IPNA

Teaching Course

VII SEPNWG Meeting

european society for paediatric nephrology

Personalised genomics in Pediatric Nephrology: from the lab bench to the bedside

Bucharest, Romania

17-18 November 2017

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Dear colleagues and friends,

We are pleased to invite you to the International Pediatric Nephrology Association (IPNA) teaching course and the VIIth Meeting of the Southeastern Europe Pediatric Nephrology Working Group (VIIth SEPNWG), which will be held together in Bucharest, Romania, between 17 and 18 November 2017,

The main topic of the meeting will be: "Personalized genomics in Pediatric Nephrology: from the lab bench to the bedside."

The purpose is to provide know-how on current views of personalized genomics of clinical importance, but also to review more familiar subjects in Pediatric Nephrology.

Besides, we aim to support the development of renal research and facilitate the delivery of high-quality healthcare in our countries

We hope that young doctors will take advantage of the many benefits this course will offer and they will use the information provided as a valuable resource for future development of their practice.

First SEPNWG meeting was in 2001 in Istanbul, and since then a beautiful group of Pediatric Nephrologists from the countries of Southeastern Europe formed scientific connections and friendships. We are convinced that this autumn in Bucharest those bonds will become even stronger and new ones will be created.

In addition to the scientific program, you will find that Bucharest is a lovely city to visit, a leading political, social and economic center of Romania. The capital city of the country was a meeting point for cultures throughout history, and you will find Roman, Greek, Turkish, Austrian, Hungarian and French influences. Also, many nearby regions in Romania offer you possibilities to explore and spend unforgettable days with your family, friends and colleagues.

We look forward to meeting all of you at our course.

Sincerely,

Constantinos J. Stefanidis, MD, PhD (Greece)
Chair of the Scientific Committee

Adrian Lungu, MD (Romania)
Course Director

IPNA Teaching Course - VIIth SEPNWG Meeting

November 17 and 18, 2017, Bucharest, Romania

Course Director: Adrian Lungu**,** (Romania)

Scientific Committee Chair: Constantinos J. Stefanidis (Athens, Greece)

Scientific Committee Members:

Varvara Askiti (Greece), Sevcan Bakkaloglu (Turkey), Bogdan Dima (Belgium), Francesco Emma (Italy), Elena Levtchenko (Belgium), Adrian Lungu (Romania), Danko Milosevic (Croatia), Fatih Ozaltin (Turkey), Ludmila Podracka (Slovakia), Danka Pokrajac (Bosnia), Brankica Spasojevic (Serbia), Stella Stabouli (Greece), VeliborTasic (Macedonia), Rezan Topaloglu (Turkey)

Local Organizing committee:

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Prof. Dr Adrian Covic

Dr Adrian Covic, MD, PhD is Professor of Nephrology at University of Medicine "Gr T Popa" Iasi, Head of Renal Transplant, Nephrology and Internal Medicine Departments at "Dr C I Parhon" Hospital, Iasi and member of Medical Science Academy and Romanian Scientists Academy.

Dr Adrian Lungu

Dr Adrian Lungu, MD is a pediatric nephrologist at Fundeni Clinical Institute, Bucharest. He has a special interest in atypical Hemolytic Uremic Syndrome.

Dr Bogdan Dima

Dr Bogdan Dima, MD of Pediatrics is working at C.H.U.Charleroi Pediatric Nephrology department.

Dr Brankica Spasojević Dimitrijeva

Dr Brankica Spasojević Dimitrijeva, MD in Pediatric Nephrology and Clinical Assistant at the Faculty of Medicine of the University of Belgrade has a major interest in the area of kidney transplantation. She sustained the Master Thesis in November 2008 titled "Scarcer Changes in Kidney Diseases in Children with Urinary Infections".

Professor Dr. Carola G Vinuesa

Carola Vinuesa was born in Spain and obtained a medical degree at the University Autonoma of Madrid. She undertook specialist clinical training in the UK and in 2000 was awarded a PhD by the University of Birmingham. As the recipient of a Welcome Trust International Travelling prize Fellowship, she did postdoctoral work at The John Curtin School for Medical Research (The Australian National University, ANU). Her work led to the discovery of genes important for immune regulation and memory and the identification of a novel pathway of posttranscriptional control of gene expression to prevent autoimmunity. Since 2006 she has been leading the Humoral Immunity and Autoimmunity Group at ANU, first supported by a Viertel Senior Medical Research Fellowship and currently by an Elizabeth Blackburn NHMRC Fellowship. Her group identified a critical role for follicular helper T (Tfh) cells in autoantibody-mediated autoimmune diseases and made significant discoveries into the function and transcriptional regulation of this cell subset. She has won several prizes including the 2008 Science Minister's

Prize (Life Scientist of the year), the 2009 Gottschalk Medal of the Australian Academy of Sciences, the inaugural CSL-Young Florey Medal and the 2015 Ramaciotti Medal for Excellence in Biomedical Research. In 2015 she was elected as a Fellow of the Australian Academy of Science. She is currently Professor of Immunology at the ANU and Head of the Department of Immunology and Infectious Disease. Since its launch in 2014, Carola has been joint Director of the Centre for Personalized Immunology (an NHMRC Centre of Research Excellence) that aims to dissect the genetic, molecular and cellular pathogenesis of immune disease in individual patients with the goal of improving diagnoses and identifying targeted therapies.

Prof. Dr Constantinos J Stefanidis

Dr. Stefanidis is Director of Pediatric Nephrology at "P. and A. Kyriakou" Children's Hospital in Athens, Greece. He is leading the Dialysis Working Group of the ESPN. He completed his medical degree at the University of Athens. He was trained in Pediatrics at the University of Athens and Western Ontario in London. He later went at the Hospital for Sick Children in Toronto to extend his training in Paediatric Nephrology. Dr. Stefanidis was councilor and president of the European Society for Paediatric Nephrology (ESPN), national representative and chair of the Tertiary Care Group of the European Academy of Pediatrics. He is presently section editor on dialysis at the journal "Pediatric Nephrology", registry representative at the ESPN/ERA-EDTA Registry and board member of the dialysis working

group of ESPN. He authored or co-authored more than 120 scientific publications, with more than 1300 citations.

Dr Danka Pokrajac

Dr Danka Pokrajac is Assistant Professor for Pediatrics at the Faculty of Medicine, University of Sarajevo and works at the Neoprola Department of Pediatric Clinics of KCU Sarajevo since 1995 until now. Dr Pokrajac was Head of Neurological Department of Pediatric Clinics KCUS from 2003 to Feb. 2016.She received the Honorable title of the Nephrologist of Bosnia and Herzegovina received by the Association for Nephrology, dialysis and kidney transplants in Bosnia and Herzegovina at the II Nephrology School held in Sarajevo on October 27, 2007.

Professor Dr. Danko Milošević

Dr Danko Miloševićis Full Professor of Pediatrics at Faculty of Medicine, University of Zagreb and Clinical Hospital Center Zagreb.

Dr Elena Levtchenko

Dr Elena Levtchenko, MD, PhD is Adjunct head of the department of Pediatric Nephrology at University Hospital Leuven, Belgium. She is the Secretary General of ESPN. Dr Levtchenko was Assistant professor in the department of Pediatric Nephrology Radboud University Medical Centre, Nijmegen, The Netherlands (2005-2008) and Coordinates of National Cystinosis Outpatient Clinic in The Netherland and is Member of the scientific board of Cystinosis Research Foundation USA. She is also Medical Advisor of International Cistinosis Patient Foundation and of commission Genetic Renal Diseases of Dutch Patients Association.

Prof. Dr Francesco Emma

Dr Francesco Emma is a Pediatric nephrologist at Ospedale Pediatrico Bambino Gesu, Roma, Member of the Scientific Review Board of the Cystinosis Research Foundations (2010), Secretary of the Scientific Committee of the ERA-EDTA Working Group on Inherited Kidney Disorders (2014), Contract Professor, School of Nephrology – La Sapienza University, Rome Contract Professor, School of Pediatrics – Tor Vergata University, Rome (2005). He is Author/ co-author of >100 articles in peer reviewed journals and 11 book chapters Associate Editor for Education of “Paediatric Nephrology” (Springer) Editor, Paediatric Nephrology 7th edition (Tecbook-Spinger).

Dr Fatih Olzatin

Dr Fatih Olzatin, MD, is Professor in Department of Pediatric Nephrology at Hacettepe University Faculty of Medicine, Ankara,Turkiye and also licensed in Pediatric Rheumatology with a special interest in genetics of nephrotic syndrome. He published several papers in international medical journals indexed in PubMed and is author of several Conference papers/abstracts.

Prof. Dr Ileana Constantinescu

Associate Professor Ileana Constantinescu: is Head Physician of Virusology - Immunology, University Lecturer of “Urology, Renal Dialysis and Transplantation” Department at the Faculty of Medicine “Carol Davila” Bucharest, Head of Immunogenetics and Virology Center of Fundeni Clinical Institute and the Director of Grants and Research, UMF "Carol Davila".

Prof. Dr. Katharina Hohenfellner

Dr. Katharina Hohenfellner, M.D., Ph.D. serves as the Chief Medical Affairs Officer of BioCision, LLC. Dr. Hohenfellner is responsible for facilitating the integration of BioCison's standardization and automation products into GMP environments and clinical programs. She oversees the development of new clinical

applications and develops regional educational and research opportunities in partnership with key medical institutions, agencies and industry leaders. Dr. Hohenfellner is Board Certified in Pediatrics at the Children's Hospital in Johannes Gutenberg-University, Germany. For more than 10 years, Dr. Hohenfeller served as an Associate Professor in the Department of Pediatrics at the University of Mainz and Salzburg. She is a Board Member of the Society of Pediatric Nephrologists. Dr. Hohenfellner has a Ph.D. and an M.D. from the University of Mainz.

Conf Dr Liliana Garneata

Dr Liliana Garneata is Associate Professor, MD, PhD in Discipline of Internal Medicine and Nephrology at "Carol Davila" Nephrology Hospital

Prof. Dr. Ludmila Podracka

Dr Podracka is Professor and Chair of the Department of Pediatrics at the Pavol Josef Safarik University in Košice, and Chief of Pediatrics at the Children's Hospital of Košice, Slovak Republic.

She developed the pediatric nephrology unit in Košice and established a pediatric renal replacement program

including kidney transplant at Košice, completed a PhD in pediatric nephrology at the University of Pavol Josef Safarik at Košice, and promoted to Associate Professor and serve as program director, reinstated the training program and trained pediatric nephrology fellows. In 1995 Dr Podracka won a prestigious scholarship of the "Olga Havel Foundation" and spent part of the subspecialty training and research at the Nephrology division of Tuff University Springfield,Mass and at the Nephrology division of Brown University, Providence, RI. In 2000, she assumed the role as Chief of the Department of Pediatrics at the University Hospital in Košice and was promoted to Professor in 2002 and appointed as a Vise Dean at Medical School, Pavol Josef Safarik University in Košice from 2007-2011.

Prof. Dr Marija Jelusic

Dr Marija Jelusic, MD, PhD was Assistant investigator Zagreb University School Medicine, 1998—2002, fellow pediatrics, 2002—2006, assistant professor, consultant pediatrics, since 2009, head of the department of Pediatric Immunology and Rheumatology, since 2009. Achievements include research in immune-pathogenesis of autoimmune diseases. Research in molecular cardiology.

Prof. Dr Mihaela Balgradean

Dr Mihaela Balgradean, MD PhD is Professor and Chief of Pediatrics at Faculty of Medicine" Carol Davila", Bucharest, Head of Pediatrics Clinic and Head of the "Nephrology and Dialysis" Department at "MS Curie" Emergency Children Hospital. Professor

Mihaela Balgradean is the coordinator of Romanian Pediatric Nephrology Specialty and she author or co-authored more than 200 scientific publications.

Dr Mihaela Gherghiceanu

Dr Mihaela Gherghiceanu, MD, Phd is Associate Professor of Morphopathology at the Faculty of Medicine "Carol Davila" Bucharest and Head of the "Ultrastructural Pathology Laboratory" at National Institute of Research and Development in the field of Pathology and Biomedical Sciences "Victor Babeş" Bucharest ". Dr Gherghiceanu has a special interest in research of epithelia - mesenchymal transdifferentiation in glomerular pathology, the involvement of the complement system in glomerular pathology and vascular lesions in glomerulonephritis.

Dr Mihai Popescu

Dr Mihai Popescu is MD of Anesthesiology and Intensive Care at Fundeni Clinical Institute and also University Assistant at "Carol Davila University of Medicine" Bucharest.

Dr Sevkan Bakkaloglu

Dr Sevkan Bakkaloglu is Professor of Pediatrics, Head of the Department of Pediatric Nephrology and Rheumatology Gazi University, Faculty of Medicine, Ankara, TURKEY, with a major interest in Pediatric Peritoneal Dialysis, Chronic Kidney Disease Mineral Bone Disorders (CKD-MBD) and Primary Hyperoxaluria. She is a board member of member of ESPN Council and member of several ESPN WG. Dr Bakkaloglu is Author/ co-author of many articles in peer reviewed journals and 6 international book chapters.

Dr Stella Stabouli

Stella Stabouli is Assistant Professor of Pediatrics at Aristotle University of Thessaloniki, Greece. She serves as a Senior Consultant at the Pediatric Nephrology Unit of the 1st Department of Pediatrics, in Hippokration Hospital of Thessaloniki, Greece. She obtained her MD and PhD degree from the National and Kapodestrial University of Athens, Greece. She is a certified Pediatrician (2004) and Pediatric Intensivist. She has served as a Senior Research Associate at the obesity Clinic of the University of Mississippi Medical Centre, Jackson, USA (2004-2005). She is recognized as Clinical Hypertension Specialist by the European Society Hypertension (2009), and a member of the European Society Hypertension Working Group on Blood Pressure in Children and Adolescents. She is also member of European Society of Pediatric Nephrology CKD-MBD working group. She has published more than 70 original articles, reviews, and editorials in peer review international journals, as well as book

chapters, and has presented more than 100 invited lectures in national and international meetings.

Prof. Dr Tanja Kersnik Levart

Assoc. Prof. Tanja Kersnik Levart, MD, PhD is Head of the Clinical Department of Nephrology, Pediatric Clinic in Ljubljana. She will be the Head of the Organizing committee for the 2020 ESPN congress

Dr Todor Arsov

Dr Todor Arsov, PhD in Biomedical Science at the Australian National University and completed postdoctoral research at Stanford University, California is currently Senior Medical Advisor Biosimilars – Hospira.

Varvara Askiti

Athens, Greece

Prof. Dr Velibor Tasic

Dr. Velibor Tasic is a Professor of Pediatrics in Medical School, Skopje and holds the position of Senior Consultant Pediatric Nephrologist, University Children's Hospital Skopje, Macedonia. He received the Medical degree from Medical School, Skopje, 1980 and did Specialization in pediatrics, he attained the Ph.D. degree in Pediatrics, from The Saints Cyril and Methodius University of Skopje,1997. He is an active member in many International Pediatric Nephrology Associations. He published several papers in international medical journals indexed in PubMed and is author of several Conference papers/abstracts.

Prof. Dr. Zoltán Prohászka

Dr Zoltán Prohászka is Full Professor of immunology at Semmelweis University Budapest and Associate Professor at the University of Vienna.
He published over 60 papers in international journals, many times awarded for research in his field. Since 1999 regularly delivered lectures and clinical practice for undergraduate /postgraduate students on internal medicine and tumor immunology. He organized and held a course for PhD students on the actual questions of the etiology of atherosclerosis in 2001. Dr Prohászka is involved in the training of PhD students and also a **reviewer of manuscripts** submitted to International Immunology, Cell Stress and Chaperones, Immunology Letters, Pediatric Research, Circulation, The Lancet.

SCIENTIFIC PROGRAM

Friday, November 17			
08:00	Registrations		
08.50	Welcomme message - Constantinos Stefanidis, Adrian Lungu		
	1st session - LUPUS ***Chairs: Todor Arsov, Constantinos Stefanidis***		
09:00	Session introduction + Speakers	Todor Arsov	China
09:05	SLE / inflammation - and the kidneys; a perspective from a clinical immunologist	Marija Jelusic	Croatia
09:25	LUPUS Nephritis - the pathologist perspective	Mihaela Gherghiceanu	Romania
09:45	SLE and genes - a perspective of a genomic immunologist	Carola Vinuesa	Australia
10:15	Centre for Personalized Immunology (CPI and CACPI) collaboration	Carola Vinuesa	Australia
10:35	The "other" side of personalized genetics/genomics	Todor Arsov	China
10:55	*Discussion*		
			Coffee break
	2nd session – Complement and Kidney disease **Chairs: *Zoltan Prohaszka, Tanja Kersnik Levart***		

11:30	Romanian outbreak of E Coli O:26 Hemolytic Uremic Syndrome	Mihaela Balgradean	Romania
11:50	Complement in Kidney Disease	Zoltan Prohaszka	Hungary
12:10	C3 glomerulopathy	Tanja Kersnik Levart	Slovenia
12:30	Eculizumab treatment in aHUS – Romanian Experience	Adrian Lungu	Romania
12:50	*Discussion*		
Lunch break		***POSTERS***	
	3rd session – CKD, HTA, Renal Transplant ***Chairs: Adrian Covic, Liliana Garneata***		
14:30	Current Concepts and Management Strategies in Chronic Kidney Disease-Mineral and Bone Disorder	Adrian Covic	Romania
14:50	Hypoproteic diets seem to delay dialysis in CKD patients. Is it valid for children?	Liliana Garneata	Romania
15:10	Challenges in histocompatibility and immunogenetics for kidney transplantation	Ileana Constantinescu	Romania
15:30	Vascular Access in Children on Hemodialysis	Constantinos Stefanidis	Greece
15:50	Practical point of pediatric hypertension management	Stella Stabouli	Greece

16:10	*Discussion*		
Coffee break			
	4[th] session - Glomerular disease ***Chairs: Fatih Ozaltin, Francesco Emma***		
16:30	Genetics of Nephrotic Syndrome	Fatih Ozaltin	Turkey
16:50	Immunology of the Nephrotic syndrome	Francesco Emma	Italy
17:10	Henoch-Schonlein Purpura nephritis - what's new?	Brankica Spasojevic	Serbia
17:30	*Discussion*		
Dinner			

Saturday, November 18			
	5th session – Tubular and metabolic kidney disease ***Chairs: Francesco Emma, Sevcan Bakkaloglu***		
09:00	The kidney and mitochondrial cytopathies	Francesco Emma	Italy
09:20	Critical Care Nephrology - Biomarkers	Mihai Popescu	Romania
09:40	Metabolic Causes for Nephro-lithiasis	Danko Milosevic	Croatia
10:00	Primary Hyperoxaluria	Sevcan Bakkaloglu	Turkey

10:20	Genetics of Nephrocalcinosis	Velibor Tasic	Macedonia
10:40	*Discussion*		
Coffee break			
	6[th] session– Tubular and metabolic kidney disease ***Chairs: Katharina Hohenfellner, Elena Levtchenko***		
11:30	Diagnostics and Genetics in Nephropatic Cystinosis	Katharina Hohenfellner	Germany
11:50	Practical experience of Nephropatic Cystinosis in Slovakia	Ludmila Podracka	Slovakia
12:10	Genetic and pathophysiology of renal Fanconi syndrome	Elena Levtchenko	Belgium
12:30	Bartter and Gitelman syndromes	Varvara Askiti	Greece
12:50	The impact of the treatment with L-Methionine for Urolithiasis (Solartium Symposium)	Adrian Lungu	Romania
Lunch break			
	7[th] session – UTI, CAKUT ***Chairs: Constantinos Stefanidis, Erik Van Hoorde***		
14:30	VUR: from the Nephrologist to the Surgeon. Who gets it first?	Bogdan Dima	Belgium
15:10	Renal parenchymal damage in the first	Danka Pokrajac	Bosnia and Herzegovina

	febrile urinary tract infection and the TNF, ACE, PAI1 and MTHFR genes		
15:40	How to prevent the development of renal scars in children with febrile urinary tract infections	Constantinos Stefanidis	Greece
16:00	*Discussion*		
Conclusions and closing remarks			

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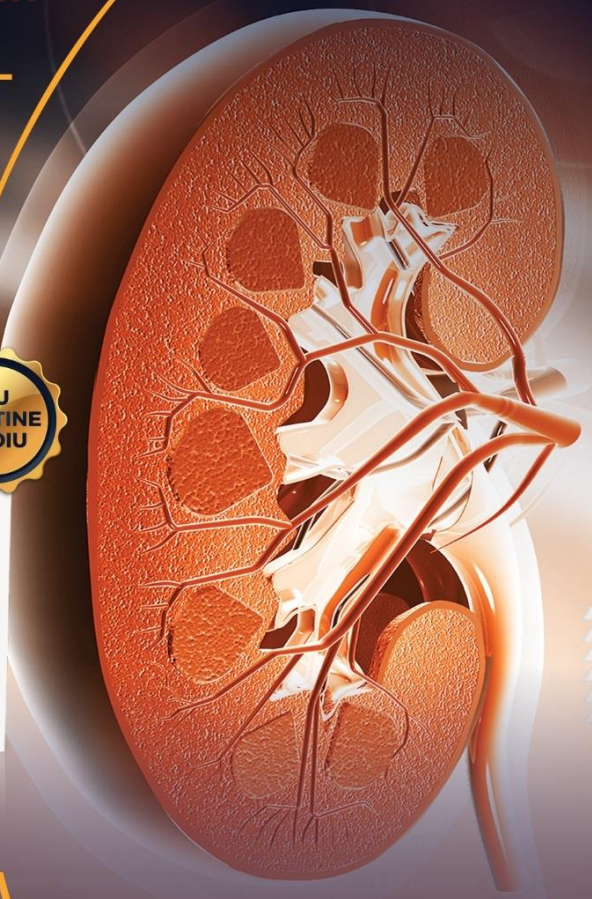

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ACCEPTED ABSTRACTS:

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P 02. MYH9-RELATED DISEASE AS A MULTIDISCIPLINARY PROBLEM
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Authors: Tripon Florin, Crauciuc George Andrei, Aldea Cornel, Bănescu Claudia, Duicu Carmen

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Authors: Iulia Constantinescu, Adrian Lungu, Anca Marin, Alexandra Niculae, Andrei Capitanescu, Ileana Negru, Raluca Slabu, Cristina Stoica

P 15. COMPLEMENT FACTOR H MUTATION ATYPICAL HEMOLYTIC UREMIC SYNDROME – 10 MONTHS ON DIALYSIS WITH PARTIAL RECOVERY OF THE RENAL FUNCTION AFTER ECULIZUMAB THERAPY – CASE REPORT

Authors: Alexandra Niculae, Adrian Lungu, DorinaTacu, Andrei Capitanescu, Cristina Stoica, Zoltan Prohaszka

ROMANIAN OUTBREAK OF E.COLI O:26 HEMOLYTIC UREMIC SYNDROME

Mihaela Balgradean, Anca Croitoru
Nephrology Department - "Marie Sklodowska Curie" Emergency Childrens Hospital, Romania

Haemolytic uremic syndrome (HUS) is a systemic disease and represents a frequent cause of acute kidney injury (AKI) in young children. The first words about HUS were in 1955 and it is defined by the triad: acute kidney injury, haemolytic microangiophatic anemia (non-immune, test Coombs- negative) and thrombocytopenia. Despite the decrease in mortality caused by sepsis, in the latest years, HUS still remains a major cause of morbidity and mortality for the children younger than five years old.
Shiga toxin are produced inside the intestine by enterohemorrhagic type of Ecoli and afterwards delivered into the blood flow. They are the main aggressive factors and are responsible for the endothelial microvascular lesions noticed in HUS. Endothelial tumefactions, accumulation of fibrinoid material and arteriolar thrombosis take place in afferent arterioles and, less frequent, in the efferent arterioles. The mortality rates is associated with extrarenal involvement of the disease, with multiple organ failure, and mainly central nervous system involvement (cerebral edema, vascular injuries, intracranial hypertension) followed by seizures and other neurological signs early in the course of the disease.
Methods: We analyzed 46 cases of Haemolytic Uremic Syndrome treated from February 2016 until September 2017 in the Nephrology Department of "Marie Sklodowska Curie" Emergency Children's Hospital, Bucharest, Romania.

Results: The age of studied patients was between 6 months and 11 years. Most of the patients presented diarrhea at the beginning. Some of them experienced important melenic stool, neurologic disorders of consciousness,

dizziness and tonic-clonic seizures due to electrolyte imbalances. 29 children needed peritoneal dialysis between 3 and 30 days.

In more than 50% of the cases the pathogen was E. Coli (most frequent serogroup O26), 1 case was diagnosed with Salmonella. Geographical distribution of the cases: most of the patients were located Arges- Pitesti, but also in: Bucharest, Constanta, Craiova. Brasov, Iasi, Galati Evolution: 3 cases died and the global evolution of the other 23 patients was favorable. As complications many of the patients presented hypertension and a few neurological manifestations (1 case remained with neurological sequelae)

Conclusions : In the great majority of the presented cases, HUS is due to STEC infections. It is a severe, life-threatening disease, but in most cases, it is self-limiting with complete resolution. The treatment is supportive and aims not only AKI but also extrarenal involvement of the disease (multiple renal failure), neurological, intestinal, pancreatic, hypertension, cardiac or pulmonary impairment.

The rapid and accurate diagnosis and correct supportive treatment is the key of a good outcome and evolution in HUS in children.

MYH9-RELATED DISEASE AS A MULTIDISCIPLINARY PROBLEM

Aksenova Marina.[1,2], Suntsova Elena.[2], Kalinina Anna.[2], Arseneva Anna.[2], Playsunova Svetlana.[2], Raikina Tatiana.[2], Machan Michail.[2], Novichkova Galina.[2]

[1] Nephrology Department, Y.Veltischev Research and Clinical Institute for Pediatrics at N.Pirogov Russian National Research Medical University, Moscow, Russia

[2] Hematology Department, Dmitry Rogachev Federal Research and Clinical Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russia

Background/Aim. MYH9-related disease is a rare autosomal-dominant disorder characterized by a considerable variability in clinical presentation: from isolated thrombocytopenia in some patients to multiple organ pathology (thrombocytopenia, deafness, nephropathy and cataract) in others. We present the clinical case of MYH9-related disease with severe phenotype caused by missense mutation in head domain.

Case diagnosis/treatment. The 9-year-old Caucasian boy was admitted to the hospital for adenectomy because of recurrent adenoiditis and progressive hearing loss. Laboratory screening revealed heavy thrombocytopenia (18-30x10^3/µl), proteinuria (1-3 g/l) and hematuria (10-20/field). The family anamnesis, pregnancy and birth were uneventful; the patient had no history of bleeding tendency. The boy had low blood platelet count from the first years of age and was treated with prednisone without any effect; sensorineural deafness grade 1 was detected at the age of 4 years, proteinuria (0,33 g/l) and hematuria (10/fields) were seen at 6-years-age. Alport syndrome was suspected. The boy was undergoing hematological examinations. Clinical and laboratory finding included: blood hypertension, thrombocytopenia (17x10^3/µl), giant platelets (mean platelet diameter 3,3 µm, N=1,69-2,63)

and Döhle bodies in neutrophils; serum creatinine 60 µmol/l, albumin 35g/l, eGFR=88 ml/min/1,73m^2; urine protein 2,14 g/day (1,79 g/m^2), hematuria (50 RBCx10^6/l). Ultrasonography did not reveal any abnormalities in either of the kidney. Audiometry showed bilateral high-pitch sensorineural deafness grade 4, no cataract was present. Mutation analysis of MYH9 gene (PCR and directly sequenced) was performed. The gene analysis showed a heterozygous c.287C>T in exon 2 [p.Ser96Leu(S96L)] in the patient.

The treatment with TPO-mimetic (Romiplostim) was started for increasing platelet count before adenectomy. The platelet count elevated to 70x10^3/µl on the 4 week of treatment. After surgery the boy was administered an enalapril 0,2 mg/kg/day. Over 3 years of follow up renal pathology slowly progresses: blood creatinine 73µmol/l, albumin – 32 g/l, eGFR=81ml/min/1,73m^2, urine protein - 3,4 g/day (2,6 g/m^2).

Conclusions. Our clinical observation demonstrates the need for close cooperation between clinicians and genetics in recognition and treatment the MYH9-related disease. We showed the efficiency of TPO-mimetic in preparation for elective surgery of patient with MYH9-associated thrombocytopenia.

ASPERGILLUS PERITONITIS IN PERITONEAL DIALYSIS PATIENTS: A CRITICAL REVIEW

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Background and aims: Fungal peritonitis in patients undergoing peritoneal dialysis(PD)is very difficultto treat and is associated with significant morbidity and mortality.Among fungal peritonitis causative organism, *Candida* constitutes the predominant. However, *Aspergillus*peritonitis presents a higher mortality rate when compared to *Candida* spp. and its identification as well as appropriate treatment remains a challenge for the physicians. Therefore, we reviewed all published cases in literature of *Aspergillus* peritonitis in PD patients.
Methods: We searched MEDLINE and Google Scholar databases and we systematically studied published cases and case series of *Aspergillus* peritonitis in PD patients. In addition, the reference list of each article was searched by hand to verify that all published cases were collected.

Results: A total of 54 cases (51% males) of *Aspergillus* peritonitis in PD patients were reported from 1968 to 2017. Mean patient age was 49.75±18.57years and mean PD duration prior to fungal infection was 38.33±36.89 months. *Aspergillusfumigatus*was isolated in 17/54 patients, *Aspergillus niger* in 15, *Aspergillus terreus* in 8, unidentified *Aspergillus* spp. in 7, *Aspergillus flavus* in 3, whereas sporadiccasesof *Aspergillus athermomutatus*, *Aspergillus nidulans*, *Aspergillus oryzae* and *Aspergillus*

sydowii were reported. *Aspergillus*spp. wereidentifiedfrom peritoneal fluid cultures in 65.8% of patientsin standard media, in18.4% in Sabouraud agar, while10.5% of patients presented a positive galactomannan test. In 5.3%of patients *Aspergillus*spp. were isolated from biopsy. As far as predisposing factors are concerned, 72.4% of patients suffered from prior bacterial peritonitis receiving antibiotic treatment, while peritoneal catheter removal was performed in 85.2% of cases. Antifungal treatment included intravenous and/or intraperitoneal administration of amphotericin B formulations in 40.5% of patients, combined with itraconazole in 23.8% or with fluconazole in 21.4%, andmonotherapy with caspofunginin 9.5%orketokonazole in 4.8%. In 2 patients,therapy concernedperitoneal catheter removal without adjuvant antifungal administration.Mortality rate was 40.7%and 74.1% of the survived patients switched to hemodialysis.

Conclusions: *Aspergillus* peritonitis diagnosis can be difficult, due to unspecific symptoms and a delay in organism growth in standard cultures. Early treatment with appropriate antifungal agents and removal of the catheter can be determinant for patient prognosis. Prior peritonitis and former antibiotic treatment are significantly associated with fungal peritonitis. Despite appropriate treatment, reported mortality remains high.

WHAT MIGHT BE THE DIAGNOSIS IN A PATIENT WITH SEIZURES, DEVELOPMENTAL DELAY, METABOLIC ALKALOSIS AND HYPOKALEMIA?

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A 14 year old refugee boy was admitted, because of generalized tonic-clonic seizures. His antenatal and previous medical history was unremarkable. His brother died at the age of six months due to an undiagnosed renal problem associated with hypokalemia. On physical examination, he had mild developmental delay with no other abnormal findings. His height and weight were on the 10th percentile. BP was normal. Initial laboratory investigations revealed metabolic alkalosis (pH: 7.48, HCO3: 47 mmol/l) and hypokalemia (serum K: 2.5 mEq/l), Na, Cl, Ca, P, Mg, were normal. Urine Mg excretion was increased (urine Mg/creatinine: 0.22). Urine volume was 1.1 L. Fractional excretion of potassium was increased (16%). Fractional excretion of Mg was also increased (6.6%). He had a mild proteinuria (Pr/Cr ratio: 0.5-1.1). Plasma renin (47 ng/ml/h, RR: 0.32-1.84) and aldosterone levels (626 pg/ml, RR: 12-340) were increased. His renal ultrasound and brain MRI were normal. EEG revealed focal abnormal seizure activity, while audiogram was normal. He was treated effectively with indomethacin and sodium, potassium and magnesium supplementation. Due to the clinical features of tubulopathy, mild developmental delay and seizures the diagnosis of SeSAME/EAST syndrome (S/E) was suspected. The results of molecular analysis of the KCNJ10 gene are pending.

S/E syndrome is a rare autosomal recessive syndrome featuring seizures, sensorineural deafness, ataxia, mental retardation and renal salt wasting. It has been associated with mutations in the *KCNJ10* gene, encoding the Kir4.1 potassium channel. *KCNJ10* is expressed in the renal distal convoluted tubule, ear and brain glial cells. The spectrum and severity of symptoms varies even with the same mutation, with some patients having predominantly electrolyte imbalance, whether others manifesting the complete phenotype.

The diagnosis of S/E syndrome should be considered in patients with a combination of neurological abnormalities and tubulopathy. Genetic confirmation of *KCNJ10* mutations is essential to establish the diagnosis.

NO RELATIONSHIP BETWEEN GLUTATHIONE-S-TRANSFERASE T1 AND M1 AND NEPHROTIC SYNDROME IN A ROMANIAN POPULATION

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The null genotypes of GSTT1 and GSTM1 (glutathione-S-transferase T1 and M1) was reported to be associated with response to IVCP (intravenous cyclophosphamide) therapy in idiopathic nephrotic syndrome and also with the risk for nephrotic syndrome (NS).
The aim of the study was to evaluate if the GST T1 and GST M1gene polymorphisms are a risk factor for NS development and if there is any correlation between this polymorphisms and NS therapy, outcome and prognostic.

Material and methods: GST T1 and GST M1 gene polymorphisms were analyzed in 73 NS patients and 165 controls. The DNA was extracted from the fresh peripheral blood and amplified using specific primers and multiplex-PCR technique.
Results: In the control group we found the following genotypes: 63GST T1/M1, 61 GST T1/T1, 12 GST M1/M1 and 28 with the null genotype. In the patients group 24 were GST T1/M1, 27 GST T1/T1, 13 GST M1/M1 and 9 with the null genotype. A significant difference between

the groups was observed for the GST M1/M1 genotype (p=0.03; OR=2.94; IC95%: 1.13-7.1).

No difference was observed between the genotypes and treatment response, disease relapse, prognostic and outcome (p>0.05).
Conclusion: The GST M1/M1 (with no activity for GST T1 enzyme) polymorphism appears to be associated with nephrotic syndrome development in this population. Given the limited sample size additional studies are needed to confirm these results.

NO ASSOCIATION BETWEEN GLUTATHIONE PEROXIDASE 1 GENE POLYMORPHISM AND YOUNG NEPHROTIC SINDROME PATIENTS

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Background and aims: Previously studies demonstrated the association between adult nephrotic syndrome (NS) patients and abnormalities in antioxidative system of NS patients. The polymorphism of GPX1 Pro198Leu (Glutathione Peroxidase 1) was reported to alter the GPX1 enzyme activity. The aim of our study was to investigate if exist a

correlation between GPX1 Pro198Leu polymorphism and young NS patients.

Methods: We obtained the ethical accord from the Ethical Committee from University of Medicine and Pharmacy Tîrgu Mureş, Romania. We

included in our study 237 children's, 73 in the patients group and 164 in the control group. The DNA was extracted from the venous blood and amplified using the RFLP-PCR technique. The amplified product was digested with ApaI Fast-digest enzyme.
Results: In the control group we found the following genotypes: 75 wild-type, 84 heterozygous and 5 homozygous with the variant allele. In the patients group 33 were wild-type, 34 heterozygous and 6 homozygous with the variant allele. No significant difference was observed between the groups ($p>0.05$).
Conclusion: The GPX1 Pro198Leu polymorphism is not a risk factor for NS development in this young population.

DIAGNOSTIC CHALLENGES OF CONGENITAL ANOMALIES OF THE GENITOURINARY TRACT

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Background

Congenital genitourinary malformations represent structural defects that originate during intrauterine development and are often associated with complications such as impaired renal function or infertility. Although progresses have been made in understanding the

underlying pathogenic mechanisms, developing new diagnostic techniques and managing congenital genitourinary malformations, due to their complexity they remain a challenge regarding diagnostic strategy and treatment alternatives.

Aim

The purpose was to report the case-specific diagnostic and therapeutic approach of a 11 year old female patient with stage V chronic kidney disease (CKD) on hemodialysis (permanent central venous catheter) with a complex genitourinary malformation.

Methods

The patient, born prematurely, small for gestational age (gestational age = 36 weeks, birth weight = 1800g) was first referred to the clinic in the neonatal period, when a urogenital sinus defect associated with clitoromegaly (Prader III) was described. Genetic testing revealed a female 46 XX karyotype. During infancy, associated congenital

anomalies of the kidney were diagnosed by abdominal ultrasound: bilateral renal hypoplasia and right renal cystic dysplasia, but with a normal sized bladder without vesicoureteral reflux (VUR). The continuous decrease in renal function imposed the need for dialysis. At the age of 4 years (stage V CKD) peritoneal dialysis was initiated and at the age 8 years and 3 months, due to recurring peritonitis, it has been decided to shift the patient on hemodialysis. Gradually, renal-related growth restriction, secondary osteodystrophy and anemia emerged as additional complications of CKD. Urinary tract infections, although expected in the presence of an underlying genitourinary malformation, were not documented in this case.

Results: Imagistic follow-up of the patient was required in order to evaluate the opportunity for renal transplantation. Abdominal ultrasound showed bilateral renal hypoplasia and right renal cystic dysplasia and a retro vesical cystic formation of fluctuating size (completely repleted within 2 days from an initial diameter of 10 cm), with a compressive effect on the bladder. MRI revealed additional megacystis with bilateral ureterohydronephrosis.

Conclusions: Contrast-enhanced ultrasound cystography is considered in this case in order to better describe the genitourinary malformation.

Case-related discussions focus on the multidisciplinary approach and the surgical management of this condition.

DIAGNOSIS AND EVOLUTION OF A ROMANIAN GIRL WITH CYSTINOSIS

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Introduction. Cystinosis is characterized by accumulation of the cystine in various organs of the body. Without specific treatment, children with cystinosis develop end stage kidney failure.

Case presentation. We present a girl who was diagnosed at one year age with cystinosis, based on the following criteria: polyuria, polydipsia, failure to thrive, hypophosphatemic rickets, metabolic acidosis, increased renal excretion of glucose, amino acids, phosphate,

and potassium, high Cystine levels in polymorphonuclear leukocytes and corneal crystals. During the first two years after the diagnosis, the treatment was targeted to metabolic acidosis and replacing electrolytes lost in the urine, but the evolution was characterized by very frequent episodes of dehydration and slow somatic development. When cysteamine therapy was available in our country, the treatment

was started with very good results: catch-up growth, disappearance of hypotonia, no gastrointestinal symptoms and normal physical activity.

PREDICTED INDIRECTLY RECOGNIZABLE HLA EPITOPES CLASS II SCORE IN PEDIATRIC KIDNEY TRANSPLANTATION – EXPERIENCE OF A SINGLE CENTER

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Background: Donor-specific HLA antibodies detected post-transplant are an independent risk factor for late deterioration of renal allograft function. Antibody mediated rejection diagnosis is the presence of HLAab directed against the allograft (dnDSA). A novel tool to predict an allo-immune response is the PIRCHE algorithm. In our study, we hypothesized that the PIRCHE II algorithm can be an independent predictor for the development of de novo dnDSA (compared with classical antigen matching).

Methods: We systematically reviewed the electronic patient record for all consecutive renal transplantations from January 2010 to August 2016. We included 70 pediatric recipients (female/male ratio = 26/44, mean age at transplantation 11.23 ± 3.86 years) of a kidney transplant with complete HLA typing (HLA-A, B, C and DR and DQ) as well as comprehensive pre- and post-transplant HLAab follow- up.

Results: The cohort included first kidney transplantations mainly from deceased donors (61 patients) with a mean waiting time for the graft of 0.93 years ±0.61 years. Transplants were allocated to recipients with a mean cumulative ABCDRDQ mismatches of 5 (1-8). The PIRCHE II score ranged between 2 and 193, with a mean of 76.05±36.92. There was a significant correlation between the number of HLA mismatches and PIRCHE II score with a $p<0.001$ and $r^2=0.19$. The mean PIRCHE II score for patients with ABCDRDQ mismatches < 5 was 61.24 ±24.89 and for patients ≥5 was 86.53 ±40.57, with a p=0.004. A total of 8 patients (11.42%) developed dnDSAduring the first year after transplantation. The mean PIRCHE II score for patients who developed dnDSA in the first year after transplantation was 61.50 ± 23.90 versus 77.93 ± 38.01 for patient who did not develop dnDSA.We divided the dnDSA negative patients into 2 groups: one with low risk (mismatches <5, n=25) and high risk (mismatches ≥5, n=37). The PIRCHE II score was 60.2 ± 24.44 in low risk patients versus 61.50±23.90 in dnDSA + patients (p=0.89), respectively 89.91 ± 41.04 in high risk patients versus 61.50±23.90 in dnDSA + patients (p=0.06). There is a statistical difference between negative dnDSA patients with low risk and high risk, p=0.001. The most discriminative cutoff values were determined from the distribution of PIRCHE II score values between dnDSA positive patients and high-risk patients versus low risk patients. The cutoff value for PIRCHE II score was 96, AUROC=0.67 and p=0.005.

Conclusions: This is a single center analysis of 70 kidney pediatric recipients on the impact of different HLA matching approaches on DSA formation. In our study the highest PIRCHE II scores were not associated with dnDSA development. The PIRCHE II algorithm is a promising tool for the allocation of organs but still needs improvements.

AUTOSOMAL DOMINANT MULTICYSTIC DYSPLASTIC KIDNEY PHENOTYPE – NO GENOTYPE IDENTIFIED (YET)

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Background and aims: Multicystic dysplastic kidney (MCDK) is a variant of renal cystic disease characterized by multiple, non-functioning, non- communicating cysts replacing the normal renal parenchyma and leading to renal dysfunction. We present a three-generation family with CKD on bilateral multicystic dysplastic kidney.

Methods: Medical histories were obtained as a part of the affected individual's clinical workup. Next generation Sequencing (NGS) was performed in the Center of Genomics Medicine Timisoara, a research

laboratory, using the Illumina TruSight One Sequencing Panel (4813 morbid genes), on MiSeq Illumina platform.

Results: ***Clinical features and family history:*** 11years old girl known with CKD IIIB since the age of 4 years, presents multiple millimeter cysts in bilateral renal parenchyma showed on MRI (one 1,4cm cyst in the inferior pole of the right kidney), no hepatic impairment and no dysmorphic features. The patient's father is in chronic dialysis programme since the age of 46years (CKD diagnosis on bilateral cystic renal dysplasia since the age of 3years) and associates bifid distal phalanx of the right thumb, bilateral sensorineural hearing loss and ostium secundum atrial septal defect; paternal grandmother shows CKD, in dialysis since the age of 55years, mild hearing loss and myopia forte. No renal biopsy was performed to this date due to patient's restraints. ***NGS result:*** No pathogenic, probably pathogenic or with uncertain significance variants (according to ACMG Guideline) were detected in relation to the patient's phenotype. The variants in the following genes were analyzed in detail: *PKHD1*, *PKD1*, *COL4A5*(Alport syndrome), *PRKCSH*, *TSC2*, *TSC1*, *EGF*, *TTR*, *FN1*, *UMOD*, *MUC1*, *SALL1*(Townes-Brocks syndrome), and other genes associated to ciliopathies. Three heterozygous variants were considered as candidates: *RET:* c.C3152T:p.A1051V; *BBS2*: c.C1229G:p.T410S; *INPP5E*: c.G304T:p.D102Y, but with poor correlation to clinical criteria. All three patients and the only sister of our patient's father with no renal impairment present a variant of debated pathogenicity in *GLA* gene: c.G937T: p.D313Y, suggesting Fabry disease.

Conclusions: We report a three-generation family with CKD and bilateral multicystic dysplastic kidney with autosomal dominant transmission and non- specific associated syndromic features. MCKD and glomerulocystic kidney disease were considered, but TruSight One sequencing was not able to identify any significant variant relevant for the phenotype. Genetic analysis will continue with SNP array to detect microdeletions/microduplications and whole exome sequencing. A renal biopsy is of high importance for a better orientation in molecular analysis and diagnosis, and is going to be performed soon as the family understands now the difficulty in a correct diagnosis and further management without it.

NEPHROGENIC DIABETES INSIPIDUS –AFFECTING THREE MALES IN TWO GENERATIONS

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Introduction: Nephrogenic diabetes insipidus is a rare X linked syndrome, secondary to mutations in the gene encoding the vasopressin V2 receptor, located at position Xq28.**Aim**: To present a family with nephrogenic diabetes affecting three males in two generations. Material and method: We report the cases of a 4 month old patient, male, admitted in our hospital for growth impairment, vomiting and fever,and his 10 year old uncle, admitted at the same time for excessive fluid intake (11 liter/day). **Results**: Family history

(two generations affected; uncle's brotherdied at the age of two with severe hypernatremic dehydration), polyuria 7.8 ml/kg/h, lab work-up (plasma hyperosmolarity, hypernatremichyperchloremic alkalosis, extremely low urine density (1002), elevated ADH levels)were suggestive for nephrogenic diabetes insipidus. Treatment with hydrochlorothiazide was initiated (2mg/kg/body), with reduction in urine output (2.85 ml/kg/h), but severe consecutive alkalosis and hypokalemia in the infant. An aldosterone antagonist (spironolactone) was added, with good response. Uncle's fluid intake was reduced to 3-4 l/day, while urine outputdecreased to 3l/day. **Discussion:** Diabetes Insipidus includes a large series of disorders. Many of the known disorders are now susceptible to symptomatic treatments or specific interventions such as dietary modification, thiazides and inhibitors of prostaglandin synthesis. However, these approaches can only ameliorate the clinical phenotype. In infants, treatment is particularly difficult. It aims to avoid episodes of dehydration and obtain a normal growth curve. Unfortunatley, the parents didn't accept the diagnosis and there was no follow-up of the patient. **Conclusions:** This highlights the importance of early diagnosis of diabetes insipidus in infants with persistent hypernatremia.

Key words: nephrogenic diabetes insipidus, infant, treatment

TREATMENT FOR INDUCTION OF REMISSION IN LUPUS, WHAT TO CHOOSE?

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Introduction: We aimed to evaluate the treatment regimens efficacy for induction in systemic lupus erythematosus (SLE) patients admitted in our referral center.
Material and methods: We performed a longitudinal retrospective study on 18 patients diagnosed with SLE between 2008-2017. The inclusion criteria were a diagnosis of SLE, clinical, laboratory and treatment data available until remission or 12 months since diagnosis date for those who did not achieve remission. We evaluated all patients and determined the Systemic Lupus Erythematosus Disease Activity Index 2000(SLEDAI2K). A decrease of 4 points or more of SLEDAI2K was used to assess the presence of the remission. We also calculated the SLEDAI2K-variance as the difference between SLEDAI2K at diagnosis and at the end of induction.

Results: The median age at diagnosis was 14.08 years [12.81;15.77], with female predominance 88.88%. Corticoid (CT) only, associations CYC with CT and MM with CT was administered to 6, 10 and 2 patients, respectively. Sixteen patients achieved remission and the median induction time was 3.5months [2;6.5]. The median SLEDAI2K at baseline was 20[10;27.25]. The median SLEDAI2K-variance was 10.5[5.75;22] (see Table I). Univariate logistic regression showed no

statistically significant differences between treatment regimens and induction with a p-value of 0.73.

Conclusions: With respect to ALMS Trial, our study confirmed that choosing a treatment regimen does not influence induction. We note an improvement of SLEDAI2K when MM is associated with CT vs. when CYC is associated with CT vs. CT only for induction. We admit as limitations of the study the number of patients and that disease activity at diagnosis may bias the selection of agents to treat.

Table I. Lot characteristics depending on treatment regimen

	Total	CT	CT+CYC	CT+MM	P value
N	*18*	*6 (33.33%)*	*10 (55.55%)*	*2 (11.11%)*	-
Male	*2 (11.11%)*	*2 (33.33%)*	*0 (0%)*	*0 (0%)*	*0.105*
Age (years)	*14.08 [12.81; 15.77]*	*15.08 [13.31; 16.83]*	*13.66 [12.36; 14.83]*	*14.04 [13.33; 14.75]*	*0.468*
Baseline SLEDAI 2K	*20 [10; 27.25]*	*10 [7.7; 14.8]*	*21 [17.6; 26.4]*	*35 [20; 50]*	*0.105*
Achieving remission	*16 (88.88%)*	*6 (100%)*	*8 (80%)*	*2 (100%)*	*0.406*
Time to remission (months)	*3.5 [2; 6.5]*	*4 [2; 6.2]*	*2.5 [2; 4.6]*	*3 [2;4]*	*0.636*
SLEDAI 2K variance	*10.5 [5.75; 22]*	*6 [4.4; 11.3]*	*12 [7.6; 22]*	*23.5 [11; 36]*	*0.22*

HEPATIC MANIFESTATIONS AT THE ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS: CASE REPORT

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Introduction: Multi-organ involvement is the hallmark of systemic lupus erythematosus (SLE). Clinically significant hepatic disease is generally regarded as unusual in SLE, but many studies showed that hepatic disease may be more common in SLE that was initially thought. Hepatic disease is not a significant cause of morbidity and mortality, but subclinical liver involvement is common. We aimed to determine if whether to classify our patient as having a primary liver disease with associated autoimmune features or having liver disease as a manifestation of SLE.

Material and methods: We investigated a 14 years old boy who presented with one-year history of elevated serum aminotransferase and complaints of daily fever in the last month, polyarthralgia, swelling of the right knee, hepatosplenomegaly. Family history was negative for autoimmune or inherited liver disease, including Autoimmune hepatitis (AIH) and SLE.

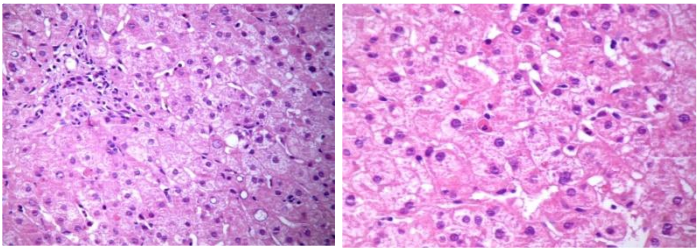
Results: SLE was confirmed by 4 clinical and 3 immunological criteria (according to SLICC Classification Criteria). Liver biopsy showed chronic hepatitis with discreet inflammatory activity, no fibrosis, no interface hepatitis, no fatty infiltration, so no specific elements were identified. Renal biopsy revealed class IIIC kidney disease.

Conclusions:

The difference between the hepatic involvement in SLE and AIH has not been clearly defined due to similarities in the clinical and biochemical features. Lupus hepatitis is a SLE-related liver dysfunction and it has been described as hypertransaminasemia owing to the fluctuations in the levels of alanine transaminase that are consistent with the activity of SLE. We consider that our patient has SLE and lupus hepatitis. Children with liver dysfunction and SLE should be investigated for Autoimmune Hepatitis (AIH) as these two entities can occur together and their complications are different. AIH may lead to end-stage liver disease, while SLE may result in end-stage renal disease. Liver biopsy might be necessary to establish the diagnostic in SLE patients with persistent increase of liver enzymes.

Images:

Hepatic biopsy



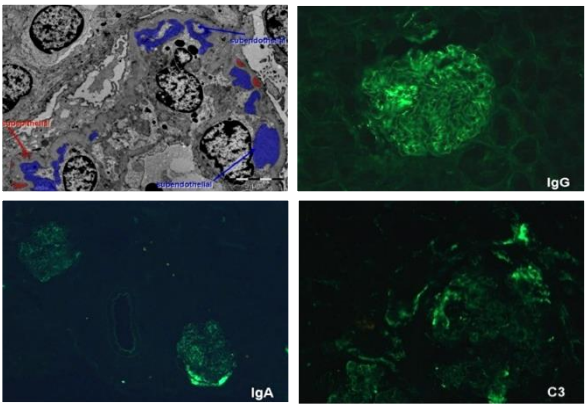
Medium-sized biopsy fragment (9mm after processing) of liver tissue with conserved lobular architecture;
3 portions of normal size, no significant inflammatory infiltration, no aspects of interface hepatitis;

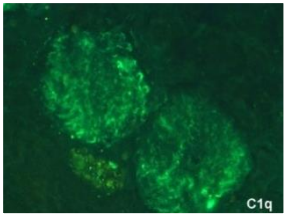
Dispersed necrosis is observed intralobular.
The peri-centrolobular area is of normal appearance;
There is no evidence of hepatic steatosis;
Perls staining (for hemosiderin) is negative.

Conclussion:

Mild lobular hepatitis without fibrosis on the examined fragment. No specificity elements are highlighted on the examined fragment, interpretation is recommended in the clinical, serological, anamnestic context (corticotherapy)

Kidney Biopsy





Three glomeruli with discrete mesangial proliferation and rare lymphocytes in the lumen. Generally permeable glomerular capillaries, some with narrow lumens due to endotheliosis.

Dense mesangial, subendothelial deposits and rare subepithelial deposits of various sizes, segmental. Rare apoptotic cells. Focal, thin MBG capillaries with disorganized architecture and ruptures. Pedicles partially deleted (<20%).

ROMANIAN CHILDREN KIDNEY REGISTRY - NATIONAL DATA REPORT

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Introduction: ESRD in children is uncommon and the reported incidence varies within Europe, being 3.6 patients per million age related population (pmarp) in Eastern Europe, 7.2 pmarp in Southern Europe and 8.1 pmarp in Northern Europe. These differences, which particularly affected younger children were related to economic factors, RRT choices in children with CKD include renal transplantation, hemodialysis and peritoneal dialysis. The choice of RRT varies particularly with age and resources
The purpose of this paper is to present the data from the ESPN/ERA-EDTA registry national report for Romania by comparing the results with 2016 data and also with the average European performance.

Methods: We estimated the incidence and prevalence of pediatric patients receiving RRT, presented as the number of patients per million age related population. We have stratified the results by age group and the treatment modality at RRT start. Country estimates for each clinical indicator (anemia, hypertension, height, overweight, hypercholesterolemia) are based on patient measurements collected

since 2007 for patients aged 0-14 years, and adjusted for the effect of age. We used funnel-plots to objectively compare the performance of Romania to the European average.

Results: The incidence of pediatric ESRD increases with age. For example, for Romania, the incidence of RRT is 3.1 pmarp in the age group 0-4 years (3 patients) , 5.7 pmarps in the age group 10-14 years (6 patients), which are all comparable to the European average. The variability in the incidence of ESRD is thought to be affected by genetic and environmental factors, the ability to diagnosis and manage children with significant renal impairment, and the threshold for when RRT is initiated.

The prevalence (number of patients receiving RRT on the 31st December 2015) stays the same in the age group 0-14 years (13.7 pmarp), compared to 2014 and is the highest in age group 10-14 years (22.8 pmarp), similar to all European countries (49.3 pmarp). Data from the Romanian Kidney Registry revealed that no patient received a pre-emptive transplant, whereas of those children who initiate RRT with dialysis and who are cared for in pediatric centers, 2.9 pmarp (9 patients) were initially prescribed HD and 0.3 pmarp (1 patient) received PD. By contrast to European countries where PD and HD were both the preferred initial choices for RRT (40% each), but also preemptive transplant occupied an important place (120 patients-19%). In Romania, as of December 31, 2016, 5% from the age group 0-14 years were transplanted vs 65% in European countries, 64% were hemodialysed vs 15% in Europe and 31 % undergone PD vs 19%. All cause mortality in the age group population 0—4 years was greater for Romania (5%) than average European mortality (1.7%).

The reports also provide insights on the performance in Romania compared to the average European performance by showing

benchmarking figures: hypertension and height in children on RRT, anemia, overweight, hypercolesterolemia. The percent of patients with height Z score <-2 was above the control limits and the mean height Z-score below control limits. Age-adjusted proportion of anemia (Hb<10 g/l) was below the control limits, age-adjusted proportion of dialysis patients with overweight was above the European average, and off the control limits. Regarding hypertension, ESA treatment the results were not statistically significant. As for hypercholesterolemia no data was provided.

Conclusion and limitations:

- The number of children starting renal replacement therapy in Romania is increasing compared to 2014 for subgroups 0-4 and 10-14 years.
- Statistics remain the same as in 2015, so worrying is that no preemptive transplantation was performed, unlike the rest of the European countries, where transplantation accounted for 19%.

- Hemodialysis was the number one choice as RRT, compared to European average, where HD and DP accounted similar percentages.
- 2 transplant centers, only one is reporting
- There is no reporting of Preemptive Tx
- Country specific mode of reporting the patients on RRT
- Sometimes, acute patients, severely ill are reported as chronic because of reimbursement protocols

We need:

- Better Nutrition
- Multidisciplinary team (with a dedicated nutritionist and psychologist in the dialysis centers)
- Better Blood Pressure control
- Better reporting to the Registry
- Directly report to ESPN Registry
- Preemptive Tx report (not reported)
- All Children Kidney Tx report (not all Tx are reported)
- Children on dialysis are reported as chronic after 7 Hemodialysis sessions (two weeks), some of them are still in the acute phase and can still recover kidney function
- Meeting with other pediatric nephrology centers from Romania and find a common way of reporting (In 2015 – there were 10 new children reported on RRT under 14. 5 of them were from the same center)
- Make internal audits
- Go to the Romanian authorities and try to make a special RRT program for children that can include also HDF (Now children and adults are in the same national program)

COMPLEMENT FACTOR H MUTATION ATYPICAL HEMOLYTIC UREMIC SYNDROME – 10 MONTH ON DIALYSIS WITH PARTIAL RECOVERY OF THE RENAL FUNCTION AFTER ECULIZUMAB THERAPY – CASE REPORT

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Introduction. Distinct genetic changes in Complement Factor H (CFH), a key regulator of the alternative pathway , are associated with atypical Hemolytic Uremic Syndrome (aHUS).

Case summary A 19 years old boy was admitted to our Hospital in July 2015 feeling sick for a couple of days, pale, hypertensive and with low urine output. Initial blood work showed decreased Haemoglobin, decreased Platelets, increased Lactic dehydrogenase (LDH), increased Urea and Creatinine, decreased Haptoglobin, decreased C3 and normal C4.

Initial diagnosis of Hemolytic Uremic Syndrome was made. He had no history of diarrhea, stool E. Coli and Shiga toxin were negative.

Treatment was started with Plasma Exchange (PEX) and Hemodialysis (HD). After a good initial response to PEX, he suffered a relapse.

Blood and serum were sent for extensive complement and genetic testing to Semmelweis University, Budapest.

The patient was found to carry several aHUS risk variation: a mutation in CFH (p.E1198Q) that is expected to have a pathogenic role in the

development of aHUS. (This mutation was not reported previously in aHUS patients or healthy individuals, but two mutations (E1198K and E1198A) affecting the same amino acid as the identified mutation were reported in aHUS patients and both mutants were shown to exhibit functional defects). He also showed two risk haplotypes: a homozygous one in CFH (H3), and a heterozygous one in MCP (MCPggaac). These variations together explain the genetic background of the alternative pathway dysregulation, hence, support the diagnosis of *complement-mediated atypical HUS*.

ECULIZUMAB treatment was started in November 2015, four months after the onset of disease.

After six months of Eculizumab therapy and ten months on hemodialysis, the kidney function recovered partially so we could stop renal replacement therapy in April 2016.

We tested C5b-9 deposits on microvascular endothelial cells (HMEC) (Instituto di Ricerca Farmacologiche MARIO Negri, Italy). The test showed normal C5b-9 deposits under Eculizumab treatment.

His kidney function is continuously improving, and now he is at an eGFR of 42 ml/min/1.73m2 (MDRD) with a creatinine of 2.23 mg/dl. He has good clinical status and well-controlled blood pressure.

He re-entered his normal social life, he finished high school and entered an economics college.

Conclusion. In many cases, the atypical Hemolytic Uremic Syndrome is caused by a sum of genetic abnormalities in the complement cascade. Late start of Eculizumab therapy could stop the progression of renal disease and the patients can partially recover the kidney function.

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