Резюмета на научните трудове на английски език

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Г7

Г7-1. Clinical Challenges – Acute Kidney Injury Following a Retained Abortion

M. Benkova-Petrova, A. Petrov, N. Harizanova, S. Stajkova, "Nephrology, Dialysis, and Transplantation," Issue 3, 2024, p. 29, ISSN 1312-5257

Acute kidney injury (AKI) during pregnancy is a complex clinical problem that requires a multidisciplinary approach due to potentially severe consequences for both the mother and the fetus. AKI in pregnant women can be caused by numerous factors, including physiological changes during pregnancy as well as specific circumstances or complications. Preeclampsia and eclampsia, obstetric hemorrhage, sepsis, thrombotic microangiopathies, dehydration, hypovolemia, and retained abortion are some of the main causes.

A review of the medical history, laboratory results, and imaging studies was conducted on a patient hospitalized with a diagnosis of retained abortion and subsequent acute kidney injury.

Early intervention and a multidisciplinary approach contributed to the favorable outcome of the disease in the patient.

Retained abortion is a type of spontaneous abortion in which the embryo or fetus loses vitality but remains in the uterus for days or weeks with a closed cervical os. Its etiology is related to intrauterine infections, severe anomalies, or hormonal imbalances. Patients may present with subtle clinical symptoms, vaginal bleeding, and/or abdominal pain. Treatment of women with a retained abortion involves timely curettage, assessment of hemodynamic stability, empirical broad-spectrum intravenous antibiotics, and intravenous rehydration.

Retained abortion may be complicated by AKI, which requires quick and targeted medical intervention. Timely diagnosis and multidisciplinary care are crucial for improving outcomes and reducing risks for both the mother and fetus.

Г7-2. Organ-on-a-Chip (I Have a Dream...) A. Petrov, M. Benkova, P. Petrov, R. Zorceva, "Nephrology, Dialysis, and Transplantation," Issue 3, 2018, pp. 20-21, ISSN 1312-5257

3D printing is a rapidly developing technology with vast potential, including applications in biomedical and engineering sciences. The creation of a complete parenchymal organ is hindered by limiting factors such as the inability to print a functional vascular system, but since the early 1990s, a new scientific discipline has proposed an alternative path to this goal. Microfluidics involves manipulating the behavior of liquids at the molecular level, and its applications are impressive:

Transfer of laboratory techniques such as ELISA, PCR, and genomic sequencing (which require large equipment and consumables) to chips the size of a human nail while maintaining their informational value.

"Organ-on-a-chip" devices are microfluidic cell cultures that, unlike conventional cell cultures, can almost fully replicate the physiology of an organ and, potentially, model diseases. Successfully functioning models have been created for "gut-on-a-chip," "lung-on-a-chip," "blood vessel-on-a-chip," "tumor-on-a-chip," "bone marrow-on-a-chip," and "kidney-on-a-chip." The "kidney-on-a-chip" model has been particularly informative in experimental conditions, with a direct observation of the nephrotoxic effect of cisplatin on proximal tubular cells (Jang KJ et al.).

In the pharmaceutical industry, testing new molecules can be done directly on human "organ-on-a-chip" models, significantly shortening the time needed to develop new drugs without side effects.

The combination of microfluidics and 3D printing will offer numerous opportunities for advancing medicine.

Г7-3. Clinical Case of a Patient with Late Onset of Familial Mediterranean Fever

M. Benkova-Petrova, A. Petrov, S. Stajkova, M. Levkova, "Nephrology, Dialysis, and Transplantation," Issue 3, 2020, pp. 20-21

Familial Mediterranean Fever (FMF) is an autosomal recessive inflammatory disorder characterized by recurrent, self-limiting episodes of fever, serous inflammation (peritonitis, pleuritis, pericarditis, arthritis), and erysipelas-like skin rashes lasting 1–4 days. The main complication is the development of amyloidosis, including kidney amyloidosis.

FMF is caused by a mutation in the MEFV gene, which encodes the synthesis of pyrin – a protein primarily found in mature granulocytes and a regulator of IL-1 mediated inflammation. Ethnic groups living along the Mediterranean Sea, such as Jews, Armenians, Turks, Arabs, and less frequently Italians and Greeks, are most commonly affected. However, in recent years, more cases have been reported outside this region. Around 60% of FMF patients have their first disease manifestations before the age of 10, and in 90% of cases, before the age of 20. Late clinical manifestations (after the age of 40) occur in only 0.5% of patients.

We present a clinical case of a 35-year-old man with newly diagnosed, advanced chronic kidney disease, erythrocyturia, moderate proteinuria, and a negative immunological panel. A renal biopsy revealed significant glomerular sclerosis, making verification of the primary disease difficult. The patient started renal replacement therapy with peritoneal dialysis. Several months later, episodes of fever, abdominal pain, arthritis in the knee and ankle joints, and erythema nodosum on the lower legs were noted, lasting 5–7 days. Laboratory tests revealed leukocytosis and elevated CRP, while abdominal CT showed generalized lymphadenopathy. Due to the presence of a microbial isolate in the used peritoneal dialysate, the symptoms were interpreted as acute peritonitis during peritoneal dialysis. The peritoneal catheter was removed, and a prolonged antibiotic course was administered. The patient switched to hemodialysis, but symptoms persisted. Molecular-genetic analysis revealed a mutation in exon 3 of the MEFV gene (arginine to tryptophan substitution at codon 354), confirming

the diagnosis of Familial Mediterranean Fever. The patient is currently being treated with colchicine (1 mg/day) and is asymptomatic. Genetic analysis of family members is planned.

Only 20 out of 4000 (0.5%) patients experience late-onset FMF. Their clinical course is much milder, they do not develop amyloidosis, and they respond well to low-dose colchicine treatment.

Г7-4. Clinical Case of No-Mutation Identified in Tuberous Sclerosis Syndrome

M. Benkova-Petrova, A. Petrov, S. Stajkova, M. Levkova, "Nephrology, Dialysis, and Transplantation," Issue 3, 2020, pp. 21-22

Tuberous sclerosis is a rare genetic multisystem disorder characterized by the formation of benign tumors (hamartomas) affecting the skin, brain, eyes, heart, kidneys, and lungs. It is most commonly caused by mutations in the TSC1 and TSC2 genes, which encode the proteins hamartin and tuberin, responsible for cell growth and division. Mutations can occur spontaneously or be inherited in an autosomal dominant pattern.

The diagnosis is based on a combination of clinical symptoms – "major" and "minor" diagnostic criteria. Major criteria include cortical tubers, subependymal nodules, subependymal giant cell astrocytomas, retinal hamartomas, pulmonary lymphangiomyomatosis, renal angiomyolipomas, cardiac rhabdomyomas, angiofibromas, ungual fibromas, hypopigmented macules, and shagreen patches. Minor criteria include skin lesions such as "confetti" type, enamel defects, intraoral fibromas, retinal achromic macules, and non-renal hamartomas. A diagnosis is certain when two major criteria or one major and two minor criteria are present, or with a positive DNA analysis. A diagnosis is considered probable when the patient demonstrates one major criterion, a combination of one major and one minor criterion, or two or more minor criteria.

We present a clinical case of a 78-year-old woman who, after a medical-genetic consultation based on clinical features – facial angiofibromas from a young age, nail and gingival changes, and bilateral renal angiomyolipomas – was diagnosed with tuberous sclerosis. The patient has no family history of the disease, and molecular-genetic analysis did not reveal a mutation in the TSC1 or TSC2 genes. The absence of mutations in these two genes occurs in 10-15% of patients clinically diagnosed with tuberous sclerosis. This could be due to large deletions, somatic mosaicism, the presence of another unidentified gene, or mutations in regulatory sequences for these genes, such as the promoter region. In a study by Qin et al., 9.17% of patients were classified as No-mutation identified (NMI), who were clinically diagnosed with tuberous sclerosis but lacked mutations in TSC1 or TSC2. NMI participants in this study were diagnosed at an older age, had preserved intellectual function, less frequent epilepsy, subependymal nodules, and subependymal giant cell astrocytomas, and were more likely to have bilateral renal angiomyolipomas. Even with the same mutation, clinical manifestations can vary due to variable expressivity. Some family members may have severe neurological involvement (seizures, intellectual disability), while others may have only skin lesions, renal angiomyolipomas, and minimal neurological involvement.

Г7-5. Causes of Erythropoietin Resistance in Dialysis Patients M. Benkova-Petrova, A. Petrov, S. Stajkova, "Nephrology, Dialysis, and Transplantation," Issue 3, 2020, p. 28

Introduction: Anemia associated with chronic kidney disease (CKD) leads to increased morbidity and mortality and reduced quality of life in dialysis patients. Recombinant human erythropoietin (rHuEPO) plays a significant role in reducing the frequency of these complications. The direct connection between CKD and erythropoietin deficiency usually does not require measurement of endogenous erythropoietin levels before starting recombinant therapy. However, sometimes rHuEPO therapy alone may be insufficient – a phenomenon known as erythropoietin resistance.

Causes: The primary cause of erythropoietin resistance is iron deficiency. Even with adequate iron supplementation, several other factors contribute, including acute or chronic inflammation, malnutrition, severe hyperparathyroidism, aluminum toxicity, neoplasms, hemolysis, folic acid and vitamin B12 deficiencies, myelosuppressive agents, PRCA (pure red cell aplasia), ACE inhibitors, angiotensin receptor blockers, genetic polymorphisms, and antibodies against erythropoietin. The adequacy of dialysis, the dialysis modality, and the biocompatibility of the dialysis membranes also play an important role. Patients with permanent tunneled catheters and PTFE grafts need higher ESA doses than those with AV fistulas.

Conclusion: Erythropoietin resistance is directly related to the frequency of comorbidities in dialysis patients and can be used as a marker for early mortality. The main factors in improving the quality of life for this group are the availability of highly qualified medical personnel in hemodialysis centers, good collaboration between patients and medical staff, proper vascular access care, frequent monitoring of laboratory parameters, and early identification of causes of erythropoietin resistance.

Г7-6. Urinary Proteomics, or the Search for New Early Diagnostic and Prognostic Molecules for Kidney Damage A. Petrov, S. Stoykova, Nephrology, Dialysis, and Transplantation, Issue 3, 2022, pp. 13-14

Chronic kidney disease (CKD) is one of the major and socially significant health issues affecting society globally. According to WHO data, the prevalence of CKD worldwide is estimated at about 13.4% (11.7-15.1%), and the number of patients who have reached the end-stage renal failure is between 4.9 and 7.08 million. Early diagnosis and timely initiation of treatment are critical aspects in preventing further kidney damage and the development of complications associated with this disease. Markers for kidney damage are still extremely limited for early diagnosis, despite the high prevalence of CKD among people (>10%). Serum creatinine levels, albuminuria, and glomerular filtration rate are cornerstones for determining and staging kidney function, but they have many limitations. Discovering new, earlier, and more accurate markers for identifying CKD will significantly improve the effectiveness of treatment initiation. The current development of urinary proteomics offers a solution to this problem. It has already proven its role in medicine by identifying antibodies against phospholipase A2 receptors in membranous nephropathy. New molecules have been identified, which, through their early expression in the urine, could significantly improve diagnostic tools for kidney damage. In addition to already known biomarkers like KIM-1 (kidney injury molecule-1), NGAL (neutrophil gelatinase-associated lipocalin), and L-FABP (liver fatty acid-binding protein), a new biomarker—translationally modified fetuin A—has been identified in patients with diabetes mellitus

before the appearance of albuminuria, thus significantly improving the diagnosis of chronic kidney disease.

Г7-7. Indicators Responsible for the Development of Anemia and Their Association with Serum Visfatin in Dialysis Patients M. Benkova-Petrova, A. Petrov, P. Petrov, S. Stoykova, Nephrology, Dialysis, and Transplantation, Issue 3, 2022, pp. 17

Abstract: Anemia is one of the main complications of chronic kidney disease and is associated with increased morbidity, mortality, and reduced quality of life. There are numerous causes for the development of anemia syndrome and erythropoietin resistance in patients with CKD—iron deficiency, folic acid and vitamin B12 deficiency, acute and chronic inflammation, malnutrition, antibodies against recombinant erythropoietin, etc. Visfatin is mainly produced and secreted by visceral adipose tissue and can induce inflammation. The study involved 50 patients in the dialysis stage of CKD. For all participants, iron status, folic acid and vitamin B12 levels, soluble erythropoietin receptor (sEPOR), hemoglobin, and serum visfatin were assessed. The results were processed using SPSS v.20.0 for Windows, and variance, comparative, and correlation analyses were conducted. The significance level was set at $p<0.05$. A significant difference in visfatin levels was found according to the lower reference limit of serum iron ($p=0.008$), with lower serum iron levels being associated with higher levels of visfatin. The analysis of the relationship between sEPOR and visfatin revealed that sEPOR serum concentrations peaked at visfatin levels between 5.62-15.66 ng/ml, after which they started to decrease significantly. With the progression of CKD to the terminal stage, higher levels of vitamin B12 were maintained, regardless of visfatin levels, which is explained by the substitution therapy administered. In this study, only 5 patients (6.25%) had a deficiency of folic acid, and they showed lower visfatin levels.

Г7-8. The Role of whole exome sequencing in the diagnosis of Primary Ciliary Dyskinesia

Benkova-Petrova M., Petrov A., Staykova S., Yahya D., Hachmeryan M., Nephrology, dialysis and transplantation,", vol 3,2023, 45

Whole exome sequencing was first described in 2009 and is a widely used method that involves sequencing the protein-coding regions of the genome (exons). The human exome represents less than 2% of the genome, but contains ~85% of known disease-associated variants, making the study a cost-effective alternative to whole-genome sequencing. For this reason, sequencing of complete coding regions (exomes) has the potential to reveal the causes of a large number of rare, mostly monogenic, genetic diseases, as well as predisposing variants of common and oncological diseases.

Ciliopathies are a heterogeneous group of diseases caused by damage to the primary cilium. Disorders of ciliary motility can lead to a wide range of clinical manifestations, including infertility, reversed visceral organs (situs inversus), lung infections and etc. Some of the ciliopathies associated with kidney disease include nephronophthisis, polycystic disease and renal cell carcinoma.

We present a clinical case of a 43-year-old man with kidney stone disease, bronchiectasis, recurrent middle ear infections and infertility. A whole exome sequencing revealed a mutation of the RSPH3 gene in the 6th chromosome NC_000006.12:g.158986423T>C. It is classified as pathogenic in ClinVar and is associated with primary ciliary dyskinesia (PCD).

Г7-9. Clinical Case of a Patient with Pseudoxanthoma Elasticum M. Benkova-Petrova, A. Petrov, S. Stajkova, "Nephrology, Dialysis, and Transplantation," Issue 3, 2022, p 39-40

Abstract: Pseudoxanthoma elasticum (PXE) or Gronblad-Strandberg syndrome is an autosomal recessive metabolic disease caused by a mutation in the ABCC6 (ATP-binding cassette transporter C6) gene, leading to ectopic mineralization of elastic tissues in the skin, eyes, cardiovascular system, and less frequently in the gastrointestinal tract. PXE affects approximately 1 in 50,000 individuals worldwide, being twice as common in females. The disease usually begins in childhood or adolescence. Clinical manifestations include skin lesions, retinal changes that may lead to significant vision loss, arterial calcification, reduced blood flow in the upper and lower limbs, and/or gastrointestinal system changes, which may result in bleeding in the stomach or intestines. The gold standard for confirming the diagnosis is genetic testing for ABCC6 homozygosity or combined heterozygosity. Other diagnostic options include characteristic skin or eye findings or histological confirmation, revealing calcium deposits, shortened and fragmented elastic fibers, and collagen fiber deformation. We present the clinical case of a 45-year-old woman, who had pruritic yellow papules on the flexor surfaces of the upper limbs and intermittent claudication. Histological and genetic analyses were conducted, and the diagnosis of pseudoxanthoma elasticum was confirmed. Subsequently, renal artery calcification was found, clinically manifesting as difficult-to-control arterial hypertension.

Г7-10. Clinical Case of Systemic Lupus Erythematosus in a Pregnant Woman T. Koleva, I. Teodorova, M. Benkova, A. Petrov, V. Ikonomov, "Nephrology, Dialysis, and Transplantation," Issue 2, 2016, p 25

Abstract: Systemic lupus erythematosus (SLE), a systemic disease, is an inflammatory autoimmune disease with an unclear etiology and a rapid course. It is the most common autoimmune disease in young women of reproductive age. The female-to-male ratio ranges from 8:1 to 31:1. In the last 20 years, cases of systemic lupus have tripled, mainly due to improved diagnostic methods. SLE can emerge or flare during pregnancy, with an approximate frequency of 1 in 1500. Among pregnant women affected by the disease, the frequency of other conditions that increase the risk during childbirth—such as kidney failure, antiphospholipid syndrome, and hypertensive diseases—is higher. Years ago, pregnancy in women with SLE was considered contraindicated because it could lead to both disease flare-ups and neonatal complications, or even fatal outcomes. Despite improved diagnostic capabilities and modern treatment methods, the prognosis for SLE in pregnant women remains serious, with a high mortality rate among patients.

We describe the case of a 25-year-old pregnant woman at 22 weeks of gestation with high-activity SLE, meeting 7 out of 11 diagnostic criteria. Despite early diagnosis and complex treatment, which began before delivery and continued afterward—including multiple pulse therapies with

corticosteroids and Endoxan, synchronized plasmapheresis, treatment with immunovennin, and hemodialysis—the patient progressed to worsening multi-organ failure and a fatal outcome**.**

Г8

Г8-1. THE ROLE OF CONTRAST-ENHANCED ULTRASOUND IN NEPHROLOGY: MODERN APPROACHES

AND CLINICAL APPLICATIONS IN THE ASSESSMENT OF RENAL FUNCTION AND PATHOLOGY

Sabri Sabri, Alexander Petrov, Svetla Staykova, Actual nephrology, Issue 1, Volume 18, 2024, pages 33-37

ABSTRACT: Contrast-enhanced ultrasound (CEUS) is a key tool in the evaluation of diverse renal pathologies due to its ability to visualize microvascular blood flow in real time without compromising renal function. CEUS enables dynamic assessment and precise quantification of microvascularization, extending to capillary-level perfusion. This article aims to succinctly review the fundamental physical properties of ultrasound (US) contrast agents, explore the technical aspects of CEUS imaging specific to the kidneys, and analyze the most common renal indications for CEUS. Additionally, imaging comparisons with baseline unenhanced US and, where applicable, computed tomography (CT) are provided.

Г8-2. ORGAN-ON-A-CHIP, OR THE FIRST STEP TOWARD CREATING A BIOARTIFICIAL ORGAN

Alexander Petrov, Svetla Staykova, Rositsa Zorcheva-Vateva, Actual Nephrology, Issue 1, Volume 13, 2019, pages 26-29

Abstract: 3D printing is a rapidly developing technology whose vast potential for application is quickly growing in the fields of biomedical and engineering sciences. While the inability to print a fully functional circulatory system remains one of the limiting factors in the creation of a complete parenchymal organ, since the early 1990s, a young scientific discipline has offered an alternative path toward this goal. Microfluidics is the study of manipulating the behavior of fluids at the molecular level. The application of microfluidics means that laboratory techniques such as ELISA, PCR, and genomic sequencing, which typically require large equipment and consumables, could be transferred onto chips the size of a human fingernail while maintaining their informational value.

Another fascinating aspect is the so-called "organ-on-a-chip" concept. This device is a microfluidic cell culture that, unlike conventional cell cultures, can almost completely recreate organ-level physiology. To date, successful functioning models of "gut-on-a-chip," "lung-on-a-chip," "blood vessel-on-a-chip," "tumor-on-a-chip," "bone marrow-on-a-chip," and "kidney-on-a-chip" have been created. The "kidney-on-a-chip" model has proven to be significantly informative in experimental conditions. Jang KJ et al. directly observed the nephrotoxic effect of cisplatin on proximal tubular cells. Cell damage was monitored over a 24-hour period, with biomarker registration. In the subsequent 72 hours after removal of the damaging agent, recovery of the damaged cells was noted through activation of

aquaporin-2 receptors and independent movement of the cytoskeleton of the tubular cells—this process has been poorly studied in experimental animal models.

Another application of this technology is found in the pharmaceutical industry, where it will greatly accelerate the development of new drug products without side effects. The combination of microfluidics and 3D printing will provide a variety of opportunities for development in medicine**.**

Г8-3. THE ART OF COMMUNICATION…. Miroslava Benkova-Petrova, Aleksandar Petrov, Svetla Staykova Actual Nephrology, Issue 1, Volume 14, 2020, pages 40-45 ISSN: 1312-0190

ABSTRACT

Every disease has consequences not only for the health but also for all aspects of human life - ability to work, social integration, emotional and mental balance of the individual. The sick person is often unable to overcome the problem on his own. Protective reactions such as anger, depression and fear occur, which worsen the disease even more. It is extremely important for healthcare professionals to have the ability to recognize such pathological changes in behavior. Calmness, confidence and empathy are some of the key factors that can help the patient to build trust and allow him to pass easily through the course of the disease, significantly improving the effect of treatment and quality of life.

Г8- 4 THE HORIZON OF 3D TECHNOLOGY – PRESENT AND FUTURE P. Vălchanov, A. Petrov, A. Tonchev, V. Ikonomov, Varna Nephrology Forum, Year 2016, Volume III, Issue №2, pages 29-33

Abstract: 3D printing is a fast developing, precise and reachable technology, which is able to operate with a variety of materials and to build 3D models with many purposes. Those qualities are allowing us to use this kind of technology in many fields of medicine. They unlock the potential for building models for demonstration, training and treating different diseases, or to personalize instruments, and even to create artificial tissues and organs. This technology has enormous potential for influencing the development of medicine.