Sonic Genetics
Douglass Hanly Moir Pathology

Reproductive carrier screening

Information for Doctors

An important part of pre-pregnancy planning

Screening for genetic disorders during pregnancy has been routine practice in Australia for many years. These screening tests include maternal serum biochemistry, fetal ultrasound and non-invasive prenatal tests, such as Harmony®. These tests are performed during pregnancy to look for new, that is, non-familial disorders in the developing fetus. Screening for genetic disorders should also address the possibility of familial disorders, and this is an important part of pre-pregnancy planning.[1]

The pre-pregnancy consultation can identify genetic disorders in the family by reviewing any history of multiple miscarriages and stillbirth; children with learning difficulties, developmental delay, or congenital abnormalities; and enquiring about consanguineous relationships in the family. Any couple suspected of being at increased risk of having a baby with a heritable genetic disorder should be referred for genetic counselling.

Whilst recognising the clinical and medico-legal significance of reviewing family histories, the reality is that most children with a familial genetic disorder do not have a family history of that disorder. The presence of a family history of a disorder is an important clue; the absence of such a history provides little information. A test to screen for genetic carriers can provide information about the risk of a familial disorder that is not evident from reviewing the family history.

Reproductive carrier screening

There are hundreds of inherited genetic disorders that cause serious illness in babies and children. The abnormal genes responsible for these disorders have often been inherited from couples who have no idea that they are at risk of having an affected child. These inherited disorders are individually rare, but together they are more common than the chromosomal disorders which have long been the focus of genetic screening in pregnancy.

Advances in genetic technologies have made it possible to test individuals or couples to determine if they carry an abnormal gene which can cause one or more of these disorders, that is, genetic carrier screening. The chance that a genetic carrier screen will identify that a person carries an abnormal gene will vary depending on the type of screen. If all genes were examined, each person tested would be identified as a carrier of at least one abnormal gene.

If the test shows that a couple are at high risk of having an affected child, they can accept that risk or consider reproductive options, such as the use of donor gametes or pre-implantation genetic testing. They could also consider prenatal diagnosis by chorionic villus sampling (CVS) or amniocentesis.

Autosomal recessive disorders

Men and women who are carriers of a mutated recessive gene located on an autosome, that is, chromosomes 1–22, are not affected by the autosomal recessive disorder caused by that gene. If both a mother and father carry a mutation in the same autosomal recessive gene, their child is at 25% risk of inheriting an abnormal gene from both parents and developing the disorder. This risk applies in every pregnancy with these parents.

X-linked disorders

If a woman is a carrier of a mutated gene on the X chromosome, she may have a family history of the disorder or she may be the first person in her family to have this mutation. She may also have subtle signs of the disorder; the presence of a normal gene on the other X chromosome modifies the impact of this mutation. If she has a son, there is a 50% chance that he will inherit the abnormal X chromosome (together with a Y chromosome from his father) and develop the disorder. If she has a daughter, there is a 50% chance that she will be a carrier. The overall risk of having an affected child is approximately 25%, and this risk applies in every pregnancy for this woman.

Types of reproductive carrier screening provided by Sonic Genetics

There are two options:

1) A three-gene panel looks for mutations responsible for three common genetic disorders: cystic fibrosis and spinal muscular atrophy (autosomal recessive), and Fragile X syndrome (X-linked). Approximately 6% of people in Australia will be identified as carriers for one or more of these disorders, and one in 160 couples will be found to be at risk of having an affected child. **Further information is available on our website, www.sonicgenetics.com.au/rcs/3p.**

2) The Beacon expanded carrier screen is a comprehensive screening test that detects mutations in 299 autosomal recessive genes and 28 X-linked genes which cause serious disorders affecting babies and children. Approximately 70% of people in Australia will be identified as carriers for one or more of these disorders, and one in 30 couples will be found to be at risk of having an affected child. **Further information is available on our website, www.sonicgenetics.com.au/rcs/beacon.**

Information on requesting the test, costs, testing limitations, detection rates, sample requirements and turnaround time for reports is available on the Sonic Genetics website, www.sonicgenetics.com.au.

Timing of carrier screening

The ideal time for testing is before conception. This gives the couple and their doctor time to consider the issues arising from the test and make informed choices about their reproductive plans.

Reproductive carrier screening can also be performed in early pregnancy. This is less suitable, as there is less time for issues to be considered and decisions made, and there are fewer options available to the couple.

Sequence of carrier screening

Testing can be performed on individuals or couples.

- **Individual testing:** If a patient is tested individually and found to be a carrier for an autosomal recessive disorder, it is then necessary to test the partner to determine the risk to their child. This slows the process of clarifying the risk for this couple. We recommend testing the woman first, as this includes testing for X-linked recessive disorders; the genes responsible for these disorders are not routinely tested in men, as their children are not expected to be affected.
- **Couple testing:** Both partners are tested at the same time to see if they carry mutations in the same gene. The woman is also tested for X-linked disorders. This is the quickest way of clarifying the couple's risk, but it is more expensive, as both partners are tested simultaneously. Please note that testing as a couple provides information about the risk of that specific couple having an affected child; if either of them re-partners, the risk assessment would need to be reviewed.

Genetic counselling

As with all pregnancy-associated tests, reproductive carrier screening can raise questions of ethics and autonomy that require time to resolve. A couple must feel free to accept or decline the offer of this test. Some people will not want to have this information – and some will insist on having it.

If both parents are found to be carriers of mutations in the same autosomal recessive gene, or if the woman is found to be carrying an X-linked disorder, it is important to discuss what it might mean for them individually and as a couple. Hearing about the carrier result will usually be unexpected. It may lead to a range of physical and emotional reactions. In the midst of this emotional confusion, there may be decisions that need to be made. Your patients require information and support when making these decisions. The only right decision is the one that is best for your patient.

Genetic counsellors are experienced in providing support and information that help patients make an informed decision. Genetic counselling is available through a number of public and private providers nationally; for a list of these services, please visit www.sonicgenetics.com.au/counsellingservices. Sonic Genetics also provides access to free counselling^ for couples who are shown to be at high risk of having an affected child; instructions will accompany any eligible results.

^Terms and conditions apply. Please refer to www.sonicgenetics.com.au/rcs/gc

Prices and rebates

Rebated testing for cystic fibrosis or Fragile X syndrome carrier status is available under certain circumstances. Please refer to the Medicare Benefits Schedule or contact us via email to info@sonicgenetics.com.au for details. Rebated testing for cystic fibrosis carrier status can only be requested by a specialist.

Please refer to the Sonic Genetics website for current pricing. A discount is available for couples that undertake the Beacon expanded carrier screen. These tests can be ordered by any medical practitioner using the dedicated request forms available on our website, www.sonicgenetics.com.au/doctors/forms.

Reference

1. Royal Australian College of General Practitioners, Genomics in General Practice. April 2018. Available online www.racgp.org.au/your-practice/guidelines/genomics [Accessed July 2018]

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