CONGRESS PROGRAM

Amsterdam, The Netherlands
March 30 – April 1, 2017

www.congressmed.com/CoPedia
### Thursday, March 30, 2017

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<td>THE FIRST UNPROVOKED VENOUS THROMBO-EMBOLIC EVENT</td>
<td>METHYLPHENIDATE BENEFITS FOR CHILDREN AND ADOLESCENTS WITH ADHD</td>
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<td>16:30-16:50</td>
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### Friday, March 31, 2017

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<td>08:30-10:00</td>
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<td>FEEDING THE NEURO-DISABLED CHILD</td>
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<td>CONTROVERSIES IN THE MANAGEMENT OF ACUTE GASTROENTERITIS IN CHILDREN</td>
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### Saturday, April 1, 2017

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<td>HOW TO IMPROVE THE ACCEPTANCE OF INFLUENZA VACCINES</td>
<td>IF CONVENTIONAL TREATMENT FAILS IN FUNCTIONAL CONSTIPATION: RECTAL THERAPY - YES OR NO?</td>
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<td>10:30-12:00</td>
<td>NON-MENDELIAN INHERITANCE: IMPRINTING DISORDERS, CONGENITAL DISEASES WITH COMMON UNDERLYING (EPI]GENETIC AETIOLOGIES</td>
<td>HELICOBACTER PYLORI: TO TEST OR NOT TO TEST; TO TREAT OR NOT TO TREAT?</td>
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<td>12:00-13:00</td>
<td>Lunch Break &amp; Poster Viewing</td>
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<td>13:00-14:30</td>
<td>ATOPIC ECZEMA</td>
<td>FUNCTIONAL ABDOMINAL PAIN: PHARMACOLOGICAL TREATMENT OR NON-PHARMACOLOGICAL TREATMENT?</td>
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<td>14:30-16:00</td>
<td>INFLAMMATORY RESPIRATORY DISEASE</td>
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<td>16:30-18:00</td>
<td>NOVEL PEDIATRIC ISSUES</td>
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Dear Colleagues,

On behalf of the Organizing Committee, we would like to personally welcome you to the 4th World Congress on Controversies in Pediatrics (CoPedia), taking place from March 30 – April 1, 2017 in Amsterdam, The Netherlands.

The aim of CoPedia is to provide a professional forum to discuss controversial topics with an emphasis on clinical solutions in cases where a consensus does not exist. This provides clinicians with valuable insight and a take-home message that ameliorates treatment in the most difficult situations. In addition, it enables the exchange of ideas and information among members of various countries.

The CoPedia scientific program deals with the most burning questions in the profession and by allowing ample time for speaker audience discussion, provides an effective forum for discussing and debating various topics.

We thank you for joining and for contributing to the success of the CoPedia Congress and hope you enjoy your time in the friendly city of Amsterdam.

Sincerely,

Ami Ballin
Israel
Sami Bahna
USA
Marc A. Benninga
The Netherlands
CME/CPD Accreditation

The 4th World Congress on Controversies in Pediatrics (CoPedia) has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide CME activity for medical specialists.

The 4th World Congress on Controversies in Pediatrics (CoPedia) is designated for a maximum of, or up to

15 European CME credits (ECMEC)

To Receive Your CME/CPD Certificate
Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity. The EACCME credit system is based on 1 ECMEC per hour with a maximum of 3 ECMECs for half a day and 6 ECMECs for a full-day event.

The CME/CPD certificate will be available after completing the online evaluation and credit claiming procedure. The process takes about 5 weeks. We thank you for your feedback as it is an important part of CME/CPD accreditation and helps improve future educational offerings.

The EACCME is an institution of the European Union of Medical Specialists (UEMS): www.uems.net

For the Italian participants
The program for the 4th World Congress on Controversies in Pediatrics (CoPedia) has been submitted for CME accreditation from the Italian Ministry of Health.

ISO 9001 Certification
This Quality certification requires all participants to fill in a scientific questionnaire and to evaluate the overall quality of the event.

CME for participants from USA and Canada
Through an agreement between the European Union of Medical Specialties (UEMS) and the American Medical Association (AMA), physicians may convert EACCME credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME credit to AMA credit can be found at: www.ana-assn.org/go/internationalcme.

Live educational activities, occurring outside of Canada, recognized by the UEMS-EACCME for ECMEC credits are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of The Royal College of Physicians and Surgeons of Canada.
General Information

**Congress Venue**
Mövenpick Hotel Amsterdam City Centre
Piet Heinkade 11
NL-1019 BR Amsterdam
The Netherlands

**Language**
The official language of the Congress is English.

**Registration Desk**
The registration desk will be open during the following hours:

- Thursday, March 30, 2017  12:00 - 19:30
- Friday, March 31, 2017  07:30 - 18:00
- Saturday, April 1, 2017  08:00 - 18:00

**Nametag**
On arrival at the registration desk you will receive your nametag. Please wear the nametag to all sessions and events.

**Certificate of Attendance (non CME/CPD)**
You may collect your Certificate of Attendance at the Registration Desk on Saturday, April 1, 2017.

**Refreshments**
A Networking Reception will be held on Thursday, March 30 at 19:30.
Coffee and lunch will be served during breaks.
Entrance will be with nametags only.

**Speakers’ Preview Room**
Invited speakers and oral presenters are invited to visit the Speakers’ Preview Room to upload their presentations.

**Poster Display**
Please check the Scientific Program for the board number on which you should display your poster(s).
Posters should be mounted between 07:30-08:30 on Friday, March, 31, 2017 and removed by the end of the sessions on Saturday, April 1, 2017.
The Organizing Committee is not responsible for posters that are not removed on time.

**Clothing**
Business casual for all occasions.

**Congress Organizer**

Powered by MCI Group
Scientific Program
Practical Algorithms in Pediatric Endocrinology
3rd, revised edition
Editor: Z. Hochberg (Haifa)
VI + 118 p., 56 graphs, 4 fig., 6 tab., spiral binding, 2017
Price: CHF 53.00 / EUR 50.00 / USD 62.00
Order at: www.karger.com/pape

Puberty from Bench to Clinic
Endocrine Development Vol. 29
Editors: J.-P. Bourguignon (Paris); A.-S. Parent (Liège)
X + 276 p., 17 fig., 5 fig in color, 27 tab., hard cover, 2016
Price: CHF 198.00 / EUR 185.00 / USD 233.00
Order at: www.karger.com/endev

SickKids Handbook of Pediatric Thrombosis and Hemostasis
2nd, revised and extended edition
Editors: V.S. Blanchette (Toronto, Ont.); L.R. Brandão (Toronto, Ont.); V.R. Breakey, (Hamilton, Ont.); S. Revel-Vilk (Jerusalem)
XX + 338 p., 31 fig., 13 in color, 80 tab., hard cover, 2017
Price: CHF 127.00 / EUR 119.00 / USD 149.00
Order at: www.karger.com/sickkids

Tumors in Adolescents and Young Adults
Progress in Tumor Research, Vol. 43
Editors: D.P. Stark, (Leeds); G. Vassal, (Villejuif)
X + 146 p., 15 fig., 9 in color, 19 tab., hard cover, 2016
CHF 198.00 / EUR 185.00 / USD 233.00
Order at: www.karger.com/pritr

Prices subject to change, VAT not included.
EUR price for eurozone countries, USD price for USA and Latin America only
Thursday, March 30, 2017

HALL A
14:00-15:00 ORAL PRESENTATIONS I

Chairperson: Itai Berger, Israel

14:00-14:09 Modelling the optimal target age group for seasonal influenza vaccination in Japan
Shinya Tsuzuki, UK

14:09-14:18 Hepatic and/or splenic abscess is a good clinical predictor for pediatric melioidosis
Supatjaree Chanvitan, Thailand

14:18-14:27 The STRONGkids nutritional screening tool in hospitalized children of a Portuguese general hospital
Juliana Costa Maciel, Portugal

14:27-14:36 The investigation of occupational experience of obstetricians in terms of drugs use in pregnancy and
teratogenicity
Ahmet Akici, Turkey

14:36-14:45 Neutrophil lymphocyte and neutrophil platelet ratios in children with autism spectrum disorders:
A preliminary study
Nagihan Cevher Binici, Turkey

14:45-15:00 Discussion

HALL B
14:00-15:00 ORAL PRESENTATIONS II

Chairperson: Ami Ballin, Israel

14:00-14:09 Anomalous gait: A very rare myopathy
Vera Gonçalves, Portugal

14:09-14:18 Pigmented hypertrichotic dermatosis and insulin dependent diabetes:
Manifestations of a rare syndrome
Siham Mansouri, Morocco

14:18-14:27 Parry-Romberg syndrome: A case report
Siham Mansouri, Morocco

14:27-14:36 Inter-rater reliability of using COMFORT-B scale in pediatric intensive care unit
Rujira Buntharikpornpun, Thailand

14:36-14:45 Successful use of recombinant tissue plasminogen activator (r-tPA) for management of chylothorax
associated with central venous thrombosis after neonatal cardiac surgery
Sameh Rabie Ismail, Saudi Arabia

14:45-15:00 Discussion
THE FIRST UNPROVOKED VENOUS THROMBO-EMBOLIC EVENT

Capsule: Venous thromboembolic disease is increasingly recognized in neonates and children. Treatment is generally extrapolated from adult guidelines. In most pediatric patients, treatment consists of heparin (unfractionated heparin or low-molecular-weight heparin [LMWH]) followed by LMWH or vitamin K antagonists. The safety and efficacy of direct oral anticoagulants (DOACs) are currently studied in children in large international, multicenter trials. The duration of antithrombotic therapy is extrapolated from adult guidelines, as well. However, do we need to treat children with a first unprovoked thrombosis indefinitely as is recommended in adults?

Chairperson: Heleen Van Ommen, The Netherlands

15:00-15:30 Antithrombotic treatment in children: Past, present, future
Heleen Van Ommen, The Netherlands

15:30-16:30 Debate: All children with a first unprovoked venous thromboembolic event should be treated with anticoagulation indefinitely

15:30 Yes: Mattia Rizzi, Switzerland
15:50 No: Claudio Molinari, Italy
16:10 Discussion

METHYLPHENIDATE BENEFITS FOR CHILDREN AND ADOLESCENTS WITH ADHD

Capsule: • Methylphenidate is commonly prescribed for ADHD.
• Methylphenidate has been used for this indication for more than 50 years.
• What is the quality of clinical research evidence on benefits for ADHD patients?
• Did something go wrong in the past?
• How can we amend and expand our evidence based on benefits of methylphenidate for ADHD?

Chairperson: Christian Gluud, Denmark

15:00-15:30 Benefits of methylphenidate for children and adolescents with ADHD? Cochrane systematic review
Ole Jakob Storebø, Denmark

15:30-16:30 Debate: What are the benefits of methylphenidate for children and adolescents with attention deficit hyperactivity disorder?

15:30 Pro: Marcel Romanos, Germany
15:50 Con: Ole Jakob Storebø, Denmark
16:00 Con: Christian Gluud, Denmark
16:10 Discussion

16:30-16:50 Coffee Break
HALL A
16:50-18:20  HPV VACCINE EFFECTIVENESS AND SAFETY

Capsule:  HPV vaccines have been introduced in over 60 countries with dramatic reductions in viral prevalence, genital warts and advanced pre-neoplastic lesions. In parallel these vaccines are implicated in non-scientific debates as responsible for a number of adverse events. These claims have resulted in serious damage to the vaccination programs in Japan, Colombia and Denmark.

Chairperson:  F. Xavier Bosch, Spain

16:50-17:20  HPV vaccines: Results after 10 years of vaccination
1) Population impact of 10 years of HPV vaccination
2) Questions and answers
F. Xavier Bosch, Spain

17:20-17:50  HPV vaccines safety assessment: Current views in Europe
1) Mechanisms of vaccine safety assessment. The HPV vaccine evaluation.
2) Questions and answers
Pier Luigi Lopalco, Italy

17:50-18:20  HPV vaccine scares: Impact in Europe and efforts to be made
1) The case of the HPV vaccination program in Denmark
2) Questions and answers
Christian Munk, Denmark

HALL B
16:50-18:20  METHYLPHENIDATE HARMS FOR CHILDREN AND ADOLESCENTS WITH ADHD

Capsule:  • Methylphenidate is commonly prescribed for ADHD.
• Methylphenidate has been used for this indication for more than 50 years.
• What is the quality of clinical research evidence on harms of ADHD?
• Did something go wrong in the past?
• How can we amend and expand our evidence based on harms of methylphenidate for ADHD?

Chairperson:  Christian Gluud, Denmark

16:50-17:20  Harms of methylphenidate for children and adolescents with ADHD?
Cochrane systematic review
Ole Jakob Storebø, Denmark

17:20-18:00  Debate: What are the harms of methylphenidate for children and adolescents with attention deficit hyperactivity disorder?
17:20  Pro: Jan Buitelaar, The Netherlands
17:40  Con: Ole Jakob Storebø, Denmark
17:50  Con: Christian Gluud, Denmark
18:00  Discussion

18:20-18:30  Break
HALL A
18:30-19:30 OPENING SESSION

18:30-18:45 Greetings by Congress Chairperson
Ami Ballin, Israel

18:45-19:30 Opening lecture:
Fatty liver in children: The emerging 21 century epidemic. How to cope? How to treat?
Shimon Reif, Israel

19:30 NETWORKING RECEPTION

Friday, March 31, 2017

HALL A
08:30-10:00 CONTROVERSIES IN NEONATAL CARE

Capsule: The currently existing prescription opioid epidemic has resulted in a dramatic increase in newborn infants born with Neonatal Abstinence Syndrome (NAS). Old and new ways of treating these addicted neonates will be discussed during this session. Total body cooling has become standard of care for the treatment of neonates with perinatal asphyxia. Many of these newborn infants are treated with a myriad of medications. This session will provide a pro/con discussion on the need for more intensified therapeutic drug monitoring in these infants during and after induced hypothermia.

Chairpersons: John van den Anker, USA/Switzerland
Karel Allegaert, Belgium

08:30-09:00 Neonatal abstinence syndrome
Karel Allegaert, Belgium

09:00-10:00 Debate: Neonates treated with hypothermia need more intensive therapeutic drug monitoring (TDM)

09:00 Pro: John van den Anker, USA/Switzerland
09:20 Con: Karel Allegaert, Belgium
09:40 Discussion
**HALL B**

**08:30-10:00 FEEDING THE NEURO-DISABLED CHILD**

**Capsule:** Many neuro-disabled children suffer from failure to thrive which might have influence on their cognitive functioning. However, depending on the severity of the cerebral palsy these children will follow their own growth chart. Feeding difficulties and intolerance are major issues in these children and there is a lot of debate about the appropriate treatment.

**Chairpersons:** Peter Sullivan, UK  
Shimon Reif, Israel

**08:30-09:00** Overview of feeding difficulties in relation with growth in neuro-disabled children  
**Peter Sullivan, UK**

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<tr>
<td>09:00</td>
<td>Pro: Jessie Hulst, The Netherlands</td>
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<td>09:20</td>
<td>Con: Peter Sullivan, UK</td>
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**10:00-10:30 Coffee Break & Poster Viewing**

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**HALL A**

**10:30-12:00 BREAST FEEDING AND CHILDHOOD IQ**

**Capsule:** A large number of studies suggest that the IQ of breastfed infants is higher than that of formula fed infants. However, there is a hot debate whether this is due to the milk/breastfeeding, or due to the characteristics and environment of women who choose to breastfeed vs those who choose formula feeding. This debate is not merely theoretical, but rather has clinical implications and ramifications for women who choose not to breastfeed.

**Chairperson:** Gideon Koren, Canada

**10:30-12:00 Debate: Does breastfeeding affect IQ?**

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<tr>
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<td>11:05</td>
<td>Con: Gideon Koren, Canada</td>
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<td>Discussion</td>
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HALL B
10:30-12:00 ORAL PRESENTATIONS III

Chairperson: Ami Ballin, Israel

10:30-10:40 How much do parents know about ADHD? 
Alexandra Fernandes, Portugal

10:40-10:50 Prevalence of infection in children with cholestasis admitted to Cipto Mangunkusumo Hospital 2010-2015
Silvi Risdia Lina, Indonesia

10:50-11:00 Space-time clustering of necrotizing enterocolitis supports the existence of transmissible causes
Margareta Ahle, Sweden

11:00-11:10 Neonatal phototherapy - turquoise is the new blue
Graham Hart, UK

11:10-11:20 Effect of guidelines based management on the early post-operative outcome after Blalock-Taussig shunt
Sameh Rabie Ismail, Saudi Arabia

11:20-11:30 Radiofrequency catheter ablation of tachyarrhythmia in small children
Liliya Svintsova, Russia

11:30-11:40 Systematic review of methylphenidate harms for children and adolescents with ADHD
Ole Jakob Storebø, Denmark

11:40-11:50 Changing attitudes in pediatric vascular access for hemodialysis
Petrut Gogalniceanu, UK

11:50-12:00 Discussion

12:00-13:00 Lunch Break & Poster Viewing
HALL A
13:00-14:30 JOINT PAIN IN CHILDREN AND ADOLESCENTS

Capsule: Joint hypermobility is a very common occurrence in the pediatric age. Occasionally it can lead to signs and symptoms, in particular to arthralgia with or without arthritis. Diagnosis is very simple and based on clinical findings alone. A correct diagnosis can avoid multiple unnecessary testing. Treatment is based on reassurance, advice, and joint protection. In severe cases physical therapy plays a major role.

Chairperson: Rolando Cimaz, Italy
13:00-13:30 Benign joint hypermobility syndrome (BJHS) Rolando Cimaz, Italy
13:30-14:30 Debate: Joint pain in children and adolescents: Clinical or laboratory investigations?
13:30 Pro: Francesco Zulian, Italy
13:50 Con: Hans-Iko Huppertz, Germany
14:10 Discussion

HALL B
13:00-14:30 FEEDING THE SICK CHILD

Capsule: It has been advocated for years that it is beneficial to start with early parenteral or enteral nutrition in sick children. However, early nutrition might interfere with the autophagy process and influence recovery.

Chairpersons: Koen Joosten, The Netherlands
Shimon Reif, Israel
13:00-13:30 Overview of the acute stress response in sick children Koen Joosten, The Netherlands
13:30-14:30 Debate: Hypocaloric feeding in sick children is harmful
13:30 Pro: Sascha Verbruggen, The Netherlands
13:50 Con: Rosan Meyer, UK
14:10 Discussion
HALL A
14:30-16:00 ROLE OF CORTICOSTEROIDS AS ADJUNCTIVE TREATMENT IN DEFINED BACTERIAL INFECTIONS: PROS AND CONS

Capsule: Corticosteroids are often considered as the magic bullet in the management of inflammatory processes. Because bacterial infections are usually associated with local inflammation, which might augment the damage caused by the infection, adjunctive steroid administration can be helpful. However, the role of corticosteroids in the treatment of bacterial infections is controversial.

Chairpersons: Pablo Rojo, Spain
Gilat Livni, Israel

14:30-14:55 Steroids in bacterial meningitis? Empiric antibiotics?
Sharon Nachman, USA

14:55-15:20 Steroids in septic arthritis? Empiric antibiotics?
Gilat Livni, Israel

15:20-15:45 Steroids in pneumonia with pleural effusion? Empiric antibiotics?
Pablo Rojo, Spain

15:45-16:00 Discussion

HALL B
14:30-16:00 KAWASAKI DISEASE

Capsule: Kawasaki disease is a febrile illness which pediatricians should know. It is in the differential diagnosis of any febrile young child, and must be recognized promptly since early diagnosis can lead to correct treatment and avoid life-threatening complications such as coronary artery aneurysms. Different treatment options are now available, in particular for refractory cases.

Chairperson: Rolando Cimaz, Italy

14:30-15:00 Update of Kawasaki disease
Mike Levin, UK

15:00-16:00 Debate: Is Kawasaki disease a common or rare disease?
15:00 Pro: Jordi Anton, Spain
15:20 Con: Constantin Tamas, Hungary
15:40 Discussion

16:00-16:30 Coffee Break & Poster Viewing
CONTROVERSIES IN THE MANAGEMENT OF ACUTE GASTROENTERITIS IN CHILDREN

Capsule: Literature review reveals considerable contrasting data regarding the management of acute gastroenteritis in children. Controlled studies have shown that antibiotic therapy is efficacious only for few causes of bacterial gastroenteritis (mainly shigellosis), ineffective in others and maybe even harm in Shiga-toxin producing E. coli (STEC) gastroenteritis by increasing toxin production and the risk of hemolytic-uremic syndrome. Likewise, when to use probiotics, anti-emetics or anti-diarrheal agents is also unclear.

Chairpersons: Marc Benninga, The Netherlands  
J. Hans Hoekstra, The Netherlands  
Shai Ashkenazi, Israel

16:30-16:55 Antimicrobial therapy in acute gastroenteritis  
Shai Ashkenazi, Israel

16:55-17:20 Probiotics in acute gastroenteritis  
Sharon Nachman, USA

17:20-17:45 Pharmacological medications in acute gastroenteritis  
J. Hans Hoekstra, The Netherlands

17:45-18:00 Discussion

AUTISM IN GIRLS

Capsule: There is a “gender gap” in autism diagnosis, commonly referenced consensus ratio of ~4:1 The male bias in autism has attracted a variety of research but currently we know shockingly little about whether and how autism might be different in girls and boys, or why. Is it possible that current screening/diagnostic instruments may not be reliable for identifying ASD in girls? In this session we will discuss the nosological and diagnostic challenge, as well as the biological theories for gender difference in autism - anatomic, genetic, hormonal theories and pathways.

Chairperson: Itai Berger, Israel

16:30-16:50 Autism in girls: Unmet needs and translational research  
Itai Berger, Israel

16:50-17:30 Autism in girls: Misunderstood, misdiagnosed or missed altogether?  
16:50 Understanding autism in the light of gender: Meng-Chuan Lai, Canada  
17:15 The nosological and diagnostic challenge: Michael Absoud, UK  
17:40 Discussion
**DEBATE: HOW TO IMPROVE THE ACCEPTANCE OF INFLUENZA VACCINES**

**Capsule:** Although vaccines against influenza are available, this infection is still associated with significant morbidity and mortality. For example, in the US seasonal influenza causes an annual average of ~220,000 hospitalizations and ~24,000 deaths (JAMA 8/2010; 59:1057-62), with the conclusion of the CDC that influenza is the leading cause of vaccine-preventable deaths in the US. This relates to frequent antigenic changes of the virus, resulting from recombination events and point mutations that occur during replication, and low coverage of influenza vaccines. How to increase the coverage of influenza vaccines is controversial.

**Chairpersons:** Ulrich Heininger, Switzerland
Pablo Rojo, Spain
Shai Ashkenazi, Israel

08:30-08:50 Introduction
Vaccination against influenza: A special challenge
Shai Ashkenazi, Israel

08:50-09:15 Targeted vaccination of high-risk groups is the key
Pablo Rojo, Spain

09:15-09:40 Universal vaccination is the key
Ulrich Heininger, Switzerland

09:40-10:00 Discussion

**IF CONVENTIONAL TREATMENT FAILS IN FUNCTIONAL CONSTIPATION: RECTAL THERAPY - YES OR NO?**

**Capsule:** Constipation is probably the most common gastrointestinal problem in childhood. In many children conventional treatment with dietary advices, toilet training and oral laxatives is sufficient to treat these children. However, in some children more intensive treatment is necessary. Is rectal therapy in those cases a good solution?

**Chairperson:** Marc Benninga, The Netherlands

08:30-09:00 Childhood constipation (definition, etiology, diagnostics, treatment)
Marc Benninga, The Netherlands

09:00-10:00 Debate: Anorectal irrigation/surgery is sometimes necessary or unnecessary in childhood constipation

09:00 Necessary: Justin de Jong, The Netherlands
09:20 Unnecessary: Alexander von Gontard, Germany
09:40 Discussion

10:00-10:30 Coffee Break & Poster Viewing
HALL A
10:30-12:00 NON-MENDELIAN INHERITANCE: IMPRINTING DISORDERS, CONGENITAL DISEASES WITH COMMON UNDERLYING (EPI)GENETIC AETIOLOGIES

Capsule: Imprinting disorders (IDs) are a group of rare but probably underdiagnosed congenital diseases affecting growth, development and metabolism. They are caused by changes in gene regulation (‘epigenetic mutation’), gene dosage and - rarely - in gene or genomic sequences. The term genomic imprinting describes the expression of specific genes in a parent-of-origin-specific manner - that is, they are expressed only from the maternal or from the paternal gene copy, but not biparentally. We will discuss these IDs describing the clinical features, and the specific imprinting defects.

Chairpersons: Dorit Lev, Israel
Arnold Munnich, France

10:30-11:10 Epigenetics, genomic imprinting: What does it mean?
Dorit Lev, Israel

11:10-11:50 The clinical and molecular findings in pediatric imprinting disorders (Angelman syndrome, Prader-Willi syndrome, growth syndromes)
Arnold Munnich, France

11:50-12:00 Discussion

HALL B
10:30-12:00 HELICOBACTER PYLORI: TO TEST OR NOT TO TEST; TO TREAT OR NOT TO TREAT?

Capsule: There is a debate if helicobacter pylori should be tested in children with abdominal pain. In the case this bacteria is found in these children, should we consequently treat these children?

Chairperson: Marc Benninga, The Netherlands

10:30-11:00 Childhood helicobacter pylori (definition, etiology, diagnostics, treatment)
Sibylle Koletzko, Germany

11:00-12:00 Debate: Diagnostics and treatment of Hp in children with abdominal pain: Necessary or unnecessary?
11:00 Necessary: Patrick Bontems, Belgium
11:20 Unnecessary: Petronella Mourad-Baars, The Netherlands
11:40 Discussion

12:00-13:00 Lunch Break & Poster Viewing
**HALL A**  
**13:00-14:30 ATOPIC ECZEMA**

**Capsule:**  
*Are children and adolescents with food allergy more prone to have eczema? Should we send children with eczema to test the possibility that they might suffer from food allergy?*

**Chairperson:**  
*Georges Casimir, Belgium*

13:00-13:35  
*Is food allergy the cause of atopic eczema?*  
*Anthony Dubois, The Netherlands*

13:35-14:10  
*Treatment of severe atopic eczema*  
*Sami Bahna, USA*

14:10-14:30  
*Discussion*

**HALL B**  
**13:00-14:30 FUNCTIONAL ABDOMINAL PAIN: PHARMACOLOGICAL TREATMENT OR NON PHARMACOLOGICAL TREATMENT?**

**Capsule:**  
*Functional abdominal pain, including irritable bowel syndrome, are common clinical entities in children. There is, however little evidence available how to treat these children, either pharmacological or non-pharmacological.*

**Chairperson:**  
*Marc Benninga, The Netherlands*

13:00-13:30  
*Functional abdominal pain in childhood*  
*Robert Mark Beattie, UK*

13:30-14:30  
*Debate: Pharmacological treatment of functional abdominal pain in childhood*  
13:30  
*Pro: Merit Tabbers, The Netherlands*  
13:50  
*Con: Arine Vlieger, The Netherlands*  
14:10  
*Discussion*
HALL A
14:30-16:00 INFLAMMATORY RESPIRATORY DISEASE

Capsule: Are there any gender differences in the prognosis of acute or chronic diseases in children and adolescents? Are there any differences associated with chromosomes? hormones? cytokines? Do animal models help us in answering these questions?

Chairperson: Anthony Dubois, The Netherlands

14:30-15:05 Sex and inflammatory respiratory diseases in children
Georges Casimir, Belgium

15:05-15:40 The dilemma of cough in children
Sami Bahna, USA

15:40-16:00 Discussion

HALL B
14:30-16:00 HYPERTENSION IN CHILDHOOD OBESITY

Capsule: Obesity associated hypertension is an emerging problem in childhood. Hypertension adds to other cardiovascular risk factors that come with obesity. Obesity induced hypertension is sometimes hard to diagnose as the rise in blood pressure in obese children may be most pronounced during the night. There is controversy about the threshold of blood pressure for starting medication as well as about the general approach of these patients. Some feel that medication should not be prescribed at all as long as weight reduction is not achieved, others promote a combined approach given the extreme cardiovascular burden in these children.

Chairpersons: Jaap Groothoff, The Netherlands
Joana Kist-van Holthe, The Netherlands

14:30-15:00 Overview of mechanisms and outcomes of hypertension in children with obesity
Elke Wuehl, Germany

15:00-16:00 Debate: Anti-hypertensive medication is always indicated in obesity-associated hypertension

15:00  Pro: Elke Wuehl, Germany
15:20  Con: Kjell Tullus, UK
15:40  Discussion

16:00-16:30 Coffee Break & Poster Viewing
HALL A
16:30-18:00  NOVEL PEDIATRIC ISSUES

Chairperson:  Sami Bahna, USA

16:30-17:05  The recent controversy in feeding infants to prevent allergy
Anthony Dubois, The Netherlands

17:05-17:40  Immunologic inflammation and cardio-metabolic disorders in cystic fibrosis
Georges Casimir, Belgium

17:40-18:00  Discussion

HALL B
16:30-18:00  ANTIBIOTIC PROPHYLAXIS IN VESICO-URETERAL REFLUX AND OBSTRUCTIVE UROPATHY

Capsule:  There is ongoing controversy about the efficacy of antibiotic prophylaxis in children with vesico-ureteral reflux. Some advocate that prophylaxis may both reduce the rate of urinary tract infections (UTI) and hence the occurrence of renal damage, others claim that antibiotic prophylaxis only reduces the rate of non-febrile UTI and may even lead to a higher number of febrile UTI's and concurrent renal damage.

Chairperson:  Tom P.V.M. de Jong, The Netherlands

16:30-17:00  Overview of renal damage caused by obstructive uropathy and vesico-urteral reflux
Per Brandstrom, Sweden

17:00-18:00  Debate: Antibiotic prophylaxis is indicated in all patients with high grade or obstructive uropathy
17:00  Pro: Per Brandstrom, Sweden
17:20  Con: Kjell Tullus, UK
17:40  Discussion
Board No.

P01  Investigation of antibiotic-contained prescriptions written by dentists for children
  Narin Akici, Turkey

P02  Reliability testing of JM-103 and JM-105 transcutaneous jaundice meters for a hospital and community based newborn screening program: A look behind the scene
  Krista Baerg, Canada

P03  Retroperitoneal paraganglioma: A rare cause of hypertension
  Mariana Amorim Branco, Portugal

P04  Vitamin D deficiency, in the scope of three clinical cases
  Mariana Amorim Branco, Portugal

P05  From neonatal jaundice to liver transplantation: Case report
  Snezana Sreten Djordjevic, Serbia

P06  Bullous dermatosis in child
  Andreia Forno, Portugal

P07  Zelesse® an intimate hygiene wash solution for the relief of symptoms and signs of non-specific vulvovaginitis in children. The Ninesse study
  Fátima García, Spain

P08  Ataxia: An unexpected diagnosis
  Vera Gonçalves, Portugal

P09  Autoimmune enteropathy in five month old female with intractable diarrhea and severe metabolic acidosis
  Martina Keeler, USA

P10  Medical problems according to karyotype in Turner syndrome
  Chan Jong Kim, Korea

P11  Long-term adiposity changes in youth with overweight or obesity enrolled in pediatric weight management
  Stephanie Anne Klein, USA

P12  Cutaneous neonatal lupus erythematosus
  Stephanie Anne Klein, USA

P13  Using classification trees to predict scoliosis
  Aleksandra Kulis, Poland
P14 Parents think they only need a prescription, it turns out it might be a serious case: 3 case reports
Ljubica Milorad Lukovic, Serbia

P15 Nephrotic syndrome in pediatrics: 20 years follow up
Cristina Madureira, Portugal

P16 Infantile colic: Symptoms upon treatment with lactobacillus reuteri
Immaculada Margarit Dalmau, Spain

P17 Risk factors for large-for-gestational age infants in pregnant women with gestational diabetes mellitus
Shinobu Nomachi, Japan

P18 Pediatric telephone triage hotline program for HIV-positive children: Implementation and the assessment of healthcare access barriers and guardians’ clinical knowledge in Chennai, India
Gabriella Odudu, USA

P19 Efficacy of ondansetron versus domperidone on vomiting due to acute gastroenteritis
Sanguansak Rerksuppaphol, Thailand

P20 School-based internet obesity prevention program for Thai children
Lakkana Rerksuppaphol, Thailand

P21 A rare complication of diabetic ketoacidosis
Alexandra Rodrigues, Portugal

P22 Acceptability of Zelesse® in the management of non-specific vulvovaginitis in pediatric patients. The Ninesse study
Syra Velasco, Spain

P23 The evaluation of the medial longitudinal arch (MLA) in youth with Down Syndrome: Pilot study
Renata Woźniacka, Poland

P24 The impact of variables related to fatness on body weight and BMI, depending on the level of physical activity in children aged 10-13 years
Renata Woźniacka, Poland

P25 Safety validation of WT1 peptide vaccine therapy for childhood solid tumor diseases
Ryu Yanagisawa, Japan

P26 Renal swelling can predict renal damage?
Paula Nunes, Portugal
Abstracts
About the Journal

Current Pediatric Reviews publishes frontier reviews, drug clinical trial studies and guest edited thematic issues on all the latest advances in pediatric medicine. The journal's aim is to publish the highest quality review articles dedicated to clinical research in the field. The journal is essential reading for all researchers and clinicians in pediatric medicine.

New Insight in Pediatric Cardiology: From Basic to Therapeutics

Editors:
Giuseppe Santoro
Giuseppe Pacileo
Maria Giovanna Russo

About the eBook

Congenital heart diseases are the most common neonatal malformations, ranging from 8 to 15/1000 live births in various communities. Improvement of knowledge in the genetic and etio-pathogenic aspects of these malformations as well as the technical advances of diagnostic and therapeutic tools have brought about a significant improvement in overall long-term patient outcome over the last few decades. This e-book is an update on the most recent genetic, diagnostic and therapeutic aspects of this pediatric cardiology.
NEONATES TREATED WITH HYPOTHERMIA NEED MORE INTENSIVE THERAPEUTIC DRUG MONITORING

K. Allegaert 1,2, J.N. van den Anker 3,4

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Introduction:
Use of therapeutic drug monitoring (TDM) in neonates aims at improving therapeutic responses and/or decreasing adverse events by integrating drug measurement with clinical decision-making. This is important because neonates do not respond similarly to exposure to the same drugs as adults or children, even when doses are normalized for body weight or, surface area. TDM shifted from an abstract, academic concept to a tool used during routine clinical care. Issues that still remain have to do with justifying the benefits of routine use of TDM in the light of the ever-increasing budgetary limits. For many standard clinical situations involving drugs for which TDM has commonly been used in the past, present reliance on the intervention may have become excessive in light of today’s knowledge. Current observations suggest that the greatest benefit of TDM might come from use in targeted or specialty populations: those with severely decompensated renal function, those at the extremes of age, and those using immunosuppressive, specific antineoplastic, psychotherapeutic or anticonvulsant drugs. Neonates undergoing whole body cooling because of moderate to severe perinatal asphyxia may be such another specific population.

Therapeutic drug monitoring in neonates: how to assess its relevance?
Limited predictability: is there a poor correlation between dose and concentration? The interindividual variability of drug disposition in neonates is – in general – pronounced: despite their small size, there is extensive variability in clearance and concentration/time profiles. This phenotypic variation in drug disposition is based on constitutional, environmental and genetic factors but in early neonatal life, mainly reflects ontogeny. To illustrate this, aminoglycosides are almost exclusively eliminated by the renal route. Birth weight, postnatal age, but also medication (ibuprofen, indomethacin) and perinatal asphyxia are the most relevant covariates of clearance, presumably because it predicts the time course of development of glomerular filtration rate. Is there a quantitative relationship between dose and concentration? If feasible and available at the bedside clinical assessment (e.g. body temperature, blood pressure, analgesia, sedation) is superior to any TDM driven approach. Bedside up- or down titration can be driven by pharmacodynamic outcome variables. Obviously, the introduction of more sophisticated tools (e.g. aEEG vs clinical seizures in neonates) may further support this kind of clinical monitoring, or may further improve the concentration (TDM)/effect relation and clinical titration. In contrast, it is much more difficult to evaluate the concentration/effect relation for antibiotics. Infectious diseases including meningitis and sepsis are among the most common reasons for TDM in neonates and can be associated with perinatal asphyxia. A narrow therapeutic index: is there a quantitative relation between concentration and side effects? Besides effects, a drug may also cause side-effects. These kind of side-effects may relate to idiosyncrasy in individual cases (e.g. genetic predisposition, allergy or pseudo-allergy). TDM may be helpful to avoid these side effects, similar to the use of the oxygen saturation monitor to avoid hyperoxia, or the measurement of thyroid function (e.g. amiodarone), liver enzymes (e.g. valproate) or renal function (e.g. ibuprofen, ACE inhibitors) with the use of specific drugs. The extended interval dosing approach for aminoglycosides has resulted in higher peak and lower through concentrations in neonates, and this practice is supported by data on reduced nephrotoxicity in children and adults, but there is only indirect evidence for this approach in neonates.

Significant consequences of therapeutic failure should be considered. Morbidity and mortality as mortality and morbidity as a consequence of infections are extremely relevant and common. Consequently, in the clinical setting, it is difficult to disentangle therapeutic failure due to immaturity, co-morbidity or inappropriate choice of antibiotics (e.g. resistant pathogen), compared to ‘just’ insufficient dosing. Similarly, prolonged low concentrations of antibiotics may also induce bacterial resistance or fungal colonization. Although clinicians may feel confident to use international ‘reference’ handbooks for drug dosing, we would like to stress that there is extensive and unexplained variability in dosing regimens between these textbooks. Moreover, most of the dosing regimens have never been validated. We recently illustrated this variability for aminoglycosides, and documented the need to validate vancomycin dosing regimens. The majority of vancomycin trough levels in neonates, achieved using 2 published dosing regimens, did not reach the target of 10 mg/L. This illustrates the urgent need for prospective validation of neonatal vancomycin dosing regimens. We anticipate that dosing regimens integrating covariates reflecting general physiological maturation and renal maturation, as well as disease characteristics, could improve vancomycin exposure in neonates.

TDM does not replace common clinical sense:
Any measurement should be integrated in the clinical setting of the individual patient. Some relevant issues relate to e.g. the time of sampling: is the patient already at steady state or not yet? Moreover, the specific methods used to measure either biomarkers (e.g. creatinine) or the drug itself (e.g. vancomycin measurements) may be relevant up to the level of clinical relevance. Finally, we should not forget that pharmacotherapy in neonates remains aiming and shooting at a moving target. This can be illustrated by the fact that maturational changes in renal function, driven by weight and gestational age, as well as postnatal age. Using the indicators of appropriateness for TDM, we conclude that neonates are in a rapidly evolving pharmacokinetics. It is clear that there is potential for better effects, less side effects) of more focused TDM.

Suggested reading:


NEONATAL ABSTINENCE SYNDROME

K. Allegaert 1,2, J.N. van den Anker 3,4

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Introduction:
Neonatal abstinence syndrome (NAS) is a withdrawal syndrome in neonates due to acute cessation of exposure to either illicit or prescribed drugs. Similar to tolerance or dependence, withdrawal may occur as a result of repeated or chronic administration of drugs, but also after short-term high dose administration as might happen during stay in the neonatal intensive care. Consequently, NAS can appear both following intentional to the newborn during their clinical care. The most commonly involved compounds are opioids, selective serotonin reuptake inhibitors (SSRIs), benzodiazepines, as well as cannabis or nicotine. The prevalence of NAS is increasing globally with an increased incidence of adverse neonatal outcomes and costs. Evidence...
regarding the effectiveness of NAS prevention and management strategies is very weak and further research initiatives are critically needed to support meta-analysis and clinical practice guidelines. In NAS research, the choice of outcomes and the use of valid, responsive and feasible measurement instruments are crucial. There is currently no consensus yet, and an evidence-based core outcome set (COS) for NAS is needed.

Opioid related NAS:

The incidence of opioid related NAS has increased significantly in the last decade, co-linear with the increased medical use of prescription opioids in adults. NAS is for sure no longer ‘restricted’ to illicit drug users, but also became a common complication following medical prescription of opioids to the pregnant woman or newborn. The clinical picture of NAS mimics to a large extent the syndrome of opioid withdrawal in adults (‘cold turkey’), and includes neurological (e.g. crying, agitation, feeding difficulties, sleep disturbances, but also seizures), but also extra-neurological symptoms (including vomiting, diarrhea, perianal excoriation, sweating, hyperthermia, and sneezing.). The timing of clinical presentation of NAS varies with the opioid (elimination half-life short or prolonged, heroin vs methadone) used, the presence of co-drug exposure, maternal drug history, placental transfer, neonatal elimination capacity, but – as recently described – also pharmacogenetics. The Finnegan score (modified version, 21 items, 0-37 points) is universally used to quantify NAS severity, reflecting the central nervous system driven but also intestinal, autonomic, or respiratory symptoms. Based on observations in non-exposed (near term) neonates, it has been suggested that Finnegan values above 8 should raise suspicion of withdrawal. When pharmacological treatment of opiate withdrawal in neonates is deemed necessary, opiates (morphine, methadone, preferably by oral route) are the first choice, with subsequent slow weaning, although there is extensive variability in dosing, weaning and discharge practices, in part reflecting different practices but also different legal approaches. In the event of non-opioid neonatal withdrawal, phenobarbital is likely the first choice. More recently, clonidine (5 µg/kg per day, divided in 8 doses) has been suggested as a novel treatment modality. Similarly, buprenorphine by sublingual route may also become a new treatment modality. Before and at least simultaneously with these pharmacological interventions, we strongly recommend considering the impact of other interventions like swaddling, traditional supportive interventions, but also breastfeeding. Although there are no prospective randomized controlled trials, there is evidence in support of breastfeeding in women who have used methadone in pregnancy (Grade C, since this reduces the incidence (NNT = 6) and severity of NAS (Grade C), without inducing clinically important sedation (Grade C). Optimal NAS treatment remains undetermined and practices vary between and within hospitals. Prolonged length of stay for NAS cases may result in patient harm, impaired maternal-infant attachment, besides a significant increase in healthcare related costs. The development of an educational program and a standard treatment protocol for NAS has been the most effective interventions to reduce this length of stay. NAS newborns suffering from NAS.

Essentials for the practitioner:

1. NAS incidence varies extensively (5-10 fold) between units, but there is an overall relevant increase in recent years.
2. Besides recreational use, this increase in NAS also reflects a significant increase in the medical prescription of opioids.
3. Fetal exposure does not necessary results in NAS.
4. The timing of NAS symptoms depends on the characteristics of the opioid: the longer the elimination half-life, the later the symptoms appear.
5. Treatment should be protocol driven, based on assessment (Finnegan) and followed by non-pharmacological as well as pharmacological interventions. Treatment should also cover the subsequent tapering of drugs used for the pharmacological intervention.
6. Neonatal seizures are the most life threatening complication of NAS. Furthermore, treatment aims to reduce distress, preserve weight gain and improve oral feeding.
7. Breastfeeding has a proven positive effect on the incidence and extent of NAS (NNT = 5-6).

8. Opioid withdrawal should be treated with opioids, but current practices on the compound used (methadone, morphine) vary.
9. Although these concepts can also be applied to withdrawal syndromes resulting from other drugs (e.g. antidepressants, sedatives), the evidence and guidance for these drugs is more limited.

Suggested reading:


CONTROVERSIES IN ANTIBIOTIC TREATMENT OF ACUTE GASTROINTESTINAL INFECTIONS IN CHILDREN

S. Ashkenazi

Schneider Children’s Medical Center, Petah Tikva; The Pickrel Professor for Pediatric Research, Sackler Faculty of Medicine, Tel Aviv University, Israel

As most cases of acute gastroenteritis in children, especially in developed countries, are non-bacterial, antibiotic treatment is usually not required. The mainstay in the management of gastroenteritis of all etiologies is replacement of fluid and electrolyte losses by oral (preferred) or IV solutions. Regarding antibiotic therapy, it is theoretically reasonable to believe that it will beneficial in bacterial etiologies of acute gastroenteritis, with the potential goals of achieving clinical improvement, fecal eradication of the pathogen to reduce infectivity and prevention of complications. Unfortunately, this is not the case: for unclear reasons, antibiotic therapy is efficacious only for few causes of bacterial gastroenteritis, ineffective in others and maybe even harm in some settings. The issue is therefore complicated and controversial. The biggest controversy relates to the antibiotic treatment of Shigella-toxin producing E. coli (STEC) gastroenteritis, as some non-randomized studies suggested that antibiotic therapy increased the risk of hemolytic-uremic syndrome without affecting the course of the acute illness. Other observational studies did not confirm this observation. Because controlled studies are not available yet, it is debated, but currently recommended not to use antibiotics in suspected or proven cases of Shiga-toxin producing E. coli gastroenteritis. It has been shown that appropriate antibiotic therapy of Shigella gastroenteritis reduces significantly the duration of fever, diarrhea, fecal excretion of the pathogen and also the risk of complications. The problem though is the increasing resistance to antimicrobial agents commonly used to treat shigellosis; current effective agents include ceftriaxone, nalidixic acid, azithromycin, fluoroquinolones (in children older than 17y) and rifaximin (no experience in children). In Salmonella gastroenteritis, antibiotics does not decrease the duration of fever or diarrhea; it is recommended only for high-risk patients to reduce complications. Antibiotic therapy is efficacious in gastroenteritis caused by enterotoxigenic E. coli and V. cholerae, and also in the dysenteric form of Campylobacter gastroenteritis. The role of antimicrobial therapy in other bacterial enteropathogens is unclear.

The etiology of acute gastroenteritis is seldom known at presentation. Empiric therapy should be considered in clinical dysentery and in moderate to severe travelers’ diarrhea; the selection of the specific antibiotic agent should be based on the local epidemiology of the causative organisms and their resistance patterns. In conclusion, antibiotic therapy is indicated in a relatively small subset of children with acute gastroenteritis, often started empirically on the basis of epidemiologic data and thorough medical history.
VACCINATION AGAINST INFLUENZA: A SPECIAL CHALLENGE
S. Ashkenazi
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Influenza virus is an important cause of respiratory illness worldwide, sometimes resulting in complications, hospitalizations and deaths. It causes a periodic high attack rate each winter with the background threat of a global pandemic. In recent years the disease burden of influenza infection among children has been well established. Prospective studies have shown that children younger than 5 years, and especially those younger than 2 years, have high rates of outpatient visit and hospitalizations, although death rates are lower than those in the elderly (NEJM 2006; 355:31-40). Moreover, children often introduce the infections into their families. Vaccination, when feasible, is the optimal way to prevent infectious diseases. Currently, the IM-administered killed or split vaccines are available; the latter is recommended for children because of its reduced adverse effects. The vaccine is now recommended not only to high-risk children, but also to health children aged 6 months to 2 years (in Israel) or six months to 5 years (in the US). Acceptance of the influenza vaccine is relatively low, mainly because of its several limitations. These include only moderate efficacy in young children (60%-70%), which is strain-limited and of short duration, with the need for an annual repetition of the vaccine; no mucosal immunity; and no cellular immunity. The CDC has concluded that influenza is the leading cause of vaccine-preventable deaths in the US! Improved influenza vaccines are needed. Several distinct approaches are currently under study. Initial studies with the intra-nasal, live-attenuated, cold-adapted influenza vaccine were encouraging. In a double-blind, placebo-controlled, multi-center study in Israel (as part of a multi-national study) – we have shown an efficacy of 82% against culture-proven influenza in children 6 to 36 months of age (Pediatrics 2006; 118:2298-312). In the first head-to-head comparison with the split vaccine – the live intranasal vaccine has shown a superior relative efficacy of 52.7% (PID 2006; 25:870-9). Recent field experience, however, showed a very low effectiveness, especially in the United States. Novel approaches, such as naked DNA, synthetic peptides and ribosomal vaccines against influenza, attempt to achieve broad heterotypic protection, hopefully also against the emerging avian influenza strains. Time will tell if these efforts are successful in bringing the new research vaccines to the clinical arena.

FUNCTIONAL ABDOMINAL PAIN: FOCUSCUSSING ON THE BIOPSYCHOSOCIAL MODEL
R.M. Beattie
University Hospital Southampton, Southampton, UK

The symptom of abdominal pain in childhood is so common that it is unusual for a child to go through school years without experiencing it at some stage.

• It is common in school-aged children
• It is poorly understood with a multitude of factors being implicated in causation
• Patients often have vague symptomatology
• Investigation usually results in a low yield of organic disease (large differential diagnosis)
• Treatment strategies are varied and often subjective with very little evidence upon which to base them

It is only when the pain impacts on the functioning of the child or family that medical help is sought. Functional Dyspepsia, Irritable bowel syndrome and Abdominal Migraine should be considered.

Functional Abdominal Pain refers to:
• Episodic or continuous abdominal pain in a school aged child
• No relationship with physiological events (e.g. eating)
• Some loss of daily functioning
• The pain is not feigned

• Insufficient criteria for other functional gastrointestinal disorders that would explain the abdominal pain
• No structural/metabolic abnormality to explain symptoms

There can be additional somatic symptoms e.g. headache, limb pain, sleep disturbance, chronic fatigue hence the term Functional Abdominal Pain Syndrome. Functional abdominal pain can co-exist with organic disease and like other functional gastrointestinal disorders organic disease can occur in children with functional abdominal pain. Stress is often a very major factor. It is important however when stress is considered to remember that is can be either physical or psychological or a combination of the two and reflects the response to external factors of the inherent personality type. Functional Abdominal Pain therefore reflects the child’s response to biological factors, influenced by temperament (the child’s developing personality) and reinforced by family and school environment

• Somatic predisposition, dysfunction or disorder
• Lifestyle and Habit
• Milieu and critical events
• Temperament and learned response patterns

Exposure by parents of this biopsychosocial model of illness is an important factor for the resolution of symptoms. Assessment is by a careful history and examination, exclusion of organic pathology and limited ‘one stop’ investigation. Evidence of environmental reinforcement of pain behavior should be considered. In particular, specific attention at the time of pain, medication at the time of pain, school absence, normal home activity during pain-free periods (especially days off school) and family illness history (how other family members deal with symptoms of this type). The diagnosis should be positive and confident. It is important. It is very important to avoid over investigation. Treatment strategies are varied and often subjective with very little evidence upon which to base them. Many cases of childhood recurrent abdominal pain respond to acknowledgement of the symptoms and reassurance regarding the lack of serious underlying organic disease.

• Explain the biopsychosocial theory of functional abdominal pain: The pain is real
• Offer reassurance: it is not life threatening, most cases improve
• Explain the aim is to manage pain and optimize daily function
• Give suggestions of lifestyle changes: including avoidance of excessive use of medication particularly non-steroidal anti-inflammatory drugs, discussion of dietary triggers, recognition of stress factors, recognition of relationship issues, recognition of family discourse

• Discuss coping strategies such as distraction, deep breathing
• Refer to psychology team if high functional disability
• Encourage graded return to school: liaise with school
• Consider discussion or referral to child and adolescent mental health services (CAMHS) if anxiety and depression is a significant feature inhibiting potential rehabilitation

• Arrange to review after the above have been addressed
• Consider medication: only if indicated

Long term follow-up rarely identifies an occult organic disorder. Adults who had functional abdominal pain in childhood are at increased risk of functional abdominal pain, headache, backache and menstrual irregularities. as adults. Adults who had functional abdominal pain in childhood are at increased risk of adult psychiatric disorders including anxiety and depression.

Case to Consider:

11-year-old boy
3-month history of abdominal pain
Generalized fatigue
School attendance less than 50%
What do you do

The parental perspective:

• What is functional abdominal Pain?
• Is it all in my son’s head?
• Why my son?
• What is wrong with him?
• Surely he needs tests?
AUTISM IN GIRLS – MISUNDERSTOOD, MISDIAGNOSED OR MISSED ALTOGETHER?
I. Berger
The Pediatric Neurology Unit, and the Neuro-Cognitive Center - Hadassah-Hebrew University Medical Centers, Israel

There is a "gender gap" in autism spectrum disorder (ASD) diagnosis. The relationship between sex/gender differences and autism has attracted a variety of research - ranging from clinical and neurobiological to etiological, stimulated by the male bias in autism prevalence. Findings are complex and do not always relate to each other in a straightforward manner. Distinct but interlinked questions on the relationship between gender differences and autism remain under-addressed. From the first published descriptions of autism, it has been a male-typical disorder. Prevalence surveys conducted since have reported a range of male biases from 1.33:1 male:female to 15.7:1, and a commonly referenced consensus ratio of ~4:1. Males are substantially over-represented among high functioning cases, and males and females are more equally represented among cases with severe intellectual disability. So, it is not uncommon for women to be repeatedly misdiagnosed. Many studies include almost only boys. We know shocking little about whether and how autism might be different in girls. What we do know is that on average, girls who have mild symptoms of autism are diagnosed two years later than boys. Scientists and service providers rarely acknowledge the additional challenges being female may bring, whether physical, psychological or societal. Researchers suggest several reasons for the existing "gender gap" in autism diagnoses: Diagnostic criteria, concepts and practices have historically been biased towards the 'conventional' (male) presentation of ASD; Current screening instruments may not be reliable for identifying ASD in females; Females may be better able to adapt to, or compensate for, aspects of ASD symptomatology than are males, sometimes referred to as the "camouflage hypothesis"; The brains of females with ASD may be anatomically different to the brains of males with ASD. One way to examine this issue is to study groups of children with 'ASD-like traits' who present for diagnostic assessment. Specifically, researchers are looking for factors that are unique to girls. It has been shown that in the absence of significant intellectual or behavioral problems, girls with ASD-like traits are more likely than boys to evade a diagnosis of ASD. These results may reflect the different strategies girls use to manage their behavioral traits. Girls tend to engage in more 'pretend play' than boys, but for girls on the autism spectrum this may involve simply imitating or repeating play or social situations they have previously encountered. Girls with ASD also appear able to demonstrate complex emotions than boys. The intense special interests often found in girls with ASD tend to more closely align with the 'mainstream' than the corresponding interests of boys with ASD. Biological theories for the sex difference in ASD prevalence most frequently take the form of a multiple-threshold multifactorial liability model, in which females have a higher threshold for reaching affection status than males. Thus, genetic studies operating under this model hypothesize that females with ASD are likely to be carrying a higher heritable mutational "load" than affected males. Sex chromosomal genes have been proposed to be key players in molecular mechanisms driving females' protection from ASD liability conferred by specific risk loci and/or by genome-wide mutational load. The Extreme Male Brain theory, born from cognitive-behavioral observations is conceptualized along two dimensions: 1) empathizing, the drive to perceive others' feelings and thoughts and respond appropriately, and 2) systemizing, the drive to interact with and understand rule-based systems. One recent attempt to explain the sex difference in ASD prevalence was the increased expression of genes involved in immune system and glial function which was observed to be up-regulated in adult autistic cortex, and sex hormones, particularly estradiol, have been shown to affect glial-neuronal interactions. Thus, it may not be the absolute levels of androgens or estrogens, but the balance between them that influences ASD risk. Due to the complex and 'unconventional' presentation of ASD in girls and women, there is a greater chance of them being misdiagnosed with conditions such as language delay, anxiety and eating disorders. Recently, an increasing number of studies from different perspectives and methodologies have revisited how gender differences are related to autism. Some have attempted to clarify how males and females with autism are similar or different in behavioral features via meta-analyses, multi-site large datasets, and by means of a male/female-balanced design. This has been extended to proteomics, anthropometrics, brain structure, and neural/somatic growth patterns. On the other hand, studies of population genetics/genomics have revisited the sex/gender- differential liability hypotheses using well-powered datasets and advanced technology. It seems that the use of adequately powered datasets and statistical design as well as multilevel approaches offer promising avenues for advancing our understanding in this debatable issue.

- Can you make him better?
- Can you give him some medicine?
- Is there anything else we can do?
- Will he get better?

This presentation will discuss:
1. The incidence and etiology of recurrent abdominal pain in childhood
2. The classification into subgroups including functional dyspepsia, irritable bowel syndrome, abdominal migraine and functional abdominal pain (syndrome)
3. The etiology of functional abdominal pain
4. Assessment including investigation
5. Evidence based management
6. Practical Approach in the child with recurrent abdominal pain
7. Long term outcome

Further readings:
Boey CC, Goh KL. Recurrent abdominal pain and consulting behaviour among children in a rural community in Malaysia. Digestive and Liver Disease 2001;33(2):140-4
Chikara DK, Rawat DJ, Talley NJ. The epidemiology of childhood recurrent abdominal pain in Western Countries: a systemic review. Am J Gastroenterol 2005;100(8):1868-75
Huertas-Ceballos AA, Logan S, Bennett C, Macarthur C. Pharmacological interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. Cochrane database Syst Reviews 2008

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THE IMPACT OF 10 YEARS OF HPV VACCINATION
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In spite of the availability of cervical cytology and HPV screening technologies and more recently, of prophylactic HPV vaccines, cervical cancer remains amongst the three most common cancers in women and consistently the second most common in developing countries. In Europe, some 50,000 new cases of cervical cancer occur yearly with a 40 to 60 % mortality rate and a 90% 5-year survival rate. Half of these cases occur in the western countries in Europe where screening activities have been in place for decades. In 2006 HPV vaccines were first licensed and introduced into the vaccination routines in many developed countries. By the end of 2014 over 60 countries did so and initiated programs targeting mostly your girls. Recent estimates on the impact of such programs indicated that 118 million girls were targeted by public programs of which 42 million received the scheduled vaccines (two or three doses depending on the time and cohort). Projections of these cohorts to their life expectancy indicate that of the 960,000 cases of cervical cancer expected 450,000 will not occur because of the vaccination received. Public programs have also reported, amongst vaccinated cohorts, a strong reduction of the viral circulation, of genital warts (in areas where the quadrivalent vaccine was used) and of High grade cervical lesions, the closets surrogate to cervical cancer. It is expected that in the coming 5 / 6 years the first confirmation of the reduction of cervical cancer will be achieved. Studies have also shown that there is a powerful herd protection effect by which in populations with over 50% vaccination rate amongst females only, reduction of viral circulation and of genital warts was also observed amongst non-vaccinated women and non-vaccinated males. Phase III clinical trials with vaccines against HPV 16 and 18 have recently shown that protection is also very high for adult women (to ages 45+) provided they are HPV DNA negative at the time of vaccination. More recently a nine valent vaccine covering up to 90% of the types found in cervical cancer has shown high efficacy and safety and trials in adult women are underway. Extending the age of vaccination to adult women combined with an adequate HPV screening and triage algorithm should be able to dramatically reduce mortality in areas of high risk. These campaign-type approaches have the potential to advance the reduction of cervical cancer incidence and mortality as compared to the time table in the reductions expected if only current programs of vaccination adolescent girls are maintained.

DIAGNOSTICS AND TREATMENT OF HPV IN CHILDREN WITH ABDOMINAL PAIN: NECESSARY OR UNNECESSARY? – NECESSARY
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Heliocobacter pylori (H. pylori) is a Gram-negative bacterium that colonizes the mucus layer on the surface of the gastric mucosa. The mechanism of transmission of H. pylori is not fully elucidated, but this bacterium is transmitted exclusively between humans, often between people living in crowded and poor hygiene condition. H. pylori is acquired most often during childhood; the disadvantaged socioeconomic environment is a well-documented risk factor for acquisition. In Europe, however, the prevalence of infection in children depends on the ethnic origin (country of birth) of the child and of the parents and acquisition occur later in life in emerging countries. If the infection is not treated, it persists throughout life. The persistence of H. pylori infection is made possible by various immune defense escape strategies. Chronicity of infection is responsible for inflammation of the gastric mucosa that can, after several decades, lead to a variable degree of gastric atrophy as well as intestinal metaplasia or dysplasia. These histological lesions may evolve into a malignant lesion. Progression from the gastritis stage to the cancer stage appears to be influenced by strain virulence factors, but also by host-related immunological factors. In 1994, the World Health Organization classified H. pylori as a group 1 carcinogen and reconfirmed this in 2015. It is frequently forgotten in low prevalence countries such as European and North-American ones that the incidence and mortality rates due to stomach cancer associated with H. pylori remains a critical health issue in the rest of the world. It is frequently not known that children do also have gastro-duodenal ulcers, probably underestimated due to frequent empiric treatment with proton pump inhibitors for suspicion of gastro-esophageal reflux disease. H. pylori is one of the most prevalent human pathogen and, besides gastric cancer, a major public health issue with serious consequences for human health such as chronic gastritis, gastric ulcers and duodenal ulcers in children as in adults. When considering evidence-based guidelines, when a child is infected by H. pylori, an eradication treatment is indicated in case of peptic ulcer disease, in case of refractory iron deficiency anemia and of immune thrombocytopenia. In case of non-ulcer dyspepsia (symptoms corresponding to Rome IV criteria for functional dyspepsia), an elimination treatment can be considered after deliberations with the patient and the family. However, in most cases, parents (and children when old enough to understand) are willing to have a treatment since, although there is no conclusive evidence, that elimination of the infection will improve their symptoms of dyspepsia. Strategy for H. pylori eradication in children is still a controversial topic in high prevalence countries. To date, there is only evidence-based guidelines for children from Europe and North America, where the approximate infection rate varies from 1 to 10%, while in developing countries, this prevalence can reach up to more than 90%. Due to this, eradication of the infection in a population can be considered a preventive measure although not currently applicable due to an elevated rate of treatment failure. Indeed, a success rate of eradication strategies must be over 90% but this goal is not achieved in most published eradication trials in children, where the observed rate remains usually between 70 and 80%. Current common accepted strategies to eliminate the infection in children are a 10-day sequential treatment and a 14-day triple therapy. A treatment based on bismuth salts is also acceptable but
there is a lack of recent data. A preventive and therapeutically vaccine is still lacking despite more than 20 years of active research. Prevention by systematic H. pylori eradication can therefore only be currently planned in adulthood where therapeutic regimen is more effective. Some recent studies suggested that H. pylori infection may have a protective role against some diseases whose prevalence are increasing in developed countries: asthma and allergic disorders, esophageal diseases and obesity. The absence of early exposure to H. pylori may be associated with an increased risk of asthma in childhood. This was confirmed by epidemiological data as well as interventional studies in mice. Two hypotheses are proposed to explain the role of H. pylori in protection against allergy: a profile of secretion of cytokines preferentially of Th1 type inhibiting the Th2 responses and the increase of Treg lymphocytes in the gastric mucosa. A correlation between the absence of allergic manifestation and a higher IL-10 and TGF-β secretion could be demonstrated in vivo. Studies in a murine model have been able to replicate a protective effect of H. pylori infection in the neonatal period on allergic pulmonary manifestations and have shown the predominant role of gastric induced Treg by secretion of IL-18 by Dendritic cells. However, this protection can only be obtained by perinatal acquisition of the infection and this is not the case anymore in European and North-American countries. The hypothesis that the eradication of H. pylori leads to an increased risk or an aggravation of gastroesophageal reflux disease has been the subject of numerous publications with contradictory conclusions in adults. The conclusions of the last consensus in adults is that: epidemiological studies show a negative association between the prevalence of H. pylori and the severity of gastroesophageal reflux as well as the incidence of esophageal adenocarcinoma but that the eradication of the bacteria does not influence the evolution of these diseases. For these reasons, H. pylori infection should be considered a dangerous threat for a population and eradication is indicated whenever objectivized by clinical findings.

OVERVIEW OF RENAL DAMAGE ASSOCIATED WITH OBSTRUCTIVE UROPATHY AND VESICO-URETERAL REFLUX
P. Brandström
Queen Silvia Children’s Hospital, Sweden

Renal damage is often diagnosed following an episode of urinary tract infection (UTI), typically in a young individual, or in assessing a child with urinary tract dilatation detected on prenatal ultrasonography. It can be detected or suspected on ultrasonography. For more accurate characterization of the extent of the damage other imaging methods are used. DMSA scintigraphy provides a very good assessment of the renal parenchyma and the split function between the left and the right kidney and has replaced the use of intravenous urography. MAG-3 renography gives a somewhat lower resolution but provides a dynamic image of the outflow. Magnetic resonance is a coming technique but still requires sedation or anesthesia to ensure the child is not moving during the investigation and computerized tomography is limited by the radiation burden it imposes. Renal damage is often, but not always, associated with obstruction in the urinary tract or dilating vesicoureteral reflux (VUR). Sometimes the kidney damage is related to one of several known congenital syndromes with associated renal parenchymal defects such as non-motile ciliopathies and multi organ malformation syndromes. These syndromes typically have a genetic cause and some of these will be addressed briefly during the talk. Non-syndromal congenital abnormalities of the kidney and urinary tract (CAKUT) comprise a wide range of structural and functional malformations in the kidneys, collecting system, bladder and urethra and are assumed to be multifactorial. VUR is strongly associated to renal damage and recurrent UTI. But VUR in itself, without recurrent UTI, does not increase the risk of renal deterioration. There is evidence of a genetic predisposition also to VUR, with VUR seen more often in siblings to children with VUR compared to other children. In boys VUR is more often associated with congenital hypo-/dysplasia of the kidneys, while in girls VUR is more often associated with recurrent UTI and acquired renal scarring. Obstruction of the urinary tract is typically located at the pelvoureteral junction (PUJO), in the vesicoureteral junction (VUJO) or in the urethra seen in boys with posterior urethral valves. There are also rarer causes of obstruction such as large ureteroceles or bladder stones obstructing the outflow from the bladder, meatal stenosis and prominent phimosis in boys. Severe neurogenic bladder dysfunction will result in a functional obstruction of the bladder due to an overactive sphincter and dyssnergy between the sphincter and detrusor muscles at voiding. In PUJO and VUJO the renal function can be surprisingly well preserved at birth even with extensive dilatation of the renal pelvis and calyces. In these cases there is probably less impact on the urine flow and over time the dilatation will usually decrease. Sometimes the obstruction worsens, as in abnormal crossing vessels or periurethralcalceal fibrosis, aggravating the restriction of urine flow. This will eventually lead to decreased renal function of that kidney, seen as decreasing split function on MAG-3 renography. The increased pressure in the renal pelvis and the collecting ducts is probably the reason for the impaired concentrating capacity sometimes seen in children with hydronephrosis, with large urine output and reduced tolerance to dehydration. Bladder outflow obstruction will often lead to bladder dysfunction, initially with small bladder volumes and increased voiding pressure with a high risk of dilating VUR. Later the bladder will become enlarged with incomplete emptying and large residual urine volumes with increased risk of UTI. The renal damage often seen in these children may be an associated congenital malformation or deranged renal development due to the increased pressure in the upper urinary tract system. If the obstruction persists the normal growth of the kidneys may be compromised. There is also an increased risk of recurrent UTI and subsequent scarring. There is a risk of deteriorating renal function in children born with urinary tract obstruction, especially when the obstruction remains or worsens. Febrile UTI is an important factor for acquired renal scarring and renal deterioration in previously damaged kidneys in all children. Children with persistent obstruction or dilating VUR are more vulnerable to the damaging effect of a UTI. And children with VUR run a greater risk of UTI recurrences. The host response to a bacterial infection is depending on the virulence factors of the bacteria, but also to genetically regulated functions of the innate immune system rendering individual’s different susceptibility to UTI and renal damage.

LONG-TERM, LOW-DOSE PROPHYLAXIS AGAINST URINARY TRACT INFECTIONS IN YOUNG CHILDREN
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Urinary tract infection (UTI) is common in children. It affects about 2 % of boys and 8 % of girls during the first 6 years of life. Escherichia coli is the predominant pathogen. Symptomatic UTI causes discomfort and distress, and carries a risk of inducing renal damage. There is a strong correlation between febrile UTI, dilating vesicoureteral reflux (VUR), and renal scarring. This has led to the introduction of antibiotic prophylaxis for children with VUR in order to reduce the rate of UTI recurrence an it became common practice not only in children with VUR but also in children with other urinary tract abnormalities. However, there has been a lack of scientific support for this policy and it has therefore been challenged by many authors. During the last ten years several randomized controlled studies have been published comparing prophylaxis to no treatment or placebo. There have also been some trials comparing anti-reflux surgery or injection treatment to prophylaxis or no treatment. These studies show that children with normal urinary tracts do not benefit from prophylaxis. In young children with VUR, especially dilating VUR, prophylaxis may still be indicated. After the first year of life, boys have very few recurrences and do not benefit from prophylaxis. Girls with dilating VUR, on the other hand, are more prone to recurrences and benefit from prophylaxis. In children with multiple recurrences prophylaxis should be deployed but carefully monitored and surgical anti-reflux interventions considered. In children with obstructive uropathy, such as pelvoureteral or vesicoureteral junction
obstruction, posterior urethral valves or neurogenic bladder dysfunction, we lack evidence for the use of prophylaxis. But it is equally true that there is also no or little evidence against the use of prophylaxis. Hence, many still argue that these children are vulnerable and should be treated with prophylaxis as a precaution.

There has been a decline in the use of prophylaxis due to questioning of its efficacy, increasing bacterial resistance, and a propensity to low adherence to medication. Alternative measures to reduce UTI recurrences should be emphasized. However, in selected patients carefully followed, prophylaxis can protect from recurrent UTI and long-term sequelae.

SEX AND INFLAMMATORY RESPIRATORY DISEASES IN CHILDREN
G. Casimir
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This lecture discusses sex differences in the prognosis of acute or chronic inflammatory diseases. The consequences of severe inflammation vary in relation to sex, depending on illness duration. In the majority of acute diseases, males present higher mortality rates, whereas continuous chronic inflammation associated with tissue damage is more deleterious in females. The recruitment of cells, along with its clinical expression, is more significant in females, as reflected by higher inflammatory markers. Given that estrogens or androgens are known to modulate inflammation, their different levels in males and females cannot account for the sexual dimorphism observed in humans and animals from birth to death with regard to inflammation. Numerous studies evaluated receptors, cytokine production, and clinical outcomes in both animals and humans, revealing that estrogens clearly modulate the immune response, but the results are contradictory and difficult to link to hormone concentrations. Even in pubescent children, the presentation of acute pneumonia or chronic diseases mimics the adult pattern. Several genes located on the X chromosome have been shown to encode molecules involved in inflammation. Moreover, 10% to 15% of the genes from silenced X chromosome may escape inhibition. Females are also a mosaic of cells with genes from either paternal or maternal X chromosome. Therefore, polymorphism of X-linked genes would result in the presence of two cell populations with distinct regulatory arsenals, providing females with greater diversity to fight against infectious challenges, in comparison with the uniform cell populations in hemizygous males. The similarities observed in males and Turner syndrome patients using an endotoxin stimulation model support the difference in gene expression between monosomy and disomy for the X chromosome. Considering the enhanced inflammation in females, cytokine production may be assumed to be higher in females than males. Even if all results are not clear-cut, nonetheless, many studies have indicated higher cytokine levels both in healthy women and animals than in females. High IL-6 levels in males correlated with poorer prognosis and shorter longevity. A sound understanding of the basic mechanisms responsible for these gender differences may lead to new therapeutic targets.

IMMUNOLOGIC INFLAMMATION AND CARDIO-METABOLIC DISORDERS IN CYSTIC FIBROSIS (CF)
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The prognosis of CF regularly improved during the last 20 years, partially due to the new drugs available as inhaled antibiotics or mucolytics (pulmozyme), to the multidisciplinarity of medical approach and to the precocious search for contamination by pseudomonas. The mid-life expectancy increases from 15 to 45 years with improvement of pulmonary function and nutritional status. As inflammatory conditions are persistent, features, collateral tissues damages are extending with age, leading to reduced organ function (lung, pancreas) but also cardio-metabolic complications, related to resistance to insulin and secondary diabetes. This lecture evaluates metabolic complications of CF according to persistent inflammation and long term duration of the disease.

BENIGN JOINT HYPERMOBILITY SYNDROME (BJHS)
R. Cimaz
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Children are defined to have hypermobile joints when they display a range of movement that is considered excessive, taking into consideration the age, gender and ethnic background of the individual. Since joint hypermobility may be associated with serious and life-threatening conditions (also reviewed here, such as Marfan syndrome and Loeys-Dietz syndrome) the term benign joint hypermobility syndrome (BJHS) is reserved to the cases of joint hypermobility associated with symptoms (mainly musculoskeletal pain) and no other causes found for them. It is estimated that at least 10–15 % of normal children have hypermobile joints. The prevalence of BJHS is not known with precision, given the lack of studies of large populations. In a cross sectional study of a cohort of healthy Italian schoolchildren, aged 8-13 years, BJHS occurred in the 13,2% of the 289 children evaluated. Hypermobility is more common in childhood and it tends to lessen during adulthood. In the majority of cases hypermobile joints are not a cause of pain, and what brings a proportion of subjects to develop BJHS is not fully understood. Joint pain is thought to be caused by microtrauma to the joint surface. The structures are dynamic, secondary to the excessive movement. Other factors may contribute to the development of the syndrome, such as poor proprioception, autonomic dysfunctions and fatigue secondary to poor sleep, although the exact impact of such abnormalities is still a matter of debate. BJHS seems to be transmitted by an autosomal pattern, first-degree relatives with the disorders can be identified in many cases and variable penetrance is generally observed. With the exception of a minority of patients, who show a deficiency of tenascin-X, no abnormality in collagen or related proteins has been identified as a cause for BJHS. The more common complaint of BJHS is pain, which may be widespread and debilitating, with easy fatigability. The most common affected sites are the lower limbs but children may also report handwriting difficulties or ‘clicking or cracking’ joints. The pain is typically elicited by activity and this characteristic is very useful in differentiating BJHS from inflammatory conditions. Occasionally, episodes of joint swelling lasting hours to days, joint dislocations, or more commonly subluxations with spontaneous reduction are reported. Back-pain is also a common complaint, heavy school bags are often an aggravating feature. Chronic pain results in a reduced exercise tolerance and can negatively impact patients’ quality of life. A significant proportion of subjects progressively quit sports and other physical activities entering into a vicious circle that amplifies fatigability and may lead to pain amplification. Some extra-skeletal manifestations may enrich the clinical picture of BJHS. These symptoms usually arise after the third decade of life, but have been described in adolescents and include functional and anatomic gastrointestinal tract abnormalities (constipation, bloating, diarrhea, hiatal hernias), autonomic dysfunctions (postural tachycardia syndrome, palpitations, orthostatic intolerance, headache, fatigue) and skin abnormalities (easy bruising, striae). These disorders may be due to connective tissue abnormalities, linking BJHS and other hereditary disorders of connective tissues, namely Ehlers-Danlos syndrome type III. Hypermobility is commonly assessed through the “Beighton score” (derived from the original one by Carter and Wilkinson) and classically hypermobility is present if 4 out of 9 points are scored. Since children are normally more flexible that adults, a score of 4 is frequently seen in normal children, for this reason it may be better to consider a Beighton score of 5 or more as positive. To diagnose BJHS the Beighton score has been incorporated into a more comprehensive set of criteria called the Brighton Criteria, which take into account the possible multisystem nature of this condition. Although these criteria have not been formally validated in a pediatric population, they have been used in some studies on children with hypermobility. The management of individuals with BJHS can be very challenging and there are no evidence-based management strategies
THE RECENT CONTROVERSY IN FEEDING INFANTS TO PREVENT ALLERGY
A. Dubois
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Historically, food allergy has been thought to originate in early life and be dependent on exposure to allergenic foods. Early strategies thus sought to prevent food allergy by postponing contact with allergenic foods until later ages. Despite quite universal implementation of restricted diets in high-risk infants, the prevalence of food allergy has continued to increase. This fact prompted studies on the effect of early food allergen avoidance on the development of food allergy. These studies showed that early avoidance was ineffective, a finding that was echoed by developments in the understanding of the development of allergic immune responses in the fetus and infant. International guidelines responded to this information by abandoning recommendations to avoid allergenic foods in the first years of life. These developments paved the way for asking the question whether early exposure rather than early avoidance might be effective for the prevention of food allergy, and several studies particularly on peanut and egg were undertaken. Despite encouraging results from many of these studies, many questions remain to be answered about when and how to carry out this strategy. Of importance are also the effective avoidance of unacceptable side effects and the optimal combination with breastfeeding so that the latter does not become compromised. Pending the outcome of further studies answering these questions, introduction of allergenic foods should follow guidelines for healthy general nutrition.

IS FOOD ALLERGY THE CAUSE OF ATOPIC ECZEMA?
A. Dubois
University Medical Center Groningen, The Netherlands

Atopic Eczema (AE) and food allergy frequently co-exist in children, and the relationship between food allergy and AE is not always clear. Based on the fact that sensitization to foods is more frequent in children with moderate or severe eczema than those with mild disease, it has been recommended in the past to limit investigations for food allergy to children with more extensive AE. We revisited this question in a study of children seen between 2001 and 2011. These children were referred to our tertiary care center and underwent double-blind, placebo-controlled food challenges (DBPCFCs) for one or more suspected food allergies. Immediate reactions were observed and recorded by allergy nursing staff, while late reactions were ascertained by semi-structured telephone interview 48 hours after challenge. To test which degree sIgE-results were predictive in the therapeutic trial? Is current practice ethical? Conclusions: We need to rewrite guidelines and consider other treatment options.

THE BENEFITS OF METHYLPHENIDATE FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): ARE THE RESULTS SO SPECIAL AND ARE THEY VALID?
C. Gluud
Copenhagen University Hospital, Denmark

When looking at the results of the systematic review Ole Jakob Storebø just presented, one should look for evidence from adjacent therapeutic areas before one makes judgements and asks: are the results likely and valid? When looking at methylphenidate for adults with ADHD, the very positive Cochrane review by Epstein, Patsopoulos, and Weiser from 2014 was retracted in May 2016 due to a plethora of severe flaws, including high risks of systematic errors (bias), high risks of random errors (play of chance), and erratic assessment of the outcomes in all trials. There was also suspicion of conflicts of interests. When looking at randomised clinical trials including adults with major depression, we could not identify one single trial out of 884 trials not being at high risk of bias (Krogh et al., J Affective Disorders 2015;179: 121-127). Trials at high risk of bias (and high risk of play of chance) are the norm. Such biased trials overestimates benefit and understimates harm. Can we then believe the average results we see on benefits presented by Storebø? Remember most treating physicians have seen more patients with benefits which seemed to outweigh harms. How can this be reconciled? First, we usually see patients at a peak of their symptoms. Ergo, any intervention will likely be connected to a fall in severity of symptoms (natural history and regression towards the mean). Second, patients vary. Some have large reductions in symptoms, others less. Let us assume that the observed mean difference in ADHD-rating scale of -9.72 points is correct (that is a decline of 18% from the maximum score of 54 points), how will patients look on methylphenidate compared with placebo or no intervention? A potential proportion of about 20% of methylphenidate patients may get and look better than placebo patients. Even if the effect is less than -9.72 points, there may still be some methylphenidate patients feeling and showing improvements compared with placebo patients. Third, physicians and researchers tend to focus on benefits and tend not to see adverse events so clearly. More on this later! The mean difference of -9.72 points [95% confidence interval -11.82 to -7.63 points] on the ADHD-rating scale is, however, likely an overestimate and not even exist. Only nocebo-controlled randomised clinical trials can assess this. Moreover, a change in ADHD-rating scale of 10 to 15 points only corresponds to a change in one level of the Clinical Global Impression-Improvement score of one level (Goodman et al., Primary Psychiatry 2010;17:44-52). With very few patients achieving such decreases in the ADHD-rating scale on methylphenidate, does this potential benefit outweigh the harms that almost 100% of the patients may suffer? Is the balance between benefits and harms an advantage for the patients at large? Can we identify such patients before considering to start a therapeutic trial? Is current practice ethical? Conclusions: We need to become better in identifying the potential subset of patients that have a high likelihood of showing clear benefits and have low risks of harms of methylphenidate. Until then, we need to rewrite guidelines and consider other treatment options.
The harms of methylphenidate for children and adolescents with attention-deficit hyperactivity disorder (ADHD): are the results so special and are they valid?

C. Gluud
Copenhagen University Hospital, Denmark

When looking at the results of the systematic review Ole Jakob Storebø just presented, one should look for evidence from adjacent therapeutic areas before one makes judgements and asks: are the results likely and valid? In 131 randomised clinical trials on selective serotonin reuptake inhibitors for adult patients with major depression, we observed that only 44 trials (33.6%) reported on serious adverse events and that usually only 5 to 78 trials (0.8% to 59.5%) reported on non-serious adverse events (Jakobsen et al., BMC Psychiatry 2017;17:58). When looking at assessments of harms in clinical research a dangerous picture of neglect and ignorance emerges. First, randomised clinical trials are not poised to detect rare harms or even common harms. The selection of participants is too ideal. The duration of treatments most often too short. The influence from co-morbidities and co-interventions are minimised. The dosing schedule tight. The reporting outright bad. The average results on harms in randomised clinical trials are likely underestimated or plain “neglected, restricted, distorted, and silenced” (Ioannidis JPA. Annals Intern Med. 2009;160: 1737-38).

Randomised placebo-controlled trials are usually better than observational studies, provided that placebo works, i.e., can blind the parties involved in the trial. However, with the many adverse events and adverse effects associated with methylphenidate, unbiased assessments of harms are not likely. We need randomised, nocebo-controlled trials to get objective and unbiased assessments of both harms and benefits. In spite of the defects of randomised clinical trials in evaluating the harms of interventions, non-randomised studies usually report less absolute risks of harm than the randomised studies. This makes the findings on methylphenidate harms in children and adolescents so perplexing.

Conclusions: We need to become better in identifying the subset of patients that have a high likelihood of showing clear benefits and have low risks of harms of methylphenidate. Until then, we need to rewrite guidelines and consider other treatment options.

Breastfeeding and IQ - Pros and Cons

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Authoritative medical and pediatric organizations such as the World Health Organization, the United Nations Children’s Fund (UNICEF) and the American Academy of Pediatrics among others, have stated that exclusive breast milk is the ideal source of nutrition for infants up to the age of 6 months, followed by 1 year or longer as complementary foods are added after 6 months. Exclusive breastfeeding is considered the single preventative measure with the greatest potential impact on child mortality; it serves as the infant first immunization, lowers the risk of diarrhea and respiratory illnesses and provides essential nutrition for the child growth and development. It also protects against obesity and other non-communicable illnesses in later life. Questions have been raised on whether or not, in addition to those essential and unquestionable benefits, feeding breast milk to infants enhances the child’s cognitive development. Most studies support that hypothesis, but the data are conflicting.

The child’s intelligence is shaped by both genetic factors and environmental circumstances. Although it remains to be determined which of either is most responsible, multiple different environmental factors influence the child’s intelligence. These influences fall into two main categories: biological (like nutrition, illnesses, and exposure to violence) and sociocultural. Studies investigating the possible effect of breastfeeding and maternal milk on the child’s IQ have considered some and various of them, such as maternal IQ, maternal age, maternal cigarette consumption, maternal alcohol consumption, maternal marital status, education of parents, ethnicity, number of pregnancies, parity, birth order, siblings at home, socioeconomic status, gestational age, birth weight, head circumference, fetal distress, gender, duration of labor, infant’s anemia, iron deficiency, chronic illnesses, exposure to medicines, exposure to pollutants, blood lead, kindergarten or nursery attendance, children books at home, exposure to stressful events, age of testing, quality of neuropsychological test, rural vs. urban residence, etc. Maternal IQ and socioeconomic status have been found to be important confounders. In addition, the more potential confounders have been included and adjusted for, the evidence of a beneficial effect of breastfeeding becomes weaker or are nullified. Studies favoring breastfeeding have not given proper importance to some other potential confounders which are associated with the child IQ and with the source of the infant nutrition. Among those factors it is relevant to mention postpartum depression, moderate to heavy alcohol consumption, genetic background and early maternal-infant contact. A Consensus Statement of the American College of Obstetricians and Gynecologists indicates that perinatal mood and anxiety disorders are conditions commonly encountered by women of reproductive age. Postpartum depression and perinatal mood disorders affect about 10%-15% of mothers and result in significant morbidity for the child. If left untreated, maternal depression and anxiety are related to adverse outcomes, such as poor adherence to medical care, poor nutrition, smoking, and inadequate maternal – newborn attachment. It has been shown that less than half of depressed mothers breastfeed their infants, and also that children of depressed mothers are at an increased risk for developmental psychopathology. Maternal depression and failed lactation seem to share a common neuroendocrine mechanism. Depressed mothers tend to express behaviors that have a negative impact on their children, and their children have been more likely to have adverse cognitive, behavioral and emotional outcomes and long-term developmental disturbances. Two quality studies that adjusted for maternal depression among several other potential confounders found that the difference between breastfed and formula fed infants in total IQ became non-significant after adjustment. The harmful effects of alcohol during pregnancy are well documented. The U.S. Center for Disease Control and Prevention (CDC) defines heavy drinking for women as consuming 8 drinks or more per week, and binge drinking as 4 or more drinks on a single occasion within about 2 hours. Some studies indicate that drinking low to moderate amounts of alcohol or any binge drinking during pregnancy are not seriously associated with the children’s intelligence. However, guidelines on safe drinking during pregnancy appear contradictory, some advocating complete abstinence and others suggesting that light to moderate use is not harmful. Different genetic variants may explain the controversy. Lewis et al. found in UK children of white European origin that four genetic variants in alcohol dehydrogenase were strongly related to lower IQ at the age of 8 years, and the effect was seen among the offspring of mothers who drank some alcohol during pregnancy. Alcohol exposure via breastmilk can inhibit lactation and reduce the amount of breast milk the infant consumes. Although several studies showed maternal smoking during pregnancy as potential confounders in the investigation of the effect of breast milk on cognitive development, heavy drinking and alcohol metabolizing genes were not analyzed. Caspi et al in New Zealand showed that the association of breastfeeding and IQ is moderated by a variant in a gene involved in the control of fatty acid metabolism. Breastfed children carrying a genetic variant in FADS2 may enhance an increase IQ to exposure to breastfeeding. It has been shown in mammals and in humans that early skin-to-skin contact effects mothers-infant interactions and maternal mood, and that has long-term effects. Early skin-to-skin contact between mother and infant improves the chances of exclusive breastfeeding for up to 4 months and the duration of breastfeeding. Skin to skin contact in Kangaroo Care premature infants has been shown to reduce maternal anxiety and enhances child cognitive development Skin to skin Care is associated with longer and more exclusive breastfeeding and higher volumes of expressed milk, as shown by randomized controlled trials and a systematic review. Skin to skin contact also improves mother’s attachment. Two cohort studies also reported that infants receiving skin-to-skin contact demonstrated higher scores on the Bailey Scales of Infant Development at 6 or 12 months.

RESULTS SO SPECIAL AND ARE THEY VALID?

R. Gorodischer1 G. Koren2

BREAST FEEDING AND IQ - PROS AND CONS
of age.) one of those studies children who received Skin-to-skin contact followed up to the age of 10 years showed better cognitive control. However, early skin-to-skin contact has been promoted mostly for preterm and sick newborns, and was not a routine practice at the time many of the studies on breastfeeding and child’s IQ were performed. Ideally, formal prospective randomized controlled studies would provide the best solution to the conflicting information. Yet, such study design is not ethical in view of the undisputable benefits of breast milk. A good quality prospective study of sibling pairs discordant for breastfeeding status and for duration of breastfeeding reached non-significant differences after adjusting for several confounders. In contrast, another good quality study also using discordant sibling pair analysis obtained higher points for ever as compared to never breastfed. Those studies did not consider maternal postpartum depression or alcohol intake during pregnancy, or genetic variants of alcohol dehydrogenase genes or in genes involved in fatty acid metabolism as potential confounders. Also, obviously infants studied belonged to the same maternal IQ but only to similar socioeconomic status and maternal mental status. A high quality investigation carried out in Belarus randomized women to receive or not receive formal education about the advantages of breastfeeding and obtained higher IQ points for breastfed infants, in parallel to much higher percentages of breastfeeding; however, mothers randomized to receive the breastfeeding education might have been influenced by improving other positive health behaviors. Also, that study did not consider above mentioned other important potential confounders. Biologically, breastmilk contains substantially higher levels of long chain unsaturated fatty acids which have been shown to improve brain development and vision in animal models. In summary, most studies seem to indicate that the child cognitive ability is favored by having been breastfed in infancy, but results are conflicting. The more potential confounders are included in the analysis, the difference between having received breastmilk or formula decreases or disappears. Yet, a group of newer studies still showed effects of breastfeeding even after correction for a wide list of variables. Performance of classical randomized controlled trials is not ethically acceptable. Some of potential confounders which may have not been adjusted properly for are postpartum maternal depression, genetic variants in alcohol and in fatty acid metabolism, heavy drinking, and early skin to skin contact among others. The beneficial effect of breast milk in determining the child’s IQ, remains dubious and if existent, seems to be minimal.

HOW TO IMPROVE THE ACCEPTANCE OF INFLUENZA VACCINES - UNIFORM VACCINATION IS THE KEY

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Influenza viruses cause respiratory tract infections in all age groups including children and adolescents which occur during yearly winter outbreaks (Northern and Southern hemispheres, respectively) or endemically year round (tropical areas). Complications, such as high fever, febrile convulsions, and secondary bacterial infections frequently lead to hospitalization, especially in young infants and patients with underlying chronic diseases. In a study of our group (Pediatr Infect Dis 2013;32:293-6) we compared characteristics of pandemic influenza A/H1N1 (which occurred in 2009/2010) to those of seasonal influenza virus types A (winters of 2006/2007; 2007/2008; and 2008/2009) in 134 children (i.e., <18 years of age) hospitalized with pandemic influenza and seasonal influenza (N = 55 and 79, respectively). Chronic underlying diseases were present in 25% and 33%, respectively. Most common symptoms were fever (87%/94%), cough (78%/86%), rhinitis (76%/76%) and pharyngitis (67%/68%). Croup syndrome (15%/3%), conjunctivitis (31%/10%) and febrile seizures (26%/13%) were more frequent in patients with pandemic influenza; 64%/53% patients had ≥1 complication and 5 (3/2) were admitted to intensive care unit. However, it should be emphasized that transmission of the virus from human to human occurs irrespective of age and underlying diseases and therefore influenza may affect any individual at almost any time. For decades, safe and effective vaccines against influenza have been available for yearly use from 6 months of age onwards. Most countries do have guidelines for influenza immunizations and current strategies primarily aim at decreasing the burden of influenza disease in certain, heterogeneously defined high risk groups and senior adults, whereas universal immunization in young children so far has only been recommended in very few countries. Unfortunately, compliance of many physicians and patients with current influenza immunization recommendations is rather poor in most settings and several barriers to immunization have been identified. It is generally known that universal immunization recommendations are easier to implement than risk group based immunization strategies. Given the fact that a number of significant benefits could be achieved by immunizing young children, universal immunization against influenza in certain age groups (primarily children) should strongly be considered. These benefits include the direct benefit for the immunized child, reduced usage of antibiotics, reduced work loss of parents, and increased indirect or herd protection for the sake of the whole population. Overcoming the existing hurdles, improving knowledge about the benefits of influenza immunization, and possibly the development of improved vaccines with long lasting immunity are areas which deserve our specific attention in the future.

PHARMACOLOGICAL MEDICATIONS IN ACUTE GASTROENTERITIS

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Acute gastroenteritis (AGE) is a leading cause of child morbidity and mortality in developing countries. In high-income countries mortality due to AGE is a rare but not completely disappeared event, and morbidity remains very important with a high health care and economic burden. In Europe AGE is a major cause of medical visits and hospitalization and leads to approximately 240,000 emergency department visits annually, and the hospitalization of 1 in every 10-25 children. The WHO has set the following therapeutic goals for the management of AGE: (1) to prevent dehydration; (2) to treat dehydration; (3) to prevent nutrition damage; (4) to reduce the duration and the severity of diarrhea and the occurrence of future episodes. The mainstay of AGE treatment is to treat with oral rehydration solution (ORS) and to continue feeding. The use of ORS has drastically reduced mortality rates, but remains underutilized. Unfortunately, proper use of ORS will not reduce the duration of diarrhea. Many anti diarrheal drugs have been marked, but based on current evidence only few of these can be recommended. In children all these anti diarrheal drugs should only be used as adjunctive therapy to ORS. The focus in this presentation will be on features of an ideal drug, mechanisms of action, current evidence, international EBM-guidelines, and costs vs. benefits. Antiemetic, antimotility or antiperistalsis drugs, adsorbents, ant secretory drugs and zinc therapy will be addressed.

TOO MANY CHILDREN WITH CEREBRAL PALSY ARE FED BY GASTROSTOMY AND TOO SOON - PRO

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Children with cerebral palsy frequently have feeding difficulties that can be associated to undernutrition, growth failure, poor bone health, and micronutrient deficiencies. There is a lot of debate about the appropriate treatment of feeding problems and about timing, route and type of enteral feeding. No evidence based guideline is available and there is currently a lack of a systematic approach to the care of these patients. For each patient the route and type of feeding should be decided upon based on the presence of oral motor difficulties, gastro-intestinal comorbidities, severity of the neurological impairment (GMF5 level) and actual nutritional status. Early enteral feeding via gastrostomy may not be the first step in a substantial portion of the children. It is essential to assess several issues before deciding on placement of a gastrostomy. First, it is important to
assess a patient’s nutritional status in terms of weight and (segmental) length, but more importantly also by including a measure of fat mass and lean body mass. When a NI child who is capable of eating and drinking has substantial subcutaneous or abdominal fat deposition, even though weight and height may be low, feeding by gastrostomy will just increase the fat mass and that will not necessarily improve outcome. Second, a thorough assessment of a child’s eating and drinking skills, nutritional intake and behavioural factors by a multidisciplinary team is essential and can lead to individualized advice on feeding management strategies to maximize safety, nutritional adequacy and hydration for these children. Third, education and explaining the benefits and possible complications of a gastrostomy should take place. Common complications reported in different studies are minor site infections and granulation tissue, occurring in 40-60% of patients. Major complications such as tube migration, tube blockage, peritonitis, major site infections, buried bumper, and colon perforation are less common, but should be considered when contemplating performing a gastrostomy procedure. For children on exclusive tube feeding, serious and unintended social deprivation may result because they may be excluded from the many social activities were eating is involved. Special attention for this negative effect should be discussed beforehand and ongoing medical and psychosocial support after gastrostomy placement is needed which is best provided through the collaborative efforts of the family and team of professionals. Immobile children with severe CP are at risk of overfeeding when fed via a gastrostomy tube, which further highlights the necessity of post-operative follow-up.

UNDERSTANDING AUTISM IN THE LIGHT OF SEX AND GENDER
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Autism is an early-onset neurodevelopmental syndrome with a prevalence of ~1% across ages. It has long been perceived as being male-predominant with a reported male/female ratio of 4:5:1 in prevalence. This may have resulted in male-biased identification and understanding of autism to date. Understanding autism in the light of sex and gender informs their moderating roles in both the presentation and emergence of this condition. First, understanding how sex and gender moderate the presentation of behavioural characteristics of autism will inform why males are more likely to be identified. Females with autism tend to be under-recognized owing to higher likelihood of subtler and partially different behavioral presentation, and possible biases on the interpretation of their behaviours by the source of referral or the clinician. Studies using standardized instruments tend to find lower levels of repetitive, restricted and stereotyped behaviour and interests in females, but social-communication differences vary greatly by age and developmental level. Males and females may meet the diagnostic criteria in partly different ways. On the other hand, anecdotal clinical and autobiographical observations suggest that compared with autistic males, autistic females may show more social interests and motivation, heightened emotion contagion or affective empathy, increased imagined, more friendships but with different quality, greater camouflage of social difficulties, and different contents of restricted interests. Second, clarifying how variables related to sex and gender contribute to the male-predominance of prevalence will further inform the diverse aetiologies and developmental mechanisms of autism. This may involve particularly the convergence of developmental pathways between the emergence of autism, typical sexual differentiation and gender socialization. The optimization of supports for girls and women with autism is best based on the understanding of their needs and characteristics considering the moderating roles of sex and gender, targeting at resilience and person-environment fit, and taking into account the influences of gendered social-cultural contexts. This often involves not only skill-building and graded exposure for the individual, but more importantly, the adjustment of the social and physical environments.

GENOMIC IMPRINTING AND DISEASES
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Mammals inherit two complete sets of chromosomes, one from the father and one from the mother, and most autosomal genes are expressed from both maternal and paternal alleles. Imprinted genes show expression from only one member of the gene pair (allele) and their expression are determined by the parent during production of the gametes. Genomic imprints are erased in both germelines and reset accordingly. Thus, they are reversible depending on the parent of origin and lead to differential expression in the course of development. Genomic imprinting has been studied in humans since the early 1980’s and accounts for several human disorders. The first report in humans occurred in Prader-Willi syndrome due to a paternal deletion of chromosome 15 or uniparental disomy 15 (both chromosome 15s from only one parent) and similar genetic disturbances were reported later in Angelman syndrome. The presentation will discuss five representative disorders useful from a diagnostic/clinical perspective. These include Prader-Willi and Angelman syndromes (the first examples of genomic imprinting in humans), Silver-Russell syndrome, Beckwith-Wiedemann syndrome, Albright hereditary osteodystrophy and uniparental disomy 14. Also, included will be an introduction and description of genomic imprinting in humans and assisted reproductive technology (ART).

HPV VACCINES SAFETY ASSESSMENT: CURRENT VIEWS IN EUROPE
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HPV vaccine programs may considerably reduce the burden of several cancer forms. Their impact at population level depends not only on vaccine efficacy/effectiveness, but also vaccine acceptance plays a key role. High vaccine uptake, especially if extended to the whole both male and female population, could warrant a serious decline of virus circulation and a greater impact on disease burden reduction. Vaccine acceptance is a determined by several factors, but fear for unexpected serious adverse event is one of the most critical issues. Since the launch of HPV vaccination programs in Europe, starting from 2008, rumors about HPV vaccine safety have spread several times severely affecting the ongoing vaccination programs. Unexpected, sudden deaths in close temporal correlation with vaccine administration have been reported and had a great influence on the media. Most of those cases have been properly assessed and public health authorities managed to restore the public confidence. On the other hand, a suboptimal management of such cases - left without a proper assessment of the real cause of death – have led to a significant vaccine uptake reduction. Psychogenic response to HPV vaccine administration have been also reported both in Europe and elsewhere. A large spectrum of psychogenic reactions, from syncope to convulsive episodes, have been reported in adolescent girls. Mass psychogenic response, involving hundreds of adolescents, got large media attention in Colombia. More recently, HPV vaccination has been allegedly linked to a series of cases of not well defined neurological syndrome in Japan. This event led to a dramatic drop in vaccine uptake from 70% to 1%. Echoes of the Japanese event reached Europe and got some media attention especially in Denmark, where a neurologist collected a series of similar cases and raised the doubt that those cases were caused by HPV vaccination. Both events, the Japanese and the Danish one, have been thoroughly assessed by EMA and WHO and the relationship between neurological symptoms and HPV vaccination has been discarded. Nevertheless, those events had a significant the impact on the media. Safety of HPV vaccines has been assessed both during the clinical development of the vaccines and in the post-marketing phase. A total of about 180 million doses of vaccines have been administered worldwide and safety data that have been collected are very robust. Communicating vaccine safety is not an easy task, even when the collected evidence is strong. An additional effort, both at local and
global level, must be carried out in order to make vaccine safety assessment even more efficient and increase vaccine confidence by the means of effective communication plans.

ALL CHILDREN WITH A FIRST UNPROVOKED VENOUS THROMBOEMBOLIC EVENT SHOULD BE TREATED WITH ANTICOAGULATION INDEFINITELY: NO A.C. Molinari and L. Banov

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THROMBOSIS IN CHILDREN:

Pediatric venous thromboembolism (VTE) is a rare but increasingly diagnosed and recognized disease in the past decade. Neonates show the greatest risk for VTE [5;1,100,000 live births per year in Caucasian children] and a second peak in incidence occurs during puberty and adolescence. The annual incidence of venous events was estimated to be 0.07 to 0.14 per 10,000 children, or 5.3 per 10,000 hospital admissions of children [1].

CURRENT AND FUTURE TREATMENTS:

Pediatric VTE are treated according to recommendations based on small-scale studies in children and guidelines adapted from adult patient protocols. Unfractionated heparin (UFH), low molecular weight heparins (LMWH), and vitamin K-antagonists (VKA) are the commonly used antithrombotic drugs [2]. A child with first provoked VTE will receive anticoagulation for at least three months; the treatment will be prolonged up to 12 months in the case of idiopathic deep venous thrombosis or pulmonary embolism [2]. Decisions on further extending anticoagulant therapy are individually based on the perceived risks of VTE recurrence and anticoagulant-related bleeding [1-4]. LMWH gained increasing importance compared to UFH and oral VKA as the low requirement for monitoring facilitates use for short or longer term, especially when young infants and toddlers are being treated. VKA are preferably used for long term anticoagulation in older, compliant children [1;4-6]. Several direct novel anticoagulants (DOAC) are authorized for adults; these new agents with improved properties are being studied in children such that they will benefit from the enhancements of the newer agents. Till now it is dangerous to simply apply adult dosing and monitoring protocols to children with VTEs, and the use of new agents should be avoided excepting in the participation of clinical trials. Completion of PK and PD trials of DOAC in children will provide the data supporting their safe use in the clinical setting [6].

VTE RECURRENCE:

Roughly reported follow-up data in children suggest a recurrence rate between 3% (neonates) and 21% (idiopathic VTE) [1]. During a ten-year-study period in an Israeli-German cohort including high-risk pediatric patients with VTE, namely carriers of Antithrombin deficiency (ATD), Protein C deficiency (PCD) and Protein S deficiency (PSD), authors observed an absolute risk of recurrence per 100 patient years of 5.4% in pediatric ATD carriers, 1.3% in children with PCD, 0.7% in pediatric individuals with PSD and 0.9% in children with no thrombophilia [7]. Children with thrombophilia are also at high risk for recurrence (OR 4.46, 95% CI 2.89-6.89)[8]. Furthermore, not surgically corrected vascular anomalies (i.e., May thurner and Paget Schroetter syndrome) could lead to recurrent VTE [2;9].

COMPLICATION OF ANTICOAGULATION:

Although anticoagulation effectively prevents recurrent VTE, the patient is at increased risk of bleeding while on therapy, as bleeding is the main complication of VKA therapy in the pediatric age [2]. There is therefore a decision problem in balancing the risks between recurrence, and bleeding. It would therefore be beneficial if therapy decisions could be tailored to patients’ risk so that, for example, a child at higher risk of recurrence if untreated could be recommended (or advised) to continue long-term anticoagulant therapy, even after having considered his bleeding risk. In children receiving VKA for mechanical prosthetic valves the risk of serious bleeding is less than 3.2% per patient year [10]. In one large cohort (391 warfarin years, variable target range) the bleeding rate was 0.5% per patient year [11]; in a randomized trial (n=41, target INR range 2.0-3.0 for 3 months) bleeding occurred in 12.2% (95% CI 4.1-26.2) [12]. A more recent single centre study, with a nurse-coordinated anticoagulant service has reported lower bleeding rates of 0.05% per patient year [13]. Non-hemorrhagic complications of vitamin K antagonists, such as tracheal calcification [14] and hair loss [15] have been described on rare occasions in young children while osteoporosis/osteopenia have been reported in children on warfarin for greater than 1 year [16-18]. LMWH use is also burdened by a significant incidence of bleeding rate (0.7 % - 8.1 %) [12;19;20]; dosing related discomfort should also be considered.

OTHER ISSUES:

Otherwise well children can have up to 8–10 viral illnesses per year, depending on age and social environment, and in those with underlying significant medical issues, this can have a huge impact on absorption and metabolism of anticoagulants. Moreover, compliance issues are vastly different. For example, small infants who cannot understand the need for therapy, adolescents who intellectually comprehend but emotionally are unable to co-operate, and children in dysfunctional families who suffer the effects of inadequate parenting. Anticoagulation in children requires the development of a close working relationship between the treating team, the patient and their family. Constant communication to deal with developmental, dietary and inter-current changes is essential. Clear and constant communication between the anticoagulant management team and the multitude of other health professionals involved in the care of most children requiring anticoagication is also critical. Furthermore, careful planning around procedures, vascular access, and medication changes significantly improves control of therapy. The involvement of social workers, psychologists and other family supports and community resources is often required to support families as they try to manage anticoagulation in children. Finally, close interaction with the coagulation laboratory and diagnostic imaging department is essential to enable appropriate diagnostic and monitoring strategies [4].

CONCLUSIONS:

Long term anticoagulation with current available drugs (namely VKA) in children is burdened by significant complications and management issues that overcome the recurrence risk in most cases; however children with unprovoked thrombosis in ATD, combined thrombophilia or uncorrected venous anomalies could be considered for long term anticoagulation. After authorization of new anticoagulants use in children, and proper experience with their use in real life, the risk/benefit ratio of long term anticoagulation for secondary prophylaxis of unprovoked venous thrombosis in children will be reconsidered.

References:
HPV VACCINE SCARES: IMPACT IN EUROPE AND EFFORTS TO BE MADE

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HPV vaccination has been available in Europe since 2006 where the qHPV vaccine was licensed. Shortly after, the bHPV was also licensed. In Europe, Denmark was one of the first countries to implement HPV vaccination in a publicly funded programme that was initiated late 2008/early 2009. The programme included vaccination of all 12-years old girls and an initial catch-up of girls 13-15 years of age was also launched. HPV vaccination is carried out as for other vaccines in the childhood immunization programme in Denmark, by general practitioners. The programme was accompanied by public media attention and endorsed by influential NGO’s such as the Danish Cancer Society. As a result, the coverage in the targeted birth cohorts reached as high as 80-90%. During the last 3-4 years, reports about suspected side effects to HPV vaccination started to appear in Denmark in the media including the social media. Case stories appeared about previously healthy young girls now being tied to wheel chairs because of adverse events of vaccination. In addition, Postural Orthostatic Tachycardia Syndrome (POTS) was reported to affect many Danish girls as a side effect of vaccination. The peak of the media attention was in autumn/winter of 2015 where a TV channel and a newspaper had stories about the ‘HPV girls’ as they were now referred to. The National Board of Health Denmark asked the European Medical Agency (EMA) for a fast-track evaluation of suspected adverse events. Even though the EMA concluded that the suspected adverse events could not be causally linked to vaccination, the compliance with the HPV vaccination programme has dropped drastically. For girls in birth cohorts 1993 (12 years in 2015) and 1994 (12 years in 2016), the uptake of the first dose of vaccination was 46% and 22%, respectively. For birth cohort 2003 only 14% have been fully vaccinated (this number cannot be calculated for birth cohort 2004 yet). Thus, the impact on vaccination coverage in Denmark has been very substantial compared to the previous birth cohorts. The same tendency with a distrust in the vaccine safety and in the authorities has been observed elsewhere in Europe. Although it may not be as pronounced as in Denmark, countries as e.g. France and Ireland has also experienced waning compliance to HPV vaccination.

Some of the considerations and efforts that can be made include:
- Realising the power of social media and the fact that social media do not ‘respect’ borders
- Taking concerns of safety issues seriously while at the same time underlining the facts about safety
- Better education of vaccine providers (paediatricians, GPs, OB/GYNs, nurses)
- Underlining the consequences of not vaccinating
- Unity within research community, clinicians and not least politicians, we need to pull together with evidence-based facts
- Educating parents and children to better understand HPV and HPV vaccination

PROBIOTICS IN ACUTE GASTROENTERITIS

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Infectious gastroenteritis continues to be a leading cause of mortality and morbidity worldwide. In Europe, it is estimated that the incidence of AGE ranges from 0.5 to 1.9 episodes per child per year in children up to 3 years of age. The cornerstone of treatment remains replacement of water and electrolyte losses with oral rehydration solution. Until a few years ago, probiotics (defined as “live microorganisms which when administered in adequate amounts confer a health benefit on the host”) were discussed primarily in the context of alternative medicine, but they are now entering mainstream medical practice. Probiotics are “generally regarded as safe”, but side effects such as septicaemia and fungaemia have very rarely been reported in high-risk situations. Although many studies conclude in a statistically significant shortening of the duration of diarrhea, the clinical relevance of this finding is limited, particularly in the era of changing pathogens and rotavirus vaccine. Current available data and the 2014 recent ESPGHAN and NASPGHAN guidelines will be discussed.

STEROIDS IN BACTERIAL MENINGITIS

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Death and long-term disabilities are common outcomes of acute bacterial meningitis, especially in developing countries, even when highly effective antibiotic therapy is given. Therefore, improvement in the outcomes of acute bacterial meningitis is unlikely to come from developments in chemotherapy but rather from measures that alleviate the damage done before the causative bacteria are killed. There are strong theoretical grounds for believing that anti-inflammatory drugs should improve the outcomes of acute bacterial meningitis. Establishing whether this is the case has taken more than 25 years, and the situation is still not entirely clear. The current use of both Hib and Prevnar has changed the meningitis landscape in children, with virtual elimination of these bacterial infections. Thus, the use of corticosteroids is even less clear in cases of acute bacterial meningitis. Current available data from both developed and developing world studies will be presented.
on the matter of anticoagulation for pediatric VTE, but it is a factual description of possible arguments. Pediatric venous thromboembolism (VTE) in children is a rare but an increasingly recognized multifactorial complication. VTE encompasses deep vein thrombosis (DVT), pulmonary embolism (PE) and cerebral sinus venous thrombosis (CSVT) and occurs most likely in the inpatient setting more than in the community. The annual reported incidence in the general population ranges from 0.7 to 4.9 per 100'000 rising to 5.3 per 10 000 hospitalized children (1-3) Among the entire pediatric population, neonates are at greatest risk of VTE accounting for 24 per 10'000 admissions to neonatal intensive care unit with a second increase in incidence during puberty and adolescence. More recent data show a significant overall increase in the hospital based pediatric VTE incidence rate rising from 5.3 in the previous decades to 58 cases per 10'000 hospital admissions in more recent reports. This is most likely due to an improved awareness of clinicians, but might also reflect an increased utilization of invasive therapeutic interventions, and improved pediatric survival rates in chronic/severe conditions. The majority of VTEs in children occurred in the setting of associated conditions and/or risk factors defining “provoked VTE”. The presence of a central venous catheter is the most frequent independent risk factor for childhood thrombosis, along with other conditions such as infections, malignancy, immobility and others. However, a minority of VTEs are “unprovoked”, i.e. in the absence of clinical risk factors. The incidence of unprovoked childhood VTE has been reported to vary between 4-41%, reflecting the heterogeneity in the types of study. A significant proportion of unprovoked VTE occur during adolescence and are frequently linked to thrombophilic predisposition (a true thrombophilic condition or a congenital venous anomaly). The estimated mortality of pediatric VTE ranges between 2.2-4.2%. Long-term morbidity can result from thrombus persistence in up to 50%, the development of the post thrombotic syndrome in about a third of the patients and/or recurrent events. These deleterious outcomes can cause chronic venous damage and venous insufficiency, leading to various degrees of impairment in quality of life. It is therefore imperative to identify (a) children at risk for VTE and (b) factors that potentially influence unfavorable outcomes such as recurrence, in order to implement preventive strategies. Avoiding immobilization whenever possible, limiting oral contraceptive use to clear indications could be complemented by educational measures and/or by the administration of interrupted anticoagulation (AC) at the time of risk exposure. On the other end, recurrence of an unprovoked first event can unlikely be prevented without AC. Current management strategies for VTE in children are based mainly on adult literature with limited data available from pediatric cohorts, and include AC therapy in the absence of known contraindications. The primary aim of AC is to prevent thrombus progression and to reduce the risk of recurrence. The duration of treatment in individuals with fixed and/or transient pro-thrombotic risk factors, is usually for 3-6 months. A prolonged duration of AC has been proposed in VTE patients with chronic acquired pro-thrombotic conditions, such as antiphospholipid antibody syndrome, and in those with unprovoked events.10

For adults as well as for children, it is recognized that patients who experienced symptomatic VTE remain at risk for a recurrent event after withdrawal of an adequate AC independently of underlying conditions. This holds true even in pediatric age groups, suggesting that these patients might benefit from longer exposures to AC.11 In adult patients with a first episode of deep vein thrombosis, the cumulative incidence rate of recurrent VTE has been reported to exceed 30% over a period of 8 years of follow-up.12 In the pediatric population, the overall reported recurrence rate of VTE has been estimated of approximately 3% in neonates and among children with a first non-central-venous-catheter-associated VTE in the presence or absence of other thrombotic associated conditions. In children with first episode of unprovoked VTE the risk of recurrence is even higher up to 23% in this latter group the risk of recurrence has been reported as high as 87% after 7 year follow up in patients carrying an inherited prothrombotic risk factors, such as deficit of endogenous anticoagulants (Antithrombin [AT], Protein C [PC] and Protein S [PS]), mutation on factor V (G1691A) or prothrombin (G20210A) gene, or elevated Lipoprotein A.11 In addition, the highest risk was observed in children with two or more combined prothrombotic risk factors. The majority of patients relapsed within a median time of 3.5 years after AC withdrawal.11 It is also noteworthy that the overall death rate at recurrence per 100 patient-years has been recently reported to be 3.5%, ranging from 0.4 to 13% in patients with major inherited thrombophilia (IT), including deficit on AT, PC, PS.9 Given their relevant risk of recurrence, and the non-negligible associated morbidity and mortality, pediatric patients with first unprovoked VTE would initially need to be tested for the presence of an underlying IT, and in the presence of single or combine positive test results could be considered for AC indefinitely. Indeed, recurrent spontaneous VTE could not be prevented without AC. The benefit of AC in this setting would potentially be outweighed by the potential risk of major bleeding, reported in children on long-term oral AC with vitamin K-antagonist to be less than 2% patient-years.13

References:

JOINT ABSTRACT FEEDING THE SICK CHILD
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The need for nutritional support in hospitalised sick children has been recognised for many years and its positive outcome on length of stay, muscle strength, macro and micronutrient status and quality of life has been shown in numerous publications. Over the years, research has expanded in our knowledge on nutritional support in specific populations including neurodevelopmental delay, cardiac disease, metabolic and gastrointestinal disease and has led to numerous national and international guidelines. Similar to the progress made in the aforementioned areas, significant advances have also been made in the nutritional support on critically ill children, which remains one of the most challenging areas for clinicians not only from a medical perspective but also nutritionally. Critical illness is characterised by cascade of neuro-endocrine, immunologic and...
Support remains the ideal for critically ill children, but the amount during the first week was clinically superior. Early enteral nutritional provision of only 25% of the energy requirement within the first week has already shown to have a positive effect of excessive provision of energy and amino acids via parenteral nutrition during critical illness. Nutrient restriction early in critical illness enhanced the central and peripheral neuro-endocrine response by further lowering T3, thyroxine and TSH levels as well as the T3/T3 ratio. The T3/T3 ratio was also further reduced by the application of a tight glucose control protocol in critically ill children. The benefits of withholding nutritional support during the acute phase may also be explained by the stimulating effect on autophagy. Autophagy is an essential survival mechanism by which cells break down their own (damaged) components to recycle intracellular nutrients and generate energy during starvation. When suppressed by forced mandatory overfeeding early in critical illness, the risk of organ failure and cell death increases, resulting in worse clinical outcome. Preservation of autophagy in skeletal muscle partially explained why parenteral nutrient restriction reduced ICU-acquired weakness and enhanced recovery. In particular, excessive amino acid delivery is associated with increased muscle atrophy in adults. Although the science behind autophagy and metabolic responses related to excessive nutrient intake is now well accepted, closely linked to this concept is the question to “what is excessive” energy intake and how do we define hypocaloric/hypercaloric intake. Resting energy requirements have long been established in ventilated critically ill children to range between 40-55 kcal/kg, which are significantly lower than patients in recovery and on the ward and assessing over and under nutrition really depends on the definition applied. Provision of only 25% of the energy requirement within the early days of critical illness have already shown to have a positive impact on mortality. A recent study in critically ill children showed the deleterious effect of parenteral nutrition to supplement insufficient enteral nutrition in the acute phase to aim energy requirements. The average energy delivery in the first week was ±85 kcal/kg/d (< 10 kg), ±65 kcal/kg/d (10-20 kg) and ±40 kcal/kg/d (> 20 kg) for early parenteral nutrition, compared to an average intake of ±45 kcal/kg/d (< 10 kg), ±30 kcal/kg/d (10-20 kg) and ±10 kcal/kg/d (> 20 kg) for late parenteral nutrition. Although according to some available guidelines the children randomized to early PN would not be considered as being overfeeding withholding PN during the first week was clinically superior. Early enteral nutritional support remains the ideal for critically ill children, but the aim amount is closer to the resting energy expenditure that ideally should be measured once a patient is in the stable or recovery phase. Both hyper and hypocaloric feeding in this setting is therefore harmful as the key lies in providing sufficient energy and protein to prevent further deterioration in nutritional status and prevent negative metabolic side effect on autophagy. In children beyond the acute phase of critical illness, that are sick and on the ward, nutritional support is significantly different. Studies have indicated the ongoing rate of malnutrition in hospitalised children that needs to be improved with nutritional support. Disease specific guidelines on energy requirements exist for cystic fibrosis, cardiac disease (not critically ill), inflammatory bowel disease, neurodevelopmental delay, burns and many other clinical conditions. In many of these patients increased metabolic demands, poor appetite and thus low dietary intake leads to weight loss (including significant loss of lean muscle mass) with associated increased morbidity. This combination requires the increased delivery of energy and proteins as well as associated micronutrients that are instrumental in catch up weight gain. Studies on insufficient energy supply in numerous disease groups (whilst hospitalised on the wards), has indicated worsening morbidity and mortality. Nutritional support, in particular energy supply in both ventilated and non-ventilated children remains important. The mainstay of this support should occur via the enteral route. Hypercaloric feeding, in particular via the parenteral route has a negative impact on morbidity and mortality in critically ill children, but should not deter from early enteral support.

SYSTEMATIC REVIEW OF METHYLPHENIDATE BENEFITS FOR CHILDREN AND ADOLESCENTS WITH ADHD

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Background: Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed and treated psychiatric disorders in childhood. Methylphenidate is the drug most often prescribed to treat children and adolescents with ADHD, and has been used for this objective for more than 50 years. Despite its widespread use, this is the first comprehensive systematic review of its benefits.

Objectives: To assess the beneficial and harmful effects of methylphenidate for children and adolescents with ADHD.

Methods: In February 2015, we searched six databases (CENTRAL, Ovid MEDLINE, EMBASE, CINAHL, PsycINFO, Conference Proceeding Citation Index), and two trial registers. We also checked for additional trials in the reference list of several hundred relevant reviews and we contacted the pharmaceutical companies for published and unpublished data. Electronic databases and other sources were searched up to February 2015 for randomised clinical trials comparing methylphenidate with placebo or no intervention in children and adolescents with ADHD. Data from parallel-group trials and first period data from cross-over trials formed the basis of our primary analyses. We used Sequential Analyses to control for type I (5%) and type II (20%) errors, and we assessed and downgraded evidence according to the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach for risk of bias, imprecision, indirectness, heterogeneity, and publication bias.

Results: We included 38 parallel-group trials (n=5111) and 147 cross-over trials (n=7134). The participants were individuals of both sexes, with boys-to-girls’ ratio of 5:1, and participants’ ages ranged from 3 to 18 years across most studies. The average age across all studies was 9.7 years. The duration of methylphenidate treatment ranged from 1 to 425 days, with an average duration of 75 days. Methylphenidate was compared with placebo (175 trials) or no intervention (10 trials). All 185 trials were assessed at high risk of bias. Methylphenidate may improve teacher-rated ADHD symptoms (standardised mean difference (SMD) -0.78, 95% confidence interval (CI) -0.92 to -0.64; 19 trials, 1601 participants; very low-quality evidence). Teacher-rated general behavior seemed to improve with methylphenidate (SMD -0.87, 95% CI -1.04 to -0.71; 5 trials, 668 participants; very low-quality evidence). Methylphenidate may also improve parent-reported quality of life (SMD 0.61, 95% CI 0.42 to 0.80; 3 trials, 514 participants; very low-quality evidence). Conclusion: Methylphenidate may improve teacher-reported symptoms of ADHD, general behavior, and parent-reported
quality of life. However, given the risk of bias in the included trials, and the very low quality of the evidence, the magnitude of the effects is uncertain. Our review questions the overall quality of the methylphenidate trials. These shortcomings have previously largely been ignored. Clinicians, parents and children have the right to know this, in order to make decisions informed by the evidence. Better designed trials are needed to assess the benefits of methylphenidate. Future trials should publish depersonalised individual participant data. This can enable researchers conducting systematic reviews to assess differences between intervention effects according to age, sex, comorbidity, type of ADHD, and dose.

Correction: Ours review has been criticised in several editorials, articles, responses, and blogs pointing at errors, shortcomings, and disagreements. All the references for these feedbacks and all our responses to the critical comments are now published in our Cochrane systematic review (Storebø et al., 2015). We have corrected all errors in our presentation, showing than correction of the errors did not change substantially any of our analyses or results.

References:

SYSTEMATIC REVIEW OF METHYLPHENIDATE HARMs FOR CHILDREN AND ADOLESCENTS WITH ADHD
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Problem statement: Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed and treated psychiatric disorders in childhood. Methylphenidate is the drug most often prescribed to treat children and adolescents with ADHD, and has been used for this indication for more than 50 years. In our systematic review of randomised clinical trials (RCTs), we found that the very low quality of the evidence made it uncertain as to whether methylphenidate offers more benefits than harms compared with placebo or no treatment. Because of the limitations of identifying and reporting adverse events in RCTs, a thorough systematic assessment of harms reported in non-randomised studies was conducted.

Objective: To assess the harmful effects of methylphenidate treatment for children and adolescents with attention deficit hyperactivity disorder (ADHD) in non-randomised studies.

Methods: This review was conducted according to Cochrane guidelines for systematic reviews on harms and based on a comprehensive search for literature in scientific medical databases, unpublished data from the U.S. Food and Drug Administration and European Medicines Agency, and data received from pharmaceutical companies. The primary outcome is the number of serious adverse events defined according to The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practices (GCP). The secondary outcomes are all other adverse events.

Results: We included 256 studies: 6 comparative cohort studies (n=1134); 4 patient-control studies (n=2455); 176 cohort studies (n=2, 844 243); and 70 patient reports or series (n=206). Altogether, these studies included more than 2,848,038 patients, and were reported in 425 publications. The comparative-cohort studies lasted from 1 days to two years, the patient-control studies from one year to 11 years, and the cohort studies from 1 day to 10 years. Most were conducted in outpatient clinics in high-income countries, particularly USA. The comparative cohort studies and the patient-control studies were assessed for quality by using the ROBINS-I tool (Risk Of Bias In Non-randomized Studies - of Interventions). All the cohort studies and reports can be regarded as having risk of bias due to no control groups. Five studies were found to be at serious risk of bias, and five were found to be at critical risk of bias. Methylphenidate compared to no intervention was associated with an increase in serious (e.g., life threatening) adverse events (18.0 % vs 0.0 %); odds ratio (OR) 5.45, 95% CI 0.31 to 95.2; 2 studies, 1,362 participants (critical risk of bias). The random-effects meta-analysed proportion of methylphenidate-exposed participants with serious adverse events in 51 cohort studies including 162,434 participants was 1.2% (95% CI 0.7% to 2.0 %). The random-effects meta-analysed proportion of participants having methylphenidate withdrawn due to serious adverse events in 5 cohort studies including a total of 645 participants was 1.5% (95% CI 0.7% to 3%). The random-effects meta-analysed proportion of participants having methylphenidate withdrawn due to adverse events of unknown seriousness in 22 cohort studies including a total of 3,708 participants was 7.3% (95% CI 5.3% to 10%).

Conclusion: The present data on serious adverse events and withdrawal of methylphenidate due to serious adverse events and adverse events of unknown seriousness show high proportions, especially when considering the very low quality of evidence of benefits as well as the costs. We also observed a high proportion of participants with one or more non-serious adverse events. The advantages of non-randomised studies, compared to RCTs, in collecting information on adverse events are their often larger size, allowing for detection of rare adverse events. Furthermore, participants can be followed up for much longer periods, allowing for detection of late adverse events. On the other hand, the disadvantage of non-randomised studies compared to RCTs is the lack of a placebo comparator, which means that any apparent association between the intervention and the observed harmful effect may be related to other factors. However, harms are generally underestimated in non-randomised studies with high risk of bias. Accordingly, the reported data likely represents underestimates. Before physicians start methylphenidate administration, they need to inform patients and parents about the low quality of evidence for any benefits as well as the risks of adverse events.

OVERVIEW OF FEEDING DIFFICULTIES IN RELATION WITH GROWTH IN NEURO-DISABLED CHILDREN
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Feeding and nutritional problems are common in children with neurodisability and occur in up to 85% of those with severe spastic quadriplegic cerebral palsy. These feeding problems lead to growth failure and are associated with decrease in cerebral function, immune function, decrease in circulation time and respiratory muscle strength. Oro motor dysfunction underlies these feeding problems and is associated with profound feeding inefficiency and makes feeding these children slow and extremely difficult and stressful for their caretakers. Feeding difficulties in these children are associated with a significant reduction in the quality of life for their caregivers and in societal participation of both the affected children and their families. Nutritional management of these children is complex and best undertaken in the context of a multidisciplinary feeding team with input from paediatricians, dietitians, speech and language therapists and clinical nurse specialists. Assessment of body composition is increasingly recognised as an essential component of the nutritional assessment of such children. Measurement of micronutrient status (e.g. vitamin D, iron status, calcium, phosphorus) should also be part of nutritional assessment of children with neurodisability. Improvement in nutritional state can come from dietary supplementation but often adjunctive tube feeding is required. Gastrostomy feeding is not a panacea for the management of these problems and can be associated with significant complications not least of which is the potential for over-feeding. Careful pre-operative assessment before gastrostomy insertion as well as adequate post-operative follow-up is required. Follow-up anthropometry (weight, linear growth and fat mass) is essential in the monitoring of nutritional status of children with neurodisability and should take place at least biannually.

Further Reading:
Functional abdominal pain disorders are a common problem in childhood with a worldwide pooled prevalence of 13.5% (95% CI 11.8–15.3), of which irritable bowel syndrome has been reported most frequently (8.8%, 95% CI 6.2–11.9). In almost 90% of these children, no explanatory organic cause can be identified. Initially this condition was referred to as “recurrent abdominal pain” (RAP) by Apley and Naish in 1957 and defined as “at least three episodes of abdominal pain, severe enough to affect their activities over a period longer than three months.” In 1996, the pediatric Rome II criteria introduced the term abdominal pain related-functional gastrointestinal disorders (AP-FGIDs); which include functional dyspepsia (FD), irritable bowel syndrome (IBS), abdominal migraine (AM), functional abdominal pain (FAP) and functional abdominal pain syndrome (FAPS). In order to meet these criteria symptoms had to occur weekly, persisting for over three months before diagnosis. With the introduction of the Rome III criteria in 2006 this criterion was redefined to persisting symptoms two months prior to diagnosis. In 2016, the Rome IV criteria were introduced and “abdominal pain related functional gastrointestinal disorders” were changed to “functional abdominal pain disorders.” The term functional abdominal pain was often used to refer to any of the abdominal pain–related FGIDs (eg, FAP, irritable bowel syndrome (IBS) and functional dyspepsia (FD)). This inconsistent use of the term functional abdominal pain was considered to be a major problem by the Rome IV committee.

For those children not meeting criteria for IBS, FD, or abdominal migraine, the term functional abdominal pain—not otherwise specified (NOS) was introduced. Children with AP-FGIDs report significantly lower quality of life (QoL) scores compared to healthy peers and AP-FGIDs are ranked as second in causing school absence. In 29.1% of patients with chronic abdominal pain, pain persists even for more than 5 years, despite frequent medical attention. Furthermore, functional abdominal pain disorders in childhood have a huge economic burden, as only the diagnostic workup is approximately 6000 dollar per child in the United States. The pathogenesis underlying AP-FGIDs remains unclear. Alzheimer’s disease, visceral hypersensitivity, abnormal brain-gut interaction, psychosocial disturbance and immune activation have been suggested as possible explanation for the symptoms. Functional abdominal pain disorders are shown to occur significantly more in girls (15.9% vs. 11.5%, pooled OR 1.5) and is associated with the presence of anxiety and depressive disorders, stress and traumatic life events. However, incomplete pathophysiological understanding still hampers management. Treatment, therefore, remains symptomatic. Based on the current literature and cases, we will discuss efficacy and safety of the following pharmacological interventions: antispasmodics, antidepressants, antihistaminic agents, antibiotics, pain medication, antireflux agents, anti-emetics, antihypertensive agents, antithrombinic agents and laxatives. Beside medications, several non-pharmacological treatment options exist, of which cognitive behavioral therapy and hypnotherapy are the two best studied options. We will discuss efficacy of both therapies, not only on pain reduction but also on depression and anxiety scores as well as their effect on cognitions and quality of life. Other non-pharmacological therapies that will be discussed are yoga and probiotics. Finally, the effects of these therapies will be compared to the efficacy of pharmacological options, taking into account costs, availability and long term results.

DEBATE: FUNCTIONAL ABDOMINAL PAIN: PHARMACOLOGICAL TREATMENT OR NON-PHARMACOLOGICAL TREATMENT? M.M. Tabbers and A.M. Vlieger

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KAWASAKI DISEASE

T. Constantin

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Kawasaki disease was first described in 1967. Kawasaki disease is a small vessel vasculitis, its most dangerous complication is developing coronary aneurysms. The majority of patients are less than 5 years old when the disease occurs. After Henoch-Schoenlein purpura, Kawasaki disease is the second most common vasculitis in Europe, the incidence is 3–6/100 000 children under the age of 5. The exact cause is unknown. Infectious trigger was suggested by many papers but so far we have not been able to identify any particular infectious cause. The incidence rate of Kawasaki disease increased in Japan, even 3 larger epidemics have been described. Epidemiologic studies suggested that infectious triggers might be one of the reasons of this increase in the incidence of Kawasaki disease. Usually a patient with Kawasaki disease is seriously ill. Fever is an obligate symptom. Fever is often shows continua pattern and characteristically high fever could be observed, fever usually responds poorly to conventional antibiotics. Non-suppurative conjunctivitis could be seen in almost all children. Similarly, mucosal oral symptoms are common: cheilitis (cracking over the lips can be caused by inflammation), strawberry tongue, and pharyngitis could be observed. It is also typical that patients develop polymorphic rash, pruritus and vesicular rash is a rarity. Cervical lymphadenopathy occurs in more than half of all patients. Kawasaki syndrome is a self-limiting disease. Acute febrile, subacute and convalescent phases could be distinguished during the disease course. In addition to fever 4 symptoms should appear among the 5 characteristic symptoms, listed previously, to fulfill the definitive diagnosis of Kawasaki disease. Not included among the criteria symptoms, but it is typical that patients general condition is alarming and most, if not all, patients seems to be severely ill. Although it is very rare, the disease might be detected by echocardiography as the patient might have coronary aneurysms, or
dilatation already at the time of diagnosis. The diagnosis can be stated in cases even there is less (2-3) symptoms observed. Incomplete Kawasaki syndrome occurs when, despite a clinical suspicion of Kawasaki syndrome, patient does not show all the required number of criterias. Kawasaki syndrome has no specific laboratory result, but in case of incomplete Kawasaki syndrome, many laboratory findings might reinforce the suspicion: elevated CRP, hypoalbuminemia, elevated transaminase levels, leukocytosis, thrombocytosis, sterile pyuria. Incomplete Kawasaki syndrome is more common in children younger than 1 year. All patients should undergo echocardiographic evaluation in case of more than 7 days of fever of unknown origin. Also, none of them belongs to the diagnostic criteria, but the following symptoms often could be observed in Kawasaki disease: perianal, vulvar erythema and gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhea, hydrops of gall-bladder) may occur. Differential diagnosis of Kawasaki syndrome includes systemic onset juvenile idiopathic arthritis and polyarteritis nodosa. High-dose (2 g / kg) IVIG infusions should be given optimally between the 5th and 7th, but no later than the 10th day of the febrile phase of the disease. IVIG is supplemented with initially high dose (80-100 mg / kg / day), aspirin treatment. In two days after the disappearance of fever, the dose should be decreased (3-5 mg / kg / day). This low dose should be continued until the time when thrombocytosis resolved. If coronary artery disease observed, then it should be continued as long as the status of coronary arteries justify it (sometimes for life-long). The correct place of glucocorticoid treatment in the treatment protocol is still an issue, but more and more data suggest that glucocorticoid treatment might further reduce prevalence of coronary aneurysms, and, in short term, steroid treatment reduces the number of febrile days and reduce the frequency of IVIG resistant disease. If the initial therapy is failed, a second IVIG infusions should be given. Many patients with IVIG resistant, refractory disease respond well to a single infusion of infliximab.

**ANTIBIOTIC PROPHYLAXIS IN VESICO-URETERIC REFLUX AND OBSTRUCTIVE UROPATHY**

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Great Ormond Street Hospital for Children, UK

Our knowledge on the efficacy of prophylactic antibiotics has developed a lot during the last decade with nearly ten studies published. This has both enlightened us and confused us. **Prevention of recurrent UTI:**

Some studies show that antibiotic prophylaxis does not reduce the number of UTI. Other studies, generally of higher quality, indicate that prophylaxis works. While again a further study of high quality showed statistically significant fewer infections in the placebo group!

One of the high quality studies, the RIVUR study, shows the counter intuitive finding that prophylaxis works only in low grade VUR but not in high grade VUR.

**Prevention of renal scarring:**

Only one study, the Swedish reflux study, has shown prevention of renal scarring; in girls between the age of 1-3 years with grad III or IV VUR. The RIVUR study showed an opposite but not statistically significant tendency. They did however conclude that their study, which had 600 treated children, was under powered to study renal scarring. That would have needed 8000 children! I wonder if an outcome that needs so many children to become statistically significant really can be clinically significant? You are thus allowed to feel confused, and realise that there is no solid proof that antibiotic prophylaxis works for its most important outcome, renal scarring. I will in the talk provide you with some more data on this.

**ANTI-HYPERTENSIVE MEDICATION IS INDICATED IN OBESITY-ASSOCIATED HYPERTENSION**

K. Tullus  
Great Ormond Street Hospital for Children, UK

There are, as I see it, two questions to answer here:

1. **How do you define that a child has got hypertension.**
2. **How do you treat obesity related hypertension.**

**Screening for hypertension:**

Should all children have their blood pressure measured regularly? Should all obese, but not other, children have their BP measured? A majority of guidelines do recommend that all children above a certain age should have regular BP check-ups. That does still not seem to happen in most parts of Europe. Why is that so? Are the guidelines wrong? Or are our colleagues not doing their job? It has during the last decade become clear that when evaluating screening you have to include both sides of the coin: The benefits and the down sides of the procedure. One well known example is breast cancer. We now know that this screening has majorly increased the number of diagnosed cancers with a suggested over diagnosis of one in three without any reduction of the incidence of advanced cancers. Could also BP screening have important down sides? The potential problems with blood pressure screening include over diagnosis and over treatment, unnecessary worry among children and families and costs to rule in or out true hypertension in children with on high blood pressure reading. Treatment of obesity related hypertension The basis of this treatment should be advice and help to get a healthy life style and to lose weight. Drugs are only the second line approach. I will in my talk review the outcome of this treatment approach.

**ANTITHROMBOTIC TREATMENT IN CHILDREN: PAST, PRESENT AND FUTURE**

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In children, anticoagulation is used for treatment of thromboembolic disease as well as prevention of thrombotic complications, for example to children with heart disease, adolescents after surgery, and critically ill patients with extracorporeal circulation. The incidence of thromboembolic disease is increasing as result of improved diagnosis, increased survival of children with severe underlying diseases and increased use of invasive procedures and instruments such as central venous catheters.(1) This higher prevalence of venous thromboembolic disease (VTE) is accompanied by an increased use of anticoagulants. Nowadays, the most frequent used anticoagulants in children include low-molecular-weight heparin (LMWH), unfractionated heparin and vitamin K antagonists (VKAs). (2) These anticoagulants were introduced in children before specific dose-finding, efficacy and safety studies were performed. Unfractionated heparin is a glycosaminoglycan, which functions as an antithrombotic agent by binding to and potentiating the activity of antithrombin. The heparin—antithrombin complex inactivates coagulation factors, especially thrombin and factor Xa. There are only two prospective studies of intravenous unfractionated heparin in children with 65 and 38 patients.(3, 4) In 1994, Andrew et al showed that infants needed higher maintenance dosages of unfractionated heparin than older children.(3) The LMWHs are derived from unfractionated heparin by chemical or enzymatic polymerization. They have shorter lengths of the polysaccharide chains resulting in a more profound effect on factor Xa than on thrombin. Compared to unfractionated heparin, LMWHs have a reduced capacity to bind to plasma proteins, endothelial cells and macrophages. Therefore, they have a greater bioavailability, a more predictable anticoagulant response, and longer half-life. Hence, LMWHs can be given subcutaneously, once or twice daily, with limited laboratory monitoring, which allows outpatient management. Therefore, LMWHs are considered the first line anticoagulant for both therapeutic and prophylactic treatment of thrombosis in children. Several dose-finding and pharmacokinetic studies
have been performed with various LMWHs. (5-9) VKA function by blocking the generation of vitamin K from its epoxide. Vitamin K is necessary for the addition of γ-carboxyglutamic acid residues to the coagulation factors II, VII, IX, and X. As a consequence, plasma concentrations of these factors are reduced in patients treated with VKA. They have one important advantage: they can be administered orally. However, these drugs have several limitations, including its narrow therapeutic index and multiple drug and food interactions, leading to the necessity of frequent monitoring and increased risk of bleeding. In children, most studies have been performed with warfarin. (10, 11) Alternative anticoagulants for children, which are not often used include argatroban, bivalirudin and fondaparinux. Bivalirudin and argatroban are parenteral direct thrombin inhibitors. Two prospective studies have been performed with bivalirudin in pediatric patients from 0-6 months and 6 months to 18 years with thrombosis. (12, 13) These studies showed early clot resolution in almost half of the patients. Argatroban was studied in 18 pediatric patients requiring an alternative to heparin due to documented or suspected HIT. (14) Fondaparinux is a synthetic, antithrombin-dependent inhibitor of factor Xa. Two pediatric studies investigated the dosages, pharmacodynamics and safety of Fondaparinux in children above one year of age. (15, 16) Direct oral anticoagulants (DOACs) are increasingly used in adults. Their direct and Betrixaban). They have proven to be safe and effective for treatment fixed dose without the necessity of laboratory monitoring, in addition to However, the use will probably rise in pediatric patients as these medications is limited, as studies have not been published yet. Moreover, the use will probably increase in pediatric patients as these anticoagulants have several advantages, including oral administration as a fixed dose without the necessity of laboratory monitoring, in addition to the efficacy and safety shown in adults. The first pediatric studies started in 2010, and results of phase III trials are expected in the coming years. A new era in pediatric anticoagulation has begun! References 1. Raffini L, Huang YS, Witmer C, Feudtner C. Dramatic increase in venous thromboembolism in children’s hospitals in the United States from 2001 to 2007. Pediatrics. 2009;124(4):1001-8. 2. Monagle P, Chan AK, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Gottlieb U, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e73S-801S. 3. 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Meta-analysis of the efficacy and safety of new oral anticoagulants in patients with cancer-associated acute venous thromboembolism. J Thromb Haemost. 2014;12(7):1116-20. OVERVIEW OF MECHANISMS AND OUTCOMES OF HYPERTENSION IN CHILDREN WITH OBESITY E. Wühl University of Heidelberg, Germany The prevalence of obesity is increasing worldwide. Between 1990 and 2010, the prevalence of overweight (Body mass index (BMI) 85th to 95th age- and sex-specific percentile or BMI >25 kg/m2) and obesity (BMI ≥95th percentile or BMI >30 kg/m2) increased by more than 50%. In 2010 almost 17% of children and adolescents in the US and up to 13% in Europe were classified as obese. A close correlation exists between BMI and blood pressure and the risk of having a higher blood pressure is increased already in children with BMI below the upper normal range. It is estimated, that for each 1 kg/m2 increase in BMI, systolic blood pressure increases by 1 mmHg. The estimated prevalence of hypertension in overweight or obese children and adolescents ranges between 4% to 14% and 23% to 37% respectively and obese children are up to 3.7 times more likely to have hypertension than non-obese children. Systolic blood pressure seems to be closer correlated to BMI than diastolic blood pressure, and overweight adolescents may have isolated systolic hypertension. Obese children also have a higher risk to present with white coat hypertension (elevated elevated office blood pressure, but normal 24-hour ambulatory blood pressure monitoring (ABPM)) compared to non-obese children and up to 50 % have masked hypertension (normal office blood pressure, but hypertension by ABPM criteria) or isolated nocturnal hypertension, conditions solely to be diagnosed by ABPM. Thus ABPM should be considered in all overweight and obese children and adolescents for screening of hypertension. Hypertension (systolic or diastolic blood pressure above 90th-95th age- and sex-specific percentile) in children is supposed to be mostly secondary. This still holds true for infants and younger children, however, the prevalence of primary hypertension - a condition formerly considered to be mainly present in adults - has increased considerably in school children and adolescents and is meanwhile estimated to account for up to 85-95% of cases. Nevertheless, also in obese children with presumed primary hypertension, secondary hypertension due to renoparenchymal or renovascular, cardiac or endocrine diseases has to be excluded. Obesity is linked to multiple comorbid conditions including cardiovascular disease, dyslipidemia, diabetes mellitus type 2, non-alcoholic steatohepatitis, or obstructive sleep apnea. Hypertension is the most common comorbidity identified in overweight or obese adolescents. The clustering of abdominal obesity, hyperglycemia, dyslipidemia and hypertension, has been described as ‘metabolic syndrome’. In combination with overweight and obesity, hypertension has a much higher risk of cardiovascular morbidity and mortality than isolated hypertension in normal-weight subjects. Even in normotensive children, obesity might be linked to increased left ventricular mass and left ventricular hypertrophy. The endogenous, familial and environmental factors influencing the risk for hypertension in obesity are manifold: a positive family history for hypertension, obesity or diabetes, a history of low birth weight, higher age and advanced pubertal status, as well as sedentary behavior with inadequate physical activity, poor sleep quality, nutritional high sodium and low potassium intake, dyslipidemia, disturbed glucose metabolism or chronic signs of
inflammation are potential predisposing factors for hypertension and cardiovascular disease. Also ethnicity seems to be an important influencing factor and children of African-American, Hispanic, Indian or Turkish descent were reported to have a higher risk of obesity-associated hypertension. The clustering of risk factors indicates a higher risk of end-organ damage. Obesity can be seen less as a symptom than a syndrome with diverse effects on body systems. With respect to hypertension, interactions with the endocrine and sympathetic nervous system are of particular interest. The hyperactivation of the sympathetic nervous system in obesity and the activation of the renin-angiotensin-aldosterone system are contributing to an elevation of blood pressure levels. In addition, not only salt-sensitivity but also salt-intake seems to be increased in obese children and adolescents and several proteins secreted by fat cells, mediating pro-inflammatory processes, may also be involved in the development of arterial hypertension. In this setting the identification of patients with a high risk for hypertension and cardiovascular disease is essential to allow timely diagnosis and treatment of hypertension and prevention of cardiovascular end organ damage. Tracking of hypertension from childhood into adulthood is strongest in adolescents > 15 years of age and it has been shown that the severity of hypertension during adolescence affects the risk of overall mortality. Furthermore, any evidence of subclinical cardiovascular pathology, regardless of the degree of blood pressure elevation, should always be considered a maker of high-risk disease in obese adolescents. Weight reduction is effective in reducing blood pressure and future cardiovascular morbidity and mortality. A BMI reduction of 0.25 SDS or greater may significantly reduce the risk not only for hypertension but also for dyslipidemia and other comorbid conditions. It has been demonstrated that reversal of obesity status prior to adulthood results in a risk reduction for hypertension in adulthood. The reduced risk was found comparable to those of subjects who never had been obese. With respect to the general impact of obesity not only on cardiovascular, but also on overall morbidity and mortality, stringent efforts are required to prevent or reverse overweight and obesity in youth.

ANTI-HYPERTENSIVE MEDICATION IS ALWAYS INDICATED IN OBESITY-ASSOCIATED HYPERTENSION - PRO

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Treatment of hypertension in obesity is as multifactorial as the underlying disorder. Weight reduction by life-style modification is a cornerstone of treatment and may result in a significant reduction of blood pressure and a reduction of cardiovascular and overall morbidity and mortality. However, the implementation and success of a reduction diet and exercise in children and adolescents strongly depends on patient motivation and family support and is extremely variable. To reduce the cardiovascular risk burden, pharmacological treatment of hypertension is indicated in any obese patients with severe hypertension or in subjects where life-style modification and weight reduction is not effective or does not result in timely blood pressure normalization. While the antihypertensive effect of the different antihypertensive drug classes (Angiotensin converting enzyme inhibitors (ACEI) or angiotensin-receptor blockers (ARB), beta blockers, calcium channel blockers and diuretics) is comparable, the spectrum of potential benefits and side effects suggests the use of ACEI or ARBs as first line medication. ACEI and ARBs are beneficial, as they have not risk of inducing diabetes or aggravating dyslipidemia, while beta-blockers may interfere unfavorably with carbohydrate and lipid metabolism and may increase the risk of weight gain and diabetes. Diuretics may increase the activity of the already activated sympathetic nervous and renin-aldosterone system in obesity. In view of the significantly increased cumulative risk for cardiovascular end-organ damage in obesity, blood pressure should be controlled timely and effectively, aiming for a blood pressure goal below the 90th percentile.

O1 SPACE-TIME CLUSTERING OF NECROTIZING ENTEROCOLITIS SUPPORTS THE EXISTENCE OF TRANSMISSIBLE CAUSES

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Problem Statement: Despite great efforts to prevent necrotizing enterocolitis (NEC) the incidence may in fact be increasing, and changes in the patient population over time seem to lead to changes in clinical presentation and risk factor spectrum as well. The presence of bacteria is an important prerequisite in the pathogenesis, but, rather than being caused by specific pathogens, inflammation and bacterial invasion are thought to be mediated through erroneous interaction between microbiota and innate immunity during colonization of the gut. There are, however, reports of episodic outbreaks of NEC, seasonal variation in incident rates, and clustering, suggesting a role for transmissible infectious agents or other environmental factors around the pregnant mother or newborn infant. In order to investigate evidence for such factors we have analyzed the occurrence of space-time clusters in Sweden over 23 years. Methods: A national register-based cohort of all children born between 1987 and 2009 in Sweden, diagnosed with NEC, was identified. The Knox test and Kulldorff’s scan method were used to analyze signs of space-time clusters at two geographical levels; the mother’s residential address and the delivery hospital. Time windows of seven, 14 and 21 days were used for closeness in time. Results: The Knox test showed clustering on hospital level in all studied temporal windows; seven days (p=0.022) 14 days (p=0.011) and 21 days (p=0.006), and Kulldorff’s scan method found seven significant clusters. On residential level, there was no indication of space-time interaction. When comparing two time periods, significant clustering on hospital level was found during 1987-1997, but not during 1998-2009. Conclusion: Space-time clustering was found on hospital level, but not on community level, suggesting a contagious environmental effect at and after delivery but not in the materno-fetal environment outside the hospital before birth. The decrease in clustering over time suggests that improved routines in neonatal care have minimized the risk of NEC precipitating contagions spreading between patients in the neonatal intensive care unit. The importance of such routines should not be forgotten while our efforts to bring down NEC incidence are directed towards other challenges.

O2 THE INVESTIGATION OF OCCUPATIONAL EXPERIENCE OF OBSTETRICIANS IN TERMS OF DRUGS USE IN PREGNANCY AND TERATOGENICITY

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Problem Statement: Drug use in pregnancy is a perinatal situation that can affect the child’s health and development in all stages of life. Nevertheless, maternal health situation should be also taken into consideration during pregnancy. There is no doubt that the investigation of maternal drug use in pregnancy may supply valuable information about the teratogenicity of drugs and the child health. In this study, the clinical experience of the obstetricians were investigated, especially how they perceive the risk of the teratogenicity of drugs and the perinatal complications in the babies of whose mothers used drugs in their pregnancies. Methods: The data are eliminated from face-to-face surveys performed to 30 obstetricians (response rate: 51.7%) who work in Northern Cyprus, between April-May 2016. There were questions about the demographic characteristics and the risks regarding the drug use in pregnancy. Results: The mean of
occupational experience in the obstetricians was 22.0±11.0 years. The doctors expressed that they diagnosed pregnancy in their patients at an average of 5.2±1.2 weeks and among the patients only 15.1% use drugs. The obstetricians also expressed that 33.9% of the pregnant women had the risk of teratogenicity. The obstetricians also categorized that the drugs they prescribed as “no risk”(75.5%), “low risk” (21.5%) and “moderate” or “high” risk (3%) groups. Seventy percent of the physicians also expressed that they had cases leading to spontaneous or medical abortion due to exposure to drugs. The most common 20 drugs were chemotherapeutics, where 45% were anti-microbial, and 15% were anti-neoplastic drugs. Among the obstetricians who participated in the study, 5 doctors (16.7%) stated that they had cases with birth anomalies and/or perinatal complications that occurred due to drug use in pregnancy. Conclusion: The results of this survey may point out the risk of birth defects occurring due to exposure to drugs during perinatal period are more common in the occupational experience of the obstetricians than that reported in the literature.

O3 INTER-RATER RELIABILITY OF USING COMFORT-B SCALE IN PEDIATRIC INTENSIVE CARE UNIT

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Problem Statement: COMFORT-B scale is a sedation level assessment tool to guide the sedation protocol in pediatric intensive care unit (PICU). However, there has never been a reliability test of COMFORT-B scale in Thailand. A cross-sectional study was conducted to determine inter-rater reliability of COMFORT-B scale at PICU of a university hospital in southern Thailand. Methods: Each pediatric patient in PICU who had no neuromuscular disorder and clinically stable were assessed by 2 independent nurses and a standardized person using COMFORT-B scale. All nurses were trained by the standardized person using learning resources from Erasmus MC-Sophia Children Hospital (30-minute-session). A bed number was randomly assigned by computer for each pair of nurses. Unit of analysis was an observation. Nurses were assigned into group 1 and 2 depending on the sequence at the randomization. Kappa statistics was used to determine inter-rater reliability between groups. Patient’s pain perceived by an observer was evaluated by visual analog scale (VAS). Correlation between groups was analyzed using Pearson’s correlation test. Results: There were 20 nurses participating. Thirty-six pairs of COMFORT-B assessment were performed. According to standardized person, most patients (76%) were optimally sedated and 18% were over-sedated. Only observations assessed within 3 minutes apart were analyzed. Overall, inter-rater reliability between standardized person and group1 was 0.72 and 0.69 in group2. In subgroup analysis, kappa could reach 0.8 in both groups. In subgroup analysis, kappa could reach 0.8 in both groups. Patient reliability between standardized person and group1 was 0.72 and 0.69 in group2. In subgroup analysis, kappa could reach 0.8 in both groups. Patient’s pain assessed by visual analog scale was significantly different between group1 and group2 (t: 2.297, p: 0.023) than children with ASD. In ASD group, when we compared PLR levels were similar. Healthy children had significantly lower neutrophil number (t: -2.376, p:0.011) but higher platelet number (t: -2.251, p:0.026) and lymphocyte number (t: -2.297, p:0.037) than children with ASD. In ASD group, when we compared NLR, PLR and all blood count parameters in terms of age, sex and subtype, there were no significant differences. Conclusion: As far as we are aware this is the first study that evaluates NLR and PLR values in children with ASD. As a strength of this study, examining young drug-naïve sample reduces the role of illness burden, psychocthopic drug usage and comorbid medical diseases on inflammatory variables. Also our study has the largest sample size among the studies evaluating neuroinflammation in ASD. The main result of this study is increased NLR levels in ASD. This finding confirm the involvement of neuroinflammation in the underlying pathophysiology of ASD. In this study, although white blood cell numbers were similar in each groups, children with ASD had higher neutrophil number and lower lymphocyte, platelet numbers. These findings indicate an imbalance of white cell distribution in ASD patients. Further studies are needed for a better understanding of the inflammatory dysregulation in the etiology of ASD.
cases were defined as children initially treated as melioidosis but culture or serology results were all negative. Results: There were 145 patients who had clinically suspected melioidosis and confirmed cases were found in 27 patients. Comparing the confirmed cases to suspected cases, the median (IQR) ages [8.4 [3.7,12.4] vs 8.0 [3.9,11.4] years), the proportions of patients who had underlying diseases including diabetes mellitus, thalassemia, or renal disease, fever, hepatomegaly, lymphadenopathy, the median (IQR) white blood cell counts [12,700 [9,200,18,600] vs 10,200 [5,975,15,632] cells/mm3) and hemoglobin levels [9.9 [.0,10.5] vs 10.1 [8.8,11.7] g/dL) were not significantly different between the two groups. The proportions of patients who had hepatic and/or splenic abscess (44.4% [8.8,11.7]) in the confirmed cases than in the non-confirmed cases. Multivariate analysis found that patients who had hepatic and/or splenic abscess had a higher risk and who had splenomegaly without abscess had a lower risk of having melioidosis with an odds ratio (95% confidence interval) of 5.4 (2.0, 14.1) and 0.2 (0.0-1.9), respectively. Conclusion: Hepatic and/or splenic abscess is a good clinical predictor for pediatric melioidosis. Patients who have clinically suspected melioidosis should be performed hepatic and splenic ultrasonography even though they have no abdominal tenderness or hepatosplenomegaly and those with hepatic and/or splenic abscess should be treated initially as melioidosis while waiting for the culture or serologic test results.

O6
HOW MUCH DO PARENTS KNOW ABOUT ADHD?
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Problem Statement: Attention-deficit hyperactivity syndrome (ADHD) is a neurodevelopment disorder characterized by an ongoing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. The aim of this study was to investigate indirectly how effective are pediatricians in explaining parents what ADHD is and how much they have learned about it. Methods: A questionnaire with 24 questions was applied to 67 parents of children with ADHD. The first 16 questions were about definition, cause, and characteristics of this syndrome and the last 8 questions were about the treatment. The results were analyzed using the SPSS program and chi-square test. Results: Sixty-seven questionnaires were completed by 53 mothers and 14 fathers (70.1% and 20.9%). We found that all parents (100%) are knowledgeable about the definition of ADHD and are aware of the goal of treatment. The issues that most failed were about the memory (53.7%) and organizational capacities of these children (32.8%), the cause of this disorder (37.3%) and about psychostimulants’ side effects (43.3%). Parents with more schooling answered correctly to more questions (p<0.05). Conclusion: This data show that parents remain in doubt about many aspects of ADHD, especially with regard to cause, treatment and other specific characteristic of this syndrome. Since psychoeducation of parents about their children’s condition is a key factor of treatment, the pediatric neurodevelopmental clinic is planning workshops with groups of parents to promote their knowledge in this matter.

O7
CHANGING ATTITUDES IN PAEDIATRIC VASCULAR ACCESS FOR HEMODIALYSIS
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Problem Statement: In the UK, most children commence haemodialysis (HD) via a central venous catheter (CVC) and few will ever have dialysis via an arterio-venous fistula (AVF). There is growing evidence that a ‘fistula-first’ policy is just as relevant in children as in adults with chronic renal failure. Many barriers (technical, psychological, cultural) exist to running a haemodialysis programme based on AVFs. However, these can be overcome by developing strategies involving parents, children, medical and nursing staff in the care of children on long term HD. We present our experience and lessons learned from developing a dedicated vascular access clinic for children on haemodialysis at Great Ormond Street Hospital, London. Methods: An integrated multi-disciplinary clinic was set up to provide paediatric vascular access services for the London area and beyond. The clinic consists of a vascular access/transplant surgeon, a paediatric nephrologist, dialysis specialist nurse and ultrasound angiologist. Results: In a 2-year period 23 patients (56% male and 44% female) were seen in the integrated clinic. 12 new AVFs were formed and 11 existing AVFs were followed-up. These consisted of 12 brachio-cephalic, 9 brachio-basilic and 2 radio-cephalic vein AVFs. At AVF formation the median age was 9.4 (3-17) years with a median weight of 26.9 (14-67) kg respectively. Pre-operative ultrasound mapping of the upper extremity veins (using a simple tourniquet) and arteries showed a maximum median diameter of 3.0 (2.5) mm and 2.7 (2.0–5.3) mm, respectively. Maturation scans 6-weeks after AVF formation showed a median flow of 1277 (432-2880) ml/min. AVF patency and successful needleing were achieved in all patients. For the 11 children with existing AVFs the maximum median vein diameter was 14.0 (8.0-26.0) mm with flow rates of 1781 (800-2971) ml/min at a median 153 weeks after AVF formation. The primary maturation rate of new AVFs was 82% (9 AVFs). Two cases required angioplasty to achieve balloon-assisted primary maturation of 100%. One child received a transplant before the AVF was used. The AVF function achieved a median kT/V of 1.97 (1.8-2.9) and a urea reduction ratio of 80.7 (79.3–86%). Conclusion: Negotiating chronic renal failure in childhood involves a ‘revolving door’ of dialysis and transplantation. A CVC may be familiar and perceived as ‘convenient’, but an AVF is the best long-term option for children requiring haemodialysis, and can be achieved with a multidisciplinary approach.

O8
ANOMALOUS GAIT: A VERY RARE MYOPATHY
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Problem Statement: Developmental screening is a central concern of paediatricians. Postural control and the ability to walk are crucial for quality of life and functional independence. Gait disturbances must be promptly evaluated so that an early intervention can be established. Methods: Clinical Case: A three-year-old girl presented with frequent falls, unstable gait and a different walking pattern. She began walking independently at 24 months of age; the other developmental milestones were all met appropriately. Her paternal aunt was hypotonic (died at three months of age of pneumonia). At physical examination, facial hypotonia, limitation of eyes’ abduction, lower limbs proximal weakness with positive Gower’s sign
and absent patellar and Achilles reflexes were noted. Muscular enzymes testing (creatinine phosphokinase, aldolase and myoglobin) were normal. A deltoid muscle biopsy revealed type 1 fibres' hyptrophy and type 2 hypertrophy, centrally placed nuclei and sarcoplasm with marked basophilia. These findings are compatible with centronuclear myopathy. Genetic testing detected ryanodine receptor type 1 (RYR1) deficit caused by heterozygous RYR1 mutations c.12063_12064dup, c.13672C>T and c.7027G>A.

Results: A diagnosis of centronuclear myopathy secondary to RYR1 deficit was established and the child is currently in treatment with physiotherapy and swimming. Genetic counselling was offered to the family. Conclusion: Centronuclear myopathy is an inherited neuromuscular disorder characterized by centrally placed nuclei in muscle biopsy, as our patient presented. Since this is not pathognomonic, clinical features are necessary for the diagnosis. The onset is usually at birth, with neonatal hypotonia and weakness (respiratory failure can occur). This was not the clinical presentation in the case reported, with delayed motor development and external ophthalmoplegia being the key to the diagnosis. Multiple genetic mutations may be involved in centronuclear myopathy. RYR 1 gene mutations are a rare cause, but its’ incidence is not known. This gene is also involved in malignant hyperthermia so, a cautious approach is determinant if the patient needs a general anaesthesia.

**O9 NEONATAL PHOTOTHERAPY - TURQUOISE IS THE NEW BLUE**

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Problem Statement: Phototherapy for hyperbilirubinaemia has been used for neonates for almost sixty years and has also been adapted for chronic conditions such as Crigler-Najjar Syndrome. The original choice of fluorescent lamps had a spectral output which overlapped the assumed peak of the absorption spectrum of bilirubin bound to Human Serum Albumin (HSA) at “about 460nm”. This spectrum was based on ‘in-vitro’ experiments. It is estimated that more than 200 million babies worldwide have been treated in much the same way since 1958 but a growing body of opinion is forming that longer wavelengths would be just as effective and possibly safer, especially for very premature babies and for long term treatment of chronic conditions. Methods: An extensive literature search was undertaken. Key researchers in this field were contacted for discussion. A further study of the photochemistry of bilirubin and the physiology of neonatal jaundice was undertaken in order to follow the more complex papers encountered. Results: Theoretical papers based on mathematical models showed that longer wavelengths in the turquoise region of the visible spectrum should be at least as effective at treating neonatal hyperbilirubinaemia as the shorter blue wavelengths currently in use in clinical treatment systems worldwide. Clinical studies using these wavelengths have shown that this is indeed the case. Conclusion: Manufacurers should introduce LED-based phototherapy units which have a narrow band spectrum having a peak wavelength in the range 480 to 490nm. This will be at least as effective at treating neonatal hyperbilirubinaemia but will avoid the possible harmful effects of shorter wavelength blue light.

**O10 SUCCESSFUL USE OF RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR (R-TPA) FOR MANAGEMENT OF CHYLOTHORAX ASSOCIATED WITH CENTRAL VENOUS THROMBOSIS AFTER NEONATAL CARDIAC SURGERY**

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Problem Statement: Postoperative chylothorax is a frequently encountered pathology occurring in up to 5% of patients undergoing surgery for repair of congenital heart disease. Neck vein thrombosis can be associated with chylothorax and may contribute to its severity and duration. Furthermore, neck vessel thrombosis resulting in permanent vessel occlusion may hinder future management, diagnostic studies and cardio-surgical interventions. Methods: In this case report we are describing a neonate who developed chylothorax on the 7th post-operative day following open-heart surgery. The chylothorax was linked to venous thrombosis in the cannulated right internal jugular vein with thrombus extending to the right atrium, diagnosis was made by bedside ultrasound. Results: After using low dose tissue plasminogen activator (r-TPA) infusion, the thrombi disappeared and the chylothorax resolved, with no complications.

**O11 EFFECT OF GUIDELINES BASED MANAGEMENT ON THE EARLY POST-OPERATIVE OUTCOME AFTER BLALOCK- TAUSING SHUNT**

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Problem Statement: Modified Blalock- Tausing shunt (MBTS) is a palliative procedure in cyanotic heart diseases to facilitate blood flow to the lung (1), though it showed significant post-operative mortality and morbidity especially in the neonatal group. to master the post-operative management and minimize complication, mortality and morbidity, we designed and implemented executive guidelines to maintain patients respiratory and hemodynamically stable especially during the critical early post-operative period. Aim of our study to evaluate the patient outcome after implementation of these guideline in our center. Methods: We conducted a retrospective chart review analysis of all children who underwent MBTS since year 2000 till December 2015, we excluded cases of...
From August to October 2015 by using retrospective cohort study toward postoperative course and outcome.

6.25) (p 0.2). Conclusion: This study prove that protocol based management of patients after MBTS can help to improve the postoperative course and morbidity after guidelines implementation. The ventilation time, reintubation rate, inotropic support duration, and postoperative complications were significantly lower in (group A), there was a trend of higher mortality in group B (15.7% VS 8%) (p 0.5), but it was more obvious in the neonatal patients group (19.41% VS 6.25) (p 0.2). Conclusion: This study prove that protocol based management of patients after MBTS can help to improve the postoperative course.

O12
PREVALENCE OF INFECTION IN CHILDREN WITH CHOLESTASIS ADMITTED TO CIPTO MANGUNKUSumo HOSPITAL 2010-2015
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Problem Statement: Infection is one of the most common comorbidity and complication found in children with cholestasis. This condition may adversely affect management of the disease and increase mortality rate among children with cholestasis. Methods: The aim of this research is to identify prevalence of infection in children with cholestasis admitted to Cipto Mangunkusumo Hospital 2010-2015. This research was conducted from August to October 2015 by using retrospective cohort study toward cholestatic children age 0-5 years old through medical records. Results: From 97 patients included, prevalence of infection in children with cholestasis was 66% (n=64). There are 35 children (36%) who manifested more than one type of infection. Infectious diarrhea (41.2%, n=40) and urinary tract infection (28.9%, n=28) were the most common types of infections found in children with cholestasis. The other types of infections found in cholestatic children were sepsis (2 0.6%, n=20), pneumonia (19.6%, n=19), and spontaneous bacterial peritonitis (13.4%, n=13). Conclusion: Prevalence of infection in children with cholestasis admitted to Cipto Mangunkusumo Hospital was high. Multiple infections were more common than single type of infection found in children with cholestasis. The most common type of infections were infectious diarrhea and urinary tract infection. Other types of infections were sepsis, pneumonia, and spontaneous bacterial peritonitis.

O13
THE STRONGKIDS NUTRITIONAL SCREENING TOOL IN HOSPITALIZED CHILDREN OF A PORTUGUESE GENERAL HOSPITAL
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Problem Statement: Children and adolescents who are admitted to the hospital have an increased risk of developing malnutrition, especially those with an underlying disease. STRONGkids, developed by Hulst Jessie et al, is a nutritional risk screening tool for hospitalized children, allowing early identification of malnutrition and early nutritional intervention. The aim of our study was to evaluate nutritional risk of children admitted to the paediatric ward of a Portuguese General Hospital, by applying the nutritional risk screening tool STRONGkids. Methods: A prospective observational study was conducted in the paediatric ward from June to September 2016 and consisted in the nutritional risk assessment of the children through the use of STRONGkids screening tool. The analyzed variables consisted of demographic data, length of hospital stay, measurements of weight, length and brachial perimeter and the STRONGkids items: (1) subjective global assessment (2) high risk disease (3) nutritional intake and losses (4) weight loss or poor weight increase. SD-scores < -2 for weight-for-height and height-for-age were considered to indicate acute and chronic malnutrition respectively. Data processing in SPSS® 22. Results: A total of 150 children met the inclusion criteria, with a median age of 7.6 years (range 25 days - 17.9 years) and no predominance of gender. The median length of hospital stay was 2 days (range 1-20 days). During hospitalization, about 30% of the children presented weight loss and of these, 20.6% (n=31) had a medium risk score. Height and brachial perimeter measurements on admission were available in 87% and 93% of children, respectively. New anthropometric evaluation was carried out in 6% (n = 9) of children, being the most of it (n=6) in children over 4 days of hospitalization. The percentage of children with acute malnutrition was 6.2% and with chronic malnutrition was 4%. Regarding Strongkids Score, 57.4% (n = 86) of children evaluated showed a medium risk score, 42% (n = 63) low risk and 0.7% (n=1) high risk. Concerning items from the STRONGkids, 34.7% (n = 52) of children had an underlying disease, mostly, 76% (n=39), a major surgery. About 4.7% of children were referred to the nutrition unit, and in all of them an individualized nutritional plan was made. The referral to Paediatric Dietary consultation was held at 57% (n = 4) of cases. Conclusion: The study applied a simple nutritional risk screening tool, easy to include in the paediatric ward and that can ensure early identification of those children at nutritional risk and therefore ensure early nutritional interventions. In our study, 6.2% of children presented with acute malnutrition and more than half of the children evaluated presented a medium nutritional risk score. Referral to nutrition unit occurred in 4.7% of children. Therefore, the authors concluded, that it is necessary to sensitize professionals to the importance of implementing more consistently the assessment of nutritional risk of children and adolescents admitted to the hospital.

O14
PIGMENTED HYPERTRICHOTIC DERMATOSIS AND INSULIN DEPENDENT DIABETES: MANIFESTATIONS OF A RARE SYNDROME
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Problem Statement: Type 1 diabetes mellitus is characterized by dysregulation of the immune system leading to inflammation and selective destruction of pancreatic beta cells. It may also be part of a syndrome occasionally involving hair and skin abnormalities. We report a case with insulin-dependent diabetes, severe exocrine pancreatic deficiency, pigmented hypertrichotic skin patches with induration and chronic inflammation. Methods: We report a case with insulin-dependent diabetes, severe exocrine pancreatic deficiency, pigmented hypertrichotic skin patches with induration and chronic inflammation. The patient developed diabetes mellitus at the age of 8 years and then presented at the age of 14 year with hypertrichosis and hyperpigmentation on the upper inner thighs, with involvement of the genitalia, trunk, and limbs. The physical examination showed an orbital proptosis, musculoskeletal abnormalities, inguinal lymphadenopathy and hepatosplenomegaly. Results: The patient had elevated laboratory markers of inflammation included an elevated ESR, CRP, and raised serum immunoglobulin levels. He had had a positive anti-GAD 65 antibody titer consistent. Biopsy specimens from the skin showed...
a chronic inflammatory cell infiltrate. Conclusion: The chronic inflammatory response is highly suggestive of some form of immune dysregulation. These inflammatory pigmented skin lesions represent a unique dermatosis associated with diabetes mellitus and systemic disease. Genetic studies to search for a candidate gene are currently in progress.

O15
PARRY-ROMBERG SYNDROME: A CASE REPORT
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Problem Statement: Parry Romberg syndrome (PRS), is a rare degenerative disease characterized by slowly progressing unilateral facial atrophy. The etiology of PRS is still not well known because of its rarity. This report presents one case with classical clinical, radiographic, histological findings and the treatment of progressive hemifacial atrophy. Methods: A 22 year old, consulted for a right progressive hemifacial atrophy that lasted for 3 years. The physical examination revealed a hemifacial atrophy non-indurated interesting all the right hemifacial without sclerosis, a frontal linear “en coup de sabre”, a slight deviation of the mouth and nose to the side reached, an achromic small macules on the neck’s anterior right side, an atrophy of the right half of the tongue and a scarring alopecia plaque on the right side of the scalp. At 2-year follow-up, the symptomatology had progressively worsened. Results: PRS is an uncommon degenerative condition characterized by a slowly progressive atrophy that is generally unilateral. PRS can coexist with several developmental deformities. This syndrome often occurs during the first and second decades of life, after which the atrophy slowly progresses over several years. Our case presented clinically and confirmed histopathologically the features of PRS. Treatment is still unsatisfactory and limited. However, cosmetic revision is not recommended until the progression of the illness is complete.

Image:

Conclusion: PRS is a developmental disorder with various manifestations and deformities. This case report documents the classical features of this rare entity, contributing towards the understanding of PRS.

O16
DOES CLINICAL GOVERNANCE APPLY TO THE ADVANCE CARE PLANS?
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Problem Statement: Does Clinical Governance Apply To The Advance Care Plans? Background: The mainstay for the Advance care plan (ACP) documentation in the United Kingdom, is a policy statement issued by the working group for the Child and Young Person’s Advance Care Plan Collaborative. This includes pro forma, information leaflets and current laws related to this very sensitive issue. Aim: To standardise the practice of Advance care plans in the West Midlands and identify potential areas of improvement. Methods: We surveyed Paediatric Consultants in the West Midlands Deanery using an online tool “Survey Monkey”. Results: 40 consultants have responded to the survey request. 100%, of them have confirmed using Trust approved proforma for doing ACPs. 87%, reported that ACPs were initiated by the lead clinician. 92%, reported that they keep the General Practitioner, Ambulance and Hospice in-loop about the ACP and review them annually. 87%, of the responders currently have fewer than 9 patients on the ACPs. 50%, reported spending about 2-4 hours in preparing an ACP. On the flip side, only 45% reported using an Incident reporting system for documenting deviations from the ACPs. Astonishingly, over 80% reported that ACPs are not audited in their trust. Conclusion: Our Survey has revealed that all the responding consultants practising in the region are familiar with the ACPs and use approved proforma to do so. Most of the ACPs are initiated by the lead clinician and shared with the other relevant agencies. Just under half of the responders use Incident reporting system to document deviations from the plan. Over three quarters of the responders reported that the ACPs are not audited in their trust. Recommendations: Considering the enormous ethical and legal implications, we strongly feel that the process of Advance care planning should be robust. Thus, Clinical Governance tools like Audit & Incident Reporting should be used more efficiently to facilitate this.

O17
SYSTEMATIC REVIEW OF METHYLPHENIDATE HARMs FOR CHILDREN AND ADOLESCENTS WITH ADHD
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Problem Statement: The use of methylphenidate for ADHD in children and adolescents has increased during the past decade. However, in our systematic review of randomised clinical trials (RCTs), we found that the very low quality of the evidence made it uncertain as to whether methylphenidate offers more benefits than harms compared with placebo or no treatment. Because of the limitations of identifying and reporting adverse events in RCTs, a thorough systematic assessment of harms reported in non-randomised studies was conducted. Methods: This review was conducted according to Cochrane guidelines for systematic reviews on harms and based on a comprehensive search for literature in scientific medical databases, unpublished data from the U.S. Food and Drug Administration and European Medicines Agency, and data received from pharmaceutical companies. The primary outcome is the number of serious adverse events. The secondary outcomes are all other adverse events. Results: We included 256 studies: 6 comparative cohort studies (n=1134); 4 patient-control studies (n=2455); 176 cohort studies (n=2 844 243); and 70 patient reports or series (n=206). The comparative cohort studies and the patient-control studies were assessed for quality by using the ROBINS-I tool (Risk of Bias In Non-randomised Studies - of Interventions). Five studies were found to be critical risk of bias, and five were found to be at critical risk of bias. All the cohort studies and reports can be regarded as high risk of bias studies due to no control group. Methylphenidate compared to no intervention was associated with an increase in serious (e.g. life threatening) adverse events (18.0 % vs 0.0 %; odds ratio (OR) 5.45, 95% CI 3.21 to 95.2; 2 studies, 1,362 participants (critical risk of bias). The random-effects meta-analysed proportion of methylphenidate-exposed participants with serious adverse events in 51 cohort studies including 162,434 participants was 1.2% (95% CI 0.7% to 2.0 %). The random-effects meta-analysed proportion of participants having methylphenidate withdrawn due to serious adverse events in 5 cohort studies including a total of 645 participants was 1.5% (95% CI 0.7% to 3%). The random-effects meta-analysed proportion of participants having methylphenidate withdrawn due to adverse events of unknown seriousness in 22 cohort studies including a total of 3,708 participants was 7.3% (95% CI 5.3% to 10%). The random-effects meta-analysed proportion of methylphenidate-exposed participants with non-serious adverse events in 49 cohort studies including 14,006 participants was 51% (95% CI 41% to 61%). Conclusion: The present data on serious adverse events and withdrawal of
methylphenidate due to serious adverse events and adverse events of unknown seriousness show high proportions, especially when considering the very low quality of evidence on benefits as well as the costs. We also observed a high proportion of participants with one or more non-serious adverse events. Harms are generally underestimated in non-randomised studies at high risk of bias. Accordingly, the reported data likely represents underestimates. Before physicians start methylphenidate administration, they need to inform patients and parents about the low quality of evidence for any benefits as well as the risks of adverse events.

O18
RADIO FREQUENCY CATHETER ABLATION OF TACHYARRHYTHMIA IN SMALL CHILDREN
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Problem Statement: The aim of the study was to evaluate the safety and efficacy of RFA in critically ill small children (< 1 year of age) with drug resistant tachycardia accompanied by arrhythmogenic cardiomyopathy and heart failure. Methods: Material: The study included 25 patients aged 5.1 ± 3.6 months. Wolff-Parkinson-White syndrome and atrial tachycardia were detected in sixteen (60 %) and ten (40 %) patients, respectively. Patients with structural heart pathology, including congenital heart diseases and laboratory-confirmed myocarditis, were excluded from the study. Results: The indication for RFA was drug refractory supraventricular tachycardia (SVT) accompanied by arrhythmogenic cardiomyopathy and heart failure. Unsuccessful ablation was observed in two 1-month-old patients who underwent successful ablation 3 months later. The follow-up periods ranged from 0.3 to 10 years (average 5.2 years). Only two patients (10%) had tachycardia recurrence 1 and 2 months after RFA, respectively. The RFA success rate was 92%. The study did not show any procedure-related complications. Heart failure disappeared within 5–7 days after RFA. Complete normalization of cardiac chambers sizes was documented within 1 month after effective RFA. A three-dimensional CARTO system was used in three patients with body weight > 7 kg. The use of the CARTO system resulted in a remarkable decrease of the fluoroscopy time without vascular injury or other procedure-related complications in all cases. Conclusion: Our study suggested that RFA may be considered as the method of choice for SVT treatment in small children when drug therapy is ineffective and arrhythmogenic cardiomyopathy progresses.

O19
MODELLING THE OPTIMAL TARGET AGE GROUP FOR SEASONAL INFLUENZA VACCINATION IN JAPAN
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Problem Statement: Selecting the most cost-effective vaccination policy for seasonal influenza is important to obtain optimal health benefits with the same resources. In Japan, the current influenza vaccination programme is selective, targeting individuals over 65 years of age and those over 60 years who are at higher risk of severe influenza, similar to many other developed countries. On the other hand, epidemics of influenza in the population are likely to be mainly driven by children, providing other potential vaccination strategies. In this study, we consider the most effective target age group for a seasonal influenza vaccination programme in Japan. Methods: We used demographic, virological, clinical, and epidemiological data to establish an age-stratified transmission model that reproduces a seasonal influenza epidemic in Japan. We constructed deterministic compartmental SEIR (susceptible-exposed-infectious-recovered) model with data from 2012/13 influenza season in Japan in order to compare different vaccination scenarios. Bayesian inference with MCMC (Markov Chain Monte Carlo) method was adapted to parameter estimation and model fitting. Results: A scenario of high vaccine coverage (amount to 90% in the end of the year) amongst children (0-14 years of age) demonstrated the largest reduction in influenza cases (13,665,455 cases reduced on average over one season), which corresponds to a 73.5% all-age reduction compared to the original vaccination scenario. An adult only (15-59 years of age) high coverage scenario reduced 9,008,580 cases (a 48.4% all-age reduction) and an elderly only (age over 60 years) high coverage scenario reduced by 1,306,279 cases (a 7.0% all-age reduction), respectively. Conclusion: With regard to incidence reduction, a vaccination programme which targets children 0-14 years of age is predicted to have much larger epidemiological impact than those targeting adult or elderly only populations. Predicting reductions in hospitalisations and deaths and a cost-effectiveness analysis of alternative vaccine strategies will be future challenges.
Problem Statement: Irrational utilization of antibiotics is a topic that irritates the whole world in terms of its potential consequences. Dentistry is a healthcare field that has compliance problems with the principles of rational use of antibiotic. The aim of the present study was to determine the antibiotic prescribing pattern of dentists to the children. Methods: The study was designed retrospectively by using the prescription data of dentists whose registered in the Prescription Information System of the Turkish Medicines and Medical Devices Agency between January 1, 2013 and August 31, 2015. A total of 2,918,321 antibiotics were prescribed for dentists for children (<18-year). ATC (Anatomical Therapeutic Chemical) was used to elucidate antibiotics, while ICD-10 (International Classification of Disease) classification was used to analyze the diagnoses in detail. Results: Total number of written prescriptions to children was 2,898,210, the number of drugs "per prescription" (PP) was 1.96 and the number of antibiotics PP was 1.01. While "amoxicillin + enzyme inhibitors" (J01CR02) was the most common prescribed antibiotic (67.4%), this was followed by amoxicillin (J01CA04), (11.0%) and sultamicillin (J01CR04), (5.6%). The most common three indications prescribed antibiotic were K04.7 coded "periapical abscess without sinus", Z01.2 coded "dental examination", and K02 coded "dental caries". Prescriptions were examined by monthly in calendar years (2013 and 2014) that could be examined each month in the study period. In these years, the antibiotics were more prescribed in November and December than the other months, respectively. Conclusion: This is the first pharmacoepidemiologic study on antibiotic prescribing patterns of dentists to the children do not have enough rational.

PO2 RELIABILITY TESTING OF JM-103 AND JM-105 TRANSCUTANEOUS JAUNDICE METERS FOR A HOSPITAL AND COMMUNITY BASED NEWBORN SCREENING PROGRAM, A LOOK BEHIND THE SCENE

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Problem Statement: Universal screening for newborn jaundice with total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) is recommended. Screening is performed by 72 hours of age and regular clinical assessment is advised in the newborn period. The aim of this study is to determine reliability of 6 JM-103 and 9 JM-105 TcB meters to be integrated into a hospital- and community-based universal newborn jaundice screening program. Methods: Ethical approval was obtained for this prospective observational study. A total of 544 Infants with 739 visits under the age of 14 days, greater than or equal to 35 weeks gestation, who had not received exchange transfusion or phototherapy were eligible for the study. The study infants received the institutional standard for screening with TSB. On each visit, each baby had 3 readings made per meter, with 2 meters. Meters remained in circulation until a minimum of 5 infant visits were recruited per meter in 3 TcB ranges (<150, 150-250, and >250 μmol/L). Meter data was excluded if TcB was not measured within 2 hours of TSB collection. Descriptive statistics was used to summarize data. A student’s t test was used to compare mean TcB and TSB. Lin’s concordance, and hierarchical clustering analysis were applied to determine agreement between mean TcB and TSB as well as similarity in performance among meters. Results: Parallel box plots describe within- and between-meter variability and bias. A hierarchical clustering method is used to organize meters to cluster meters with similar precision (Pearson correlation) and accuracy (bias correction factor). Both dendrogram and side-by-side box plots show that two meters need more attention to use in practice due to the concerns with false negatives. Conclusion: Reliability varies from meter to meter. Meters should undergo testing to determine compatibility prior to integration into a hospital- and community-based universal jaundice screening program.

PO3 RETROPERITONEAL PARAGANGLIOMA: A RARE CAUSE OF HYPERTENSION

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Problem Statement: Paragangliomas are rare tumors in the pediatric age that derive from sympathetic tissue of extra adrenal location or parasympathetic tissue. Some of these tumors secrete catecholamines and are a rare cause of hypertension. Methods: The case of an adolescent with a paraganglioma is described. Results: Female adolescent, 14 years old, with no relief personal history. Referred to Pediatric consultation for episodes of holocranial headache associated with blurred vision with 6 months of evolution. The physical examination was normal. The brain magnetic resonance imaging was normal. At the visit, stage 1 hypertension was detected and confirmed with ambulatory blood pressure measurement, without nocturnal dipping. The analytical study (blood count, urea, creatinine, electrolytes, fasting glucose, Plasma cholesterol (total, HDL and LDL) and triglycerides, Urinalysis and microalbuminuria), chest X-ray, electrocardiogram and echocardiogram were normal. Renal echography revealed "heterogeneous mass in contiguity with the left renal sinus with 5.6 cm with cystic and necrotic areas and with internal vascularization". The abdominal computed tomography revealed "retroperitoneal lesion in the medial side of the left perirenal space, totally exophytic, multiloculated, with irregular wall and areas of parietal thickening with fine and gross septations with a maximum diameter of 5.5 cm". The anamnesis revealed that her mother had undergone surgery for a jugulo-tympanic paraganglioma. Catecholamines were required in the urine for 24 hours. Due to the suspicion of a retroperitoneal paraganglioma, the patient was referred to the Portuguese Institute of Oncology of Porto, where she underwent surgical excision of the lesion. The anathomopathological diagnosis confirmed the diagnosis of sympathetic paraganglioma. Conclusion: Although rare in the pediatric age, paragangliomas represent the most common endocrine tumor. The biochemical and imaging diagnosis are essential. After the diagnosis, a genetic study is recommended for its relevance in the approach and follow-up of patients. The treatment consists of surgical excision, achieving the complete remission in about 90% of the cases.
Problem Statement: Vitamin D is unique among vitamins because in addition to its effects on phosphocalcic metabolism, vitamin D deficiency is associated with an increased risk of developing other non-bone diseases.

Methods: Three cases with vitamin D deficiency are described. Results: Male child, 17 months old, referred to the emergency room with febrile seizure. The physical examination was normal. The laboratory study revealed hypocalcemia (calcium 5.7 mg / dL, ionized calcium 0.58 mmol / L). Parathyroid hormone levels were elevated (523.6 pg / mL) and had a severe deficiency of 25-hydroxyvitamin D (3 ng / mL). In nutritional history irregular vitamin D supplementation was detected during the first year of life and a daily milk intake of less than 500 mL. Initiated supplementation with vitamin D3 (cholecalciferol) and calcium carbonate and after 6 weeks of treatment the values normalized. Female child, 21 months old, practicing vegetarian diet since the second year of life. The laboratory study revealed hypocalcemia (calcium 5.7 mg / dL, ionized calcium 0.58 mmol / L). Parathyroid hormone levels were elevated (523.6 pg / mL) and had a severe deficiency of 25-hydroxyvitamin D (3 ng / mL). In nutritional history irregular vitamin D supplementation was detected during the first year of life and a daily milk intake of less than 500 mL. Initiated supplementation with vitamin D3 (cholecalciferol) and calcium carbonate and after 6 weeks of treatment the values normalized. Adolescent male, 14 years old, with no relief pathological history. Occurrence of tibia fracture in a jump during basketball practice. He performed a laboratory study that revealed a deficiency of 25-hydroxyvitamin D (10.5 ng / mL). Initiated vitamin D3 supplementation and after 6 weeks of treatment the values normalized. Conclusion: Several international studies and publications enhance the importance of vitamin D supplementation in pediatric age. These three clinical cases aim to alert to inadequate vitamin D supplementation and decreased sun exposure that occurs in different countries and the need to protocol recommendations on vitamin D supplementation and the need to monitor its deficit.
Problem Statement: Vulvovaginitis is an inflammatory disease of the vulvar and vaginal area. Vulvovaginitis of non-specific etiology is very prevalent (up to 75%) among prepubertal and preschool girls. The most annoying and relevant symptoms are pruritus and burning. Zelesse® an intimate hygiene wash solution, based on Chamomile, Burdock and Aloe Vera, with soothing, antipruritic and antiseptic properties, may be effective in the symptomatic relief of non-specific vulvovaginitis in girls. The aim of this study was to evaluate the efficacy, tolerability and acceptability of Zelesse® in the relief of non-specific vulvovaginitis in girls. Methods: This is a prospective, observational and multicenter clinical study. Girls aged 2 to 8 years with symptoms and signs of non-specific vulvovaginitis received Zelesse® as single treatment, once or twice daily during 15 (+/-5) days. Symptoms and signs were individually evaluated at baseline and after treatment using a validated scale. The Global Symptom and Sign Score (GSS), a composite score of symptoms and signs, was calculated in both visits. A T-Test was used to compare the effect of Zelesse® on all individual symptoms and signs taken as a whole. After treatment, pediatrician’s opinion on Zelesse® contribution to progression of symptoms and signs was evaluated, as well as the parent’s perception of girls improvement. Tolerability was evaluated by parents. Acceptability, treatment compliance and time to improvement was also evaluated. All analyses were considered significant if p < 0.05. Results: 71 girls (4.5±1.9 years) were studied. At baseline 89% of girls reported pruritus, 92% burning, 97% erythema and 79% edema. 98% of the girls with pruritus at baseline improved after treatment (intensity reduced from 1.8 to 0.1 [p<0.001]). Furthermore, 97% of girls with burning and 93% with erythema at baseline improved after treatment (intensity reduced from 1.7 to 0.1 [p<0.001] and from 1.7 to 0.2 [p<0.001] respectively). Zelesse® also showed beneficial effect on the rest of the evaluated symptoms and signs. At baseline 100%, 98% and 97% of girls with moderate or severe pruritus, erythema and burning respectively, presented after treatment with mild or absence of these symptoms and signs. GSS reduced from 7.4 to 0.5 (p<0.001). Pediatricians considered Zelesse® contributed significantly to the improvement of 86% of patients. 91% of the parents also perceived this improvement. Zelesse® was well/very well tolerated by 96% of patients. No serious adverse event were reported. Conclusion: Zelesse® is a safe and well-tolerated wash solution for the relief of symptoms and signs of non-specific vulvovaginitis in girls. Its significant effect on pruritus and burning is considered clinically relevant, as these are very distressing and persistent symptoms that usually do not resolve without treatment.

PO9
AUTOIMMUNE ENTEROPATHY IN FIVE MONTH OLD FEMALE WITH INTRACTABLE DIARRHEA AND SEVERE METABOLIC ACIDOSIS
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Problem Statement: Autoimmune enteropathy is a rare cause of intractable diarrhea. The primary method of treatment is elemental formula and/or parenteral nutritional support along with immunosuppressive therapy. However, treatment response is variable with many patients requiring long-term immunosuppressive therapy associated with significant morbidity and mortality. The diagnosis of AIE is difficult, as the disease is heterogeneous and there is no standard diagnostic criteria. Methods: A 5-month-old female infant was hospitalized for several weeks of intractable diarrhea and severe metabolic acidosis. Her initial laboratory results revealed HCO3 8 mmol/L (normal 20-26), anion gap 22 mmol/L (normal 4-15) and venous pH 7.08 (normal 7.35-7.45). She was initially treated with IV fluid resuscitation and replacement of bicarbonate. Attempts at use of elemental formulas and withholding all food did not remit her symptoms. Total parental nutrition was initiated. She underwent upper and lower endoscopies. The small bowel biopsies showed chronic duodenitis with

PO7
ZELESSE® AN INTIMATE HYGIENE WASH SOLUTION FOR THE RELIEF OF SYMPTOMS AND SIGNS OF NON-SPECIFIC VULVOVAGINITIS IN CHILDREN: THE NINENSE STUDY.
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Problem Statement: Vulvovaginitis is an inflammatory disease of the vulvar and vaginal area. Vulvovaginitis of non-specific etiology is very prevalent (up to 75%) among prepubertal and preschool girls. The most annoying and relevant symptoms are pruritus and burning. Zelesse® an intimate hygiene wash solution, based on Chamomile, Burdock and Aloe Vera, with soothing, antipruritic and antiseptic properties, may be effective in the symptomatic relief of non-specific vulvovaginitis in girls. The aim of this study was to evaluate the efficacy, tolerability and acceptability of Zelesse® in the relief of non-specific vulvovaginitis in girls. Methods: This is a prospective, observational and multicenter clinical study. Girls aged 2 to 8 years with symptoms and signs of non-specific vulvovaginitis received Zelesse® as single treatment, once or twice daily during 15 (+/-5) days. Symptoms and signs were individually evaluated at baseline and after treatment using a validated scale. The Global Symptom and Sign Score (GSS), a composite score of symptoms and signs, was calculated in both visits. A T-Test was used to compare the effect of Zelesse® on all individual symptoms and signs taken as a whole. After treatment, pediatrician’s opinion on Zelesse® contribution to progression of symptoms and signs was evaluated, as well as the parent’s perception of girls improvement. Tolerability was evaluated by parents. Acceptability, treatment compliance and time to improvement was also evaluated. All analyses were considered significant if p < 0.05. Results: 71 girls (4.5±1.9 years) were studied. At baseline 89% of girls reported pruritus, 92% burning, 97% erythema and 79% edema. 98% of the girls with pruritus at baseline improved after treatment (intensity reduced from 1.8 to 0.1 [p<0.001]). Furthermore, 97% of girls with burning and 93% with erythema at baseline improved after treatment (intensity reduced from 1.7 to 0.1 [p<0.001] and from 1.7 to 0.2 [p<0.001] respectively). Zelesse® also showed beneficial effect on the rest of the evaluated symptoms and signs. At baseline 100%, 98% and 97% of girls with moderate or severe pruritus, erythema and burning respectively, presented after treatment with mild or absence of these symptoms and signs. GSS reduced from 7.4 to 0.5 (p<0.001). Pediatricians considered Zelesse® contributed significantly to the improvement of 86% of patients. 91% of the parents also perceived this improvement. Zelesse® was well/very well tolerated by 96% of patients. No serious adverse event were reported. Conclusion: Zelesse® is a safe and well-tolerated wash solution for the relief of symptoms and signs of non-specific vulvovaginitis in girls. Its significant effect on pruritus and burning is considered clinically relevant, as these are very distressing and persistent symptoms that usually do not resolve without treatment.

PO8
ATALAXIA: AN UNEXPECTED DIAGNOSIS
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Problem Statement: Ataxia is a common emergency and its differential diagnosis is wide. Therefore, the underlying aetiology may be very unexpected. Only a systematic investigation allows an effective diagnosis.
villus blunting and prominent lymphocytosis along with chronic esophagitis, proctitis and gastritis with acute cryptitis. Further staining, revealed an abundance of CD4 cells in the lamina propria and CD8 cells in the intraepithelial layer. She tested negative for circulating anti-enterocyte antibodies. She was started on methylprednisolone at 1.5 mg/kg/day with dramatic clinical improvement. She was able to tolerate elemental formula and was transitioned to oral prednisolone at 1.5 mg/kg/day. Over the next three months, her prednisolone was weaned weekly. At 9 months of age, she has been successfully weaned from prednisolone and is tolerating elemental formula and solid foods without issue. Results: The pathophysiology of AIE is not completely understood. It is known that intestinal lesions are generated by an immune mechanism and that activated T lymphocytes play a role in the pathogenesis of the villous atrophy. Therefore, this process is interrupted by corticosteroids and immunosuppressants. The importance of autoimmune antibodies in the pathogenesis and diagnosis of AIE is debatable. Their presence is neither sensitive nor specific to AIE and is quite variable. They are found in 20-70% of patients diagnosed with AIE (1, 2, 3). In fact, these autoantibodies seem to appear only after the onset of mucosal damage and disappear before the restoration of normal mucosa (1). Conclusion: Malnutrition in AIE frequently necessitates total parenteral nutrition support and refractory diarrhea most typically requires corticosteroids and/or immunosuppressants. The majority of case reports and case series on AIE focus on failure of corticosteroids alone to control symptoms, which makes our case different in that steroids as the sole medical therapy has been successful. More research must be done to better understand the pathophysiology, diagnosis and treatment of this disease. If a physician chooses to treat with corticosteroids or immunosuppressants, it is important to consider the potential severe side effects of these treatments and should frequently reassess the ability to wean therapy.

P10 MEDICAL PROBLEMS ACCORDING TO KARYOTYPE IN TURNER SYNDROME C. J. Kim
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Problem Statement: Turner syndrome (TS) is one of the most frequently encountered chromosomal abnormalities. Many studies reported higher incidence of cardiac, renal, thyroid and auditory problems in patients with TS than general population. The aim of this study is to identify the incidence of these disorders in patients with TS according to the karyotype. Methods: We reviewed medical records of patients with TS diagnosed by chromosomal analysis. At diagnosis, we performed renal US, 2-D echocardiography, thyroid function test and hearing test. The patients were divided into 3 subgroups by cytogenetic results as classic monosomy (45,X karyotype), mosaicism and structural aberration group, respectively. Then, we evaluated distribution of various karyotypes and incidence of 4 common medical problems (renal, cardiac, thyroid and auditory disorder) according to karyotype. Results: The distribution of karyotypes were 45,X (47.3%), mosaic pattern (34.1%) and structural aberration group (18.7%), respectively. Renal anomalies, cardiovascular anomalies, thyroid disorders and auditory problems are accompanied in 4.4%, 9.9%, 11.0% and 5.3%, respectively. 45,X group had renal anomalies (7.0%), cardiovascular anomalies (18.6%), thyroid disorders (9.3%) and auditory problems (11.6%). Mosaic group had renal anomalies (3.2%), thyroid disorders (12.9%), no cardiovascular anomalies and auditory problems. Structural aberration group had cardiovascular anomalies (5.9%), thyroid disorders (11.8%) and no other 2 problems. Patients with 45,X group had a significant higher incidence of cardiovascular anomalies (p=0.025). Conclusion: TS patients showed high frequency of kidney anomalies, cardiovascular anomalies, thyroid diseases and hearing loss, as mentioned in previous researches. Especially, incidence of cardiovascular anomalies is higher in classic monosomy with significant statistical difference.

P11 LONG-TERM ADIPOSITY CHANGES IN YOUTH WITH OVERWEIGHT OR OBESITY ENROLLED IN PEDIATRIC WEIGHT MANAGEMENT S.A. Klein
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Problem Statement: Childhood obesity is a serious, multifactorial, and difficult to treat disease and is increasing in prevalence exponentially. FitKids360 (FK) is an evidence-based pediatric weight management program designed to improve physical activity, nutrition, sleep, and sedentary behaviors among 5-16 year olds with overweight and obesity and their families. Over the 7-week program, participants have improved their obesity-related health behaviors and age- and sex-adjusted body mass index z-scores (BMIz), on average, but the long-term durability of these outcomes has not been adequately examined. This study aims to determine long-term trends in adiposity changes in youth both before and after completing FK. Methods: This is a retrospective cohort study of patients who completed FK from 2011-2013 and were patients at the Helen DeVos Pediatric Clinic. Anthropometry data were collected from medical records 2 years prior to FK participation through 2 years after the program, and the earliest and latest measures were used to index pre-FK and post-FK adi posity, respectively. Participants with at least one pre-FK and post-FK measure were included. Repeated measures ANOVA was used to evaluate BMIz changes from pre-FK to FK and from FK to post-FK across all participants. Results: Participants (n=46) were 64% female and 10.6 ± 3.2 years at FK. On average, pre-FK measures were taken 13.0 months prior to FK and post-FK measures were assessed 18.8 months after FK. Before treatment, patients had a nonsignificant upward trend in BMIz from Pre-FK (2.26 ± 0.59) to FK (2.33 ± 0.66) (p=0.206), and then significantly decreased BMIz from FK to Post-FK (2.22 ± 0.52) (p=0.036). Conclusion: Overall, children and adolescents who completed the FK program changed their BMI z-scores from an upward trend over the year preceding class to decreasing significantly over the 18 months after participation. This is one of the first studies to describe long-term BMI changes in pediatric weight management within the context of BMI changes prior to treatment. These results add to the evidence supporting the efficacy of FitKids360 and suggest the program may provide an impetus to reversing excess adiposity gains.

P12 CUTANEOUS NEONATAL LUPUS ERYTHEMATOSUS S.A. Klein1, M. Keeler2
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Problem Statement: Neonatal lupus erythematosus (NLE) is an autoimmune disease caused by transplacental transmission of maternal antibodies to SSA and/or SSB. NLE occurs in 1-2% of infants born to mothers with autoimmune disease. Cutaneous disease occurs in 50% of infants with NLE and is often mistaken for a fungal infection. Infants with NLE are also at risk of cardiac, hepatobiliary, and hematologic complications. These typically resolve as maternal autoantibodies are cleared from the infant’s circulation. Cardiac disease, most commonly complete heart block, is the most severe manifestation and is often irreversible. It is important to be aware of cutaneous and extracutaneous manifestations of this disease in order to diagnose and treat infants. Methods: N/A. Results: 4 month old
male presented for a well exam. Parents were concerned about a rash for the past 2 months. There were 4 erythematous circular lesions on his abdomen and 2 on his head. The rash had not spread, was not painful or pruritic, and did not drain. Clotrimazole did not improve or worsen the rash. He was feeding well and meeting developmental milestones appropriately. He was born full term and had a normal postnatal course. His newborn screen was normal. Family history was positive only for maternal hypertension. No known history of autoimmunity or skin disease. His physical exam was unremarkable except for four annular, erythematous patches with scalloped edges and central clearing on his abdomen and two over his scalp. There was no scaling. His laboratory evaluation included a normal CBC, CMP, urinalysis, and fungal culture of rash. His autoimmune panel was positive for ANA, dsDNA, and SSB antibodies. SSA antibodies were negative. These findings were consistent with NLE diagnosis. EKG was normal. His mother was screened for autoimmune disease and had the same positive antibodies as her son. As the patient had no systemic manifestations of NLE, no further workup was done. Conclusion: The prognosis is excellent for infants with exclusively cutaneous manifestations. The rash appears a few weeks after birth and resolves by six to eight months. Resolution of symptoms is concurrent with the disappearance of maternal autoantibodies. The rash is photosensitive and typically develops after exposure to UV light. Lesions are most commonly located on the scalp and periorbital area. The characteristic rash is erythematous annular macules with slight central atrophy and raised margins. NLE may cause serious disease involving the cardiac, hepatobiliary, and/or hematologic systems. Congenital heart block is the most common systemic complication, occurring in half of affected infants. It develops around 18-24 weeks gestation. Congenital heart block is usually irreversible and associated with significant mortality (20-30%). Hepatobiliary complications occur in 10% of cases, are typically transient, and include liver failure, conjugated hyperbilirubinemia, and/or elevated transaminases. Hematologic complications are also transient, occur in 10% of cases, and include cytopenias. Treatment is aimed at prevention. If maternal SSA and/or SSB antibodies are detected during pregnancy, the fetus should be closely monitored for congenital heart block via monitoring heart rate between 18 and 24 weeks. Glucocorticoids can decrease the inflammation that leads to heart block. In third degree heart block, a pacemaker is often necessary. After birth, photoprotection is important to prevent cutaneous manifestations.

P13 USING CLASSIFICATION TREES TO PREDICT SCOLIOSIS
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Problem Statement: The aetiology of adolescent idiopathic scoliosis (AIS) is still unclear. A multifactorial theory is the most frequently adopted one, and potential factors are supposed to take part in the processes that trigger the disorder, as well as in the progression of AIS. Methods: The study encompassed 200 girls in total: 100 girls with scoliosis and 100 girls without scoliosis (control group). Each of the studied groups was divided into two equal subgroups: Group 1 (non-menstruating girls with scoliosis), Group 2 (menstruating girls with scoliosis), Group 3 (non-menstruating girls without scoliosis) and Group 4 (menstruating girls without scoliosis). All girls underwent diagnostic tests that allowed for measuring 10 blood parameters; the following parameters (variables) were measured: FSH, progesterone (PROG), phosphorus, HGH, calcium, LH, oestrone, PTH, osteocalcin and vitamin D. Diagnostic strength of the variables was determined with cluster analysis conducted with a STATISTICA software. Pearson r=2 coefficient was used in the calculations, which allowed for determining the degree of the correlation between the variables. The C&RT module of the STATISTICA system was used to construct a classification tree, which allowed for classifying the girls into four groups. The classification was carried out by determining the variability ranges of the measured hormone levels. Results: The clustering method yielded two clusters of strongly correlated variables (progesterone and phosphorus, and HGH and calcium) and a larger cluster that also encompassed the FSH variable. Oestrone and PTH, and osteocalcin and vitamin D, which are strongly related with the occurrence of scoliosis, constitute a separate and non-correlated group of parameters (variables). The LH variable was found to be the most distant from both groups. The STATISTICA system chose this parameter as the most important diagnostics attribute, and it was assigned to the root of the classification tree. The analysis of the LH values distinguished the majority (86) of menstruating girls (Group 2 and Group 4) from the studied set. Further on, the tree was constructed recursively, following the principle according to which the attributes yielding the greatest information gain, guaranteeing the optimal division of a studied sample, are assigned to the root. Oestrone, osteocalcin and PTH were assigned to split nodes of the constructed tree. The question about the level of calcium, the value of which allows for distinguishing the group of menstruating girls with scoliosis (6 girls) from the girls without scoliosis (37 girls), was assigned to node no. 5. Conclusion: Only 6 girls from the studied group were classified incorrectly, which, with respect to the number of girls in the studied group (200), yields a mean correctness of classification equaling 96%. Such effectiveness of the classification system created on the basis of data obtained from an experiment can be considered a very good result. The prognostic properties of the constructed decision system can be used in diagnosing scoliosis. At the same time, it should be observed that, in order to obtain a high accuracy of diagnosis, it is enough to measure the level of only 5 hormones in a patient’s blood out of the proposed list of 10 hormones.

P14 PARENTS THINK THEY ONLY NEED A PRESCRIPTION, IT TURNS OUT IT MIGHT BE A SERIOUS CASE: 3 CASES REPORTS
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Problem Statement: Do parents sometimes need just the prescription for the drug another specialist suggested, or they need a paediatrician’s opinion too? Methods: 3 Cases reports. Results: A 4 year-old boy was taken for the pulmonologist upon experiencing breathing problems. The next day his mother came to Primary Health Centre in Kaludjerica asking the nurse if the paediatrician could just write the prescription, solutio salbutamol. She did not bring the child along and she had no time to wait. Before prescribing the medicine, the paediatrician wanted more information. Asked if she gave the boy the inhalation treatment, she answered that she did not have inhalator but the boy took the solutio per os. They had bought sol salbutamol the previous night but were already out of it. Instead of taking sir Spalmotil (salbutamol) 3x1 mg, she gave him per os sol salbutamol, form for inhaling, 3x12.5 mg. She was asked to bring a boy for examination immediately. The boy had tachycardia 160/min and was sent to cardiologist for observation. Fortunately, everything turned out well. Impatient mother of 16 years old girl didn’t want to talk to the doctor and only asked for the prescription for Efilt (Malproin acid + natrium valproat). Than she added she wouldn’t be coming if her daughter didn’t take several doses at once, leaving a note that she wanted to commit a suicide. Paediatrician spent 30 min explaining to her how serious it may be and convincing her to immediately take her daughter to see a psychiatrist. Five month old baby
Intestinal flora modulates inflammatory response, depending on good results when Lactobacillus reuteri probiotic was used for treatment.

I. Margarit Dalmau

REUTERI

NEPHROTIC SYNDROME IN PEDIATRICS: 20 YEARS FOLLOW UP

P. Matos2, P. Teixeira1

Problem Statement: The Nephrotic Syndrome (NS) is characterized by alterations of the glomerular capillary wall that cause urinary protein loss, resulting in proteinuria and hypoalbuminemia frequently associated with edema and hyperlipidemia. The estimated annual incidence is 2 to 7 new cases per 100000 children under 18 years of age. The objective of this study was to analyse the presentation and evolution of patients hospitalized for Nephrotic Syndrome. Methods: Retrospective study of the clinical files of patients hospitalized for NS and their follow-up in an out patient setting in the period between January 1996 and January 2016. Results: There was a total of 16 children with NS, with a median age of 30 months (16-86 months) at the time of diagnosis, 68.8% (n=11) of which were males. In the first episode, all the children presented with edema, 3 had arterial hypertension and 6 hematuria. Thirteen cases responded to initial treatment with prednisolone, entering remission a median of seven days after hospitalization (minimum 4, maximum 16). Of these, 61.5% recovered in the first 6 months. Renal biopsy was done in 2 children (steroid-dependent) that revealed minimal change disease. At the present time 62.5% are in remission (including steroid resistant) and 37.5% remain steroid dependent. Conclusion: As observed in other studies, the majority of NS patients are steroid responsive although with high frequency of relapse and steroid dependency. Many children need alternative treatment options because both of steroid resistance their secondary effects.

P15

NEPHROTIC SYNDROME IN PEDIATRICS: 20 YEARS FOLLOW UP

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Problem Statement: The Nephrotic Syndrome (NS) is characterized by alterations of the glomerular capillary wall that cause urinary protein loss, resulting in proteinuria and hypoalbuminemia frequently associated with edema and hyperlipidemia. The estimated annual incidence is 2 to 7 new cases per 100000 children under 18 years of age. The objective of this study was to analyse the presentation and evolution of patients hospitalized for Nephrotic Syndrome. Methods: Retrospective study of the clinical files of patients hospitalized for NS and their follow-up in an out patient setting in the period between January 1996 and January 2016. Results: There was a total of 16 children with NS, with a median age of 30 months (16-86 months) at the time of diagnosis, 68.8% (n=11) of which were males. In the first episode, all the children presented with edema, 3 had arterial hypertension and 6 hematuria. Thirteen cases responded to initial treatment with prednisolone, entering remission a median of seven days after hospitalization (minimum 4, maximum 16). Of these, 61.5% recovered in the first 6 months. Renal biopsy was done in 2 children (steroid-dependent) that revealed minimal change disease. At the present time 62.5% are in remission (including steroid resistant) and 37.5% remain steroid dependent. Conclusion: As observed in other studies, the majority of NS patients are steroid responsive although with high frequency of relapse and steroid dependency. Many children need alternative treatment options because both of steroid resistance their secondary effects.

Conclusion: Excessive gestational weight gain was greater risk factor of LGA (SMD 1.83-9.24, p<0.01) folds higher risks of LGA, compared with women with appropriate-for-gestational weight gain (GWG), neonatal birth weight and sex. LGA was defined as a birth weight greater than 90th percentile, and appropriate-for-gestational age (AGA) was defined as a birth weight between 10th and 90th percentile. Maternal weight gain was classified into three categories of the World Health Organization. Women with excessive gestational weight gain (GWG) had 4.16 (95% CI: 1.83-9.24, p=0.01) folds higher risks of LGA, compared with women with below and adequate GWG, adjusted for HBa1c levels. No significant difference was found in pre-pregnancy BMI, HBa1c level, insulin treated infants with the women with AGA infants. Of the 118 GDM women, LGA was present in 19.5%, AGA was present in 74.6%. The average HBa1c level was 5.6±0.38 %, percentage of insulin treated was 9.3%. Women with excessive GWG had 4.16 (95% CI: 1.83-9.24, p<0.01) folds higher risks of LGA, compared with women with below and adequate GWG, adjusted for HBa1c levels. No significant difference was found in pre-pregnancy BMI, HBa1c level, insulin treated infants with the women with LGA infants and the women with AGA infants. Conclusion: Excessive gestational weight gain was greater risk factor of LGA.
P18

PEDiATRIC TELEPHONE TRIAGE HOtLINE PROGRAM FOR HIV-POSITIVE CHILDREN: IMPLEMENTATION AND THE ASSESSMENT OF HEALTHCARE ACCESS BARRIERS AND GUARDIANS' CLINICAL KNOWLEDGE IN CHENNAI, INDIA

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Problem Statement: In 2015, it was estimated that 36.7 million people were living with HIV and approximately 2.1 million of those people live in India (UNAIDS, 2016). Children living with HIV (CLHIv) are a very vulnerable sub-population, often who are unable to receive the healthcare that they need to grow and thrive. The southern part of India bears the nation’s largest HIV burden, and since 2005, the Chennai-based NGO, known as the International Alliance for the Prevention of AIDS (IAPA), has been caring for CHIV by offering free once monthly well-check visits & robust food & nutritional supplementation packages. Currently, IAPA cares for 43 CHIV. Between their once-a-month visits, children may fall ill. As of now, only one IAPA staff member fields calls from families to assist sick children to get the care they need, but this has proven to be an unsustainable model, as staff burnout is high, and one child previously passed away from undiagnosed meningitis. In Tamil, “uthavi” means help, and to ensure IAPA’s CHIV get the care they need, the present study examined the implementation of the UTHAVI Project, a web-based telephone triage database that trained triage coordinators can use to document phone calls with the families and give instructions on how to care for their sick child. Prior to full implementation, guardian’s healthcare access barriers (HAB) and clinical knowledge were to be assessed. Methods: We surveyed 31 Indian guardians of CHIV receiving care from IAPA. Study components were conducted with a translator. HAB were assessed with novel surveys & clinical knowledge assessed by pre- & post test design. An ANCOVA was conducted to compare the difference in pre & post test scores, with HAB as the covariate. Health education curriculum was adapted from the WHO’s Integrated Management of Childhood Illness (IMCI) handbook (WHO, 2016). Results: Of the 31 participants surveyed, 63.1% reported multiple HAB & 63.2% of these reported 3 or more HAB. The most commonly reported HAB was “HIV stigma deters health-seeking behavior” (n=15). Cough & Difficulty Breathing was the most commonly incorrect category from the guardian clinical knowledge pre test, with the average score being 43.75%. After a health education module, the average score was 84.38%. Although there was no significant difference in pre test & post test scores while using HAB as a covariate, the results are approaching statistical significance (p=0.066). Conclusion: Due to multifaceted HAB in a vulnerable population & lack of proficient guardian clinical knowledge, a pediatric telephone triage for HIV-positive children is a promising tool in the resource-limited, global health setting. Given the limited sample size, the trend towards statistical significance suggests that HAB account for some variance observed in test scores. Future research looks to expand the sample size & create a control & treatment to assess the impact of the teaching module on pre & post test scores.

P19

EFFICACY OF OndANSETRON VERSUS DompERIDONE ON VOMITING DUE TO ACUTE GASTROENTERITIS

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Problem Statement: Acute gastroenteritis (AGE) is a common cause of morbidity and mortality in children that is frequently accompanied by vomiting. Several anti-emetic drugs are used for the management of vomiting; however, their efficacy is limited and comes at the cost of some side effects. Currently, there is no standard guideline for pharmacological treatment of vomiting in children with gastroenteritis. Methods: Seventy-six Thai children under the age of 15 with AGE were randomized to receive either ondansetron or domperidone. In ondansetron group, the prescribed dose was 2 mg for children weighing less than 15 kg, 4 mg for children weighing 15-30 kg, and 8 mg for children weighing more than 30 kg. The prescribed dose of domperidone was 2.5 mg for children weighing less than 15 kg, 5 mg for children weighing 15-30 kg and 10 mg for children weighing more than 30 kg. The primary outcome of the study was the proportion of the patients in each group who had no episode of vomiting 24 hours after the start of treatment. Results: Primary outcome was met in 62% of patients in ondansetron group and 44% of patients in domperidone group (P=0.16). Patients in domperidone group received more doses of the drugs within 24 hours after the start of the treatment compared to ondansetron group (P=0.01). No adverse effect was observed in any of the two groups. Conclusion: Ondansetron can be considered a safe comparable alternative to commonly-used domperidone in Thai children who suffer from symptoms of gastroenteritis. Larger clinical trials are needed to further explore the effectiveness of the two medications.

P20

SCHOOL-BASED INTERNET OBESITY PREVENTION PROGRAM FOR THAI CHILDREN

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Problem Statement: School-based Internet obesity prevention programs have been advocated as one strategy to address the rising prevalence of childhood obesity; however, their efficacy is not seen consistently. This study aims to assess the efficacy of internet-based obesity prevention program in Thai schoolchildren. Methods: Healthy children studying in public schools in one township of central Thailand were randomly assigned to either the intervention (Internet-based) program or the control group. Anthropometric characteristics were recorded at baseline and for the next four following months at monthly intervals. Changes in the percentage of overweight/obese children and changes in BMI at the end of study were considered as the primary and secondary outcome, respectively. Results: 217 children, mean age of 10.7 years, were included into the final analysis. Baseline anthropometric parameters and percentages of overweight/obesity were not significantly different between groups. At the end of the study, the control group had a higher percentage of overweight/obesity than the intervention group (56.6% vs. 39.6%, respectively; p-value=0.009). Children in the control group had a significantly higher increase in net BMI gains than those in the intervention group (1.24kg/m2 vs. 0.40kg/m2, p-value=0.027). The intervention group had no changes in BMI z-score (-0.001, 95%CI -0.19 to 0.18, p-value=0.988), contrary to those in the control group, which had a significant gain of BMI z-score (0.45, 95%CI 0.27 to 0.63, p-value<0.001). Conclusion: The school-based Internet obesity prevention program was effective in modifying the percentage of overweight/obese children and significantly increased BMI z-score in the control group.
examination revealed tachycardia, painful abdominal palpation, bilateral pain radiated to both thighs, and he had associated dysuria. Physical examination revealed tachycardia, painful abdominal palpation, bilateral doubtful Murphy sign and cold lower limbs with bilateral edema. The dorsalis pedis pulse was weak but present in both sides. Laboratory tests revealed increased D-dimer (485 ng/ml) and C reactive protein (89.1 mg/L). In the abdominal ultrasound the inferior vena cava could not be identified, so a CT scan was performed. The CT scan demonstrated increased diameter of the distal segment of the inferior vena cava and common iliac veins, internal and external, suggesting extensive acute inferior vena cava and common iliac veins thrombosis. The patient was then admitted to the infirmary and treated conservatively with subcutaneous enoxaparin, aided by compression hosiery and bed rest, followed by oral rivaroxaban. After 3 days of treatment, the symptoms had significantly improved. The patient was discharged at the 14th day. The lower limb swelling resolved 4 weeks later. The patient remains well 5 months later and continues treatment was discharged at the 14th day. The lower limb swelling resolved 4 weeks later.

Problem Statement: Type 1 diabetes (T1D) is a common disease in the pediatric population. In children with T1D, diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality due to the associated complications, involving multiple systems. Type 1 diabetes (T1D) is a common disease in the pediatric population. In children with T1D, diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality due to the associated complications, involving multiple systems. Methods: We report the case of a 17 year-old male, with T1D treated with insulin, discharged from hospital care one week before due to gastroenteritis with an underlying DK. The patient was admitted in the emergency department with a 4 days history of severe lower back pain. The pain radiated to both thighs, and he had associated dysuria. Physical examination revealed tachycardia, painful abdominal palpation, bilateral doubtful Murphy sign and cold lower limbs with bilateral edema. The dorsalis pedis pulse was weak but present in both sides. Laboratory tests revealed increased D-dimer (485 ng/ml) and C reactive protein (89.1 mg/L). In the abdominal ultrasound the inferior vena cava could not be identified, so a CT scan was performed. The CT scan demonstrated increased diameter of the distal segment of the inferior vena cava and common iliac veins, internal and external, suggesting extensive acute inferior vena cava and common iliac veins thrombosis. The patient was then admitted to the infirmary and treated conservatively with subcutaneous enoxaparin, aided by compression hosiery and bed rest, followed by oral rivaroxaban. After 3 days of treatment, the symptoms had significantly improved. The patient was discharged at the 14th day. The lower limb swelling resolved 4 weeks later. The patient remains well 5 months later and continues treatment was discharged at the 14th day. The lower limb swelling resolved 4 weeks later.

Conclusion: Zelesse® is an effective treatment for the relief of symptoms and signs of non-specific vulvovaginitis in children. Methods: This is a prospective, observational and multicenter clinical study. Zelesse® was administered to the girls as single measure once or twice daily for 15 (+/−5) days. Individual symptoms and signs, as well as a composite score of symptoms, were individually evaluated at baseline and at the end of treatment. Comparisons were performed between baseline and post-treatment and all analyses were considered to be significant if p <0.05. At final visit, parents were asked about their daughters’ acceptability to Zelesse® using an ad-hoc 5-point Likert scale (from “very well accepted” to “very poorly accepted”). Zelesse® was considered very poorly accepted if girls refused vaginal wash, or simply cried during administration. At final visit, parents were also asked about their perception of improvement of their daughters’ condition, treatment compliance and time to improvement. Tolerability and adverse events incidence were also evaluated. Results: 71 girls, aged 2 to 8 years (mean age 4.5±1.9 years) with suggestive symptoms or signs of non-specific vulvovaginitis were studied. At baseline erythema (97%), burning, (92%) and pruritus (89%) were the most frequent symptoms and signs, which were present at final visit in 23%, 9% and 10% respectively (p<0.001). At the end of treatment 66% of the girls reported absence of symptoms and signs of vulvovaginitis. At final visit, 91% of the parents perceived that Zelesse® greatly improved or solved symptoms and signs of their daughter’s pathology and 87% of those that improved, experienced improvement during the first week of treatment. Compliance and acceptability was excellent: 94% of children showed high adherence, and the acceptability of Zelesse® was reported as “very good/good” in 93% of the girls. No serious adverse events were reported. Conclusion: Zelesse® is an effective treatment for the relief of symptoms and signs of non-specific vulvovaginitis in pediatric patients. Zelesse® has a very good safety profile and is very well tolerated and accepted for girls with vulvovaginitis.
Problem Statement: Down syndrome is the most common genetic disorder and occurs in 1 out of 1000 live births as a result of the presence of an extra copy of chromosome 21. There are a number of medical problems that are associated with the syndrome, including musculoskeletal defects such as hypotonia, ligament laxity, body posture disorders including feet pathology. Children with Down syndrome are very often overweight or obese. This excessive body weight can also affect feet shape especially medial longitudinal arch (MLA). The aim of the study was the evaluation of the medial longitudinal arch (MLA) in youth with Down syndrome.

Methods: The research involved 31 youth with Down syndrome, including 13 female and 18 male of the Complex of Special Schools in Cracow, Poland, aged 10-23, with the average age of 17.34±4.26, the average height of 147.2±11.53 cm and the average weight of 55.28±17.54 kg. The measurement of weight and height allowed the calculation of body mass index (BMI) 25.1±11.06. All the subjects had documented moderate mental handicap, (IQ 36-51). All participants were subjected to a podoscopic foot examination in order to determine the height of the longitudinal arch. In the following research, a 2D scanner was used to determine the longitudinal arching in youth and young adults with Down syndrome. Additionally, each individual’s height and weight were measured. The results were evaluated by means of descriptive statistics and statistical analysis (t-student test and Mann-Whitney test). Results: In the examined group, the most common type of the longitudinal arching was a flat foot that was observed in 25 persons in the left foot and in 23 persons in the right one. Gender had no significant influence on foot arching distribution, excluding the high arched foot which was observed only in male group (3 cases). Conclusion: The obtained results suggest that flat foot seems to be the most common pathology in the examined group.
Of the 24 patients that were enrolled during the study period, 20 patients completed the seven scheduled vaccinations. They had the following diseases: brain tumor, 11 patients; rhabdomyosarcoma, 4 patients; neuroblastoma, 3 patients; clear cell sarcoma of the kidney, 1 patient; and osteosarcoma, 1 patient. WT1 expression was confirmed by immunostaining of primary tumors in all cases, except for one case wherein no specimen could be obtained. No side reactions were observed for four patients throughout the entire course of the seven vaccine injections. The remaining 16 patients had local skin symptoms (redness and subcutaneous induration). In one case, anaphylactic and respiratory symptoms emerged at the time of the final injection, but these were quickly ameliorated by the treatment. Four patients developed a fever exceeding 38°C. All symptoms improved over time in all cases. After seven vaccinations, immunological assessment confirmed a positive response in four patients (20%).

Conclusion: WT1 peptide vaccine therapy appears to be a relatively safe treatment that can also be administered to children. However, the rate of acquisition of active immunity is only 20%. Presumably, this rate largely depends on the state of the original disease, patient immunological conditions, and concomitant use of chemotherapy, steroids, etc. in addition to childhood-specific characteristics. Further studies are necessary to confirm safety and efficacy in a larger number of patients.

P26
RENAL SWELLING CAN PREDICT RENAL DAMAGE?

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Problem Statement: Renal imaging can provide valuable information in urinary tract infection (UTI) diagnosis. The objective was to determine whether renal swelling is correlated to fever and C-reactive protein value.

Methods: 264 infants <1 year old were examined with renal ultrasound (US) in the acute phase of urinary tract infection and at follow-up after 8 weeks. Longitudinal length and the volume of the kidney were assessed by renal ultrasound and correlated to fever and C-reactive protein in infants with first UTI. Results: The mean renal length and volume at the first US examination were 2.1 SDS (±1.6) and 1.8 SDS (±1.5) for the larger kidney and 0.92 SDS (±1.2) and 0.87 SDS (±0.98) for the smaller kidney respectively. We observed a significant decrease in renal length and volume between the first and second US with a mean difference in renal length and volume between the first and the second US with a mean difference 1.01 SDS (±1.34) and 1.12 SDS (±1.38) for the larger and 0.51 SDS (±0.98) and 0.53 SDS (±0.99) for the smaller kidney respectively (p<0.0001).

Length of the largest kidney correlated with the degree of fever (p<0.001) and serum CRP (p<0.0001) and renal volume of the largest kidney correlated with serum CRP. Conclusion: The degree of swelling of the larger kidney correlates with inflammatory signs. Early US can be of value to identify children with risk of renal damage. Measurement of renal length and volume US in the acute and late phases of UTI in infants can identify renal swelling.
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