Fragile X syndrome

Summary

- Fragile X syndrome is the most common inherited cause of intellectual disability.
- About 1 in 3,600 boys and 1 in 4,000–6,000 girls have Fragile X syndrome.
- The effects of Fragile X syndrome vary widely but most people experience lifelong difficulties.
- Both men and women can be carriers of the Fragile X gene. Female carriers of the Fragile X gene are at risk of having one or more children with Fragile X syndrome.

Fragile X syndrome is a genetic disorder caused by a change to one of the genes on the X chromosome. It is the most common inherited cause of intellectual disability. Fragile X syndrome is also linked to features of autism spectrum disorder.

Fragile X syndrome affects around 1 in 3,600 boys and between 1 in 4,000 – 6,000 girls. Fragile X syndrome causes a wide range of physical, developmental, behavioural and emotional difficulties although the level of severity between people with the condition varies enormously.

Effects of Fragile X syndrome

Fragile X syndrome can cause a range of physical, developmental, behavioural and emotional difficulties in people. Although there is no typical presentation, some boys with Fragile X syndrome have a long narrow face, prominent forehead and large testicles.

The most significant effects of Fragile X syndrome are:

- global developmental delay, including speech, language and communication difficulties
- intellectual disability and learning problems
- anxiety
- autism-like behaviours such as hand flapping, repeating words and sentences, and difficulty with social interactions
- attention deficit hyperactivity disorder (ADHD)
- poor eye contact
- difficulty processing sensory information.

The level of severity of these effects varies considerably and not every person with Fragile X syndrome will have every one of these characteristics.

Cause of Fragile X syndrome

Fragile X syndrome is caused by a change to a gene on the X-chromosome called the FMR1 gene. This gene produces a protein that helps the brain to function normally. If this gene is changed or altered in any way, it cannot produce its normal protein, which can result in Fragile X syndrome.

Fragile X syndrome is inherited in a way that is known as 'X-linked', as the changed gene is on the X chromosome. This means that men with Fragile X syndrome are often more severely affected than women. This is because men only have one X chromosome, whereas women have two X chromosomes, only one of which is changed.

Carriers of the Fragile X gene

Although Fragile X syndrome is not that common, affecting around 1 in 3,600 boys and between 1 in 4,000 – 6,000 girls, the number of men and women who are carriers of the Fragile X gene is significantly higher.
It is estimated that 1 in 150 women and 1 in 800 men are carriers of the gene. These people are known as ‘Fragile X pre-mutation carriers’. Pre-mutation carriers may not have any symptoms of Fragile X syndrome but they are at risk of passing on the changed \textit{FMR1} gene and having a child or grandchild with Fragile X syndrome.

People who are Fragile X pre-mutation carriers may also be at risk of developing health problems later in life. Around 20 per cent of female Fragile X pre-mutation carriers experience reduced fertility or early menopause. This is called Fragile X-associated Primary Ovarian Insufficiency, or FXPOI.

Older male and female Fragile X pre-mutation carriers are also at risk of developing a neurological condition called FXTAS, or Fragile X-associated Tremor Ataxia syndrome. Problems with balance and gait, tremors and gradual intellectual decline are common in FXTAS. These conditions are called Fragile X-associated Disorders.

\textbf{Testing and diagnosis of Fragile X syndrome}

Fragile X syndrome (and Fragile X-associated disorders) can only be diagnosed by DNA testing -- usually by a blood test but sometimes via cheek swab or mouthwash. If possible, testing should be done at a \textbf{recognised genetics service}.

If there is a diagnosis of Fragile X syndrome, it is important that immediate and extended family members are also tested to identify others who may have the changed \textit{FMR1} gene. This is called cascade testing.

DNA testing is recommended for:

- people with a family history of Fragile X syndrome or intellectual disability
- people with intellectual disability, developmental delay or learning disability together with features of Fragile X syndrome such as anxiety, ADHD or characteristics of autism spectrum disorder
- men or women over 50 with balance or gait problems, tremor or dementia
- any woman with problems with fertility or early menopause (under 40)
- women with family history of primary ovarian insufficiency (loss of function of the ovaries before age 40) for testing before or during pregnancy.

Unfortunately diagnosis of Fragile X syndrome is often delayed and it is not uncommon for families to have had a second child born with Fragile X syndrome before the first child has been diagnosed. A prompt diagnosis of Fragile X syndrome is important so that families can get access to appropriate early intervention services to help their child reach their full potential.

\textbf{Genetic counselling services and Fragile X syndrome}

The facts about Fragile X syndrome are complicated and the ramifications for families can be serious. It is recommended that parents and family members ask their doctor to refer them to a genetics service, both for testing and follow-up counselling.

Genetic counsellors are health professionals qualified in both counselling and genetics. As well as providing emotional support, they can help you to understand Fragile X syndrome and what causes it, how it is inherited, and what a diagnosis means for your child's health and development, and for your family. Genetic counsellors are trained to provide information and support that is sensitive to your family circumstances, culture and beliefs. A genetics counsellor can also provide information about the range of reproductive options that are now available.

\textbf{Clinics in Victoria} are located in metropolitan Melbourne and major regional centres.

\textbf{Where to get help}

- Your \textbf{GP (doctor)}
- Paediatrician
- \textbf{Fragile X Association of Australia} Tel: \textbf{1300 394 636} (freecall)
- \textbf{Victorian Clinical Genetics Services} Tel: (03) \textbf{8341 6212} or \textbf{1300 11 8247}
- \textbf{Fragile X Alliance Clinic} Tel: (03) \textbf{9528 1910}
- \textbf{Genetic Support Network Victoria} Tel: (03) \textbf{8341 6315}
- \textbf{Carers Victoria} Tel: \textbf{1800 242 636} (freecall)

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