Endocrine Track 1: Symposium 1

S1.1

Newborn screening for congenital hypothyroidism: performance and outcomes of the UK programme.

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Introduction
Early detection of congenital hypothyroidism (CHT), and treatment with oral thyroxine, supports the critical period of early brain development, improves growth and prevents the metabolic effects of adult hypothyroidism. Screening for CHT, involving an assay for thyroid-stimulating hormone (TSH), has been included in the UK newborn blood spot screening programme since 1981. Since the introduction of screening, the number of CHT cases has increased, although the reasons for this are unclear. There has been limited evaluation of the performance of the current UK programme.
Methods
UK-wide active surveillance to estimate the current incidence of CHT in infancy and to evaluate perfomance of the newborn screening programme. Surveillance was conducted through the British Paediatric Surveillance Unit and newborn screening laboratories from 2011 to 2012 to identify children aged <5 years who were investigated after a presumptive-positive screening result or clinical presentation. Children were followed for 3 years to confirm CHT diagnosis and clinical management. Differences in the TSH assay cut-off used by English laboratories provided an opportunity to explore the optimal screening test cut-off.
Results
Six hundred and twenty nine newborns (58.3% girls) were reported after presumptive-positive screen and an additional 21 children (52.4% girls) after clinical presentation. 508 children commenced thyroxine but this was discontinued in 76 (15%) children. 432 (85%) remained on treatment at three years. Incidence of CHT was 5.3 (95%CI 4.8, 5.8) per 10,000 live-births. Screening programme sensitivity, specificity and positive predictive value were 96.76%, 99.97% and 66.88% respectively. Evaluation at different TSH cut-offs suggested that the optimal cut-off was likely to be lower than the recommended standard.
Discussion / Conclusion
Performance of the UK screening programme for CHT is good, however standardisation of screen test cut-offs is advisable and re-evaluation of the recommended cut-off is warranted. Clinical follow-up is essential to avoid unnecessary continuation of therapy, and ascertain longer-term outcomes.

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S1.2

Congenital hypothyroidism – lessons from a tertiary service

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Congenital hypothyroidism (CH) occurs due to dysgenesis or dyshormonogenesis of the thyroid gland. Newborn screening for CH was introduced in the UK over 30 years ago and has almost eliminated the severe intellectual deficits caused by the deficiency of thyroxine to the developing brain. The recognised incidence of CH increased immediately post introduction of screening due to the improved detection and diagnosis of cases. However, further increases in the incidence of CH have been reported internationally and this is variably suggested to be due to a combination of lower screening detection thresholds, changes in population demographics and iodine status. Using data from over 1700 infants who have been referred to a single centre with positive CH screening results, lessons have been learnt in terms of the impact of changing screening TSH thresholds, underlying the physiology and genetics of CH and outcome data. In this cohort, we demonstrated that the group of infants classified as Asian/British Asian and Chinese by the UK Office of National Statistics have higher TSH cut points than the group of infants classified as white. This Asian group is also over-represented in the cohort referred from the CH screening laboratory compared to the background population. In addition, there is a high incidence of genetic mutations in the DUOX2 pathway for infants with borderline screening results. These mutations are reported most frequently in populations from the Asian subcontinent. They may be associated with transient CH. Using data from this same cohort, we have studied audiology outcomes. These suggest that there in an increase in hearing loss in infants with CH, and this is not detected by newborn hearing screening. In summary, 30 years after the introduction of newborn CH screening, there are still many unanswered questions regarding the physiology, genetics and outcomes of infants with CH.

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S1.3

Subclinical hypothyroidism – lessons from clinical studies in adults

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Subclinical hypothyroidism (SCH) is a relatively common endocrine condition characterised by raised serum thyrotropin (TSH) levels in the presence of normal circulating thyroid hormones. It is generally recognised that SCH – especially if it is sustained - is a mild form of hypothyroidism but whether it should be treated or not is a matter of a long-standing debate amongst both paediatric as well as adult endocrinologists. In adults, there are conflicting data on the long-term outcomes of SCH with some studies suggesting adverse metabolic, cardiovascular, pregnancy-related and quality of life outcomes. On the other hand, there is emerging evidence to suggest that SCH may not be detrimental to health (or may even be beneficial) in the very elderly. Clinical trials of treatment of SCH have mostly shown modest benefit in reduction of cardiovascular risk factors: mainly dyslipidaemia, but little or no improvement in other areas. Therefore, current evidence does not support the view that all patients with SCH should be treated. However, there may be certain groups of individuals that may gain from treatment in adult populations. This overview will identify such groups that may be at risk of the adverse effects of SCH and could potentially benefit from treatment. Furthermore, how the lessons learnt from adult SCH populations could be applied to younger groups will be discussed.

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Endocrine Track 1: Symposium 2

S2.1

Abstract unavailable.

S2.2

APS1 – an expanding disease spectrum

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Autoimmune Polyglandular Syndrome (APS1), also known as Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED), is a rare but frequently debilitating disorder, usually presenting in childhood and adolescence; it is typically caused by homozygous AIRE mutations. The cardinal manifestations are chronic mucocutaneous candidiasis, autoimmune hypoparathyroidism and autoimmune adrenal insufficiency; the development of any two of these three classic features leads to the diagnosis. There are many associated minor manifestations and these may be the main presenting features. It is becoming increasingly apparent that the involvement of non-endocrine tissues can play a significant role in the morbidity and mortality associated with this condition. This presentation, with the aid of cases, will consider:

- The variability of the early clinical picture and the difficulties that this poses when making a diagnosis of APS1.
- The underlying immune deficit in APS1 and the immune markers that can facilitate the diagnostic process.
- The diverse clinical picture that we have observed in local patients and the management challenges associated with the non-endocrine organ-specific manifestations.
- The need for input from multiple different paediatric specialities due to this widening clinical picture and the role of a specialised APS1 clinic.