

Insights into MAnaging Growth for Endocrine nurses

Prague, Czech Republic, 9–10 October 2014



The event was held in the beautiful city of Prague

“The aim is to give the nurses knowledge, and by giving them knowledge you give them confidence, and by giving them confidence you empower them”

Martin Savage, Programme Director

Getting ‘under the skin’ of endocrinology

The Insights into MAnaging Growth for Endocrine nurses symposium took place in Prague, Czech Republic, over a day and a half in October 2014. A total of 44 paediatric endocrine nurses from seven European countries plus Canada attended the event.

The event was designed to bring paediatric endocrine nurses together, giving an opportunity for “formal education”, according to Programme Director Martin Savage (Barts and the London School of Medicine & Dentistry, UK). “The aim is to give the nurses knowledge, and by giving them knowledge you give them confidence, and by giving them confidence you empower them.”

Meeting Chair Kate Davies (Great Ormond Street Hospital, London, UK) agrees. “There’s more nurses taking on more autonomous roles now, leading our own clinics.” But to do that, she says, nurses need education, and opportunities for education are, in general, “pretty limited”.

The programme therefore aimed to provide a broader view than routine clinical practice, to go, in the words of Savage, “under the skin of endocrinology”.

“We don’t get taught all this in-depth growth information at nursing college,” says Davies. But patients and their families assume that nurses know all about the IGF-1 system, and the effect of genetics on growth and treatment response.

Rather than learning the background science in a structured manner, nurses pick it up through experience with patients and interaction with consultants. “I think you learn the hard way,” observes Faculty member Peter Bang (Linköping University, Sweden). But he says that, at least in some countries, younger doctors lean heavily on the experience of the endocrine nurses, making it vital that nurses are fully informed.



Watch: Martin Savage outlines the aims of the IMAGE programme

Meet the committee



Kate Davies

Meeting Chair Kate Davies has spent 15 years working as a Clinical Nurse Specialist in Paediatric Endocrinology at Great Ormond Street Hospital, London, and

has a thorough knowledge of all the growth hormone preparations on the UK market and their indications.



Martin Savage

Meeting co-Chair and Programme Director Martin Savage is Emeritus Professor of Paediatric Endocrinology at Barts and the London School of Medicine and Dentistry and

consults at The London Clinic Centre for Endocrinology. He has 30 years' clinical experience in paediatric endocrinology and treatment with growth hormone and recombinant human IGF-1. He has written many publications on growth disorders and on growth hormone resistance states. He was a member of the Organising Committee for the 2008 Consensus Meeting on the management of idiopathic short stature.

Pierre Chatelain

Meeting co-Chair Pierre Chatelain is Professor of Paediatrics at Université Claude Bernard, Lyon, France. He is Chairman of the Collège de Pédiatrie and coordinator of



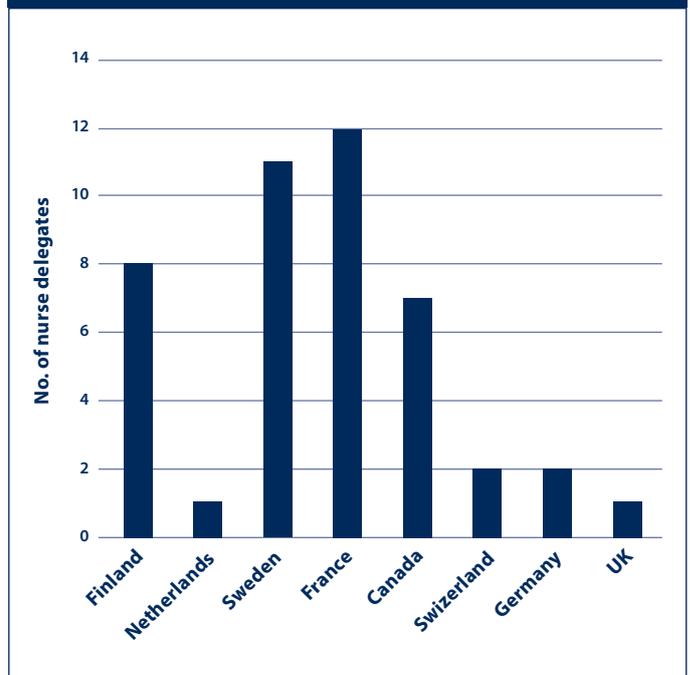
the French National Reference Centre of Rare Diseases of Sex Differentiation and Development. He has authored or co-authored more than 170 publications in the field of paediatric endocrinology, diabetology and paediatrics, and has been involved with the endocrine nurses symposia from their inception.

The programme covered

- Determinants of normal and abnormal growth
- Rationale and indications for growth hormone treatment
- Response to hormone therapy in specific patient groups
- Managing idiopathic short stature
- Treatment responses in children with growth hormone deficiency
- Psychological issues associated with short stature
- Tackling adherence issues

As well as filling in nurses' background scientific knowledge, the programme was also designed to encourage dialogue, with case presentations and panel discussions, and to tackle controversial issues.

44 nurses from 8 countries attended IMAGE 2014



The nitty gritty

“Normally when you are at a medical congress, the level is higher, so it’s sometimes difficult to understand for nurses.”

Nurse delegate at IMAGE 2014

Three talks in the first day, given by endocrinologists, got down to the basic science behind the growth disorders nurses encounter every day. A few of the most experienced nurses were familiar with the underlying biology, but most were not, and found it extremely useful knowledge.

Inside the IGF system

Peter Bang opened with an overview of the growth hormone–insulin-like growth factor (IGF) axis, discussing how the system regulates growth throughout childhood, the contribution of insulin, nutrition and pubertal stage, and techniques and pitfalls in measuring the axis components.

“The value of coming to this has been, unexpectedly, greater than I anticipated.”

Nurse delegate at IMAGE 2014

“In general, I think it’s important to have a high knowledge of the system,” he said.

Importantly, he revealed that growth velocity is not always down to growth hormone. Before birth and up to the age of 1 year, IGF-I and II and insulin control growth, after which growth hormone and IGF-I predominate until puberty, when oestrogens and androgens also come into play. And a child’s genetic growth potential plays a part throughout their growth years.

Therefore, growth hormone is not the only culprit in a child with short stature; defects in IGF-I and II can have a profound effect. So, for example, “short stature in a child

less than 1 year is unlikely to be growth hormone dependent; it’s more likely to do with primary IGF problems.”

IGF is an extremely important measurement, said Bang. However, IGF levels fluctuate throughout the day, change with age, and are affected by many transient factors.

“It’s very important for nurses to know when they can sample and when they can interpret IGF-I levels, because it’s such an important measurement,” he said. “They need to take into consideration whether the child has been well – not any acute infections or periods of poor nutritional intake, because in that context you cannot interpret the levels.”

Guiding treatment with genetics

Marie-José Walenkamp (VU University Medical Center, Amsterdam, the Netherlands) then delved deeper into the genetic mutations that lead to defects in the growth hormone–IGF axis. She explained the fundamentals of genetic mutations, showing how a change of a single base in the gene encoding IGF-I can lead to a defective IGF-I protein and thus a child with short stature.

Then she showed some of the mutations that have been uncovered in other components of the growth hormone system, and their consequences for children who carry these mutations.

These genetic defects are very rare, she noted, but it is important to identify them, “because it has consequences for treatment and other symptoms.”

A multidisciplinary challenge

In the third presentation, Martin Savage looked at the biology underlying growth hormone resistance, in which patients have normal or increased growth hormone levels, but impaired postnatal growth and a poor or absent response to growth hormone treatment. Again, these conditions are caused by defects in the components of the growth hormone–IGF-I axis.

“It’s wonderful to spend this amount of time on one aspect of endocrinology. You can really immerse yourself.”

Nurse delegate at IMAGE 2014

“You cannot expect the same magnitude of response in the child with Turner syndrome, small for gestational age, etc, as you will get with growth hormone deficiency,” said Savage.

But there is a continuum of response, he noted, and pinpointing the exact genetic cause will help to predict the response, if any, to growth hormone. It may also reveal the

potential for other treatments that may boost growth; for example, recombinant human IGF-I is successfully used to treat children with short stature and growth hormone resistance due to defects in the growth hormone receptor or other components required to produce sufficient levels of IGF-I.

Even more complicated to treat is growth hormone resistance secondary to chronic diseases such as Crohn’s disease and juvenile chronic arthritis, in which the production of inflammatory cytokines interferes with the action of growth hormone. Relative to primary growth hormone resistance caused by genetic defects, secondary growth hormone resistance is a lot more common.

“But these children are not looked after by paediatric endocrinologists,” said Savage. “They’re looked after by subspecialists – gastroenterologists, etc. And persuading them that their patients may benefit from treatment with either growth hormone or IGF-I is difficult. So that’s a real multidisciplinary interactive challenge.”



The meeting hosted 44 nurse delegates from 8 countries

An international affair

“We do it exactly the same... but completely different!”

Kate Davies, Meeting Chair

One key theme to emerge from the meeting was the rich variation in practice between, and even within, countries.

Symposium delegates came primarily from Finland, Sweden, France and Canada, but also from Switzerland, Germany, the Netherlands and the UK. And the situation of paediatric endocrine nurses varied considerably, ranging from the Netherlands, which has just one paediatric endocrine nurse practitioner, to Canada, which has a large number of nurses who further specialise in their particular areas of interest, and whose input is “taken very seriously”.

Martin Savage observed: “I was impressed by the confidence of some of the nurses, particularly from Canada, where the role of the nurse practitioner in paediatric endocrinology is established and recognised, and that was very nice to see.”

Indeed, the Canadian paediatric endocrinology community has an annual conference, and “the physicians value us so much that they pay for our attendance!” revealed Susan Rybansky (Children’s Hospital, London Health Sciences Centre, Ontario, Canada). “This has allowed us to organise ourselves across Canada as paediatric endocrine nurses.”

The programme included a number of interactive sessions, in which del-

egates and Faculty discussed case presentations or issues such as treatment adherence. Many country and cultural differences emerged, from the specific tests ordered in children with short stature to the age and height criteria that must be met before patients can be started on growth hormone.

Speaking after case presentations on treatment response in children who are small for gestational age (SGA), session Chair John Chaplin (Göteborg University, Sweden) said: “It was interesting to see the opinions of people from different countries. We had some differences of opinion about how to treat SGA and whether you should double the dose or increment the doses, and I think it’s important that everybody is aware of those issues and aware that there are differences between countries and also within countries and within the clinics.”

Rybansky, after chairing a session on treatment response in Turner syndrome, was taken by the trans-Atlantic differences in initiation of oestrogen therapy, with European patients tending to start treatment earlier than the 13 years of age that is usual for Canadian patients.

“To hear that the Europeans begin at our standard beginning dose, which is 0.5 mg daily, they begin by 11 or 12 – certainly 12 they consider late – so that’s interesting. And I know what the comments will be around that, they will be: well, what about the effect on growth potential?”



John Chaplin (Göteborg, Sweden) in discussion with Martin Savage (London, UK)



Susan Rybansky (Ontario, Canada) co-chairs a session on “Responses to growth hormone therapy in GHD”

However, recent research suggests that starting with very low doses of oestrogen from around the age of 8 years – the age at which girls without Turner syndrome begin to produce oestrogen – actually improves growth outcomes and normalises thelarche.

Adherence: a sensitive issue

There were a number of case presentations and panel discussions on the topic of response to growth hormone treatment, and a recurring theme in this area was adherence: how do nurses distinguish between poor response and poor compliance?

Pauline Mussen (Southampton Children's Hospital, UK), who presented a case of a poor response to growth hormone, pointed out that nurse-led clinics, while enhancing hospital-based practice and care for patients, "have been at the price of liaison and understanding of the home life and the support that they need at home."

Families arrive in the clinic and "present a front", she said, making it hard to identify those who are missing multiple doses.

There are many methods of gauging adherence, ranging from asking patients, to pill counting and in-clinic administration. More recently, devices such as the easypod® (EMD Serono, Germany) have appeared on the market, which simplify administration for patients, as well as providing an accurate record of missed doses and the timing of taken doses.



Faculty member Lee Martin (London, UK) joins in the discussion

Less-than-ideal patient adherence has a proven effect on outcomes, with height velocity standard deviation scores ranging from less than 1 in patients with low adherence to nearly 3 in those with high adherence.

So if it is not identified and addressed, poor patient adherence can lead to unnecessary testing to determine why a patient is failing to respond to treatment. Continuing to prescribe medication that is not taken is a waste of money, but stopping treatment is difficult in a patient who has a demonstrable good response to treatment, but which is compromised by nonadherence.

"It's really hard to stop treatment when it's obvious it works so well," Lee Martin (Royal London Hospital, UK) commented. "It's really hard to have that conversation where you say: 'We are going to stop this treatment.'"

Patients give many reasons for missing injections, and there are an even larger number of underlying causes. These, outlined in a presentation by Svante Norgren (Karolinska University Hospital, Stockholm, Sweden), include not realising the consequences of missed doses, dislike of injections, age, socioeconomic and cultural factors, dissatisfaction with the results and long duration of treatment.

The impact of family dysfunction also arose during discussions, and a delegate commented that, to address all these problems, endocrine nurses need to be teachers, psychologists and social workers, as well as nurses.

Family dysfunction, however, can be partly in the eye of the beholder. John Chaplin observed that endocrinologists and endocrine nurses should also address their own issues with adherence. "Families that we may be classifying as 'bad' families – they don't see themselves as bad families, they see themselves as good families. They're not giving an injection because the child doesn't want an injection; they're doing the best thing for the child."

Susan Rybansky noted that "there are ways in which we communicate that facilitate honesty from the patient." She said she gives the patient "permission" to admit to nonadherence, by mentioning that missed doses are very common, and that she asks about adherence while doing other things, such as taking measurements, "so that I'm not putting them on the spot".

Martin Savage noted that there is a "specific training need" to help all nurses to adopt non-confrontational strategies to accurately gauge adherence, and to then work with families in a non-judgemental manner to improve treatment compliance.

Tackling controversy: when is growth hormone justified?

In his presentation, Meeting Co-Chair Pierre Chatelain (Université Claude Bernard, Lyon, France) examined the process behind establishing therapeutic need for growth hormone, which besides being used in patients with growth hormone deficiency, is also indicated in several conditions in which patients produce endogenous growth hormone, but respond to treatment nonetheless.

He stressed the point that growth hormone indication should always be considered on an individual basis; the benefits and efficacy of the treatment vary according to the patient and their particular condition, creating a different risk-benefit ratio in each case.

The medical need for growth hormone may be considered low in many conditions of growth hormone sufficiency, as the drug improves height but otherwise has little effect on health. However, Chatelain noted the psychological issues associated with

short stature, and epidemiological evidence linking it to coronary heart disease and suicide.

And then there's the cost of growth hormone: the medical cost of treating patients and the cost to society of not treating them.

"But the practice is that people tend to be happy when they get the growth hormone drug to prescribe," said Chatelain. "And most of the time it's the end of the story when actually it should be the beginning."

Martin Savage further expanded on the theme with a presentation about growth hormone in patients with idiopathic short stature (ISS), a heterogeneous group of patients with a variety of as-yet unidentified causes of short stature. It is, indeed, the diagnosis that remains for children with a height standard deviation score below 2 after all else has been excluded, with conditions to exclude ranging from coeliac disease and Crohn's disease to Noonan syndrome and psychosocial deprivation.

"... it's a question of the doctor having some degree of humility..."

Martin Savage, Programme Director

Use of growth hormone in ISS patients is a highly divisive subject, with the 2003 approval of the indication by the US Food and Drug Administration, set against the continuing refusal of the European Medicines Agency, creating a trans-Atlantic divide. The indication is also approved in Canada, a fact that did not sit well with several of the Canadian endocrine nurses at the symposium.



Peter Bang (Linköping, Sweden) asks a question

Savage described the long-term data for ISS children treated with growth hormone as “relatively unimpressive”, but, of course, the average data encompass a variety of responses ranging from poor to good, and there are social pressures to be taller, particularly in parts of the world like South-East Asia.

“The question is: how do you strike a balance?” asked Savage. Children who are inappropriately short for their families and have marginal growth hormone levels “do deserve a chance at growth hormone treatment”, he suggests.

But he stressed that clinicians have to be honest and say they don’t know what the response is likely to be. In this case, treatment can easily be stopped if unsuccessful.

Because growth hormone is expensive, with the cost per cm adult height gained amounting to €16–33K (US\$ 21–44K). Savage quoted Jerry Wales, from Sheffield Children’s Hospital, UK, who wrote in the *BMJ* that “the cost of increasing adult height by 4 cm using [growth hormone] treatment in a child with ISS would provide 200,000 doses of measles vaccine or 28 village pumps for sub-Saharan Africa.”

“So it’s a question of the doctor having some degree of humility, admitting that he’s not quite sure how the child is going to respond,” said Savage.

This gives the doctor a “let-out”, allowing them to call a halt to an expensive treatment if it proves to be ineffective.

“...the practice is that people tend to be happy when they get the growth hormone drug to prescribe...”

Pierre Chatelain, Meeting Co-Chair

Reflections

This year’s meeting covered a lot of ground, attempting both to delve into the background and to communicate recent findings.

“We tried to look critically at growth,” said Martin Savage. “And this is rather new, you may be surprised to hear, but in fact when recombinant human growth hormone first became available the aim seemed to be to show everybody how effective it could be in every possible situation.”

So several of the case presentations focused on poor response to growth hormone and the multitude of underlying reasons, generating discussion of how to manage such patients. Post-symposium feedback from the nurses indicates that 70% of them intend making changes to their practice based on what they learned, either immediately or after further information/training.

A major positive for the delegates was the opportunity to meet and talk to other endocrine nurses, and to hear how practices in other countries meet the many challenges of caring for children with growth disorders.



Watch: Kate Davies, Pierre Chatelain, Lee Martin and Peter Laing reflect on the meeting

Future meetings will hopefully build on this theme, promoting interaction and support between paediatric endocrine nurses across the world.

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Paediatric Endocrinology

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