NATIONAL FRAGILE X FOUNDATION

FRAGILE X SYNDROME (FXS)

An Overview for Families and Providers

ABOUT THE NFXF

The National Fragile X Foundation (NFXF) was founded in 1984 to support individuals with Fragile X syndrome (FXS), their families, and the professionals who work with them. Today, it is a comprehensive resource not only for FXS, but also for the conditions of Fragile X-associated tremor/ataxia syndrome (FXTAS), Fragile X-associated primary ovarian insufficiency (FXPOI), and other premutation carrier issues. The organization offers help for today and hope for tomorrow with personalized support, community, education, awareness, advocacy, and research. Get your free Fragile X 101 e-book, Welcome Packet, connect with your local chapter, learn about the upcoming conference, and more at fragilex.org/welcome.

If you have specific questions about what to expect, treatments, clinics, well, just about anything, please email treatment@fragilex.org or call (800) 688-8765.

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FRAGILE X SYNDROME: AN OVERVIEW FOR FAMILIES AND PROVIDERS

OVERVIEW

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

Fragile X syndrome (FXS)

An inherited condition affecting intellectual, behavioral, 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 in males. It causes tremors, memory 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 in some female carriers.

Other Premutation Carrier Conditions

Research is currently underway looking at various issues that may be seen in people with the premutation.

THE FMR1 GENE

The FMR1 gene can undergo changes which cause these Fragile X-associated conditions. These changes affect a pattern of DNA called CGG repeats. Typically, the FMR1 gene has up to 54 CGG repeats. A premutation in the FMR1 gene results in 55–200 CGG repeats, and a full mutation in more than 200 CGG repeats.

CHARACTERISTICS OF FRAGILE X SYNDROME

The following characteristics of Fragile X syndrome are usually more evident in males, but females can also demonstrate a range of features. No one individual will have all the features listed below.

Physical features may include:

- Large ears
- Long face
- Soft skin
- Flexible joints -particularly fingers, wrists, elbows
- Low muscle tone
- Flat feet
- High arched palate
- Large testicles (called "macroorchidism") in post-pubertal males

Some of the features are due to poor connective tissue, such as flexible joints, flat feet, and high arched palate.

Behavioral characteristics may include:

- Sensory processing challenges (sensitive fabric/ clothing, loud noises, crowds, food textures, etc.)
- Hand-flapping, hand-biting
- Poor eye contact
- ADHD (attention deficit/hyperactive disorder)
- Anxiety
- Autism spectrum disorders
- Increased risk for aggression
- Sleep disorders

Cognitive abilities may include:

- Cognitive abilities in FXS include a range from mild learning disabilities to more severe intellectual disabilities. The majority of males with Fragile X syndrome demonstrate moderate intellectual disability.
- Speech and language delay
- Motor delay (late crawling, walking, toileting)

Medical issues may include:

- Ear infections
- Strabismus (crossed eyes)
- Seizures

Disposition characteristics often include:

- Very social and friendly
- Excellent imitation skills
- Strong visual memory/long-term memory
- Especially nice, likes to help others
- Wonderful sense of humor

INTERVENTIONS AND TREATMENTS

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

- Early intervention such as infant development therapy and special needs preschool
- Speech and occupational therapy, particularly sensory integration
- Behavioral therapies
- Special education (though many children with FXS are able to be “fully included” in an age appropriate classroom)
- Medications for symptom-specific issues such as anxiety, ADHD, seizures, etc.
- Fragile X clinic referral for consultation regarding educational and therapeutic strategies
- To see the latest studies and trials, visit MyFXResearch.org

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

INHERITANCE OF FXS

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, normal X often compensates for the FMR1 mutation. That frequently results in milder symptoms of FXS. 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.
- Female premutation carriers have a 50 percent chance in each pregnancy to pass the premutation to their children of either gender. The risk of a premutation to expand to a full mutationis dependent on its number of CGG repeats.
- Only premutations carried by women expand to the full mutation that causes Fragile X syndrome.

TESTING FOR FRAGILE X

- Any individual who has unexplained developmental disabilities, speech delay, ADHD, autism, or learning disabilities should be tested for Fragile X.
- The Fragile X test, also called the FMR1 DNA test, is not the same as a chromosome analysis or microarray, which examine all 46 chromosomes. However, a provider may order a number of tests in a child who exhibits unexplained delays in development. The test can be ordered by any health care provider, including genetic counselors or physicians.
- Genetic counseling 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. A physician can refer you to a local genetic counselor or you can find one at www.nsgc.org. Also, the genetic specialist at the National Fragile X Foundation can assist you—call (800) 688-8765.
- For more information about testing, visit fragilex.org/testing.