

# ARCHIVES OF THE BALKAN MEDICAL UNION

**THE 23<sup>rd</sup> BALKAN MEDICAL DAYS**  
*THE BALKAN MEDICINE DURING COVID-19 PANDEMIC*  
online event

**ORGANIZED BY**  
**The Romanian National Section  
of the Balkan Medical Union**



01-02 October 2021

# BOOK OF ABSTRACTS

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# BALKAN MEDICAL UNION

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## HISTORY OF MEDICINE

### H1. Short comparison between British and Romanian Sanitary organization in 1926

Baran D

*"Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania*

Medical connections between Romania and Great Britain intensified in the XXth century. In terms of hygiene - the main concern in the post-war years -, relationships were greatly enhanced through the collaboration between the Romanian Ministry of Health and the Health Commission of the League of Nations in Geneva. Among the delegates of the Romanian Ministry of Health who visited hospitals and got acquainted with the details of the British sanitary organization was a pioneering hygienist, chief physician Moise Enescu (1878-1943), health inspector of the Roman County. In 1924 he traveled to England and Wales, attended conferences and continued his documentation for three months. In 1926, he returned to Albion, participating in the Royal Sanitary Institute Jubilee Congress. Back home, he published in national specialized journals detailed comparative analyses of both health organization and population health in Great Britain and Romania, formulating conclusions and suggestions. As things happen nowadays, too, challenging hygiene and sanitation problems were communicable diseases and epidemics, beside cancer, as an emerging disease. According to Dr. Enescu, in 1926 Romania looked like England five decades earlier. In his country post-war reconstruction was delayed in many ways: sanitary houses with bathrooms and sewerage system scarcity, household waste mismanagement, imperfect burial and cremation strictness, relative observation of hygiene principles. Almost as nowadays, differences between the sanitary status of the United Kingdom and Romania were due to impaired central and regional administration, insufficient funds, lack of health education and health promotion, few sanitary doctors: as many lessons from the past.

### H2. The COVID-19 pandemic and a possible budding new medical order

Baran D

*"Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania*

The ancient knights of the apocalypse have recently been updated and imagined by some as represented by World Health Organization (WHO), global corporations, militant (servant) press, and "progressive" non-governmental organisations. Once again, epidemics –such as the one SARS-CoV-2 caused – proved to be critical states, able to change everyday life coordinates, cultural and behavioural paradigms, revealing new dimensions of interpersonal relationships, of medical and social structures. A challenging experience, COVID-19 pandemic has not been conveniently answered yet, but it repositioned the importance of health science, human condition and medical consciousness in the "economy of life". New epistemological approaches emerged: COVID-19 could be interpreted in terms of either pathocenoses, i.e. dynamic "biocenotic pathologies" (particularly epidemics), or syndemics, i.e. "synergistic endemics".

Concurrently it has entrained infodemic aspects, along with moral, ethical and deontological debates. Information has developed from “conspiracy”, to “coincidence theories”, often involving “u-l-tra-crepidarianism”. As already noticed, coevolution of politics and science occurred, and the science-based society has gained ground. The ongoing pandemic - highlighted relationships between vaccines, SARS-CoV-2 transmission and their immunological impact; - uncovered medical, social and political vulnerabilities; - identified communication problems both at the medical and media level; - emphasized the necessity of increasing medical safety, education for health, and -determined fundamental changes in the interaction of individuals, social groups, societies, nation states, world systems, economic orientation. The future would require assessment of the pandemic overall impact in the immediate, medium and long term, reconsideration of WHO authority, restructuring transnational cooperation for disease prevention and control, while facing epidemiological globalization.

### **H3. Antivax: trois siècles de polémiques**

Karamanou M<sup>1</sup>, Laios K<sup>1</sup>, Androutsos G<sup>1</sup>

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Les vaccins constituent sans aucun doute une grande réalisation scientifique. Cependant, si on jette un regard rétrospectif sur l'histoire des vaccins qui ont combattu de manière drastique des maladies infectieuses mortelles, on va constater qu'ils ont été traités avec suspicion, faisant remonter à la surface les peurs et les inquiétudes, les plus profondes de l'espèce humaine. La variole a été une maladie virale terrible, avant son éradication en 1979 grâce à la vaccination. Les Chinois étaient les premiers à utiliser une méthode de prévention de la maladie qui sera ensuite introduite en Occident, sous le nom d'inoculation. La méthode, mentionnée pour la première fois au XI<sup>e</sup> siècle, consistait à introduire dans les narines des croûtes des pustules varioliques enroulées dans du coton ou réduites en pâte avec de l'eau. En Europe, l'inoculation a été préconisée par les médecins grecs Emmanuel Timoni (1669-1720) et Jacob Pylarinos (1659-1718) qui pratiquaient à Constantinople et puis par Lady Mary Wortley Montagu (1689-1762), épouse de l'ambassadeur britannique auprès de l'Empire ottoman. Pourtant, en Europe, les débats suscités par la technique étaient nombreux puisque elle présentait le risque de pouvoir communiquer la maladie. En plus, des objections inspirées par la religion et la morale s'ajoutent. Une amélioration dans la prévention de la maladie était introduite par le médecin anglais Edward Jenner (1749-1823), en 1798, qui préconisa au lieu de la variolisation, la vaccination, une variante atténuée de la variole chez les bovins. Cependant, la méthode de Jenner a suscité d'importantes controverses. A la fin du XIX<sup>e</sup> siècle, Louis Pasteur (1822-1895) a élaboré des nouveaux vaccins préventifs contre une série de maladies infectieuses. Malgré ses inventions importantes, il a reçu des attaques par des médecins et des défenseurs des animaux qui s'opposaient aux courants novateurs. Cependant, l'œuvre de Louis Pasteur a inauguré une nouvelle période en immunologie et les découvertes de vaccins se succèdent jusqu'à nos jours. Si les vaccins nous avons aidé d'éradiquer des maladies et même de contrôler des pandémies, ils suscitent encore polémiques et doutes, comme dans le cas de COVID-19 où des questions d'éthique sont omniprésentes.

#### **H4. Epidemics in history: the case of the Great plague of London (1665-1666)**

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The Great Plague of London was the last major epidemic of the bubonic plague in England. It took place during the second plague pandemic period that started with the black death, which reached Europe in 1348 and killed around half of the population of Eurasia within four years. The Great Plague of London killed between 75,000 and 100,000 of London's rapidly expanding population of about 460,000. Medical writers of that era describe the clinical features of the disease and the measures that had to be taken in order to prevent its spreading. Quarantining of ships as well as isolation of the sick had been widely adopted as a means of limiting the extend of the outbreak. The study of the current literature also allows us to understand the views held by physicians on the cause of the disease and its impact on society. It was a "dark" final chapter to three hundred years of plague in England which disappeared almost entirely after the Great Fire in 1666.

#### **H5. Asclepias: a divine name for one celestial therapeutic herb ... or two**

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Asclepias, an old plant named after the patron of ancient Hellenic medicine, the god Asclepius, was classified among the classical herbs of medical botanology in antiquity and Renaissance. Its name was originally used by Pedanius Dioscorides (40-90 AD) in his book *Materia Medica* to refer to plants identified as *Vincetoxicum officinale* and *Apocynaceae*, nowadays known as swallowwort. According to medico-philosophers of the ancient Hellenic peninsula, drunk with wine, the roots of Asclepias help the colicky and those bitten by wild animals. Meanwhile, the leaves when plastered on have the same effect. Plant species of the same family were considered suitable for breast and uterine malignancies. The *Juliana Anicia Codex* of 512 (Der Wiener Dioskurides) illustrating Dioscorides' *Materia Medica* has two illustrations of swallowwort. One identified as Asclepias and another named Apocynum (dogbane) as *Cynanchum erectum* L., whose leaves kill dogs, a synonym of *Vincetoxicum* family, which includes *Asclepias syriaca* L. plant from Asia Minor. Carl Linnaeus (1707-1778), the Swedish naturalist and explorer in his *Species Plantarum* published in 1753, described common milkweed, an American species, as *Asclepias Syriaca* due to confusion with an *Apocynum* species from Asia Minor. It was then, when convoluted iconographic and nomenclatural history due to this confusion led the two species to be wrongfully considered as one. An American plant became a celestial herb, falsely taking its place beside the ancient species. The main representative of the family, Asclepias

curassavica, was native to South America but soon has become a naturalized weed in tropical and subtropical areas, disturbed throughout the world due to its therapeutic properties. It was considered to have antimicrobial, anticancer, cardiovascular, analgesic and antipyretic effects and it was used as an emetic, purgative, haemostatic in bleeding wounds and haemorrhoids. It was said that it could cure gonorrhea, inflamed spleen, pneumonia, mastitis, warts, malignancy, caries, fever and pyoderma, tonsillitis, pneumonia, bronchitis and urethritis. Two completely different plants, with origin from different continents, one from the era of the eve of medicine and one from an epoch when medicine had been reborn after the Dark Ages, became one herb family with great value in herbal, folklore and modern medicine.

#### **H6. The first pharmacies in some countries in the Balkans**

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**The objective of the study** was to perform a comparative analysis of the emergence of the first pharmacies in 4 countries in the Balkans with different political and economic development during the Middle Ages.

**Methods and materials.** The comparative-historical and comparative method, document analysis, as well as the methods of analysis and synthesis of the studied problems were applied.

**Results.** The study includes the Republic of Bulgaria, Croatia, Serbia and the Republic of Turkey. The countries are characterized from ancient times to the end of the 19th century. Pharmacies in Turkey first appeared in hospitals during the Anatolian Seljuk dynasty between the 11th and 13th centuries. As one of the oldest hospitals, including a pharmacy, Gevher Nesibe Darussifasi (Caesarea) was built in the city of Kayseri in 1206. In the Ottoman period, the first pharmacy called the Two-Door Pharmacy (Iki Kapili Eczahane) was opened in the Bahçekapı district of Istanbul in 1757 The first pharmacy of a Turkish pharmacist in Istanbul is registered in 1880 in the name of the pharmacist Ahmet Hamdi Bey. Document dated October 29, 1271. proves the existence of a pharmacy in Trogir, Croatia. The first private Serbian pharmacy of the modern type was opened on April 30, 1830 in Belgrade by Mateja Ivanovic, a pharmacist from Zemun by decree of Prince Milos Obrenovic. Ludovico Melanesi graduated in pharmacy in Padua in 1855 and was elected a member of the Academy in Naples. In 1866 he founded a pharmacy in Vidin on a European model.

**Conclusion.** The political and economic-social differences between the studied Balkan countries are the reason for a different start of the opening of the first pharmacies of modern type during the Middle Ages.

#### **H7. Professor doctor Nicolae Hortolomei (1885 – 1961) - founder of the cardiovascular surgery in Romania**

Tesoiu NJ

*Institute of Emergency for Cardiovascular Diseases “Prof. Dr. C.C. Iliescu”, Bucharest, Romania*

Professor Doctor Nicolae Hortolomei (Husi, November 27, 1885 – Bucharest, January 3, 1961), considered to be the founder of the physiologic surgery in Romania and the founder of the most

important school of surgery in Romania after professor Doctor Toma Ionescu, reaches the maximum of his impressive career as: member, Romanian Academy (1945), chief of section, Institute of therapy, Romanian Academy (1948) and head, Chair of surgical clinic, Faculty of specialization and perfecting in medicine and pharmacy (1952).

The climax of his activity is constituted by founding the cardiovascular surgery in Romania, from experimental stage to clinical practice and from complex evaluation to surgical, anesthetic and intensive care aspects, with a group of young enthusiasts, at Coltea Hospital, Bucharest; his disciples continue at Fundeni Hospital, Bucharest, the present day cardiac surgery, vascular surgery and endovascular surgery being fully represented in five institutes and in one center dedicated to the diagnosis of the cardiovascular diseases and to the treatment of the patients with this pathology, as well as in numerous hospitals in our country.

His prestigious scientific activity includes 368 medical works, co-editor with Professor Doctor Ion Turai, the first Romanian Treatise on Surgery, participation to international Congresses, presenting the contribution of the Romanian school of surgery to the universal medical scientific patrimony and member of numerous international societies: International Society of Surgery, International Society of Urology, French Association of Surgery, French Association of Urology, Academy of Surgery from Paris, Society of Surgeons from USSR and Society of Surgery "Pirogov" – Leningrad.

#### **H8. Ethical and equity aspects in the advancing of the medicine – “errare humanum est”**

Tesoiu NJ

*Institute of Emergency for Cardiovascular Diseases “Prof. Dr. C.C. Iliescu”, Bucharest, Romania*

Past, present and future are parts of a continuous present time through which we can freely travel using two mechanisms, feed - back and feed – forward, allowing us to learn the facts from the past and to foresee the facts from the future with their everchanging significances, implications and interpretations and interfering in an interesting and intriguing manner; events from the present have been events from the future and will be events from the past.

The disease is human; we should be conscient of the existence of our biological, structural and functional, limits and we should have the wisdom to do not surpass them in order to preserve our inseparable individual and social integrity, to remain united and to be prepared to face the aggressions. The prevention would represent the first step and the greatest part of the diagnosis and of the treatment.

The error is human; we should be able to recognize the errors made in the past aiming to do not repeat them and, much more than that, to prevent the appearance of new others.

We should be curious and we should have a friendly, hopeful and a peaceful attitude while being characterized by modesty and by self – criticism in preparing our perspective and our interpretation on the names and on their facts from the past, present and from the future; as working, united, solidary, integrated and cooperating, in our domain of activity, we have solid bases for the continuous advancing of the medicine.

### **H9. Theodoros Zaimis (1848-1922): the philanthropist surgeon**

Laios K<sup>1</sup>, Michaleas SN<sup>1</sup>, Papaioannou TG<sup>1</sup>

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Theodoros Zaimis was one of the most distinguished figures in Greek Surgery during the second half of 19<sup>th</sup> and early 20<sup>th</sup> century. He was awarded a Doctorate from the Medical School of the University of Athens, then so-called Ethnikon (Greek: National) University, in 1870. He continued his studies and specialized in surgery in Vienna and Graz. He returned to Greece in 1881 and until 1882 worked as an assistant at the Astyclinic. He then took over the Management of the Surgical Department of the Municipal Hospital of Patras, where he was recognized as a distinguished surgeon, as he was the first in Greece at that time to perform laparotomies for ovarian cyst resection, echinococcal liver cyst resection, as well as surgical treatment of gastric ulcers. From 1902 to 1918, Theodoros Zaimis would be appointed Professor and Director of the 1<sup>st</sup> Surgical Department of Medical School of University of Athens. During the academic year 1907-08 he was Dean of the Medical School and in 1912-13 Rector. He took an active part in the political life of Greece, as he was elected Member of Parliament representing Kalavrita, his place of origin, during the years 1895-1898 and 1899-1902. During the period 1920-22, he was elected Plenipotentiary of Achaioilidos in the 3<sup>rd</sup> National Assembly, while he served as Minister of Ecclesiastical and Public Education in the governments of the G.A. Rallis, N. Kalogeropoulos and D. Gounaris, from 4/11/1920 to 2/9/1922 with a rich legislative work. He died on October 18, 1922 due to a heart attack, while it is considered that his sudden death was the result of intense emotion due to the tragic national and political events of the time. He was great for his charitable work, as he never practiced medicine privately in his surgical career.

## INTERNAL MEDICINE

### IM1. The analysis of COVID-19 patients hospitalized in the Internal Medicine Department of a hospital from Bucharest, Romania

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**Introduction.** The coronavirus pandemic, which began in December 2019 and continues to this day, is currently the most important health problem worldwide, with important financial and human resources being directed to limit the number of deaths and prevent infection. However, despite the significant efforts made by doctors and researchers, the number of infected patients and the number of deaths reach impressive figures.

**Materials and methods.** We have conducted a retrospective study that included 692 patients infected with SARS-CoV-2 virus, hospitalized between March 1, 2020 and March 1, 2021 in the internal medicine department of the Clinical Emergency Hospital of Bucharest. The main inclusion criteria used were: SARS-CoV-2 infection diagnosed by RT-PCR test in the Emergency Department, the existence of a chest CT-scan and the presence of non invasive ventilation. 692 patients met the aforementioned criteria, their data being entered into a database by four independent investigators. The study aimed in addition to evaluate the biological parameters and the number of comorbidities of hospitalized patients, the treatment received and the response to it, as well as the survival rate according to the characteristics mentioned above.

**Results.** Following the statistical analysis of the group, it was found that most patients have multiple comorbidities and preexisting conditions at the time they contracted the virus. Among the prescribed treatments, the most frequent are represented by Remdesivir, Dexametazone. and parenteral anticoagulation, such as dalteparin or enoxaparin, with a favorable evolution in a significant percentage.

**Conclusions.** Although in the last year all the attention of the medical world has been directed towards the treatment of COVID-19 patients and finding optimal therapeutic guidelines, they are far from perfect, once again drawing attention to the complex pathophysiological mechanisms of this new, yet poorly understood disease.

## IM2. Late hypoxia – a medical challenge in COVID-19 era

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**Introduction.** The long term follow up of patients after COVID-19 put in evidence a huge panel of complication. A main part of these are focused on troubles of haematosis with chronic hypoxia. Various post-COVID-19 symptoms have been reported in different studies. Post-COVID-19 symptoms can develop even in mild cases. Most studies have reported fatigue, cough, respiratory distress, and headache as the dominant feature. Viral infection-related immune system alterations may be the cause of fatigue.

**The objective of the study.** We follow up a number of 30 cases, initially with COVID-19.

**Material and methods.** The follow up consists of clinical visit, check of inflammatory syndrome, saturation of O<sub>2</sub>, chest X-ray, ECG. All of cases has comorbidities.

**Results.** In our study, a significant proportion of patients had sleep disturbances, including insomnia and circadian rhythm sleep disturbances. Previous experience with other SARS-CoV infections has revealed that involvement of the hypothalamus might be the reason for such symptoms. We also found a large number of patients with adjustment disorders. Mental stress due to COVID-19 might have a role in developing adjustment disorders.

**Conclusions.** Cough and respiratory distress can be explained by persistent squeal lung damage. A recent study from China reported decreased diffusion capacity for carbon monoxide in 25% patients 3 months after hospital discharge.

## IM3. Acute renal injury with an unexpected etiology

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**Introduction.** Acute renal injury (ARI) is a pathology with multiple etiologies, which can result in permanent loss of kidney function. Uncommon causes include tumors of the urinary tract or other adjacent anatomical structures.

**Case presentation.** An 83-year-old patient presented for pain in the hypogastrium, with no specific irradiation, polakidysuria and weight loss of 5-10 kg, symptoms that began about 2 months prior. The patient has a history of paroxysmal atrial fibrillation, arterial hypertension, chronic heart failure, mitral regurgitation, and a transient ischemic attack. During clinical examination, the patient was pale, with a blood pressure of 150/70 mmHg and 100 mL of a clear, dark urine already in the urine bag. During a previous hospitalization in the urology



department, an enlarged prostate was detected, along with bilateral grade I-II uretero-hydronephrosis and the increased values of the following parameters: creatinine 6.6 mg/dL, BUN 229 mg/dL and K<sup>+</sup> 6.86 mmol/L. Laboratory tests showed leukocytosis with neutrophilia, mild normochromic anemia, nitrogen retention, hyperuricemia, hypernatremia, hyperkalemia. By corroborating the clinical and paraclinical data, the diagnosis of ARI was established and specific treatment was initiated. Abdominal ultrasound and computed tomography were also performed, which revealed an enlarged prostate with a diffuse inhomogeneous structure, bilateral uretero-hydronephrosis, and circumferential stenosis of the rectosigmoid lumen, as well as retroperitoneal and meso-gastric adenopathy block. Further, a colonoscopy was performed, which reveals a circumferential recto-sigmoid constriction with a normal-looking mucosa. A transrectal prostate biopsy is subsequently done, followed by histological analysis, which confirms the presence of a poorly differentiated prostate cancer with a Gleason score of 9 (4 + 5). **Conclusions.** Postrenal ARI may be a complication of a gastrointestinal, urological, or hematologic neoplasm that requires further investigation in order to establish the exact etiology.

#### **IM4. How intricate is the relationship between serum magnesium and dyslipidemia?**

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**Introduction.** Dyslipidemia has become a common discovery in our clinical practice and its association with cardiometabolic disorders, i.e., diabetes, metabolic syndrome, obesity, hypertension, chronic kidney disease, is troublesome. In the last decade, a myriad of studies has revealed a direct link between the serum concentration of several micro- or macro-nutrients and serum lipids. However, the interplay of serum magnesium and serum lipids remains unclear.

**Materials and methods.** A dedicated search was conducted in several international databases to assess the relationship of serum magnesium concentrations and dyslipidemia. Relevant studies were selected and summarized.

**Results.** There seems to be a link between serum magnesium concentrations and lipid abnormalities. Magnesium supplementation via dietary interventions or exogenous supplementation might positively impact the management of dyslipidemia. Magnesium supplementation has been explored in a variety of studies, including randomized clinical trials, but the data available in the literature is sometimes conflicting. Magnesium deficiency can arise from primary or secondary causes, i.e., drug-induced.

**Conclusions.** The relationship of serum magnesium concentrations and serum lipids, as well as dyslipidemia, is intricate and requires further investigation. Future studies should focus on the

discovery of efficient means to target and treat magnesium deficiency and explore the benefits of magnesium supplementation. Magnesium orotate could emerge as an interesting alternative in the management of lipid abnormalities.

#### **IM5. Renal anemia – an early complication in diabetic kidney disease**

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**The aim of the study** was to identify risk factors for the presence of anemia in chronic kidney disease (CKD) because of diabetic kidney disease (DKD).

**Material and methods.** We performed a case-control study in which we included 134 patients with DKD-associated CKD and anemia, and 139 patients with DKD-associated CKD without anemia. Independent risk factors for anemia were identified using logistic regression by SPSS ver. 20.0.

**Results.** Patients from study group had important signs of malnutrition- significantly lower albuminemia (3.3±0.7 g/dl vs 4.2±0.6 g/dl, p<0.001) and lower body mass index (BMI) (27.8±4.9 vs. 31.5±5.9 kg/m<sup>2</sup>, p=0.02). We found a higher incidence of anemia in patients with advanced CKD stages (stages 4 and 5, p<0.001), but even in mild CKD (stage 2) patients had lower Hb levels. We found strong positive correlations between Hb and eGFR (r=0.565, p<0.001) and albuminemia (r=0.543, p<0.001), and moderate negative correlation between Hb and phosphatemia (r=-0.377, p=0.01). Patients in study group had evidence of abnormal mineral metabolism- significantly higher phosphatemia (4.9±0.6 mg/dl vs 3.7±1.1 mg/dl, p<0.001) and significantly lower calcemia (9.06±0.4 mg/dl vs 9.6±0.8 mg/dl, p=0.005). Proteinuric patients had a 3-fold increased risk of anemia (OR 3.3, 95%CI 1.6-7.1, p=0.01). We found as independent risk factors for anemia: treatment with renin-angiotensin-aldosterone system (RAAS) blockers (OR 6.6, 95%CI 1.8-26.1), and proteinuria (OR 5.5, 95%CI 1.9-24.9).

**Conclusions.** Patients with CKD due to DKD have an increased incidence of renal anemia, starting from early CKD stages. Malnutrition and abnormal mineral metabolism are involved in the development of anemia in these patients and may be treatable factors in order to improve Hb levels in DKD.

#### **IM6. Why are acute stroke patients not receiving IV tPA in the Republic of Moldova**

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**Background.** Stroke is one of the leading causes of morbidity and mortality, accounting for 11.13% of total deaths worldwide. The development of hyper-acute treatments such as thrombolysis, organization of stroke units and a better understanding of secondary prevention has changed considerably in recent years the field of stroke medicine. In Republic of Moldova stroke in 2019 were registered 5937 new cases of stroke, including 4810 cases (81%) of ischemic stroke, 1009 cases (17%) of hemorrhagic stroke and 118 cases of subarachnoid hemorrhage

(SAH). Prevalence of cerebrovascular diseases is 274.8 and incidence is 30.3 per 10 000 population.

**The aim of this study** was to identify the reasons why patients with acute stroke did not receive thrombolysis.

**Materials and methods.** A retrospective hospital-based study was conducted in the Emergency Medical Institute, Chisinau, Republic of Moldova. All medical records with a diagnosis of stroke were identified based on the ICD, R10, from January 01, 2020 to December 31, 2020.

**Results.** Out of 456 patients, 248 (54.4%) were male and 208 (45.6%) were female, the mean age of the patients was  $60.4 \pm 17.4$  years and the mean age at the time of stroke was  $59.4 \pm 16.9$  years. 79.4% of acute ischemic stroke patients did not receive thrombolytic therapy (n=362). The incidence of different risk factors in ischemic stroke (IS) was as follows: 42.6% hypertension, 32.7% smoking, 32.2% alcohol intake, 24.8% diabetes mellitus, 22.6% coronary artery disease, 18.6% dyslipidemia, 16.6 % dysrhythmia, 13.4% previous stroke, 10% inactivity, 8.8% transient ischemic stroke in the past. Stroke is mostly a disease of advancing age, the most affected categories of age are 61-70 years (23.0%), 71-80 years (33.0%); patients over 80 years were 17.0%, patients over 70 years were 50.0%. About 56.0% of stroke patients were in the age group 61-80 years, 17.0% patients were in the age group 20-40 years, and 18.0% of patients were more than 80 year-old. The following most common reasons they did not receive thrombolytic therapy were: exceedance of time window 38.2%; low or improved NIHSS 19.8%; uncontrolled blood pressure 6.8%; stroke mimics 5.6%; history of stroke in the past 3 months 8.2%; history of gastrointestinal bleeding 2.8%; uncertain onset 2.6%; family refusal 1.4%, and no alteplase availability 2.0%.

**Conclusions.** In the Republic of Moldova, only 12.6% of ischemic stroke patients currently receive thrombolytic treatment. The most common reasons were: exceedance of time window, low or improved NIHSS, uncontrolled blood pressure, stroke mimics, and history of stroke in the past 3 months.

#### **IM7: Diabetes, obesity and insulin resistance in COVID-19**

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**Introduction.** Patients with diabetes are at high risk for developing severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and usually present severe forms of the coronavirus disease 2019 (COVID-19), with respiratory insufficiency. An increased body mass index (BMI) is also correlated with a high risk of developing a severe form of COVID-19. New-onset diabetes was observed after SARS-CoV-2 infection due to endothelial dysfunction, inflammatory state, and insulin resistance, induced by the disease.

**Objectives.** Our study aimed to evaluate the bidirectional relationship between COVID-19 and diabetes and the importance of BMI in patients with COVID-19.

**Material and methods.** We analyzed the data of 130 patients with COVID-19 admitted to the Clinical Pneumology Hospital of Constanta, Romania. The diagnosis was sustained by positive real-time polymerase chain reaction (RT-PCR), or imaging changes and symptoms suggestive for COVID-19.

**Results.** Of the 130 cases diagnosed with COVID-19, 32 (24.6%) presented obesity, and 8 (6.15%) of them have been known with diabetes. 4 (50%) patients with diabetes associated also obesity. 26 cases (20%) presented hyperglycemia. From the cases with hyperglycemia, 5 cases (19.23%) presented diabetes and 10 cases (38.46%) presented obesity. Of the 32 cases with obesity, 21 cases were female (65.6%), with a ratio between women: men of 1:2.

**Conclusions.** Patients with diabetes develop more severe forms of COVID-19, with prolonged hospital stay and subsequent sequela. The SARS-CoV-2 infection can determine the disequilibrium of known diabetes, or even diabetes de novo.

#### **IM8. NOONAN syndrome with multiple lentigines - a case report**

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**Introduction.** Noonan syndrome with multiple lentigines (NSML) (formerly called LEOPARD syndrome) is a rare autosomal dominant monogenic disorder with complete penetrance and variable expressivity. LEOPARD is an acronym for the characteristic abnormalities associated with the disorder: (L)entigines, (E)lectrocardiographic conduction abnormalities, (O)cular hypertelorism, (P)ulmonary stenosis, (A)bnormalities of genitalia, (R)etardation of growth, (D)eafness. The term RASopathies includes disorders with mutation in the genes that code for the proteins of the RAS/MAPK pathway, such as neurofibromatosis type 1, Noonan syndrome, Legius syndrome, Costello syndrome and cardiofaciocutaneous syndrome. The diagnosis of NSML is established either by clinical findings or if clinical findings are insufficient, by identification of a heterozygous pathogenic variant in one of four genes (PTPN11, RAF1, BRAF and MAP2K1) by molecular testing. NSML is often caused by missense mutation in the PTPN11 gene.

**Case presentation.** The authors present a family case of LEOPARD syndrome, the mother and two brothers who are registered in the Genetics Department of Municipal Clinical Hospital "Dr. Gavril Curteanu", Oradea, Romania. Both siblings present at clinical examination proportionate short stature (-3DS), dysmorphic facial features (elongated facies, eyelid slits with antimongoloid orientation, small eyes, hypertelorism, prominent elongated nose), thin, fine skin, with multiple lentigines, thoracic and level lenses neck, facial eczematides, cryptorchidism. Interdisciplinary consultations revealed neurosensory hearing loss, mild intellectual disability, sinus arrhythmia. Paraclinically, much lower levels of growth hormone were reported for both siblings. Molecular diagnosis could not be made due to the consent of the family. The mother has a small stature, multiple lentigines present on the face, neck, chest. The established treatment was with growth hormone, the clinical evolution being favorable, the final waist reaching the level of the 3rd percentile at both patients.

**Conclusions.** In the absence of a molecular diagnosis, clinical examination, family history, paraclinical investigations and interdisciplinary consultations are essential for the correct

management of the disease and appropriate genetic counseling. Growth hormone treatment has a beneficial role, improving the speed of growth in patients with LEOPARD syndrome.

## CARDIOLOGY

### C1. Heart failure and sodium-glucose co-transporters-2 (SGLT-2) inhibitors

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**Background.** Diabetes mellitus is a well-established risk factor for cardiovascular diseases, including heart failure. The coexistence of type 2 diabetes mellitus (T2D) and heart failure carries a higher risk of hospitalization, cardiovascular mortality and overall mortality. Previous large scale cardiovascular studies with sodium-glucose co-transporters-2 inhibitors (SLGT-2) in patients with T2D have suggested that these agents may help prevent primary and secondary hospitalization due to heart failure and cardiovascular death among these patients.

**Material and methods.** 60 patients (45 males and 15 females) with heart failure with reduced ejection fraction (HFrEF) and T2D were enrolled in the prospective study. The mean age was 72±12.4 years. The structural and functional state of the left ventricle myocardium and ejection fraction were assessed through echocardiography. Patients were randomized to receiving once-daily dapagliflozin 10 mg.

**Results.** Patients with HFrEF and T2D were divided in 3 subgroups according to their age. 7% (4) patients had age < 45 years, 30% (18) patients between 46-59 years and 63% (38) patients > 60 years. The most prevalent comorbidities were hypertension (43.1%), coronary heart disease (40%), and obesity (33.2%). Also, mitral regurgitation was found in the subgroup of patients aged > 60 years, representing 75%. Study drug discontinuation and serious adverse events were not frequent in the subgroups, in either men or women.

**Conclusions.** SGLT-2 inhibitors are a novel class of antidiabetic agents that have demonstrated positive efficacy and safety outcomes in the setting of HFrEF. Until now, in our study, dapagliflozin was safe and well-tolerated, irrespective of sex.

### C2. Clinical presentation of patients with hypertensive emergencies, comorbidities, and target organ involvement

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**Introduction.** Hypertensive crisis is defined as levels of systolic blood pressure >180 mmHg and/or levels of diastolic blood pressure >120 mmHg and is usually seen in patients with essential hypertension. In addition, hypertensive crisis is a severe clinical condition in which a sudden increase in arterial blood pressure can lead to acute vascular damage of vital organs, so

timely detection, evaluation and adequate treatment are crucial to protect target organ function, ameliorate symptoms, reduce complications, and improve clinical outcomes.

**Materials and methods.** A retrospective study was conducted in the Emergency medical services in Chisinau, Republic of Moldova. All medical records with a diagnosis of hypertensive emergencies were identified based on the ICD, R10. The study was conducted from January 01<sup>st</sup>, 2020 to December 31<sup>st</sup>, 2020, and included 630 subjects of both sexes, aged 28-92 years, with a diagnosis of hypertensive crises. All subjects were divided into two groups: hypertensive urgencies (492 subjects) and hypertensive emergencies (138 subjects). The aim of this study was to evaluate the hypertensive emergencies in the Emergency medical services in relation to clinical presentation, comorbidities, and target organ involvement.

**Results.** The study results indicate that female subjects were significantly over-represented compared to men (285 (57.9%) vs. 207 (42.1%),  $p=0.007$ ). The average age of the male subjects was  $56.6 \pm 16.6$  years, while the female mean age was  $58.4 \pm 12.6$  years. The majority of subjects belonged to the age group of 60-69 (36.4%) years: 28.8% hypertensive urgency and 38.6% hypertensive emergency. The average blood pressure in subjects with hypertensive crisis was 212.46/122.16 mmHg. Hypertensive emergencies frequently present with chest pain (30.4%), dyspnea (28.6%) and neurological deficit (29.4%). The types of end-organ damage associated with hypertensive emergencies include cerebral infarction (26.4%), acute pulmonary edema (24.8%) and hypertensive encephalopathy (28.6%), as well as cerebral hemorrhage (4.5%) and congestive heart failure (12%). Other clinical presentations associated with hypertensive emergencies include aortic dissection (0.8%), renal failure (1.02%), preeclampsia and eclampsia (2.6%), as well as acute coronary syndromes (20.4%) and hypertensive retinopathy (6.8%).

**Conclusions.** Patients with hypertensive emergencies require immediate reduction of elevated blood pressure to prevent and arrest progressive end-organ damage. Clinical manifestations of hypertensive emergency were cerebral infarction, acute pulmonary edema, hypertensive encephalopathy, acute coronary syndromes, cerebral hemorrhage, congestive heart failure, aortic dissection, preeclampsia and eclampsia. The types of end-organ damage associated with hypertensive emergencies include central nervous system (cerebral infarction, hypertensive encephalopathy, cerebral hemorrhage), cardiovascular system (acute pulmonary edema, acute coronary syndromes, congestive heart failure, aortic dissection). Other end-organ damage associated with hypertensive emergencies include renal failure, preeclampsia and eclampsia, and hypertensive retinopathy.

### **C3. Echocardiographic techniques used to identify the myocardial damage associated with SARS-COV-2 infection**

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**Introduction.** The prevalence of myocardial damage in patients with COVID-19 disease is unknown because it lacks specific diagnostic tools.

**Materials and methods.** 2D transthoracic echocardiography is usually the first imaging tool performed in suspected cardiac damage. Speckle tracking echocardiography could detect subclinically contractility abnormalities.

**Results.** Most studies suggested that 2D echocardiographic features of myocardial involvement are increased ventricular wall thickness, ventricular dilatation, pericardial effusion, decrease of

systolic function. Wall motion abnormalities could be regional or diffuse. The amount of myocardial damage varies widely in patients with SARS-Cov-2 infection. If the affected area is small, 2D echocardiography may not be sensitive enough to detect the typical findings for diagnosis. Patients with acute myocarditis were found to have decreased longitudinal and circumferential strain and strain rate values. Modified regional strain values correlated with the late gadolinium enhancement changes. A novel parameter derived from speckle tracking echocardiography is myocardial work, which measures the LV pressure-strain relationship. It provides a more detailed assessment of segmental and global left ventricle function and is less load-dependent. The findings of myocardial damage in COVID-19 patients on echocardiography are not specific. Cardiac magnetic resonance remains the imaging diagnostic tool.

**Conclusions.** Different echocardiographic methods can be used to identify cardiac lesions in patients with SARS-Cov-2 infection. The features are nonspecific, and other pathologies must be excluded. Clinicians must provide adequate diagnosis, monitoring, and treatment because the long-term impact of COVID-19 myocardial damage is still unknown.

#### **C4. Coronavirus disease 19 (COVID-19) pandemic effects on admissions and in-hospital outcomes of acute myocardial infarction in Albania**

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**Introduction.** Worldwide reports have shown a significant decrease in admissions and divergent results regarding complication rates in acute myocardial infarction (AMI) patients. We aimed to study the impact of the COVID-19 outbreak on admission rates and in-hospital outcomes of AMI patients.

**Methods.** Was conducted a retrograde single-center study, collecting data for all-AMI admissions from March 9<sup>th</sup>, 2020 (first COVID-19 case) until April 30<sup>th</sup> compared with the same period of 2019. AMI admissions were classified as ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI). Incidence rate ratio (IRR) was used to compare AMI admissions and revascularization procedures, and risk ratio (RR) to compare mortality and cardiogenic shock.

**Results.** Admissions for AMI declined during the COVID-19 period from a total of 311 patients in 2019 to 219 patients in 2020 (-29.6%) representing an IRR=0.704 ( $p<0.0001$ ). Reduction in admissions for all AMI types, including both STEMI (IRR 0.719;  $p=0.033$ ) and NSTEMI (IRR=0.67;  $p=0.001$ ); and in invasive procedures performed respectively, in coronary-angiography (IRR= 0.683;  $p<0.0001$ ), and in percutaneous coronary interventions (IRR=0.64,  $p<0.0001$ ) were observed. No significant increase in all-AMI mortality during pandemic outbreak compared to 2019 (RR= 1.59;  $p=0.12$ ), but a significant increase in STEMI mortality (RR=1.91;  $p=0.037$ ) and in all-AMI cardiogenic shock (RR =1.79;  $p=0.013$ ) were observed.

**Conclusions.** Admissions and coronary procedures significantly reduced in all-AMI patients associated with a non-significant increase in mortality during the COVID-19 pandemic outbreak. Meanwhile, the STEMI mortality and cardiogenic shock substantially increased. Public education to seek medical care and the safety of health care services are the best response to the situation created by the pandemic.

## C5. Overweight, obesity and cardiovascular risk

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**Introduction.** In Bulgaria overweight and obesity are associated with a number of chronic non-communicable diseases. The aim of the present study is to investigate the anthropometric indicators and indices in patients with cardiovascular diseases and their relationship to cardiovascular risk.

**Material and methods.** A representative sample of 100 subjects at the age of  $55.4 \pm 9.7$  was selected from practices of general practitioners in Pleven, diagnosed with cardiovascular diseases. Weight, body mass index, body fat percent, fat free mass were measured by Tanita Body Composition Analyzer. Height, waist and hip circumferences were measured by standardized stadiometer and special measuring tape. Overweight, obesity and cardiovascular risk were assessed, according to the WHO definitions and cut-off values of waist circumference, waist to hip ratio (WHR), and index of visceral obesity (IVO).

**Results.** The prevalence of obesity was 46% and the overweight was 33%. Every third female was with overweight and every second male was obese. Increased cardiovascular risk according to the cut-off criteria of waist circumference was assessed in 71% of the studied group, in 83% by the IVO, and in 73% by the WHR. Significantly more males had higher risk in comparison with the women according to the WHR (91% vs. 64%) and the IVO (97% vs. 76%).

**Conclusions.** A very high percentage of overweight and obese subjects was identified in a Bulgarian population suffering from cardiovascular diseases. Men were found to be at higher future health risk according to the applied anthropometric indicators in this study.

## C6. Aortic stenosis in patients with heart failure and atrial fibrillation: impact on mortality

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**Background.** Aortic stenosis (AS) is a degenerative and progressive disease, that usually remains asymptomatic for decades, but once symptoms appear, survival is significantly compromised. When associated with heart failure (HF) and atrial fibrillation (AF), aortic stenosis leads to a high risk of mortality.

**The objective** was to determine the risk of one-year mortality in patients with HF, AF with AS, compared to patients with HF, AF without AS, according to their left ventricular ejection fraction (LVEF).

**Materials and methods.** This is a prospective, observational, case-control study that included 727 patients with HF, AF, of whom 119 with moderate or severe AS, hospitalized in the Clinical Emergency Hospital of Bucharest, Romania, between January 2018 – December 2019. The inclusion criteria were: age more than 18 years, diagnosis of chronic HF and AF (paroxysmal, persistent or permanent), informed written consent to participate to this study. The exclusion criteria were: the absence of echocardiography data, suboptimal ultrasound view, other cardiac



rhythms than AF. Patients were divided in three subgroups: subgroup A – 278 patients with HF with preserved ejection fraction (HFpEF), subgroup B – 112 patients with HF with mid-range ejection fraction (HFmrEF), subgroup C – 337 patients with reduced ejection fraction (HFrEF). AS was present in 61 patients in subgroup A, 15 in subgroup B and 43 in subgroup C. 2D transthoracic echocardiography was performed in all patients. Statistical analysis was performed in R software, version 4.0.2 2020. The study respected the ethical standards of the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law.

**Results.** The one-year mortality rates were 27.69% in subgroup A, 27.67% in subgroup B and 36.49% in subgroup 3. AS was associated with the increase of one-year mortality only in the subgroup of patients with HFrEF (OR 2.00, 95%CI 1.04 to 3.83), while in the two other subgroups of patients, did not increased statistically significant the risk of mortality.

**Conclusions.** Patients with HFrEF, AF and AS had a higher risk of one-year mortality compared to patients with HFrEF and AF without AS.

## GASTROENTEROLOGY

### G1. MicroRNA in the diagnosis and prognosis of pancreatic cancer

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One of the molecular targets with potential diagnostic, prognostic and therapeutic role in pancreatic cancer, that has received special attention in recent years, is represented by Micro-Ribonucleic Acid (miRNA). MiRNAs are small (~ 19–25 nucleotide) noncoding RNA molecules involved in the regulation of biological processes such as cell development, cell differentiation, and cell survival. To date, approximately 2469 miRNAs have been identified in humans and it is estimated that approximately one-third of all genes are regulated at the posttranscriptional level by these molecules. Also, single miRNA has the ability to regulate multiple genes. Recent data highlight the aberrant expression of a series of miRNAs in patients with pancreatic cancer and their role in tumor development, invasion and metastasis. For example, the combined evaluation of miR-16, miR-196a and CA19-9 in biopsy tissue or pancreatic juice samples had a sensitivity of 92% and a specificity of 95.6% in differentiating pancreatic tumor cells from normal tissue. Other overexpressed mi-RNAs in pancreatic tumor cells, with a role in the diagnosis of this neoplasm, are miR-376a, miR-301, miR-155, miR-21, miR-221 and miR-222. Given the poor prognosis of patients with pancreatic cancer, the use of miRNA in the diagnosis of this neoplasm may lead to improved morbidity and mortality in these patients.

### G2. Approach to gastrointestinal bleeding in the emergency department

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**Introduction.** Digestive bleeding is a major medical emergency that can compromise patients' lives.

**Material and methods.** The retrospective study included the evaluation of 353 medical records of patients who went to the Emergency Department (ED) of Institute of Emergency Medicine (IEM) with complaints of gastrointestinal bleeding. The selected data were statistically processed using the Excel program.

**Results.** Of the 353 cases of gastrointestinal bleeding (GIB) who addressed in the ED, 305 (86.4%) had superior gastrointestinal bleeding (SGIB), 48 cases (13.6%) had lower intestinal bleeding (LIB). The ratio between men and women with a presumptive GIB diagnosis was 4:1. Patients suspected of GIB were served in the yellow area or in the red area, depending on the parameters of vital signs. All were investigated clinically and paraclinically. In the case of SGIB,

video esophagogastroduodenoscopy was performed in ED, in 199 cases (65.24%) the presence of SGIB was excluded, and in 106 cases (34.76%) it was confirmed. Endoscopic hemostasis (EH) by injecting hemorrhagic lesions was performed in 40.57% of cases confirmed by SGIB (43 patients). Endoscopic banding of esophageal varices was scheduled in 37 patients. In 26 cases, hemorrhagic erosions (19 cases) and not identifying the source of SGIB (7cases), it was not possible to provide EH. Patients with LIB were hospitalized for colonoscopy.

**Conclusions.** Endoscopic examination of the digestive tract is the method of choice for the diagnosis of gastrointestinal bleeding. Endoscopic hemostasis is the minimally invasive method of choosing treatment.

### G3. Clostridium difficile infection in cirrhotic patients

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**Background.** Clostridium difficile infection (CDI) is associated with higher mortality in hospitalized liver disease patients. Cirrhotic patients are more susceptible to developing CDI due to the particular risk factors. In the first place, during the therapeutic management of this pathology, it is common to administer antimicrobial therapy for the prophylaxis of spontaneous bacterial peritonitis with the consequence of disturbing the intestinal microbiome. In addition, symptomatic therapy with proton pump inhibitors (PPI) increases the risk of CDI and the multiple long-term hospitalizations imposed by decompensation episodes place the patient in a high-exposure environment. The aim of this study emphasizes the importance of knowing the risk factors associated with the increased incidence of CDI in patients with cirrhosis in order to initiate optimal prevention measures, focusing on the balance between risks and benefits in the evolution of liver disease.

**Material and methods.** This study included a total of 278 patients admitted to the gastroenterology department between 1st of June 2020 and 30th of June 2021, diagnosed at admission or during hospitalization with CDI. Among these patients, a significant percentage (20.14% - 56 of 278) was represented by patients previously diagnosed with liver cirrhosis with various etiologies. In this subgroup of patients, we analyzed the following data: age, sex, previous hospitalizations, laboratory parameters, duration of current hospitalization and previous administration of antibiotics.

**Results.** The study group consisted of 37 (66.07%) male patients and the mean age was  $54 \pm 12.87$  years. 12.5% (7 of 56) of cirrhotic patients diagnosed with CDI had at least one previous hospitalization during the same year. The average length of stay in the hospital was slightly longer than 8 days. Data from the subanalysis correlate the prolongation of the hospitalization period with the presence of pathological conditions such as hypoproteinemia, hepato-renal syndrome or hepatic encephalopathy. A significant percentage of cirrhotic patients (73.21% - 41 of 56) were exposed to antibiotics prior to diagnosis of CDI.

**Conclusions.** Cirrhotic patients have an increased risk of CDI due to pathophysiological features, therapeutic agents and high levels of exposure during prolonged hospitalizations. Knowing the risk factors requires a preventive approach by carefully choosing the recommended antibiotics, establishing on strict criteria the prophylaxis indication of spontaneous bacterial peritonitis and avoiding the excessive administration of PPI.

#### **G4. Controversies of long-term antibiotherapy in advanced colorectal cancer patients with cutaneous adverse reactions to EGFR inhibitors**

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Colorectal cancer (CRC) is an important public health issue, with increasing incidence and mortality. The development of new targeted therapies such as those based on EGFR-inhibitors (epidermal growth factor receptor inhibitors) have led to better outcomes for patients. However, these novel treatments are frequently associated with significant adverse reactions. Cutaneous manifestations induced by EGFR-inhibitors often require long-term antibiotherapy with tetracyclines. Clinicians (oncologists, dermatologists, infectious diseases specialists, and others) may find difficulties in their management due to scarce information and controversial opinions regarding the impact of antibiotic therapy in this category of already vulnerable CRC patients. We aim to discuss the main challenges raised by long-term use of tetracyclines in advanced CRC patients under EGFR-inhibitors.

#### **G5. Neurocognitive impairment among patients with chronic liver disease**

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**Introduction.** In Romania, the diagnostic methods for neurocognitive impairment encountered in minimal hepatic encephalopathy (HE) are not standardized. In this ongoing prospective study,

we aimed to evaluate the presence of minimal HE, using the psychometric hepatic encephalopathy score (PHES) which is recommended by ISHEN (International Society for Hepatic Encephalopathy and Nitrogen Metabolism) as the “gold-standard” method.

**Material and methods.** A total of 55 patients with chronic liver disease were enrolled between December 2020 and May 2021. We excluded patients with overt HE, neurological or psychiatric comorbidities.

**Results.** We divided the patients in 2 groups: study group included 32 cirrhotic patients and control group which included 23 non-cirrhotic patients (e.g. steatosis, hepatitis). In the study group mean age was  $62.6 \pm 8.7$  years and the average number of years of education was  $10.9 \pm 2.7$ . Non-cirrhotic patients had a significantly lower mean age ( $55.3 \pm 6.7$ ) and higher number of years of education ( $13.1 \pm 2.4$ ). The five neuropsychological tests comprising the PHES were administered to all enrolled subjects. The cut-off between normal and pathological values for PHES score was set at  $-4$  points. In the study group the mean PHES was  $-2.91 \pm 2.51$ , significantly lower than in the control group,  $1.39 \pm 0.72$  respectively. The prevalence of minimal HE was 27.2% (15 patients).

**Conclusions.** Minimal HE is highly prevalent in patients with liver cirrhosis and affects both the individual and the society, by reducing workplace and driving performance. Besides impairing the quality of life, minimal HE also has an increased risk of progression towards overt HE.

## G6. Upper gastrointestinal bleeding - key aspects of management

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Upper gastrointestinal bleeding is one of the most common medical emergencies presented in the gastroenterology department. Starting from the case of an 18-year-old man with a clinical picture suggestive for an acute episode of digestive bleeding, contact with a COVID-19 case confirmed by PCR test, we will highlight the key features of acute upper gastrointestinal bleeding management (AUGIB). Patients with AUGIB clinical picture require adequate initial management, focused on simultaneous intensive care interventions and clinical-biological evaluation in order to stabilize hemodynamics to a permissive condition for diagnostic and therapeutic interventions. The integration of significant developments in the endoscopic and medical treatment of the AUGIB episode helps to guide case management according to the standards of good clinical practice. In patients suspected of being infected with SARS-CoV-2, opting for endoscopy requires unique management decisions. Also, it is important to impose prompt evaluation using validated screening tools for identifying patients at increased risk of death, rebleeding and establishing an endoscopic intervention or surgical hemostasis. This cascading approach to case management will allow both the etiology and risk factors for rebleeding to be specified, as well as the medical and endoscopic therapeutic interventions available to reduce these risks.

## NEUROLOGY

### N1. A comprehensive overview of vascular aphasia

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Aphasia is a central, acquired disorder of language that damages a person's ability to produce and/or understand spoken and written language. It is induced by a localized/diffuse lesion (vascular pathology: ischemic and hemorrhagic stroke, cerebral veins and dural sinuses thrombosis – known as vascular aphasia; traumatic brain injury: subdural hematoma; brain tumors; neuroinfections - especially Herpes simplex encephalitis; neurodegenerative diseases: Alzheimer disease), situated usually in the dominant cerebral hemisphere, in proven right-handed persons. Vascular aphasia affects more than one-third of all stroke patients. It improves during the first 4 weeks in one-third of the patients and in the first 6 months in almost half of them. The language disturbances observed in practice are usually combined into aphasic syndromes, which are components of different vascular syndromes (that include aphasia, hemiparesis, hemianopia, etc). The most determinant factor of the type of aphasia is the infarct location (especially left superficial anterior, left superficial posterior or left complete middle cerebral artery ischemic stroke). The importance of studying vascular aphasia rises from the failure in establishing an effective treatment for this patients (different therapies have been studied overtime, from different drugs to experimental methods of transcranial stimulation – magnetic TMS or direct current tCS). Also is considered a marker of stroke severity (is associated with a higher risk of mortality, poor functional prognosis) and increased risk of post-stroke dementia.

### N2. Multiple sclerosis patients safely navigating during the COVID-19 pandemic

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**Introduction.** The COVID-19 pandemic was a challenge for the multiple sclerosis (MS) patients. MS do not expose people to a higher risk of SARS-CoV-2 infection, but some specific immunosuppressive disease modifying treatments needed a special attention, as well as the vaccination.

**Material and methods.** We present the data collected, the 1<sup>st</sup> of May 2021, using a special created questionnaire, from 668 (84.02%) MS patients (436 women and 232 men) out of the 795 treated and monitored in the Neurology Department of the Colentina Clinical Hospital Bucharest.

**Results.** 83 patients had mild forms of COVID-19 while treated with: Interferon (IFN) beta 1b 7 cases (12.2% of the patients treated with the same drug), IFN beta 1a im 18 cases (11.61%), IFN beta 1a sc 17 cases (13.28%), Glatiramer acetate 10 cases (7.81%), Teriflunomide 18 cases (14.51%), Natalizumab 11 cases (16.41%), Ocrelizumab 2 cases (28.57%). Only 6 were hospitalized. We encouraged vaccination, so that 205 patients (30.68%) received the COVID-19 vaccine in the first 4 months, although at the beginning of the vaccination program, the MS patients were not considered at high risk. All the patients who were infected with SARS-CoV-2 were not vaccinated before and 27 of them got vaccinated after recovering from COVID-19.

**Conclusions.** Our MS patients started, continued or switched treatments. Respecting the protection rules and getting vaccinated limited the number of COVID-19 cases to 12.42%. The disease modifying treatments did not worsen the outcome of COVID-19, and vaccination didn't induce relapses or adverse events different from the healthy population.

### **N3. Morbidity through acute stroke in adult population of the Republic of Moldova**

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**Background.** Stroke remains one of the leading causes of death and the largest cause of disability in the Republic of Moldova, being the third leading cause of death (159.1: 100000). In 2019 there were registered 7320 new cases of stroke. The prevalence of cerebrovascular diseases is 274.8:10 000 and incidence is 30.3 per 10 000 population. The medical-economic importance of stroke prevention for the Republic of Moldova is argued by the presence in the population on 01.01.2020 of 79691 patients who suffered a stroke and who constitute 1.98% of the total population and 2.46% of the adult population. At stationary treatment in 2020, 5.03% of hospitalized adults or 23976, who spent 211835 days-bed, which is 4.79% of the total days-hospitalization per republic.

**Materials and methods.** A retrospective hospital-based study was conducted at the clinical base of the Department of Emergency Medicine, USMF "Nicolae Testemitanu" (IMSP Institute of Emergency Medicine) from January 01st, 2020 to July 31st, 2020. The statistical processing of the results was performed using programs SPSS 22.0(SPSS inc). Out of 480 patients, 54.4% were male and 45.6% were female, the mean age of the patients was 59.8±17.4 years and the mean age at the time of stroke was 58.4 ±15.9 years. 83.0% had ischemic stroke and 17.0% had hemorrhagic stroke.

**Results.** Stroke is mainly a problem of advancing age, the most affected categories of age are 61-70 years (23.0%), 71-80 years (33.0%) and patients over 80 years were 17.0%, patients over 70 years were 50.0%. Age distribution overall about half (67.0 %) of stroke patients were in the age group 61-80 years, 17.0% patients were in the age group 20-40 years, and 18.0% of patients were having age more than 80 years. The analysis of the incidence of different risk factors in ischemic stroke (IS) were as follows: 42.6% hypertension, 32.7% smoking, 32.2% alcohol intake, 24.8% diabetes mellitus, 22.6% coronary artery disease, 18.6% dyslipidemia, 16.6% dysrhythmia,

13.4% previous stroke, 10% inactivity, 8.8% transient ischemic stroke in the past. The major risk factors in hemorrhagic stroke (HS) were: 57.0% hypertension, 39.3% smoking, 36 alcohol intakes, 26.8% coronary artery disease, 26.3% dyslipidemia, 21.2% obesity, 26.3% dysrhythmia, 20% diabetes mellitus, 19.8% inactivity. In our study, the most common clinical presentation was motor weakness (90.0%) followed by headache (39.0%), speech involvement (35.0%), altered sensorium (33.0%). In ischemic stroke, motor weakness was seen in 92.0%, speech involvement in 38.0%, headache in 33.0%, and altered sensorium in 20%. In hemorrhagic stroke, altered sensorium was present in 93.0%, motor weakness in 79.0%, headache and vomiting 64.0% of patients, and it was statistically highly significant ( $p < 0.001$ ).

**Conclusions.** In Republic of Moldova, stroke is predominantly a problem of advancing age, the most affected categories of age are 61-70 years (23.0%), 71-80 years (33.0%) and patients over 80 years were 17.0%, patients over 70 years were 50.0%. In our study, most common clinical presentation was motor weakness, followed by headache, speech involvement, altered sensorium. In the ischemic stroke, motor weakness was seen in 92.0%, speech involvement (38.0%), headache (33.0%), and altered sensorium (20%). In hemorrhagic stroke, altered sensorium was present in 93.0%, motor weakness in 79.0%, headache and vomiting 64.0% of patients, and it was statistically highly significant ( $p > 0.001$ ). The analysis of the incidence of different risk factors in ischemic stroke (IS) was as follows: hypertension, smoking, alcohol intake, diabetes mellitus, coronary artery disease, dyslipidemia, dysrhythmia, previous stroke. Informative programs for the population are required taking into consideration that only 1 of 5 patients that has reached the emergency services were aware of the problems a consequence caused by stroke.

#### **N4. The importance of emergency medical assistance at the prehospital stage in initiating the specific therapy of stroke**

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**Introduction.** Thrombolytic therapy in ischemic stroke has major efficacy within the first 3 hours of onset.

**Objective.** Determination of stroke onset to emergency call and to arrival of the emergency team, with the as quickly possible transportation to the Emergency Department (ED), given the decisive importance of time in applying specific treatment.

**Materials and methods.** We analyzed the cases of stroke patients who have call to the Emergency Medical Service (EMS), the results of clinical examination and patient monitoring during pre-hospital transport of 384 patients from disease onset to ED. Gender, age of the patients, type and onset of stroke, and time from onset until arrival in the ED were assessed.

**Results.** Of the 384 patients enrolled in the study, 246 patients (64.1%) were registered by family doctor with hypertension and received treatment and in another 138 (35.9%) the blood pressure was within the normal range. The gender distribution: 186 (48.4%) were men and 198 (51.6%) women. Stroke rate by age group showed a gradual increase in the incidence with every decade since the age of 50, being the maximum among the patients aged 60-70 years. The most frequent EMS was requested by relatives in 247 cases (64.3%), followed by the family doctor in 67 cases (17.4%) and only in 26 cases (6.8%) the patient alone call for ambulance. In 44 cases



(17.4%), pre-hospital EMS was announced by other people, such as neighbors and others. Regarding the duration from first symptoms to emergency call found, the addressability under 1 h was 8 patients (2.1%), 1-3 hours – 209 patients (54.4%), 3-4.5 hours – 53 patients (13.8%) and more than 4.5 hours – 114 (29.7%). Namely, people living with relatives were able to request EMS within 3 hours of stroke onset. Also, according to statistical analysis, it was found that not all people knew the exact time of the illness onset. The exact time of stroke onset was known in 306 (79.7%) patients and 78 (20.3%) were found by relatives. Of the 306 patients whose relatives know the exact stroke onset time, 217 patients (70.0%) reached the DMU within 3 hours, between 3-4.5h – 53 patients (17.3%), more 4.5 hours – 36 patients.

**Conclusions.** Initiating the specific treatment in less than 3 hours in patients with ischemic stroke is the main condition for the survival and rapid recovery of these patients. Early recognition of the onset of stroke, as well as minimizing the time from the onset of symptoms to the initiation of treatment are the main factors that can be influenced. Therefore, the role of SAMU in ischemic stroke management is essential.

#### **N5. Peculiarities in a familial case with neurofibromatosis**

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**Introduction.** Neurofibromatosis 1 (NF1) is a autosomal dominant disorder with an incidence of 1/3000 individuals worldwide. Males and females are affected equally. Neurofibromatosis 1 does not affect a particular ethnic group. The primary cutaneous manifestations are café-au-lait spots, neurofibromas and freckling in the axillae and inguinal regions. Other diagnostic criteria includes a first-degree relative with neurofibromatosis 1, tumors, ophthalmologic, musculoskeletal, vascular and neurological findings. Tendency for malign degeneration of neurofibromas is described. Cognitive and behavioral disorders affect between 50-80% of all children with NF1.

**Material and methods.** The authors present a familial case with neurofibromatosis type 1 who are registered in the Regional Center for Medical Genetics of Municipal Clinical Hospital "Dr. Gavril Curteanu" Oradea. Three family members are affected, the father and two children.

**Results.** The father presents café-au-lait spots, multiple neurofibromas found on the anterior and posterior thorax, axillary freckling and Lisch nodules. Both children have disseminated café-au-lait spots, freckles in the axillae and inguinal region, macrocephaly and short stature. Also, the children present social difficulties, attention-deficit/hyperactivity disorder, delay of expressive language.

**Conclusions.** Cognitive problems are common in children with NF1 and they can often complicate treatment. Early recognition of developmental impairments is important for the

effective treatment of these patients. A multidisciplinary team is required for the evaluation, monitoring and social integration of a patient with complex NF1.

## **N6. Clinical and radiological aspects in cerebral venous thrombosis during the COVID period**

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**Introduction.** Deep vein thrombosis as well as pulmonary embolisms were found to be frequent complications of SARS-CoV-2 infection.

**The objective of the retrospective study** was to evaluate the frequency of the cerebral vein thrombosis during the COVID-19 period compared to a reference period before the COVID-19 pandemic. Furthermore, we tried to find MRI differences between the two periods regarding the radiologic features this pathology usually presents.

**Material and methods.** The population selected for this study was a group of patients diagnosed with cerebral vein thrombosis at the Hospital Fondation A. De Rothschild, a medical center in Paris focusing primarily on neurological pathologies. The reference for the non-COVID-19 period was the year 2019, and the reference for the COVID-19 period was the entire year 2020. The patients we excluded were the ones addressed for cerebral vein thrombosis check-ups, along with the patients who presented aspects of sequelae from older thrombosis on their MRI.

**Results.** During the non-COVID-19 period (2019), 20254 MRIs were performed and 44 patients were diagnosed with cerebral venous thrombosis, which corresponds to an occurrence of 2.17/1000 for this pathology. During the COVID-19 period, 15436 MRIs were performed, and 31 cerebral venous thrombosis were discovered, corresponding to an incidence rate of 2/1000. During the COVID-19 period (2020) and compared to the reference period, more thrombosis of the sagittal superior sinus as well as the cortical veins were found, whereas the lateral sinuses were overall less affected.

**Conclusions.** Even though the incidence rate of the cerebral vein thrombosis seems unaltered by the COVID-19 outbreak, the cortical thrombosis, and to a lesser extent the superior sagittal sinus thrombosis, were found more frequently in proportion to the reference period. Nonetheless, given the limited number of patients we were able to gather, in addition to the rarity of this disease, these results would benefit from the backing of a study involving a bigger cohort of patients.

## RHEUMATOLOGY

### R1. New approaches in the treatment of systemic vasculitides with biological medicinal products

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**Introduction.** Systemic vasculitides are rare and heterogeneous disorders that affect different organs and organ systems, with varying degrees of severity depending on the size, location, and significance of the affected vessels. The etiology and pathogenesis of primary vasculitides are still unknown. The pathogenesis included different mechanisms: deposition of immune complexes onto vessel walls, autoantibodies (e.g. anti-endothelial and anti-neutrophilic cytoplasmic antibodies), cell-mediated and humoral immune responses, granuloma formation and endothelial damage. Treatment consists in glucocorticosteroids and immunosuppressants. The mortality rate for some vasculitides can exceed 90% for a 5-year period. From 2018, the biological product Rituximab is available as an alternative in the treatment of vasculitides associated with antineutrophil cytoplasmic antibodies.

**The objective of the study.** We analyzed the available therapeutic strategies and mechanisms of action of the different therapies and evaluate their structural and functional characteristics, with an emphasis on the biological product Rituximab.

**Materials and methods.** Using published registration data and clinical trials and through graphical static and dynamic models, we will present the mechanism of action of Rituximab in systemic vasculitides treatment.

**Results.** The overall survival rate in vasculitides, associated with antineutrophil cytoplasmic antibodies after the inclusion of Rituximab in therapeutic regimens is expected to exceed 87% for a 5-year period. Biological medicinal products are expected to ameliorate systemic vasculitides prognosis - from a disease with high short-term mortality to a fully treatable one.

**Conclusions.** Knowledge of the pathogenetic mechanisms of vasculitides and the mechanisms of action of biological medicinal products by medical professionals is essential to the success of the therapy.

### R2. Clinical trials of immunosuppressive agents for organ transplantation

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**Introduction.** The organ transplantation is fast growing part of medicine during the last few decades that includes the development of surgery, immunology, appearance of new drugs and health care. The aim of immunosuppression is to control the unwanted immune response and if it's possible to prevent from drug complicate which are obtained because of the immunodeficiency. The immunosuppression is achieved through ablation; change of location

and migration of lymphocytes; change of lymphocytes and dendrites function or affecting the lymphokines. These interventions can be physical or pharmacological. The aim of the study is to review scientific and regulatory requirements when clinical trials of immunosuppressive agents for organ transplantation is made. To analyze the main guidelines of conducting clinical trials in transplant patients, types of design, outcome measures, analyze of evidence of effective immunosuppression etc.

**Materials and methods.** Documentary analysis and content analysis of published guidelines and standards of EMA, FDA and scientific publications are used.

**Results.** The law bases for clinical trials with transplant patients are Directive 2001/83/EO, Regulation (EO) 141/2000 about orphan drugs and Regulation (EO) 726/2004, in particular conditional approval of marketing authorization and all the guidelines of CHMP. The potential claims of immunosuppressors in transplantation must include 3 main elements: induction prevention; initial or prolonged prevention; treatment of acute rejection.

**Conclusions.** We present the main requirement of population selection, primary and secondary endpoints, donor, recipient and transplant requirements, evaluation of efficacy methods, selection of comparator ect. Clinical trials with transplant patients are serious challenge and require multidisciplinary approach.

### **R3. Health related quality of life in patients with antineutrophil cytoplasm antibody associated vasculitis conducting biological treatment - a systematic review of scientific publications**

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**Introduction.** In severe forms of ANCA-associated vasculitis (AAV), the rapid onset of ischemia and blockage of blood vessels can lead to organ failure and death. The aim of the study was to evaluate the health-related quality of life in patients with AAV and assessed as suitable for treatment in accordance with the EULAR and Bulgarian national specific criteria for treatment with biological products with INN Rituximab.

**Materials and methods.** A systematic review of scientific publications in accordance with the PRISMA guideline was performed. We prepared a survey protocol with predefined: topic, design, search strategy, inclusion and exclusion criteria, data collection methods, data analysis and statistical evaluation, conclusions. The PICOS tool has been developed for patients with AAV.

**Results.** We conducted a literature search by keywords: systemic vasculitis, biological treatment, rituximab; HRQoL in MEDLINE and PubMed databases for the period 2002 - 2020. We found a total of 190 publications – 177 publications in MEDLINE and 13 in PubMed. We removed 27 articles because they are not in English. 159 articles do not contain the keyword HRQoL. The other 4 do not contain information about Rituximab.

**Conclusions.** We did not find any scientific publications that deal with quality of life (HRQoL) in patients with AAV and treated with Rituximab. The lack of literary publications in the world-famous databases gives us reason to believe that the topic we have chosen is original in nature,

not only for Bulgaria, but also internationally. The importance of rituximab in the treatment of AAV is still an unexplored scientific area.

#### **R4. Novel insights into the relationship between oxidative stress, gut microbiota and psoriasis**

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Reactive oxygen species (ROS) are highly reactive entities that participate in a series of chemical and biochemical processes. An increase in ROS, not compensated by antioxidant mechanisms, leads to oxidative stress (OS). The involvement of OS in diseases with a chronic inflammatory background has been intensively studied, and elevated ROS levels and a decrease in the total antioxidant capacity have already been shown to be involved in the pathophysiology of cancers, cardiovascular disease, obesity and particularly inflammatory bowel diseases (IBD). The association of psoriasis (PSO) with the above-mentioned disorders has directed the attention of the scientific community towards the study of the role of OS and of gut microbiota in the onset and progression of PSO. Recent research has depicted correlations between biomarkers of OS, e.g., malonyldialdehyde (MDA), superoxidismutase (SOD), catalase (CAT), the quantitative and qualitative alteration of the gut microbiota and PSO severity. Thus, patients with PSO have elevated levels of SOD assessed in the blood and skin (both in the affected and the normal skin), emphasizing once again the systemic nature of the disease. A correlation was also observed between elevated MDA levels, blood cholesterol levels and the Psoriasis Assessment Severity Index (PASI) score in PSO patients. Regarding the composition of the microbiota, patients with PSO show a decrease in the commensal species of *Lactobacillus* and *Bifidobacterium* spp, with an increase in the pathogenic ones, among which the most frequently mentioned are *E. Coli.*, *Salmonella*, *Helicobacter* and *Candida albicans*. The same changes are present in other diseases characterized by an increase in OS, such as IBD, even in the absence of PSO. All these data suggest an interrelationship between OS, gut microbiota and PSO, with the possibility to reduce OS levels and PSO severity via an adequate, low-fat diet (in order to lower cholesterol metabolism products), rich in antioxidants and supplemented with probiotics according to the alterations of the gut microbiota.

#### **R5. Osteogenesis imperfecta – a case report**

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**Introduction.** Osteogenesis imperfecta (OI) is a group of rare disorders of the connective tissue. It is caused by mutations in the COL1A1 and COL1A2 genes that codify the alpha 1 and alpha 2 chains of type 1 collagen. The incidence of OI is approximately 1 per 20.000 births. The main signs include spontaneous fracture or fracture from minor trauma, joint hypermobility, especially of the small joints, skin fragility, easy bruising. Hearing loss is a variable feature of OI. Inherited thrombocytopenia (IT) represents a group of hereditary disorders characterized by a reduced number of platelets and sometime abnormal platelet functions, which can subsequently lead to impaired hemostasis. The clinical spectrum of IT ranges from severe bleeding diatheses, during the first few weeks of life, to mild conditions that may remain undetected even in adulthood.

**Case presentation.** The authors present the case of a boy, 11 year-old, with OI associated with IT, who is registered in the Genetics Department and Hematology Department of Municipal Clinical Hospital "Dr. Gavril Curteanu" Oradea, Romania. His father, brother and two sisters were also diagnosed with IT. The boy presents craniofacial dysmorphism: microcephaly (head circumference below percentile 5), low insertion of the hair, mild exophthalmia, blue sclera, full lips; short stature (-3SD), abnormal joint flexibility, skeletal deformities as a result of repeated fractures of the upper and lower limbs, with a vicious consolidation of the callus. In addition, he presents low counts of platelets detected since birth. The treatment was substitutive, including blood transfusions during infancy, calcium supplements and folic acid, orthopedic (immobilization of fractures in splints), kinetotherapeutic. The platelets number remained between 70000-80000/mm<sup>3</sup>; he suffered no fractures in the past 3 years.

**Conclusions.** OI is a rare genetic disease with no curative treatment. The association with IT requires a multidisciplinary approach in order to better evaluate and monitor the patients.

## R6. Systemic lupus erythematosus patients during COVID-19 pandemic

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**Introduction.** During COVID-19 pandemic, patients with systemic lupus erythematosus (SLE) experienced a limited access to doctors and medical tests.

**The objective of the study** was to determine the availability of local Healthcare resources for patients with SLE during COVID-19 pandemic.

**Material and methods.** A group of 98 lupus patients (group 1) was examined during the period of 01.04.2019–31.03.2020, using a questionnaire investigating SLE activity, treatment, addressability, QoL (SF8), hospitalization, Lupus Impact Tracker (LIT), the COVID-19 diagnosis and vaccination. Using the same questionnaire, patients (n=95, group 2) had a repeated phone interview, a year later (01.04.2020 – 31.03.2021).

**Results.** The data from two groups revealed a reduction of site visits number from 3.2 to 0.9 vs. phone consultations, which increased from 3.6 to 9.8 times. PGA was 46.9 and 49.7 points, in group 1 and 2. The SF-8 physical component score decreased from 38.7 to 36.7 and the mental component – from 41.8 to 32.9. The number of hospitalizations decreased during the COVID-19 pandemic from 17.3% to 5.2% cases. The treatment recorded a reduction in the use of immunosuppressants to 8.4% and an increase of NSAIDs prescription to 29.4%. SARS-CoV-2 infection occurred in 9.4% of lupus patients and vaccination was performed in 40.5% of cases. The disease impact on lupus patients, as initially assessed by LIT, increased from 52.4 to 65.1 points ( $<0.05$ ), in both groups.

**Conclusions.** The addressability of systemic lupus erythematosus patients to a rheumatologist and hospitalizations decreased significantly during the COVID-19 pandemic, which led to increased activity and burden of the disease in these patients.

### **R7. An antiphospholipid -antibody syndrome with renal involvement**

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**Background.** Antiphospholipid syndrome (APS) is an acquired, immune-mediated thrombophilia occurring alone (primary APS, PAPS) or in association with other autoimmune diseases, mainly systemic lupus erythematosus (SLE), (secondary APS), characterized by recurrent venous or arterial thrombosis and /or pregnancy morbidity in association with antiphospholipid antibodies (aPL) and/or lupus anticoagulant (LA).

**Case report.** A 36-year-old woman was admitted to the hospital because of acute renal failure and thrombocytopenia. This woman presented with an acute illness characterized by a prodrome of respiratory symptoms and fever that were unresponsive to antibiotic therapy, followed by the progressive involvement of multiple organs. There was enzymatic and functional evidence of myocardial necrosis leading to intermittent, severe heart failure, as well as acute renal failure requiring dialysis, laboratory evidence of pancreatic injury, pulmonary infiltrates with respiratory failure, and central nervous system involvement, with confusion. After a renal biopsy was detected a perinephric hematoma and thrombocytopenia. The laboratory criteria for the diagnosis of the antiphospholipid-antibody syndrome are an elevated value for IgG anticardiolipin antibody, a positive test for lupus anticoagulant, and an elevated value for IgM anticardiolipin antibody.

**Conclusions.** This patient has the antiphospholipid antibody syndrome, with an acute thrombotic angiopathy that caused ischemic damage in the myocardium, pancreas, kidneys and lungs. The renal interstitial inflammation is more severe than that expected from the ischemic injury alone and many reflect either a hypersensitivity drug reaction or in view of the dry Sjogren's syndrome.

### **R8. Psoriatic arthritis during COVID-19 pandemic**

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**Introduction.** During the COVID-19 pandemic, psoriatic arthritis patients had limited access to health care. The objective of the study was to assess the impact of the COVID-19 pandemic on medical care accessibility for psoriatic arthritis patients, and related consequences.

**Material and methods.** A group of 46 psoriatic arthritis (PsA) patients were examined between 01.04.19-31.03.20 (gr 1) by a 12-item questionnaire investigating addressability, QoL, hospitalization, and PsAID. During 01.04.20 -31.03.21 the same patients (n=44) were repeatedly interviewed by phone (group 2) including COVID-19 diagnoses and vaccination.

**Results.** Comparing general addressability in both groups, we noticed a reduction of visit numbers from 2.8 to 0.8 whereas phone consultations increased by 2.5-7.8 times. PGA was  $58.9 \pm 18.6$  and  $49.7 \pm 11.9$  points, respectively; the SF-8 physical component decreased from  $42.5 \pm 3.4$  to 39.7 and the mental component from 45.8 to 43.9. We noticed a reduction of patients' global state and mental component of quality of life. The number of hospitalizations decreased from 78.2 to 18.2%. The treatment included a decrease in the use of immunosuppressants to 17.4%, and increase in the use of NSAIDs from 73.9 to 88.6%. Among 46 patients (gr1) with psoriatic arthritis, COVID-19 occurred in  $10.8 \pm 2.9\%$ . Vaccinations were performed in 23.4% of psoriatic arthritis patients. The impact of the disease in psoriatic arthritis patients, assessed by Psoriatic arthritis impact of the disease-PSAID questionnaire increased from  $3.9 \pm 2.3$  to  $5.9 \pm 2.4$  points ( $p < 0.05$ ).

**Conclusion.** During the COVID-19 pandemic, psoriatic arthritis patients' addressability decreased significantly, which led to increasing of the activity and impact of the disease in these patients.

## **R9. Application of therapeutic drug monitoring to assess the therapeutic response and safety of biological therapy in patients with rheumatic diseases**

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**Introduction.** Therapeutic drug monitoring (TDM) is a set of pharmacokinetic (PK), pharmacodynamic (PD) and pharmacogenetic methods aimed to providing effective and safe personalized pharmacotherapy. TDM reduce the individual variability of the therapeutic response and pharmacokinetic parameters in real clinical practice, by effective control of blood and/or plasma concentrations of the respective medicinal product. TDM improves effectiveness and reduces the risk of adverse reactions. Biological products (BMP) containing antibodies become the main options for treatment of rheumatic diseases. The aim of study is to present the PD effects as a direct consequence of basic PK parameters.

**Materials and methods.** The literature review of scientific publications was performed.



**Results.** The pharmacokinetics of BMP are highly dependent on their route of administration, dose regimen, body weight and/or body surface, clearance and immunogenicity. The wide interindividual pharmacokinetic variability of BMP has been demonstrated - clearance, volume of distribution and elimination half-life are highly variable;  $T_{max}$ ,  $C_{max}$ , AUC, as well as their medians are in a wide range; the median half-life  $T_{1/2}$  is about 30 days, in the range of 10 to 90 days and etc.

**Conclusions.** There are serious difficulties in predicting the therapeutic and clinical response in the individual patient. The effectiveness of biologic treatment may be affected by low plasma concentrations due to incorrectly selected dose and dosing interval, and due to the lack of measurable plasma concentrations and formation of anti-drug antibodies. The introduction and application of TLM is a reliable method for improving therapeutic efficacy and achieving the optimal benefit/risk ratio in biological treatment.

#### **R10. Sarcoidosis in a patient with a history of cancer - causality or coincidence?**

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**Introduction.** Sarcoidosis is a systemic inflammatory disease, characterized by the presence of non-caseating granulomas. The most common pattern of sarcoidosis is the appearance of intrathoracic lymphadenopathies, usually mediastinal or hilar, associated or not with damage to the pulmonary parenchyma.

**Case presentation.** We present the case of a 46-year-old non-smoking patient, known with breast cancer operated and radio-chemo-treated in 2014, ovariectomy in 2015, mediastinal lymphadenopathies, acute conjunctivitis in both eyes, recently diagnosed uveitis in the right eye. The patient presented to our hospital complaining of dry cough and anterior chest pain accentuated at deep breath. Biological samples revealed a mild inflammatory syndrome. The spirometry highlighted a distal obstructive syndrome. TLCO (transfer factor for carbon monoxide) values were normal. Computed tomography of the thorax with contrast substance described rare micronodules and small bilateral lung nodules associated with an area of nodular ground-glass opacity located in the lower-left lobe and subdiaphragmatic lymphadenopathies. The histopathological examination of the lymph nodes revealed an appearance compatible with non-necrotizing chronic granulomatous lymphadenitis, without carcinomatous infiltrates. After the corroboration of clinical and imaging data with the histopathological examination, the diagnosis of stage II sarcoidosis was made.

**Conclusions.** The association between sarcoidosis and malignancy is not yet well-defined. The incidence of sarcoidosis was found to be higher in patients with a history of breast cancer than in the general population. The high frequency of sarcoidosis after certain cancers suggests the possibility of a causal association between malignancy and the development of sarcoidosis.

## ENDOCRINOLOGY

### E1. Thyroid and parathyroid conditions requiring endocrine surgery: COVID-19 pandemic data

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**Introduction.** Considering the global aspects with respect to the first 18 months of COVID-19 pandemic, endocrine conditions management has been changed in some areas like disorders requiring surgery at the level of thyroid and parathyroid glands, an approach that continued at different levels from emergencies due to calcium metabolism anomalies and neck obstruction to suspected/confirmed malignancies.

**Objective.** Up-to-date on endocrine conditions referred to surgery during pandemic.

**Results.** Thyroidectomy-related complications on a patient with infection might aggravate hypocalcemia, and cardiac status. PanSurg-PREDICT, a study including 12 countries, with a prospective, observational design, included 380 endocrine surgery patients within first 6 months of pandemic (224 Tx, 116 PTx). The results showed: 97% elective procedures, COVID-19 status was unknown in 92%/30% concerning before/after surgery evaluation.<sup>4</sup> THYCOVIT study included thyroid surgery in Italy, a retrospective, multi-centric (N=28) cohort with a multi-phasic approach as reflected by pandemic status. 3892 subjects were enrolled: 38% during pandemic versus 62% operated during the similar period of time in 2019. No particular increase of post-operative risk was found, but a decrease in number of procedures was identified between 5.1% and 64%. Vitamin D deficiency might aggravate the parathyroid disorders as well as COVID-19 infection itself. In cases with severe hypercalcemia, PTx was considered an emergency unless the medical therapy, including cinacalcet controlled serum calcium levels.

**Conclusions.** While pre-operative management and delay of procedures was feasible via telemedicine in certain cases, endocrine emergencies were essentially referred to surgery even during lockdown.

### E2. COVID-19 pandemic: pitfalls of approaching the adrenal tumors

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**Introduction.** Multiple endocrine diseases, including adrenal tumors, associate a higher risk of contracting an infection, including COVID-19.

**Objective.** Up-to-date on COVID-19 pandemic concerning a multidisciplinary approach of adrenal tumors. We mention 5 major aspects on patients with adrenal tumors regarding COVID-19:

1. These patients have a higher risk of diabetes mellitus, high blood pressure, anomalies of coagulation profile and obesity (involving Cushing syndrome, primary hyperaldosteronism and pheochromocytoma) thus a higher risk of COVID-19 infection and more severe form in adults and pediatric population.
2. Uncontrolled values of arterial hypertension make the subject a candidate to emergency adrenalectomy including during lockdown.
3. Glucocorticoid excess due to Cushing syndrome represents a particular hit concerning COVID-19 infection.
4. Very severe oncologic profile in adrenal carcinoma needs immediate intervention if it is feasible.
5. A limited number of adrenal hemorrhages due to COVID-19 infection itself were reported.

**Conclusions.** Overall, adrenal tumors display a heterogeneous profile concerning the risk of developing a COVID-19 infection from no particular risk as seen in non-functional incidentalomas to very high risk in tumors with positive secretion of catecholamines, aldosterone or glucocorticoids. Cardio-metabolic and oncologic complications required intervention including during lockdown while medical therapy was followed-up through telemedicine in most of the cases during peak periods of time amid pandemic.

### E3. Thyroid dysfunction post COVID-19

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**Introduction.** Observations on the clinical course of coronavirus disease 2019 (COVID-19), show a number of short- and long-term adverse effects on human health. Along with life-threatening damage to the respiratory, cardiovascular, coagulation and nervous system, this infection can lead to long-term abnormalities in thyroid function. The aim of this study was to assess the effect of COVID-19 on thyroid function in patients without history of thyroid disease.

**Material and methods.** An observational, prospective study was performed on 60 patients (40 women and 20 men) two months after initial COVID-19. In all observed patients, anticoagulants or antiplatelet agents were used in the treatment of COVID-19. In six patients, glucocorticoid therapy was administrated. Thyroid function tests were performed on all patients, including thyroid-stimulating hormone (TSH), free thyroxine (FT4), antithyroglobulin antibodies (TAT) and anti-thyroperoxidase antibodies (anti-TPO). TSH was tested at baseline (2 months after COVID-19) and again one month later.

**Results.** The mean age of the patients was 42.5 years. Two months after COVID-19, in 66.6% of the patients a thyroid dysfunction was diagnosed. Eighty percent of these patients had elevated TSH and the remaining 20% had low or low-limit values. Positive antithyroid antibodies was observed in 73.3% of patients. Because of evidence of clinical hypothyroidism in four patients a hormone replacement therapy was initiated. The remaining patients with thyroid dysfunction were tested again a month later. Thirteen patients (21.6%) developed subclinical hypothyroidism in the third month after COVID-19.

**Conclusions.** Our findings show that COVID-19 could have a long-term, negative effect on thyroid function. These results indicate the need to include thyroid function testing in the follow-up algorithm of survivors from COVID-19.

## HEMATOLOGY

### H1. Novel strategies of evaluation and management in myeloproliferative neoplasms

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**Introduction.** Myeloproliferative neoplasms (MPNs) are clonal disorders of the hematopoietic stem cell in which mature myeloid cells are abnormally produced independent of cytokine stimulation. The most commonly studied MPNs are polycythemia vera, essential thrombocythemia and primary myelofibrosis which are classified by the World Health Organization as Philadelphia-negative or BCR-ABL1-negative MPNs. MPNs are characterized by a chronic evolution but these blood cancers are associated with an increased risk of thrombosis which is often the most reported cause of morbidity and mortality in patients diagnosed with the aforementioned diseases.

**We aimed** to report on novel strategies of evaluation and management in MPNs.

**Materials and methods.** A dedicated search was conducted in several international databases to identify novel strategies of evaluation and management in MPNs. Relevant studies were selected and summarized.

**Results.** The evaluation and management of MPNs requires the assessment of peripheral blood samples as well as the employment of a bone marrow biopsy particularly useful in differentiating between essential thrombocythemia and prefibrotic myelofibrosis. We have identified several biomarkers that can be used in the near future to evaluate and manage patients with MPNs, specifically in terms of thrombotic risk assessment.

**Conclusions.** MPNs are complex disorders which are characterized by phenotypic mimicry and risk of thrombosis, progression towards secondary myelofibrosis and (or) transformation to acute myeloid leukemia. Future research is needed to identify new clinical biomarkers with direct applicability in the evaluation and management of these hematological malignancies.

## **H2. Clinical outcome of patients with COVID-19 infection and hematological diseases. Experience of Moldavian hematological center**

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**Introduction.** COVID-19 is an extreme challenge to health systems around the world. Patients with hematological disorders (HD) are known to be more predisposed to and have higher morbidity and mortality rates from COVID-19 than the general population.

**The aim of the present study** was to analyze the clinical evolution of patients with HD who contracted COVID-19.

**Material and methods.** The study included 111 patients with various HD who contracted COVID-19 between April 2020 and March 2021, being monitored in the Hematology Center of the Oncology Institute in Chisinau, Republic of Moldova. The cases were evaluated to analyze the impact of this pathology on the hematological patient (HP).

**Results.** In the study group, 52 (46.8%) were women and 59 (53.2%) men. The mean age of the patients was 57.2±13.1 years. The HD associated with COVID-19 were: non-Hodgkin's lymphoma (NHL) – 56 pts (50.45%), multiple myeloma – 18 pts (16.22%), acute leukemia - 12 pts (10.81%), Hodgkin lymphoma – 9 pts (8.11%), idiopathic myelofibrosis – 6 pts (5.41%), chronic lymphocytic leukemia – 5 pts (4.5%), others – 5 pts (4.5%). Mild forms of COVID-19 were established in 17 pts (15.3%), moderate in 43 pts (38.7%), severe in 51 pts (45.9%). SARS-CoV-2 pneumonia was found in 86 (77.5%) cases. SARS-CoV-2 mortality in the study group was 42 (38.2%) cases. Among the predictors of severe forms were: active disease, old age, use of monoclonal antibodies and intensive chemotherapy. From patients who overcame COVID-19 in 8 (7.3%) cases, the progression of hematological disease was found during the of COVID-19.

**Conclusions.** HP are a sensitive population to SARS-CoV-2 infection. The most common HD associated with COVID-19 was NHL (50.45%). Severe forms of COVID-19 were detected in 45.9% of cases. The mortality associated with SARS-CoV2 infection was 38.2%.

## **H3. Impact of COVID-19 on the prognosis of non-Hodgkin's lymphoma patients**

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**Introduction.** Non-Hodgkin's lymphomas (NHL) represent a heterogeneous group of hematological malignancies. The prognosis depends on NHL subtype, disease stage, cytogenetics, age at diagnosis, ECOG status, presence of anemia, number of lymph node areas affected, LDH and  $\beta$ 2-microglobulin levels. SARS-CoV-2 is a single-stranded RNA-enveloped virus. Gene fragments express structural and nonstructural proteins. A special attention was given to the S proteins that cover the surface of SARS-CoV-2 and bind to the host cell receptor angiotensin-converting enzyme 2. NHL patients are more vulnerable to the SARS-CoV-2

infection due to immunosuppression caused by the disease per se and its treatment, neutropenia, lymphopenia, hypogammaglobulinemia, chemotherapy.

**The objective** was to analyze the impact of COVID-19 on the prognosis of NHL patients.

**Material and methods.** We searched PubMed/MEDLINE for articles on NHL and COVID-19. The search terms were “hematological malignancies”, “non-Hodgkin’s lymphoma”, “NHL”, “coronavirus”, “COVID-19”, “SARS-COV2”, “prognosis”, “comorbidities”.

**Results.** From a total of 230 articles evaluating hematological malignancies, we selected the most important studies on NHL and COVID-19. The studies were conducted in France, Italy, Spain, Turkey, included 738 patients and highlighted the impact of COVID-19 on NHL evolution based on NHL subtype, stage, affected lung area, comorbidities. Mild symptoms (fever, dry cough, fatigue, diarrhea) were reported both in the general population and immunosuppressed patients, but in immunocompromised patients the disease duration was longer in terms of virus clearance and hospitalization. As opposed to solid cancers, hematological malignancies were linked with worse outcomes and higher mortality. Hypertension, lymphopenia and high CRP were risk factors for severe COVID-19 pneumonia. Age  $\geq 70$  years, uncontrolled hematological disease, ECOG performance status 3-4, neutropenia  $< 500/\text{mmc}$  and high CRP were linked with increased COVID-19 mortality. Pre-existing comorbidities (diabetes, chronic pulmonary disease, cardiovascular disease) increased the risk of COVID-19 and its severe manifestations and predicted poor overall survival. Duléry et al. (2021) revealed that age  $\geq 70$  years, relapsed/refractory NHL and recent administration of anti-CD20 therapy were risk factors for prolonged length of in-hospital stay and higher mortality after COVID-19.

**Conclusions.** Refractory/relapsed NHL, age  $\geq 70$  years, recent administration of B-cell depleting immunotherapy, progressive disease and comorbidities (diabetes, obesity, chronic pulmonary disease, hypertension) were risk factors for prolonged hospital stay and higher mortality in NHL patients hospitalized for COVID-19.

#### H4. The burden of SARS-COV-2 infection on patients with non-Hodgkin's lymphoma

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**Introduction.** COVID-19 pandemic continues to affect the global healthcare systems in profound and unprecedented ways. Patients with non-Hodgkin lymphomas (NHL) are immunocompromised because of the disease and its treatments.

**Material and methods.** This retrospective study included adult patients with NHL diagnosed in the Institute of Oncology from Chisinau, Republic of Moldova, confirmed with COVID-19 between April 2020-March 2021. The characteristics of NHL and COVID-19 were collected from medical charts.

**Results.** Of 56 examined patients, 29 (51.79%) were females, the median age was 57.8 years (27–79 years). In 40 (71.42%) cases, COVID-19 was associated with aggressive NHLs, in other 16 (28.57%) with indolent NHLs. The most common types of NHL were diffuse large B-cell lymphoma (DLBCL) – 34 pts (60.71%), small lymphocytic lymphomas – 8 pts (14.81%), follicular lymphoma – 5 pts (9.25%). Among the patients from the study group, 35 (62.5%)

received treatment for first remission induction, 16 (28.57%) for a relapsed/refractory NHL, and 5 (8.9%) received maintenance therapy. Rituximab was used in 42 (75%) of patients. Mild forms of COVID-19 were established in 9 pts (16.1%), moderate in 22 pts (39.3%), severe in 25 pts (44.6%). SARS-CoV-2 pneumonia was found in 44 (78.5%) cases. SARS-CoV-2 mortality in the study group was 14 (25%) cases, being higher in the group of patients who received Rituximab as therapy.

**Conclusions.** NHL patients are at risk for COVID-19 due to frequent need of hospitalization. The most common type of NHL associated with COVID-19 was DLBCL (60.71%). Moderate and severe forms of COVID-19 were found in 47 (83.92%) of cases. The mortality rate was 14 (25%) cases.



## SURGERY

### S1. Laparoscopy for the management of nontraumatic acute abdomen

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**Introduction.** Laparoscopy for acute abdomen is important either for diagnosis, when there is uncertainty in establishing the etiology, and also has a therapeutic role with the well-known advantages of mini-invasive surgery.

**Material and methods.** Our study evaluates 873 patients of nontraumatic acute abdomen (excepting acute cholecystitis), approached laparoscopically between 2016-2020. The following factors were pursued: the concordance between pre and postoperative diagnosis, the establishment of a certain intraoperative diagnosis, incidence of laparoscopic interventions and their complications.

**Results.** There were 653 (75%) cases of acute appendicitis, 146 patients with gynecological diseases (ruptured ovarian cyst, extrauterine pregnancy, inflammatory pelvic disease), 52 (6%) patients with perforated ulcer, 22 cases with other pathologies (acute pancreatitis, enteral perforations, perforations of Meckel diverticulum, entero-mesenteric infarction, tuberculous peritonitis), confirmed laparoscopically. Incidents and accidents were encountered in 56 (6.5%) cases, there were 33 (3.7%) conversions to open technique and 37 (4.2%) patients had postoperative complications.

**Conclusions.** Diagnostic laparoscopy is an optimal method of diagnosis confirmation for cases of non-traumatic acute abdomen, especially for acute appendicitis, gynecological emergencies and peritonitis of unknown etiology, with the possibility of laparoscopic treatment of these pathologies, being also the last option for diagnosis and the first solution for treatment.

### S2. A case of Meckel's diverticulum perforated in the abdominal wall

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**Introduction.** Meckel's diverticulum represents the most common congenital abnormality of the gastrointestinal tract. It is encountered in approximately 2% of the normal population. The most frequent localization of Meckel's diverticulum is 20 cm proximal to the ileocecal valve. In most patients it is totally asymptomatic. However, it can produce gastrointestinal symptoms or develop complications like: perforation, enteroumbilical fistula, intussusception, obstruction or tumors.

**Case presentation.** We present the case of a 45 year-old patient, with a medical history of type 2 diabetes and high blood pressure, who presented to the emergency room with severe pain in right

iliac fossa. The ultrasonography showed 10 mm fluid in the right iliac fossa and dilated small bowel loops. The CT scan diagnosed an abscess in the abdominal wall (right iliac fossa) with a small bowel loop in contact with the abscess. Intraoperative, we diagnosed a Meckel's diverticulitis perforated in the abdominal, which produced an abscess at this level. After we evacuated the abscess and excised the inflammatory tissue, we performed resection of the Meckel's diverticulum followed by double layer enteroraphy. Postoperative, the evolution was favorable with no complications.

**Conclusions.** In some cases, it is very hard to make the differential diagnosis with other acute abdominal conditions because the radiological and clinical findings can be similar. Even though Meckel's diverticulum is a rare pathology, it can produce severe complications, which can threaten the life of the patient if not treated promptly. Knowing all the clinical, radiological, embryological and pathological aspects of Meckel's diverticulum will help the surgeon to rapidly diagnose and then choose the best treatment for patients with this pathology.

### S3. Gallbladder volvulus

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**Introduction.** Gallbladder volvulus (GV) is a rare and potentially life-threatening condition if not promptly diagnosed and treated. It was first described as a "floating gallbladder" by Wendel in 1898.

**The objective of the study** was to search the specialty literature and highlight the mechanisms of formation, characteristics of clinical manifestations, methods of diagnosis and management of the GV.

**Material and methods.** A systematic literature review was performed in PubMed and Google Scholar, using the mesh terms: „gallbladder volvulus”, with the identification of 500 cases of gallbladder volvulus reported until 2021.

**Results.** GV is rotation of the gallbladder along the axis of the cystic duct and vascular pedicle. The gallbladder torsion may be complete (>180°) degree resulting in strangulation of the vascular supply and gangrenous cholecystitis or incomplete (<180°) degree with intermittent symptoms of biliary colic with clockwise direction (most common) or anticlockwise. The age of the patients ranged from 5 days to 100 years. A female preponderance has been established at a 3:1 ratio, with the highest incidence occurring in the seventh and eighth decades of life. Clinical findings include sudden onset of abdominal pain, early emesis and tender mass in the right upper quadrant. The best therapeutic option is gallbladder detorsion and cholecystectomy.

**Conclusion:** GV is an uncommon clinical entity and a difficult condition to diagnose preoperatively. Early diagnostic imaging investigations can lead to a more rapid definitive treatment (open or laparoscopic cholecystectomy) and reduce the risk of the potentially fatal sequel of gallbladder necrosis and perforation.

#### **S4. Acute abdomen approach in the Emergency Department**

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**Introduction.** Acute abdominal pain represents 10% of the presentations to the Emergency Department (ED). The acute abdomen (AA) approach, according to the algorithms proposed by the National/Institutional Clinical Protocols (CP), prevents the development of complications and the patient's death.

**Material and methods.** A retrospective study included the evaluation of 1457 medical records of patients with a presumptive diagnosis of AA in the ED of the Institute of Emergency Medicine, Chisinau, Republic of Moldova, was performed. The statistical evaluation of the selected data was performed through the Excel program.

**Results.** Out of 1457 evaluated medical records, with the presumptive diagnosis of AA, 346 cases were identified with acute appendicitis (AAp), 352 with acute pancreatitis (AP), 306 with acute cholecystitis (AC), 167 with strangled hernia (SH), 165 with intestinal occlusion (IO), 14 with perforated ulcer (PU), 107 with acute gynecologic abdomen (AGA). AAp was confirmed in 183 cases, 97% were treated surgically. AP were confirmed 148 cases, 99.3% were treated conservative. AC was confirmed in 178 patients, 85.96% were treated surgically. SH was confirmed in 132 patients, 93% were treated surgically. IO was confirmed in 153 patients, in 38% surgery was required. PU was confirmed in 10 patients. AGA was confirmed in 107 cases.

**Conclusions.** The management of patients with AA in the ED corresponds to the analyzed national/institutional CP. In the case of AP, in 37.5% of cases, compared to the recommendations of the International CP of the AP, the severity of pancreatitis according to the 2012 Revised Atlanta classification was not mentioned.

#### **S5. Emergency anesthesia in urological patients after COVID-19**

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**Introduction.** Urological emergency (UE) anesthesia is always a challenge and a test for the doctor, especially in patients who have recently had COVID-19, with lung damage of 25% to 70% and one of the kidney blocked with stones.

**Material and methods.** In the last 15 months, there have been 295 patients with unilateral kidney block (KB). In 78 patients the UE appeared after 2-3 weeks of COVID treatment. In all patients, aged between 45-65 years, there were changes on the ECG: myocardial overload, repolarization syndrome, heart rate increased by 20-25%, and hypertension grade II. Anesthesia was performed with Propofol, Fentanyl and support with Sevoflurane for 15-25 minutes, during which time the ureteral stent was fitted. Oxygen saturation was maintained at 96%, with a flow of 4L/minute of oxygen.

**Results.** Anxiety in patients who had COVID-19 was greater. They had hypertension that was more difficult to control. It has been observed that patients with COVID-19, after the same type of anesthesia, find it very difficult to restore adequate breathing. Four of the patients developed

severe depression, which required the intervention of a neurologist, possibly the influence of newly developed COVID-19 and overlapping urological disease.

**Conclusions.** Patients who have had a history of COVID-19 are more vulnerable, physically and mentally, and the anesthesia performed on them must be safe, to create a state of post-anesthetic comfort, which together with the prescribed treatment and the operation performed give patients optimism about the future.

#### **S6. Ectopic retroperitoneal pregnancy: a type of rare ectopy**

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**Introduction.** Retroperitoneal ectopic pregnancy (REP) is a type of rare variants of ectopia, with many management challenges. It does not show pathognomonic clinical signs, ranging from the absence of symptoms or the presence of mild signs, to hemorrhagic shock.

**Material and methods.** The bibliographic sources from the PubMed database were examined, with the keywords: "ectopic", "pregnancy", "extraperitoneal", "retroperitoneal". Information about characteristic clinical manifestations, diagnostic methods and treatment options was researched and processed.

**Results.** We identified 38 cases of REP – 21 of them between 2010-2021. Age: from 19 to 38 years, average 32.2 years. Most of patients with aggravated gynecological anamnesis: right salpingectomy (n=6), left salpingectomy (n=2), bilateral (n=5), salpingostomy (n=1). IVF – 9 patients: 3 procedures (n=5), 2 procedures (n=2) and one procedure (n=1). The average time of the apparition of the symptoms was 38.6 days after IVF. In 9 cases the gestational sac was related to the aorta. The average length of the amenorrhea – 54.4 days (min. - 35, max. - 140 days). The average amount of blood loss was 1750 mL (max. 2500 mL). The most frequently reported imaging exam was transabdominal ultrasonography (n=15). The level of  $\beta$ -HCG was elevated in all cases, average 26,018 mIU/mL.

**Conclusions.** REP is a very rare variant of ectopia, with an undefined etiopathogenetic mechanism, IVF being one of the main risk factors. The preoperative diagnosis is difficult. Ultrasonography, CT and MRI are eloquent imaging methods, providing information about the size, location and involvement of adjacent structures. The elective method of treatment is surgical removal.

#### **S7. Ectopic pregnancy after hysterectomy**

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**Introduction.** Post-hysterectomy ectopic pregnancy (EP) is a very rare variant of ectopia, with a limited number of cases reported in the literature. Depending on the time from intervention to diagnosis is divided into two types: early and late.

**Material and methods.** The resources available in PubMed, using the keywords: "ectopic", "pregnancy", "hysterectomy" were analyzed and we identified 76 cases of EP after hysterectomy, 15 between 2010-2020.

**Results.** The average age was 35 years. The reported cases were divided into 2 groups: early (n=31) and late (n=45). In the group of early EP: vaginal hysterectomy (n=15), abdominal approach (n=14), in 2 cases total laparoscopic hysterectomy and one laparoscopic supracervical hysterectomy. The average time of diagnosis of early EP was 55.2 days post-hysterectomy. In the group of patients with late EP: vaginal HE (n=21), subtotal transabdominal HE (n=12), cesarean hysterectomy (n=4) and 2 cases – laparoscopic approach. 46.5% of EP – after vaginal hysterectomy. The average level of  $\beta$ -hCG was 1247 mIU/mL. In 52% of cases – tubal location. The volume of hemoperitoneum varies: minor – up to 500 mL, massive hemoperitoneum – 500 - 3000 mL and the highest reported volume – 4500 mL. In the cases reported in the literature in the period 2010-2020, the average reported volume of hemoperitoneum was 1543 mL. The mortality rate reaches 7.4%, compared to 0.9% in case of ectopic pregnancy with intact uterus.

**Conclusions.** EP after uterine ablation interventions, regardless of approach and type, are very rare, but should not be neglected and should be considered as a differential diagnosis in patients with intact uterus, regardless of the time of hysterectomy.

#### **S8. Clinical and morphological features of rhinosinusitis in patients with post-COVID-19 syndrome**

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**Introduction.** COVID-19 is characterized by damage of various organs and systems in the human body in acute phase and frequent development of post-COVID-19 syndrome. In literature, there is a little data about such manifestation of post-COVID-19 syndrome as rhinosinusitis. The aim is to characterize the clinical and morphological features of rhinosinusitis that developed in patients with post-COVID-19 syndrome.

**Materials and methods.** The clinical course of rhinosinusitis was analyzed in 5 patients who had COVID-19. All patients underwent maxillary sinus punctures. A morphological study of the operating/biopsy material was carried out.

**Results.** In 5 cases, the patients complained of nasal congestion, difficulty in nasal breathing, purulent-hemorrhagic nasal discharge, predominantly one-side soreness in the nose, headaches, fever, general weakness. These complaints were combined in 4 cases with eyelid edema and decreased vision. In all patients the phenomena of marked atrophic purulent-necrotic processes with the formation of dense stony masses was noted in one-side of the nose. Pansinusitis was identified mainly in all cases. Morphological examination revealed blood-soaked necrotic tissues with inflammatory cell infiltration (predominantly leukocytes, lymphocytes and macrophages).

These changes were combined in one case with the presence of mucorous fungi filaments and in one case with *Aspergillus* mycetoma.

**Conclusions.** In 5 patients with post-COVID-19 syndrome, rhinosinusitis with one-side purulent atrophic-necrotic rhinitis was diagnosed, which was characterized by the presence of mucorous fungi filaments in one case and *Aspergillus* mycetoma in one case.

## FAMILY MEDICINE

### FM1. The role of the family physician during the COVID-19 pandemic

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**Introduction.** Doctors fighting a pandemic is nothing but new on the course of the human history – we have been exposed to multiple plagues since ancient times, sometimes with catastrophic results, and physicians have been in the frontline most of the time. Still, the new age is fighting COVID-19 and managing the trauma it causes on the social and personal level. Our aim was to elicit the very important role the family physician plays in dealing with COVID-19 cases.

**Material and methods.** We reviewed the charts of approximately 200 patients with suspected and confirmed SARS-CoV-2 infection, diagnosed and monitored between September 2020 and May 2021. The symptoms have been charted and their evolution recorded, as well as the treatment received. Most of the patients have been followed by daily phone calls and media devices, and this proves once more the importance of telemedicine nowadays. We retrospectively asked the former patients about their experience in communicating with the family doctor, to be able also to evaluate the degree of psychological support they have received.

**Results.** The symptoms recorded have been consistent with the clinical picture described in the literature (e.g. fever, cough, headache, fatigue). The treatment administered was mostly symptomatic, but we underline the importance of the supplements in improving general condition. Fortunately, only 12 patients required hospitalization, with two fatalities recorded. Over 90% of patients described their interaction with the family medicine doctor or nurse as a positive one, aimed at stress reduction and better coping with their condition.

**Conclusions.** A pandemic of such proportion reaches the top as well the bottom of society – no one is spared of the fear and anxiety it produces. While most of the cases in our study have been mild and moderate, we underline the importance of fast diagnosis, constant communication and proper symptomatic and supportive treatment with major impact on recovery. The Family Physician and the office team plays an important role in monitoring and assisting the SARS-CoV-2 patients, with the aim of reducing hospitalization, the patient anxiety and other negative outcomes.

### FM2. COVID-19 prevention: vaccination in pregnancy and lactation

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**Introduction.** Pregnant women with severe forms of SARS-CoV-2 infection have an increased risk of premature birth and intrauterine death. Furthermore, compared to non-pregnant women, pregnant women may be at higher risk for severe forms and death from COVID-19.

**Objective.** We aimed to make a mini-review concerning vaccination against COVID-19 in pregnant and lactating women.

**Material and methods.** We selected 50 articles and medical guidelines from medical databases on the topic of the article.

**Results.** In SARS-CoV-2 infection, pregnant and lactating individuals should be vaccinated according to product characteristics and the national guidelines. According to the WHO Declaration of 2021, pregnant women at a high risk of exposure to SARS-CoV-2 (eg. medical staff) or who have comorbidities that add to their risk of severe disease may be vaccinated after consulting their doctor. Regarding the breastfeeding woman, the lipids in the structure of the mRNA vaccine are unlikely to enter the bloodstream and reach the mammary gland. Additionally, it is even less likely that the mRNA will transfer to breast milk. As a result, breastfeeding individuals are recommended to receive a COVID-19 vaccine and may choose to be vaccinated.

**Conclusions.** In the last year, we have learned a lot about the effects of COVID-19 on pregnant women and the general practitioner will have to constantly update his knowledge related to the management of SARS-CoV-2 infection and how to prevent it.

### **FM3. Pediatric vaccination during COVID-19 pandemic**

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Vaccination is considered to be one of the most important preventive public health interventions. In Romania, the vaccination program is conducted in the primary care setting, with family physicians who know their patients and put in all their efforts in order to perform this preventive action in safe conditions. According to data centralized by the WHO Regional Office for Europe in 2019, the vaccination coverage for most vaccines in Romania was below the 95% target. The SARS-CoV-2 pandemic struck Romania while it was facing the measles pandemic, ongoing since 2016 due to a progressive decline of vaccination coverage (75% for the MMR second dose) secondary to patient refusal. The COVID-19 pandemic transformed vaccination from a routine activity into a discouraging and stressful one due to restrictive measures and health risks associated with the spread of SARS-Cov-2. As vaccination cannot be performed through telemedicine and cannot respect the physical distancing recommendation, the family physicians have continued to offer this preventive service in a new, reconfigured setting. The useful measures preventing SARS-Cov-2 infection until the medical personnel and population received access to anti-COVID-19 vaccination (since December 2020) were: reducing face-to-face time, telephone triage, controlled access in the family care practice with separation of preventive and curative activities, wearing protective personal equipment and ensuring a good ventilation. The ongoing COVID-19 pandemic is a reminder of the importance of vaccination, with the family physicians playing a central role in educating patients and performing preventive activities for the community.



## PEDIATRY

### P1. Dermatological manifestations in multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2

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**Introduction.** Multisystem inflammatory syndrome in children (MIS-C) was first described in April 2021. Since then, there have been reports all over the world about this new entity. MIS-C is characterized by fever, increased inflammatory evidence, multiorgan damage. Dermatological findings in MIS-C are often and variable, from erythematous, purpuric/petechial maculopapular rash to erythema multiforme.

**Material and methods.** We want to share our experience related to dermatological manifestations in MIS-C in a series of children diagnosed from August 2020-June 2021 in the Paediatric Department of Constanta County Clinical Emergency Hospital, Romania. The diagnosis of MIS-C was established according to Centre Disease Control and Prevention criteria. An electronic file was made with all the skin findings, which were photographed. The informed consent was obtained from the parents in all cases.

**Results.** There were diagnosed 32 patients with MIS-C. 26 patients (81%) had mucocutaneous manifestations: 10 boys and 16 girls. We also included 3 patients in whom we had no evidence of SARS-CoV-2 infection, but who had a Kawasaki-like form of MIS-C. Erythem of palmes and soles was found in 24 patients (92%), conjunctival injection in 22 patients (84%).

**Conclusions.** Dermatological manifestations in MIS-C are common. A multidisciplinary team is needed to correctly establish the diagnosis of MIS-C/ Kawasaki like. In order to better understand the pathophysiological phenomena of skin findings, the inclusion of skin biopsy in MIS-C cases with mucocutaneous findings should be considered.

### P2. Cholesterol levels in human colostrum: influence of maternal age, dietary and smoking habits

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**Introduction.** Human milk is the most valuable nourishment for infants as contains all the necessary nutrients needed during this crucial period. Among the sterols found in human milk, cholesterol is the main one which plays an important role as a structural component of cells membranes and in the formation of new tissues and organs, especially as a constituent of myelin during the brain development in early life. The objective of our study was to determine the cholesterol contents in colostrums samples obtained from different maternal age groups and to assess its potential relationship with dietary and smoking habits during pregnancy.

**Material and methods.** Colostrums samples were collected from healthy mothers who delivered healthy term babies. All participants were divided in two groups: A (aged  $\geq 35$ ,  $n=29$ ) and B (aged  $<35$ ,  $n=34$ ). Maternal dietary and smoking habits were obtained through questionnaires. Total lipids concentration was measured by gravimetric method and quantification of total cholesterol was performed by GC-MS.

**Results.** In older group, significantly elevated levels of total cholesterol and lipids ( $27.34 \pm 6.17$  mg/100 mL;  $3.46 \pm 0.29\%$ ) were noticed compared to younger group ( $21.26 \pm 7.25$  mg/100 mL;  $2.43 \pm 0.34\%$ ) ( $p < 0.01$ ). Also, strong positive correlations were found between cholesterol levels with maternal age and total lipids ( $r=0.70$  and  $r=0.64$ , respectively). Comparing cholesterol contents with dietary habits we observed weak positive correlations (A:  $r=0.38$ ; B:  $r=0.34$ ), as well as, weak negative correlations with smoking habits (A:  $r=-0.13$ ; B:  $r=-0.18$ ) for both groups.

**Conclusions.** Mean cholesterol level in colostrums obtained from mothers with advanced maternal age is considerably higher compared to younger mothers. Primarily, these findings might be greatly related to higher total lipids content, as well as, in minor extent with maternal dietary and smoking habits during pregnancy. Acknowledgements: This research was supported by grant TR 31060 from the Ministry of Education and Science of the Republic of Serbia.

### P3. HPLC assay of metformin in obese pediatric patients with asthma

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**Introduction.** Nowadays, most pediatric professionals recognize that obesity and asthma symptoms are common conditions in pediatric population. Metformin is a biguanide oral agent that is generally well tolerated, and, is commonly prescribed to obese children in order to promote weight loss. The aim of this study was optimizing and validating HPLC method for determination of metformin in plasma obtained from obese asthmatic children both genders.

**Material and methods.** Blood plasma samples were collected from obese pediatric patients with asthma (aged  $\geq 12$ ,  $n=17$ ), 2-3hrs after the dosing. Single step extraction with acetonitrile was performed, followed by centrifugation. An aliquot of supernatant was filtered through  $0.45 \mu\text{m}$  syringe filter and analyzed by HPLC. The separation of metformin was achieved at  $30^\circ\text{C}$  on Zorbax-NH2 column using isocratic elution. The mobile phase was consisted of 100% acetonitrile with flow rate  $0.725 \text{ mL/min}$  and  $20 \mu\text{L}$  of sample was injected. The detection was performed at  $232 \text{ nm}$  and quantification was done by calibration curve method.

**Results.** Under the optimized experimental conditions, good linearity was found in the range of  $0.1-5.0 \text{ mg/L}$  ( $r=0.9997$ ), while detection and quantification limits were  $0.053 \text{ mg/L}$  and  $0.175 \text{ mg/L}$ . Also, the optimized method showed good accuracy (recovery  $>89\%$ ) and precision ( $\text{RSD} < 9\%$ ). The obtained mean metformin concentrations were in the range from  $1.27 \pm 0.06 \text{ mg/L}$  to  $1.92 \pm 0.17 \text{ mg/L}$ .

**Conclusions.** The proposed method has been successfully applied for the analysis of metformin in plasma collected from obese pediatric patients with asthma with satisfactory analytical

parameters in terms of validation. Also, this method could be easily applied for the therapeutic drug monitoring and pharmacokinetics studies of this drug in different patients groups and from other types of biological samples.

#### **P4. Polychlorinated biphenyls in human breast milk: preliminary research in Varna, Bulgaria**

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**Introduction.** Polychlorinated biphenyls (PCBs) are widespread lipophilic persistent organic pollutants (POPs) in the environment and in food chains. Because of its high lipid content, human breast milk might be used the newborn exposure to PCBs to be evaluated.

**The objective of the study** was to assess the levels of PCBs in the breast milk of women, living in Varna, Bulgaria and to identify important factors that determinate the presence of PCBs.

**Material and methods.** Breast milk samples were collected from mothers aged 25 to 40 years from the region of Varna in 2020. The mandatory inclusion criteria were age, breastfeeding period and inform consent. Factors that may influence PCB levels such as age, body mass, dietary habit, smoking and others were investigate using a questionnaire. The inclusion criteria and the questionnaire were based on the protocol of the WHO/UNEP 2007 coordinated surveys on POPs in human milk. The congeners of PCBs were determined by capillary gas chromatography system with mass spectrometry detection (GC-MS).

**Results.** The concentrations of six indicator PCBs were measured in milk samples from 25 both primiparae and multiparae mothers. The lipid content of the tested samples was from 1.41 to 5.77%. The average value of calculated total PCBs was 43.6 ng/g lipid weight. PCB 153 was the most abundant congener in the milk samples, followed by PCB 138, PCB 180.

**Conclusions.** Age and body mass index were the most important factors affecting transfer of PCBs and have positive associations with PCBs levels. Total PCB levels in human milk from Varna, Bulgaria were found comparable to similar surveys in the Balkan countries.

#### **P5. Epidemiology of pediatric burns in pandemic times: changes and challenges**

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**Introduction.** Burns represent a major public health issue worldwide. There are some recognized patterns regarding the causes and situations leading to these devastating accidents, and young children are a population showing a high propensity of suffering burns, especially caused by contact with hot fluids. The ongoing COVID-19 pandemic has brought numerous changes for healthcare systems, and burn epidemiology reports also showed differences with regard to pre-pandemic times.

**Material and methods.** We retrospectively analyzed our burn patients emergency presentations and burn ward admissions during the years 2019 and 2020, comparing the different aspects related to demographic data, geographic distributions, etiology, burn extent and depths, and outcomes.

**Results.** There was a general decrease of emergency room presentations and admissions for burns in 2020, with reference to the previous year. Most of this difference was due to less frequent occurrence of minor burns, involving less than 10% TBSA. However, when analyzing the number of moderate and extensive cases, over 20% TBSA, the number was similar to what was registered in 2019. Causes of burns did not show major changes, although we noticed the occurrence of burns due to alcohol disinfectant firing. Most importantly, we registered a significant decrease of mortality rate.

**Conclusions.** As a direct consequence of “stay home” messages and social distancing, less minor accidents occurred. However, analyzing the epidemiology of pediatric burns during the pandemic, we may conclude that serious accidents or aggression occur following the same patterns as in normal times, but we can ensure the same quality of care for our patients.

## PUBLIC HEALTH

### PH1. Hesitancy towards COVID-19 vaccines: an analytical cross-sectional study

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**Introduction.** Vaccination is the most promising strategy to counter the spread of Coronavirus Disease 2019 (COVID-19). Vaccine hesitancy is a serious global phenomenon, and therefore the aim of this cross-sectional study was to explore the effect of educational background, work field, and social media on attitudes towards vaccination in Jordan.

**Material and methods.** We compared between medical personnel who were in direct contact with patients and non-medical individuals at Jordan University Hospital in terms of demographics, knowledge about COVID-19 vaccines, rumors received via social media, their trust in these vaccines, and the encouraging factors for vaccination.

**Results.** 646 individuals were enrolled in this study, of whom 287 (44.4%) were from medical field, and 359 (55.6%) from non-medical field. 226 (35%) were planning to take the vaccine once available, with a positive response from 131 (45.6%) medical field workers, compared to 94 (26.2%) non-medical individuals ( $p<0.001$ ). The social media rumor that was believed the most was the unsafety of these vaccines ( $n=283$ ; 43.8%). Only 163 (56.8%) of medical persons did not believe any of the circulated rumors, compared to 126 (35.1%) of non-medical persons ( $p<0.001$ ). The effect of medical personnel advice ( $OR=0.83$ ; 95%  $CI= 0.70$  to  $0.98$ ;  $p=0.026$ ) and social media ( $OR=1.21$ ; 95%  $CI= 1.04$  to  $1.41$ ;  $p=0.012$ ) were significantly associated with the willingness to take COVID-19 vaccine once available.

**In conclusion,** medical personnel and social media play a crucial role in increasing the society's inclination towards vaccination by providing the community with updated evidence-based information about COVID-19 vaccines as an efficient medical countermeasure and by correcting the previously spread misinformation.

### PH2. A single-center, open-label, longitudinal, prospective study of health-related quality of life in pharmacy students

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**The aim of study** was to assess the health status of pharmacy students through self-assessment of their condition, using the HRQoL tool SF-36 v2, in four main domains: physical, social and behavioral functioning, mental health and general perceptions of health.

**Materials and methods.** Design - single-center, open-label, longitudinal, prospective study. Survey period: November 2017-January 2021. We used the "Direct Individual Questionnaire" method, the survey being software-based, licensed, standardized and validated questionnaire SF-36 version 2. Respondents are pharmacy students of the 5<sup>th</sup> year of study. The research included 135 students, aged between 22 and 25 years, after they duly signed an informed consent form and were informed of the conditions for completing the questionnaires.

**Results.** In a preliminary conversation, none of the participants reported on diagnosed past and present diseases, there is no data on the use of medicinal products for general and chronic diseases. Over 25% of the study group have a higher risk of developing depression, which is higher compared to the general population and is unusual of the study age group. ¼ have psycho-emotional problems with the character of a borderline nature. More than half of the respondents did not describe themselves as absolutely healthy. Only ⅓ think that they have psycho-emotional comfort. According to indicators of social and emotional functioning - over 50.00% of the respondents described their condition as unsatisfactory, especially in social aspect.

**Conclusions.** The mental functioning, social, emotional and behavioral functioning are in sharp contrast to the declared physical functioning, vitality and presence of pain.

### PH3. Death by SARS COV-2 - A Romanian COVID-19 multi-centre comorbidity study

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**Background.** Evidence regarding the relation between SARS-CoV-2 mortality and the underlying medical condition is still scarce.

**Material and methods.** We conducted an observational, retrospective study based on Romanian official data about location, age, sex and comorbidities for COVID-19 fatalities in a multi-case, multi-center approach. Descriptive methods and exploratory statistical testing were applied to characterize comorbidity patterns and their differences between categories of sex or age.

**Results.** Hypertension, obesity, diabetes and chronic kidney disease as well as diseases of the circulatory system, endocrine, nutritional or metabolic diseases, and diseases of the genitourinary system have the largest prevalence in the sample and show differences in relative counts between age levels. Men and people aged between 70 – 79 have the largest individual relative frequency, 65.3% respectively 29.63% while patients with a mild severity of the disease had a relative frequency of 91.20%. The median multimorbidity was 2, the median CCI equaled 1 and the 1-year median prognosis for survival probability was 87%. Differences between patterns of co-occurrence between men and women were observed both pairwise and in the cluster analysis. The large number of clusters confirms the low median number of multimorbidity.

**Conclusions.** The comorbidity profile of the Romanian COVID-19 mortality study confirms previous results about hypertension, diabetes obesity and chronic kidney disease as conditions that co-occur more frequently in the COVID-19 fatalities. Our findings indicated that the burden of disease was low and the prognosis for 1-year survival probability was high in the sample.

#### **PH4. Incidence of Clostridium difficile infection in COVID-19 patients**

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**Introduction.** Clostridium difficile, a Gram-positive, anaerobic, sporulated, enterotoxin-producing bacillus, is currently considered the major etiological agent of diarrhea syndrome after antibiotic therapy. The objective of our study was to evaluate the incidence of Clostridium difficile infection in patients admitted to COVID-19 intensive care unit and their mortality rate.

**Material and methods.** We conducted a retrospective study on 430 patients admitted to the COVID-19 intensive care unit of the Modular Hospital Brasov (Romania), between January 1, 2021 and June 15, 2021, who required at least 7 days of care. The age, gender, comorbidities, number of days of hospitalization, diagnosis of infection with Clostridium difficile were assessed. Only 29 patients were eligible for the study. The data were analyzed by Chi-test and Student t-test.

**Results.** The maximum affected age group was 65-70 years, with a number of 8 patients. There are no statistically significant differences between the mean age of deceased patients and survivors (T-test p value 0.866). The distribution men:women was 1.23. There was no association between age and survival (Chi-test, p=0.91) or between patients' sex and survival (Chi-test, p=0.989). There was a statistically significant association between more than 8 days spent in the intensive care unit and survival (Chi-test, p=0.04).

**Conclusions.** Despite the treatment administered, the mortality rate of our patients was statistically significant with the number of days of hospitalization, without showing statistical significance with comorbidities, age or sex.

## **PH5. Understanding the psychological ramifications of the COVID-19 pandemic among mental health professionals in Romania**

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**Introduction.** Viral outbreaks have posed complex challenges for healthcare systems globally not only from a medical standpoint, but also through their negative psychological implications, which have been thoroughly documented and investigated. Acute psychological distress, as well as long-term psychopathology have been identified among front line healthcare workers especially. There is sparse scientific work in the current literature that describes the perspective of mental health professionals during or after a pandemic.

**Purpose.** This study aims to investigate the psychological ramifications of the COVID-19 pandemic among mental health professionals in Romania. Furthermore, different factors that may positively or negatively influence the response of this specific group will be explored.

**Material and methods.** Questionnaires were sent electronically to mental health professionals working at two important mental health centers in Romania: Bucharest and Iasi, that inquired into the emergence of potential negative psychological effects in relation to the pandemic.

**Results.** The 300 participants comprised of 54.9% psychiatrists, 23.7% nurses, 19.4% psychologists. 87.6% worked in psychiatric hospitals and were constantly exposed to infected patients. Anxiety directly related to SARS-COV-2 was noted among 5.9%. Respondents exhibited depression (5.2%), anxiety (2.65%) and stress (6.2%). Correlations between psychopathology and individual characteristics were investigated.

**Conclusions.** There is evidence of psychological distress determined by the pandemic among mental health professionals that was most saliently experienced through an increased struggle with psychiatric patients’ level of proper compliance to the constantly evolving recommendations. Properly grasping the complexity of this phenomenon may allow for a clearer viewpoint of the mental health system for potential further improvement.

## **PH6. Mesure d’impact d’une campagne de sensibilisation aux infections sexuellement transmissible portant sur l’erotisation du port du preservatif aupres d’un public jeune (moins de 25 ans)**

Charasse C

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Dans un contexte d’augmentation constante de l’incidence des infections sexuellement transmissibles et des grossesses non volontaires en France chez les jeunes de moins de 25 ans, une étude de terrain portant sur les représentations personnelles, les représentations sociales et les pratiques de ce public quant au securisexe a été menée pour l’Agence Régionale de Santé Nouvelle Aquitaine. Nous avons pu mettre en évidence la nécessité de retravailler l’image du



préservatif afin d'en augmenter son usage. La littérature en sciences comportementales et en psychologie sociale a mis en avant l'intérêt de l'érotisation du port du préservatif dans le changement comportemental du public cible. La présente étude porte sur l'intégration de leviers de neuro-marketing, de psychologie sociale, et des sciences comportementales dans la réalisation d'une nouvelle campagne d'affichage pour la promotion du sécurisexe. Dans différents lieux cibles, fréquentés par des personnes moins de 25 ans, nous avons exposé alternativement cette néocampagne, la campagne étalon utilisée par Santé publique France, et une campagne témoin portant sur le port du masque chirurgical dans les maisons de santé pluridisciplinaires. Les résultats ont pu montrer une augmentation de 350 % du nombre de préservatifs récupérés par chaque personne, cependant, après traitement ANOVA, nous ne pouvons rejeter l'hypothèse nulle. Ces résultats encourageants ne sont donc pas significatifs mais incitent à explorer les initiatives portant sur l'usage de nouveau leviers de communication.

#### **PH7. Depression among inmates - interference with SARS-CoV-2**

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**Introduction.** After SARS-CoV-2 infection, patients often present malfunction of various body systems, usually occurring months after resolution of the acute respiratory syndrome.

**The objective of the study** was to assess the most significant symptoms of depression and the neurophysiology of the referred mental malfunction in inmates. The study aimed to answer the following question: are the incidence of depression increased among inmates because of increased incidence and prevalence of SARS-CoV-2 in this group, or is this statistics different due to different conditions of habitation and lifestyle?

**Material and methods.** The period of the study was February 2020 – July 2021 (beginning with the first reported case of COVID-19 internationally, as police facilities have in custody migrant population as well). The first group of study includes 404 healthy individuals from the general population (police officers working in the same facility for the entire period of study), while the second one includes 1,054 inmates from the police-operated correctional facilities, who have been in custody in the same center for at least 30 consecutive days.

**Results.** Inmates often present depression, though statistics of the past 18 months show evidence of increasing incidence and prevalence of depression among population in correctional facilities, as compared to the first group of the study (because the population in both groups experienced an increased number of acute episodes of various diseases during the period of study, a statistical comparison has been performed).

**Conclusions.** Depression among inmates occurs more often than in the general (healthy) population. In order to better prevent depression among inmates, we propose a different approach which includes a more active screening and immediate medication and therapy, along with appropriate treatment for all comorbidities.

#### **PH8. Clostridium difficile infection – a risk factor for unfavorable outcome in SARS-CoV-2 infected patients - a case series**

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**Introduction.** COVID-19 is a mostly a respiratory disease with variable degrees of severity. One of its possible complications consists of bacterial pulmonary superinfections, which are treated with antibiotics. Combination antibiotic therapies are a risk factor for the occurrence of *Clostridium difficile* infections (CDI), which could lead to severe forms of colitis.

**Materials and methods.** 187 SARS-CoV-2 infected patients were admitted in the Neurology Department of Colentina Clinical Hospital, Bucharest (Romania), between the 1<sup>st</sup> of October 2020 and the 15<sup>th</sup> of December 2020. Out of these patients, 24 acquired CDI during hospitalization. We compared CDI and non-CDI patients in terms of sex, age, COVID-19 pulmonary involvement, inflammatory markers, number of prescribed antibiotics, days of hospitalization and outcome.

**Results.** Surprisingly, CDI patients had a lower percentage of COVID-19 pulmonary involvement than non-CDI ones (32.63% vs. 53.97%). The mean number of administered antibiotics was similar for the two groups (1.92 for non-CDI patients and 2.34 for CDI patients). Hospitalization periods, as well as mortality rates, were higher among CDI patients versus non-CDI patients (27.38 vs. 15.03 days, respectively 10 cases (41.6%) vs. 52 cases (31.9%)). There was a statistically significant association between the presence of CDI and prolonged hospitalization period ( $p < 0.01$ ) and unfavorable outcome (4 patients (16.66%) were admitted in Intensive Care Unit). 10 of the CDI patients (41.66%) were treated with the combination Ceftriaxone-Pantoprazole, a well-known risky association for induced CDI.

**Conclusions.** Excessively prescribed antibiotics and certain drug combinations may lead to potential risks, so their use must be restricted especially in viral infections.

#### PH9. Sleep in COVID-19 period

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Sleep is and remains an important feature in difficult times as: wars, bankrupt, stress periods but also in pandemic times. COVID-19 is in train to change our life. Sleep is analysed by the authors, looking to all the potential effects on human organism, population, authorities, health workers and patients with sleep disturbances. Finally, there are also described by these specialists some treatment solutions for all people suffering from coronavirus infections.

#### PH10. Response of the Bulgarian pharmacists to the first wave of the coronavirus pandemic - a pilot project

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**Introduction.** The first registered case of COVID-19 in Bulgaria from the beginning of March 2020 followed a series of anti-epidemic measures. The Bulgarian pharmacists along with other medical care providers were challenged to respond to the pandemic and provide service and care.

It is important to assess the impact of the first wave of COVID-19 pandemic on the community pharmacies in anticipation of future mass-scale disruptions.

**Materials and methods.** A cross-sectional study including pharmacists working in community pharmacies was carried out between December 2021 and March 2021. An anonymous online questionnaire was distributed to pharmacies from different regions of Bulgaria. Overall, 118 community pharmacists participated in the survey. A web-based 10-item questionnaire was developed.

**Results.** The major events that were identified by pharmacists are changes in everyday responsibilities and demand surges that lead to distribution issues. Over 59% of pharmacists experienced high-stress levels. Counseling of patients with underlying conditions that are predisposed to severe illness and advice on the prevention of the spread of the disease were among the additional services provided by pharmacists.

**Conclusions.** In the early days of the pandemics, pharmacists faced unprecedented changes that emphasized the preexisting problems and challenges. To conclude pharmacists have a significant social role as front-line workers and providers of evidence-based information to the public during times of crisis.

### **PH11. Major ethical issues in the context of the COVID-19 pandemic**

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**Introduction.** The COVID-19 pandemic is the latest life-threatening disease affecting the health and economic sector in the world. The COVID-19 pandemic worsened health and social unequalness. Due to the rapid spread of infection in many countries, health systems have reached the limit of their resources. This overview article discusses the ethical issues raised during the COVID-19 global pandemic.

**Material and methods.** We performed a systematic review of scientific publications in accordance with the recommendations of the Cochrane Collaboration and the Guide to Preferred Elements for Reporting Systematic Reviews and Meta-Analyzes (PRISMA guidelines).

**Results.** We conducted an active search for scientific publications on the following keywords: Ethics, COVID-19, Health Care, Medical professionals in MEDLINE and PubMed databases. We found a total of 156 publications. We removed 16 articles because they are in a language other than English or no abstract available. This overview article aims to explain ethical problems in relation to five different areas: Distributive and social injustice, Health care collapse /patient intake and sorting, distress among healthcare workers/, informed consent and protection of personal data in the developing digital world, pandemic exit strategies /movement restrictions, isolation, mass vaccinations/ and ethics of and research studies in pandemic conditions.

**Conclusions.** The uncertainty we face during the pandemic has raised fundamental ethical questions. All health care professionals who sacrificed their lives are examples of high morality, honesty, and responsibility to the decisions made. Only after the passage of the COVID-19 pandemic results will be evaluated in order to agree on global issues that affect human health, well-being, and survival.

## **PH12. Learning from community-led 3D-printing of personal protective equipment during the first months of the COVID-19 pandemic**

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The first months of SARS-CoV-2 (COVID-19) pandemic have led to significant Personal Protective Equipment (PPE) and other critical medical devices' shortage worldwide, due to the surge in global demand and lockdown restrictions affecting the supply chain. Consequently, the U.S. Centers for Disease Control and Prevention suggested the implementation of crisis capacity strategies and applied a relaxation in relative regulatory requirements. 3D-printing and open-source innovation allowed for prompt action to meet the increased need in hospitals and clinics. As part of a global effort by 3-D printing companies, academic institutions and citizens, our team collaborated with five other research labs to produce face shields for hospitals in need. Initially, three separate designs, which became available as open-source files online, were tested in regards with filament usage, production speed, minimal set-up and ease of use on behalf of the healthcare workers. One of these designs was adjusted and optimized for our specific printers and users' needs. Finally, in one and a half months' time, about 2500 face shields were printed, sterilized and distributed. More than a year now into the pandemic, the supply and availability of PPE have increased significantly over the last several months, however, important lessons can be drawn from the community-led response to the initial shortages; open-source technology can accelerate medical innovation and allow for customized design, while 3D-printing can allow for distributed, on-demand manufacture.

## **PH13. Changes in vitamin and microelement supplementation during SARS-CoV-2 pandemic**

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**Introduction.** Although there are still no scientifically confirmed benefits related to COVID-19 treatment, most people are advised to ensure their daily intake of vitamins and micronutrients. This study used a web-based survey to investigate how perceived COVID-19 threats are related to change in supplementation with vitamins and/or microelements.

**Material and methods.** The study employed the online platform (google.doc/forms) to create and distribute a questionnaire during April 2021. It was freely available and anonymous. The questions aimed to collect socio-demographic characteristics, general health status, COVID-19 morbidity, and habits of vitamin and microelement intake.

**Results.** Among 229 respondents, 79.0% were females. More than a half of them usually takes micronutrients, while 56.1% increased vitamin and/or microelement intake during the pandemic. Generally, supplements are consumed more often by females ( $p=0.004$ ), those who respect precautionary measures ( $p=0.001$ ), and adults younger than 40 years ( $p<0.05$ ). There was a

significant change in vitamin D, vitamin C, zinc, and selenium consumption ( $p < 0.001$ ). Most respondents (36.2%) report that an influence on their decision to increase supplementation had direct advice from a physician or pharmacist. There was a significant positive relationship between the change in supplementation and an opinion that supplements can help in COVID-19 treatment ( $p = 0.001$ ), as well as for zinc and selenium intake related to previous COVID-19 ( $p = 0.027$ ).

**Conclusions.** The tendency to use vitamin and/or microelement supplements increased during SARS-CoV-2 pandemic in Serbian population. Understanding of peoples habits, attitudes and trusted information sources can help clinicians on how to modify future activities in order to promote healthy behaviours.

#### PH14. Study of the impact of the COVID-19 pandemic on medicinal advertising

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**Introduction.** Advertising of medicinal products is regulated by European and Bulgarian legislation and there are restrictions on the method of distribution, advertising channels, type and consumers and advertising materials. An interesting factor is the appearance of some kind of cataclysm (Great abrupt change in public life, turmoil) such as the COVID-19 pandemic.

**The objective was to study** the impact of the COVID-19 pandemic on the advertising of over-the-counter drugs.

**Materials and methods.** The advertisements for OTC products in the advertising commission of BDA in 2019 and 2020 were analyzed.

**Results.** It was established that the appearance of COVID-19 did not affect the number, type and different advertised medicinal products according to the ATC classification. These results are an indication of the need to pharmacist when dispensing both prescription and OTC drugs.

**Conclusions.** Due to the fact that the pharmacist is the most accessible medical specialist and the pharmacy the most accessible health institution, the provision of pharmaceutical care seems to be of great need for the people of the population.

#### PH15. COVID-19 case management in GP's practice office

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**Introduction.** Although several COVID-19 vaccines have been approved for use in different countries, and immunization programs are well underway, the COVID-19 pandemic continues to

impact countries around the world. Many are experiencing further waves of infection, and the number of new coronavirus cases worldwide has risen again.

**Material and methods.** The study took place in a GP's practice office between March 2020 and June 2021, on a number of 136 cases of COVID-19. Patients were diagnosed by RT-PCR testing or rapid SARS-CoV-2 antigen testing.

**Results.** 49% (67 cases) had mild infection or were asymptomatic, 34% (46 cases) moderate infection, and 17% (23 cases) had severe infection and were hospitalized. Almost all cases of mild and moderate infection were treated at home, except for those who were diagnosed during a hospitalization for another condition. In symptomatic patients, administration of treatment at the onset of symptoms has led to a faster recovery and a lower rate of complications.

**Conclusions.** COVID-19 patients need careful assessment, especially those with comorbidities, to avoid asymptomatic/ mild and moderate cases to become severe.

#### **PH16. Effects of COVID-19 lockdown on surgical dental emergencies and related interventions in Albania**

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**Introduction.** Many studies report contradictory effects of the COVID-19 pandemic on surgical dental emergencies. During the pandemic outbreak in Albania, the dental ambulatory service was suspended beside the University Dental Clinic (UDC) and oral and maxillofacial hospital services. We investigated the impact of the COVID-19 pandemic on oral surgical emergency/urgency admission and management.

**Material and methods.** A retrospective single-center analysis of all consecutive patients with surgical dental emergency/urgency was conducted from 9th of March to 17th of May (lockdown period) and using as a control period the same weeks in 2019. All data were collected from the medical files. Admissions classified as oral surgical emergencies and urgencies were included. Total and weekly emergency/urgency admissions, related surgical procedures, and conservative treatment were assessed. The incidence rate ratio IRR was used to compare emergent dental surgical admissions and interventional and conservative treatments.

**Results.** Dental surgical emergent admissions significantly increased during the 10 week COVID-19 compared with control period 181 versus 35 patients with an IRR=5.17 95% confidence interval [95%CI] 4.46-5.97;  $p<0.0001$ ; dental abscess also increased IRR=4.41 [3.49-5.50]. Significant augmentation in all-surgical procedures IRR 3.46 [2.78-4.23], dental extraction IRR=2.85 [2.18-3.67], dental drainage IRR=6.00 [3.25-10.2]; and in conservative medical treatment IRR=10.11 [8.19-12.36] during COVID-19 compared to control period were observed.

**Conclusions.** Important augmentation of dental surgical emergencies/urgencies and related interventions were observed during the COVID-19 pandemic in our center. The augmentation probably is related to the activity restriction of all dental clinics and the later stage of the disease presentation during the lockdown period.

## VARIA

### V1. Special procedures for marketing authorization of medicinal products and their impact on pharmacovigilance

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**Introduction.** The objective of the study was to define the "special procedures" for marketing authorization of medicinal products as part of the common procedures for marketing authorization: centralized, decentralized, mutual recognition procedure, national procedure and to make a critical analysis of their impact of pharmacovigilance systems. Secondary objectives: to analyze various new initiatives in regulatory practice such as: accelerated assessment, priority medicines, adaptive pathways, etc., and to analyze their impact on pharmacovigilance.

**Materials and methods.** Documentary analysis and content analysis were conducted on published EU Directives and Regulation and EMA guidelines.

**Results.** Granting of marketing authorization of new medicines in Europe should be based on the benefit/risk ratio, after objective assessment of criteria for quality, safety and efficacy only and to exclude all kinds of economic concerns. We have established that in the past few years in regulatory practice of EMA accelerated procedure, conditional approval, exceptional circumstances and rolling review procedure are the ones mainly used. The decision for early access is a serious challenge due to limited available clinical evidence for reliable conclusion regarding the benefit/risk ratio and the relative effectiveness of new medicines.

**Conclusions.** Pharmacovigilance systems are burdened with post-registration non-interventional studies for additional safety data, against the background of ongoing additional pre-registration studies for new indications. Are the potential benefits for public health from the immediate availability of a medicine outweigh the potential risks, related to the high level of uncertainty of benefit/risk ratio?

### V2. In-depth analysis of the role and involvement of pharmacists in clinical studies, clinical trials and non-interventional studies of medicinal products

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**Introduction.** Regulation (EU) No 536/2014 has fundamentally changed the understanding of clinical trials of medicinal products (MPs) and the functions of healthcare professionals. The Regulation introduced a new conceptual system for "Clinical study", "Clinical trial", "Low-intervention clinical trial", "Non-interventional study", etc. Authorization/approval procedures, the role of the Ethics committees, monitoring, etc. have completely changed.

**The aim of the study** is to identify the opportunities of participation of pharmacists in clinical trials and for professional development.

**Materials and methods.** We conducted a content analysis of the regulations at European and national level, enabling masters of pharmacy to participate in clinical trials.

**Results.** We identified five main areas: 1. Pharmacy as a fundamental science of applied nature in the design of MPs, is actively involved in the preparation of the dossier of the investigational MP and its evaluation; 2. All medicines intended for clinical trials must be obtained at the hospital pharmacy by Master Pharmacist - member of the clinical research team. Involvement of hospital pharmacists leads to a reduction in the risk of discrepancy in therapy and the prevention of adverse reactions. According to data from the Professional Organization of Hospital Pharmacists in Bulgaria, 56% of hospitals have their own hospital pharmacy as of 2018; 3. Sponsors are seeking for pharmacists as part of the monitoring process; 4. Pharmacists can realize themselves as Good Clinical Practice inspectors at the national competent authorities. 5. There is a demand of pharmacists to participate in non-interventional studies.

**Conclusions.** Clinical trials are the most dynamic part of the pharmaceutical sector, importance of the pharmacist profession is continuously growing, as well as the knowledge in GCP is a big challenge. Despite the results achieved, pharmacist participation in clinical trials in Bulgaria is still limited.

### **V3. Ethical dilemmas and burnout syndrome in healthcare professionals during COVID-19 pandemic**

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**Introduction.** Healthcare professionals have faced unprecedented challenges during the COVID-19 pandemic. In addition to issues related to the large number of infected patients, overwork, personal risk of infection, healthcare professionals have been confronted with difficult ethical dilemmas such as: limiting professional autonomy, the obligation and responsibility to care for patients versus personal protection, allocating resources, promoting the autonomy and well-being of patients, including those who are unable to take part in the decision-making process. Burnout syndrome is characterized by feelings of exhaustion, cynicism, anxiety, irritability, fatigue, withdrawal and reduced professional efficiency.

**Material and methods.** The authors conducted an analysis of the literature to identify the psychological impact of the ethical dilemmas and their role in generating burnout syndrome in healthcare professionals.

**Results.** Healthcare during the COVID-19 pandemic has been marked by difficult ethical dilemmas and medical decisions. These are likely to cause moral injury and moral distress for healthcare professionals, which can lead to burnout and mental health problems, followed by decreased work efficiency and increased error rates.



**Conclusions.** The well-being of medical professionals must be a priority for medical systems. Thus, medical professionals must be supported to solve the ethical dilemmas they face and to make problematic decisions. In this context, effective organizational measures are needed by creating an ethical work climate, streamlining the activity of clinical ethics commissions and creating psychological support mechanisms for healthcare professionals.

#### **V4. Doctor-patient relationship: a review of one and a half year of COVID-19 pandemic**

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**Introduction.** It is already universally acknowledged that the COVID-19 pandemic has produced changes at all levels of human existence, and medical practice was deeply affected. The aim of this paper was to identify the consequences of the COVID-19 pandemic on the doctor-patient relationship from its beginning to the present.

**Material and methods.** The authors conducted an analysis of the literature to identify the impact that the COVID-19 pandemic has had so far on the relationship between the two protagonists of the medical act.

**Results.** Medical practice has been affected in multiple directions: difficult access to medical services, overcrowding of intensive care units, exhaustion of medical staff in these departments, exposure to infectious risk, difficulties in decisions on equitable allocation of resources- which have often been limited. All of these had a direct impact on the doctor-patient relationship, which suffered profoundly. Limiting the time of interaction with the patient and the direct physical contact, and wearing a protective mask have created additional difficulties both in effective communication and in the level of trust of patients in the quality of the medical act. At the same time, studies show that using effective communication skills with patients suffering from COVID-19 have improved the psychological status of these patients.

**Conclusions.** COVID-19 has created unprecedented difficulties for contemporary medical practice. Despite the protective measures imposed to reduce the transmission of the disease, it must not be forgotten that the patient remains in the center of the medical act. Thus, in addition to adapting to medical practice in pandemic conditions, it is necessary to identify measures to preserve to the maximum the relationship between the doctor and patient.

#### **V5. The effect of verapamil administration on aluminium tissue accumulation after chronic exposure in rats**

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**Introduction.** Aluminium is ubiquitous and widely used. It accumulates in the body and exhibits toxic effects (dialysis encephalopathy, osteomalacia with osteodystrophy, microcytic anemia, neurodegenerative diseases). The mechanisms of toxic aluminium action are: oxidative stress, alteration of membrane function, disruption of intracellular signaling, and alteration or inhibition of enzyme functions.

**The aim of the study** was to investigate the role of disruption of calcium homeostasis in aluminium toxicity and effect of the pretreatments with calcium blocking agent verapamil. **Material and methods.** 36 male Sprague Dawley rats were divided randomly in six groups: E1 - E4, C and V. Groups of animals were treated daily as follows: E1 (10 mg/kg BW AlCl<sub>3</sub> i.p.); E2 (5 mg/kg BW verapamil by gavage, and after 60 minutes 10 mg/kg BW AlCl<sub>3</sub> i.p.); E3 (20 mg/kg BW AlCl<sub>3</sub> i.p.); E4 (5 mg/kg BW verapamil by gavage, and after 60 minutes 20 mg/kg BW AlCl<sub>3</sub> i.p.); V (5 mg/kg BW verapamil by gavage), and control group C i.p. with saline. After 8 weeks of treatment the animals were euthanised and tissue samples were analyzed. **Results.** The highly significant increase in aluminum tissue deposition in liver and testicles ( $p < 0.001$ ) was registered in groups of animals treated with AlCl<sub>3</sub> compared to deposition in same tissues of animal groups previously treated with verapamil. Aluminium deposition in kidney did not show significant change after verapamil application. **Conclusions.** The results emphasize the significance of calcium homeostasis preservation in chronic aluminum exposure and propose possible toxicity alleviation.

#### **V6. To do or not to do a biopsy? Is reflectance confocal microscopy sensitive and specific enough?**

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Reflectance confocal microscopy is a non-invasive diagnostic technique that provides in vivo images of the epidermis and the underlying papillary dermis with near-cellular resolution. Originally used for the diagnosis of skin cancers, reflectance confocal microscopy shows a continuous progression both in terms of training and in terms of image resolution in order to improve this diagnostic method. This determines major advantages in the differential diagnosis, establishing with more precision the right place to take biopsies and broad therapeutic lines. A systematic search was performed using the PubMed / MEDLINE platform with the following key terms "confocal microscopy", "basal cell carcinoma", "squamous cell carcinoma", "melanoma", "actinic keratosis". The included articles were selected by removing those articles whose title and abstract were not appropriate to the topic, were not in English and did not present the full text version. The analysis of the final articles aimed to assess the role of confocal microscopy in the diagnosis of the most common skin tumor pathologies, the level of specificity and diagnostic sensitivity for each of these pathologies and the extent to which this non-invasive technique can guide the therapeutic decision. Despite the increasing awareness campaigns of the risk of ultraviolet radiation in the pathophysiology of skin cancers, they are still an important health problem, both for the elderly and the younger generations, despite photoprotection. Confocal microscopy can thus be an essential diagnostic tool with high specificity and sensitivity, while avoiding unnecessary excision or diagnostic biopsies in patients with unclear dermatoscopic appearance.

## V7. Instrumental methods in analytical toxicology

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**Introduction.** The application of methods used to detect possible toxins in the test sample is area of research of analytical toxicology. Instrumental methods: saves time (resources), provide greater accuracy, lower the limit of detection, allows the analysis of small amounts of samples, do not destroy the sample, provide work without previous separation processes.

**Materials and methods.** The analysis of inorganic compounds is done by: molecular spectroscopy in visible spectrum; atomic absorption spectroscopy; atomic emission spectroscopy; electron spectroscopy; thermogravimetric analysis; electrochemical methods. Analysis of organic compounds: spectroscopy in UV spectrum; infrared spectroscopy; nuclear magnetic resonance; gas chromatography; liquid chromatography.

**Results.** Instrumental methods are applied for: colorimetric determination of iron content in drinking water; determination of vitamins B1 and B2 in biological extracts; determination of metals in geological researches; determination of metals in cosmetic products; environmental monitoring; detection of metal in samples in quantities parts per billion; chemical composition of essential oils; chemical composition of tomato.

**Conclusions.** Instrumental methods in analytical toxicology are required for detailed analysis of various samples. They provide qualitative and quantitative data about sample of analysis. With application of instrumental methods, it is possible to do many analysis during one working day.

## V8. Rhodiola root as a platelet enhancing agent – a case report on oncology patient

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**Introduction.** Since thrombocytopenia is common in oncology patients undergoing radiotherapy, effective and rapid treatment for the increase of oncology patients' platelet count is needed.

**Case presentation.** A 45-year-old female was on radiotherapy due to her oncologist's recommendation. Yet, after admission of a total of 20Gy, the platelet count was 75,000/mm<sup>3</sup>, which indicated urgent interruption of radiotherapy. On the same day, high doses of vitamin B12, unsaturated omega 3,6,9 fatty acids, folic acid, vitamin D, vitamin C, medium dose of Zinc, and commercial Rhodiola root product alongside a diet with a lot of fresh vegetables and fruit were prescribed. *Rhodiola rosea* L. is for centuries considered as an adaptogen. European Medicinal Agency recommends it for temporary relief of symptoms of stress, such as fatigue and sensation of weakness. Vit. D 2000 IU/day supplementation fits into current suggestions (1.000 to 3.000 IU vitamin D) for subjects at high risk of COVID-19, to maintain its optimum serum concentrations that could significantly benefit both in the prevention and treatment of the COVID-19. Vitamin C and Zinc, alongside omega-3-6-9 fatty acids, herbal food, and phytonutrients are well-known activators of the immune response and often necessary factors for organism homeostasis. In addition, the supplementation approach included vitamin B12 and folic acid since their importance for hematopoiesis. After a three-day treatment, an increased platelet count was measured, and patient continued her radiation therapy.

**Conclusions.** This case report suggests a possible positive impact of Rhodiola extract in combination with selected vitamin-mineral supplements in the prevention of thrombocytopenia in cancer patients during therapy.

#### **V9. The use of OTC medicinal products and nutritional supplements**

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**Introduction.** Advertising, as an element of the Marketing Mix, is designed to provoke, form or maintain interest in people, goods, ideas, services and endeavors so that they can be realized. Advertising of medicinal products and food supplements aims to arouse, form or maintain interest in people who need short-term treatment or supplementation of their diet.

**Material and methods.** The aim of the present study was to assess the extent to which advertising shapes the demand for over-the-counter drugs and dietary supplements and stimulates self-medication. A mixed methodology of documentary analysis, survey and statistical analysis was applied.

**Results.** Two online surveys were conducted among patients and pharmacists with a total number of respondents  $n = 400$ .

**Conclusions.** Patients are guided by factors such as knowledge, attitudes and experiences regarding health, illness and treatment, as well as other cultural and social factors. Advertising is the most accessible source of health information for patients and therefore needs to be strictly regulated. Although focusing consumers on the potential risk of a product could have a negative impact on its sales when it comes to medicinal products, the focus should be on the health and benefits of society.

#### **V10. The peculiarities of body composition indices among overweight and obese adults**

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**Introduction.** The modifications in physiological indices produced among population with overweight and obesity constitute an objective basis that allows to study the action of different factors on the human organism.

**The objective of the study** was to assess the peculiarities of body composition among subjects with a body mass index  $\geq 25$  kg/m<sup>2</sup>.

**Material and methods.** The study included: group I - 243 persons with hereditary family history of excess of body mass, and group II - 180 persons without hereditary family history of excess of body mass.

**Results.** The results of the study show that the percentage of water (group I:  $51.7 \pm 3.7\%$ , group II:  $52.1 \pm 3.2\%$ ), of skeletal muscles (group I:  $30.9 \pm 1.9\%$ , group II:  $31.1 \pm 2\%$ ) and bones mass (group I:  $2.4 \pm 0.6$  kg, group II:  $2.5 \pm 0.6$  kg) decrease in the same time with increasing of body mass index values.

**Conclusions.** The decrease of the percentage of water can retard the metabolism as ingested water stimulates the increase of energy consumption in the body. In result, the body weight is maintained within the normal body mass index. At the same time, insufficient physical activity can reduce the percentage of skeletal muscles as well as the bones weight, which can influence the appearance of bones fragility and fractures among subjects with overweight and obesity.

#### **V11. Blockade of CB1 receptors differentially modulates acetylcholine release in rat hippocampus in vitro**

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**Introduction.** Studies have shown stimulatory effects of cannabinoid antagonists on electrically evoked [3H]-acetylcholine (ACh) release in hippocampus. The aim of the present study was to evaluate the differences in the release of [3H]ACh in slices from left (LH) and right (RH) rat hippocampus and the effect of cannabinoid CB1 antagonist SR 141716A on spontaneous and evoked release.

**Material and methods.** Slice preparations dissected from rat hippocampus were used for the experiments. The release of [3H]-ACh in response to field stimulation was determined radiochemically, the ACh content was assayed by HPLC. S1 and S2 are the mean values of the evoked release following the first and second stimulations.

**Results.** The spontaneous [3H]-ACh release in LH was greater than that in RH. The evoked release in LH was higher at re-stimulation (S2 > S1); in RH S1 and S2 values were close. The control experiments with SR 141716A solvent (DMSO) confirmed the differentiation between the spontaneous release in slices from RH and LH. In the presence of SR 141716A we observed the following effects: LH - the spontaneous release decreased compared to the controls; there was a peak in response to stimulation (S1); RH - spontaneous release increased; greater evoked release was present (S2).

**Conclusions.** The cannabinoid CB1 antagonist SR 141716A showed a differential modulatory effects on acetylcholine release in slices from R and L rat hippocampus. In LH the spontaneous release was inhibited; the evoked one increased, in RH there was an increase in both spontaneous and evoked release.

#### **V11. Antioxidant activity of supercritical CO<sub>2</sub> extracts of some medicinal plants of *Lamiaceae* family**

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**Introduction.** Lamiaceae (mint family) is a large plant family of mainly shrubs and herbs, and some of the members are economically relevant aromatic plants. They are used as culinary herbs and grown for edible leaves, such as basil, mint, sage, thyme, marjoram, and oregano.

Also, Lamiaceae is a significant medicinal plant family widely used in traditional medicine to treat various disorders. In this study, we have determined the total phenolic content (TPC) and antioxidant activity of supercritical (Sc) carbon dioxide (CO<sub>2</sub>) extracts of six Lamiaceae medicinal plants, which have been used in the traditional medicine of Serbia.

**Material and methods.** The investigated ScCO<sub>2</sub> extracts were obtained from the Faculty of Technology and Metallurgy, University of Belgrade, Serbia. Plant material of the following species of the Lamiaceae family was extracted and examined: mountain tea (*Sideritis scardica* Griseb.), thyme (*Thymus vulgaris* L.), lemon balm (*Melissa officinalis* L.) sage (*Salvia officinalis* L.), mint (*Mentha piperita* L.) and oregano (*Origanum vulgare* L.). The TPC of ScCO<sub>2</sub> extracts was measured by the modified Folin-Ciocalteu colorimetric method, while antioxidant activity was determined using the ferric reducing antioxidant power (FRAP) and by  $\beta$ -carotene bleaching (BCB) assays.

**Results.** We found that TPC levels ranged between 17.16 $\pm$ 0.06 mg Gallic acid equivalents (GAE)/g dry extract in mountain tea extract and 170.57 $\pm$ 0.70 mg GAE/g in oregano extract. High TPC was also found in sage and thyme extract, 91.92 $\pm$ 0.62 and 82.69 $\pm$ 0.25 mg GAE/g, respectively. The highest reducing capacity using FRAP assay was determined in the sage extract (1.21 $\pm$ 0.09 mmol Fe<sup>2+</sup>/g dry extract), followed by the oregano extract (0.73 $\pm$ 0.01 mmol Fe<sup>2+</sup>/g). Using the BCB assay significant antioxidant activity was estimated for oregano and sage extracts, IC<sub>50</sub> value was 0.25 $\pm$ 0.03 and 0.35 $\pm$ 0.06 mg/mL, respectively. A very high correlation was determined between the TPC and BCB assay ( $r = -0.928$ ) ( $p < 0.01$ ).

**Conclusions.** Our results showed that analyzed extracts possessed a considerable amount of phenolics and reducing properties. Oregano and sage ScCO<sub>2</sub> extracts were most promising for use as a source of natural antioxidants.

## V12. Orthodontic treatment in the context of COVID-19 pandemic

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**Introduction.** At the beginning of last year, the COVID-19 pandemic put its stigma on the whole world, changing the naturalness of our personal and professional lives. From that moment we all started looking for solutions to continue our life and activity. The current level of scientific research has helped us to slowly decipher this virus, to draw measures to prevent infection.

**Material and methods.** The literature now abounds in articles on the SARS-CoV-2 virus. The sources accessed on Google were PubMed, Scopus, the WHO archives and the Journal of the American Orthodontic Association, and the keywords were *COVID-19*, *orthodontics in pandemic* and *oral health*.

**Results.** The transmission of the virus in the orthodontic office was done by direct contact with blood or saliva or indirectly, through contaminated surfaces, respectively through aerosols. Specific preventive measures were: prioritization of patients with fixed devices, scheduling at the end of the program of aerosol-generating procedures, telemedicine use, disinfection of instruments before sterilization in 2% glutaraldehyde or 0.1% hypochlorite solution, disinfection of orthodontic appliances with alcoholic solution 75%, ultraviolet disinfection, natural

ventilation, use of high volume saliva vacuum and Hepa filter, mouth rinse with hydrogen peroxide solution or povidone iodine. Only a quarter of orthodontic patients showed up at the office, only for fixed appliances emergencies, but all said they want to continue treatment. This prolonged the duration of orthodontic treatment.

**Conclusion.** The control of the infection transmission in the office must be done on a scientific basis, constantly updated.

### V13. Oral health and the fluor resources

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The importance of fluoride in the body's economy is reviewed, as it plays a particularly important role in the defense mechanisms against the aggression of cariogenic agents. The authors make an analysis of the theoretical notions in the literature, to note some important aspects for specialists, for the public health system and services, but also for updating knowledge of medical culture and health. The importance of knowledge of fluoride resources and how to use them in dentistry is relevant to the oral health clinic. The analysis of the theoretical notions from the specialized literature brings back to the present some important aspects for the specialists in the system, for the public health services, but also for the categories of population at cariogenic risk. This review of the literature brings useful reflections on the dental role of fluoride and its resources, providing educational information for prophylactic purposes for oral health.

### V14. Telemedicine as a tool during the pandemic in Romania

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**Introduction.** During the last year telemedicine became a reliable tool for medical professionals in Romania. The use of electronic information and telecommunications technologies to support remote clinical care, education in the field of patient and doctor health, public health and health administration were regulated by law.

**Material and method.** This study analyzes the telemedicine applications developed and used in Romania in the last year and their contribution to preventing and combating the SARS-CoV-2 pandemic. Specialized publications, reports of competent national institutions, legislation etc were analyzed and evaluated.

**Results.** In the last year, almost a quarter of specialized consultations in private health units in Romania were performed through telemedicine services. It is shown that most consultations are made by telephone and almost half of patients accessing telemedicine services are between 35 and 44 years old. During this period with restrictions to access hospitals, telemedicine has proved its usefulness especially for chronic patients and especially for oncologic patients. Doctors were able to communicate and prescribe treatment to patients in quarantine or isolation for SARS-CoV-2 infection. Medical data regarding SARS-CoV-2 infection is reported and analyzed, being used in the strategy to combat and prevent the spread of coronavirus in Romania.

**Conclusions.** Telemedicine has become an increasingly useful tool both for regular consultations and for monitoring patients at risk, in pre-hospital emergency care, intaking and sending patients as well as for rural, disadvantaged areas, distance education and also for crisis management.

#### **V15. The impact of COVID-19 pandemic in patients with rheumatic diseases**

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The COVID-19 pandemic has brought a huge burden on both healthcare workers and patients suffering from rheumatic inflammatory diseases (RID). The latter carry a higher risk of contracting the infection because of the underlying disease and are frequently immunosuppressed because of their condition or associated treatments. Moreover, the breakthrough of the anti-COVID-19 vaccine has been down sided by its unclear efficiency in this category of rheumatic patients: are they as protected from the administration as other patients? The European League against Rheumatism (EULAR) has provided useful information targeting these points, based on increasing scientific evidence and registry data. Thus, rheumatologists should be updated on managing RID patients associating SARS-CoV-2 infection or adjusting therapeutic scheme in a tailored manner when receiving the vaccination so that efficacy can reach its highest peak.