifestyles, unfavorable living conditions, and dietary habits that do not adhere to recommended guidelines.
This paper aims to complement preventive measures. Our focus is on ensuring food safety by implementing good hygiene practices throughout food production, processing, and preparation. Public awareness campaigns addressing safe food handling, proper cooking temperatures, and personal hygiene also play a pivotal role in reducing the incidence of this infection.
The recommendations we propose are designed to lower the risk of gastroenteritis

among children aged 0-10 years and enhance the effectiveness of children's healthcare during the summer season.

Key words: Epidemiological situation, Gastroenteritis risk, Holiday season, Infection.

MTHFR C677T GENE POLYMORPHISM AND ASSOCIATION WITH DISORDERS

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Abstract

The Methylenetetrahydrofolate reductase (MTHFR) is a general and important enzyme in human cells, which is involved in metabolism reactions of homocysteine and folate. The genetic material for MTHFR enzyme synthesis is situated on 1 chromosome p arm in 1p36.3 position. There are a lot of single nucleotide mutations in this mentioned locus, but among them well-studied is the C677T gene mutation. The C677T/MTHFR polymorphisms impact MTHFR enzyme activity, leading to alterations in methionine and folate metabolism, elevated homocysteine levels, and in most cases subsequent effects on DNA methylation. This literature review compiles information about the MTHFR C677T polymorphism and explores its potential association with various complex, multifactorial disorders, including cancer, cardiovascular complications, neurological conditions, and diabetes mellitus, among others. The review synthesizes findings from diverse global populations, providing valuable insights for master's and doctorate students, as well as researchers specializing in this field.

Key words: MTHFR C677T Gene, polymorphism, multifactorial disorders, complication.