Carriers of Fragile X

Fragile X-associated Disorders
Fragile X-associated Disorders are a group of associated genetic disorders (FXDs) that include:

- **Fragile X Syndrome (FXS)**
  The most common cause of inherited intellectual disability, behavioural disorders and speech and language delays that manifest in early childhood

- **Fragile X-associated tremor/ataxia syndrome (FXTAS)**
  Neurological disorder which may affect carriers at age 50 years or over, causing tremors, balance and memory problems, and cognitive decline, and

- **Fragile X-associated primary ovarian insufficiency (FXPOI)**
  Causes irregular menstrual cycles, infertility and premature menopause in female carriers.

What is a fragile X carrier?
A fragile X carrier is a person with a repeat number of between 55 and 200 and is classed as being in the ‘premutation’ range.

Figure 1: Normal, Intermediate, Premutation and Full Mutation

![Graph showing normal, intermediate, premutation, and full mutation ranges.]

Source: GOLD Service, Hunter Genetics, Newcastle.

When there are more than 200 repeats, the gene is switched off, leading to the symptoms seen in fragile X syndrome. The intermediate range or grey zone is 45-55 repeats.

The number of repeats may increase when the mother passes on her X chromosome to her child. Therefore, an apparently unaffected woman – with fewer than 200 repeats – may have an affected son or daughter with greater than 200 repeats.

Who can be a fragile X carrier?
A carrier can be any male or female who has an altered form of a gene that can lead to having a child or grandchild with a genetic disorder. We are all carriers of gene mutations, many of which are ‘silent’. This means we can pass the gene on but suffer no ill effects from it ourselves. It is only through genetic testing that we know which ones we carry.
How is fragile x passed on?
A man who is a carrier will pass on the premutation fragile X gene to all his daughters—making them carriers. But he will not pass it on to his sons in any form.

A woman who is a carrier has a 50 percent chance of passing the fragile X gene on to each of her sons and daughters, often with an increase in the number of repeats. Her children may be carriers or may be in the fully affected range.

Only female carriers can go on to have fully affected children of either sex. The fragile X premutation can be passed silently down through generations in a family before a child is born with full mutation fragile X syndrome.

Do fragile X carriers have symptoms?
Traditionally, a carrier of a genetic mutation is defined as a person who inherits an altered form of a gene but shows no effects of that mutation.

However, in fragile X this definition does not exactly fit, as carriers of a premutation are at risk of developing Fragile X-associated Disorders (FXDs) including Fragile X-associated primary ovarian insufficiency (FXPOI) and Fragile X-associated tremor/ataxia syndrome (FXTAS).

Approximately 25% of women with a fragile X premutation experience FXPOI—which causes early menopause and ovary impairment.

Men and women who are carriers can also develop FXTAS—which affects balance and memory and causes tremors and other neurological problems. Men are more likely than women to develop FXTAS and it usually develops after the age of 50 (see Fragile X Association Fact Sheet 6).

Though most women with a premutation show no significant mental health issues, some have reported increased general anxiety, shyness and social anxiety. In addition, there is evidence that women with the premutation are at increased risk for depression.

Reproductive options
When a woman or man finds out that they are a fragile X carrier they ask “what are my options for the future?” or “how can I increase my chance of having a child without fragile X syndrome?”

There are a number of ways for carriers to exercise choice in building a family, including conceiving naturally and testing the pregnancy at 11 weeks (prenatal diagnosis), testing a fertilized egg outside the woman’s body and implanting only unaffected embryos (Prenatal Genetic Diagnosis), using an egg donor, adoption and conceiving naturally and proceeding without any testing. (See Fragile X Association Fact Sheet 5, from the NSW GOLD Service, for more detail on Reproductive Options).

Where to get help
Further information is available from the Fragile X Association of Australia:
www.fragilex.org.au or call 1300 394 636 or email support@fragilex.org.au

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