

Tay Sachs Disease carrier screening in the Ashkenazi Jewish population

A needs assessment and review of current services



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EXECUTIVE SUMMARY AND RECOMMENDATIONS

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Executive Summary and Recommendations

This report is a needs assessment and review of screening services for Tay Sachs Disease commissioned by the National Screening Committee and undertaken by a joint project team from Guy's and St Thomas' NHS Foundation Trust Clinical Genetics Service and the PHG Foundation, Cambridge.

Tay Sachs disease (TSD) is an autosomal recessive degenerative neurological disease caused by deficiency of the enzyme hexosaminidase A (HexA). It is one of a small number of conditions that is more common in Jewish populations of Ashkenazi origin (Jews originating from Central or Eastern Europe) than in the overall population. The most common form of the disease is lethal in infancy or early childhood. There is currently no cure or effective treatment. Increased incidence of the disease in Ashkenazi Jews is due to a higher carrier frequency - around 1 in 25 to 1 in 30, compared to a carrier frequency of about 1 in 250 to 1 in 300 in the general population.

Carrier testing can be undertaken either using a biochemical test, which looks for the relevant enzyme activity, or a molecular (DNA) test that aims to detect one of the mutations responsible for the condition. Carriers so detected can reduce their risk of having a child affected by Tay Sachs disease, either by avoiding marriage to another Tay Sachs disease carrier or, if both partners are carriers, opting for prenatal diagnosis and termination of affected pregnancies. In some communities (particularly the Strictly Orthodox community) carrier screening has been used as part of the procedure for arranging marriages, to avoid bringing together carrier couples. The provision of carrier screening to individuals through an NHS programme is important in ensuring that people can decide for themselves whether to be tested and what to do with the results. Carrier screening was approved in 1999 by the National Screening Committee (NSC) and funded as an NHS service. Carrier testing for Tay Sachs disease and several other conditions is also available on a private basis through the international Dor Yeshorim programme and a number of companies.

Tay Sachs disease carrier screening in the UK offers reproductive choice to the Ashkenazi Jewish population and has been welcomed by the Jewish community. Nearly a decade after the introduction of the service within the NHS however, it has been recognised that there is a need to review the service in order to assess whether it meets both the quality standards set by the NSC and the needs of the Ashkenazi Jewish community.

Main findings

The condition

Tay Sachs is a very rare condition that can include classical, late onset and other variant forms. Both classical and late onset forms are more common in Ashkenazi Jews. The typical clinical features for the classical form include a gradual neurological degeneration beginning in the first 3-6 months of life and progressing by the age of two to a vegetative state, cortical blindness and the requirement for continual nursing care, with death by the age of four years.

In Ashkenazi Jews between 94 and 98% of cases are caused by one of three Tay Sachs disease

mutations in the *HEXA* gene (+TATC1278, +1IVS12 and G269S). These mutations are less common as a cause of TSD in Jews of other ethnic origins and non-Jewish populations, which have a much wider set of disease causing mutations.

Before the advent of screening, TSD was 60-100 times more common in Ashkenazi Jews than in the overall population in the US. In the UK, without screening, the small size of the Jewish population (about 2,700 children born each year) means that we would still expect only one birth of an affected child per year. Nevertheless, this condition is of concern to the Jewish community in UK and internationally. There is some limited evidence in our report that, since the availability of carrier testing in the UK, the number of affected children has been approximately halved, with Jewish cases now being fewer than those from the non-Jewish population.

The Jewish population

Screening for Tay Sachs carrier status is focused on the Ashkenazi Jewish population, which is the ethnic origin of about 95% of British Jews. The project team used data from the 2001 census, which was analysed in a report prepared by the Institute for Jewish Policy Research, to provide a description of the population and its distribution in the UK. The size of the Jewish population in the UK is relatively small at about 270,000.

Almost 97% of UK Jews live in England, with major concentrations in certain areas of London and to a lesser extent in Manchester. Our report on distribution showed that the majority could be reached by focussing efforts on a small number of districts in the London region (including parts of Hertfordshire and Essex) and Greater Manchester. For school children, about 30% of all Jewish secondary-school children could be reached by targeting 7 mainstream Jewish secondary schools in London (4), Manchester (1) and Hertfordshire (2). 62% of Jews who are married have a spouse who is also Jewish; this relatively high level of endogamy indicates a continuing need for carrier screening.

The current carrier screening service

In this report we differentiate where possible between screening - the systematic, proactive identification and offer of a test to individuals who are at increased risk, and testing - the provision of a test in response to an individual who seeks advice.

For the screening programme overall, our review has highlighted the fact that there is no routine or readily available information about the service, its activity or its outcomes. Information collected by the project group through ad hoc analysis, surveys and a questionnaire to patients is summarised below.

Tay Sachs disease carrier testing is available through NHS laboratories in London (Guy's Hospital) and Manchester (Willink laboratory). In London, weekly walk-in clinics are run by a genetic counsellor at Guy's Hospital (provided by the Guy's and St Thomas' NHS Foundation Trust Clinical Genetics Service) and the Barnet District General Hospital. Individuals elsewhere in the country can request referral to their regional genetics centre in order to obtain carrier testing. Samples are sent either to the Guy's laboratory or to the Willink.

Outreach community screening sessions are run on a voluntary basis in Jewish schools and

community organisations. All samples are sent to Guy's Laboratory for testing provided by the NHS.

In Manchester, community screening sessions are run by voluntary organisations in schools and universities, with samples sent to the Manchester Willink laboratory for testing that is paid for by the voluntary sector.

Carrier testing is also available on a private basis through two UK-based companies, the international Dor Yeshorim organisation, and other private laboratories based outside the UK.

Outreach carrier screening in the Jewish community thus currently depends heavily on the commitment and voluntary work of individuals and charitable organisations from the Jewish community. There has been no NHS support for this activity (except for the laboratory testing itself, and then only in London) and many of the people who have organised outreach community screening sessions over the last 10 years are nearing retirement. The future viability of community screening in Manchester, in particular, is seriously in doubt.

The offer of carrier screening in the antenatal service was reviewed in detail through a survey of antenatal screening coordinators. There were no clear and consistent protocols or pathways for Tay Sachs carrier screening within the antenatal setting; no agreed question for seeking information about Ashkenazi Jewish family origin; no evidence that midwives even in areas with substantial Jewish populations are routinely suggesting screening to Jewish patients; and little or no awareness of local Jewish populations and their uptake of screening. Finally there was confusion about the appropriateness of offering screening in different situations and many coordinators acknowledged that they needed further advice on this issue.

A survey of patients attending the Guy's walk-in clinic corroborated some of these findings and provided further information about the patients who were attending for testing. The ethnic background of individuals and couples attending for testing was predominantly Ashkenazi Jewish. Most individuals were aware of their ethnic origins and able to say how many of their grandparents were Ashkenazi Jewish, suggesting that it would be feasible to ask such a question as a way of identifying individuals who might benefit from carrier screening. It was of concern to find that most people had found out about screening from family, friends or the internet rather than through health care professionals such as GPs or midwives. About one third of the testing was in the antenatal period - however there was no evidence that midwives in areas with substantial Jewish populations are routinely suggesting Tay Sachs disease screening to Jewish patients at the antenatal booking-in appointment, as in the 7 month period of the survey, none of the patients surveyed described this route to testing. Interestingly, just under one fifth of patients attending for testing were aware of known carriers of Tay Sachs disease in their family, or a family history of Tay Sachs disease, indicating that there is a cascade effect occurring naturally which influences who attends for testing. Five of the 7 carriers in the surveyed sample of patients came from this group.

The laboratory testing service

Two laboratories (Guy's Hospital in London and the Manchester Willink) currently test samples for Tay Sachs disease carrier screening. Testing at the Manchester Willink has been unfunded since a one-year research project finished at the end of 1989, and since then has been running at a loss. Dr Alan Cooper has indicated that the Willink intends to stop

performing carrier screening tests for Tay Sachs disease when Dr Sybil Simon (who organises the community outreach programme) retires. This would leave Guy's as the only laboratory offering carrier screening tests.

Data collection from laboratory testing needs to be improved. In particular, the Guy's database has not in the past distinguished carrier screening tests from diagnostic tests, or recorded the ethnic origins of those tested, making accurate audit of the programme impossible. There has been no standardisation between the Guy's and Manchester Willink databases. Between 1999 and 2007 the Guy's laboratory performed a total of 26,152 assays on samples from 5,330 individuals, of whom approximately 55% were female and 45% male. Overall, 6.1% of those tested, or 1 in 16, were recorded as carriers of Tay Sachs disease. This carrier frequency is significantly higher than the expected figure of 1 in 25-30 for the Ashkenazi Jewish population again suggesting that the data may contain an appreciable number of results from professional- and patient-initiated cascade testing in families (both Jewish and non-Jewish) in which there was a known carrier.

At the Willink laboratory in Manchester 36 carriers were found out of a total of 462 individuals tested, a carrier frequency of 1 in 12.8. 368 of those tested were of Ashkenazi Jewish origin, but it is not known how many of the carriers were Ashkenazi Jewish. The high carrier frequency suggests that a significant percentage of those tested probably had a family history of Tay Sachs disease.

The testing protocol for Tay Sachs disease carrier screening has not been standardised or fully evaluated. Manchester Willink uses only biochemical testing in leucocytes. Both biochemical testing and mutation testing are carried out at Guy's but the testing protocols have developed in an ad hoc way.

Overall, screening coverage by the NHS programme appears to be very low, possibly as low as 6% of the Jewish population. A major difficulty in obtaining an accurate estimate of screening coverage throughout the whole Ashkenazi population is the lack of data both from private non-UK testing services used by the Association for the Prevention of Jewish Diseases, and from Dor Yeshorim. There is some anecdotal evidence that an increasing proportion of the Jewish population, perhaps particularly in the Strictly Orthodox community, is choosing private testing in preference to the NHS service because the private services offer testing for a wider panel of up to 9 or 10 diseases.

Other models for carrier screening in recessive disorders

The review built on the experiences of genetic counsellor Sara Levene in undertaking international visits to Tay Sachs screening programmes in Israel, Canada, Australia and the United States under the Department of Health-funded Visiting Fellowships in Genetics in Health Care Programme. The Advisory Group also examined the UK Sickle Cell and Thalassaemia screening programme to see if there were valuable learning points.

Tay Sachs disease carrier screening programmes in Israel, Australia, Canada and the US have both strengths and weaknesses that may be relevant in considering options for the UK programme. The Israeli system is universal and systematic but such a system may not be feasible in countries where Jews constitute a much smaller proportion of the population. Antenatal screening programmes (Israel, New York) target the population at a time when

screening is directly relevant, but have the disadvantage that additional stress and worry may be caused at this time, and that they are not acceptable to Strictly Orthodox Jews. Preconception screening (Canada, Australia and Philadelphia) may be less traumatic but is not systematic and is dependent on high-quality education programmes to ensure that test results are understood and recalled correctly. This approach also potentially tests twice as many people as necessary because it is not couple-based.

There is a tendency in most Tay Sachs disease screening programmes to move towards offering molecular-genetic (DNA) Tay Sachs disease carrier testing rather than the biochemical test, mainly because screening can then be readily extended to include other genetic conditions. Pressure for this change is coming largely from the Jewish community itself.

The antenatal carrier screening programmes for haemoglobin disorders in the UK provide another example of carrier screening for recessive conditions. This programme is already well developed, and many aspects of its standards and operating procedures are likely to be relevant to the development of antenatal carrier screening for Tay Sachs disease. However, the target population for these screening programmes is larger and the carrier frequencies higher than for Tay Sachs disease in the Ashkenazi Jewish population. Thus it may not be feasible to achieve a comparably systematic, national carrier screening programme for Tay Sachs disease.

The Family Origin Questionnaire (FOQ) has proved to be an effective tool for systematically identifying couples at high risk of having a child affected by a haemoglobin disorder. The FOQ is the result of a process of extensive consultation and validation involving a range of clinical, community and religious groups; however, it should be possible (after due process) to add a question to ascertain ethnic Jewish origin. Educational initiatives among antenatal health professionals across the country would be essential to ensure understanding of the reason for the question and the referral pathway for women taking up the screening offer.

Evaluation of different methods of laboratory testing

Carrier testing for Tay Sachs disease can be carried out by a biochemical assay of hexosaminidase A (HexA) activity in serum, leucocytes or platelets, and/or by direct DNA testing for one or more of the known causal mutations in the *HEXA* gene. At present the laboratories provide testing by the biochemical assay method in leucocytes, and the Guy's laboratory also provides DNA testing for further characterisation of those identified as carriers and for those whose biochemical test result is inconclusive.

Members of the PHG Foundation team undertook a literature review and carried out modelling to provide an evaluation of the performance of the two testing methods.

Insufficient information is available to enable full evaluation of the biochemical and DNA tests. In particular, the true sensitivity of the DNA test and the true specificity of the biochemical test in leucocytes cannot at present be accurately estimated. DNA tests for Tay Sachs disease are not currently included in the UK Genetic Testing Network's list of tests approved for use in the NHS, and have not yet had Gene Dossiers prepared for them. (Gene Dossiers assess the available evidence regarding a DNA test's analytical validity, clinical validity and clinical utility). Preparation of a Gene Dossier for the Tay Sachs disease mutation test, which is currently being undertaken by Dr Christine Patch, is a useful step.

From the limited data available, the risk that a mutation-negative Ashkenazi Jewish person could still have an affected child lies in the range 1 in 22,000 - 234,000 if their partner is an unscreened Ashkenazi Jew, and in the range 1 in 206,000 - 2,168,000 if their partner is an unscreened non-Jew. The higher residual risk figures relate to a sensitivity of 87.3% for the DNA test in Ashkenazi Jews. However this figure, calculated from the performance of the DNA test in people identified as carriers by use of the biochemical test in screening programmes, is almost certainly an underestimate. A more reliable 'gold standard' for judging the test may be the detection of obligate Tay Sachs carriers; by this criterion, the sensitivity of the DNA test is 98.8%. Nevertheless, if a decision were made to use DNA testing rather than the biochemical test as the initial screening test, it might be prudent to advise both members of a couple to be screened if both are Ashkenazi Jews.

The extremely high sensitivity of the biochemical test (at least 99%) means that the residual risks for those tested by this method are very low. However, this sensitivity comes at the cost of reduced specificity, leading to significant numbers of (probably) false positive results if this test is used as a screening test, and creating additional costs and counselling difficulties.

We have suggested that screening should be offered to those with at least one Ashkenazi Jewish grandparent. This policy would represent a cut-off for screening at a prior risk of 1 in 80 (corresponding to a risk of having an affected child of 1 in 8,640 with an unscreened Ashkenazi Jewish partner, or 1 in 80,000 with an unscreened non-Jewish partner). If mutation testing became the screening test, and a couple was of mixed Ashkenazi Jewish/non-Jewish ancestry, it would be advisable to ensure that the partner with the higher number of Ashkenazi grandparents had been tested.

There are additional issues about the best method of screening for a small group of Jews of North African Sephardi origin. These individuals also have an increased carrier risk, but due to a different set of mutations, meaning that, if mutation testing were to replace biochemical testing, the latter would need to be retained for use in certain circumstances. Similarly whichever test is chosen as the initial screening test, biochemical testing should be used in the antenatal setting to test the partner of any known carrier (whether Jewish or non-Jewish).

Opinion in the Advisory Group was divided on the question of whether the NHS Tay Sachs disease carrier screening programme should continue to offer the biochemical test as the initial screening test, or move towards replacing the biochemical test by a DNA test. The arguments for and against the different protocols are discussed in this Report. It should be kept in mind that the reason for offering screening to the Jewish community is the higher risk that individuals from this community carry one of three specific mutations. Use of a screening test that goes beyond a test for these mutations, therefore, needs careful justification. One important factor about which we have insufficient information is the view of the Jewish population itself. There appears to be a trend, particularly in the Strictly Orthodox community, towards a preference for services that offer DNA carrier testing for a panel of 'Ashkenazi Jewish diseases', rather than Tay Sachs disease alone. It is possible that individuals may prefer to offset the (possibly) lower sensitivity of the DNA test against the perceived advantage of testing for a wider range of conditions. A survey of attitudes on this question would be useful in helping to formulate NHS screening policy.

Recommendations for developing the Tay Sachs disease screening programme

The Advisory Group was charged with the task, following review of the current service, of making recommendations to develop a more systematic screening programme with equity of access. Based on our analysis of need, our review of current services and our evaluation of evidence from the literature and from other services worldwide, we set out here a series of recommendations for the development of the Tay Sachs disease National Screening Programme.

The rarity of the condition and the relatively small size of the Ashkenazi Jewish population in the UK mean that the screening programme should be viewed, not as solving a major public health problem in disease incidence, but as putting in place a service for a community that is identified and sees itself as high risk. Benefits thus arise from the ability of carrier testing to reduce anxiety in Jewish communities for individuals and couples for whom prenatal diagnosis is acceptable and to enable carrier couples to enter into or continue relationships with the option to avoid the birth of an affected child. In some communities (such as the Strictly Orthodox community) where there is a tradition of arranged introductions leading to marriage, carrier testing has also helped to avoid bringing together carrier couples. The provision of carrier screening to single individuals through an NHS programme is important in ensuring that people can decide for themselves whether to be tested and what to do with the results.

Worldwide, communities with high Jewish populations have put carrier screening programmes in place, with high degrees of success in reducing the birth prevalence of Tay Sachs disease in Ashkenazi Jews to below the overall population rate. In 1999 the case was made for a carrier screening programme in the UK and the programme gained formal agreement from the NSC. It was not, therefore, the role of this Advisory Group to revisit whether or not Tay Sachs disease screening fulfilled all the screening criteria, but to review the implementation of the programme against a current assessment of need and evaluation of available services.

Our review has shown that the present programme has built on considerable NHS laboratory resources, professional expertise and voluntary sector experience and commitment. Nevertheless, it is currently running without formal agreements, documentation, channels of accountability, quality assurance and evidence of effectiveness. We identified several important gaps in the service, such as lack of a systematic approach to the offer of screening in antenatal services, and vulnerability of the community and laboratory elements in the Northwest. Most importantly, this means that there is risk of a child with Tay Sachs disease being born to an unscreened couple. Also important is the likelihood of suboptimal services for users and potential users, inequity, poor cost effectiveness and low responsiveness to technological, clinical or patient-desired changes. Putting these aspects of the service in order is not only vital to proper implementation of Tay Sachs disease carrier screening but would also provide a valuable basis for introduction of carrier screening for other conditions for which the Ashkenazi Jewish population is at increased risk, should the NSC wish to do so following formal evaluation of such conditions against screening criteria.

The Advisory Group has made the following recommendations, grouping them into *immediate recommendations* to ensure the continuation of the Programme, *programme recommendations*, to ensure that over time the Programme achieves necessary quality

standards and *longer term recommendations*, which includes consideration of the related issue, not addressed by this Report, of including a wider panel of diseases exhibiting higher frequency in the Ashkenazi Jewish population.

Immediate recommendations

Recommendation 1: Continuation of the programme

The Advisory Group recognises the clinical need for Tay Sachs disease carrier screening and the valuable work being undertaken in clinical, laboratory and voluntary services. We recommend that the UK National Screening Programme (NSP) for Tay Sachs disease carrier screening should continue but with renewed commitment to achieving a high quality and equitable service that maximises choice for high risk individuals and couples.

Recommendation 2: Formal constitution of the programme

The Advisory Group recommends that the Tay Sachs disease programme should be formally constituted as with any other screening programme.

Recommendation 3: Linked antenatal and community programmes

The National Screening Programme for Tay Sachs should include antenatal and community carrier screening and these programmes should be linked.

The Tay Sachs screening programme is included in the antenatal section of the National Screening Programme. The principle for carrier screening for pregnancies at high genetic risk in antenatal care is well established through the UK Sickle Cell and Thalassaemia programmes. Like Tay Sachs disease, the antenatal screening programme focuses on identifying carrier couples and offering prenatal testing with the option of termination of pregnancy if the fetus is affected.

Although the antenatal service provides an important safety net for at risk couples, ideally Tay Sachs carriers, and more specifically carrier couples, would be identified before pregnancy so that couples at risk of having an affected child could carefully consider their options before conception. They could be referred to the appropriate genetic services and, when pregnant, could receive early referral (as a high risk pregnancy) to obstetric services for counselling and advice. If they wish they could then proceed to testing, decision making and possible pregnancy termination in a timely and unhurried fashion. Chapter 4 shows that the current provision of Tay Sachs disease screening in UK does indeed include a service for adults prior to conception, including couples, single adults and older school children. This service is also important for individuals who would not consider prenatal diagnosis or termination of pregnancy, but wish to reduce their risk of having an affected child by avoiding marriage to another carrier.

Recommendation 4: Developing antenatal carrier screening

The Advisory Group recommends that consolidation and development of the quality of antenatal screening should be the first priority and that this should be first focussed on Trusts serving large Jewish communities.

For antenatal screening, Chapter 5 shows that there is no effective system for screening Jewish patients. This represents a risk to the NSP of a child with Tay Sachs disease being

born to a Jewish carrier couple who had received no information about screening. This is of particular concern in areas where there are large Jewish communities.

Recommendation 5: Securing carrier testing and community carrier screening in the short term

The Advisory Group recommends that lead commissioners for the Programme should urgently put in place interim contractual measures to secure current carrier testing and screening services in the short term, pending further development and integration with the antenatal screening programme. These services include current clinical 'walk-in' services (e.g. the Guy's Hospital service), testing provided on request to regional genetics services, and community carrier screening services provided by voluntary organisations; all with associated laboratory elements. This is likely to require provision of some further NHS resources for these services.

For community carrier screening, Chapter 4 shows that NHS walk-in clinics and voluntary organisations such as Jewish Care and the Association for the Prevention of Jewish Diseases provide access to testing through the NHS laboratory testing service, although these services are not running as a coherent screening programme. The Advisory Group notes the potential vulnerability of all these services, and particularly that services in the Northwest are likely to come to an end in 2009 with the retirement of key personnel.

Programme recommendations

Following agreement in principle about the continuation of the Tay Sachs disease Screening Programme as set out in Recommendations 1 - 4, the NSC should set out its programme in detail. In the following sections we make recommendations about some of the key issues that the Programme will need to consider.

Recommendation 6: Target group

The NSP will need to decide who will be the target group for the Programme. The Advisory Group recommends that the Programme should be focussed primarily on the Jewish population of Ashkenazi Jewish origin, with a cut-off for an offer of screening at a prior risk for carrier status of approximately 1 in 80 (the risk of an individual who has one Ashkenazi Jewish grandparent). In practice, individuals with other Jewish origin (eg Sephardi) should not be excluded but are likely to be small in number. This decision might need to be reviewed at a later stage. In the antenatal setting screening should be offered if either partner is Jewish or part-Jewish. If only one partner is Jewish or part-Jewish that partner should be tested first.

Recommendation 7: Target population

The Advisory Group recommends that antenatal carrier screening should be developed first in those London and Manchester Trusts that serve the largest Jewish populations. Community screening should first be offered in mainstream Jewish secondary schools. Information should also be provided in Strictly Orthodox schools (if possible), in private schools that have a large number of Jewish pupils, and through Hillel houses (Jewish Halls of Residence) in universities.

The Advisory Group considered the question of equity and in particular whether it was fair to develop carrier screening programmes to reach specific populations based in particular locations such as schools or geographical areas, rather than Jews in the population as a whole. Chapter 3 provides a detailed description of the structure of the Jewish population throughout the UK. The Advisory Group noted the relatively small total population and the particular concentration in certain boroughs in and around London and in the Northwest and, for children, in a small number of Jewish schools.

Recommendation 8: Developing an ethnic screening questionnaire for Jewish patients

Work needs to be done in the antenatal setting to develop a tool for systematically identifying Jewish couples and offering them testing. The Advisory Group recommends that work is undertaken in conjunction with the Sickle Cell and Thalassaemia Programme to add a question on Jewish ethnicity to the Family Origin Questionnaire.

Recommendation 9: Integration of antenatal screening into antenatal care

The Tay Sachs disease Programme needs to work with antenatal services to introduce carrier screening into the care pathway for maternity services to ensure a systematic offer of screening at an appropriate stage of pregnancy. The Advisory Group recommends that this should be achieved by the end of the first trimester. The Advisory Group recommends that such work should be led by the antenatal screening coordinators and will require investigation of feasibility, practicality and resource aspects as well as a substantial awareness-raising and educational programme with midwives, health visitors, primary care teams and GPs and the development of high quality information for patients. Initial work should be undertaken in areas of high Jewish populations where there will be greater motivation of health professionals and more immediate outcomes for patients.

Recommendation 10: Development of community screening

Community screening is currently undertaken by voluntary organisations such as Jewish Care and the Association for the Prevention of Jewish Diseases. The Advisory Group recommends that interim measures to secure these services should be followed by development of a contractual agreement that integrates these services with NHS services and includes protocols, standards and reporting arrangements.

Recommendation 11: Choice of initial screening test

The NSP will need to take a major decision on whether the biochemical or the DNA test should be the initial screening test. The NSP should ask laboratory providers and clinical services to look into the advantages and disadvantages of moving to DNA testing as the initial screening test, with retention of the biochemical test where clinically appropriate. In particular, a distinction should be made between the testing that is done to screen potential carriers, and testing for high-risk couples.

The Advisory Group recommends that services should consider using DNA testing as the method of choice in the screening programme for:

1. All specimens from individuals where there is not a pregnancy.
2. All specimens where there is a pregnancy and one or more partners is an Ashkenazi Jew. If both partners are Ashkenazi Jewish, both should be tested.

As a preliminary, laboratories should work with services to agree an optimum panel of mutations to be tested for in the UK and provide practical and literature based evidence for its likely sensitivity in the UK Jewish population.

Biochemical testing should be retained for:

1. All specimens where there is a pregnancy and one or more partners is of known or suspected North African Sephardi origin.
2. All partners of known carriers (both Jewish and non-Jewish).

Laboratories should develop detailed protocols and standards for the agreed tests.

The debate about the choice of screening test is set out in Chapter 7. Chapter 4 also demonstrates the current lack of information about the laboratory performance of the tests currently in use, and included recommendations for development.

Recommendation 12: Developing information systems

Laboratories and clinical providers should develop a standardised database and IT infrastructure recording essential patient information and able to produce standard reports, to support audit and monitoring requirements of the programme and to link with relevant diagnostic laboratories.

Longer term recommendations

Recommendation 13: Extending carrier screening to other genetic conditions

The Advisory Group recommends that the NSC also consider whether to extend the Tay Sachs disease NSP to include other genetic diseases that are more common in the Ashkenazi Jewish population, following on from the work previously submitted to the NSC in 2006 and which is enclosed as Appendix 8.

Although consideration of this issue was outside of the scope of this report, the view has frequently been expressed within the Jewish community and was endorsed by members of the Advisory Group that screening should be extended to a wider panel of conditions with increased frequency in the Ashkenazi Jewish community.



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