UK NATIONAL SCREENING COMMITTEE

Newborn Screening for Severe Combined Immunodeficiency

20 March 2013

Aim

1. To agree the UK National Screening Committee's (UK NSC) formal policy position on newborn screening for Severe Combined Immunodeficiency (SCID).

Background

2. This is the first time the UK NSC has assessed the evidence for newborn screening for SCID. There is no current policy recommendation for this condition.

3. SCID was included in the US newborn screening core panel in 2010. Previously, in work undertaken in 2005, the condition was excluded from the core panel as no suitable test was available. At present 16 States have implemented screening, are in the process of doing so or plan to do so. Two States (Arizona and Pennsylvania) have introduced a selective approach which targets high risk populations and / or provides testing on request. In 2011 the US Secretary's Advisory Committee on Heritable Disorders in Newborns and Children listed the following as obstacles to implementation:

- lack of cost benefit information,
- budgetary concerns (cost estimates for technology infrastructure estimated at $500,000–$1 million),
- prior commitment to implement other screening tests mandated by State legislation,
- lack of the widespread availability of experts in immunodeficiency within a State for diagnosis and treatment,
- lack of an FDA approved or cleared assay

4. Pilots are being planned in Sweden and areas of Germany and a multicentre study was reported by the IPOPI website to be under consideration in France.

5. The UK NSC received a request to review the case for newborn screening for SCID. This centred on a vignette produced by Professor Bobby Gaspar (Consultant in Paediatric Immunology at Great Ormond Street Hospital for Children). The stated aim of screening in the vignette was to improve survival outcomes in infants born with SCID.

UK NSC review of screening

6. Bazian were asked to consider each criteria and the review was considered at the July 2012 Fetal, Maternal and Child Health Co-ordinating Group meeting. The review, which is attached, evaluated the criteria positively in some cases but many criteria are not met, partly met or uncertain. Some of the outstanding issues from the review relate to:

Epidemiology – there has been no UK study to establish the epidemiology. The review concluded that this criteria was only partly met but the only way to understand the true rate is by introducing a screening programme.
Test - screening using T cell receptor excision circles (TREC) levels appears to have a poor positive predictive value, a consequence of detecting high numbers of related conditions (14 infants with SCID out of 364 screen positives), false positives in premature babies. An appropriate TREC cut off level has not been defined and the practicality of using PCR as the primary screening test has not been established. The review concluded that criteria relating to the test were only partly met. In the UK, Professor Bobby Gaspar is in the process of studying 2000 bloodspots to establish TREC levels in unaffected babies and in premature infants.
Treatment – these criteria were said to be met but there was uncertainty about the treatment and management of infants with non – SCID conditions. This latter issue is becoming more of a concern in the wider literature on expanded newborn screening. The summary of criteria 15 (benefit and harm from the screening programme) which was partly met, emphasised that the 'management of children with non-SCID T-cell lymphopenia will need to be agreed before the benefits and harms related to the overall screening and treatment pathway can be evaluated.'
Cost effectiveness – this criteria was said to be uncertain, no UK study has been undertaken.
Other options for management – again this criteria was said to be uncertain.
Managing, monitoring and Quality Assurance – this was said to be not met but the US approach would provide a model for the UK.
Staffing etc – this was said to be not met. The review suggests that an impact assessment of some type would be required for us to understand what would be needed to implement and maintain what would be the first DNA based screening test in the UK.
Research recommendations – These help clarify what remains unknown. Bazian recommend 'A study of screening for SCID in pilot sites/states of the US to compare time to transplant and outcomes in infants identified by a population screening programme with those identified outside these programmes'. As such the incremental benefit of introducing screening over and above current practice, which seems to be improving, might be considered uncertain.

Consultation and responses

7. A consultation closed on January 14th 2013 and 247 responses were received. These are attached for consideration.

8. There were 119 responses received as part of a campaign by the parents of one child who was treated at Great Ormond Street Hospital. A further 82 were received from individuals using a proforma provided by UK Primary Immune-deficiency Patient Support (UKPIPS), 15 healthcare professionals submitted individual responses. The following national organisations submitted responses: Genetic Alliance UK, British Paediatric Allergy, Immunology and Infectious Diseases Group, Save Babies Through Screening Foundation, International Nursing Group for Immunodeficiencies, Ataxia Telangiectasia Society, Chronic Ganulomatous Disorder Society, CLIMB, UK Primary Immunodeficiency Network, International Patient Organisation for Primary Immunodeficiencies, Primary Immunodeficiency UK (PID UK).

9. While the overwhelming majority of responses favoured screening a range of concerns and uncertainties are articulated within them. These include:

- the epidemiology in the UK remains uncertain
- while screening in the USA provides a valuable source of experience there are outstanding issues relating to standardisation of TREC cut off levels and the test has not yet been validated
- the distribution of test values would need to be established locally
- the false positive rate (those with low TREC levels but non SCID conditions) was highlighted in several responses and in several ways eg concern about detection of conditions of uncertain clinical significance, uncertainty about the treatment options and outcomes for patients identified in this way, concern about parental anxiety in term and preterm infants, workload issues
- variation in statements relating to the comparative effectiveness of bone marrow transplantation in clinically diagnosed and screen detected cases and uncertainty about the proportion of treated babies who would require ongoing medication
- uncertainty about the cost of screening
- management of information from test results was raised as a practical issue as a SCID screening programme would be the first DNA based programme.

10. While these are not, in the main, seen as obstacles to the introduction of a screening programme a number of the responses suggest that a pilot would be beneficial in the UK. Since the consultation closed the National Institute for Health Research – Health Technology Assessment has been approached informally by the UK NSC regarding a mechanism to evaluate the impact of screening for SCID.

11. It is proposed that the UK NSC policy should reflect these concerns and that, while screening for SCID appears to be a means of improving outcomes in affected babies, a screening programme should not be recommended in the UK until an evaluation has been undertaken.

Recommendation

12. The UK NSC is asked to agree the policy position on newborn SCID screening as follows:-

Newborn screening for SCID is not recommended outside of well designed evaluations to assess the impact of screening. At present there is insufficient information on:

- the epidemiology of the condition in the UK
- the performance of the test
- the management and outcomes of babies who are detected by screening but do not have SCID
- the clinical and cost effectiveness of screening compared to current practice

13. The UK NSC is asked to agree that the policy should be reviewed in three years time unless there is significant new peer reviewed evidence in the meantime.