Insights into MAnaging Growth for Endocrine Nurses

November 5 – 6 2015, Nice, France

A Springer Healthcare Independent Medical Education Event for Paediatric Nurses

Session Summaries

Springer Healthcare IME

IMAGE 2015: Insights into MAnaging Growth for Endocrine Nurses

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Thank you for attending this year's IMAGE symposium. We hope you found the sessions helpful and made many useful contacts with colleagues from other countries.

This year's meeting contained nearly 9 hours of presentations and discussion, packed into one and a half days: a lot of information to absorb! To help refresh your memories, here is an overview of the key teaching sessions to complement the presenters' slides you were given at the close of the symposium. We also provide a summary of the popular "My Week" feature.

A view of Nice, France where the meeting took place.

Organising Committee

Kate Davies – Chair

Senior Lecturer in Children's Nursing
London South Bank University, UK

As a qualified children's nurse for over 20 years, Kate spent 15 of them working as a Clinical Nurse Specialist in Paediatric Endocrinology. She has always held a passion for teaching and education, and has now moved into this realm, teaching pre- and post-graduate children's nurses. A new post-graduate module at BSc / MSc level in paediatric endocrine nursing will shortly be launched by Kate in her new role.

Martin Savage – Co-Chair

Emeritus Professor, Professor of Paediatric Endocrinology
Barts and the London School of Medicine & Dentistry, UK

Professor Savage has 30 years' clinical experience in paediatric endocrinology, treatment with GH and recombinant human IGF-1. He is the author of many publications on growth disorders and on GH resistance states, and was also a member of the Organising Committee for the 2008 Consensus Meeting on management of idiopathic short stature.

Pierre Chatelain – Co-Chair

Professor of Paediatrics
Hôpital Mère-Enfant de Lyon, France

Professor Chatelain contributed as Principal Investigator or Investigator to the pivotal/ registration trials of GHD in Paediatrics, Turner Syndrome and Small for Gestational Age. He also contributed to the development of prediction models of response to GH for these conditions, as well as the development of Pharmacogenomics of GH Treatment.

John Chaplin – Co-Chair

Professor of Paediatrics
University of Gothenburg, Sweden

Professor Chaplin is a Chartered Psychologist in the UK and Sweden, Associate Fellow of the British Psychology Society and Associate Professor of Experimental Paediatrics in Sweden. He has worked in a number of medical fields, with both paediatric and adult focuses. His main research concerns the cognitive and behavioural aspects of illness and treatment. He has developed various instruments for the measurement of quality of life and psycho-social effects of living with a chronic medical condition and its treatment. He currently works with the Paediatric Growth Research Centre, Sahlgrenska Academy, at Gothenburg University, Sweden, where his research interests are the cognitive and psychosocial consequences of hormone imbalance and replacement. He campaigns for the incorporation of patient-reported outcomes to be a routine part of medical assessment and medical quality control. Other research interests include good clinical practice in clinical trials and the understanding of the child's perspective of health messages via social media.

Key teaching presentations

GH Therapy Throughout Life

(See session 1 slides)

Stefano Cianfarani, Martin Savage, Stephen Shalet, Tanya Urquhart

The first session began with overviews of growth hormone (GH) treatment in infancy and in later childhood and puberty. Although focusing on different stages of childhood, two points common to both were:

The more severe the GH deficiency, the better the response to treatment.

The younger the age at the start of treatment, the better the response.

Diagnosis in infants

For children older than about 2 years, the size of response to GH stimulation that indicates deficiency is reasonably well defined and accepted. But for younger children, the situation is less clear. So for infants, the results of magnetic resonance imaging (MRI) assume particular importance. There are some clear MRI indicators of GH deficiency:

- Ectopic posterior pituitary
- Anterior pituitary hypoplasia/aplasia
- Pituitary stalk agenesis

Children small for gestational age

An important category of short stature in infants is small for gestational age (SGA). Although the majority of these children will naturally catch up to a normal height, and may take up to 4 years to do so, about 10–15% of SGA children will remain short for their age.

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GH deficiency is rare among SGA children, although they may have slightly reduced IGF-1 and IGFBP-3 levels. However, GH treatment can be efficient in SGA children, adding an average of 6 cm to their adult height, although the response is highly variable, with some children not benefiting at all.

GH treatment can be efficient in SGA children, adding an average of 6 cm to their adult height

The continuum of GH sensitivity/deficiency

There is huge variability among children with defects in the GH/IGF-1 axis, and their response to therapy depends partly on the balance of how much GH they secrete and how sensitive they are to exogenous GH.

For example, a child who secretes almost no GH, but otherwise has no faults in the GH signalling pathway (severe GH deficiency), will have an excellent response to treatment. Whereas a child who secretes normal amounts of GH but is deficient in IGF-1 (and is therefore GH insensitive) will have a poor treatment response.

This has consequences for the dose of GH required: children with severe GH deficiency will respond well to even a small rhGH dose. Other, more complex conditions, such as Turner syndrome, require a higher

Children with severe GH deficiency will respond well to even a small rhGH dose

dose to achieve similar results.

Predicting response and managing expectations

Predicting growth response is complicated; even within the category of GH deficiency, responses vary according to the underlying aetiology. But the best outcomes in terms of adult height occur when children:

- Have peak stimulated GH below 3 µg/L
- Have subnormal IGF-1 and/or IGFBP-3
- Begin treatment at a young age
- Have tall parents
- Achieve a good response during the first year of treatment

It is vital to be honest about treatment expectations, to allow for reassessment and stopping of treatment if there is a poor response during the first year, especially in conditions such as idiopathic short stature, where the underlying cause is unknown.

Be honest about treatment expectations

Transitioning to adult care

Studying GH deficient children at the point of transition into adult care, when they are about 19 years of age, can be revealing. Patients with larger gaps between their target height and the height they achieved with therapy have poorer body composition than those with smaller gaps, with lower bone mineral content and lean body mass.

So optimising GH treatment is vital for more than just increasing growth velocity.

However, it is vital to retest patients at the point of transition, as most who were severely GH deficient in childhood will no longer be so in adulthood. And the likelihood of continued severe deficiency guides the testing strategy; a patient who had isolated GH deficiency should undergo more than one test to ensure accurate results, whereas a single positive test in a patient with multiple pituitary hormone deficiency arising from childhood cancer can be trusted.

The effects of GH on body composition have implications for the transition period, as patients without a break in treatment continue to reap the benefits of GH on bone turnover. For this indication, an adult dose (0.25 IU/kg per week) is as effective as a paediatric dose (0.5 IU/kg per week), with the two doses having similar effects on bone mineral content and lean and fat mass.

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Transition in action

The session was rounded off by a case study of a patient transitioning into adult care within the UK health system. The case illustrated that transition should be highly personalised, occurring at the right age for individual patients. It also showed the importance of listening to patients' views; the girl in question had disliked GH treatment as a child and had not wished to continue it in adulthood, but was willing to reconsider when she became unhappy with her body composition.

Presentation by Tanya Urquhart on day one.

Addressing the psychological challenges of short stature

(See session 3 slides)

John Chaplin, Barbro Jonsson, Birgit Lidwall

Many studies have addressed the effects of short stature on people's wellbeing. As outlined in this session, observational studies of patients being assessed and treated for short stature are unequivocal: short stature reduces self-esteem and leads to depressive symptoms and behavioural problems, which are alleviated by treatment.

But population-based studies are less clear, showing perhaps an increase in bullying but no other effects. The very largest studies refine the associations further, suggesting that short stature is more of an issue in younger people and is relative; people are affected by how their height compares with their friends' rather than by their absolute height.

However, there is also evidence that shorter stature is associated with suicidality and lower income.

The latter point seems to be both reality and stereotype, as research demonstrates that people assume the shorter of two men will have the smaller salary. Such stereotypes extend to sports commentators speaking more favourably of taller athletes, and of people more readily associating negative words with short men than tall men – even when they believe they hold no such bias.

So short stature patients and their families will inevitably encounter such stereotypes. The endocrine nurse can support families in recognising and combating height-related stereotypes.

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When to investigate the short child

(See session 4 slides)

Martin Savage, Stefano Cianfarani

For all that short stature is considered the preserve of paediatric endocrinologists, endocrine causes of short stature are actually very rare, making it important to:

Approach diagnosis as a general paediatrician, not an endocrinologist.

Diagnosing short stature needs a comprehensive approach combining auxology, anthropometry, biochemical and endocrine testing, neuroradiology and, in some cases, genetic analysis.

The most common categories of short stature are constitutional delay of growth and puberty ("late developers"), genetic short stature and idiopathic short stature. After this come non-endocrine causes, including syndromes such as Turner syndrome, chronic conditions such as coeliac disease, and being born short for gestational age. Pure endocrine causes are the least common.

Accurate auxology and medical history are critical, so that a reliable growth record can be gathered before

referral to an endocrinologist. This identifies the children who are most likely to have a genuine pathology and should be referred. These children have:

- Height between –2 and –3 SDS
- Height at a percentile clearly below their mid-parental height
  - But note that where parental heights are markedly different, a child may inherit their height primarily from one parent
- Growth velocity of less than 4 cm/year

The power of observation

Children's physical features can be telling – for example, wide-set eyes and low-set ears are characteristic of Noonan syndrome. Identifying these features immediately removes the child from the idiopathic category, and guides treatment.

Children's physical features can be telling

Pitfalls of laboratory investigations

After excluding known non-endocrine causes, the most tested endocrine causes of short stature are GH, IGF-1 and IGFBP-3. But GH stimulation testing is invasive, the threshold for a normal GH response is arbitrary, and patients have variable responses.

There is a high risk of false–positive GH stimulation results.

On top of this, there is up to 25% variability between the different commercially available assays, no consensus about sex steroid priming and the presence of obesity can produce false–positive results.

The accuracy of IGF-1 testing is adversely influenced by a range of factors including age, nutritional status, genetic variability, and the fact that measurements in the same patient can be vastly different on different days. The IGF-1 assay cannot be relied upon to identify all children with GH deficiency; about a quarter of children with a normal IGF-1 test will actually be GH deficient. But it has a fairly low false–negative rate; about 90% of children with abnormally low IGF-1 will prove to be GH deficient.

IGFBP-3 testing misses an even larger proportion of children with GH deficiency, but, again, children with very low levels are highly likely to have GH deficiency.

The combination of IGF-1 and IGFBP-3 levels below –1.9 SDS is therefore a very strong indicator of GH deficiency.

Conversely, normal values for both IGF-1 and IGFBP-3 strongly suggest no GH deficiency.

A false–positive GH result should therefore be suspected in obese children who have a blunted GH stimulation test but normal IGF-1/IGFBP-3 results.

For selected children, genetic testing can be informative. Patients can be considered for genetic testing if they have:

- Early onset of growth failure
- Family history of growth disorders
- Parental consanguinity
- Severe growth failure (SDS below –3)
- Very poor response to GH stimulation testing
- Very low IGF-1 and/or IGFBP-3 levels

Whatever the eventual diagnosis, it is important to keep an open mind. If a patient has a poor response during the first year of GH treatment it should trigger reassessment, especially if their baseline neuroimaging findings were normal.

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Pathology in organic pituitary disorders in childhood and adolescence

(See session 5 slides)

Martin Savage, Stephen Shalet

Anterior pituitary hormone	Target in body
Thyroid stimulating hormone	Thyroid
Adrenocorticotropic hormone (ACTH)	Adrenal cortex
Gonadotropins (follicle-stimulating hormone and luteinizing hormone)	Reproductive system
Prolactin	Mammary glands
Endorphins	Pain receptors in brain
Growth hormone	Whole body

Complex gland, complex disease

The anterior pituitary gland secretes a range of hormones that affect multiple systems. So pituitary pathology frequently results in abnormal levels of several or all pituitary hormones, leading to complex disease with many non-endocrine comorbidities requiring lifelong multidisciplinary care.

Even patients who have abnormal levels of just one pituitary hormone have multiple health problems

Pathology is also influenced by the underlying cause. For example, a genetic mutation in the *Pit1* gene causes abnormalities in multiple pituitary hormones, and an ACTH-secreting pituitary neoplasia causes Cushing's syndrome, whereas a GH-secreting neoplasia leads to excessive growth. But even patients who have abnormal levels of just one pituitary hormone have multiple health problems; for example, patients with excess GH production can have hypertension, diabetes, heart failure and skeletal problems, with even more problems possible if the excess GH production results from a macroadenoma.

Ask about previous head injuries when taking a patient's medical history

Other aetiologies include inflammatory and infective, treatment-induced, and developmental. Another important cause is traumatic brain injury, so it is crucial to ask about previous head injuries when taking a patient's medical history.

The complexity of these conditions raises equally complex management issues, when multiple treatments are often required. It is important to consider the effect of hormone replacement on endogenous hormone levels; for example, GH replacement reduces levels

of free thyroxine and cortisol. Also, correcting levels of some hormones may unmask further problems requiring treatment.

It is important to consider the effect of hormone replacement on endogenous hormone levels

Treatment-induced pituitary damage comes with an additional set of problems, as hypopituitarism resulting from radiation damage can take a long time to fully appear. In the meantime, patients need monitoring, raising issues such as how many hormones to screen, how often and whether to measure mostly baseline hormone levels or to undertake more labour-intensive stimulation tests.

My Week: Highlights and common themes

(See session 2 slides)

In the "My Week" sessions, nurses from Canada, Sweden and the UK gave accounts of their working weeks, giving insights into how the role of a paediatric endocrine nurse varies from country to country.

Although the three sessions were held in separate rooms and featured six different speakers, the discussions after the presentations frequently touched on the same themes, most notably the variable availability of GH delivery systems and the frequent lack of formal training and qualifications for paediatric endocrine nursing.

Availability of GH formulations and devices

It emerged that the choice of GH administration methods that nurses can offer their patients varies widely between countries, and even between institutions within the same country.

In some countries, such as Italy, the endocrinologist selects the GH formulation, thus restricting the number of devices nurses can offer to families. In others, such as Canada, the choice of GH formulation and delivery system is entirely led by nurses. But even where the choice is nurse-led, it can be restricted by availability between countries and within countries, and by funding constraints.

So some nurses can offer only two devices, some will show patients an example of each type, and others will give families links to device websites and ask them to select a small number that they would like to see demonstrated.

This raised the point that the online and DVD-based device information varies in tone, and that the "glitzier" advertising might sway patients towards a device that is not wholly appropriate for them.

Training and qualification

In most countries, paediatric nurses learn the specialist endocrine aspects of their role informally, "on the job". In France, for example, there is no formal training leading to a recognised paediatric endocrine nursing qualification, while in Sweden there is a 1-year course but it is currently only run once every 10 years, because of the small numbers of nurses wishing to participate.

From next year, UK nurses will be able to do an endocrine nursing course as part of a Bachelor's or Master's degree. However, some countries have addressed the problem by partnering with their national nursing bodies to develop competency frameworks. These specify which skills an endocrine nurse should have at what level of experience, so nurses can work towards higher levels. In Canada, for example, the competency levels are based partly on procedures performed in the clinic and partly on undertaking learning modules about specific endocrine conditions.

As well as encouraging continuing education, having a competency framework in place protects endocrine nurses' roles against cutbacks and ensures that only nurses with the appropriate skills are employed in these positions.

Of note, such competency frameworks take considerable time to write – 5 years in the case of the UK framework – but organisers can reduce the task by adapting existing competencies from other countries.

Communication and sharing

Related to this are nurses' efforts to promote communication and sharing of information within and between countries. By sharing protocols, educational materials and similar items that can be adapted to suit local circumstances, nurses can "work smarter, not harder". In a similar vein, the newly formed European Society of Paediatric Endocrine Nurses (ESPEN) has a half-day meeting within the wider ESPE conference and plans to build a multilingual website.

Within countries, endocrine nurses in Canada have an online portal and an organised email group to facilitate rapid communication, sharing of information, and support between nurses in different clinics. In France, by contrast, communication tends to be between doctors, rather than between nurses.

Ambulance service registries

In one session, it emerged that some ambulance services in the UK have a registry of patients on hydrocortisone replacement. Although the ambulance crews don't carry hydrocortisone, the registry means that they are prepared to give emergency injections using medication kept at patients' homes and schools if no one at the scene is able to do so. This was felt to be of particular help if school staff were unwilling to give emergency injections.

The impetus for setting up a registry comes from the paediatric endocrine team, rather than from the ambulance service. If anyone is interested in setting up a registry, please contact Lee Martin (lee.martin@bartshealth.nhs.uk) or Kate Davies (kate.davies@lsbu.ac.uk) for further advice and a protocol.

Panel discussion during a breakout session on day two.

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Achieving Adherence to Growth Hormone Therapy

Martin Savage and Svante Norgren have written a 'roadmap' summarising key steps in the initiation of a program to assess and improve adherence.

The successful establishment of such a program will be of considerable value to patients receiving GH therapy and bring rewards to the medical and nursing team involved in their management.

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