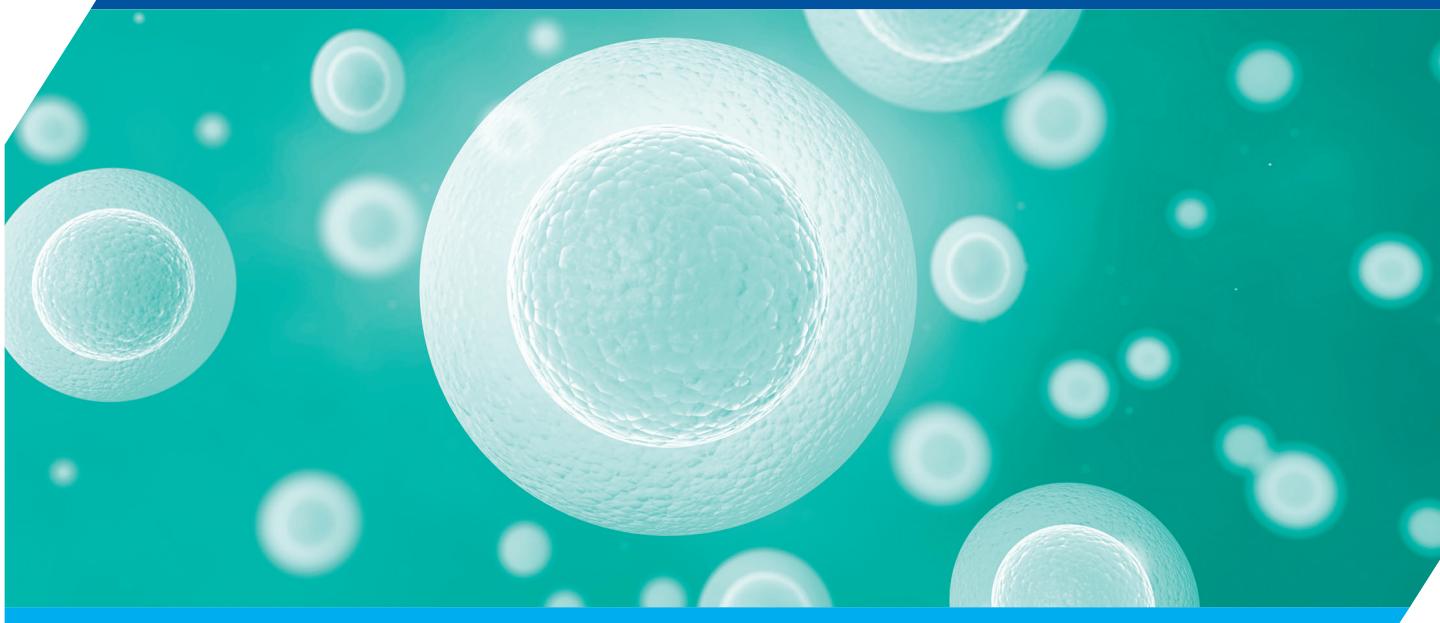




Pre-Conception Health Special Interest Group



Genetics and genomics

Applications of genetics and genomics are flooding into clinical medicine and personal genotyping will influence many medical and health decisions in the future. This is particularly important in peri-conception care where couples have the opportunity to evaluate, prevent or get early diagnoses of genetic diseases. New technologies are expanding at an ever increasing pace and new developments in gene array, proteomics and detection of fetal DNA will become commonplace in peri-conception and early pregnancy. All clinicians and health services seeing couples planning a pregnancy should be aware of their responsibility in eliciting an appropriate history, obtaining specialist advice and diagnoses, and counselling couples or individuals on the options available to them before commencing fertility treatment. Some recommendations will be applicable to everyone while others apply to those with specific risk factors. The diversity and range of diseases mean that referral to specialised genetic services must be available to the clinical service treating the couple or individual.



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Evidence review

Table 1. Examples of advice for specific ethnic groups

Ethnicity of at least one of the couple	Disorders with recommended testing or counselling	Type of test
Caucasian	Cystic fibrosis, spinal muscular atrophy and Fragile X	DNA of the relevant gene
Askenazi-Jewish	Cystic fibrosis, Tay-Sachs disease, Gaucher's disease, Niemann-Pick disease, Fanconi anaemia etc	Variety of appropriate genetic tests
African	Sickle-cell disease trait, thalassaemia	Complete blood picture, haemoglobin electrophoresis
Mediterranean	Thalassaemia	Complete blood picture, haemoglobin electrophoresis
Asian	Thalassaemia	Complete blood picture, haemoglobin electrophoresis

Table 2. Personal or family history that should prompt further counselling

Chromosomal disorders such as trisomy; clotting disorders; developmental delay/mental retardation (eg Fragile X)

Early infant death; heart defects; known genetic disorders (eg phenylketonuria, Marfan's, sickle cell disease, thalassaemia, thrombophilia)

Neural tube defects; familial cancer syndromes; family history of abnormalities; neural tube defects

Orofacial clefts; recurrent miscarriages; SIDS

Advice to people with no relevant history

A number of professional organisations now recommend people planning a pregnancy should be aware of pre-conception DNA testing. Couples planning a pregnancy should be aware of the option of having a preconception test for common gene disorders.

This is offered by several laboratories who will test for a limited set of more common gene disorders or may offer a wide range of rare genetic tests.

One of both members of a couple could be tested with further testing dependent on the results in one individual.

Adequate genetic counselling should be available before and after the test to enable informed decision making.

At present, individuals will cover the cost of testing which can range from \$300 – \$700 for general testing.

If a significant gene variation is detected, people may choose to:

- i. Not become pregnant
- ii. Use donor sperm or eggs
- iii. Have preimplantation genetic testing (PGT-M) of embryos through an IVF procedure
- iv. Have chorionic villus sampling or amniocentesis
- v. Have fetal DNA tested in the last weeks of the first trimester.

Ethnicity-related genetic advice

It is important to ascertain couples' or individuals' ethnic origins as some genetic conditions are more common in certain ethnic groups. Evaluation of ethnicity and family background may highlight increased propensity to carrier status that could lead to homozygous disease if pregnancy is achieved with a heterozygote partner. Screening or testing should be based on the couple's or individual's informed decisions. Table 1 highlights some of the conditions that should be considered.

Advice to people with specific family history

If a specific condition is identified in a person's history, specialist genetic advice should be offered with appropriate testing if available (Table 2). Decisions can be made depending on the findings.

Advice to people with genetic risk factors based on reproductive history

History of recurrent pregnancy loss or failed implantation after IVF may indicate a need for chromosomal testing for a variety of conditions including hereditary thrombophilias. Preimplantation genetic screening or anticoagulation may be indicated.

Most menstrual disorders are not associated with genetic abnormalities although von Willebrand's disease is more common in teenage years. Deep vein thrombosis or pulmonary embolus while on the oral contraceptive pill may indicate the need to investigate for Factor V disorders. A raised FSH or lowered AMH for age and early menopause may indicate the need for chromosomal assessment or examination of the pre-mutations in the fragile X gene.



Genetics and genomics

Advice to people with identified conditions

To individuals with known genetic conditions obstetric and perinatal advice can be offered regarding their pregnancy and the early life of their baby. This may include referral to an obstetric physician or paediatrician. Examples include risks of premature delivery in sickle cell anaemia, aortic aneurysm in Marfan's syndrome, increased requirement for folate in sickle cell disease, low phenylalanine in phenylketonuria.

Summary

Medical practitioners and other clinicians need to be aware of their responsibility in obtaining an adequate three generation family history, performing appropriate testing, seeking specialist advice and planning for pregnancy and paediatric life in light of genetic test results. There are many internet based resources and excellent consumer information sites about specific diseases. Relationships with hospital-based genetic departments are essential for adequate counselling.

Recommendations

General advice

All individuals should have a full three generation medical history comprising ethnicity, medical diseases and reproductive history across both sides of the family. This will include grandparents, parents, siblings and children of the couple or individual and should take into account half siblings and step-parents. Adopted children may not know their biological genealogy and those from donor conception may have incomplete information on their medical history.

Learning about conditions in their family allows for appropriate counselling, to help couples decide whether to:

- attempt to conceive spontaneously or with ART with their own gametes
- use pre-implantation genetic diagnosis or screening
- use donor gametes and/or surrogacy or seek other alternatives such as adoption to avoid genetic risk.

Technologies such as early genetic diagnosis allow decisions about termination to occur in the first trimester.

For more information about pre-conception health visit



www.yourfertility.org.au

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References

1. Solomon BD, Jack BW, Feero G. The clinical content of preconception care: genetic and genomics. American Journal of Obstetrics and Gynaecology 2008; 199: S340-4.