

## Fragile X Syndrome (FXS, Martin-Bell Syndrome) — Symptoms and Treatment

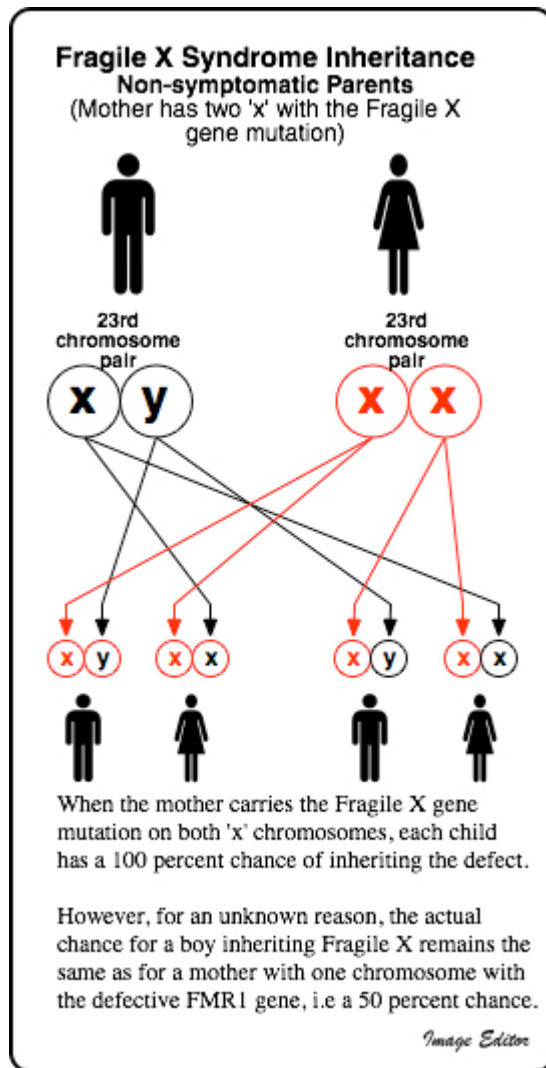
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**Fragile X Syndrome results from a mutation in the promoter region of FMR1 gene. A characteristic physical phenotype of FXR includes a long face, prominent forehead, high arched palate, large ears and flat feet. Learning disability, social anxiety, hypersensitivity to different stimuli, attention deficit hyperactivity disorder and lack of clarity in speech are some of the clinical features of FXR. Molecular genetic testing is used for diagnosis. Treatment is aimed at improving psychiatric issues and associated physical conditions.**



### Overview and Definition of Fragile X Syndrome

Fragile X syndrome, also known as Martin-Bell Syndrome, is a genetic condition which results due to *FMR1* gene mutation on the X chromosome. This mutation prevents the formation of **fragile X mental retardation 1 protein** which is essential for normal functioning of the nervous system. It, therefore, results in a range of developmental issues including cognitive impairment and learning disabilities.



Females are less severely affected by FXR as compared to males due to X inactivation.

*Image:* "Fragile X Syndrome Inheritance - Mother Two." By Image Editor. License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

*FMR1* gene mutation results in **trinucleotide (CGG) repeat disorder in the promoter region of the FMR1 gene**. CGG expansion causes abnormal methylation, silencing of the *FMR1* gene and loss of the FMRP protein which is essential for brain and testicular development.

Over 200 CGG repeats are seen in individuals who have FXS. A repeat expansion of more than 200 results in silencing of the *FMR1* gene and therefore, the lack of its product. More repeats in subsequent generations lead to worse symptoms.

Fragile X syndrome accounts for 1 in 4000-6000 births in females and 1 in 3600 to 4000 births in males. Females are less severely affected as compared to males due to X inactivation.

FXR is the most common genetic cause of intellectual disability.

Autism is frequently associated with FXS.

Life expectancy of individuals with Fragile X Syndrome is 12 years less than others.

# Sign and Symptoms of Fragile X Syndrome

Signs and symptoms vary among individuals. Females are likely to show mild symptoms as compared to males. Common features that are found in people with Fragile X syndrome are as follows:

## Physical phenotype



A boy with Fragile X Syndrome. Long face and prominent ears are visible.[Image](#): "Boy with Fragile X syndrome smiling." By Peter Saxon. License: [CC BY-SA 4.0](#)

These individuals have characteristic physical features including **long face**, prominent forehead, high arched palate, **large ears**, flat feet, low muscle tone, **macroorchidism after puberty**, hyperextensible thumbs and finger joints and soft skin. These physical signs may not be present at a young age; they do show as puberty hits and become more prominent with age.

## Speech

Affected individuals often begin to talk later than other children. They eventually start talking, but some of them remain nonverbal. These individuals are mostly unclear in their speech and have difficulties in understanding others' social cues.

## Vision

Patients with FXS are common to have refractive errors. **Strabismus** is a frequent ophthalmologic problem, and if not treated early, it can lead to amblyopia.

## Neurological

According to literature reports, 10 to 40 percent of the affected individuals have seizures. Others are also at a higher risk.

## Intellectual development

Individuals with FXS are likely to experience the following difficulties:

- Learning disabilities (females tend to be less affected)
- Short term memory
- Visual memory
- Visual Spatial Perception

## Social interaction

- Social anxiety
- Shyness (75 %) may lead to mild to severe social withdrawal
- Panic attacks (50 %)
- Gaze aversion and poor eye contact lead to challenges with face encoding
- Forming peer relationships is challenging for these individuals.

## Hypersensitivity and repetitive behavior

Individuals with FXS, especially children, have hyperactivity, hypersensitivity to different stimuli and short attention spans. Children are more likely to experience tantrums in large crowds due to loud sounds. They tend to show repetitive behaviors such as talking about the same subject repeatedly. Self-talking is common in these children. Children with FXS usually find the texture of things irritating.

## Psychiatric

Attention deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder in Fragile X syndrome. Inattentive symptoms continue to affect the individuals throughout their life. Disruptive behavior and hyperactivity, however, declines with age.

Behaviors like nail biting and hand flapping are common. Obsessive-compulsive disorder (OCD) is found in the minority. However, individuals feature obsessive-type symptoms. Fluctuating mood, self-harm, aggression and irritability are all seen as a reaction to stressors. However, these are usually transient.

## Diagnosis of Fragile X Syndrome

Methods to diagnose Fragile X Syndrome are as follows

### 1. Count CGG repeats on X chromosome with the help of

- Polymerase chain reaction (PCR)
- Methylation status with the help of Southern blot analysis

Greater than 200 repeats on one allele mark the diagnosis in females.

### 2. Prenatal testing:

- Chorionic villus sampling
- Amniocentesis

Echocardiography is used to rule out cardiac anomalies.

# Treatment of Fragile X syndrome

There is no specific treatment for FXS. Available treatment options are to improve the symptoms and functionality of life.

## Supportive therapy includes:

- Special education
- Avoidance of stimulants which trigger hypersensitivity and specific behaviors in FXS individuals
- Early intervention
- Vocational training
- Medical conditions related to heart, vision, hearing and connective tissues are treated.
- ADHD is treated with stimulants under strict monitoring to prevent adverse events.
- SSRIs are used for anxiety and mood swings.
- Anticonvulsants to control seizures; they also help alleviate the mood.
- Antidepressants and antipsychotics are used to treat self-injurious and aggressive behaviors in these individuals.

## References

Garber, KB; Visootsak J, Warren ST. (2008). "Fragile X syndrome". *European Journal of Human Genetics*. 16 (6): 666-72. doi:10.1038/ejhg.2008.61. PMID 18398441.

Hagerman RJ; Berry-Kravis E; Kaufmann WE; Ono, M. Y.; Tartaglia, N.; Lachiewicz, A.; Kronk, R.; Delahunty, C.; Hessler, D.; Visootsak, J.; Picker, J.; et al. (2009). "Advances in the treatment of fragile X syndrome." *Pediatrics*. 123 (1): 378-90. doi:10.1542/peds.2008-0317. PMC 2888470 Freely accessible. PMID 19117905.

U.S National Library of Medicine (2017). Retrieved from:

<https://ghr.nlm.nih.gov/condition/fragile-x-syndrome>

US Department of Health and Human Services | National Institutes of Health (2017).

Retrieved from:

<https://www.nichd.nih.gov/health/topics/fragilex/conditioninfo/Pages/commonsymptoms.aspx>

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