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Fragile X syndrome

What is fragile X syndrome?

Fragile X syndrome is an X-linked disease of intellectual disability with variable severity.[1] Expansions of CGG repeat sequences in the *FMR1* gene account for 99% of mutations causing fragile X syndrome. Interpretation of CGG repeat expansion results is based on the following ranges: Negative: <45 repeats; intermediate: 45-54 repeats; premutation: 55-200 repeats; full mutation: >200 repeats. Greater than 99% of males and approximately 50% of females with the full mutation are intellectually disabled.[2]

What are the symptoms of fragile X syndrome and what treatment is available?

Fragile X syndrome is associated with a range of symptoms. Early signs include delayed speech and language skills.[1] Intellectual problems vary from mild learning disabilities to severe intellectual disability.[3] Behavioral characteristics include autism and hyperactivity.[1] Physical features, such as a long face and large or prominent ears, are usually more noticeable in adults than in children, and in males more than females.[3] There is no cure for fragile X syndrome. Treatment is supportive and focuses on educational and behavioral support and management of symptoms.[2]

Individuals with a premutation do not have fragile X syndrome, but may have an increased risk for fragile X-related disorders. Females may have fragile X-associated primary ovarian insufficiency (FXPOI), which can cause infertility or early menopause. Most males with a premutation and some females are at risk for fragile X-associated tremor and ataxia syndrome (FXTAS), which can affect balance and is associated with tremor and memory problems in older individuals.[3]

Intermediate numbers of CGG repeats are not associated with symptoms and there is no increased risk to have children with fragile X syndrome.[2]

How is fragile X syndrome inherited?

Fragile X syndrome is an X-linked disease caused by mutations in the *FMR1* gene.[1] When a premutation is passed from a mother to her offspring, the number of CGG repeat sequences may expand in length from a premutation to a full mutation.[2]

If a female carries a full mutation, the risk for each son or daughter to inherit the full mutation is 50%.[4] If a female carries a premutation, the risk that the premutation will expand to a full mutation depends on the repeat size of the premutation.[2] Men who are carriers pass the premutation to all of their daughters but none of their sons.[4]

Who is at risk for fragile X syndrome?

Fragile X syndrome can occur in individuals of all races and ethnicities. It affects approximately 1 in 4,000 males and 1 in 8,000 females.[1] One (1) in 259 females and 1 in 813 males are carriers of a premutation.[5]

Having a relative who is a carrier of fragile X syndrome or a relative who has been diagnosed with fragile X syndrome or a fragile X-associated disorder increases an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a fragile X premutation or full mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for at-risk family members.

What does a negative test result mean?

A negative result means an individual does not have a premutation or full mutation and therefore is not at increased risk of having a child with fragile X syndrome due to an expansion mutation.

Where can I get more information?

National Fragile X Foundation: https://fragilex.org/fragile-x/fragile-x-syndrome/

March of Dimes: http://www.marchofdimes.org/complications/fragile-x-syndrome.aspx

Genetics Home Reference: http://ghr.nlm.nih.gov/condition/fragile-x-syndrome

References

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