ESPE Newsletter

bringing the latest in paediatric endocrinology to you

The newsletter of the ESPE
European Society for Paediatric Endocrinology
Improving care of children with endocrine diseases by promoting knowledge and research

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ESPE News Contents *(click on a link below)*

Welcome to **Milan!**

I LOOK FORWARD TO GREETING YOU very shortly at the 9th Joint Meeting of Paediatric Endocrinology on 19–22 September in Milan, Italy. This reunion of ESPE with its sister societies will provide a truly international forum in which clinicians, scientists, psychologists and nurses from around the globe can share the latest research and developments in paediatric endocrine care.

Entitled 'Predictive medicine to improve the care of children', this meeting will highlight the importance of scientific research and technological advances, and the insights they provide, in our ability to provide the best patient care. This theme will be made manifest, fittingly, by a schedule of inspiring plenary lectures on topics ranging from innovative research into stem cells as a cure for type 1 diabetes to endocrine disruptors, via genetics of growth, early programming, obesity and disorders of sex development. Read more on pages 4–5.

Read previews of exciting plenary lectures on pages 4–5.

Visit www.jointmeeting2013.org for further details

All aspects of endocrine care in childhood will be explored in the array of symposia, controversies and meet-the-expert sessions, and all delegates will be encouraged to discuss their latest findings with experts in the many free oral communications and poster presentations.

As always, it is your participation that will make this meeting a success, and so I extend my warmest invitation to you to come and sample for yourself the cuisine, architecture, music, history and culture for which Milan and Italy are renowned. Remember the ***deadline for registration is Friday 2 August 2013***. Make sure you submit your registration now!

Professor Franco Chiarelli, chiarelli@unich.it
President, European Society for Paediatric Endocrinology (ESPE)
Chairman of the Joint Programme Organising Committee (JPOC)

Milan 2013

Welcome to issue 22

DEAR FRIENDS AND COLLEAGUES,

We are looking forward to the 9th Joint Meeting of Paediatric Endocrinology, which takes place in Milan, Italy, in September – now only a few weeks away.

The Joint Meetings give a special flavour to our academic life. New friends and colleagues from different countries all over the world, broader perspectives from different societies and a busier and tighter schedule. We wish every success to the President of the Milan meeting, Franco Chiarelli, and to the Organising Committee, comprising members of the different societies, who have brought together an excellent scientific programme. Read Franco Chiarelli's message on this page, then turn to pages 4 and 5 for keynotes from some of the plenary lectures to inspire you (we thank the speakers for these contributions). Make sure to mark your calendar and register for the meeting by 2 August, if you have not already done so.

We continue to introduce national societies in the Newsletter, and in this issue brings news from the French Society (page 6). We thank them for telling us about their activities. Please

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New dates

Please note the 2014 ESPE meeting in Dublin will take place on **18–20 September 2014**, and the 2015 ESPE meeting in Barcelona on **1–3 October 2015**.

Accreditation and Syllabus update

The Accreditation and Syllabus Subcommittee has updated the Training Syllabus in Paediatric Endocrinology and Diabetes. See www.eurospe.org/education/education_training.html to review the latest version.

We welcome your feedback and suggestions to finalise the syllabus. Please send them to espe@eurospe.org.

Lars Sävendahl, *ESPE Secretary General*

Welcome *continued from page 1*

share news from your own national societies with us.

We also report from the very successful ESPE Winter School (page 8) and the equally successful academic ESPE Science School, as well as the Bone and Growth Plate Working Group (both on this page). You will find perspectives on paediatric endocrinology in China (also below) and Africa (page 3), and an interview with a new member of ESPE (page 7), who explains what our Society brings to her academic life.

We continue our series previewing the *Yearbook of Pediatric Endocrinology*, courtesy of its editors, Ze'ev Hochberg and Ken Ong (pages 6–7). This initiative is greatly appreciated by members, and we are pleased to highlight some new articles. We thank the editors cordially.

We also thank Mark Dunne and Karen Cosgrove from the University of Manchester, UK, for sharing their research on congenital hyperinsulinism (page 3). We hope articles such as this will foster increased collaboration throughout Europe.

We, as your Editorial Board, will do our best to continue to maintain the quality of the Newsletter and enrich it with feedback from all members.

I would also like to thank my colleagues in the Newsletter team and Caroline Brewser from Bioscientifica, with whom I have a chance to always work with much enthusiasm and in excellent collaboration.

Yours sincerely,
Professor Feyza Darendeliler
Editor, ESPE Newsletter
feyzad@istanbul.edu.tr

ESPE Science School

THE 2013 ESPE SCIENCE SCHOOL IN ACRE, ISRAEL, on 9–12 May was attended by 23 students (13 with MD/PhD). They came from countries across Europe, but also included two delegates from the Sociedade Latino-Americana de Endocrinología Pediátrica, two from the Asia Pacific Paediatric Endocrine Society, two from the Pediatric Endocrine Society and one from India.

The faculty comprised 10 ESPE members and 15 guest speakers, with a Scientific Committee including George Chrousos (Chair), Ze'ev Hochberg (Co-ordinator), Dov Tiosano (Local Organiser), Jean-Claude Carel, Olle Söder, and Nicolas de Roux (the next Science School Organiser).

On the programme were:

- a general research topic (e.g. career development, ethical consideration, or scientific approach)
- group work to discuss students' research and review a grant application
- leading science concerning 'Human evolution and perspectives in child health'

The scientific element was of the highest quality and very relevant to paediatric endocrine practice, moreso than any previous ESPE Science School or New Inroads in Child Health Conference. About half the lectures will be published in the prestigious journal *BMC Medicine* (impact factor 6).

Following a decision by Council, the Science School will continue at 2-yearly intervals, with the next in Paris in 2015.

Ze'ev Hochberg, *Haifa, Israel*
z_hochberg@rambam.health.gov.il

Bone and Growth Plate Working Group

THIS WORKING GROUP'S SESSION IN MILAN will include top speakers from America and Europe on the development of growth plate cartilage and the skeleton, as well as management of leukaemia-induced growth and bone disease and vitamin D.

Vitamin D is a hot topic, with much debate about deficiency and insufficiency thresholds, supplementation and treatment doses, whether extra-skeletal effects exist and what relevance they have from a global point of view. Last but not least – how should all nations adjust their health policies and at what cost?

We are planning a worldwide paediatric consensus conference on vitamin D, and have started setting up a working group of experts to formulate consensus questions. I have been busy communicating with the ESPE Clinical Committee and raising the necessary funds. As we now have CPC approval, we will contact sister societies and proceed with the consensus in the next 12 months.

In its second year, the European Bone and Growth Plate Network is being actively used to encourage discussion of supra-regional public health issues (such as vitamin D), collaborative research and audit, distribution of information on meetings and updates, and *ad hoc* discussions. I encourage ESPE members interested in being included in this network to contact me.

Wolfgang Högler, wolfgang.hogler@bch.nhs.uk

ESPE represented in China

ESPE HAS BEEN FORGING LINKS with the Chinese Society of Paediatric Endocrinology and Metabolism (CSPEM).

The CSPEM generously invited Jan Lebl (Prague, Czech Republic) and Olle Söder (Stockholm, Sweden) to their meeting in Yantai in October 2011. Both ESPE delegates presented at their respective plenary sessions and participated in a postgraduate training programme for budding Chinese endocrinologists.

In 2012, it was the turn of Gary Butler (London, UK) to represent ESPE, while in October 2013, the baton will pass to Gabriele Haeusler (Vienna, Austria).

Although language remains an issue, all our ESPE speakers have commented on the great enthusiasm among local paediatric endocrinologists, which helps to break down such barriers and fosters closer collaboration. ESPE feels privileged to continue to support CSPEM activities. We hope to include news and scientific updates from CSPEM 2013 in a future issue of the Newsletter.

Congenital hyperinsulinism in infancy

NEONATES AND INFANTS WITH THE RARE CONDITION congenital hyperinsulinism in infancy (CHI) are the focus of integrated basic science and clinical research in our laboratories at the University of Manchester, UK.

Working closely with the Northern Congenital Hyperinsulinism Service based at Manchester Royal Infirmary and led by Dr Indi Banerjee, the academic research team are exploring new ways to diagnose and treat this devastating condition (for review see Banerjee *et al.* 2013 *Clinical Endocrinology (Oxford)* **78** 803–813).

We employ novel approaches to understand disease pathogenesis, using post-genomic technologies such as proteomics and metabolomics on patient serum, in combination with more traditional studies of cell biology and function on insulin-secreting cells removed during pancreatectomy (e.g. Powell *et al.* 2011 *Diabetes* **60** 1223–1228).

Currently fewer than 50% of patients with transient or persistent CHI have identified gene mutations, and this makes both prediction of disease outcome and selection of the most appropriate treatment difficult. By understanding the disease processes using a network biology approach, we hope to identify new prognostic disease biomarkers and personalised treatment strategies (Stevens *et al.* 2013 *Orphanet Journal of Rare Diseases* **8** 21).

The research team regularly collaborate with clinical colleagues throughout Europe to share protocols, samples and know-how. Any ESPE colleagues who would like to participate in multi-centre studies, donate post-operative tissue or collaborate directly are welcome to contact mark.j.dunne@manchester.ac.uk or karen.e.cosgrove@manchester.ac.uk.

Mark Dunne *and* **Karen Cosgrove**, *University of Manchester, UK*

4th Annual Scientific Meeting of ASPAE

DURBAN, SOUTH AFRICA, was the setting for the African Society for Paediatric and Adolescent Endocrinology (ASPAE)'s Annual Meeting, on 15–17 May 2013.

In total, 39 paediatric endocrinologists took part, from 8 countries. Most were from South Africa or Nigeria (host of ASPAE 2012 and home of the second PETCA (Paediatric Endocrine Training Centre for Africa)), while others travelled from Botswana, Ghana, Kenya and Tanzania, with guests from India and the Czech Republic.

Abiola Oduwole, ASPAE Past President, welcomed delegates, commenting, 'This is our fourth meeting, and it is wonderful to see how we have grown. I clearly remember the first meeting in 2010, with all the excitement and expectation that finally, a dream I had, and felt might never materialise, was going to be fulfilled. We must recognise Lucy, our Foundation President, and the team – Tom, Renson, Risper, Paul, Kerstin, Ze'ev, Ragnar, Faisal and the PETCA Fellows – who succeeded against great odds in making that date a historic one.'

Kubendran Pillay, 2013 Conference Chair and ASPAE President, summarised the current needs of African countries: 'As they emerge from a colonial and oppressive past, positive political, economic and social changes take hold. As epidemics of infectious disease start declining, non-communicable and chronic conditions are increasingly recognised as causes of significant morbidity and mortality. The maturing healthcare system is diagnosing more children with endocrine disorders. These changes are leading the demand for more skilled clinical care and scientific research in this area.'

The 3-day scientific programme included 20 invited lectures and meet-the-expert sessions, with numerous oral presentations and posters. It clearly demonstrated the recent major achievements in African paediatric endocrinology and the increasing capability to provide high quality patient care in low income countries. The invited guest from India, Dr Virmani from New Delhi, shared her great experience in establishing comparable levels of up-to-date care for diabetic children who originate from a range of socio-economic backgrounds, and in building an infrastructure for chronic paediatric patients in general.

Meeting African colleagues and friends brought inspiration for both parties. Europeans have much to learn from Africa, such as how to use, and not overuse, the available resources.

Thanks are due to the Organising Committee: Kubendran Pillay, Abiola Oduwole, Yasmeen Ganie, Dipeselema Joel and Edna Majaliwa. The next Annual Meeting of ASPAE takes place in May 2014 in Dar-es-Salaam, Tanzania, with Edna Majaliwa as the Local Chair.

Jan Lebl *and* **Stanislava Kolouskova**, *ESPE delegates*

Milan 2013 – Plenary lecture preview

Here is a taste of the advances in paediatric endocrinology that will be on offer at the 9th Joint Meeting of Paediatric Endocrinology in Milan. Register now at www.jointmeeting2013.org to ensure your place!

Long-term follow-up in DSD

THE CHALLENGE OF DIAGNOSING and treating patients with disorders of sex development (DSD) is exacerbated by the lack of long term follow-up data. Our update on the long term follow-up of DSD patients over 3 decades is mainly retrospective, with patients investigated by a multidisciplinary team using a 152-point questionnaire to analyse the impact on patients' social, professional and sexual behaviour.

We studied 55 patients with the classical form of virilising congenital adrenal hyperplasia (CAH; 52 with 21-hydroxylase deficiency and 3 with 11-hydroxylase deficiency), and 96 patients with 46,XY DSD in four categories: testosterone biosynthetic defects, 5α-reductase type 2 (5α-RD2) deficiency, androgen insensitivity syndrome and indeterminate DSD.

Attribution of female social sex was predominant in both 46,XX and 46,XY DSD groups. Social sex change to male occurred in 18% of 46,XY DSD and in 10% of 46,XX DSD patients. Childhood male or neutral games significantly associated with the change of social sex to male in patients registered as females ($P < 0.05$). In the 46,XX DSD group, CAH patients who had been inappropriately treated changed to a male social sex. In the 46,XY DSD group, 5α-RD2 deficiency was associated with a change to male social sex. Heterosexual orientation was reported by 94% of the 46,XY DSD patients and by 80% of the 46,XX DSD patients. There was a predominance of homosexual/bisexual behaviour in the virilising CAH group. Patients with 5α-RD2 deficiency had the smallest penile length before and after therapy, whereas the undetermined group presented the largest penis size, with most with a final penile length less than –2 SDs.

Most patients reported being happy with their professional activities. Five patients with female social sex (4.7%; 3 from the 46,XX group and 2 from the 46,XY group) worked in typically male oriented jobs, in contrast with the male social group, in which all of the patients worked in male oriented or neutral jobs.

Berenice Bilharinho de Mendonça
Faculdade Medicina Universidade São Paulo, Brasil

Stem cell-derived islet cells for transplantation

DIABETES MELLITUS AFFECTS over 350 million patients worldwide. The most severe form is the type 1 variant, with destruction of pancreatic β cells. Strategies aimed at restoring β cell mass generally use replacement (islet transplantation and stem cell differentiation), reprogramming (from non-insulin-producing cells) or regeneration (replication and induction from endogenous precursors/stem cells). The aim is to reverse the disease condition and prevent the development of severe chronic complications that can affect many organ systems over time.

The additional challenge is to abrogate autoimmunity, so that the immune system can no longer destroy the new insulin-producing cells introduced into the body. This involves tolerance induction strategies or immune protection, whilst avoiding side effects such as those associated with life-long immunosuppression. There is a broad consensus on the idea that stem cells will replace islets in the near future, although candidate cell type(s) and approaches need to be refined.

Mesenchymal stem cells have been investigated extensively in adult stem cell research, but problems remain. Current methods to differentiate adult stem cells to β cells are variable and inefficient. On the other hand, reprogramming (or transdifferentiation), where a terminally differentiated tissue might be converted into another under the appropriate conditions, may be another option. Ferber and colleagues pioneered this approach by delivering a pancreatic regulatory gene, Pdx1, into recipient mice by adenoviral vehicles. Ectopic expression in the liver led to the activation of β cell genes and dramatic reductions in blood glucose levels. Other groups reported similar results either with Pdx1 alone or with other reprogramming genes, such as Ngn3 and MafA.

While a multicentre phase III trial of transplantation of adult pancreatic islets has recently completed enrolment and is moving towards a biological licence application in the USA, the selection of the most appropriate source for insulin-producing cells is still not defined, and the selected alternatives between replacement, reprogramming and regeneration strategies should be further developed.

Camillo Ricordi, *University of Miami, Florida, USA*

Dietary causes of the obesity epidemic

AN IMPORTANT CLUE TO THE dietary causes of obesity comes from demonstrations that animals including insects, birds, fish and mammals have separate appetite systems for protein, carbohydrate and fat. These species regulate intake of protein more strongly than carbohydrate and fat when confined to diets of fixed macronutrient composition.

Simpson and Raubenheimer proposed that this predominant protein appetite may play a key role in the human obesity epidemic – the protein leverage hypothesis (PLH). The PLH predicts that when the proportion of dietary protein falls, the powerful protein appetite stimulates increased energy intake in an attempt to gain limiting protein. Hence, if the diet shifts towards an increased proportion of foods that are higher in carbohydrate and/or fat, thereby diluting available protein, energy intake will increase, as will the risk of obesity and metabolic disease.

Such a shift has occurred in the Western diet over the past 50 years, driven by factors including increased reliance on processed foods, economic drivers impacting consumers and the food production industry (protein is more expensive than fat and carbohydrate), and our evolutionary predisposition to find sugar and fat highly palatable. There is growing evidence for the PLH from animal studies, clinical trials, population surveys and large trials. The implications for health are profound.

Stephen J Simpson, *University of Sydney, NSW, Australia*

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Milan 2013 – Plenary lecture preview *continued from page 4*

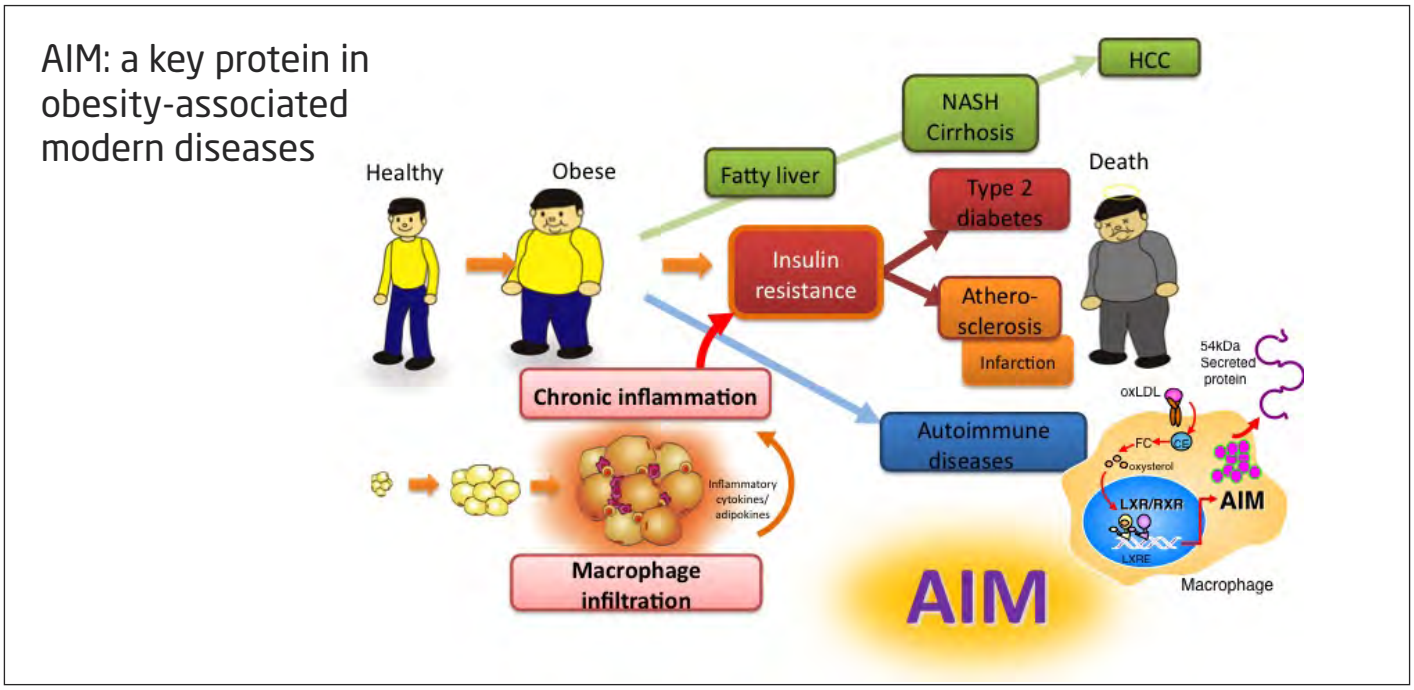
AIM: a key player in modern diseases

THE NUMBER OF PATIENTS SUFFERING multiple diseases associated with obesity is rapidly increasing. Obesity induces various metabolic and cardiovascular diseases, caused by chronic, low-grade inflammation, and correlates strongly with autoimmune disease. Obesity is accompanied by fatty liver diseases including non-alcoholic steatohepatitis (NASH) and hepatocellular carcinoma (HCC). We hypothesise that there might be underlying key molecules involved in the regulation of these diseases.

We have identified a macrophage-derived secreted protein, apoptosis inhibitor of macrophage (AIM), that may be a key player. In obesity, augmentation of blood AIM levels induces vigorous lipolysis in adipose tissue, thereby inducing chronic inflammation followed by diabetes and atherosclerosis. AIM also binds to IgM and contributes to production of multiple autoantibodies under obese conditions.

In contrast, AIM strongly inhibits fatty liver associated HCC development. Thus, AIM acts as a key factor that defines the 'disease lineage' in obesity, either to inflammatory diseases or to liver diseases. Currently, we are conducting a large scale human cohort study to assess correlation between blood AIM levels and multiple diseases, which may lead to diagnostic and therapeutic strategies.

Toru Miyazaki, *University of Tokyo, Japan*



Genetic regulation of growth

IN THE FETUS AND NEWBORN, body growth is rapid because of swift cell proliferation in multiple tissues. During later childhood, both cellular proliferation and growth slow down. This deceleration is briefly interrupted by the pubertal growth spurt, but then resumes until growth ceases in adulthood.

The mechanisms for growth deceleration are not well understood. Although the decline in cell proliferation occurs concordantly in multiple organs, it does not appear to be co-ordinated by a change in hormone levels. In organ transplantation, the growth rate of the organs depends on the donor's age, not the recipient, suggesting that the decline in growth rate is due to local, not systemic, mechanisms.

From work in mice and rats, it appears the decline in cell proliferation in juvenile life is due to a growth-regulating genetic programme occurring simultaneously in multiple tissues to downregulate multiple growth-promoting genes. This programme appears not to be driven by time *per se* but by the process of growth itself. So, if growth is temporarily inhibited, e.g. by nutritional deficiency, the growth-limiting genetic programme slows, thus at least partially retaining growth potential for the future. This putative growth-limiting programme is conserved among different mammalian species.

Recent studies suggest the downregulation of these growth-promoting genes during juvenile life is orchestrated in part by a transcription factor, E2f3. In early life, E2f3 expression is high, driving expression of many growth-promoting genes, such as Igf2. With increasing age, E2f3 levels decline, leading to downregulation of these genes. Evidence suggests that this growth-limiting control system is defective in some malignancies, where overexpression of E2f3 appears to drive overexpression of Igf2, probably contributing to unrestricted growth of cancer cells.

Jeffrey Baron, *NIH, Bethesda, MD, USA*

Other plenary lectures in Milan include:

Prevention of type 1 diabetes in children
Michael Knip
(Helsinki University Central Hospital, Finland)

Programming effects of early life adversity
Wayne Cutfield
(University of Auckland, New Zealand)

Endocrine disruptors and their effects on child health
Niels Skakkebæk
(University of Copenhagen, Denmark)

Yearbook of Pediatric Endocrinology: Editors' preview

Editors Ze'ev Hochberg and Ken Ong pick out some of the outstanding papers published recently in the Yearbook of Pediatric Endocrinology.

Ethical and policy issues in genetic testing and screening of children

American Academy of Paediatrics, American College of Medical Genetics and Genomics *Pediatrics* 2013 **131** 620–622.

With rapid growth in both genetic knowledge and consumer interest, the genetic testing and genetic screening of children are now commonplace. The decisions about whether to offer these tests should be driven by the best interests of the child. The growing evidence regarding the psychosocial and clinical effects of such testing and screening should inform best practice. This policy statement represents recommendations developed collaboratively by the American Academy of Pediatrics and the American College of Medical Genetics and Genomics. They apply to many of the scenarios in which genetic testing and screening may occur, including: diagnostic testing, newborn screening, carrier testing, predictive genetic tests, histocompatibility testing, adoption, disclosure, and direct-to-consumer testing.

COMMENTARY

For children who present with clinical features of genetic illnesses or with a family history of a genetic condition, paediatric endocrinologists have an increasing number of genetic tests available in our clinics, even without having to consult with our medical genetics colleagues. More and more, we are put under pressure to perform these tests by families. These recommendations from the USA are therefore timely and will be very valuable reading for many paediatricians worldwide. In addition to the wide range of scenarios described above, the authors provide two important general recommendations, which most paediatricians would no doubt whole-heartedly endorse. First, that the decisions regarding the use of testing should be driven by the best interests of the child. Secondly, that genetic testing is best offered in the context of genetic counselling.

A key strength of these recommendations is that they are informed by the published evidence regarding the psychosocial, clinical and reproductive harm and benefit of genetic testing and screening, which was comprehensively reviewed and published at the same time (Ross *et al.* 2013 *Genetics in Medicine* **15** 234–245). Evidence on key issues such as informed consent or assent, voluntary agreement, privacy and confidentiality is presented and interpreted. An interesting distinction is made between 'predictive' testing, for mutations that will almost certainly give rise to disease, typically childhood-onset conditions, versus 'predispositional' testing, for mutations with incomplete penetrance that may never become manifest, such as adult-onset cancer syndromes.

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SFEDP
Société Française d'Endocrinologie et Diabétologie Pédiatrique

SFEDP, the French Society for Paediatric Endocrinology and Diabetology, was founded in 1996 as a part of the French Society of Paediatrics and currently has 196 members. The President and Secretary are Regis Coutant (Angers) and Agnes Linglart (Paris) respectively.

Unlike many other national societies, SFEDP is not organised around multisite collaborative working groups, but supports the development of reference centres for the diagnosis and management of rare paediatric endocrine diseases. These are centres for rare growth diseases (J Leger, Robert Debré Hospital, Paris), rare diseases of phosphorus and calcium metabolism (A Linglart, Bicêtre University Hospital, Paris), rare diseases of hormone signalling pathways (P Rodien and R Coutant, Angers University Hospital), sex differentiation disorders (P Chatelain, Lyon University Hospital, and C Bouvattier, Bicêtre University Hospital, Paris), rare pituitary diseases (T Brue and R Reynaud, Marseille University Hospital), Prader-Willi syndrome (M Tauber, Toulouse University Hospital) and rare adrenal diseases (J Bertherat, Cochin University Hospital, Paris). There are review publications once a year in the *Quotidian du Médecin*, a French journal for general practitioners.

SFEDP organises a 1-day annual meeting, with outstanding workshops and meet-the-professor sessions. Each year, it supports 3–4 grants and 2–3 prizes of various sizes.

Currently, the national accreditation in paediatric endocrinology is the National Certificate for Paediatric Endocrinology and Diabetology, which uses, in part, the ESPE Training Programme.

For further information or to get in touch, visit www.sfedp.org or contact the SFEDP Secretariat at secretariat.sfedp@gmail.com.

Yearbook of Pediatric Endocrinology: **Editors' preview** *continued from page 6*

100 years of CAH in Sweden: a retrospective, population-based cohort study

Gidlöf S, Falhammar H, Thilén A, von Döbeln U, Ritzén M, Wedell A & Nordenström A
The Lancet Diabetes & Endocrinology, Early Online Publication, 28 February 2013

CONTEXT: The authors aimed to assess the effect of historical medical improvements in managing patients with congenital adrenal hyperplasia (CAH) and of neonatal screening in Sweden.
METHODS: Data sources, including the registry at the Swedish National Screening Laboratory, were used to identify patients with CAH for this retrospective, population-based cohort study. The authors collected data from 2010/2011. They also identified patients via the neonatal screening programme, late-diagnosed patients reported to the laboratory, and patients who underwent genetic analysis or were known to the authors through clinical contacts.
RESULTS: 606 patients with the disorder, born between 1915 and 2011, were identified. The *CYP21A2* genotype was known in 490 patients (81%). The female-to-male ratio was 1.25 in the whole cohort, but close to 1 in patients detected by screening. There was a sharp increase in diagnoses in the 1960s and 1970s. After the introduction of neonatal screening (1986), the proportion of patients with the salt-wasting form increased in both sexes, from 114 (47%) of 242 individuals between 1950 and 1985 to 165 (57%) of 292 individuals between 1986 and 2011 ($P = 0.038$). Before 1970, 5–10 children were missed annually.
CONCLUSION: The authors found that, contrary to current belief, boys and girls with salt-wasting CAH were equally missed clinically. Screening improved detection of the salt-wasting form in both sexes, saving lives in boys as well as girls. The non-classic form was diagnosed more often in females, explaining the female preponderance in this cohort.

COMMENTARY

Using a national screening registry containing almost 100 years of data, the authors assessed the impacts of treatment advances and of screening for CAH. It has been assumed that screening is important for detecting simple virilising CAH and salt-wasting CAH in males because ambiguous genitalia at birth already alerts to the diagnosis and anticipation of salt-wasting in females. Whilst CAH screening is adopted in many 'developed' countries, a high proportion of false positives can lead to parental anxiety and extra healthcare costs. Therefore, CAH screening programmes should be evaluated in terms of both mortality and morbidity reduction. Well-being, not just survival, is important, and there remain many surgical and psychological issues in relation to treatment timing, efficacy, compliance etc.

This paper is important because the authors found that screening improved detection in girls as well as in boys. Contrary to received wisdom, girls with salt-wasting CAH were missed clinically as often as boys, despite a highly developed healthcare system. Apparent increases in incidence over time reflected improvements in diagnosis and increased awareness of CAH arising from healthcare improvements and the development of paediatric endocrinology as a specialty.

Earlier detection of salt-wasting CAH through screening means that both sexes escape adverse effects (neonatal hyponatraemia/hyperkalaemia/hypoglycaemia/acidosis) at this important window for brain development. Healthcare benefits are maximised by integrating molecular genetics with specialised care, and a healthcare system that collects universal data; this has been shown to be beneficial even in a 'developing country', such as Cuba (Gonzalez *et al.* 2013 *Clinica Chimica Acta* **421** 73–78).

MEET A MEMBER ...

Ece Böber

If you have recently joined ESPE, or if you have been a member for some time, and you would like to tell us what inspired you to join, and what you find most useful about your membership, please contact espe@eurospe.org.

Professor Ece Böber works in the Paediatric Endocrinology Unit at Dokuz Eylül University, in Izmir, Turkey. Here, she tells us why she values her membership of ESPE.

I have been impressed with the scientific and clinical content at ESPE for some time, and have attended almost all ESPE meetings over the last 10 years. The standard of presentations is very high, but at the same time accessible and usable. My involvement with ESPE's Turner Syndrome Working Group has been very gratifying. I decided to take the next step and applied to be an ESPE member. I am delighted that I was chosen.

Now that I am a member, I hope I will be able to follow the latest progress in diagnostic and therapeutic approaches in paediatric endocrinology closely. This will help my clinical practice in a significant way.

I would definitely advise other budding and established paediatric endocrinologists to apply for ESPE membership. Apart from the huge amount of valuable information, ESPE membership also offers advantages like discounts on ESPE meeting fees and subscription to *Hormone Research in Paediatrics*. There's no good reason not to apply if you are linked to paediatric endocrinology in any way!

18th ESPE Winter School

WINTER SCHOOL RETURNED TO POLAND this year, taking place on 15–21 February at the magnificent castle Zamek Baranów, near Rzeszów.

The faculty comprised 25 students selected from nearly 60 applications, and 7 teachers. We gave preference to students from Poland and the surrounding countries, and were keen to build on the success of the 2012 Winter School in Ukraine by encouraging further applications from east and (especially) west Ukraine.

Our Host Co-ordinator, Artur Mazur, showed extraordinary commitment and attention to detail, so the event went very smoothly. Other members of the Winter School faculty were Malcolm Donaldson (Co-ordinator; Glasgow, UK) and John Gregory (Cardiff, UK), Christa Flück (Berne, Switzerland), Angela Hübner (Dresden, Germany) and Margaret Zacharin (Melbourne, Australia). We were also joined by David Metreveli, next year's Host Co-ordinator (Tbilisi, Georgia).

As usual, the 5-day course covered all main aspects of paediatric endocrinology and diabetes. The format was a combination of interactive plenary lectures and small group sessions involving student case presentations, student research proposal rehearsals, and the ever-popular 1½-hour sessions on teachers' cases.

The research component of Winter School was led for the third time by Christa Flück and consisted of evening sessions on how to do research and audit, critical evaluation of two papers sent out by Christa beforehand, and presentation of 10 selected student research or audit projects to the plenum.

The excursion was to the town of Sandomierz, where we walked a famous underground route, attended a church organ concert, and visited an armoury to learn about weapons through the ages, from a young man dressed as a crusader. We finished by climbing the town tower – a very stimulating if cold (–10˚C) experience! Back at the castle we enjoyed a firework display and a meal in a cave with a three-piece

band, punctuated by a visit from two gate-crashing 'soldiers' to ravish one of the students ('a virgin') and put the Winter School Co-ordinator in the stocks, before challenging faculty members to rescue their hapless colleagues!

The meeting was another resounding success with a particularly high standard of student cases and research presentations, and the best ever student feedback for the research sessions. This is a huge credit to Christa Flück, and a fitting tribute at this, her final ESPE Winter School; she has served us brilliantly since 2009. Seven of the 25 students have since had abstracts accepted for the 9th Joint Meeting of Paediatric Endocrinology in Milan this September.

I shall stand down as Co-ordinator after Georgia 2014; the post will be advertised shortly. In 2015, Winter School will visit the Balkans for the first time, with Zoran Gucev (Skopje, Macedonia) as Host Co-ordinator.

We thank Ferring Pharmaceuticals (especially their Global Brand Manager Phil Boothroyd) for sponsoring our meetings, as they have done from the inception of Winter School in 1995.

Malcolm Donaldson, *Glasgow, UK*
ESPE Winter School Co-ordinator 2008–2014

BOOK YOUR PLACE!
Winter School 2014

21–26 February, Kachreti, Georgia

Our venue will be the friendly and intimate Ambasadori Hotel in Kachreti, 85km from Tbilisi. Application forms will be available at www.eurospe.org from 1 August and the deadline for their submission is 25 October 2013. Applications will be particularly welcomed from Georgia, Armenia, Azerbaijan, Turkey, countries of the Middle East, Russia and Ukraine.

ANNOUNCEMENT: Shortage of Increlex® (mecasermin)

In April, Ipsen informed the Regulatory Agencies of the EU, ESPE and the public of a market shortage of Increlex® (mecasermin) in the EU from early August 2013.

The shortage is due to difficulties in manufacturing the active ingredient of Increlex®. These issues are not related to the safety or efficacy of Increlex® currently on the market. Ipsen is making every effort to resume a normal supply as soon as possible, but the duration of the shortage is currently unknown and resupply before the end of 2013 is not anticipated.

Increlex® is recombinant human insulin-like growth factor-1 (rhIGF-1) approved for the long-term treatment of growth failure in children and adolescents of 2–18 years with severe primary IGF-1 deficiency (IGFD). Ipsen recommends that remaining product should only be used for patients who already receive Increlex®. Treatment of new patients should not start until normal supplies are re-established. There are no alternative treatment options for severe primary IGFD available in the absence of Increlex®.

Ipsen recommends that physicians follow-up all patients during the off-treatment period. For patients in the European Increlex Growth Forum Database (EU-IGFD) Registry, this enforced break will provide the possibility of documenting information on the clinical consequences of treatment interruption and reintroduction, which could be extremely valuable.

Ipsen has established an Advisory Board of EU clinicians, expert in the management of paediatric growth disorders, who will answer your medical management questions in an independent and confidential manner: Peter Bang (peter.bang@liu.se), Michel Polak (michel.polak@nck.aphp.fr), Martin Savage (m.o.savage@qmul.ac.uk), Joachim Woelfle (joachim.woelfle@ukb.uni-bonn.de).

Future meetings

See www.eurospe.org/meetings for details of all future meetings

Other Events

ESPE Summer School
22–25 September 2013
LAKE MAGGIORE, ITALY

3rd ESPE Maghreb School
20–25 November 2013
ALGERS, ALGERIA

ESPE Winter School
21–26 February 2014
KACHRETI, GEORGIA

Deadlines

Please note these fast-approaching deadline dates and submit your applications as soon as possible.

ESPE Visiting Scholarship applications	31 Jul 2013
9th Joint Meeting Standard Fee Registration	2 Aug 2013
ESPE Winter School Applications	25 Oct 2013
ESPE Visiting Scholarship	31 Oct 2013
ESPE Andrea Prader Award nominations	10 Dec 2013
ESPE Research Award nominations	10 Dec 2013
ESPE Young Investigator Award nominations	10 Dec 2013
ESPE Outstanding Clinician Award nominations	10 Dec 2013
ESPE International Award nominations	10 Dec 2013
ESPE Henning Anderson Award nominations	10 Dec 2013
ESPE Visiting Scholarship	31 Jan 2014

See the ESPE website www.eurospe.org for further details and application forms

ESPE
European Society for Paediatric Endocrinology

Improving care of children with endocrine diseases by promoting knowledge and research

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ESPE Office

The ESPE Office is managed by Bioscientifica Ltd, headed by Managing Director Leon Heward-Mills.

Hannah Bonnell, Bioscientifica's Association Services Manager, oversees the day-to-day relationship with ESPE, liaising with the ESPE Council and committee members as well as being the main point of contact for ESPE enquiries. She undertakes projects requested by the Secretary General, providing him with assistance and attending ESPE Council and committee meetings. The ESPE Office handles membership renewals and payments and deals with subscriptions to *Hormone Research in Paediatrics*.

Bioscientifica also manages the Corporate Liaison Board which deals with industry sponsors, and is also responsible for publication of the ESPE Newsletter.

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