Sonic Genetics
Melbourne Pathology

Preconception carrier screening

Information for Doctors

Preconception carrier screening can identify individuals or couples at high risk of having a child with a serious heritable disorder. This test is becoming an essential part of prenatal care planning. It allows patients the opportunity to explore their reproductive options, and helps ensure they can make properly informed decisions.

The importance of preconception carrier screening

Cystic fibrosis (CF), spinal muscular atrophy (SMA) and Fragile X syndrome (FXS), three of the most common familial disorders in Australia, affect 1 in 1,500 babies; this is the equivalent to the combined risk of trisomy 18, trisomy 13 and Turner syndrome. Many people have no family history and are unaware they are carriers.

Current guidelines* recommend that screening for common genetic disorders, including CF, SMA and FXS, may be offered to all women. It is also recommended that individuals with an increased likelihood based on ethnicity be offered screening for haemoglobinopathies.

* Prenatal screening and diagnosis of chromosomal and genetic conditions in the fetus in pregnancy (C-Obs59), RANZCOG College Statements and Guidelines

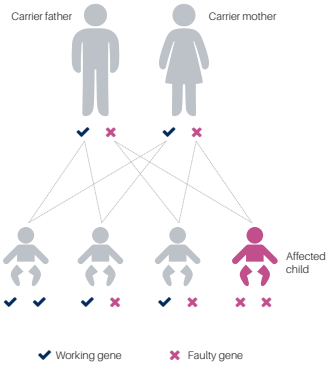
Condition	People with the condition	Carriers of the condition
CF	1 in 3,000 births	1 in 25
SMA	1 in 6,000–10,000 births	1 in 35
FXS	1 in 7,000–11,000 people	1 in 250
Data from:	www.cysticfibrosis.org.au www.fragilex.org.au www.smaaustralia.org.au	

Why you should choose Sonic Genetics

We are Australia's largest private genetics referral laboratory. Our genetic pathologists and medical scientists work in NATA-accredited laboratories throughout Australia to provide quality testing and clinical support.

We are part of Sonic Healthcare, an acknowledged world leader in the provision of diagnostic services, and Australia's largest pathology provider.

We are supported by Sonic's extensive network of state and regional laboratories and benefit from the interdisciplinary collaboration between a large cohort of pathologists and scientists working across all specialities. Many of our pathologists are recognised nationally and internationally; they have established academic reputations and are actively involved in professional and regulatory oversight in Australia and overseas.

Preconception screening identifies carriers by testing for mutations that cause most cases of CF, SMA and FXS		
The disorder	**The test**	**The risk**
Cystic fibrosis (CF) is the most common inherited disorder in Caucasians. It affects respiratory and gastrointestinal function, resulting in progressive lung disease, recurrent respiratory tract infection, pancreatic insufficiency and male infertility.	50 common mutations in the CFTR gene, responsible for >85% of cases of CF in the Australian population.	A couple can only have a child with CF or SMA if they are both carriers. When both partners are carriers, they have a 25% risk of having an affected child. 
Spinal muscular atrophy (SMA) is the most common genetic cause of mortality in children under two. It is characterised by progressive symmetric muscle weakness and atrophy that can be complicated by respiratory, orthopaedic and nutritional comorbidities.	Deletions of the SMN1 gene, responsible for 96% of cases of SMA.	
Fragile X syndrome (FXS) is the most common form of inherited intellectual disability, developmental delay and behavioural abnormalities, including autism.	Expansions of the CGG triplet repeat region of the FMR1 gene, responsible for 99% of cases of FXS.	Female carriers are at 50% risk of passing the mutation to their children. The risk of having a child with FXS depends on the size of the expansion. Male and female carriers of premutations are at increased risk of tremor-ataxia syndrome and premature ovarian insufficiency (women).

Requesting preconception carrier screening

After discussion with your patient, request preconception carrier screening using our dedicated request form.

Family history can modify carrier risk assessment and interpretation of genetic test results. Please ensure that any details regarding family history, including relationship to the patient and previous genetic test results, are included on the request form. This information may also indicate whether the patient is eligible for a Medicare rebate for part of the test cost.

The best time to establish carrier status is before conception; however screening can still be performed in early pregnancy. Please indicate the patient's pregnancy status on the request form.

Testing procedure

Testing can be performed on individuals or couples. There are two options for carrier testing of couples:

- A sample is collected and tested from the female partner first. If she is found to be a carrier of CF or SMA, a sample can be collected from the male partner for carrier testing for the same disorder. Testing of the male is not required for FXS as this is an X-linked disorder.
- Samples are collected from both partners and tested. The advantage of this is that in the event of a positive screen, anxiety while waiting for the second can be avoided.

Results

Results are typically available within two weeks of sample collection. They indicate whether a mutation was found, and the implication for the patient.

Result	Interpretation
Carrier for CF or SMA	Individual is at increased risk of having affected children. Testing of reproductive partner is recommended. Genetic counselling is recommended if both partners are carriers.
Carrier for FXS (females)	Individual is at increased risk of having affected children. This result also has potential medical implications for the individual being tested. Genetic counselling is recommended.
Carrier for FXS (males)	Carrier testing of males should be considered carefully. Male mutation carriers are not considered to be at risk of having children with FXS; however, their daughters will inherit a premutation and be at risk of having affected children themselves. This result also has potential medical implications for the individual being tested. Genetic counselling is recommended.
Carrier status for CF, SMA and FXS unlikely	A mutation was not detected but the possibility that the patient is a carrier cannot be excluded.

Our clinical and scientific experts have selected the mutations most relevant to these conditions and use the most appropriate technology to detect them. However, the test does not detect every mutation that can cause CF, SMA and FXS, or mutations in other genes responsible for other disorders. If no mutation is found, the risk of the patient being a carrier is greatly reduced, however the possibility cannot be eliminated. The patient's ethnicity may also affect carrier risk. For more details, please phone Sonic Genetics on 1800 010 447 or email info@sonicgenetics.com.au.

Your patients may require genetic counselling and/or further discussion of their reproductive options. A list of private and public providers of clinical genetics and genetic counselling services is available on request or visit www.sonicgenetics.com.au/doctors/resources.

Sample requirements

Samples may be collected by the requesting clinician or at any Melbourne Pathology collection centre. We also recommend that the patient or another adult check the labelling of request forms and sample tubes.

4 mL blood in EDTA is required.

Cost*

CF, SMA and FXS panel	$400
CF and SMA or FXS	$400
CF only	$310
SMA only	$220
FXS only	$101.30

Useful references

GeneReviews entries for cystic fibrosis and congenital absence of the vas deferens, spinal muscular atrophy and FMR1-related disorders, at: www.ncbi.nlm.nih.gov/books/NBK1116.

*Prices correct at time of printing. Please refer to www.sonicgenetics.com.au/pricing for current price.

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How to Access

Sonic Genetics is a member of the Sonic Healthcare group of companies.

Please contact your local Sonic Healthcare laboratory listed below:

ACT	Capital Pathology
NSW	Douglass Hanly Moir Pathology Barratt & Smith Pathology Southern.IML Pathology
QLD	Sullivan Nicolaides Pathology
SA	Clinpath Laboratories
TAS	Hobart Pathology Launceston Pathology North West Pathology
VIC	Melbourne Pathology
WA	Clinipath Pathology

For further information, including scientific and peer-reviewed publications, please refer to our website, www.sonicgenetics.com.au or call us on 1800 010 447

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