

## What is Cystic Fibrosis (CF)?

CF is a serious life-shortening genetic disease. Generally, people with CF produce thick, sticky mucous in their lungs and digestive tract, causing frequent lung infections and poor absorption of nutrients from food. Other parts of the body can also be affected. Treatment involves daily therapies including physiotherapy and medications (including antibiotics and pills to assist with the digestion of food) and frequent stays in hospital are often required. There is no cure for CF. For more information on CF please visit [www.cysticfibrosis.org.au](http://www.cysticfibrosis.org.au)

## What is Spinal Muscular Atrophy (SMA)?

SMA is a disease that results in a weakening of the muscles in the body due to the breakdown and loss of specific nerve cells in the spinal cord. The age at which symptoms begin can vary from birth to early adulthood. In its most severe form a baby is born with weak muscles and as the disease progresses will lose the ability to breathe, resulting in death before two years of age. Pneumonia, curvature of the spine, joint contractures, poor weight gain and sleep difficulties are common complications. There is no cure for SMA. For more information on SMA please visit [www.smaaustralia.org.au](http://www.smaaustralia.org.au)

## What is Fragile X Syndrome (FXS)?

Fragile X syndrome (FXS) is the most common inherited form of intellectual disability. You do not need to have a family history of FXS to be at risk of having children with the condition. Approximately 1 in 250 females in the general population carry a genetic change that puts them at risk of having a child affected with FXS. The disease is seen across all ethnic groups and affects an estimated 1 in 3,600 males and 1 in 5,000 females. Individuals with FXS have a normal life expectancy and may be variably affected, with females typically less severely affected than males. Symptoms can include:

- Intellectual disability / developmental delay. The average intellect of an individual with FXS is similar to that of a child affected by Down syndrome.
- Behavioural / emotional problems. This can include features of autism and/or attention deficit hyperactivity disorder and anxiety.
- Epilepsy (20% of males), leaky heart valve, eye squint and recurrent ear infections.

*Our genetic carrier screen gives patients information regarding their chances of having a child with a genetic condition like cystic fibrosis (CF), fragile X syndrome (FXS) or spinal muscular atrophy (SMA).*

## Who should have the carrier screening for CF, SMA or FXS?

Carrier screening is recommended for couples who wish to clarify what their risk is of having a child with one of these conditions. Note – FXS carrier screening is recommended for females as it is inherited in a different way to CF and SMA and only requires that the female have the gene change for there to be a risk of having a child affected by FXS.

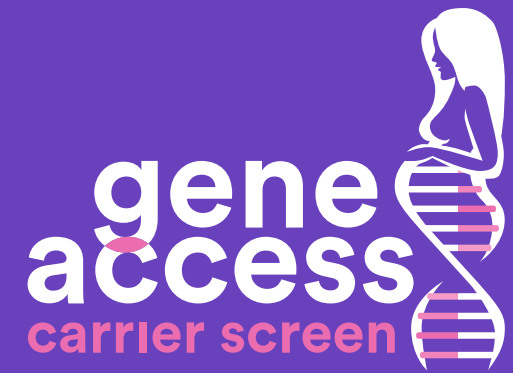
## What if I have a family history of CF, SMA or FXS?

If you or your partner has a family history of one of these conditions, your chances of being a carrier may be higher. In such cases, it is recommended that you contact your local clinical genetics service for expert advice as testing may be free of charge in this setting.

## What if I am found to be at risk of having a child affected with CF, SMA or FXS?

If you are identified as a carrier for one of these conditions, you will be contacted by your doctor or a genetic counsellor to discuss your results in detail. If you are a carrier for CF or SMA, testing of your partner will be offered free of charge to further clarify your risk of having an affected child.

For those identified as at risk during an existing pregnancy, testing is available to determine whether or not the developing baby may be affected. If the developing baby is found to be affected, a genetic counsellor will discuss your options with you, which may include termination of pregnancy. For individuals identified as at risk before they are pregnant, additional options are available to avoid having a child affected with these conditions, e.g. pre-implantation genetic diagnosis through IVF, the use of donor eggs (or donor sperm for CF and SMA), donor embryos or adoption.



*A cystic fibrosis, fragile X syndrome and spinal muscular atrophy screening test.*

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## What causes CF and SMA?

CF and SMA are both genetic disorders. Everyone has two copies of the different genes involved in CF and SMA as we inherit one copy of each of the genes from each of our parents. Sometimes a change is present in a gene (called a mutation), which prevents the gene from working normally. Having a change in one copy of the gene has no effect on your health as you still have another working copy of the gene. Such people are referred to as 'carriers'. Approximately 1 in 25 Caucasians are carriers for CF while approximately 1 in 37 are carriers for SMA. As shown in Figure 1, when both parents are carriers for the same genetic disorder, every time they have a child there is a 1 in 4 (25%) chance that child will inherit two changed copies of the gene and be affected with that genetic disorder. Most parents of children with CF or SMA are unaware that they are carriers for one of these conditions before their child is diagnosed. Usually there is no known family history of the disease to warn couples of the risk. This test can identify couples who are at increased risk of having a child with either CF or SMA.

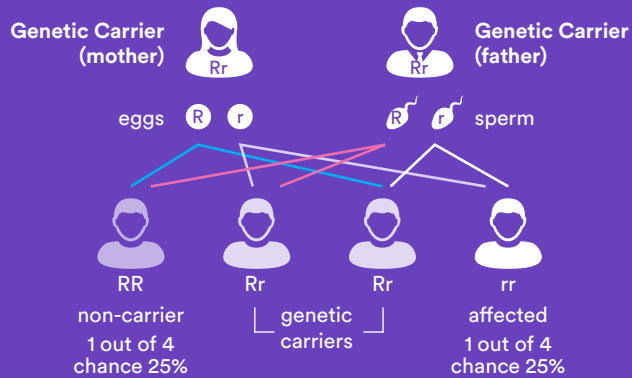


Figure 1. For CF or SMA, each parent passes on one copy of the gene to each of their children.

## What do the results of the CF and SMA test tell me?

There are two possible outcomes when being tested for CF or SMA. Your results may indicate you are either:

**A Carrier** – This means the test has identified that you carry a change in a copy of your CF or SMA gene. If this occurs, then testing of your partner is recommended to further clarify your risk of having a child affected with that condition.

**A Non-Carrier** – This means that you were not found to carry any of the common gene changes tested for and testing of your partner would not be indicated. Importantly, the test cannot detect all possible changes in the CF or SMA gene, and thus cannot completely exclude the possibility that you are a carrier of a less common mutation. By excluding you as a carrier of one of the common gene changes, your risk of being a carrier, or having a child with CF or SMA, is significantly reduced.

## What do the results of the FXS test tell me?

FXS carrier screening aims to identify women at risk of having children affected with FXS by analysing the number of repeats present in the FMR1 gene. Table 1 shows the four different types of test results from FXS carrier screening based on the number of repeats detected. Importantly, this test cannot detect other changes in the FMR1 gene that account for less than 1% of FXS.

Possible FXS test results	Number of repeats identified
Normal Range	5 to 44 repeats
Intermediate Range	45-54 repeats
Premutation Range	55-200 repeats
Full Mutation Range	>200 repeats

Table 1. Classification of FXS screening result based on the number of repeats detected.

**Results in the normal range:** Women with repeats within the normal range are not at increased risk of having a child affected with fragile X syndrome.

**Results in the intermediate range:** Women with repeats in the intermediate range are not at increased risk of having children affected with FXS. However, the number of repeats may increase when that copy of the FMR1 gene is passed on to their offspring. If the number of repeats increases from being in the intermediate range to being in the premutation range when passed from mother to offspring, then future generations may be at risk of having children affected with FXS. For this reason, genetic counselling is recommended for individuals with results in the intermediate range.

**Results in the premutation range:** Women with repeats in the premutation range, though not affected by FXS themselves, are at increased risk of having children affected with FXS. This is because the number of repeats can increase into the full mutation range when this copy of the gene is passed on to their offspring. Individuals identified as having a result in the premutation range should arrange referral to a clinical geneticist or genetic counsellor for expert advice.

Women found to have repeats in the premutation range are at increased risk of developing the following conditions themselves:

1. Premature menopause (before age 40): approximately 20% of women who carry a premutation will experience premature menopause.
2. Fragile X – Associated Tremor Ataxia Syndrome (FXTAS): approximately 16% of female premutation carriers over age 50 will develop FXTAS. This is a condition that results in worsening unsteadiness (ataxia) and tremors.

**Results in the full mutation range:** Women with repeats in the full mutation range are at increased risk of having children affected with FXS and should arrange referral to a clinical geneticist or genetic counsellor for expert advice. Unlike women with a result in the premutation range, women with a result in the full mutation range are not at increased risk of premature menopause or FXTAS.

## What causes FXS?

Greater than 99% of FXS is caused by a specific change (or mutation) which affects the number of times a particular part of the DNA code is repeated in the FMR1 gene. Once the number of repeats is beyond 200, a state known as a "full mutation", the FMR1 gene is typically switched off and so produces insufficient amounts of a protein that is required for normal brain development, resulting in that individual being affected with FXS.

## Is there a fee and is it covered by Medicare?

Unfortunately, Medicare does not cover the fee for carrier screening. When all three tests are requested at the same time the total fee is \$350.

(Prices may vary. Current as of 1st January, 2017.)

## What sample is required for testing?

A small 4ml blood sample (EDTA tube), regardless of whether one or all three tests are requested. Alternatively, these tests may be performed using a cheek swab.

## How long does testing take?

Results will be available, via your doctor, within 7-10 business days of your sample being received in the laboratory.

## Further questions?

Please contact Australian Clinical Labs on 1300 453 688

