Clinical update:
Hidden co-morbidities present in obese children & adolescents

News from Europe:
The 6th Europaediatrics 2013 preview
Glasgow - a fun, exciting and welcoming host city

EPA Newsletter / Issue 17/ April 2013
## Contents of EPA/UNEPSA Newsletter  Issue 17

Cover page photo: A classic European children’s hospital - The Bambino Gesù Children’s Hospital in Rome.

<table>
<thead>
<tr>
<th>Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Letter of the Editor</strong></td>
<td></td>
</tr>
<tr>
<td>The upcoming Europaediatrics Congress</td>
<td>3</td>
</tr>
<tr>
<td><strong>Clinical update</strong></td>
<td></td>
</tr>
<tr>
<td>Hidden co-morbidities present in obese children &amp; adolescents</td>
<td>4</td>
</tr>
<tr>
<td><strong>News from Europe</strong></td>
<td></td>
</tr>
<tr>
<td>The 6th Europaediatrics 2013 Preview</td>
<td>6-7</td>
</tr>
<tr>
<td>Glasgow - a fun, exciting and welcoming host city</td>
<td>8</td>
</tr>
<tr>
<td><strong>Announcement</strong></td>
<td></td>
</tr>
<tr>
<td>Join the most extensive paediatric network in Europe!</td>
<td>9</td>
</tr>
<tr>
<td><strong>Calendar of events</strong></td>
<td></td>
</tr>
<tr>
<td>List of upcoming paediatric conferences in 2013</td>
<td>10</td>
</tr>
<tr>
<td><strong>Information</strong></td>
<td></td>
</tr>
<tr>
<td>List of member countries 2013</td>
<td>11</td>
</tr>
<tr>
<td><strong>Acknowledgments</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
</tr>
<tr>
<td><strong>Publication identity</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>13</td>
</tr>
</tbody>
</table>
Dear colleagues and friends,

The upcoming Euopaediatrics Congress is a strong pole of attraction. Our activities are revolving around speakers and topics. The speakers are from all over the World although most come from our own region i.e. Europe. This work has been possible because of the firm dedication of the Congress management unit. Some changes and subtle modifications of topics keep us on our toes. Nevertheless the program is ready; when one takes an objective look, two main features define better its quality: 1) the balance of topics for clinical updates, and 2) the importance ascribed to paediatric health promotion. Please see the next article in which the scientific content of the Congress is analyzed. The joint Opening Ceremony with the Royal College of Paediatrics and Child Health, the Keynote speech or the joint special symposium with WHO, are small parts but with an impact that will persist.

This Congress has another point of interest that although administrative in nature, is no less important. New elections are going to take place at the General Assembly. I am convinced that EPA will continue in the right direction.

In this pre-Congress atmosphere I would like to encourage you all to attend. Apart from the aforementioned scientific pole and the proved hospitality of the Scots, there are other geographical reasons. Once there and apart from Glasgow itself and the nearby Edinburgh, you can take a look at the Firth of Clyde and if possible go to the unique islands in the North Atlantic.

I hope to see you there!

Manuel Moya

P.S. If you wish to receive an e-alert for new issues, all you have to do is send an e-mail to epa-unepsa@2eic.com
Metabolic syndrome (Met S)

Metabolic syndrome (Met S) is a determining common factor for co-morbidities and they are furthermore related to the metabolic syndrome. Met S encompasses a series of findings with clear cut limits, easily defined in clinical terms and highly predictive of CVD and T2D particularly when these appear in obese children and adolescents. This predictive character has been considered with growing interest particularly since the moment at which the International Diabetes Federation (1) unified and established the cut off points for adult and pediatric patients. The four parameters of Met S are: Abdominal obesity, altered glycemic homeostasis, dislipemia and hypertension (Table 1). There is a series of surrogate factors such as fasting insulinemia, uric acid, Hb A1c and hs C-reactive protein, which increase predictive accuracy. The identification of Met S at any age implies a tighter control of obesity and this is a clear necessity at present. We should remember that according to the Center for Disease Control (Atlanta) in the US there are more than 80 million people, children and adolescents included, suffering from T2D. As we know that the number of overweight and obese people is similar on both sides of the Atlantic, this problem is also likely to be present here. In this context the WHO has stressed that to avoid such co-morbidities, obesity prevention should be started in pediatric ages.

Factors leading to insulin resistance.

Dietary habits, sedentary attitudes and socio economic factors are related to Met S (but also to obesity). The Australian Rayne study shows how a greater glycemic load, estimated after a three-day questionnaire, increases independently the risk of Met S (2). High consumption of sugared drinks is an additional risk. Raised plasma uric acid indicates cardiometabolic risk according to the NHANES 99-06. Sedentary lifestyle. When evaluated through screen time, figures greater than 35 hours per week imply by themselves a greater prevalence of Met S. The counterproof came after using the accelerometers that show how greater physical activity is associated with lower BMIzs. Insufficient sleep (< 8hr/day), together with environmental changes (use of machinery, heating &c) is also associated with the chain of obesity, insulin resistance and co-morbidities (3).

Mechanisms of insulin resistance.

There are three phases in the genesis of IR: Compensation when normal glycemia is maintained but at the expense of higher insulinemia levels; postprandial hyperglycemia despite higher insulinemia levels; and continuous hyperglycemia, which signals the transit from IR to T2D in which beta cells are unable to produce enough insulin to maintain homeostasis. High insulinemia levels increase the fat content of the abdominal adipocytes due to activation of lipoprotein-lipase that facilitates the fatty acids uptake. Insulin also facilitates the uptake of glucose, the natural precursor of glycerol, then the increase synthesis of triacylglycerols which are almost the only component of the fat vesicle. Fasting hypoglycemia is due to hepatic gluconeogenesis.

### Table 1. The IDF definition of the at risk group and metabolic syndrome in children and adolescents

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Obesity (WC)</th>
<th>Triglycerides</th>
<th>HDL-C</th>
<th>Blood pressure</th>
<th>Fasting plasma glucose</th>
</tr>
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<tbody>
<tr>
<td>6-10</td>
<td>≥ 90th percentile</td>
<td>≥ 150 mg/dL</td>
<td>&lt; 40 mg/dL</td>
<td>Systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg</td>
<td>FPG 100 mg/dL or known T2DM</td>
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<tr>
<td>10-16</td>
<td>≥ 90th percentile or adult cat-off if lower</td>
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<td>16+ (Adult criteria)</td>
<td>WC ≥ 94 cm for Europid males and ≥ 80 cm for Europid females, (with ethnic-specific values for other groups)</td>
<td>≥ 150 mg/dL, or specific treatment for high triglycerides</td>
<td>&lt; 40 mg/dL in males and 50 mg/dL in females, or specific treatment for low HDL</td>
<td>Systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension</td>
<td>FPG 100 mg/dL or known T2DM</td>
</tr>
</tbody>
</table>

* For clinical purposes, but not for diagnosing the MetS, if FPG 5.6-6.9 mmol/L (100-125 mg/dL) and not know to have diabetes, an oral glucose tolerance test should be performed. Diagnosing the metabolic syndrome requires the presence of central obesity plus any two of the other four factors.
**Nonalcoholic fat liver disease (NAFLD)**

NAFLD is a co-morbidity of obesity caused by accumulated macrovesicular fat in the hepatocyte, worsened by hyperinsulinemia with a poorly and unpredictable progression to steatohepatitis. NAFLD merits special mention here because it is the most common liver abnormality in children and adolescents. Fatty liver develops when fatty acid uptake and the novo fatty acid synthesis exceed fatty acid oxidation and export as very low-density lipoproteins or triglycerides. Prevalence varies according to the method, if for example high definition ultrasound plus AST /ALT elevation is used, then prevalence ranges between 10-77%, which clearly implies a low specificity. Schwimmer (5) reviewed 742 autopsies on children and adolescents after accidental death. Fatty liver (> 5% of hepatocytes containing macrovesicular fat, droplet diameter > nucleus) was found in 97 cases, 38% of whom were overweight or obese. This gives a more realistic figure for prevalence. Fat liver histo (type II) is habitual in pediatric obesity, it is characterized by macrovesicular steatosis plus portal inflammation and perportal mononuclear cell infiltration. Different from the adult type which in addition shows ballooning degeneration, perisinusoidal fibrosis and PMN infiltration. Figure 1 shows an area in which a portal space and fatty liver tissue of one of our patients appear with a typical pediatric pattern (no ballooning macrovesicular steatosis and inflammatory pattern with mononuclear cells). In the image on the right (trichromic acid) a portal fibrosis can be seen. Probable histology is the current gold standard for evaluating fat liver, but liver biopsy is quite an invasive procedure. Consequently strict criteria are required in our Unit: trunk fat > 40%, raised AST,ALT and gamma GT and fasting insulinemia >15 uU/ml.

**Clinical clues.** Despite the high prevalence, NAFLD is largely underdiagnosed, probably because NAFLD is a clinico-pathological diagnosis and most children are asymptomatic. Diagnosis depends on the eventual finding of hepatomegaly and elevated aminotransferases. If waist circumference is above 90th percentile, then the suspicion grows and even implies liver fibrosis (6). Serum liver enzymes have low sensitivity and specificity according to their levels prior to the biopsy but when measuring AST, ALT and gamma-GT in an obese patient, they can be helpful. Image techniques. Liver biopsy remains as the gold standard, it can qualify the degree of steatosis, stage liver fibrosis and assess the degree of liver cells injury, but percutaneous biopsy has a certain risk of bleeding and requires experience and a hospital setting. Prior to the biopsy, MRI can be used to allow a fairly accurate diagnosis and an evaluation of the evolution of the fat liver deposit. Recent techniques using intravenous contrast permit us to assess the degree of fibrosis. Ultrasound, although less precise, is the most often employed modality because of safety, availability and cost. Its weak points: it only detects steatosis greater than 30%, the attenuation of the US beam by fat outside the liver and its subjectivity. Ultrasonic transient elastography is used more for following hepatic fibrosis in chronic patients. It is important to consider that NAFLD precedes T2D and probably metabolic syndrome itself, therefore the importance of its diagnosis.

**Prognosis.** Fat liver is associated with cardiovascular disease and type 2 diabetes to a greater extent than obesity without this co-morbidity. Chronic NAFLD evolution to non alcoholic steatohepatitis (NASH), to fat with fibrosis and finally cirrhosis and hepatocellular carcinoma depends on genetic (gene polymorphisms) and environmental factors, the latter being the only ones that can be modified, thus the importance of treating (abdominal) obesity (7, 8).

**Treatment.** Multidisciplinary lifestyle intervention is the only effective way of approaching NAFLD, even a minimal reduction of overweight led to an improvement. Metformin added or not of vitamin E were not superior to placebo (9).

Manuel Moya  
Nutrition Growth & Metabolism Unit  
HUSJ Alicante Spain

**REFERENCES**


**Briefly there are two underlying mechanisms.** The first is the high postprandial rise of fat and free fatty acids and glycemia. The former causes triacylglycerols to increase in the muscle and liver cells and once there, a part of them become diacylglycerols which in turn alter a protein known as insulin-receptor substrate 1(IRS 1) which makes the high affinity transporter for glucose GLUT 4 unable to reach the external membrane of the myo / hepatocyte. In adequate amounts and subsequently hyperglycemia results (4). In normal conditions once insulin is bound to its receptor, it activates GLUT 4 through IRS 1 and consequently normoglycemia is restored. More and fascinating aspects of the cellular basis for insulin resistance are beyond the scope of this text. The second is the inflammatory mechanism after the proinflammatory cytokines produced and excreted by the white adipose tissue particularly when it is situated in the abdominal cavity. Genome-wide studies probably will throw some light on the fact that not all obese people develop insulin resistance.

**Figure1.** NAFLD histopathology. HUSJ patients: Type II 5, NASH 1, other 1.
6th Europaediatrics
jointly held with the
RCPCH Annual Conference,
and the 2nd PNAE Conference
in the beautiful city of Glasgow

On the next page you will find detailed content of the scientific programme at Europediatrics 2013. In summary, we have 45 sessions plus the poster presentations that we have carefully prepared. It is worth mentioning the three plenary sessions. They will bring cutting edge knowledge of the role of pediatric sub-specialties; the breakthrough on important clinical care; and the challenge we have before us of promoting health in European children.

From the longer list of symposia it is worth highlighting the joint symposia with some of the European sub-specialized societies such as ESPID, ESPGHAN, ENS etc. Some of the symposia have a clear intention to homogenize paediatric care and child health in Europe. The symposium on Eradication of measles, rubella and congenital rubella syndrome requires special mention. First, because it will be given by real experts in this field. Second, because it can provide the present picture of this problem in our Region. Third, because of the implication of EPA, AAP and IPA plus WHO authorities, which gives an idea of the crucial point which we are witnessing similar to that of smallpox some decades ago.

One traditional chapter in our congresses is the early-bird ‘Meet the Professor’ sessions. The short presentation of hot clinical topics followed by a long question and answer section will continue. The Lecture Sessions are intended to follow this pattern: after more detailed updated information the questions/answers will take place. Finally, the poster sessions. If you have an accepted abstract you can be sure that it is of interest, very expert reviewers have fixed a high level of quality for abstracts and as mentioned the presentations will be instructive and constructive.

We cannot end without stating the importance of the joint meeting with the Royal College of Paediatrics and Child Health which gives us the opportunity to share their high standards and pragmatic way of applying childcare and also to benefit from the clinical research which has been so well-established in the UK since the birth of paediatrics. The cooperation and understanding with the RCPCH has not only facilitated this combined congress but also extends to wider aspects of pediatric child health.

Manuel Moya
Plenary sessions
1. KEYNOTE SPEECH: Children, mental health and primary care
2. Clinical breakthroughs
3. European paediatrics: Challenges and opportunities

Symposia
1. Respiratory
2. Neonatal
3. Child health & environment
4. Endocrine
5. Infection symposium I - jointly organised with ESPID
6. Strategic paediatric alliance for children I
7. Strategic paediatric alliance for children II
8. Emergencies
9. Childhood hypercholesterolaemia
10. Gastroenterology - jointly organised with ESPGHAN
11. Primary care psychiatry
12. Evidence based medicine in paediatric primary care
13. Nephrology
14. Autism
15. Infection symposium II - jointly organised with ESPID
16. Genetics
17. Obesity
18. Current inflammatory diseases of the liver
19. Paediatric trials
20. Migraine
21. Nutrition update - jointly organised with EPNS

Special symposium
Global elimination of measles, rubella and congenital rubella syndrome - organised by EPA/AAP/WHO

Meet the professor
1. Seizures in primary care
2. Substance use and abuse
3. The best approach for the use of antipyretics
4. Chronic cough
5. Assessment of acute diarrhoea disease in paediatrics
6. Children with anemia
7. The adolescent and child living with a chronic condition
8. Sports medicine
9. Practical clues for skin manifestation of systemic diseases

Lectures
1. Child health in countries with limited financial resources
2. Advances in the diagnosis of asthma
3. Nutrition in Europe
4. Obstructive sleep apnea
5. Triggers and preventive mechanisms of anaphylaxis in children
6. Basic developmental themes
7. The relationship between breastfeeding, maternal mood and hospital practices
8. New global projects for quality paediatric care - a collaboration between the WHO and the Russian Federation
9. Vitamin D: A necessary update
Glasgow will be a fun, exciting and welcoming host city for the 6th Europaediatrics, 5th - 8th June 2013

Named as the top UK city in the Tripadvisor Travellers’ Choice Destinations on the Rise 2012, Glasgow is trendy and one of Europe’s most exciting destinations. It combines the energy and sophistication of a great international city with some of Scotland’s most spectacular scenery.

Compact and easy to walk around, as a delegate in the city you will enjoy a wealth of attractions. Glasgow is home to more than 20 museums and art galleries offering free admission. Enjoy the magnificent Kelvingrove Art Gallery & Museum, which exhibits an internationally renowned collection of over 8,000 objects. The iconic Riverside Museum on the banks of the River Clyde was designed by world famous architect Zaha Hadid and houses the city’s transport collection with more than 3,000 exhibits in over 150 displays.

Enjoy the many works of Glasgow born architect, designer and artist, Charles Rennie Mackintosh, who is celebrated around the world as one of the most creative figures of the early 20th century. A pioneer of Art Nouveau, he has left a legacy of his work throughout the city including the Glasgow School of Art, considered by many to be his architectural masterpiece.

With the best shopping in the UK outside of London’s West End, Glasgow is the perfect place to indulge in some retail therapy. You can find high street favourites, malls and popular department stores on the city’s Style Mile, an area which includes the shopping thoroughfares of Buchanan Street, Sauchiehall Street and Argyle Street. Designer stores and chic boutiques can be found in the Merchant City and, if you’re looking for something a little more quirky, the West End has great vintage stores on offer.

If you are looking for a great night out, Glasgow is unsurpassed. Enjoy the outstanding choice of cafes, restaurants and bars where the eclectic restaurant and café scene cater for every taste.

Also, if you are looking for some tranquillity, Glasgow means ‘Dear Green Place’ in Gaelic, and there are over 90 parks and gardens to explore. Just beyond the city lies some of Scotland’s most beautiful scenery including ancient castles, quaint distilleries, stunning lochs and miles of unspoilt coastline.

Glasgow’s is easy to get to, with excellent air, rail and road infrastructures. There are three international airports within easy reach of the city offering:

- Direct flights from over 135 destinations
- Low cost direct European flight connections
- Over 40 return flights from London per day
- Flight time from London just 1 hour

Glasgow has two major train stations, Glasgow Central servicing the South and Glasgow Queen Street servicing Edinburgh and the North.

- 20 direct trains from London
- Journey time from London just 4.5 hours

Glasgow has a great choice of accommodation to choose from, including three onsite hotels at the conference venue the Scottish Exhibition + Conference Centre. The city’s hotels include a variety of international brand hotels, deluxe boutique properties, quality budget and student hotel accommodation. Book your accommodation now for the 6th Europaediatrics at www.seeglasgow.com/unepsa2013

For more information on what to see and do in Glasgow:

- Download the free Glasgow city guide app, available from the App Store and Google play, search ‘Glasgow’
- Website seeglasgow.com
- Twitter @see Glasglow
- Facebook GlasgowScotlandwithstyle

The above information was kindly provided by Glasgow City Marketing Bureau (GCMB) is the official destination marketing organisation (DMO) for the city of Glasgow.
European Paediatric Association (EPA/UNEPSA)

Join the most extensive paediatric network in Europe!

Since the launch of the individual membership scheme, the European Paediatric Association (EPA/UNEPSA) embraces a constantly increasing number of individual members from all over Europe.

EPA/UNEPSA welcomes all doctors who are certified as paediatricians in Europe and are members of their respective National Paediatric Society/Association participating in EPA/UNEPSA.

By joining EPA/UNEPSA, you gain access to a network of 41 national European associations and open yourself to a new world of opportunities.

Benefits
The individual membership is offered at a privileged 50 Euro annual fee and encompasses a set of benefits that aim to provide value to the wide community of European paediatricians.

• On line access to the The Journal of Pediatrics is a core benefit of individual membership to our association and we are excited by the prospect of making such a valuable resource widely available to paediatricians across Europe.

• Our members will enjoy reduced registration fees to Europaediatrics as well as to other events organised by our Association.

• The quarterly e-newsletter aims to be a source of current information relevant to the interests of European paediatricians.

• Finally, our members will find in our new website a valuable tool and resource

Individual membership is offered on an annual basis starting on the 1 January of each year and ending on the 31 of December.

You may apply on line for an individual membership. Please visit our website www.epa-unepsa.org for more details and to fill out a registration form.

We look forward to welcoming all of you in EPA/UNEPSA!

Did you know... that all individual members of EPA now also get a free subscription of The Journal of Pediatrics?
Upcoming conferences in 2013

European meetings by EPA/UNEPSA

6th Europaediatrics Congress jointly held with the Royal College of Paediatrics and Child Health
5-8 June 2013, Glasgow, United Kingdom

4th International Conference HUS-MPGN-TTP & related disorders
9-11 June, 2013, Austria

The 4th Annual Conference of the European Confederation of Primary Care Paediatricians – ECPCP
3-5 July 2013, Tel Aviv, Israel

Member and Affiliated Societies’ Meetings

10th National Congress of the Slovakian Paediatric Society
25-27 April 2013, Bratislava, Slovakia

International Congress of Pediatrics – ICP 2013
24-29 August 2013, Melbourne, Australia

12th World Congress of Pediatric Dermatology
25-27 September 2013, Madrid, Spain

8th World Congress on Pediatric Infectious Diseases
19-22 November 2013, Cape Town, South Africa

14th National Congress of the Portuguese Paediatric Society
3-5 October 2013, Porto, Portugal

Excellence in Paediatrics 2013
4-7 December 2013, Doha, Qatar

Other Meetings

2nd International Conference and Exhibition on Nutritional Science & Therapy, and Symposium by World Health Organization, July 15-17, 2013, Philadelphia, USA

Other Paediatric Meetings

46th Annual Meeting – ESPGHAN 2013
8-11 May 2013, London, United Kingdom

2nd PNAE Congress on Paediatric Nursing
7-8 June 2013, Glasgow, United Kingdom
## List of Member Countries 2013

<table>
<thead>
<tr>
<th>Country</th>
<th>Society/Association</th>
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<tbody>
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EPA is an association for medical professionals. Our network is a fantastic talent pool of 60,000 paediatric healthcare professionals, who every year share their brilliant questions and suggestions on how to best understand and improve general paediatric practice. EPA always responds to such important feedback. Importantly, however, to be able to address shared issues, unmet needs or to develop good ideas and exciting initiatives, even after prioritisation, we need external financial resources.

EPA has therefore developed a corporate partnership programme that allows companies to support our work provided they share our mission and values, and comply with our ethical principles and Guidelines for Relations with Industry. Jointly we can understand diverse issues better, and develop targeted activities to effectively meet paediatricians’ needs for medical education, best practice guidelines, and interactive communication. By working, learning and developing together – by proactively combining our strengths - we can develop and improve the clinical standards, and ultimately also European child health.

EPA would like to welcome its corporate partners and acknowledge their support in the development of the following exciting initiatives:

“Good Health begins with Good Hygiene”
EPA and Reckitt Benckiser (RB), believe that good hygiene is a key ingredient to good health and work jointly to educate the public on the benefits of adopting good hygiene habits, both personal, in the home, and to explain why good health begins with good hygiene.