Guy's and St Thomas' NHS
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Tay Sachs Carrier Screening

a review for the National Screening Committee

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Tay Sachs Disease

Tay Sachs disease (TSD) is an inherited degenerative neurological disease caused by deficiency of the enzyme hexosaminidase A (HexA). It is inherited in an autosomal recessive manner, so that individuals with one copy of a disease-associated genetic variant are carriers, and individuals with two copies have the disease. The most common form of the disease is lethal in infancy or early childhood, and there is no cure or effective treatment.

The carrier frequency for TSD in Ashkenazi Jews is between 1 in 25 and 1 in 30, much higher than for the general population (about 1 in 250-300 in the general population). The increased risk of TSD in Ashkenazi Jews is due to a higher frequency of three specific TSD mutations in this population.

A biochemical test for TSD carrier status became available in the 1960s, and DNA testing for TSD mutations in the late 1980s. The availability of these tests has enabled Ashkenazi Jews who test positive for carrier status to reduce their risk of having a child affected by TSD, either by avoiding marriage to another TSD carrier or opting for prenatal diagnosis and termination of affected pregnancies.

Screening for Tay Sachs

In the UK, carrier screening for TSD in the Ashkenazi Jewish population has been available since the 1980s. In 1999 it was approved by the National Screening Committee (NSC) and funded as an NHS service. The international Dor Yeshorim programme also offers carrier testing for TSD and several other conditions to the Strictly Orthodox population, on a private basis.

Since the advent of carrier testing, the birth prevalence of TSD in Ashkenazi Jewish populations in several countries, including the UK, USA and Israel, has fallen to below that of the general population. Nearly a decade after the introduction of the service within the NHS, the NSC has recognised the need to review the service, to assess whether it meets both the quality standards

set by the NSC and the needs of the Ashkenazi Jewish community. In particular, a national meeting examining the Tay Sachs carrier screening programme at Guy's Hospital (the main service in London) concluded that the programme required review to ascertain how it could be made more systematic and provide equity of access across the NHS.

Project aim and scope

Guy's invited the PHG Foundation to join with them in proposing a review of this area to the NSC, which responded with the request that an expert group be convened to direct a needs assessment and review of current service provision for TSD screening in the UK, and to make recommendations on future actions. This work was limited to Tay Sachs disease screening and testing for an at-risk population of people of Ashkenazi Jewish descent, but included screening and testing programmes provided both within and outside of the NHS in England, Wales, Scotland and Northern Ireland

The work was undertaken by Sara Levene and Chris Patch from Guys Hospital and Corinna Alberg, Hilary Burton, Alison Stewart and Calvin Cheah from the PHG Foundation. An Advisory Group was chaired by Dr Sue Halliday from the Eastern Public Health Observatory and included experts on clinical, laboratory and population screening aspects of TSD and representatives from Jewish religious and community organisations involved in Tay Sachs screening.

The National Screening Committee was represented on the Advisory Group by the Strategic Director for the National Newborn Screening Programme and more general expertise on screening by the Programme Director for the NHS Sickle Cell and Thalassaemia Programme and two regional antenatal screening coordinators.

Timescale

The report and recommendations to the NSC will be completed in autumn 2008.

Project overview

The needs assessment and service review comprises:

1. **An overview of Tay Sachs disease and UK epidemiology in the UK, including cases and numbers of prenatal diagnostic procedures**
2. **Definition of the 'at risk' population and who is included as being of 'Ashkenazi Jewish descent'.**
3. **Demographics of the Ashkenazi Jewish population in the UK**
4. **Collated data on the numbers of Ashkenazi Jewish adults (and teenagers) in the UK who have previously utilised TSD screening and the routes through which they have accessed this service**
5. **An overview of the facilities and methods available across the UK for TSD sceening, both in the public and private sectors**
6. **Stakeholder engagement and consultation on available services, gaps in the services and the need for service improvement**
7. **Description and evaluation of available testing technologies**
8. **Current and likely future gaps and deficits in the service and changing needs**
9. **Assessment of alternative models of screening programmes (including screening in the UK for other recessive disorders, and TSD screening abroad) and their appropriateness, including care pathways for areas of high and low prevalence and the different cultural needs of population sub-groups**
10. **Proposal of a screening algorithm including stages of screening, sensitivity and specificity of the tests.**

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