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As the results of the Human Genome Project are realized, it has become technically possible to identify carriers of numerous autosomal and X-linked recessive disorders. Couples at risk of having a child with one of these conditions have a number of reproductive options to avoid having a child with the condition should they wish. In Australia the haemoglobinopathies are the only group of conditions for which population screening is widely offered and which is government funded. In some Australian states there are also population screening programs for cystic fibrosis and autosomal recessive conditions more common in Ashkenazi Jewish individuals which are generally offered on a user pays basis. It is predicted that as consumer demand increases and testing becomes cheaper, that many people planning or in the early stages of pregnancy will have carrier screening for multiple genetic conditions. This will have significant implications for genetic counseling, laboratory and prenatal testing resources. In addition such screening raises a number of ethical issues including the value of lives of those born with genetic conditions for which screening is available.

Keywords: screening, carrier, cystic fibrosis, thalassaemia, Tay Sachs disease

There are more than 2,000 autosomal, X-linked and mitochondrial disorders whose genetic basis is known (McKusick, 2008). It is theoretically possible to offer testing for heterozygous mutation status (so called carrier testing) for all autosomal recessive and X-linked disorders whose genetic basis is known and therefore to provide advice about the risk of any couple having a child affected by these conditions. In reality it is only practical to offer population genetic screening for few conditions largely because of the cost of identifying carriers, the length of time it takes to do testing and the rarity of most genetic disorders in any community. Population screening refers to testing for carrier status in individuals who are not at increased risk of being a carrier because of a family history of the condition.

Carrier testing programs for genetic disorders began formally in the early 1970s for Tay Sachs disease (TSD) by measurement of serum hexoseaminidase A (Kaback et al., 1997). This was followed by carrier screening programs for β thalassaemia by measurement of mean corpuscular volume and haemoglobin electrophoresis (Davies et al., 2000). This highlights the fact that genetic screening is not always by DNA testing. Indeed the genetic basis of TSD and β thalassaemia only became known some years after screening programs were introduced. If both members of a couple are carriers of the same autosomal recessive condition or a woman is a carrier of an X-linked condition there is a 1 in 4 (25%) chance of having a child with the condition.

The most often cited rationale for carrier screening is to offer couples reproductive choice by identifying those who are at high risk of having a child with a genetic condition (Davies et al., 2000). The reduction in incidence of genetic conditions through prenatal diagnosis and pregnancy termination as well as preimplantation genetic diagnosis is often used to measure the success of carrier screening (Marteau & Anionwu, 1996). Indeed if few couples identified by screening as being at high risk of having a child with a particular genetic condition acted on the information, screening programs could not be justified on economic grounds (Haddow, 1997; Zeuner, 1997). Similarly, the uptake of screening, whilst often used to measure the success of a program, is only one measure by which the value of a program should be assessed (European Society of Human Genetics, 2003). Other important aspects to assess the success of programs are the level of informed consent among those screened and those declining screening, the proportion of the target population offered screening, harms in those screened and economic outcomes (European Society of Human Genetics, 2003).

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Table 1
Reproductive Options Available to Couples Where Both are Carriers of the Same Autosomal Recessive Condition or the Female is a Carrier of an X-linked Condition

<table>
<thead>
<tr>
<th>Reproductive option</th>
<th>Nonpregnant</th>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal testing with pregnancy termination of affected fetuses</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pre-implantation genetic diagnosis</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Donor gamete or embryo</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Adoption</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Note: The pregnancy status refers to whether the female is pregnant at the time the couple's carrier status is identified and whether the specific reproductive option is available for that pregnancy.

Couples may wish to know their carrier status to be prepared for the birth of a child with a genetic condition or to avoid having a child affected by the condition. Couples at high risk have a number of reproductive options to enable them to avoid having a child affected by the condition. These are outlined in Table 1.

Criteria for the Introduction of Carrier Screening
The decision to offer population carrier screening for a genetic condition is generally arrived at because the condition fulfils a number of criteria. The basic principles of population screening were developed by Wilson and Junger in 1968 (Wilson & Junger, 1968). A significant recent addition to the principles of population screening is that appropriate education should be provided so that individuals can make informed decisions about having testing and that the individual's decision is respected and they are protected from stigmatisation and discrimination (Andermann et al., 2008). The principles of population genetic screening are listed in Table 2.

Cascade Testing
Cascade testing refers to testing for carrier status of relatives of individuals with a genetic condition or where an individual is identified as a carrier of such a condition (Barlow-Stewart et al., 2007). The rationale is that genetic relatives are at much higher than background risk of being a carrier of a genetic condition in their family. If the causative mutation(s) is known in the family, carrier testing is available and can be offered to relatives irrespective of the population frequency of the condition.

Population Genetic Screening in Australia
Population genetic carrier screening is widely conducted in Australia for haemoglobinopathies (Metcalfe et al., 2007). Population screening is offered in some places for cystic fibrosis (Barlow-Stewart et al., 2003; Christie et al., 2006; Massie et al., 2005) and autosomal recessive conditions more common among Ashkenazi Jews (Barlow-Stewart et al., 2003; Gason et al., 2005). These will therefore be discussed in some detail.

Haemoglobinopathies
The haemoglobinopathies are a group of autosomal recessive conditions that affect the function of haemoglobin. They are the most common global recessive conditions with about 270 million people (4.5% of the world's population) being carriers and at least 300,000 individuals are born each year who are affected by one of the haemoglobinopathies (Angastiniotis & Modell, 1998). Haemoglobinopathies can be divided into structural variants, the commonest of which is sickle cell disease, and those that have quantitative effects on haemoglobin chains. The quantitative haemoglobinopathies are the thalassaemias: the globin proteins are structurally normal but there are insufficient α- or β-globin chains (Old, 2007).

The two main forms of thalassaemia, α and β, result from mutations in the α- and β-globin genes, respectively. The genetics of α-thalassaemia is complicated by the fact that there are four rather than two α-globin genes. Thalassaemia is most common in people from Mediterranean countries, including the Middle East, India, Africa and south-east Asia (Davies et al., 2000).

β thalassaemia major results in chronic anaemia requiring regular blood transfusions and iron chelation therapy (Birgens & Ljung, 2007). Because there are four α-globin genes, an individual may have 0–4 functioning α-globin genes. If a fetus has no functional α-globin genes, they will have haemoglobin Bart's hydrops fetalis syndrome and will usually not survive (Birgens & Ljung, 2007). The presence of a single functional α-globin gene results in haemoglobin H disease and may require regular blood transfusions and iron chelation if the affected individual has a moderately severe haemolytic condition. Individuals with two or three functional α-globin genes are healthy carriers of α-thalassaemia. Their partner

Table 2
The Principles of Population Genetic Screening (Khoury et al., 2003; Wilson & Junger, 1968)

<table>
<thead>
<tr>
<th>Principle</th>
<th>Corresponding number</th>
</tr>
</thead>
<tbody>
<tr>
<td>It screens for an important problem</td>
<td>1</td>
</tr>
<tr>
<td>There is acceptable treatment</td>
<td>2</td>
</tr>
<tr>
<td>There are facilities for diagnosis and treatment</td>
<td>3</td>
</tr>
<tr>
<td>There is a recognized latent or early symptomatic stage</td>
<td>4</td>
</tr>
<tr>
<td>The natural history is understood</td>
<td>5</td>
</tr>
<tr>
<td>There is a suitable test acceptable to population</td>
<td>6</td>
</tr>
<tr>
<td>There is an agreed policy on who to treat</td>
<td>7</td>
</tr>
<tr>
<td>The cost of case finding is balanced against total expenditure</td>
<td>8</td>
</tr>
<tr>
<td>There is a continuous process of case finding</td>
<td>9</td>
</tr>
<tr>
<td>Appropriate education should be provided</td>
<td>10</td>
</tr>
</tbody>
</table>
should be offered DNA testing to ascertain if they are a carrier of α-thalassaemia.

In considering screening for thalassaemia, the practitioner should establish whether there is a family history of a haemoglobinopathy, the ancestry of the individual and arrange a full blood examination (FBE) (Old, 2007). Further testing is indicated when:

- there is a positive family history
- the individual is from one of the high-risk ethnic groups
- there is a low mean corpuscular volume (MCV) and/or mean corpuscular haemoglobin (MCH).

Further testing includes haemoglobin electrophoresis, iron studies and, if indicated, DNA studies (Old, 2007). In β-thalassaemia carriers (so-called β-thalassaemia minor) the FBE generally shows a low MCV/MCH and there are elevated levels of HbA2 in the haemoglobin electrophoresis.

In carriers of α-thalassaemia haemoglobin electrophoresis is normal (American College of Obstetricians and Gynecologists, 2007). Therefore, specific genetic testing should be carried out if a person has low MCV or MCH and/or is from one of the high-risk ethnic groups to identify whether they are a carrier of α-thalassaemia.

Thalassaemia screening is done in the majority of pregnant women because the initial investigation is an FBE, a test undertaken on most women early in pregnancy. Further testing with haemoglobin electrophoresis and/or genetic testing is carried out if the result of the FBE dictates that this is appropriate or if the woman is from a high-risk ethnic background. An FBE is done in pregnant women for a number of reasons in addition to screening for thalassaemia including assessing for anaemia. It is doubtful that many women are aware they are screened for thalassaemia until they are found to be a carrier.

**Cystic Fibrosis**

Cystic fibrosis (CF) is the commonest severe autosomal recessive condition in childhood among Caucasian individuals. About 1 in 25 people from this ethnic background are carriers with about 1 in 2,500 being affected by the condition (Massie et al., 2000). CF results in affected individuals having some or all of suppurrative lung disease, malabsorption, reduced fertility, liver disease and meconium ileus and generally results in a significantly reduced life span.

CF results from mutations in the CFTR gene (Rommens et al., 1989). More than 1500 different alterations have been identified in this gene (Cystic Fibrosis Consortium, 2007). The p.F508del mutation accounts for about 70% of mutations among Caucasians. Because so many different mutations can result in CF, screening programs test for the most common mutations in the community where the program is being offered. The American College of Obstetricians and Gynecology and American College of Medical Genetics recommend that mutations which occur with a frequency of greater than 0.1% in the CF population should be tested meaning screening for 23 mutations is currently recommended in the USA (Watson et al., 2004). In Australia, current programs vary in the mutations tested for. In the Hunter Region, NSW, screening is initially for p.F508del alone and if one member of a couple is found to carry this mutation, the other member of the couple is tested for a panel of 28 other mutations (Christie et al., 2006). By contrast, in Victoria, 12 mutations are tested which will identify about 83% of carriers (Massie et al., 2005). Currently there is no government funding for population screening for CF in Australia.

**Screening in the Ashkenazi Jewish Community**

Ashkenazi Jews are those whose ancestors originated in Eastern Europe. The majority of Jews in Australia are Ashkenazim. There are a number of autosomal recessive conditions that are more common in this community (Leib et al., 2005). These include Tay Sachs disease, Canavan disease, Niemann Pick disease type A, Bloom syndrome, Fanconi anaemia, familial dysautonomia, mucolipidosis type IV and Gaucher disease (Table 3). In addition, CF occurs with about the same frequency in Ashkenazi Jews as it does among the broader Caucasian community. Testing for the most common mutations for all of these conditions is available to individuals of Ashkenazi Jewish ancestry and formal programs exist in Sydney (Burnett et al., 1995) and Melbourne (Gason et al., 2003). Screening for Tay Sachs disease can be by mutation detection or measurement of hexoseaminidase A. Both will identify > 97% of carriers (Bach et al., 2001). The enzymatic assay is technically more complex in pregnant women and can only be done on blood samples whereas the genetic test is the same irrespective of the individual’s pregnancy status and can be done on cheek cells as well as blood (Gason et al., 2005).

The ultra-orthodox Jewish Community have developed a unique program to meet their specific cultural needs. The Dor Yeshorim program tests young people for carrier status for nine conditions (Ekstein & Katzenstein, 2001). The test result is not released to the individual but rather they are issued with a personal identification number (PIN). In this community pregnancy termination is problematic and marriages are generally arranged. The PINs of a prospective couple are presented to the central laboratory and only if at least one of the couple is not a carrier for each of the conditions does the marriage proceed.

Screening for Gaucher disease is somewhat controversial. Although mutations that underlie Gaucher disease are the commonest of the autosomal recessive conditions amongst Ashkenazi Jews, only about one third of individuals who are homozygous or compound heterozygous for the commonest mutations have symptomatic disease (Beutler, 2006). In addition, there is an effective, albeit expensive treatment,
Fragile X Syndrome

Fragile X syndrome is the commonest inherited cause of intellectual disability with around one in 4,000 males and one in 8,000 females affected (Murray et al., 1997). It is virtually always due to an expansion of a CCG trinucleotide repeat at the 5' end of the FMR1 gene on the X-chromosome. About one in 150 females carry a so-called premutation meaning they are at risk of having a child with a full mutation (Berkenstadt et al., 2007). Essentially all males and some females with a full mutation have intellectual disability often accompanied by severe behavioral problems with autistic features being prominent (Reiss & Hall, 2007). One of the challenges of offering population genetic screening for fragile X syndrome is that identifying full mutations in a timely fashion has been technically difficult as Southern blotting is often required. These technical issues can mean that providing pregnant women with a result in time to enable prenatal diagnosis and, if necessary, pregnancy termination, may not always be possible. New technology using a rapid polymerase chain reaction based screening method may mean that these problems can be overcome, paving the way for the introduction of widespread screening (Tassone et al., 2008). Screening for fragile X syndrome has been undertaken for a number of years in Israel (Berkenstadt et al., 2007) with an uptake of about 24% (Sher et al., 2003).

A significant issue to consider related to population screening for fragile X syndrome carrier status is that individuals with an FMR1 premutation may develop the fragile X-associated tremor/ataxia syndrome (FXTAS) (Jacquemont et al., 2007). Features of FXTAS include cognitive decline, tremor, ataxia and autonomic dysfunction. FXTAS affects over 50% of male premutation carriers over the age of 70 years (Jacquemont et al., 2004) and about 8% of female premutation carriers over 40 years (Coffey et al., 2008). Population screening will identify women who will go on to develop this neurological syndrome and such screening is thus a form of presymptomatic testing. It is therefore important that women are made aware of this risk prior to screening.

Spinal Muscular Atrophy

Spinal muscular atrophy (SMA) is an autosomal recessive condition that affects about one in 10,000 individuals meaning about one in 50 people are carriers (Pearn, 1980). The most severe form referred to as type I SMA or Werdnig Hoffman disease, results in an infant having progressive muscle weakness, never being able to walk and results in death before two years. Almost all SMA is due to deletions involving the SMN gene (Lefebvre et al., 1995). Carriers can be diagnosed by dosage studies. There are complexities with carrier testing due to the possibility of point mutations that cannot be diagnosed by dosage studies and the fact that people can have two normal SMN genes on one chromosome and none on the other (Ogino et al., 2004). In this situation, the individual is a carrier as they can pass on a chromosome with a deleted SMN gene but dosage studies reveals two copies of the gene. The frequency of this occurrence has been studied enabling the residual risk to be calculated (Ogino et al., 2004). There are no studies reported in the literature of formal population screening programs for SMA.

### Table 3

<table>
<thead>
<tr>
<th>Disease</th>
<th>Carrier rate</th>
<th>Test sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gaucher disease</td>
<td>1 in 15</td>
<td>96%</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1 in 25</td>
<td>97%</td>
</tr>
<tr>
<td>Tay Sachs disease</td>
<td>1 in 28</td>
<td>98%</td>
</tr>
<tr>
<td>Familial dysautonomia</td>
<td>1 in 30</td>
<td>99%</td>
</tr>
<tr>
<td>Canavan disease</td>
<td>1 in 40</td>
<td>98%</td>
</tr>
<tr>
<td>Mucolipidosis type IV</td>
<td>1 in 80</td>
<td>95%</td>
</tr>
<tr>
<td>Fanconi anaemia</td>
<td>1 in 90</td>
<td>99%</td>
</tr>
<tr>
<td>Niemann-Pick disease type A</td>
<td>1 in 90</td>
<td>92%</td>
</tr>
<tr>
<td>Bloom syndrome</td>
<td>1 in 100</td>
<td>99%</td>
</tr>
</tbody>
</table>

### Other Genetic Diseases for Which Screening is Possible

There are a number of other conditions that are considered common enough that population genetic screening is being considered. These include fragile X syndrome and spinal muscular atrophy.

### Reproductive Screening for Single Gene Disorders

Timing of Testing

In theory, carrier testing can be done at any time from preimplantation onwards. In practice, such screening is generally offered in high school, pre-pregnancy or in early pregnancy. As discussed above, the first two of these result in more reproductive options being available than the third (Table 1).

### High School Screening

High school screening for Tay Sachs disease and thalassaemia have been offered since the mid-1970s in Montreal, Canada (Mitchell et al., 1996). High school screening for Tay Sachs disease has more recently been introduced in Sydney (Burnett et al., 1995) and Melbourne (Gason et al., 2003). The advantage of this
approach is that a large percentage of the population can be offered education about screening and be offered screening with relative ease. In addition, students who are educated about screening have much better knowledge at the time of screening than adults screened in other settings (Barlow-Stewart et al., 2003; Gason et al., 2003; Gason et al., 2005; Mitchell et al., 1996). Concerns that individuals will forget their test result by the time reproduction occurs have not generally been borne out for carriers (Mitchell et al., 1996). Similarly, long term negative psychological sequelae are rare. Critics nevertheless have raised concerns about whether high school students are sufficiently mature to provide fully informed consent for such screening (Frumkin & Zlotogora, 2008) and that peer pressure may result in individuals having screening when they may otherwise not choose to do so (Ross, 2006).

Prepregnancy
Prepregnancy adulthood is considered an ideal time for testing (Frumkin & Zlotogora, 2008). At this time individuals are often already in a relationship with a person with whom they plan to have children. Therefore if one is found to be a carrier of a genetic condition, the other can be quickly tested to define their risk of having a child with the condition in question. If both are carriers, all reproductive options are open to them (Table 1). The practical barrier to screening at this time is that individuals/couples often do not consider screening until a pregnancy ensues. If screening is offered on a user-pays basis, such testing may not be a financial priority until a pregnancy occurs.

Pregnancy
Pregnancy is the time when screening is most commonly done. The reasons are that this may be that the first contact with a health professional does not occur until the woman is pregnant or that screening does not become a priority until this time. In addition couples may not believe they need to consider screening until pregnant. There are two major disadvantages to screening in pregnancy. The first is that the only option where a couple are both found to be carriers of a condition and wish to not have a child with that condition, is to have prenatal diagnosis and termination of an affected pregnancy. Secondly, the couple often needs to make major decisions in a short space of time during a period that is often already emotionally charged.

The Health Belief Model
The Health Belief Model (HBM) was designed to explain the relationships between health beliefs and health behavior (Sheeran & Abraham, 1996). The HBM has four dimensions:

- perceived susceptibility — subjective perception of risk of being a carrier/having a child with the condition in question
- perceived severity — medical and social consequences of the condition
- perceived benefits — effectiveness of various actions in reducing disease threat or reducing anxiety
- perceived barriers — potential negative aspects of the action.

A screening program should aim to have as many people as possible aware of the availability of screening so as to make an informed choice about having testing and remove as many barriers as possible. Given the issues with each of the three major times for offering screening outlined above, it is appropriate to give individuals the opportunity for screening at a number of life stages and in a number of settings.

Evolution of a Screening Program: A Case Study
The Melbourne Tay Sachs Disease Prevention Program began in 1998. It has three main arms: (a) a high school screening program where screening is free, (b) biannual community screening days where screening is offered at a discount rate and (c) promotion of the program through religious leaders and obstetricians. A number of research studies have been done to gauge the views of users and potential users with the results being used to improve the program (Gason et al., 2003; Gason et al., 2005). For example, in the high school program, where testing was initially through a blood sample, a significant minority of students wanted screening but did not have it due to needle phobia. Testing was therefore changed to cheek brush sampling. The uptake increased from 85% to 96% ($p < .0001$). Testing packs were developed whereby the individual can self-administer the cheek swab test and post it to the laboratory, meaning they do not need to attend a pathology collection facility. Major community awareness campaigns were conducted including newspaper articles and flier distribution. Outside the school program, awareness of the program has escalated and uptake is slowly increasing.

Genetic Screening: Harms and Benefits
It is very important that screening programs are culturally sensitive if they are to succeed. The introduction of screening for carrier status of sickle cell disease in the United States in the 1970s resulted in discrimination due to misunderstanding that being a carrier of this disorder caused illness (Beutler et al., 1971). The Dor Yeshorim program described above is an excellent example of where a community has designed a screening program that is culturally acceptable and widely utilized as a result (Ekstein & Katzenstein, 2001).

Carrier testing should have no implications for life and disability insurance (health insurance is community rated in Australia meaning all pay the same rates irrespective of their health and family history). All individuals have heterozygous mutations, the majority of which have no implications for their health and some of which reduce the risk of disease such as the carrier status for haemoglobinopathies which reduce...
the risk of falciparum malaria. Nevertheless there is some evidence that people are concerned about the insurance implications of being identified as a carrier by population screening (Quinlivan & Suriadi, 2006; Williams & Schutte, 1997).

A number of studies have examined the psychological impact of being identified as a carrier. In general these studies have found minimal impact from this in cystic fibrosis (Denayer et al., 1996; Gordon et al., 2003; Marteau et al., 1997) and Tay Sachs disease (Childs et al., 1976; Mitchell et al., 1996). The anxiety levels are generally higher when carriers are identified in pregnancy than when not pregnant. Unsurprisingly, anxiety is highest when both members of a couple are found to be carriers particularly if the female is pregnant. There is a negative correlation between knowledge level and anxiety of those screened. That is, those who are more knowledgable about screening and the condition being screened for are less anxious about the prospect of being found to be a carrier than those less knowledgable (Gason et al., 2005).

Concerns have been raised that by offering screening for carrier status with the option of carrier couples utilizing technology to prevent the birth of children with specific genetic disorders, that the value of the lives of those with genetic disorders is diminished (Knoppers et al., 2006). Indeed there is evidence that where children are born with Down syndrome in the current era of widespread screening, that some parents are questioned about why the condition wasn’t picked up in pregnancy and the birth of the child prevented (Marteau & Drake, 1995). Others believe that it is possible for society to both accept prevention of genetic conditions and respect and care for those with disabilities. It has also been argued that when some individuals choose to use preventive reproductive technologies, more resources are available for those in society with disabilities (Soini et al., 2006).

Is Informed Consent Always Possible?

As noted above, it is considered essential that individuals are given sufficient information upon which to base an informed decision on whether or not to have screening (Andermann et al., 2008). How informed is decision making in screening? In high school screening programs where students are exposed to detailed education by oral or CD ROM education, knowledge levels are very high and consent, at least in terms of education by oral or CD ROM education, knowledge levels are very high and consent, at least in terms of education, is generally well informed (Gason et al., 2005). Where education is by brochure with or without information from a health practitioner, knowledge levels are generally lower (Gordon et al., 2003; Mennie et al., 1997). It is common for individuals to prefer to obtain detailed knowledge only if they are found to be a carrier of the condition being tested for. In addition as more conditions become available for carrier testing the challenge of providing sufficient information becomes even more demanding (Chadwick et al., 1998). People at low risk, as participants in screening programs generally are, are less inclined to access information than people at higher risk such as those with disease symptoms or those with a family history. It is nevertheless critical that individuals have access to accurate unbiased information upon which to base screening decisions. A review of brochures related to CF carrier screening in the USA and UK found significant variability in the information presented including how the condition was portrayed (positive, neutral and negative statements) and whether or not termination of pregnancy is discussed (Loeben et al., 1998). However, people cannot be forced to access education and it must be accepted that many will be screened or refuse screening without being fully informed.

Health Economic Considerations

As noted above, screening criteria state that for a screening program to be introduced, it needs to be cost effective (Wilson & Junger, 1968). It is generally agreed that economic considerations should not be the ultimate arbiter of whether screening programs for a condition should be introduced, but nevertheless economic considerations are important in deciding whether or not to introduce a program. Governments are unlikely to fund programs that are not cost effective.

A review of the literature regarding economic evaluation of CF screening found much heterogeneity in study design, modeling and reporting (Radhakrishnan et al., 2008). Nevertheless, the majority of studies reported that the cost of a screening program is less than the potential healthcare costs averted through the birth of fewer individuals with CF. This was by no means universal, however. One study compared CF screening to other established screening programs, including newborn screening for PKU and mammography, and concluded that CF screening represents good value for money by comparison (Rowley et al., 1998).

There are fewer economic data for TSD screening (Nelson et al., 1978; Warren et al., 2005). The cost of screening for TSD is similar to CF screening but the lifetime medical costs of a child with TSD is considerably less than for an individual with CF (Warren et al., 2005). Nevertheless an argument has been mounted that the emotional (to the family) and physical (to the affected child) costs are greater for TSD than CF and this makes the value of preventing the birth of child with TSD much higher than preventing the birth of a child with CF (Warren et al., 2005).

Studies have consistently shown screening for haemoglobinopathy carrier status to be cost effective (Cronin et al., 2000; Ostrowsky et al., 1985).

There are limited economic data for single gene reproductive screening in Australia and such data are very important to inform government decisions regarding funding screening programs. Calls have been made to collect such data and indeed, a health economic evaluation of CF screening in Australia is currently underway (Radhakrishnan et al., 2008).
The Future

Genetic screening for reproductive risk is largely in its infancy in Australia. The only single gene disorders for which screening is government funded are the haemoglobinopathies. Other programs have been set up by individuals interested in providing couples with more options. Peak bodies including the Royal Australian and New Zealand College of Obstetrics and Gynaecology and the Human Genetics Society of Australasia do not have policies regarding when and for which single gene disorders screening should be offered. These bodies need to take the lead in this area as governments are unlikely to fund screening unless the leaders in these fields make recommendations that screening should be offered and in the interests of equity that it is freely available to all.

The laboratory costs of screening have decreased rapidly and are likely to continue to do so as technology improves. In addition, it is likely that there will be increased consumer demand for testing. In Israel for example, where screening for Tay Sachs disease has been widely taken up since the 1970s, screening for up to 14 conditions is commonly requested (Professor E Levy-Lahad, pers. comm.). Apart from the test for Tay Sachs disease which is government funded, individuals pay for testing. The more conditions that are screened for the more carriers that will be identified. Funding for genetic counseling of carriers and prenatal testing for carrier couples therefore needs to be included in costing whether programs are funded by payment by those tested or by government.

It is possible that in the not too distant future, screening will be cheap enough to test for carrier status for over 100 single gene autosomal and X-linked disorders. Pre-test knowledge of all conditions will be essentially impossible making post-test counseling of carriers of even greater importance (Chadwick et al., 1998).

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