Inheritance of Fragile X

The FMR1 gene is on the X chromosome. Males have one X and one Y chromosome; females have two X chromosomes. In females with a full mutation, their other, unaffected X often compensates for the FMR1 mutation which frequently results in milder symptoms of fragile X syndrome. In males the Y chromosome cannot compensate for the effects of the fragile X mutation.

- Both males and females can be FMR1 carriers and can pass the premutation on to their children
- Male premutation carriers will pass the premutation on to all their daughters and none of their sons.
- Only premutations carried by women expand to the full mutation that causes fragile X syndrome in their children. Female premutation carriers have a 50 percent chance in each pregnancy of passing the premutation to their children of either gender. The risk of a premutation expanding to a full mutation is dependent on its number of CGG repeats.

Testing for Fragile X

Any individual who has unexplained developmental disabilities, especially when they are associated with speech and language delay or an autism spectrum disorder, should be tested for fragile X. The fragile X test, also called the FMR1 DNA test, is not the same as a chromosome analysis. However a healthcare provider may order a number of tests in a child who exhibits unexplained delays in development. The fragile X test can be arranged by your GP/family doctor, any physician or genetic counsellor. Genetic counselling is recommended for any individual or relative of someone who has a positive test result, or a relative diagnosed with any of the Fragile X-associated disorders. Your GP/family doctor can refer you to a local genetic counsellor. For more information about testing and genetic counselling visit **www.fragilex.org.uk** click on information and then on genetic testing.

About the Fragile X Society

The Fragile X Society was founded in 1990 to provide support and information to fragile X families, to raise awareness of fragile X and to encourage research into all aspects of fragile X.

The Society offers support and information through its family support workers, website, regular newsletters and other publications. It also organises annual conferences and supports research through the participation of its family members in fragile X studies.

For more information on fragile X syndrome and other topics related to fragile X, email: info@fragilex.org.uk or telephone 01371 875100

Special thanks for assistance on this leaflet to:

The National Fragile X Foundation and the families affected by fragile X whose photos appear

Produced in cooperation with the European Fragile X Network, www.fragilex.eu

EUROPEAN FRAGILE X NETWORK

Additional copies of this leaflet available free of charge. Other leaflets in this series which explain FXTAS and FXPOI also available free of charge.

The Fragile X Society

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FXS

FRAGILE X SYNDROME

An Introduction for Families and Healthcare Providers

The Fragile X Society

A Fragile X Overview

Fragile X is associated with changes in the Fragile X gene. The gene (also known by its scientific name of "FMR1") can be normal, but it can also exhibit a "premutation" or "full mutation". When a premutation or full mutation is present, it can result in a Fragile X condition. These include:

- **Fragile X syndrome (FXS):**
  An inherited condition affecting intellectual, behavioural, language and social development. It occurs in both males and females who have a full mutation of the FMR1 gene.
- **Fragile X-associated tremor/ataxia syndrome (FXTAS):**
  An adult onset (over 50 years of age) neurological condition, more common and more severe among males, that causes tremor, memory difficulties and balance problems in those with a premutation of the FMR1 gene. (Both males and females who have a premutation are also referred to as "carriers".)
- **Fragile X-associated primary ovarian insufficiency (FXPOI):**
  A condition affecting ovarian function that can lead to infertility and early menopause. It occurs in some female carriers, who have a premutation of the FMR1 gene.

The FMR1 Gene

The FMR1 gene can undergo changes which cause these fragile X conditions. These changes affect a pattern of DNA called CGG repeats. Typically, the FMR1 gene has up to about 54 CGG repeats. A premutation in the FMR1 gene results in approximately 60–200 CGG repeats, and a full mutation in more than 200 CGG repeats.

www.fragilex.org.uk

Characteristics of Fragile X syndrome

The following physical, cognitive and behavioural characteristics of fragile X syndrome are usually more evident in males, but females can also demonstrate a range of features.

Physical features may include:

- Large/protruding ears, long face, soft skin
- Flexible joints – particularly fingers, wrists, elbows
- Low muscle tone
- Flat feet
- Large testicles (at puberty)
- Seizure disorder (epilepsy)

Behavioural, intellectual and social characteristics may include:

TODDLERS/CHILDREN

- Learning disabilities
- Speech and language delay and continuing difficulties
- Motor delay (late crawling, walking, toileting)
- Tactile defensiveness and sensory overload (high sensitivity to fabrics/clothing, loud noises, crowds, food textures and tastes, etc.)
- Overactivity, impulsivity, poor concentration/ short attention span
- Autistic-like features including dislike of eye contact, difficulty relating to other people, anxiety in social situations, insistence on familiar routines, hand flapping or hand biting
- Dislike of transitions

ADOLESCENTS/ADULTS

Extra difficulties arising in adolescents and adults may include:

- Managing independent living skills such as independent travel and using money
- Making and sustaining friendships

FEMALES

with mild or no learning disabilities may show:

- Concentration problems and particular difficulties with maths
- Social, emotional and communication difficulties related to extreme shyness and anxiety in social situations
- Oversensitivity to perceived rejection or criticism.

Their problems and difficulties need to be acknowledged so that appropriate support can be offered. Otherwise repeated failure to achieve may further increase their social anxiety and low self-esteem.

Interventions and Treatments

Research and clinical experience have shown that children with fragile X may benefit from the following treatments and interventions:

- Early intervention e.g. home based teaching schemes like portage and special needs nurseries
- Speech and language therapy, physiotherapy and occupational therapy, particularly sensory integration therapy
- Behavioural therapies
- Special education (though many children with fragile X are able to be "fully included" in an age-appropriate classroom)
- Medications for symptom-specific issues such as anxiety, ADHD, seizures, etc.

Adolescents and adults with fragile X also benefit from educational opportunities that help them acquire appropriate life skills. These programmes can begin in secondary school and extend into adulthood, and should include education and guidance in matters of employment, social activity, recreation, independent living, and sexuality.