ES-PCR

since 22.06.2007

European Society of Pediatric Clinical Research
Europäische Gesellschaft für klinische pädiatrische Forschung
formaly known as Paediatric Research of Central European Countries

President : Prof. R. Urbanek
Vice-President: Prof. L.B. Zimmerhackl

25-27, JUNE 2009 VILLA BLANKA Innsbruck (Austria)

18th Meeting of ES-PCR

Contact and Info:
www.ES-PCR.jimdo.com
Claudia.Lenz@uki.at
Tel: + 43 - 512 504 23501
Fax: + 42 - 512 504 25450

ABSTRACT DEADLINE MAY 15, 2009

INNSBRUCK

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

tilak Universitätskliniken LKH Innsbruck

VILLA BLANKA CAFÉ - RESTAURANT

ÖSTERREICHISCHE GESELLSCHAFT FÜR KINDER- UND JUGENDHEILKUNDE

KINDERKLINIK INNSBRUCK PÄDIATRIE EINS

Dear friends of the 18th Meeting of European Society of Pediatric Clinical Research – ES-PCR (previously: Meeting of Paediatric Research of Central European Countries)!

This year the 18th Meeting of ES-PCR will again take place in Innsbruck, Austria. In Innsbruck we will gather together at the "Villa Blanka" above Innsbruck. The location is in a historical place overlooking the whole Inn valley.

The programme of the meeting is outstanding. You will see that Paediatric Research is at an International top level. Listen, contribute and judge for yourself.

Be reminded that our new society ES-PCR will have its second general assembly. Each participant is invited to join the society.

We will have two lectures. The invited speaker is Prof. Lukas Huber, our head of the Biocenter. He is a world reknown scientist and particularly keen in proteomics. He will talk on use of the mouse for excellent research.

Prof. Urbanek and I will touch the problem of Pediatric studies. Academic and pharmaceutical studies in Pediatrics are usually multicentric und multinational. We will discuss if ES-PCR can provide a platform for such studies.

Our banquet will be again in the "Weiherburg" and members of the student orchestra will accompagny our evening.

The mayor of Innsbruck ***Hilde Zach*** is again actively supporting our meeting as patroness.

Welcome to Innsbruck!

Lothar Bernd Zimmerhackl
Vice-President of ES-PCR

Radvan Urbanek
President ES-PCR

(Fotonachweis: Martin Vandory, Innsbruck)

Under the auspices of
Hilde Zach, Mayor of Innsbruck, Austria

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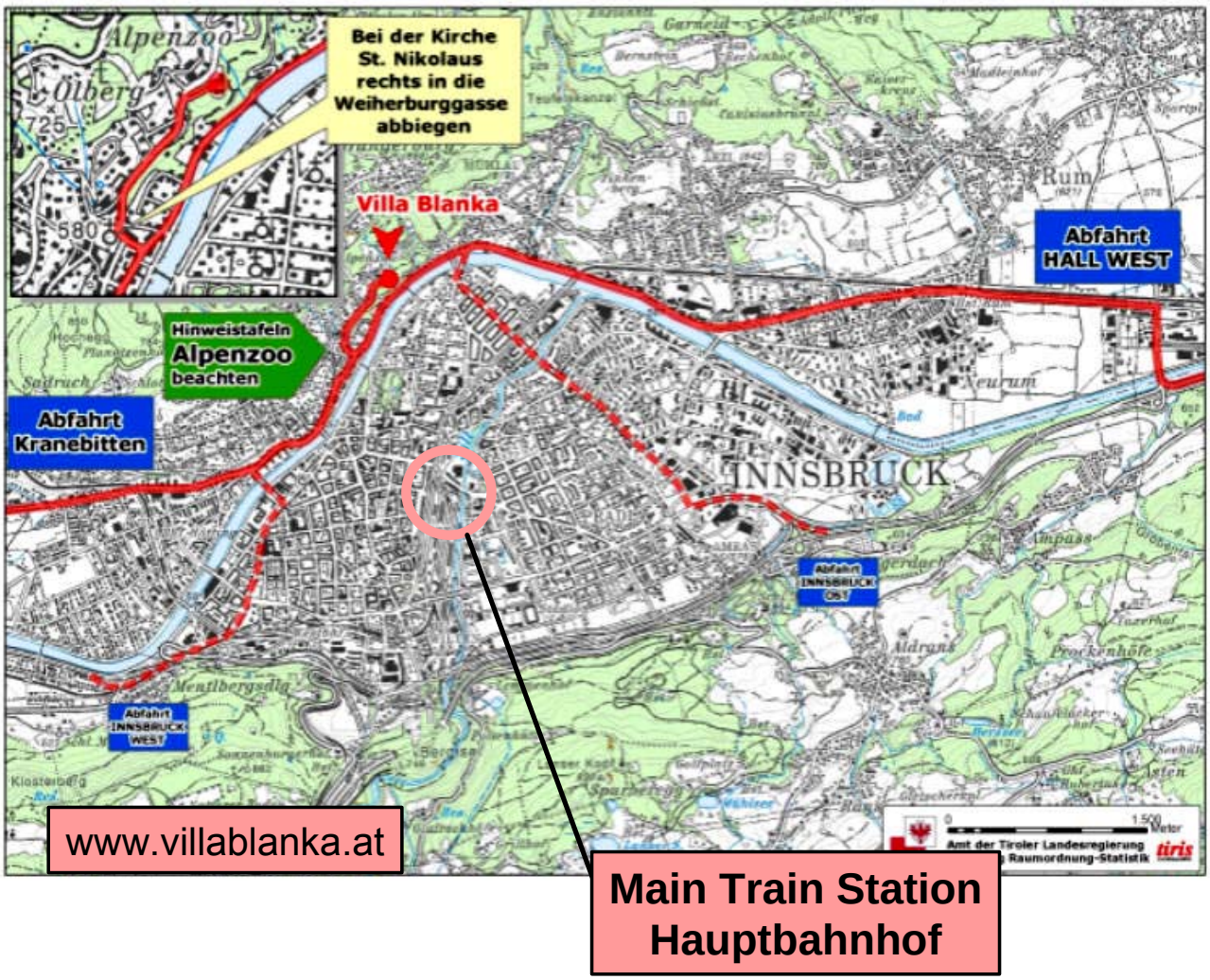
ARRIVAL



Villa Blanka
Weiherburggasse 21, 6020 Innsbruck
Tel: +43-512-292413, Fax: +43-512-292413-11

3rd WORKSHOP:
LABORATORY METHODS IN PEDIATRIC RESEARCH
Thursday, June 25, 2009

Outline of the workshop

The workshop provides insight in currently used techniques in pediatric research. After the successful workshop in 2007 and 2008, we will focus this year again on advanced staining techniques in FACS analysis. The first half of the workshop will be dedicated to practical aspects of FACS analysis. We are going to demonstrate 4- to 5-colour staining techniques. The second half of the workshop gives you detailed information in techniques to investigate apoptosis.

What can you learn: New ELISA applications

We are going to give you a view on a new ELISA application to test antibody avidity, useful in evaluation of humoral immunity against various viral infections.

What can you learn: FACS

The workshop shows you how to plan an experiment with FACS and how to arrange the colours. Together with our laboratory team you will perform and interpret a 4-colour staining FACS analysis for detection of apoptosis and cell proliferation.

What can you learn: Apoptosis assays

Assays for investigation of apoptosis are important tools to analyze programmed cell death on cells and tissues and is necessary for answering of many research questions. The workshop shows you a detailed view into apoptosis assays and provides practical approaches.

Organization and Information:

PD Dr. Martina Prelog (e-mail: Martina.Prelog@i-med.ac.at)

PROGRAM Thursday, June 25, 2009
3rd Workshop

08:00 - 08:45 Registration (Secretary Lenz)

09:00 – 09:15 Introduction (Zimmerhackl)
Location: Seminar room Tyrolean Cancer Research Institute, Innrain 66, ground floor

09:15 – 10:00 Theoretical background "Apoptosis" by Labi, Manzl
Location: Seminar room Tyrolean Cancer Research Institute

10:05 - 12:15 Wet workshop: **Apoptosis detection with FACS and TUNEL**
Group A: FACS - practical instruction by Labi, Manzl, Zlamy, Jeller
Group B: TUNEL – practical instruction by Mayerl, Prelog
Location: Pediatric Research Laboratory (4th floor)
& FACS room (3rd floor)

12:15 – 13:15 **Lunch**
Location: Hospital Mensa

13:30 – 15:30 → Wet workshop: **Apoptosis detection with FACS and TUNEL**
Group A: FACS - practical instruction by Labi, Manzl, Zlamy, Jeller
Group B: TUNEL – practical instruction by Mayerl, Prelog
Location: Pediatric Research Laboratory (4th floor)
& FACS room (3rd floor)

15:30 – 17:00 **→ Antibody avidity**
Location: Seminar room Tyrolean Cancer Research Institute, Innrain 66, ground floor and Pediatric Research Laboratory (4th floor)

- Theoretical background (Prelog)
- Practical demonstration (Jeller, Zlamy)

17:00 Conclusion – Questions (Prelog) and distribution of certificate

Coffee breaks will be held spontaneously during incubation times!

Additionally a guided tour through our new Children's Hospital Building is offered!

Lecturers:
PD Dr. Martina Prelog (Pediatrics I)
Dr. Manuela Zlamy (Pediatrics I)
Mag. Verena Jeller (Pediatrics I)
Mag. Christina Mayerl, BMA (Biocenter)
Dr. Claudia Manzl (Division of Developmental Immunology)
Dr. Verena Labi (Division of Developmental Immunology)

Fee: 100 € (after April 30, 2009), 80 € (before April 30, 2009), (40 € for students)

Registration dead line: May 15th, 2009

The fee of the seminar include all breaks, lunch and non-alcoholic beverages.

Hotel Accommodation in the Villa Blanka for Euro 30 per night (student housing)

Registration: Claudia Lenz claudia.lenz@uki.at
☎ +43-512-504-23501
🖷 +43-512-504-25450
Department of Pediatrics
Anichstraße 35, A-6020 Innsbruck

Meeting point: Research laboratories Medical University Innsbruck
Seminar room Tyrolean Cancer Research Institute,
Innrain 66, ground floor
Innsbruck

This workshop is supported by (as of May 31, 2009):

PROGRAM 18th Meeting

Thursday, June 25, 2009

16.00–19.00 Registration Villa Blanka

Friday, June 26, 2009

07.00 – 08.00 Registration Villa Blanka

Chair: Podracka/Zimmerhackl

08.15 Welcome
Zimmerhackl

08.30 WHAT ARE THE WAYS TO EXCELLENCE IN PEDIATRICS: ES-PCR AS BASIS FOR COOPERATIVE STUDIES?
Urbanek/Zimmerhackl

09.00 DELAYED ANTIBODY RESPONSE TO TICK-BORNE ENCEPHALITIS VIRUS VACCINATION IN CHILDREN AFTER THYMECTOMY
Zlamy

09.15 CHARACTERISATION OF REGULATORY T CELLS,NATURAL KILLER CELLS, AND OTHER LYMPHOCYTE SUBPOPULATIONS IN NEWLY DIAGNOSED PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE
Molnar

09.30 – 10.00 COFFEE BREAK

Chair: Hrstkova/Urbanek

10.00 INCREASED HEAT SHOCK PROTEIN 72 EXPRESSION IN COELIAC CHILDREN
Gál

10.15 HAEMATOCHESIA : ALLERGIC BOWEL INFLAMMATION IN INFANTS?
Szalay

10.30 PHENOTYPING OF LYMPHOCYTES AND COMPLEMENT SYSTEM ANALYSIS OF CHILDREN AND ADOLESCENTS WITH LUPUS NEPHRITIS
Riedl

10.45 IMMUNOSENESCENCE IN CHILDREN WITH TYPE 1 DIABETES MELLITUS
Hofer

11.00 CYTOKINES IN BREAST MILK RECEIVED BY INFANTS WITH EOSINOPHILIC COLITIS
Durilova

11.15 BRAIN NATRIURETIC PEPTIDE AS POSSIBLE MARKER OF ABNORMAL HEART GEOMETRY IN CHILDREN WITH CHRONIC KIDNEY DISEASE
Hedvig

11.30 URETERIC JET DOPPLER WAVEFORM: IS IT A RELIABLE PREDICTOR OF VESICOURETERIC REFLUX IN CHILDREN?
Kljucevsek

11.45 DELETIONS OF THE FACTOR H RELATED PROTEIN 1/3 GENES AND FREQUENCY OF FACTOR H AUTO ANTIBODIES: ROLE FOR PATHOGENESIS OF ATYPICAL HEMOLYTIC UREMIC SYNDROME?
Rosales

12.00 – 13.30 LUNCH

Chair: G. Kovacs/Weber

13.30 SUCCESSFUL RENAL TRANSPLANT IN A 10 YEAR OLD BOY WITH FACTOR H MUTATION USING ECULIZUMAB®
Jungraithmayr

13.45 RARE CASE OF RESPONSIVNESS TO CYCLOSPORINE IN AUTOSOMAL RECESSIVE SRNS
Malina

14.00 MAILLARD REACTION PRODUCTS IN DIET OF 6 MONTH-OLD INFANTS: SKIN AUTOFLUORESCENCE AND BIOLOGICAL EFFECTS
Klenovicsova

14.15 NEW PHARMACOKINETIC DATA OF METHOTREXATE IN CHILDHOOD LEUKEMIA
Csordas

14.30 THE CLINICAL SPECTRUM OF METAPHYSEAL ANADYSPLASIA IS DETERMINED BY MUTATIONS IN *MMP9* AND *MMP13*
Lausch

14.45 THE RELATIONSHIP BETWEEN AMBULATORY BLOOD PRESSURE MONITORING AND CARDIOVASCULAR PARAMETERS AFTER ANTHRACYCLINE THERAPY
Stastna

15.00 – 15.30 COFFEE BREAK

Chair: L. Kovacs/Würzner

15.30 PANCREAS: A QUANTITATIVE ANALYSIS OF THE SENSORY AND SYMPATHETIC INNERVATION
Hager

15.45 DEHYDROEPIANDROSTERONE (DHEA) AND CASTRATION IMPROVES KIDNEY FUNCTION FOLLOWING ISCHEMIA/REPERFUSION (IR) INJURY: ROLE OF NA/K ATPASE (NKA) AND HSP72
Banki

16.00 CONTINUOUS GLUCOSE MONITORING SYSTEM (CGMS) AFTER KIDNEY TRANSPLANTATION IN CHILDHOOD
Pasti

16.15 THE CLINICAL IMPORTANCE OF THE N363S GLUCOCORTICOID RECEPTOR POLYMORPHISM IN THE PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY
Eipel

Chair: Tulassay/Urbanek

16.30 Invited Lecture:
MOUSE, MODELS FOR INVESTIGATION FOR PEDIATRIC DISEASE
Huber

17.15 Conclusion
Urbanek

17.30 – 18.15 *2nd General Assembly of ES-PCR*

19.30 Reception at the historic "Weiherburg" (close to conference site)

Music: "Trio of student orchestra"

Best presentation Award sponsored by milupa

International Scientific Advisory Board

Helmut Gadner, Wien
Gerhard Gaedicke, Berlin
Manfred Gahr, Dresden
Alojz Gregoric, Maribor
Georg Hoffmann, Heidelberg
Hana Hrstková, Brno
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Gabor Kovacs, Budapest
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Felix Sennhauser, Zürich
Tivadar Tulassay, Budapest
Radvan Urbanek, Freiburg
Lothar B. Zimmerhackl, Innsbruck

ABSTRACT COMMITTEE (best presentation award)

Radvan Urbanek, Freiburg
Ludmila Podracka, Kosice
Lothar Bernd Zimmerhackl, Innsbruck

REFERENT LIST

Dr. Nóra Fanni Bánki
1st Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

cand.med. Katalin Csordás
2nd Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Dr. Marianna Durilova
2nd Faculty of Medicine, Charles University, Prague, Czech Republic

cand.med. Olivér Tamás Eipel
2nd Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Dr. Krisztina Gál
1st Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Dr. Thomas Hager
Institute of Pathology, Medical University Innsbruck, Austria

Dr. Juraj Hedvig
1st Dept. of Pediatrics, Medical Faculty UPJS, Kosice, Slovakia

Dr. Johannes Hofer
Univ.-Klinik für Pädiatrie I, Medical University Innsbruck, Austria

Univ.-Prof. Dr. Hana Hrstková
1st Dept. of Pediatrics, Faculty of Medicine, Brno, Czech Republic

Univ.-Prof. Dr. Lukas Huber
Biocenter, Division of Cell Biology, Medical University Innsbruck, Austria

Dr. Therese Jungraithmayr
Univ.-Klinik für Pädiatrie I, Medical University Innsbruck, Austria

Dr. Kristína Klenovicsova
2nd Dept. of Pediatrics, Comenius University, Bratislava, Slovakia

Dr. Damjana Kljucevsek
Children's Hospital, University Medical Centre, Ljubljana, Slovenia

Univ.-Prof. Dr. Gábor Kovács
2nd Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Univ.-Prof. Dr. Laszlo Kovács
2nd Dept. of Pediatrics, Comenius University, Bratislava, Slovakia

Dr. Ekkehart Lausch
Zentrum für Kinderheilkunde und Jugendmedizin, Univ.-Klinik Freiburg, Germany

Dr. Michal Malina
2nd Faculty of Medicine, Charles University, Prague, Czech Republic

cand.med. Kriszta Molnár
1st Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Dr. Krisztina Pásti
1st Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Univ.-Prof. Dr. Ludmila Podracká
Dept. of Pediatric, Medical School Safarik, Kosice, Slovakia

cand.med. Magdalena Riedl
Univ.-Klinik für Pädiatrie I, Medical University Innsbruck, Austria

Dr. Alejsandra Rosales
Univ.-Klinik für Pädiatrie I, Medical University Innsbruck, Austria

Dr. Jana Stastna
1st Dept. of Pediatrics, Faculty of Medicine, Brno, Czech Republic

Dr. Balázs Szalay
1st Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Univ.-Prof. Dr. Radvan Urbanek
Emeritus, Chairman of Pediatrics, Medical University Vienna, Austria

Univ.-Prof. Dr. Tivadar Tulassay
1st Dept. of Pediatrics, Semmelweis University Budapest, Hungary

PD Dr. Lutz Weber
Dr. von Haunersches Kinderspital, Munich, Germany

Univ.-Prof. DDr. Reinhard Würzner
Dept. of Microbiology, Medical University Innsbruck, Austria

Univ.-Prof. Dr. Lothar Bernd Zimmerhackl
Univ.-Klinik für Pädiatrie I, Medical University Innsbruck, Austria

Dr. Manuela Zlamy
Univ.-Klinik für Pädiatrie I, Medical University Innsbruck, Austria

ABSTRACTS

DEHYDROEPIANDROSTERONE (DHEA) AND CASTRATION IMPROVES KIDNEY FUNCTION FOLLOWING ISCHEMIA/REPERFUSION (IR) INJURY: ROLE OF NA/K ATPASE (NKA) AND HSP72

Bánki NF[1], Prókai Á[1], Rusai K[1], Vannay Á[1], Müller V[2], Vér Á[3], Wagner L[4], Szabó AJ[1], Fekete A[1]// [1]1st Dept Pediatrics, [2]Dept Pulmonology, [3]Dept of Medical Chemistry, Molecularbiology and Pathobiochemistry, Semmelweis University, Budapest, [4]2nd Dept. Medicine, University of Pecs, Hungary

BACKGROUND: DHEA pretreatment diminishes IR injury. Renal IR injury impairs the function of NKA and decreases HSP72 expression in male vs female rats. Here we tested the effect of DHEA pretreatment and gonadectomy on IR survival, renal damage and expression of NKA and HSP72.
METHODS: Rats treated with DHEA (4mg/kg/d, 7d) (G_{DHEA}), castrated (G_{Cast}) and control (G_C) male Wistar rats had left renal pedicle clamped for 55 min. followed by 2h or 24h of reperfusion and compared to shams (n=6/group). We measured renal function, histology, mRNA expression and protein level of NKA and HSP72, as well as localization. Additional groups were followed for 7d-survival.
RESULTS: DHEA treatment and castration were associated with better post-ischemic survival at 7d. Renal function and histology was less impaired in G_{DHEA} and G_{Cast} vs. G_C at 2h and 24h. Post-ischemic changes in mRNA and protein levels showed the same pattern in all groups vs. shams (NKA: acute decrease at 2h followed by an increase at 24h; HSP72: progressive increase at 2h and 24h). Moreover both NKA and HSP72 levels were higher in G_{DHEA} and G_{Cast} vs. G_C. Translocation of NKA from the membrane was less pronounced in G_{DHEA} and $G_{Cast,,}$ and NKA was co-localized with HSP72 in these groups.
CONCLUSIONS: DHEA treatment and castration improves survival and is protective against post-ischemic renal damage. Increased NKA and HSP72 expression as well as diminished translocation may contribute to better kidney function. All these effects may be attributed to the absence (castration) or ”inactivation” (DHEA treatment) of testosterone rather than the absence of estrogens.
This work was supported by OTKA F048842-68638 Semmelweis and Magyary grants.

NEW PHARMACOKINETIC DATA OF METHOTREXATE IN CHILDHOOD LEUKEMIA

K. Csordas, MZ Hegyi, M. Csoka, *E. Pap, *J. Kralovanszky, GT. Kovacs//2nd Dep. of Pediatrics, Semmelweis University and *National Institute of Oncology, Budapest

Methotrexat (MTX) is a widely used anticancer agent in childhood malignancies, however the exact dose and mode of application is not clearly defined.
The aim of our study was to analyse the pharmacokinetic parameters and toxicity of HD-MTX treatments in children with acute lymphoblastic leukemia (ALL) at the 2nd Department of Paediatrics at Semmelweis University between 1998-2006.
Patients, methods: 43 children were treated with 5 g/m2/24 h MTX and 39 children with 2 g/m2/24 h MTX according to the ALL BFM-1995 and 2002 protocol. The mean age of the patients was 7.1 years (0.5-16.7). Totally 283 MTX infusions were analysed. Serum MTX and 7-OH-MTX levels were measured with HPLC at 24, 36, 48 hours, while the liquor MTX concentration was determined at 24 hours after the start of MTX infusion. Considering the toxicity of the treatments we measured the serum GPT, GGT, bilirubin, creatinine, protein levels before therapy and one day, two days and one week after treatment.
Results: Mean MTX level at 24. hours and 7-OH-MTX level at 36. hours was significantly lower after 2 g/m2 courses than after 5 g/m2 courses (MTX2: 29.7+/-17.4 µmol/l; MTX5: 89.5+/-55.0 µmol/l; 7-OH-MTX: 4.1+/-1.7 µmol/l and 7.6+/-5.2 µmol/l; $p<0.05$). In more than 50% of the cases with 2 g/m2 MTX serum levels were below 30 µmol/l (therapeutic level by american researchers). Comparing liquor MTX concentrations we did not find significant difference between the two doses (after 2g/m2: 15.1+/-41.7 µmol/l; after 5g/m2: 23.3+/-41.5 µmol/l). In children who received 5 g/m2 MTX significantly more cases of hepatotoxicity, trombocytopenia, mucositis occurred, however these side effects were mild and reversible. 7-OH-MTX levels showed closer correlation with the toxicity parameters than MTX ($p=0.0004$).
Conclusion: With 5 g/m2 MTX we could reach more reliable therapeutic serum levels with slightly more toxicity. 7-OH-MTX measurements might be more useful than MTX levels to detect toxicity. However, further randomised studies are necessary to determine the optimal dose of MTX.

CYTOKINES IN BREAST MILK RECEIVED BY INFANTS WITH EOSINOPHILIC COLITIS

Durilova M., Tesarova-Flajsmanova K., Stechova K., Stavikova V., Ulmannova T., Nevoral J. *Dpt. of Paediatrics, 2nd Faculty of Medicine, Charles University in Prague, Czech Republic*

Aim: Aim of the presented study was to analyze breast milk composition of cytokines received by infants diagnosed with eosinophilic colitis (EC) and compare it to composition of breast milk received by healthy infants. **Methods**: Breast milk samples were collected from mothers of infants diagnosed with EC (n=20) at time of examination at Dpt. of Paediatrics (at the infant's age of 16.8 weeks average (min-max 2-27 weeks) and from mothers of healthy infants (n=20) with negative history of allergy at the infant's age of 12 weeks. Commercial ELISA kits were used for detection of the following cytokines, chemokines and growth factors: interleukin (IL)-4, IL-6, IL-10, IL-17, IL-18, IL-23, interferon-gamma (IFN-gamma), transforming growth factor 1 (TGF-beta1), epidermal growth factor (EGF) and eotaxin. Statistical analysis was performed with SPSS programme, differences between groups were analyzed by Mann-Whitney U test and probability level $p<0.05$ was considered to be statistically significant. **Results:** Significant difference was seen in concentration of IFN-gamma (Th1 cytokine), which was higher ($p<0.001$) in breast milk received by infants with EC in comparison with healthy infants. On the other hand, breast milk received by healthy infants contained significantly higher levels of IL-18 (Th1-inducing) ($p=0.001$), but at the same time it contained higher levels of regulatory TGF-beta1 compared to infants with EC, although the difference was not significant for the latter ($p=0.07$).
Conclusion: Cytokines present in breast milk may influence the developing immune system of the breast-fed infants. Inter-individual differences in their composition are known, as well as the fact that it depends on many factors including mother’s atopy status. In the present study we found Th1 or Th1-inducing cytokines in breast milk received by infants with EC and healthy infants, but in the group of healthy infants, regulatory cytokine TGF-beta1 was also present in the breast milk. TGF-beta1 is considered to have a protective effect from development of allergic diseases. The results of this preliminary study show rather risk pattern of cytokine composition in breast milk of mothers whose infants present with eosinophilic colitis, but the results need to be confirmed on larger groups.

Supported by grant IGA MZ CR NR 8310-5.

THE CLINICAL IMPORTANCE OF THE N363S GLUCOCORTICOID RECEPTOR POLYMORPHISM IN THE PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY

OT Eipel, K Nemeth, D Török, DJ Erdélyi, M Csoka, GT Kovács

2nd 2nd Department of Paediatrics, Faculty of Medicine, Semmelweis University, Budapest

Introduction: According to the published data the role of the polymorphisms of the glucocorticoid receptors is ambiguous regarding the efficiency and toxicity of the therapy. Present study investigated the relationship between the N363S glucocorticoid receptor polymorphism and acute toxicity of the chemotherapy in children with acute lymphoblastic leukemia (ALL).
Patients and methods: 188 pediatric ALL patients were involved in this research. These children were screened for N363S polymorphism. After their DNA was isolated from the peripheral blood lymphocytes, the polymorphism was identified by allele-specific PCR. Main toxicities of carriers and non-carriers were analyzed and compared retrospectively.
Results: 32 of these patients were heterozygotic carriers (17%) and 156 were non-carriers. There was a significant difference in hepatotoxicity and glucose intolerance between the two groups. Among the carriers the frequency of hepatotoxicity (37,5 % vs 20 %, p=0,015) and glucose intolerance (15,6 vs 2,6 %, p=0,002) was significantly higher than in the case of non-carriers. The frequency neither of pancreatitis nor of hypertonia showed statistical association with the polymorphism. Surprisingly encephalopathy occurred more often in non carriers (25,8 vs 6,4 %, p=0,04).
Discussion: The genetic variants of glucocorticoid receptors may influence the severity of toxicity during the chemotherapy. Our results raise the prospective opportunity of an individual dosing of chemotherapeutic drugs.

INCREASED HEAT SHOCK PROTEIN 72 EXPRESSION IN COELIAC CHILDREN

Krisztina Gál[1], Beáta Szebeni[2], Erna Sziksz[1], Ágnes Prókai[1]; Áron Cseh[1], Ádám Vannay[1], Gábor Veres[1], Antal Dezsőfi[1], Anna Ónódy[1], IR Korponay-Szabó[3], Veronika Müller[4], András Szabó[1], Tivadar Tulassay[1,2], András Arató[1]

[1]First Department of Pediatrics, Semmelweis University, Budapest, Hungary, [2]Research Group for Pediatrics and Nephrology, Semmelweis University and Hungarian Academy of Sciences, Budapest, Hungary; [3]Department of Gastroenterology-Nephrology, Heim Pal Children's Hospital, Budapest, Hungary; [4]Department of Pulmonology, Semmelweis University, Budapest, Hungary

Aim: Heat shock protein (HSP) 72 can be released from cells during the response to stress and injury. Extracellular HSP72 activates monocytes, macrophages and dendritic cells and upregulates the expression of proinflammatory cytokines by binding Toll-like receptor (TLR) 2 and TLR4. Recently we have found higher TLR2 and TLR4 protein levels in the duodenal mucosa of children with untreated coeliac disease (CD) and children with treated CD compared to controls. Since the role of HSP72 in CD is unknown, our aim was to characterise the expression of HSP72 in duodenal biopsy samples taken from children with CD and from controls.

Methods: Duodenal biopsy specimens were collected from 16 children with untreated CD [median age (range): 6.7 (3.7-13.9)], 9 children with treated CD [median age (range): 6.7 (4.9-12.7)] and 10 controls [median age (range): 8 (1.7-13)]. The mRNA expression of HSP72 was determined by real-time reverse transcription- polymerase chain reaction (RT-PCR), HSP72 protein levels were determined by Western blot. HSP72 localization was examined by immunofluorescent staining.

Results: We found higher HSP72 mRNA and protein levels in the duodenal mucosa of children with untreated CD as well as children with treated CD compared to controls ($p<0.05$). In the duodenal mucosa of children with treated CD, HSP72 mRNA expression was decreased and HSP72 protein levels were lower than in children with untreated CD ($p<0.05$). HSP72 staining intensity was stronger in duodenal villous enterocytes and in the immune cells of the lamina propria of children with untreated CD compared to treated CD.

Conclusion: Our results of increased expression of HSP72 in untreated CD and decreased expression in treated CD suggest that this heat shock protein should mediate cellular protection against gliadin induced cytotoxicity. HSP72 may act as a „danger signal" via TLR2 and TLR4 to the innate immune system, so the distressed cells can warn neighboring cells of potential injury.

PANCREAS: A QUANTITATIVE ANALYSIS OF THE SENSORY AND SYMPATHETIC INNERVATION

Thomas Hager[1], Helga Fritsch[2], Joseph Hager[3], Consolato Sergi[1]

[1]Institute of Pathology,[2]Division of Clinical Functional Anatomy, Dept. of Anatomy

[3]Dept. of Pediatric Surgery / Medical University Innsbruck, Austria

Aims and Backgrounds: The delineation of pancreatic nerve innervation during fetal life may aid to understand postnatal pancreatic pain modalities.
Materials and Methods: To define the peripheral sensory and sympathetic fibers involved in transmitting and modulating pancreatic pain, immunohistochemical analysis was performed to examine the sensory and sympathetic innervation of the head, body and tail of normal human fetal pancreas using tissue samples from 15 fetuses (13-36 weeks of gestation) following intrauterine death or legal interruption of pregnancy. Myelinated sensory fibers were marked with an antibody raised against neurofilament (NF) and post-ganglionic sympathetic fibers were labeled with an antibody raised against tyrosine hydroxylase (TH). Choline acetylase (ChAT) at cholinergic synapses was marked with a conventional antibody.
Results: NF, TH, and ChAT reactive fibers were present in parenchyma of the head, body and tail of the pancreas at changing density, but the relative density of both NF and ChAT expressing fibers seemed to be increasing from tail to head, whereas for TH, an almost homogeneous distribution was noticed. In addition to this set of sensory and sympathetic nerve fibers that terminate in the pancreas, there were large bundles of bypassing nerve fibers in the dorsal region of the pancreas associated with the superior mesenteric plexus.
Conclusion: This on hand data suggests that the pancreas receives a significant sensory and sympathetic innervation during fetal life. Understanding the factors and disease states that may alter the distribution of nerve structures can be of significance for developing therapies in pancreatic disorders of child and adulthood.

BRAIN NATRIURETIC PEPTIDE AS POSSIBLE MARKER OF ABNORMAL HEART GEOMETRY IN CHILDREN WITH CHRONIC KIDNEY DISEASE

J. Hedvig[1], Ľ. Podracká[1], D. Potočeková[2]

[1]I. Dept. Paediat., Medical faculty UPJS and DFN,

[2] Institute of Informatics, Medical faculty UPJS, Košice, Slovak Republic

The aim of the study: Cardiovascular diseases are the leading cause of morbidity/mortality in children with chronic kidney disease. Recent studies have shown that brain natriuretic peptide is a suitable cardiac marker for stratification of cardiovascular risk in adults. It remains yet to be established whether brain natriuretic peptide has the same diagnostic potential in children with chronic kidney disease. The aim of the study was to establish whether brain natriuretic peptide might predict cardiac dysfunction in children with chronic kidney disease.
Methods: The relation between serum level of brain natriuretic peptide, echocardiography and cardiovascular risk factors (hypertension, anemia, lipids, C-reactive protein, secondary hyperparathyreoidism) were investigated in 46 children (10 predialysis patients, 14 on dialysis, 11 children with kidney transplants and 11 healthy controls).
Results: Brain natriuretic peptide (log of BNP) was significantly higher in dialysis patients compared to healthy children (2.09±0.78 vs. 1.43±0.34, p=0.012)[1] and both, patients in pre-dialysis stage (2.09±0.78 vs. 1.52±0.42, p=0.039) and after kidney transplant (2.09±0.78 vs. 1.71±0.46, p=0.19). An abnormal heart geometry was found in 19 patients (54.28%). Compared to the control, higher levels of brain natriuretic peptide were seen in children with excentric hypertrophy than in children with concentric hypertrophy (2.178±0.956 vs. 1.496±0.395, p=0.05, or 1.982±0.618 vs. 1.496±0.395, p=0.04). A significant correlation was observed between brain natriuretic peptide and ventricular hypertrophy (p=0,00l) as well as intact parathyroid hormone (p=0,03) and anemia (p=0,027).
Conclusions: Brain natriuretic peptide might predict an abnormal geometry in children with chronic kidney disease. Our preliminary results suggest that it is a suitable marker of cardiovascular stratification in pediatric CKD population.

IMMUNOSENESCENCE IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

Hofer J[1]., Hofer S[1]., Zimmerhack L. B.[1], Koppelstätter C.[2], Brandstätter A.[3], Kern H.[4], Koehle J.[1], Prelog M.[1]

[1] Medical University Innsbruck, Department of Pediatrics I

[2] Medical University Innsbruck, Department of Internal Medicine

[3] Medical University Innsbruck, Department of Medical Genetics, Molecular and Clinical Pharmacology, Division of Genetic Epidemiology

[4] Medical University Innsbruck, Department of Pediatrics III

Aim: T1DM results from a cellular mediated autoimmune destruction of the pancreatic β-cells and is considered primarily a T-cell mediated autoimmune disease. Premature ageing, associated thymic involution and compensatory autoproliferation could play an important role in the pathogenesis of autoimmunity. To evaluate whether patients with T1DM demonstrate premature immunosenescence, three indicators of ageing were measured for 38 T1DM patients compared to 37 age-matched controls (HC): (1) the amount of peripheral blood naive T-cells; (2) the frequency of T cell receptor excision circles (TRECs) in naive T-cells; (3) telomeric erosion as estimate of replicative history and proliferation
Methods: We measured concentrations of different peripheral blood mononuclear cells by FACS analyses and performed DNA isolation from CD4+ and CD8+ naive T-cells (CD45RA+ T-cells) to determine the TREC amounts and RTL by real-time PCR.
Resullts: For children with T1DM, TRECs were increased in CD4+ and CD8+ naive T-cells and RTLs were higher than for HC. Nevertheless, CD4+CD45RA+ naive T-cells were significantly lower for T1DM, whereas CD4+CD45RO+ memory T-cell levels were increased. Our findings are unique for children with T1DM and pose some questions. Most likely, our findings reflect the result of increased thymic output provoked by T1DM-specific factors, predominantly insulin therapy, and a decreased proliferation rate leading to a lower number of naive T-cells, which, at the same time, are of a more recent origin, as expressed by a high RTL value.
Concludion: Our data suggests that diabetes-specific factors like insulin therapy interfere with autoimmunity-linked premature immunosenescence to generate a T1DM-specific immune milieu. It seems conceivable that, insulin therapy has a clear impact on thymus output and thereby remodels effects of premature immunosenescence. It is possible that, for older T1DM patients, the effects of premature immunosenescence prevail.

SUCCESSFUL RENAL TRANSPLANTATION IN A 10 YEAR OLD BOY WITH FACTOR H ASSOCIATED ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) WITH PLASMAPHERESIS AND ECULIZUMAB

Therese C. Jungraithmayr[1], Johannes Hofer[1], Walter Mark[1], Reinhard Würzner[1], Franz Schäfer[3], Kay O. Kliche[2], Lothar B. Zimmerhackl[1#]

[1]Medical University Innsbruck, Tirol, Austria; [2]Alexion Pharma Germany GmbH, Munich, Germany; [3]Pediatric Nephrology, Ruprecht-Karls-University, Heidelberg, Germany

Purpose: Patients with aHUS and mutations in factor H have a high risk for recurrence after renal transplantation. Here we report for the first time a successful treatment with the C5 antibody Eculizumab after transplantation in a child.

Method: Complement was determined in serum as C3 and C4 level and by concentration of C5b-9 before and after activation with Zymosan (Elisa).

Results: A now 10 year old boy with onset of the disease at age 4years with a heterozygous mutation of factor H (W1183C) received a renal transplant. After the initial episode with hemolytic anemia (Hb 4,5, LDH 2,800 U/l), low platelets (16,000) and renal failure he received dialysis and plasm therapy. Despite continuous weekle plasma exchange (PE) his renal function declined with time. In November 2008 he received a cadaver kidney from a 15 year old donor with immediate function. Immunosuppression consisted of prenisone, mycophenolate mofetil and tacrolimus. Before and after transplantation he received daily PE. In between the session platelets decreased and complement C3 remained low. At day 10 after transplantation he received Eculizumab 600 mg i.v. in NaCl 0,9% over 2 hours. The infusion was repeated on postoperative day 18. C3 and thrombocytes normalized and no PE was performed after infusion. Eculizumab is a humanized monoclonal antibody against C5 which inhibits formation of C5b-9 marketed as Soliris for paroxysmal nocturnal hemoglobinuria. 6 months after transplantation the boys renal function is excellent an no signs of hemolysis or complement activation as measured by C3 and C5b-9 are present.

Conclusion: Eculizumab normalized activated complement after renal transplantation and a successful transplantation of this high risk patient could be achieved. Eculizumab is a promising new drug for treatment of atypical HUS. www.hemolytic-uremic-syncrome.org

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MAILLARD REACTION PRODUCTS IN DIET OF 6 MONTH-OLD INFANTS: SKIN AUTOFLUORESCENCE AND BIOLOGICAL EFFECTS

Klenovicsová K[1,2], Boor P[1], Saavedra G[3], Zumpe C[3], Somoza V[4], Birlouez-Aragon I[3], Šebeková K[1], Kovács L[2]
[1]Slovak Medical University, Bratislava, [2]2nd Pediatric Department of Children's Faculty Hospital and Comenius University, Bratislava, Slovakia; [3]Polytechnic Institute LaSalle Beauvais, Beauvais, France; [4]German Institute for Food Chemistry, Garching, Germany

Introduction: Maillard reaction products (MRP) originate in highly thermally processed (e.g. fritted, grilled) foods. Excessive intake of dietary MRP is associated with body weight gain, diabetogenic and nephrotoxic effects, increase of oxidative stress and inflammatory markers, both in adult humans and animals. Infant formulas are heat-sterilized during their industrial processing which results in 70-fold higher concentration of carboxymethyllysine (CML, a widely used MRP) compared to mother milk. Consequently, infant formula-fed (FF) infants have higher plasma CML and urinary CML excretion than breastfed (BF) infants.
Aim: Here we examined whether a) MRP absorbed from infant formulas might accumulate *in vivo* on tissue (skin) proteins and b) the different diet (BF versus FF) of infants is associated with similar biological effects as mentioned above.
Methods: We measured skin autofluorescence (indicator of MRP accumulation) non-invasively using the AGE Reader (loaned by DiagnOptics Technologies B.V., Groningen, The Netherlands) in 1-29 month-old BF (n=44) vs. FF (n=35) children. In the second part of study we compared 45 BF and 51 FF infants (mean age: 6.1±0.8 vs. 5.9±0.9 months) in biochemical parameters measured by routine biochemistry, ELISA and RIA methods in plasma and urine samples.
Results: Skin autofluorescence rose age-dependently in both groups of children and FF group had significantly higher mean values during the first 6 months of life. Despite of lower plasma glucose (p=0.031) FF infants had higher plasma insulin levels (p=0.005) and higher homeostatic model assessment (HOMA) index (p=0.017) compared to BF infants. Urinary excretion of 8-OH-deoxyguanosine (marker of oxidative DNA damage), plasma nitrotyrosine (protein nitrosation marker) and WBC count were increased in FF infants (p=0.001, p=0.044 and p=0.049, respectively). BF children had higher ferric reducing ability of plasma, which is a marker of antioxidative capacity (p=0.012), however they displayed higher plasma concentration of advanced oxidation protein products (AOPP, marker of oxidative protein damage by myeloperoxidase, p=0.004). Urinary protein excretion rate was within the normal range, but higher in FF compared to BF infants (p=0.004).
Conclusion: Our data suggest that higher consumption of dietary MRP may result in higher MRP accumulation already in early childhood. FF infants had reduced insulin sensitivity, were more sensitive to oxidative stress and had higher protein excretion. The exact contribution of high load of dietary MRP to the observed effects requires further elucidation.
This study was supported by 6FP EU, project ICARE: COLL-CT-2005-516415.

URETERIC JET DOPPLER WAVEFORM: IS IT A RELIABLE PREDICTOR OF VESICOURETERIC REFLUX IN CHILDREN?

Ključevšek D(1), Ključevšek T(2), Kersnik Levart T(1), Kenda RB(1)

1)University Medical Centre, Children's hospital, Ljubljana, Slovenia

2)University Medical Centre, Clinical Institute for Radiology, Ljubljana, Slovenia

THE AIM OF THE STUDY: The progress of diagnostics particular in pediatrics is directed towards finding diagnostic procedures that are less harmful and burdensome for patients, but that at the same time they ensure enough information for further decisions if more invasive diagnostic procedures are necessary or not. The aim of our prospective study was to evaluate the sensitivity and specificity of a ureteric jet Doppler waveform (UJDW) in identifying patients with vesicoureteric reflux (VUR) compared with the established direct method of echo enhanced voiding urosonography (VUS), which demands catheterization of a bladder and the use of contrast medium.
METHODS: Among 75 children (57 girls and 18 boys, aged 3 to 12 years, mean 4,82 years) who were admitted for echo enhanced VUS either as a part of a follow-up of previously detected VUR or after proven urinary tract infections, UJDW was successfully performed in 70 children. The procedure was considered as successful if at least 10 UJDW measurements from each ureteric unit were detected. Than the sequences of UJDW per ureteric unit was determined and were classified into three groups: monophasic - suggestive of VUR, complex - not suggestive of VUR and mixed sequence - suggestive of VUR when a certain ratio between monophasic and complex UJDWs was achieved. Sensitivity and specificity of UJDW measurement compared with echo enhanced VUS were calculated.
RESULTS: Monophasic or complex sequences were detected in 91/139 ureteric units. The sensitivity and specificity of monophasic sequences in detecting VUR were 85.7% and 94%. The sensitivity and specificity of mixed sequences (48/139 ureteric units) in detecting VUR depend on the ratio between monophasic and complex UJDWs. Combining all three sequences of UJDWs with a cut-off point of 30% of monophasic UJDWs in mixed sequences, the overall sensitivity and specificity of this method in detecting VUR in ureteric units were 88.5% and 82.3% and relating to the patients 90% and 82%. This means that on the basis of the results of UJDW measurement 61.5% of children wouldn't need a more invasive procedure.
CONCLUSION: The present study has shown that, compared to echo enhanced VUS, the measurement of UJDW seems to be sensitive enough to detect VUR in children older than 3 years and can be proposed as screening method. A biphasic approach is recommended: first, children should be screened for VUR by detection of a UJDW sequence, and only those with findings suggestive of VUR should be investigated further with one of the more invasive direct methods.

THE CLINICAL SPECTRUM OF METAPHYSEAL ANADYSPLASIA IS DETERMINED BY MUTATIONS IN *MMP9* AND *MMP13*

Ekkehart Lausch[1*], Romy Keppler[1], Katja Hilbert[1], Valerie Cormier-Daire[2], Sarah Nikkel[3], Gen Nishimura[4], Sheila Unger[1,5], Jürgen Spranger[1], Andrea Superti-Furga[1], and Bernhard Zabel[1].

[1] Zentrum für Kinderheilkunde und Jugendmedizin, Universitätsklinikum Freiburg, Freiburg, Germany

[2] Department of Genetics and INSERM U781, Hôpital Necker Enfants Malades, Paris, France

[3] Department of Genetics, Children's Hospital of Eastern Ontario, Ottawa, Canada

[4] Department of Radiology, Tokyo Metropolitan Kiyose Children's Hospital, Kiyose, Tokyo, Japan

[5] Institut für Humangenetik, Universitätsklinikum Freiburg, Freiburg, Germany

Aim and scope of the study: Matrix metalloproteinases (MMPs) are believed to be key factors in development and homoeostasis of the skeletal tissues. Of those highly expressed in bone, MMP9 and MMP13 appear to be essential for endochondral ossification, bone remodelling, and repair. In mice, both enzymes degrade native collagens and other extracellular matrix (ECM) components in the growth plate, and cleave or release biologically active molecules stored in the ECM, thereby regulating proliferation, differentiation, and apoptosis of different cell types in skeletal development. Targeted ablation of either *Mmp9*, *Mmp13*, or both, causes severe alterations of the growth plate which are, however, transient, and only apparent during embryonic development and early postnatal growth. Adult animals have a normal or subtle phenotype with a slight reduction of body length. **Methods and results:** Guided by the striking similarity of clinical and radiographic findings in *Mmp9* and *Mmp13* knock-out mice to a rare human genetic disorder, Metaphyseal Anadysplasia (MAD, MIM), we here describe mutations in either of the two genes as molecular basis of the disease in familial and sporadic cases. Functional studies resolve the controversial issue of inheritance, as dominant MAD is associated with heterozygous missense mutations in the prodomain of MMP13 resulting in aberrant autoactivation of the enzyme, while homozygous loss of either MMP9 or MMP13 function causes recessive MAD. **Conclusions:** In dominant MAD, MMP9 appears to be degraded intracellularly by autoactivated MMP13, thus providing an explanation for the more severe clinical picture. Nevertheless, as adult patients affected by MAD are of average height and do not show any obvious signs of skeletal pathology, our results suggest that neither MMP9, nor MMP13 are undispensable for skeletal development and homeostasis in man.

RARE CASE OF RESPONSIVNESS TO CYCLOSPORINE IN AUTOSOMAL RECESSIVE SRNS

Michal Malina, Ondrej Cinek, Tomas Seeman
Department of Pediatrics, University Hospital Motol and 2nd Faculty of Medicine, Prague, Czech Republic

Introduction: Autosomal recessive steroid resistant nephrotic syndrome is a rare genetically determined nephropathy caused mainly due to mutation in the *NPHS2* gene. This type of nephrotic syndrome is usually resistant also to other immunosuppressive therapy. However, very few cases of cyclosporine A induced partial remission of inherited nephrotic syndrome have been reported.

Case report: We present a boy that developed nephrotic syndrome at the age of 18 months. There was no decrease of proteinuria on the standard prednisolone therapy. The diagnosis of steroidresistant nephrotic syndrome was established. However, the proteinuria decreased significantly after introducing cyclosporine A therapy (from 1280 to 380 mg/m^2/day) without negative influence on renal function (GFR stable 130-150 ml/min/1.73 m^2). Molecular genetic test revealed homozygous R138Q mutation in the *NPHS2* gene.

Conclusion: Our case demonstrates that cyclosporine A can induce partial remission in patients with genetic forms of nephrotic syndrome without influencing glomerular filtration rate. However, its long term effect and safety in children with hereditary forms of nephrotic syndrome has yet to be investigated.

CHARACTERISATION OF REGULATORY T CELLS,NATURAL KILLER CELLS, AND OTHER LYMPHOCYTE SUBPOPULATIONS IN NEWLY DIAGNOSED PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

Molnar K, Cseh A, Vasarhelyi B, Veres G.

1st Dept. of Pediatrics, Semmelweis University, Budapest, Hungary

Aim: Animal experiments and human data indicate that the immunopathogenesis of Crohn's disease (CD) and ulcerative colitis (UC) differ at the level of T cell differentiation and activation although the underlying mechanism responsible for these differences have not been completely understood. $CD4^+CD25^+$ regulatory T cells (Treg) can prevent or treat experimental colitis, however, little is known about their potential role in paediatric patients with inflammatory bowel disease (IBD). Therefore, the aim of our study was to examine the presence of regulatory T cells, natural killer cells, and other lymphocyte-subpopulations in the peripheral blood of newly diagnosed patients with IBD.
Methods: Ten CD patients (mean age, 10.4 years, range, 4-17 years), 5 UC patients (mean age, 13.8 years, range, 8.5-17 years) and 10 controls (mean age, 8.4 years, range, 2-17 years) were enrolled. Activity markers (CD45, CD25, CD69, CD62L, HLA-DR), Thelper1/Thelper2 phenomenon (CXCR3/CCR4), iNKT/NKT/NK cell-markers (CD3, 6B11, CD161) in the peripheral blood were assessed by flow cytometry. Treg cells were characterised by the presence of CD4, CD25, FoxP3.
Results: Thelper1/Thelper2 ratio was significantly increased in CD and UC in comparison to controls ($p=0.009$, $p=0.002$, respectively). Moreover, there was elevated CD45R0/CD45RA ratio in patients with CD ($p=0.026$) suggesting increased T cell activity. Presences of Treg cells, NK cells, and other lymphocyte-subpopulations in the peripheral blood were similar in all groups studied.
Conclusions: Our results showed increased T cell activity in CD, nevertheless, there was increased Thelper1/Thelper2 ratio in CD and UC also, suggesting the importance of T cells in early phase of both disorders. Based on our results, Treg cells and NK cells play no important role in this process, at least in the peripheral blood. However, further studies will be required to analyse these cells in the intestinal mucosa of paediatric patients with IBD.

CONTINUOUS GLUCOSE MONITORING SYSTEM (CGMS) AFTER KIDNEY TRANSPLANTATION IN CHILDHOOD

Krisztina Pásti[1], Ágnes Prókai[1], György Reusz[1], Péter Sallay[1], Nóra Pekó[1], Róbert Langer[2], Tivadar Tulassay[1], Attila J Szabó[1]

[1]1st Department of Pediatrics, Semmelweis University, Budapest, Hungary,

[2]Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary

Background: Posttransplantation diabetes mellitus (PTDM) and impaired glucose tolerance (IGT) are well known consequences of immunosuppressive therapy after transplantation. PTDM plays a role in decreasing graft and patient survival and in increasing cardiovascular morbidity. Early detection of this entity is important. In a cross sectional analysis in 2006 we found overall incidence of a glucose metabolic disorder 29 % (13 % manifest diabetes mellitus, 16 % IGT) in our pediatric renal transplant recipients.
Purpose: Answer the question whether CGMS provides more accurate information of the glucose metabolism than fasting glucose and oral glucose tolerance test after the renal transplantation and whether it's necessary to modify the screening protocol by accessory CGMS in certain cases.
Methods: We screened and followed up 8 (4 boys and 4 girls) pediatric renal transplant recipients by fasting blood glucose and oral glucose tolerance test with insulin level measurements and as a pilot study they were additionally studied by CGMS. Age of the young recipients was between 14-21,5 years (median age: 15,5 years), 7 of them got tacrolimus based combined immunosuppressive therapy. We used Medtronic minimed set and provided a limited diet containing 180 g carbohydrate per day.
Results: Interstitial fluid glucose levels correlated with capillary blood glucose all over the study. Analysis of the 8 CGMS results established that all of the studied curves differed from normal CGMS curves. Studied curves were mostly depressed; we recorded hypoglycemia in 37,7 % and hyperglycemia in 12,5 % of the studied patients. Additionally measured insulin levels showed impaired glucose tolerance in the majority of the patients.
Conclusions: CGMS seems to be helpful in detection early, mild deviations, however further prospective studies involving more patients would be necessary to determine the exact role of CGMS in screening of PTDM.
This work was supported by grants OTKA NNF 78846 - K 71730

PHENOTYPING OF LYMPHOCYTES AND COMPLEMENT SYSTEM ANALYSIS OF CHILDREN AND ADOLESCENTS WITH LUPUS NEPHRITIS

Magdalena Riedl [1], Andrea Griesmacher[2], Reinhard Würzner[3], Lothar Bernd Zimmerhackl[1], Monika Edelbauer [1]

Departments of [1] Pediatrics I, [2] Medical and Chemical Laboratory Medicine and [3] Mikrobiology, Medical University Innsburck, Austria.

Introduction: Lupus nephritis is a chronic potentially fatal autoimmune disease. In childhood the risk of progression to end-stage renal disease is up to 50 %. The etiology and pathogenesis of this complex disease is not fully understood yet.The aim of this study was to gain more information concerning the dysregulation of the immune system in pediatric patients with lupus nephritis, with special regard to the WHO classes of renal biopsy, disease activity and treatment regime.
Methods and Patients: Therefore a FACS analysis of 24 different surface markers was performed. Another focus was laid on the Complement System. The Terminal Complement Complex (TCC, C5b-9) concentration, the end product of all 3 complement pathways, was measured with an ELISA. 18 patients with lupus nephritis, 5 patients with nephrotic syndrome and 6 healthy children were so far included in the study.
Results: The results show significant decreased values of lymphocytes, CD19+ B cells, T cells, CD4+ T cells, CD8+ T cells, double negative T cells and NK cells in patients with lupus nephritis compared to patients with nephrotic syndrome or healthy children. HLA-DR+ activated T cells as well as the expression of CD134, a secondary co-stimulatory marker, on CD4+ T cells was increased in children with LN. In contrast to that show patients with lupus nephritis reduced absolute counts of CD28 expressing CD4+ T cells, another co-stimulatory molecule. Peripheral circulating CXCR3+CD4+ and CXCR3+CD8+ T cells were decreased in lupus nephritis patients. Furthermore, we were able to demonstrate decreased values of CD25+ regulatory T cells in patients with lupus nephritis. The percentage of CD4+ T cells coexpressing FOXP3, another marker for Tregs was higher in patients with lupus nephritis than in control subjects. Naïve T cells, CD4+ as well as CD8+, were reduced in our cohort of patients with lupus nephritis compared to patients with nephrotic syndrome and healthy children, as well as CD4+ memory T cells. No difference concerning central memory T cell and effector memory T cell was found.
The analyses of the Complement System revealed elevated concentrations of the Terminal Complement Complex (TCC), while the Ratio (TCC in activated serum/TCC in serum), which gives information concerning the ability for further complement activation , was in the normal range
Conclusion: We can conclude that pediatric patients with lupus nephritis show a variety of abnormalities in the regulation of the immune system and an activated state of the Complement System.

DELETIONS OF THE FACTOR H RELATED PROTEIN 1/3 GENES AND FREQUENCY OF FACTOR H AUTO ANTIBODIES: ROLE FOR PATHOGENESIS OF ATYPICAL HEMOLYTIC UREMIC SYNDROME?

A. Rosales[1], J. Hofer[1], B. Petzlberger[1], J. Scheiring[1], Pawlik M.[1], Ziegler A.[1], Peer E.M.[1], Schennach S.[1], T Giner[1], H. Fehrenbach[2], M. Kirschfink[2], P. Zipfel[2], R. Würzner[2], A. Janecke[2], R. Ullmann[2], L.B. Zimmerhackl1,[1,2]

[1] Department of Pediatrics, Medical University Innsbruck, Austria;

[2] For the European HUS study group

Purpose of the study: Despite our increasing level of “know how” during the last years of aHUS research, there's still a need for innovative research to deeply understand this multifactorial disease, and to afford a custom and evidence based therapy for the patients. Our studies’ aims derived from this precept:

- identification and validation of genetic and acquired risk factors for aHUS
- establishment of a comprehensive evidence based model for aHUS pathogenesis
- establishment of a “complement profile” as indication for an individualized therapy

In order to reach these goals we established methods for genetic and functional analyses of the complement system. This study correlates genetic (homozygous Factor H related protein 1/3 deletions [FHR-1/3]) and acquired (Factor H Antibodies [FH-Abs]) risk factors as a novel 2 hit model for aHUS pathogenesis.

Methods : Genomic DNA was prepared from peripheral blood cells of >50 patients. The obtained genomic DNA was analysed for FHR-1,2,3,4 and 5 by comparative genomic hybridization (CGH) and compared to 118 healthy controls. The deletion of FHR-1 was additionally confirmed by allele specific PCR.

FH-Ab status was determined in the serum of 68 aHUS patients and 42 controls using an ELISA method. Results were verified by Western blot analyses.

Results: 20/36 patients, compared to 14/118 controls showed deletions of FHR-1/3. 13 patients and 4 controls were found to be positive for homozygous FHR-1 deletion (χ^2 = 35.57, $p < 0.001$; Fishers Exact $p < 0.001$; odds ratio = 21.13). In addition, 7 aHUS patients compared to 10 controls were found to show heterozygous FHR-1 deletion (χ^2 = 8.26, $p < 0.004$; Fishers Exact $p < 0.010$; odds ratio = 4.55). All patients with FHR-1 deletions had an additional deletion of FHR-3.

Factor H antibodies were found only in aHUS patients. The FH-Abs positive aHUS patients showed significant higher age at disease onset than the FH-Abs negative group (mean 93.3 vs. 22.3; t-test $p<0.001$). 79/12 FH-Ab positives showed homozygous FHR-1/3 deletion and 3/11 showed no FHR-1/3 deletion.

Conlusion:Homozygous deletion of FHR-1/3 is a significant risk factor for aHUS, however, homozygous FHR-1/3 deletions were also found for healthy controls suggesting it to be a rather predisposing mutation than directly disease causing.

FH-Ab positivity is a significant risk factors for aHUS (27% in this cohort!)

The significant correlation of FH-Abs with homozygous FHR-1 deletion is suggesting a genetically determination of FH-Ab positivity.

THE RELATIONSHIP BETWEEN AMBULATORY BLOOD PRESSURE MONITORING AND CARDIOVASCULAR PARAMETERS AFTER ANTHRACYCLINE THERAPY

J. Šťastná[1], H. Hrstková[1], Z. Nováková[2], N. Honzíková[2], B. Fišer[2], E. Závodná[2], *[1]I-st Department of Paediatrics, Faculty of Medicine, Masaryk University and Faculty Hospital in Brno; [2]Department of Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic*

The aim of the study: The relationship between ambulatory blood pressure monito-ring and cardiovascular parameters at rest and during exercise in oncological patients after complete antitumour therapy with anthracyclines was the aim of the present study.
Methods: We examined 37 children, adolescents and young adults after anthracycline treatment for leukaemia (the mean period between the end of the treatment and the examination was 9.7±3.1 years; a total cumulative dose of anthracyclines of 227±42mg/m*m). Ambulatory blood pressure measurement was evaluated by cosinor analysis (fit of the cosine curve with a period of 24 hours) and the mesor (midline-estimating) and amplitude of the sinusoidal curve of systolic and diastolic blood pressures (SBP, DBP) were estimated. A continuous exercise test with an increment of 25 Watts/2min until the exhaustion of the subjects by bicycle ergometry and echocardiography (a complete two-dimensional record of four standard views of the left ventricle, the biplane Simpson rule to calculate the ejection fraction - EF, %) were performed with each subject.
Results: We did not find any significant correlation between age and the following parameters: mesor and amplitude SBP (mmHg), mesor and amplitude DBP (mmHg), ejection fraction (EF;%), transport of oxygen (O_2;ml/min), symptom-limited maximal work load (WLmax;W), body mass index (BMI;kg/m^2). Significant correlations were found: between mesor of SBP and O_2 ($r=0.4399$; $p<0.01$), and WL ($r=0.4177$; $p<0.01$); between mesor of DBP and EF ($r=0.4416$; $p<0.01$).
Conclusion: The data support our hypothesis that anthracycline therapy damages the sympathetic nervous system (SNS). The damage of SNS results in a decrease of SBP and DBP mesor. The decrease of SBP mesor is accompanied by decreased transport of oxygen and by diminished symptom-limited maximal work load. The decrease of DBP mesor is accompanied by a diminished ejection fraction.
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HAEMATOCHESIA : ALLERGIC BOWEL INFLAMMATION IN INFANTS?

Balázs Szalay[1], Áron Cseh[1], Beáta Szebeni[1], Barna Vásárhelyi[1,2], András Arató[2], Krisztina Gál[2], Gábor Veres[2]

[1]Research Group for Pediatrics and Nephrology, Semmelweis University and Hungarian Academy of Sciences, Budapest, Hungary;

[2]First Department of Pediatrics, Semmelweis University, Budapest, Hungary

The aim of the study: Haematochesia (HC, fresh blood in the stool) is an alarming symptom of otherwise healthy infants that can be cured in most cases with maternal elimination diet. While several data suggest an allergic disorder, its pathomechanism is still unclear. The objective of our study was to describe the alteration of adaptive immune system in HC infants.

Methods: 10 infants with histologically verified eosinophilic or allergic colitis were recruited. None of them had evidence of a bleeding diathesis, bacterial enteritis or fissures. Peripheral blood Th1 and Th2 cytokines were measured with a cytokine chip before and after the introduction of a 3-months long maternal eliminating diet. In addition the prevalence of lymphocyte subgroups (i.e. activated CD4 and CD8 lymphocytes expressing CD45, CD25, CD69, CD62L or HLADR markers) along with the iNKT/NKT/NK cells (CD3, 6B11, CD161 markers) and Treg cells (FoxP3 positive) were investigated with flow cytometry. 10 healthy infants without HC served as controls.

Results: The levels of total Th2 cytokines were higher in HC before the diet ($p=0.02$) compared to the controls. The CD4CD45R0/CD4CD45RA was lower in HC patients before the diet than in controls ($p=0.03$). The iNKT and NKT cell prevalence were increased ($p=0.008$, $p=0.03$ respectively) before the diet than in control patients. The prevalence of Treg cells was lower before the diet than in controls ($p=0.03$) and compared to the prevalence after the diet there was an increase in the number of Treg cells ($p=0.02$).

Conclusion: These results support the notion that the immune system of HC infants is skewed toward Th2 directions, indicating that an allergic reaction may be responsible for the development of HC.

DELAYED ANTIBODY RESPONSE TO TICK-BORNE ENCEPHALITIS VIRUS VACCINATION IN CHILDREN AFTER THYMECTOMY

Zlamy M[1], Gögele C[1], Würzner R[2], Wilk C[1], Geiger R[3], Zimmerhackl L.B.[1], Prelog M[1]

(1) Department of Pediatrics I, Medical University Innsbruck, Austria

(2) Department of Hygiene, Microbiology and Social Medicine, Medical University Innsbruck, Austria

(3) Department of Pediatrics III, Medical University Innsbruck, Austria

Background: Thymectomy in early childhood due to open heart surgery leads to premature aging of the immune system (immunosenescence), which is characterized by a decrease of naive T cells in later life. The study was aimed to investigate whether children after thymectomy may show a poor antibody response to new antigens like vaccines.
Methodes: Thus, 44 thymectomized and 56 non-thymectomized age-matched children were vaccinated with tick-borne encephalitis virus (TBEV) vaccine (FSME Immun Junior, Baxter, Vienna) following a three-dose regimen. IgG antibody levels were evaluated 4 weeks after each vaccine administration.
Results: Thymectomized children showed 2.2-fold lower TBEV IgG antibody levels after the second vaccination when compared to controls (p=0.03), but a normal response after the third vaccination.
Conclusion: Our results showed a delayed increase of TBEV IgG antibody levels after vaccination in thymectomized children. This may indicate alterations of the primary T cell immune response to new antigens but a normal memory function. Thus, it is mandatory to monitor the antibody response to new antigens and vaccinations as well as infection rates in thymectomized children to avoid long-term complications.

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Impressum

Claudia Lenz (claudia.lenz@uki.at)
Univ.-Prof. Dr. L.B. Zimmerhackl
(lothar-bernd.zimmerhackl@uki.at)
Tel. +43-512-504-23501
Fax +43-512-504-25450
Department of Pediatrics
Anichstraße 35, A-6020 Innsbruck

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