

Fragile X Syndrome



The most common inherited cause
of mental retardation

 **Integrated**
GENETICS

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LabCorp Specialty Testing Group

Fragile X Syndrome

This brochure contains information about fragile X syndrome, fragile X related disorders, and fragile X carrier testing. We hope that you find this information helpful. If you have any additional questions please contact your healthcare or genetics professional.

What is fragile X syndrome?

Fragile X syndrome is the most common cause of inherited mental retardation, affecting approximately 1 in 4,000 males and 1 in 8,000 females.¹ Often there is a family history of mental retardation, but sometimes there is not.

Fragile X syndrome causes a range of symptoms. Early signs include delayed speech and language. Intellectual problems vary from mild learning disabilities to severe mental retardation. Behavioral characteristics include autism, hyperactivity, and poor eye contact. 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.²

How is fragile X syndrome inherited?

Fragile X syndrome is caused by a change in the Fragile X Mental Retardation (FMR1) gene. This altered gene can be passed from generation to generation. Only one parent needs to have the altered gene for fragile X to be passed on to the child.

"Fragile X carrier" is a term used to describe someone who has an altered FMR1 gene, but does not show any obvious symptoms of fragile X syndrome. Women who are fragile X carriers have up to a 50% chance (or one in two chance) to have a child with fragile X syndrome and both sons and daughters can be affected. Men

who are fragile X carriers pass the altered gene to all of their daughters but none of their sons. Daughters of carrier men are unlikely to be affected with fragile X syndrome, but are at risk to have affected children.¹

Can anyone be a fragile X carrier?

Yes. Fragile X syndrome is found among a variety of ethnic backgrounds and racial groups.¹ Additionally, women of all ages can have a child with fragile X syndrome, whether or not they have had previous healthy children. Approximately 1 in 260² women and 1 in 800 males³ in the general population is a fragile X carrier.

Are certain people at a greater risk to be fragile X carriers?

Yes. Individuals are considered to have an increased risk to be fragile X carriers if they have:

- Family history of fragile X syndrome or fragile X related disorders.
- Family history of unexplained intellectual disabilities (mental retardation), developmental delay, or autism.
- Unexplained infertility problems, ovarian insufficiency or failure, elevated FSH levels, early menopause.
- Unexplained problems with balance or tremor.

What are fragile X related disorders?

Fragile X carriers may also have symptoms of the following fragile X associated disorders:

- Fragile X-associated primary ovarian insufficiency (FXPOI), which is a cause of unexplained infertility or early menopause.²
- Fragile X-associated tremor and ataxia syndrome (FXTAS), which is a condition that affects balance and is associated with tremor and memory problems in older individuals (greater than 50 years of age) and is seen more commonly in males.²

What is fragile X carrier screening?

Fragile X carrier screening will detect approximately 99% of individuals who are fragile X carriers and at risk of having a child with fragile X syndrome.⁴ The test is performed on a small sample of blood and results are usually ready within two weeks. Other causes of mental retardation are not identified through this test.



What do the results mean?

There are four different results from the fragile X test: **negative, intermediate, premutation, and full mutation.**²

Test result	What this means for you	What this means for your children
Negative	<ul style="list-style-type: none">■ You are not considered a carrier for the most common alteration in the fragile X gene	<ul style="list-style-type: none">■ Your children are not at increased risk for fragile X syndrome
Intermediate	<ul style="list-style-type: none">■ You are not considered a carrier for the most common alteration in the fragile X gene	<ul style="list-style-type: none">■ Your children are not at increased risk for fragile X syndrome■ Future generations may be at risk for fragile X syndrome■ Genetic counseling can be considered
Premutation	<ul style="list-style-type: none">■ You are a carrier for fragile X■ You may be at risk for FXPOI or FXTAS	<ul style="list-style-type: none">■ Your children are at risk for fragile X syndrome■ Genetic counseling is recommended*■ Prenatal diagnostic testing is available
Full mutation	<ul style="list-style-type: none">■ You have an altered FMR1 gene. Full mutations are associated with a wide range of symptoms, including intellectual disabilities.	<ul style="list-style-type: none">■ Your children are at risk for fragile X syndrome■ Genetic counseling is recommended*■ Prenatal diagnostic testing is available

*The American College of OBGYN recommends genetic counseling for all carriers of a premutation or full mutation.

Is prenatal testing available?

Yes. Prenatal testing by amniocentesis, usually at 15–20 weeks of pregnancy, or by chorionic villi sampling (CVS), usually at 10–12 weeks, can be performed to determine whether or not the unborn baby has an altered fragile X gene that could lead to fragile X syndrome.

Is fragile X testing required?

No. Your doctor may recommend that you consider fragile X testing, but all testing is voluntary. The choice is yours.

For additional questions:

Your health care provider can help answer additional questions, or may refer you to a genetic counselor to:

- Review how fragile X is inherited
- Help you understand why fragile X testing has been recommended for you or a family member
- Explain your fragile X test results
- Explain fragile X prenatal testing
- Discuss other concerns you may have

References:

1. Sherman, S, et al. Fragile X syndrome: Diagnostic and carrier testing. ACMG Practice Guideline *Genet Med* 2005; 7(8):584-587.
2. Carrier Screening for Fragile X syndrome. ACOG Committee Opinion, Number 469. October 2010.
3. Drombrowski, C., et al. Premutation and intermediate-size FMR1 alleles in 10,572 males from the general population: loss of an AGG interruption is a late event in the generation of fragile X syndrome alleles. *Hum Mol Genet* 2002; 11(4):371-378.
4. Maddalena, A, et al. Technical Standards and Guideline for Fragile X: The First of a Series of Disease-Specific Supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics. *Genet Med* 2001; 3(3):200-205.



Informed Consent/Decline for Fragile X Carrier Screening

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My signature below indicates that I have read, or had read to me, the above information and I understand it. I have also read or had explained to me the specific disease(s) or condition(s) tested for, and the specific test(s) I am having, including the test descriptions, principles and limitations.

I have had the opportunity to discuss the purposes and possible risks of this testing with my doctor or someone my doctor has designated. I know that genetic counseling is available to me before and after the testing. I have all the information I want, and all my questions have been answered.

I have decided that:

I want fragile X carrier testing.

I do not want fragile X carrier testing.

Patient Signature

Date

Obtained by

This model informed consent form is provided by Integrated Genetics as a courtesy to physicians and their patients.

Informed Consent/Decline for Fragile X Carrier Screening

You should be certain you understand the following points:

1. The purpose of my genetic testing is to determine whether I, or my baby, have mutation(s) known to be associated with fragile X syndrome.
2. This testing is done on a small sample of blood. For the baby, testing is done on amniotic fluid, CVS, or fetal blood.
3. Mutations are often different in different populations. I understand that the laboratory needs accurate information about my family history and ethnic background for the most accurate interpretation of the test results.
4. When fragile X testing shows a mutation, then the person is a carrier or is affected with the condition or disease tested for. Consulting a doctor or genetic counselor is recommended to learn the full meaning of the results and to learn if additional testing might be necessary.
5. When the fragile X testing does not show a known mutation, the chance that the person is a carrier or is affected is reduced. There is still a chance to be a carrier or to be affected because the current testing cannot find all the possible changes within a gene.
6. In some families, fragile X testing might discover non-paternity (someone who is not the real father), or some other previously unknown information about family relationships, such as adoption.
7. In the case of twins or other multiple babies, the results may pertain to only one of the babies.
8. In the case of abnormal diagnostic results, the decision to continue or terminate the pregnancy is entirely mine.
9. The decision to consent to or to refuse fragile X testing is entirely mine.
10. No test(s) will be performed and reported on my sample other than those authorized by my doctor; and any unused portion of my original sample will be destroyed within 2 months of receipt of the sample by the laboratory.
11. My doctor may release my pregnancy outcome or ultrasound and amniocentesis results to Esoterix Genetic Laboratories, LLC, to be used for statistical analysis of the laboratory's performance.
12. Esoterix Genetic Laboratories, LLC, will disclose the test results only to my doctor or to his/her agent unless otherwise authorized by me or required by law.

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About Integrated Genetics

Integrated Genetics has been a leader in genetic testing and counseling services for over 25 years.

This brochure is provided by Integrated Genetics as an educational service for physicians and their patients.

For more information on our genetic testing and counseling services, please visit our web sites:
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