Genetic carrier screening

Objectives: To provide health professionals with advice on the counselling of women and couples prior to and in the early stages of pregnancy in relation to genetic carrier screening.

Table of contents

1. Plain language summary

There are many hundreds of inherited genetic conditio

diagnosis. The most common conditions for which carrier screening is available are thalassaemia, cystic

status for X-linked conditions is relevant) and the second member of the couple is only screened if the first member is a carrier of one or more autosomal recessive conditions. In couple screening both members of the couple are screened at the same time.	
Recommendation 5	**Grade**
Women wanting more information about carrier screening should be given the opportunity to have a more detailed discussion about carrier screening with an informed clinician. Informed consent for	

3. Introduction

Population carrier screening is defined as the detection of carrier status of autosomal and X-linked recessive diseases in couples or people who do not have an a priori increased chance of being a carrier based on their or their partners' personal or family history[1]. It does not refer to testing an individual with a strong family history of a known or possible genetic condition – these people should be offered direct referral to a specialist clinical genetics service.

Carrier screening for genetic conditions has been available since the 1970s with screening for Tay Sachs disease by testing of hexosamindase A levels in blood and for haemoglobinopathies by full blood examination and haemoglobin electrophoresis[2]. Since the late 1980s, screening by directly testing for genetic mutations has been possible.

Carrier screening for selected genetic conditions of highest population frequency

Testing has been widely offered for conditions common in particular ethnic groups such as cystic fibrosis in Caucasians, Tay Sachs disease and a number of other conditions in Ashkenazi Jewish individuals, and haemoglobinopathies in those of Mediterranean, African and Asian ethnicity. The carrier and affected frequencies for cystic fibrosis, spinal muscular atrophy and fragile X syndrome are shown in table 1. The results from an Australian study found that approximately 1 in 20 individuals accessing self-funded carrier screening were carriers of cystic fibrosis, spinal muscular atrophy and/or fragile X syndrome[3].

Table 1- frequency of carrier and affected individuals for cy

2. Conceiving naturally and having diagnostic testing during pregnancy to determine if the fetus is affected. This is usually performed with an invasive test (amniocentesis or chorionic villus sampling).
3. Conceiving the pregnancy by in vitro fertilisation (IVF) and testing embryos by preimplantation genetic diagnosis (PGD). Unaffected embryos would then be selected for achieving pregnancy.
4. Using donor sperm, egg or embryo from unaffected individuals.
5. Adoption.
6. Not having children.

4. Discussion and recommendations

4.1 Family history

All women/couples should be questioned about genetic conditions that are present in their family as well as the presence of consanguinity. This information may inform specific carrier screening and/or chromosomal testing for the couple. Referral to a clinical genetic health professional should be considered where a family history of a genetic condition is identified.

4.3 What conditions should be offered?

The conditions for which genetic screening is offered should be a cause of major diminution of quality of life and/or reduction in lifespan.

Information on carrier screening for the most common inherited genetic conditions in our population, that is **thalassaemia**, **cystic fibrosis, spinal muscular atrophy, and fragile X syndrome**, should be offered to all women planning pregnancy or in early pregnancy. Screening the general population for a limited range of high frequent single gene disorders is called **panethnic screening**.

For individuals of Eastern European (Ashkenazi) Jewish descent, additional **ethnic-specific screening** for Tay Sachs disease, Niemann Pick disease type A, Fanconi anaemia group C, familial dysautonomia, Bloom syndrome, Canavan disease and mucolipidosis type IV should be offered.

With the introduction of new genomic sequencing techniques, carrier screening for multiple autosomal and X-linked recessive conditions – "**expanded carrier screening**" - is now available for couples who have no family history of a genetic disorder.[8] Clinicians should be aware that expanded carrier panels may vary substantially in their content, mutation coverage, and reporting strategies, depending on the provider[9]. This is a rapidly evolving field and the Federal Government has invested in a large trial of expanded carrier screening which is expected to inform future service delivery and funding[10]

All individuals/couples having screening should provide written informed consent that should include:

(i) Acknowledgement that screening will not identify carrier status for all mutations in the tested genes and therefore that there is a residual chance of the couple ha

4.7.2 If a couple are found to have an increased chance **during pregnancy**, genetic counselling and prenatal diagnosis should be offered. Diagnostic testing (usually involving amniocentesis or chorionic villus sampling) may allow couples to prepare for the birth of a child with a genetic condition, to consider the option of terminating an affected pregnancy, or, in some rare cases, to allow *in utero* treatment.

representatives, health advocacy groups and other stakeholders to ensure that community values and distributive justice are maintained within our health system.

6. Other suggested reading

ACOG Committee Opinion No. 690, March 2017. Carrier screening in the Age of Genomic Medicine. https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Genetics/Carrier-Screening-in-the-Age-of-Genomic-Medicine

ACOG Committee Opinion No.691 March 2017 Carrier screening for Genetic Conditions. https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Genetics/Carrier-Screening-for-Genetic-Conditions

ACMG position statement on prenatal/preconception expanded carrier screening. Genetics in Medicine volume 15, pages 482–483 (2013). https://www.nature.com/articles/gim201347

7. Links to other College statements

Prenatal screening and diagnostic testing for fetal chromosomal and genetic conditions (C-Obs 59)

8. Patient information

A range of RANZCOG Patient Information Pamphlets can be ordered via:

https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets

9. Appendices

Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair and Board Member
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Scott White	Deputy Chair, Obstetrics and Subspecialties Representative
Associate Professor Ian Pettigrew	Member and EAC Representative

Genomics Advisory Working Group

Appendix B Overview of the development and review process for this statement

i. Steps in developing and updating this statement

This statement was originally developed in March 2018. The Genomics Advisory Working Group & Women's Health Committee carried out the following steps in reviewing this statement:

Declarations of interest were sought from all members prior to reviewing this statement.

Structured clinical questions were developed and agreed upon.

An updated literature search to answer the clinical questions was undertaken.

At the March 2018 face-to-face committee meeting, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

ii. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women's Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women's Health Committee members were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts
process 9f updating this statement.

iii. Grading 9f recommendations

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines.[14]
was sufficient consensus within the Women's Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based
committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category		Description
Evidence-based	A	Body of evidence can be trusted to guide practice
	B	Body of evidence can be trusted to guide practice in most situations
	C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D	The body of evidence is weak and the recommendation must be applied with caution applica

Appendix C Full Disclaimer

This information is intended to provide general advice to practitioners, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its prmati84ion, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.

Whilst the College endeavours to ensure that information is accui84e and cuirent at the time of prmati84ion, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available.