IPNA

International Pediatric Nephrology Association

RARE DISEASES IN PEDIATRIC NEPHROLOGY

(IPNA Sponsored Teaching Course)

Hotel Holiday Inn
Skopje, Republic of North Macedonia

Course Director: Velibor Tasic (Skopje)

Scientific Committee: Constantinos J. Stefanidis (Athens), Yaacov Frishberg (Yerusalem), Danko Milosevic (Zagreb), Velibor Tasic (Skopje), Detlef Bockenhauer(Leuven), Bodo Beck (Cologne), Dimitar Roussinov (Sofia), Adrian Lungu (Bucharest), Sandra Habbig (Cologne), Adrijan Sarajlija (Belgrade), Julia Hoefele (Munich), Valbona Nushi Stavilleci (Prishtina)

Organizing Committee: Velibor Tasic, Nora Abazi Emini, Aleksandra Jancevska, Ardiana Beqiri Jashari, Nikola Gjorgjievski, Ivan Akimovski

LIFE CHALLENGES

РЕТКО Е ДА СИ РЕДОК

4th-6th April 2024

IPNA

International Pediatric Nephrology Association

ABSTRACT BOOK

7th MSNDTAO Congress

and IPNA Teaching Course

"Rare Diseases in Pediatric Nephrology"

April 04-06, 2024

Hotel "Holiday Inn"

Skopje, North Macedonia

TABLE OF CONTENTS

ORGANIZERS

Course Director

Tasic Velibor, Skopje

Scientific Committee: Stefanidis J. Constantinos (Athens), Frishberg Yaacov (Jerusalem), Milosevic Danko (Zagreb), Tasic Velibor (Skopje), Bockenhauer Detlef (Leuven), Beck Bodo (Cologne), Roussinov Dimitar (Sofia), Lungu Adrian (Bucharest), Habbig Sandra (Cologne), Sarajlija Adrijan (Belgrade), Hoefele Julia (Munich), Nushi Stavilleci Valbona (Prishtina)

Organizing Committee: Tasic Velibor (Skopje), Abazi Emini Nora (Skopje), Jancevska Aleksandra (Skopje), Beqiri Jashari Ardiana (Skopje), Gjorgjievski Nikola (Skopje), Akimovski Ivan (Skopje)

WELCOME MESSAGE

Dear colleagues and friends,

Thanks to the sponsorship of the International Pediatric Nephrology Association, a Teaching Course entitled "Rare Diseases in Pediatric Nephrology" is being held in Skopje this year. Although rare diseases are by definition rare, their cumulative number is significant, so pediatric nephrologists will often encounter rare nephrological diseases in their practice.

The complexity of these diseases stems from the fact that the diagnosis is made late after the diagnostic Odyssey, that in addition to the kidneys, there are also serious extrarenal manifestations, which require a multidisciplinary approach. Many children end up with terminal uremia, which requires renal replacement therapy. It should be added that only a small number of these diseases have adequate etiological therapy, which is difficult to access, which is extremely expensive and available only in countries with a strong economy.

Fifteen renowned experts from neighboring countries and Europe have been invited to this course, who, in addition to standard lectures, will work interactively with the participants of this course, through clinical quizzes, challenging cases and images in nephrology.

I hope that this course will take place in a pleasant and friendly atmosphere and meet your expectations. I also hope that you will enjoy visiting Skopje in your free time, because April is a very pleasant month to visit Skopje.

Sincerely Yours

Velibor Tasic

Course Director

SCIENTIFIC PROGRAM

April 04, 2024 (Thursday)

20:00 Welcome and Opening, Hotel Holiday Inn, Skopje

April 05, 2024 (Friday)

Session I (Hall B)
Moderators: Danko Milosevic, Velibor Tasic
08:30 - 09:00 Adrian Lungu, Bucharest, Romania
Images in rare kidney diseases
09:00 - 09:30 Liesbeth Siderius, Amsterdam, Netherlands
From recognizable feature to diagnosing a rare kidney disease
09:30 - 10:00 Dijana Plaseska-Karanfilska, Skopje, North Macedonia
Genetic testing for rare kidney diseases
Discussion

10:10 - 10:30 Coffee break

Session II (Hall B)
Moderators: Constantinos Stefanidis, Detlef Bockenhauer
10:30 - 11.00 Detlef Bockenhauer, Leuven, Belgium
Renal tubular acidosis: the difference between a defect in secretion and absorption
11:00 - 11:30 Constantinos Stefanidis, Athens, Greece
How to investigate pediatric nephrolithiasis for a rare disease?
11:30 - 12:00 Yaacov Frishberg, Jerusalem, Israel
Nephropathic cystinosis – un update
12:00 - 12:30 Adrian Lungu, Bucharest, Romania
Complement role in kidney pathology
12:30 - 13:00 Velibor Tasic, Skopje, North Macedonia
Renal glucosuria and beyond

13:00 - 14:00 Symposium

Session III (Hall B)
Moderators: Nora Abazi-Emini, Julia Hoefele
14:00 - 15:15 Young nephrologists
Clinical Quizz 1
Clinical Quizz 2
Clinical Quizz 3

Session IV (Hall B)
Moderators: Bodo Beck, Dimitar Roussinov
15:15 - 15:45 Bodo Beck, Cologne, Germany
Genetic landscape of steroid resistant nephrotic syndrome
15:45 - 16:15 Julia Hoefele, Munchen, Germany
Type IV Collagen related nephropathies
Discussion

16:15 - 16:40 Coffee break

Session V (Hall B)
Moderators: Valbona Nushi Stavilleci, Sandra Habbig
16:40 - 17:05 Detlef Bockenhauer, Leuven, Belgium
Challenging case 1
17:05 - 17:30 Nora Abazi Emini, Skopje, North Macedonia
Challenging case 2

17.30-18.30 Symposium

Dinner for the Speakers
20.00-24.00

April 06, 2024 (Saturday)

Session VI (Hall B)
Moderators: Bodo Beck, Julia Hoefele
09:00 - 09:30 Dimitar Roussinov, Sofia, Bulgaria
Fabry disease
09:30 - 10:00 Sandra Habbig, Cologne, Germany
Congenital nephrotic syndrome
10:00 - 10:25 Daniel Turudic, Zagreb, Croatia
Complement activation in autoimmune hemolytic anemia

10:25 - 10:45 Coffee break

Session VII (Hall B)
Moderators: Adrijan Sarajlija, Yaacov Frishberg
10:45 - 11:15 Danko Milosevic, Zagreb, Croatia
Kidney in methylmalonic acidemia
11:15 - 11:45 Adrijan Sarajlija, Belgrade, Serbia
Genetic counselling in rare kidney diseases

Session VIII (Hall B)
Moderators: Valbona Stavilleci, Nora Abazi-Emini
11:45 - 13:00 Nora Abazi-Emini, Skopje, North Macedonia)
Adrijan Sarajlija, Belgrade, Serbia
Images in rare kidney diseases; Challenging Cases

13:00 - 14:00 Symposium (Genesis)

14:00 - 16:30 All participants
Clinical Quizz 1
Clinical Quizz 2
Clinical Quizz 3

16:30 - Closing remarks

Venue

Hotel Holiday Inn, Skopje
Republic of North Macedonia
Language of the Meeting: English

Certificates of Attendance will be provided by Prof. V. Tasic

INVITED SPEAKERS

ADRIAN LUNGU

Dr. Adrian Catalin Lungu is a consultant Pediatric Nephrologist in Fundeni Clinical Institute, Bucharest, Romania, one of the largest University hospitals in his country. Besides his daily clinical work of taking care of the small patients, he is also involved in teaching activity and research projects.

He had the opportunity to organize the first IPNA teaching course in Romania in November 2017, which was a real success with more than 200 participants and 20 international speakers.

His interests in research cover areas like Immunology and genetics of renal diseases, SLE, aHUS, C3 nephropathy, Complement, FSGS, ADPKD, tubular disorders and they involve collaborations with colleagues from Hungary, Germany, Italy, USA, Australia, Turkey, Macedonia, Croatia, Slovakia, and Slovenia.

Starting with 2022, he is leading the Bucharest, Fundeni Clinical Institute, ERKNet Reference Center, part of the European Reference Network for Rare Kidney Diseases. From 2019 he is part of IPNA council, representing ESPN and having active roles in Juniors and Specific priorities in Low Resourced Countries Committees.

He is involved in registries work and in reviewing activities for International Journals and in the scientific selection of abstracts for national and European medical meetings.

He represented Romania for Young Nephrologists Platform (YNP) at the ERA-EDTA, being involved in the webinars project. He is responsible for the Romanian events linked to World Kidney Day, and is also involved in advocacy and awareness with local patient associations. He is the secretary of the National Committee for Pediatric Nephrology from the Romanian Ministry of Health.

He is curious by nature and has always enjoyed embarking on new challenges.

IMAGES IN RARE KIDNEY DISEASES

Adrian Lungu - Romania

Rare kidney diseases encompass a diverse array of disorders, each presenting unique challenges in diagnosis and management. This abstract provides a short review with clnical cases of the role of imaging modalities in the assessment and characterization of several rare renal conditions, including Dent disease, distal renal tubular acidosis (dRTA), cystinuria, nephrocalcinosis, cystic kidney disease (ADPKD, ARPKD), ciliopathies, nephronophthisis.
Ultrasound serves as an initial screening tool, facilitating the detection of structural abnormalities, cysts, and calcifications, while magnetic resonance imaging (MRI) offers detailed anatomical and functional insights, particularly valuable in delineating cystic lesions in conditions like ARPKD and ADPKD. Computed tomography (CT) complements MRI, providing additional information on stone burden and nephrocalcinosis extent in mineral metabolism disorders.
While imaging plays a crucial role, integration with genetic testing and histopathological examination remains pivotal for definitive diagnosis and tailored management strategies.
In conclusion, a nuanced understanding of imaging findings is indispensable for navigating the diagnostic landscape of rare kidney diseases, emphasizing the need for a multidisciplinary approach to optimize patient care and outcomes.

Key words: Dent, dRTA, Cystinria, Nephrocalcinosis, ARPKD, ADPKD, Ciliopathies, Nephronophtisis.

COMPLEMENT ROLE IN KIDNEY PATHOLOGY

Adrian Lungu - Romania

Complement dysregulation plays a pivotal role in various kidney pathologies, contributing significantly to the progression of diseases such as C3 glomerulopathy (C3GN), atypical hemolytic uremic syndrome (aHUS), vasculitis, lupus nephritis, IgA nephropathy (IgAN), and post-infectious glomerulonephritis (PIGN). This review aims to elucidate the multifaceted involvement of the complement system in these renal disorders.

C3 glomerulopathy (C3GN) is characterized by dysregulated activation of the alternative complement pathway, leading to deposition of C3 in the glomeruli and subsequent inflammation and tissue damage. Genetic mutations and acquired dysfunctions in complement regulatory proteins contribute to the pathogenesis of C3GN.

Atypical hemolytic uremic syndrome (aHUS) is primarily caused by genetic abnormalities affecting complement regulation, resulting in endothelial damage and thrombotic microangiopathy. Dysfunctional complement control exacerbates renal injury and can lead to end-stage renal disease (ESRD).

Vasculitis encompasses a spectrum of autoimmune disorders characterized by inflammation and necrosis of blood vessels, including those in the kidneys. Complement activation amplifies vascular injury and perpetuates immune-mediated damage in vasculitic glomerulonephritis.

Lupus nephritis, a common complication of systemic lupus erythematosus (SLE), involves immune complex deposition and complement activation within the glomeruli. Complement components contribute to the pathogenesis of renal inflammation and fibrosis in lupus nephritis.

IgA nephropathy (IgAN) is characterized by the deposition of IgA immune complexes in the glomerular mesangium. Dysregulated complement activation, particularly via the alternative pathway, exacerbates glomerular inflammation and fibrosis in IgAN.

Post-infectious glomerulonephritis (PIGN) results from immune complex deposition following certain infections, with complement activation playing a crucial role in the pathogenesis. Complement-mediated inflammation contributes to glomerular injury and impaired renal function in PIGN.

Understanding the intricate involvement of the complement system in these kidney pathologies is crucial for developing targeted therapeutic strategies aimed at modulating complement activity and mitigating renal damage. Further research into the precise mechanisms underlying complement dysregulation in each disease entity is warranted to advance the field of renal immunology and improve clinical outcomes for affected patients.

Key words: C3GN, aHUS, Vasculitis, Lupus, IGAN, Post-infectious GN.

ADRIJAN SARAJLIJA

Adrijan Sarajlija, MD, PhD, is the associate professor of paediatrics at the University of Belgrade Faculty of Medicine. He specialized in paediatrics and clinical genetics and has decades-long experience as clinical genetics consultant at Mother and Child Health Care Institute of Serbia "Dr Vukan Cupic". His postgraduate experiences include observerships at Duke University Rare Disease Center and University Children Hospital at Heidelberg. He has authored and co-authored dozens of research articles and acts regularly as a reviewer for many leading scientific journals. Field of interest of Adrijan Sarajlija includes inborn errors of metabolism, neurodevelopmental disorders, and hereditary bone diseases.

GENETIC COUNSELING IN RARE KIDNEY DISEASES

Adrijan Sarajlija

Mother and Child Health Care Institute of Serbia “Dr VukanCupic”

Faculty of Medicine University of Belgrade

The role of genetic counselors and clinical geneticists in the field of inherited kidney diseases (IKD) is becoming paramount, given the expanding landscape of genetic testing and the complexity of genetic conditions affecting kidney. The evidence suggests that at least 10% of adult patients and most children with chronic kidney disease (CKD) suffer from IKD, underscoring the importance of genetic diagnostic tools. Genetic counselors need training and experience to navigate the intricate genetics of CKD and other renal disorders.

Several hundred monogenic causes of IKD have been identified so far, presenting diverse inheritance patterns, different pathophysiology and phenotypic variability. Only the subset of inherited metabolic disorders encompasses many different entities with plethora of heterogeneous renal manifestations.

Genetic counselors help in identifying of patients in need of genetic testing, offering expertise in test selection and result interpretation. Pre-test counseling can also include discussions of the usefulness and rationale for genetic testing in children for the adult-onset conditions. Post-test counselling consists of personalized guidance, emotional support, and access to resources for patients and their families. As indications for genetic testing expand, improved education for patients and nephrologists is crucial, addressing topics such as genomic medicine, informed consent, potential benefits, implications of genetic results, and current limitations in interpretation.

Key words: Chronic kidney disease (CKD), Inherited kidney diseases (IKD), genetic counseling.

BODO BECK

Bodo Beck, MD, is a pediatric nephrologist at the Medical School University of Cologne, Germany. He has a board certification in pediatrics, pediatric nephrology and human genetics. He has authored and co-authored dozens of research articles, following his research fellowship in human genetics.

GENETIC LANDSCAPE OF STEROID RESISTANT NEPHROTIC SYNDROME

Bodo Beck

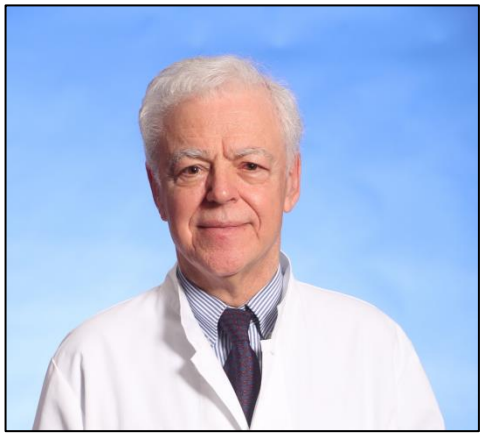
Medical School University of Cologne, Germany

Focal segmental glomerulosclerosis (FSGS) and its clinical correlate of syndromal or non-syndromic steroid resistant nephrotic syndrome (SRNS) and overlapping conditionsare a leading cause of end-stage renal disease (ESRD) in children, adolescents and adults. Recent progress in genetics allowed for the identification of a growing number of causative genes defining monogenic forms of FSGS/nephrotic syndrome. While congenital and infantile SRNS/FSGS has a high genetic yield, the genetic basis of FSGS in older children, adolescents, and adults is much more diverse and less well understood. Especially adult patients are still underserved with genetic testing and only fragmented data on their genotypes are available.With the exception of Alport syndrome targeted/causal treatment options are largely missing, however the identification of genetic causes already has many clinical implications on the treatment strategy, the prognosis, and for family counseling (recurrence risk, other family members at risk etc.).

In my presentation I will refer to the classic causes of SRNS as well as newly identified entities from the spectrum across all age groups, discuss their phenotypes and clinical hallmarks. I will also comment on the problem of variant classification in rare (proteinuric) kidney disease and the limits current genomics platforms.

Key words: Nephrotic syndrome, proteinuria, steroid resistant nephrotic syndrome, focal segmental glomerulosclerosis, monogenic kidney disease, syndromal kidney disease, proteinuria,

CONSTANTINOS STEFANIDIS



Dr. Constantinos J. Stefanidis is *Head of Pediatric Nephrology, "Mitera" Children's Hospital. Athens, Greece.* His main research interests are: Pediatric dialysis, nutritional and bone disorders management of children with Chronic Kidney Disease, Acute Kidney Injury in children.

Interesting facts: in 1973 he got his Medical Degree (Magna Cum Laude), valedictorian of the class in the University of Athens, Greece. In 1978 - Certified Pediatrician (Greece) also Certified by the College of Physicians and Surgeons of Ontario Canada. In 1982 - part of the American board of pediatrics eligibility. In 1984 he got his PhD (Magna Cum Laude), University of Athens, Greece. In 2021 - Fellow of the European Society of Pediatric Nephrology.

In 1997 - President of the 31st Meeting of European Society of Pediatric Nephrology (ESPN). From 1999-02 - Councilor of ESPN. From 2007-11 - Chair of the Tertiary Group of European Academy of Pediatrics. Since 2009- Editor of the journal "Pediatric Nephrology" of the International Pediatric Nephrology Association (IPNA). In 2010 - Chair of the Organizing Committee of the 3rd Congress of the European Academy of Pediatric Societies, Copenhagen 2010. From 2012-19 - ESPN-ERA Registry representative. From 2013-21 - Board member of the Dialysis Working Group of ESPN. Since 2020- Associate Editor of the journal Frontiers in Pediatrics -Pediatric Nephrology.

HOW TO INVESTIGATE PEDIATRIC NEPHROLITHIASIS FOR A RARE DISEASE?

Constantinos J. Stefanidis, MD, PhD, FESPN

"Mitera" Children's Hospital, Athens, Greece.

Nephrolithiasis is frequently diagnosed in adults, in contrast it is rare in children and adolescents.Recent population-based studies have demonstrated that the prevalence of pediatric nephrolithiasis has been increasing for the past decades. Nephrolithiasis is not a disease, but a symptom of different diseases. Therefore, a prompt diagnostic evaluation has to be performed to identify its cause. Most pediatric patients with nephrolithiasis have a combination of low urinary volume, hypercalciuria, hyperoxaluria, and hypocitraturia. These predisposing factors lead to elevated supersaturation of calcium phosphate and/or calcium oxalate. Primary idiopathic hypercalciuria is the leading cause of nephrolithiasis. This is a multifactorial disease in which complex interaction of environmental and individual genetic factors lead to hypercalciuria /hypercalcemia and often to nephrolithiasis. Up to 50% of these patients have a positive family history. The association with congenital anomalies of the kidney and urinary tract (CAKUT) andabnormalities of metabolismor raremonogenic kidney stone diseases should be diagnosed on time. Recently, a number of patients with hypercalcuria /hypercalcemia and elevated 1.25-dihydroxy-vitamin D3were diagnosed with mutations of SLC34A1, SLC34A3 and CYP24A1. Primary hyperoxaluria might be another rare diagnostic consideration. Preventive management is primarily based on the reduction of the concentration of lithogenic or increased excretion of antilithogenicfactors in urine. A high fluid intake (>1.5 - 2L/1.73m^2) is recommended regardless of the underlying disease. A low Na and high K diet is recommended in children with hypercalciuria. A reduced calcium intake should be avoided in these patients, because it leads to an even riskier increase in oxalate excretion.Crystallization inhibitors, mostly potassium citrate increase the solubility product of urine.The management of pediatric nephrolithiasis is challenging, because of its variable clinical presentation and its high recurrence rate. In addition, these patients have a lower rate of spontaneous passage of the stone(s) and may more often require surgical intervention.

Key words: Nephrolithiasis, children, hypercalciuria.

DANIEL TURUDIC

Dr. Daniel Turudic is a graduate of the University of Zagreb Medical School. He has recently completed his training and residency at the Department of Pediatrics of the University Hospital Centre Zagreb, where he is currently working as a pediatrician. He has received the dean's award for academic excellence on the research paper "Age-Specific Excretion of Calcium, Oxalate, Citrate, and Glycosaminoglycans and Their Ratios in Healthy Children and Children with Urolithiasis." He has co-authored dozens of research articles and regularly acts as a reviewer for many leading scientific journals. He is also a co-investigator on several international Pfizer and Takeda phase III clinical trials. He is a member of the Croatian Society for Pediatric Nephrology (HDPN), European Society of Pediatric Oncology (SIOPE), Croatian Society for Pediatric Neurology, Section for Metabolic Diseases of the Croatian Pediatric Society, and the Croatian Cooperative Association for Hematological Diseases (KROHEM). He was a part of the organizational committees for the IX South Eastern Pediatric Nephrology Working Group (SEPWNG) meeting and Neonatology 2022, a regional meeting of Croatian neonatal intensive care physicians. His special interests are coagulation disorders, rare diseases, and complement-mediated diseases. His Ph.D. thesis focuses on clinical applications of machine intelligence in the early diagnosis of rare diseases.

COMPLEMENT ACTIVATION IN AUTOIMMUNE HEMOLYTIC ANEMIA

Daniel Turudic, MD
Department of pediatrics
University Hospital Centre Zagreb

Autoimmune hemolytic anemia (AIHA) caused by anti-RBC autoantibodies may occur via direct cell lysis with or without complement activation (complement cascade membrane attack complex, or by antibody-dependent cell-mediated cytotoxicity (ADCC)[1(Barcellini, 2015)]. Complement activation and consumption have rarely been reported in AIHA so far. Hemolysis in AIHA causes the time- and concentration-dependent increase in free iron and pro-oxidative reactive oxygen species (ROS) acting as endothelial aggressors. As a consequence, antibody-mediated RBC hemolysis (hemoglobin and heme) acts as a second "hit" phenomenon, causing tissue and organ injury by triggering prothrombotic and proinflammatory pathways (sC5b-9)[2(Turudic et al. 2023)]. Additionally, free heme promotes rapid exocytosis of VWF from Weibel–Palade bodies with a membrane expression of P-selectin. P-selectin is an anchoring platform for the C3b and C3, activating alternate pathways and releasing the ultra-large von Willebrand factor (UL-vWF)[3,4(Frimat et al. 2013, Roumenina et al. 2016)]. The formation of C3b is a focal point in activating three complement pathways, namely, classical, alternate, and lectin. Free heme also inhibits the cleavage of the UL-vWF by ADAMTS13. The interaction of heme with the complement components can activate the alternate complement pathway either via C1q inhibition or via C3 activation, forming an overactive C3/C5 convertase[3,4(Frimat et al. 2013, Roumenina et al. 2016)]. The resulting proinflammatory oxidative attack promotes RBC apoptosis-like programmed cell death (eryptosis)[5(Pretorius et al. 2016)].

We encountered complement activation and consumption in a 5-year-old boy, with both positive direct [anti-IgG (1+), anti-IgG-C3d (3+)] and indirect antiglobulin (Coombs) tests triggered by concomitant EbV and CMV infection. The treatment consisted of intravenous methylprednisolone, immunoglobulins, FFP, Rituximab, plasma exchange, and vitamin B9 and B12 substitution. Final remission was achieved with plasma exchange, IVIG, and FFP. However, the disappearance of long-lived circulating plasma cells caused by Rituximab as its late and decisive effect cannot be completely ignored.

We believe that EBV and CMV trigger AIHA, which, in turn, activates the complement cascade. Additionally, the heterozygous gain-of-function C3 mutation found in the patient (c.600-14C > T) can increase the formation of C3bBb[6(Han-Mou, 2013)]. Complement activation should not be treated immediately with a complement blockade, except for case-sensitive complement overactivation and overconsumption, as most patients, after onset, should be amenable to self-complement regulation. Complement activation with a genetic background should be assessed in all severe warm and cold hemolytic anemias caused by autoantibodies[2(Turudic et al. 2023)].

Key words: Autoimmune hemolytic anemia (AIHA), complement activation.

DANIKO MILOSEVIC

I was born on January 5, 1955, in Brčko, Republic of Bosnia and Herzegovina. After completing primary education and high school in the Republic of Croatia, I entered the Faculty of Medicine at the University of Zagreb, where I graduated in 1979. After completing my studies, I enrolled in a postgraduate course in oncology, and then on in 1988, I defended my master's thesis under the title "Neutron activation analysis of tumor and normal brain tissue". After working as a general practitioner at the Kutina Health Center, I began my specialization in pediatrics at the Clinical Hospital Center in the Children's Disease Clinic in Šalata. I completed postgraduate studies in Clinical Pediatrics. In 1987, I was elected to the teaching position of expert associate at the Faculty of Medicine of the University of Zagreb, and then in 1990, to the teaching position of assistant. In 1998, I defended my doctoral dissertation entitled "Idiopathic Urolithiasis in Children: a study of Promoting and inhibitory factors in Urine for stone formation". The doctoral dissertation resulted in four papers in international scientific journals indexed in CC. In 2001, I was elected to the scientific-teaching position of assistant professor at the Faculty of Medicine of the University of Zagreb, with a cumulative working relationship in the Department of Pediatrics, for the scientific field of biomedicine and Healthcare, scientific field of Clinical Medical Sciences, the branch of Pediatrics, for the subject of Pediatrics, with a position at the Pediatric Clinic in Šalata. I acquired the title of primarius in 2003. I was recognized as a specialist in pediatric nephrology in 2004. I was elected to the scientific title of senior research associate in 2007. In 2013 and in 2014, I was elected to the scientific title of scientific advisor to a full-time professor in a cumulative employment relationship for the scientific field of Biomedicine and Health, the field of Clinical Medical Sciences, the branch of Pediatrics with a position in the Clinic for Pediatrics, Clinical hospital center Zagreb. I am a member of professional organizations in the Republic of Croatia and abroad (ESPN, IPNA, EAP). I have published 66 articles that are cited in the Scopus database, and in 2023 8 works that are cited in the CC database and 2 works indexed in the CC have been accepted for publication. My h-index is 13, and the works have been cited 685 times. I am the current president of the Croatian Pediatric Nephrology Society (HDPN) in the second term.

KIDNEY IN METHYLMALONIC ACIDEMIA

Prof. dr. sc. Danko Milošević, MD, PhD
Croatian Academy of Medical Sciences, Zagreb, Croatia

Hyperammonemias belong to a considerable variety of diseases. All hyperammonemias should be considered with utmost clinical attention. The common hyperammonemia include N-acetyl glutamate synthetase deficiency (NAGS, methylmalonic acidemia (MMA), propionic acidemia (PA), isovaleric acidemia (IA), ornithine transcarbamylase deficiency (OTC), and carbamyl phosphate synthetase deficiency (CPSID).

Methylmalonic acidemia is the most common for pediatric nephrologists because it leads to chronic renal disease and kidney failure. Accumulation of ammonia in the proximal tubule through mitochondrial dysfunction in the proximal renal tubule and metabolic acidosis-producing endothelin is the most probable explanation for progressive renal function deterioration[1,2,3](Frassetto et al. 2009, Chandler et al. 2009, Wesson et al. 2023). The majority of patients with methylmalonic acidemia develop renal impairment at the young age [4](Alkhunaizi et al. 2017). A deficiency of the methyl malonyl-CoA mutase adenosyl-cobalamin, or methyl malonyl-CoA epimerase deficiency, causes it. The broad spectrum of symptoms includes nervous system disorders (hypotonia, developmental delay, movement disorders, seizures), pancreatitis, cardiomyopathy, growth retardartion, vomiting, feeding difficulties, and hematologic disorders (neutropenia). Serum and urine methylmalonic acid are variable, and their rise is often triggered by a secondary infection such as a viral infection [5](Manoli et al. 2023). A liver or combined liver-kidney transplantation is better for lowering plasma methylmalonic acid levels than isolated kidney transplantation and is associated with better preservation of kidney function [6](Dello Strologo 2022). Recently, carglumic acid has been used for the treatment of hyperammonemia.

We present 3 cases of methylmalonic acidemia in children. The first two in early infant age presented with hematuria and thrombocytopenia with petechial bleeding. The third case is a male child with chronic presentation of recurrent vomiting with periodic serum ammonia above average level (samples taken considerable time after vomiting), anorexia (body weight stagnant at about 20 kg), failure to thrive, and developmental delay (learning disabilities, intellectual disability). Extensive search for infection included parvo B19, neonatal immune thrombocytopenia (NAIT), specific thrombocyte antibodies in all family members and immunohematology tests for erythrocyte antibodies were found negative. The signal pathway RAS/MAPK appears to be disrupted in the third patient.

In all cases, we found elevated methylmalonic acid in urine and occasionally in plasma. Genetic analysis revealed a heterozygous mutation c.1741C>T. We treated these children with carglumic acid (Carbaglu®) with no side effects, as well as with Vitamin B12 and a dietary regimen. After a 4-year follow-up, there were no signs of kidney deterioration, and the children gained average weight for their age. Following treatment, the absence of vomiting was achieved, and children gained regular physical activity and improved overall condition (excellent in school). No signs of kidney involvement is found, all patients can acidify the urine, have no overt proteinuria, and have no electrolyte abnormalities.

Key words: Methylmalonic acidemia, hyperammonemia, methyl malonyl-CoA

DETLEF BOCKENHAUER

Detlef Bockenhauer is a Professor and Head of Paediatric Nephrology at the Katholic University and University Hospital Leuven. He has a special interest in inherited kidney diseases, tubulopathies and renal physiology. He uses genetics and clinical observations in patients to gain insight into the molecular basis of kidney function and disease.

Detlef Bockenhauer went to Medical School in Hamburg and Lübeck, Germany and trained in general paediatrics in Hamburg and New York City. At Yale University, he subsequently trained in paediatric nephrology and physiology and in 2000, he joined the faculty. In 2004, he moved to Great Ormond Street Hospital and University College London, where he was Professor and clinical lead for nephrology until his departure to Leuven in 2023.

RENAL TUBULAR ACIDOSIS: THE DIFFERENCE BETWEEN A DEFECT IN SECRETION AND ABSORBPTION

Detlef Bockenhauer

1) Paediatric Nephrology, UZ Leuven and Department of Cellular and Molecular Physiology, KUL, Leuven, Belgium
2) Great Ormond Street Hospital for Children and Department of Renal Medicine, UCL, London, UK

Renal Tubular Acidosis (RTA) refers to impaired maintenance of acid-base homeostasis by the renal tubule. Most cellular processes are pH dependent, which is reflected in the very tight normal range for arterial pH. An impairment of acid-base homeostasis thus affects the whole body and can result in multiple complications. Broadly, we distinguish proximal RTA (pRTA) from distal RTA (dRTA), but a combination of both is also possible. PRTA is characterised by impaired proximal tubular reabsorption of bicarbonate, whereas dRTA is a disorder of distal acid secretion. In this talk, I will provide examples of RTA, discuss clinical manifestations, review the underlying causes including genetics, propose a diagnostic algorithm and discuss how the different disease mechanisms affect patient management

Key words: pH, acid-base homeostasis, nephrocalcinosis, acid load, alkali supplementation.

DIMITAR ROUSSINOV

Dr. Dimitar Roussinov is Pediatric Nephrologist, Hospital "The Health", Sofia. He is also a Member of the Paediatric Committee of European Medicines Agency and a Member of the Editorial Board of "Pediatria", Sofia. He is also a Representative of Bulgaria in ESPN / ERA-EDTA Registry.

In 1985 – M.D., Medical University, Sofia. From 1985-1987 – District pediatrician, Pazardjic City. From 1987-2004 – Assistant Professor, Dialysis Unit, Department of Pediatric Nephrology, University Pediatric Hospital, Sofia. From 2004-2005 – Head Department of Pediatric Nephrology, University Pediatric Hospital, Sofia. From 2005-2019 – Assistant Professor, Dialysis Unit, Department of Pediatric Nephrology, University Pediatric Hospital, Sofia. From 2019-2021 – CEO, University Pediatric Hospital, Sofia. In 2021 – Associated Professor, Department of Pediatric Nephrology, University Pediatric Hospital, Sofia. In 1991 – B.C. in Pediatrics. In 2006 – B.C. in Pediatric Nephrology. In 2016 – Ph.D. From 2015 – 2021 – Member of the Management Board of Bulgarian Nephrology Society.

FABRY DISEASE

Dimitar Roussinov

Department of Pediatric Nephrology, University Pediatric Hospital, Sofia

Fabry disease is a an X-linked type of lysosomal storage disorder. Mutations in GLA gen produce full or partial deficiency ofα-galactosidaseA (α-GAL A) enzyme. Without its function harmful levels of sphingolipids build up in different tissues. Fabry disease is a rare, but with increasing frequency due to improved diagnosis. It affects mainly, not only heart, kidneys, brain, vessels, eyes and skin. It is believed is a disease of adulthood. However, symptoms although nonspecific, start during childhood. Agalsidasealfa (Replagal®) over 7 years of age and Agalsidase beta (Fabrazyme®) over 2 years of age was approved for use as an enzyme replacement therapy (ERT) in 2001 by European Medicine Agency. The first α-GAL Astabilizer, migalastat (Galafold®), was approved for treatment of adults with an amenable GLA variant in 2016. Additionally, Pegunigalsidasealfa (Elfabrio®) was approved for treatment of adults in 2023. Accumulated significant clinical experience shows as early diagnosis is made and therapy started as successful is. However, it is clear current therapeutic options can stop or greatly slow down progression of the disease, but deposits of sphingolipids in tissues were almost not reduced. That is why, all consensuses recommend treatment to be started if symptoms or organ damage are present. There is still a discussion when to treat asymptomatic patients with more voices that to happen in childhood. Future options in management of Fabry disease are gene therapy products with few of them under development.

Key words: Fabry disease, lysosomal storage disorder, GLA mutations.

JULIA HÖEFELE

Dr. Julia Höefele is a Senior Consultant at the Institute of Human Genetics, Klinikum rechts der Isar, Technical University of Munich, School of Medicine, Munich, Germany. She had her medical training at the Medical School at the Rostock University, Rostock, Germany; Medical School at the Ruprecht-Karls University, Heidelberg, Germany; and Medical School at the Albert-Ludwigs University, Freiburg, Germany. She finished her doctorate in 2007, Prof. Dr. Friedhelm Hildebrandt; Positional cloning of the gene causing nephronophthisis type 4; Albert-Ludwigs University, Freiburg, Germany.

Her engagement in the Research System is as follows:

2009 Establishment of an own working group focusing hereditary nephropathies;

Since 2016 Medical Advisory Board of the German Alport Syndrome Foundation;

Since 2020 Expert Group of the International Alport Syndrome Foundation (alportuk);

Since 2023 Chair of the Working Group CAKUT/UTI/Bladder Dysfunction of the European Society for Paediatric Nephrology.

TYPE-IV-COLLAGEN-RELATED NEPHROPATHIES

Julia Hoefele

Institute of Human Genetics, Technical University of Munich, Munich, Germany

The genes *COL4A3, COL4A4* and *COL4A5* encode the α3, α4, and α5 chains of the type IV collagen, an essential component of the glomerular basement membrane. Disease-causing variants ([likely] pathogenic variants) in one of these genes are associated with the type-IVcollagen-related nephropathy, comprising Alport syndrome (AS) and thin basement membrane nephropathy (TBMN).
AS is characterized by microscopic hematuria and proteinuria leading to progressive loss of kidney function. Additionally, sensorineural hearing impairment, and eye abnormalities as extrarenal manifestations can be observed. AS can be inherited in an X-linked (XLAS; hemizygous [male] or heterozygous [female] variant in *COL4A5*) or autosomal form (recessive or dominant; variants in *COL4A3*/*COL4A4*). Furthermore, digenic inheritance has also been discussed as a possible cause in these individuals.
TBMN is a histopathology-derived term defined as uniform thinning of the glomerular basement membrane and phenotypically characterized by persistent microscopic hematuria, minimal if any proteinuria, and normal renal function. In up to 20% of individuals with TBMN, disease progression to late-onset kidney failure (> 50 years of age) can be observed, probably related in part to the development of focal segmental glomerulosclerosis. The presentation will focus on the different clinical phenotypes of individuals with a type-IV-collagen-related nephropathy as well as the monogenic causes and the diagnostic tools.

Key words: Type-IV-Collagen-Related Nephropathies, Alport Syndrome, Thin basemenet membrane nephropathy.

LIESBETH SIDERIUS

Liesbeth Siderius is trained in general paediatrics (Maastricht, the Netherlands) and clinical genetics (Seattle U.S.A.). She has experience working in clinical genetics as well asprimary and secondary paediatrics in the Netherlands.In 2009 EURORDIS (European Patient Organisation for Rare Diseases) reported on "12000 voices of patients with a rare disease". The lack early diagnosis, multidisciplinary care and social support are common problems for people with a rare condition. Acknowledging most rare diseases manifest at young age within the European Academy of Paediatricsworking group on rare diseases was initiated. The European Health Data Space is welcomed by the European Academy of Paediatrics and European Confederation of Primary Care Paediatricians stating : Digital child health: opportunities and obstacles (December 2023).

FROM RECOGNIZABLE FEATURE TO DIAGNOSING A RARE KIDNEY DISEASE

L Siderius S Perera

The WHO Pocket Book on Primary health care for Children and Adolescents (the Pocketbook), 2022, includes standards for the quality of care provided to children and adolescents, which should be applied in all primary care settings.The European Commission launched the European Health Data Space (EHDS) as one of the central building blocks of a strong European Health Union. The EHDS offers a consistent, trustworthy, and efficient framework to use health data for research, innovation, policymaking, and regulatory activities while ensuring full compliance with the EU's high data protection standards.

The EHDS directive of the EU and WHO Europe's Pocket Book of Primary Healthcare for Children and Adolescents, if used in synergy, could contribute to significant progress towards improving the quality of care for every child in Europe.

How can well-child visits contributes to early diagnosis of rare renal diseases?

Children and adolescents may present with symptoms of renal disease with an incidental finding during examination, e.g. high blood pressure, blood or protein in the urine.Moreover , a large variety of recognizable features at the well-child visit may indicate a rare condition at risk for renal involvement.

A selection of features demonstrates how typically renal features as well as non-renal features such as cataract, short stature, depigmentation, nail dystrophy, hearing deficit can be recognized at well-child visit.

These signs and symptoms can be assigned to one or more interoperable standards and classifications leading to a possible diagnosis.

Rare conditions such as Fish eye syndrome, Lowe syndrome, Hypophosphatemic rickets, tuberous sclerosis, nail patella syndrome, Alport syndrome present in childhood with recognizable features. Early diagnosis leads to manage preventable renal disease and treatments. Findings at recommended well-child visits can be implemented as universal interoperable data in electronic and or personal health records.

Prioritise integrating health information systems enables seamless sharing of child health data and facilitate efficient collaboration among healthcare providers involved in the child's care. This can improve care coordination, enhance decision-making, and optimise health outcomes for children.

Key words: Rare diseases, digital health, primary care

NORA ABAZI EMINI

Nora Abazi Emini was born in 1976 in Gostivar, North Macedonia. Graduated from Medical Faculty Skopje in 2002. Completing training in pediatrics in 2011. Since 2013 she is working in the nephrology department, at University Children's Hospital. Current position: Head of Department for Pediatric Nephrology, Dialysis and Renal Transplantation.

Also, she is a Ph.D. candidate in pediatric nephrology, her research field is familial hematuria. She has a special interest on congenital anomalies of the urinary tract, rare inherited renal diseases, glomerular and tubular diseases.

During her career, she participated in several national and international projects, large number of scientific meeting and congresses. She is the author and co-author of several publications in professional journals. Also, participant in ESPN/ERA-EDTA registry and European National/Regional registries for children on renal replacement therapy.

She enjoys spending her time with her daughters, travelling and reading.

CLINICAL QUIZZES IN PEDIATRIC NEPHROLOGY

Nora Abazi Emini

University Children's Hospital, Medical School, Skopje, North Macedonia

Clinical quiz is an attractive and interesting method in educating young doctors at the beginning of their clinical work.Through a sequential presentation of a case interspersed with questions about how you would proceed in the diagnostic processing of the patient and his treatment, the young doctor is encouraged to think and keeps his attention the whole time.The goal of the clinical quiz is not to guess the final diagnosis, but to create a wide differential diagnostic array from which the most probable diagnostic option will emerge. During the clinical quiz, young doctors should exchange ideas and proposals that will discuss all possible diagnostic paths for solving the given case.For example, a case with a girl admitted with fever, high inflammatory markers, vomiting and gross hematuria.What are the next steps that will be taken.First, a good physical examination will be done, which reveals attenuated breathing sounds in the right lung.Further in the quiz, a question is asked which laboratory tests will be performed.All the necessary tests that will lead us to the diagnosis are discussed.In the end you are developing a differential diagnostic array, starting with postinfectious acute glomerulonephritis, IgA nephropathy, SLE nephritis etc. At the SEPNWG Teaching Course 2024, young doctors will present several clinical quizzes. They arise from everyday practice. Through discussion and arguments, they will practice clinical/critical thinking, which is very important in the career of every young doctor.

Key words: Clinical quiz, young doctors, clinical thinking.

SANDRA HABBIG

Prof. Dr. Sandra Habbig is a Leading Attending of the Outpatient Clinic for Pediatric Nephrology, Hypertension and Immunology at the University Children´s and Adolescents´ Hospital, Medical Faculty, University of Cologne (UoC), Cologne, Germany.

She had her medical training in the Medical School at the University of Bonn, Germany, La Laguna, Spain and in Montpellier and Paris, France. Finishing with a doctorate in 2006 at the University of Freiburg, Germany. Since then she has had a several fellowships, followed by a residency in pediatrics, which then got her board certified in pediatrics and intensive care medicine. Since then she has been an attending physician at the University of Cologne, Germany.

Her reviewer activities are: Pediatrics, Pediatric Nephrology, Nephrology Dialysis Transplantation, European Journal of Medical Genetic, Frontiers in Pediatrics etc.

CONGENITAL NEPHROTIC SYNDROME

Sandra Habbig

University of Cologne, Faculty of Medicine and University Hospital Cologne, Department of Pediatrics, Pediatric Nephrology, Cologne, Germany

The diagnosis of congenital nephrotic syndrome (CNS) is defined by the manifestation of nephroti csyndrome as early as in utero or during the first 3 months of life. The patients presen twith nephrotic-range proteinuria, hypoalbuminaemia and oedema. Genetic mutations in genes encoding podocyte proteins are the most frequent cause of CNS, in rare cases, CNS is also caused by maternal allo-immune disease or by congenital infections. Manangement of patients with CNS is challenging and requires multi-disciplinary teams. This talk will focus on the clinical presentation of infants with CNS, the diagnostic measures and especially the multi-disciplinary management of the severy specific patients according to their clinical condition as recently outlined by a consensus statement experts from the European Reference Network for KidneyDiseases (ERKNet) and the European Society for Paediatric Nephrology (ESPN).

Key words: nephrotic syndrome – Podocin – Nephrin – WT1 - nephrectomy – albumin infusion – kidney transplantation.

VALBONA NUSHI STAVILECI

Valbona Nushi Stavileci, Paediatric Nephrologist.

Specialized on Pediatrics on 2007, and worked at University Clinical Centre of Prishtina -Kosovo with children with renal problems. During 2010, fellowship at Great Ormond Street Hospital for Children, London UK. Training on managing kidney diseases , dialyses and transplant. Attended subspecialized course on Dialyses at Royal free Hospital, London 2010. And Kidney biopsy hand on course on 2013, Laipzig Germany. During 9 years was part of a joint work project and team training by Swedish Urodinamic team of Linkping University.

Completed Pediatric Nephrology, IPNA ESPN Master Classes 2014-2016. And during 2022 at Wilhelmina Childrens Hospital, Nederland, trained for VideoUrodinamike and Urotherapy.

During 2014 and further four years was Coordinator of National team on Assessment of Childrens Hospital services in Republic of Kosova, joint project of Kosovo MofH and WHO. Contributed as a lecturer at University of Medical Sciences in Gjakova. Giving profesional experience contribution, participated in several Nephrology Meetings and Other Pediatric meetings. A special expertize on modern diagnostic techniques as Voiding contrast enchanced Ultrasound and Urodynamic studies.

Workes as Consutant Nephrologis in Prishtina at Elita Plus Diagnostic Center, and in Gjakova at European Clinic Hospital.

VELIBOR TASIC

Graduated: Medical School, Skopje, 1980, Employment: Clinic for Children's Diseases, Skopje 1980, Specialization in pediatrics: 1986. Stipends: The British Council 1991- London; International Society for Peritoneal Dialysis 2001 Hannover. Training in pediatric nephrology: Belgrade 1986, London 1991, Birmingham 1991, London 1998, Hannover 2001. PhD: "Clinical, biological and prognostic aspects of acute poststreptococcal glomerulonephritis in children, University Sv. Kiril i Metodij-Skopje, 1997. Academic degree: Full Professor of Pediatrics and Pediatric Nephrology, Medical School, Skopje

Membership: International Pediatric Nephrology Association, European Society for Pediatric Nephrology, EDTA-ERA, European Academy of Pediatrics, Macedonian Pediatric Association

Working Groups: South Eastern European Pediatric Nephrology Working Group, Inherited Renal Disorders (ESPN), CAKUT/UTI/Bladder dysfunction (ESPN), WGIKD (ERA-EDTA), Tertiary Working Group for Rare Disease (European Academy of Pediatrcis). Secretary General, Macedonian Pediatric Association 2004-2006. Council Member of the European Society of Pediatric Nephrology 2009-2012. Director, SEPNWG Teaching Course Ohrid 2012. Skopje 2016, 2023, 2024. Scientific Chair, BALKAN Alport Meetings, Ohrid 2018,2022. Invited Lecturer at ESPN/IPNA/EDTA teaching courses in Pediatric Nephrology; Moderator and Lecturer in Nephrology Session at Serbian, Croatian, Kosovo and Macedonian Pediatric School. Scientific Chair of Rare Disease Conferences Skopje 2012, 2013. Publications: >200 Pubmed Papers. Conference papers/abstracts ≈400

RENAL GLUCOSURIA AND BEYOND

Velibor Tasic

University Children's Hospital, Medical School Skopje, North Macedonia

Renal glucosuria is the excretion of glucose in the urine in the presence of normal plasma glucose levels. Renal glucosuria may occur without any other abnormalities of renal function or as part of a generalized defect in proximal tubule function (Fanconi syndrome). It also may occur with various systemic disorders, including cystinosis, oculocerebrorenal syndrome (Lowe syndrome), Wilson Disease, tyrosinemia and others. Familial renal glucosuria (FRG) is a rare disorder due mainly to mutations in the sodium-glucose cotransporter 2 (SGLT2) gene (*SLC5A2*), which is responsible for most cases. To date, over 86 mutations of the *SLC5A2* have been identified, including missense mutations, nonsense mutations, small deletions, and splicing mutations. In general, renal glucosuria is a benign condition and does not require any specific therapy. What is the meaning of this rare, benign, trivial disease? Great for the community! Thanks to the study of the pathophysiology and genetics of this disease, drugs called SGLT2 inhibitors were created, which proved to be very useful for the treatment of type 2 diabetes, chronic heart failure and chronic kidney disease. In this lecture, I will elaborate on SGLT2 inhibitors "gliflozines"(approved by FDA: dapagliflozin, empagliflozin, bexaglifloxin, canagliflozin, ertugliflozin), mechanisms of their action, benefits and adverse effects. I will emphasize the need for conducting controlled randomized studies for management children with chronic and rare kidney diseases with SGLT2 inhibitors..

Key words: renal glucosuria, SGLT2, SLC5A2, chronic kidney diseases, SGLT2 inhibitors.

YAACOV FRISHBERG

I was born in Israel and graduated from the Faculty of Medicine, The Hebrew University of Jerusalem. Following a pediatric residency at the Beilinson Medical Center in Petah-Tikva, I completed a fellowship in Pediatric Nephrology at the Children's Hospital of Philadelphia in the USA. During my fellowship I conducted research in molecular renal immunology.

Upon my return to Israel, I joined the division of Pediatric Nephrology at the Shaare Zedek Medical Center in Jerusalem. Currently, I am a Professor of Pediatrics at the Hebrew University of Jerusalem and the Director of the Division of Pediatric Nephrology at the Shaare Zedek Medical Center, Jerusalem.

My main scientific interests are hereditary kidney diseases in children including: kidney stone disease with special focus on the hyperoxalurias, nephrotic syndromes and mitochondrial cytopathies. My clinical interests include renal replacement therapy in children composed of various modalities of dialysis and kidney transplantation.

NEPHROPATHIC CYSTINOSIS – AN UPDATE

Yaacov Frishberg

Division of Pediatric Nephrology, Shaare Zedek Medical Center, Jerusalem, Israel

Cystinosis is a recessively inherited lysosomal storage disorder, caused by mutations in the *CTNS* gene, encoding cystinosin, a lysosomal cystine/H+ symporter. Nephropathic cystinosis is the most frequent and severe form.The disease causes progressive accumulation of cystine in virtually all tissues. Kidney involvement is responsible for the initial symptoms, namely Fanconi syndrome, occurring during the first year of life.This is followed by dysfunction of many additional organ systems including: the eye, thyroid, pancreas, growth and the neuro-muscular system. The diagnosis is based on increased leukocyte cystine levels and confirmed by the detection of bi-allelic mutations in the *CTNS* gene. Early diagnosis, for timely medical treatment, is of utmost importance in determining long-term outcomes. This may justify implementing newborn screening program for infantile nephropathic cystinosis.

Throughout adolescence and into adulthood, many extra-renal manifestations of cystinosis become apparent. The transition to adult service, during this period of fragility, mandates the establishment of a multi-disciplinary approach.

Advances have been made, during the last decade, in our understanding of the mechanisms underlying the pathogenesis of cystinosis beyond the physical damage caused by lysosomal cystine accumulation. These have been mostly derived from studies in animal models and include reduced endocytic uptake, increased proliferation and defective lysosomal dynamics and autophagy.

Review of the advances in therapeutic approaches will include the transition from immediate- release to delayed-release cystine depleting agents, kidney replacement therapy and hematopoietic stem cell gene therapy.

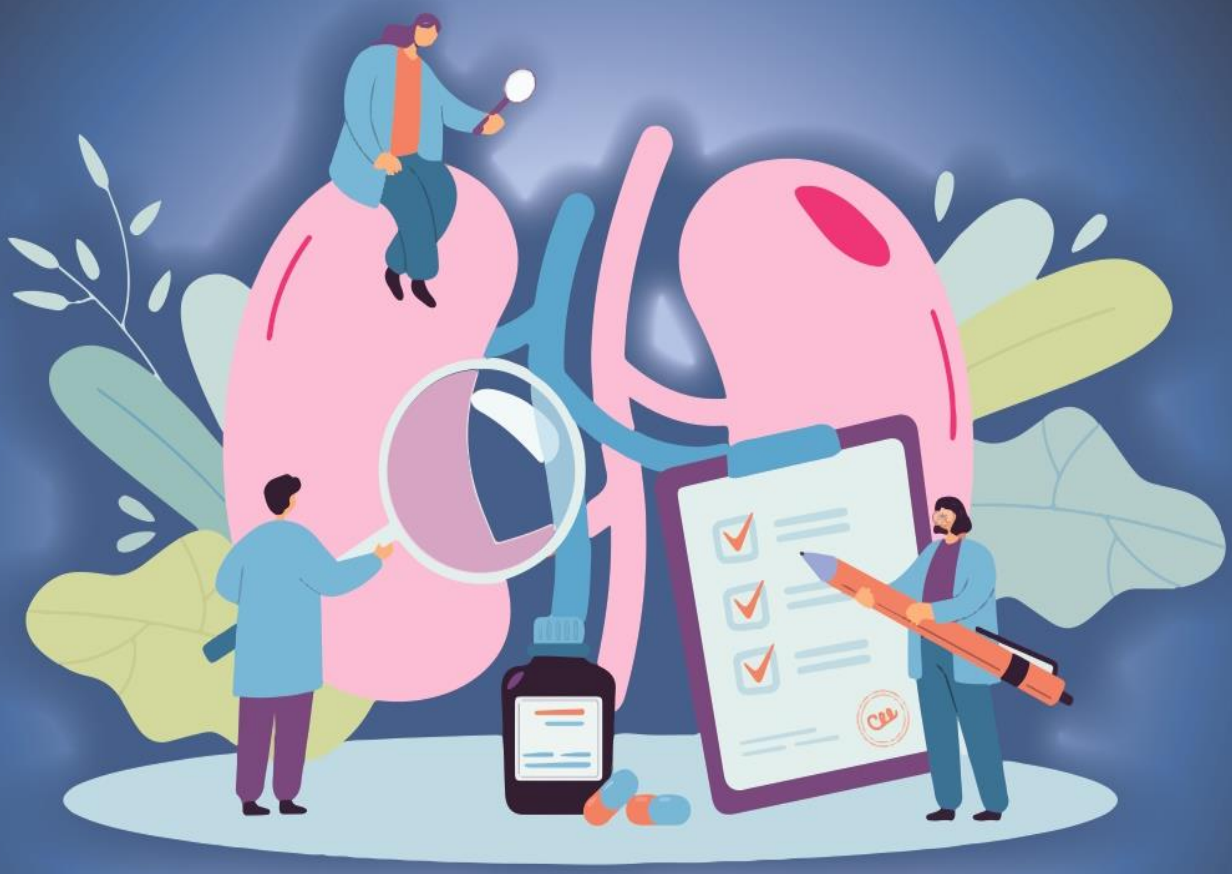
Key words: nephropathic cystinosis, lysosomal storage, cystinosin, Fanconi syndrome, corneal deposits, rickets, cystine-depleting drugs.

IPNA

International Pediatric Nephrology Association

RARE DISEASES IN PEDIATRIC NEPHROLOGY

(IPNA Sponsored Teaching Course)



Macedonian Society for Rare Diseases

LIFE with CHALLENGES
Life is a puzzle, collect it.

РЕТКО Е ДА СИ РЕДОК
RRALLË ËSHTË TË JESH I RRALLË
RARE IS TO BE RARE

Hotel Holiday Inn
Skopje, Republic of North Macedonia

4th-6th April 2024