Fragile X Syndrome

What is Fragile X Syndrome?

Fragile X syndrome is a hereditary condition which causes a wide range of cognitive impairment, from mild learning disabilities to severe intellectual disability (ID). It is the most common cause of genetically-inherited cognitive impairment. In addition to mental impairment, fragile X syndrome is associated with a number of physical and behavioral characteristics.

What are the Common Symptoms?

Common parental concerns that might bring such a child to a pediatrician's attention include:

- cognitive impairment, ranging from learning disabilities to intellectual disability
- attention deficit and hyperactivity
- anxiety and unstable mood
- autistic behavior
- long face, large ears, flat feet
- hyper extensible joints, especially fingers
- Seizures (epilepsy) affect about 25% of patients with fragile X

Boys are typically more severely affected than girls. While most boys have ID, only one-third to one-half of girls have significant intellectual impairment; the rest have either normal IQ or learning disabilities. Emotional and behavioral problems are common in both sexes.

About 20% of boys with fragile X meet full criteria for autism. Most boys and some girls have some symptoms of autism, but many of them are very social and interested in interacting.

What Causes Fragile X?

In 1991, scientists discovered the gene (called FMR1) that causes fragile X. In individuals with Fragile X, a defect in FMR1 (a "full mutation") shuts the gene down. Like a defective factory, FMR1 cannot manufacture the protein that it normally makes. Other individuals are carriers: they have a small defect in FMR1 (called a "premutation") but do not show symptoms.

The FMR1 gene is located on the long arm of the X chromosome. Within this gene lies a region of DNA which varies in length from one person to another. Ordinarily, this stretch of DNA falls within a range of length that would be considered "normal".

In some people, however, this stretch of DNA is somewhat longer; this gene change is called a "premutation". Although a person who carries the premutation does not typically have symptoms of Fragile X, the stretch of DNA is prone to further expansion when it is passed from a woman to her children. When the stretch of DNA expands beyond a certain length, the gene is switched off

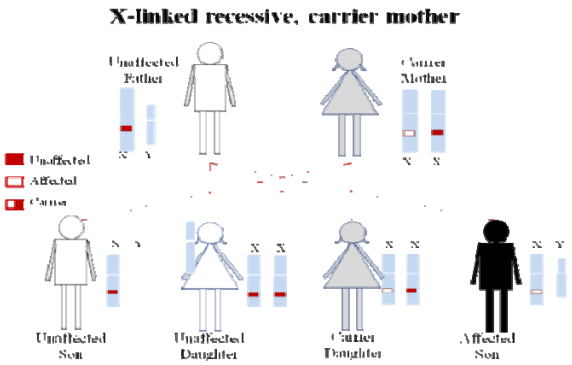
and does not produce the protein that it is normally makes. This gene change is called a "full mutation".

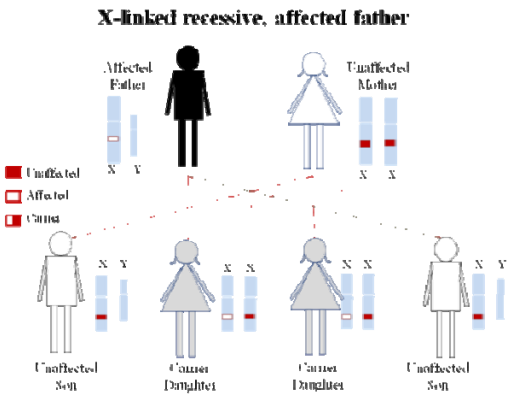
A male who inherits a full mutation exhibits characteristics of Fragile X syndrome because his only X chromosome contains the defective gene. A female may not be as severely affected as a male because each cell of her body needs to use only one of its two X chromosomes and randomly inactivates the other (usually the defective X).

How is Fragile X inherited?

Fragile X is inherited. Males and females carrying a premutation are unaffected. Carrier men (transmitting males) pass the premutation to all their daughters but none of their sons. These daughters are unaffected, but are at risk of having affected offspring. Each child of a carrier woman has a approximately 50% chance of inheriting the gene.

Variable clinical severity is observed in both sexes. Most, but not all, males with a full mutation are mentally retarded and show typical physical and behavioral features. Of females with a full mutation, approximately one-third are of normal intelligence, one-third are of borderline intelligence, and one-third are intellectually disabled.





Individuals for Whom Testing Should Be Considered

- Individuals of either sex with ID, developmental delay, or autism, especially if they have (a) any physical or behavioral characteristics of fragile X syndrome, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed ID
- Individuals seeking reproductive counseling who have (a) a family history of fragile X syndrome or (b) a family history of undiagnosed ID.

Detection of fragile X in your unborn child

- Fragile X can be detected in your unborn child during your pregnancy by analyzing samples of your unborn child (prenatal diagnosis).
- Sample is collected from 3 months (11-12th weeks) of pregnancy till 4 months (16-18th weeks) of pregnancy.
- Depending on the duration of pregnancy, sampling of the unborn child can be done by either chorionic villi sampling (CVS) or amniocentesis (AF). Both the procedures carry a small risk of abortion (0.5-2%).
- After sampling, DNA is extracted from either CVS or AF and analysis is carried out. Reporting takes about a week to ten days

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