

What is Fragile X?

Fragile X Syndrome (FXS) is the most common known cause of inherited mental impairment. People with FXS have a range of intellectual, behavioral and physical changes. Both males and females may be affected. Approximately 1 in 250 females and 1 in 800 males carry the gene that causes FXS, usually without knowing it. FXS affects people of all races and ethnic groups worldwide.

Learning about FXS is like learning a new language. Here are some definitions you may not know:

Syndrome: a grouping of unusual physical, behavioral and/or intellectual features which occur together in a single person.

Gene: the biochemical instruction within the body's cells that tell the cells how to work. The gene changed in people with FXS is called FMR-1.

FMRP: the protein made by the FMR-1 gene

Developmental Disabilities: changes in a person's abilities which affect his/her daily skill level. Most people with FXS qualify for special services due to a range of developmental disabilities.

What Causes Fragile X?

FXS occurs when a gene (FMR-1) becomes altered, or mutated. The mutation in the FMR-1 gene is an expansion (repeat) of the specific chemical components of DNA (CGG). Although everyone has a FMR-1 gene, with approximately 5 to 40 repeats, people who are carriers of fragile X have between 55 and 200 repeats: this is called a "premutation." Most carriers are unaffected intellectually because they have normal levels of the FMR-1 protein.

The number of CGG repeats is increased to over 200 in individuals with fragile X. This expanded number of repeats is called a "full mutation" and it causes the FMR-1 gene to "turn off" or not work properly. A FMR-1 gene that is turned off doesn't produce

enough, or any, of the protein it is designed to produce. It is not fully understood how the protein affects brain functioning. However, the protein is known to be critical to intellectual development and functioning.

Females with a full mutation usually have milder symptoms than boys with a full mutation. Females can inherit the fragile X gene from their mother or their father. Since females have two X-chromosomes, the unaffected X chromosome can usually compensate for the one with the fragile X mutation.

Diagnosis

It is believed that the majority of affected children and adults have never received a diagnosis. The following individuals should be considered for FMR-1 testing to rule out fragile X syndrome:

- Individuals with mental impairment or autism of unknown cause
- People with significant hyperactivity, learning disabilities and/or mild cognitive deficits
- People with any of the physical or behavioral features of fragile X syndrome, regardless of gender or family history
- Any person who has a family member with a diagnosis of fragile X syndrome or a family history of mental impairment

The testing for fragile X syndrome involves taking a small blood sample. This sample can be taken by a physician at a genetic testing center, or at a lab drawing station. A physician can help determine the most appropriate method for each situation. It is very important to request the FMR-1 gene test, which is a direct DNA test for fragile X syndrome, and to ask that both PCR and Southern Blot testing be performed. When these tests are performed together, the diagnosis can be better than 99 percent accurate.

When specifically requested, the direct DNA test also can detect changes in the FMR-1 gene in a developing fetus. Prenatal diagnosis for FXS can be made as early as 11 weeks in the pregnancy. All couples with a his-

tory of FXS or unexplained mental impairment in their family may want to seek genetic counseling prior to becoming pregnant in order to discuss the most current prenatal diagnostic procedures.

Treatment for Fragile X Syndrome

At this time there is no cure for FXS; however many treatments are available. Treatment is primarily provided through various forms of therapy including special education, speech and language therapy, occupational therapy, and physical therapy.

Many parents report that Sensory Integration therapy has helped improve motor planning, motor coordination, joint stability, and coordination of visual, auditory and tactile information into an appropriate motor response. The occupational therapist can also help teach parents calming techniques and manage their child's sensitivity to sensory input.

Medication is often helpful in managing hyperactivity and short attention spans. Other medications can be helpful for aggression, anxiety and depression. In order to create and provide an optimal educational, therapeutic or vocational program, it is important to assess an individual's overall development and to access the best informational resources available. For help accessing these resources, please contact the National Fragile X Foundation.

Genetic Counseling

Those diagnosed with FXS, those who learn someone in their family has FXS, or those with unexplained mental impairment within their family, should receive genetic counseling. A genetic counselor familiar with FXS can offer extensive information and support regarding testing, inheritance patterns and available family planning options. Genetic counselors also can help families cope with a positive diagnosis.

Characteristics of Fragile X Syndrome

The clinical characteristics of FXS can be divided into three major areas: cognitive, physical, and behavioral. Males are usually more severely affected than females. Approximately 1 in 3,600 males and 1 in 4,000 to 6,000 females have mental retardation due to FXS. Approximately 1 in 2,000 people have milder problems.

Cognitive: The spectrum of intellectual involvement ranges from subtle learning difficulties and a normal IQ to severe cognitive disabilities and autism. Common problems include delayed milestones (walking, talking, toileting), attention deficit, hyperactivity, and difficulty with math.

Physical: Adult males often have a long face, large and/or prominent ears, and enlarged testicles (macroorchidism). Problems with loose connective tissue (i.e. ligaments) are frequent, including double-jointed fingers, flat feet, and a heart murmur (mitral valve prolapse). Females and younger children also may have some of these features, or may look no different than the general population.

Behavioral: Behavior ranges from socially engaging and friendly to autistic-like and occasionally aggressive. People with FXS can become easily overwhelmed by sensory stimuli such as crowds, noises, or light touch.

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The National Fragile X Foundation

The National Fragile X Foundation unites the fragile X community to:

- Enrich lives through education and emotional support,
- Promote public and professional awareness, and
- Advance research toward improved treatments and a cure for fragile X syndrome.

The NFXF was founded in 1984 as a 501(c)(3) non-profit charitable organization charged with increasing awareness and education, supporting research, aiding families, and encouraging collaboration among professionals involved with fragile X syndrome.

We act as a vital resource for parents and professionals worldwide providing information on diagnosis, treatment, research, and education. We accomplish these goals through our 1200-plus page website at www.FragileX.org, our quarterly newsletter, **The Foundation Quarterly**, the sale of books and audiovisual materials covering a broad range of topics, and the sponsorship of regional and international conferences devoted to fragile X research, collaboration, and education.

The National Fragile X Foundation is supported entirely by private contributions from individuals like you. We do not receive any government funding. As we provide many services for free, we hope that you will consider making a contribution to cover the costs of providing you with this information. Your gift will insure that resources are available to others in need in the future.

If you wish to receive more comprehensive materials, and be updated on new information and research as it becomes available, consider becoming a member of the National Fragile X Foundation. Membership options range from \$25.00 to \$500.00 annually, and can be paid by phone, fax, mail, or email.

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National Fragile X Foundation

The National Fragile X Foundation

Serving the Fragile X Community since 1984



Understanding Fragile X Syndrome

An Overview

