

WHAT IS FRAGILE X SYNDROME?

Fragile X (Fra X) syndrome is the most common inherited type of mental retardation. It occurs in about 1 in 3600 males and 1 in 4000 females. Early diagnosis allows genetic counseling, therapy and testing of at risk relatives.

WHAT ARE THE MOST COMMON SIGNS OF FRAGILE X?

The most common signs of Fra X are mental retardation, learning disabilities, and developmental delay. An individual with Fra X may be hyperactive, show signs of autism such as poor eye contact, have rapid repetitive speech, hand biting and flapping, hypersensitivity to light or sound, and difficulty in adapting to changes.

Physical signs are most noticeable in adults and include enlarged testes after puberty, large head and hands, long narrow face with prominent chin and forehead and large flat ears. Children may have few identifiable physical characteristics. Females maybe less severely affected and the facial features are rarely seen. The majority of boys with Fra X fall in the range of mild mental retardation or an IQ below 70 points. About 80% of boys and 30% of the girls with the full mutation are at least mildly mentally retarded.

HOW IS FRAGILE X INHERITED?

Fra X is inherited in an X-linked dominant manner. X-linked means the abnormal gene is located on the X chromosome, which is a sex chromosome. Males are usually more severely affected by Fra X than females. This occurs because females have two X chromosomes; one X contains the normal functioning version of the gene. The normal gene can partially compensate for the non-functioning gene. Males have one X chromosome and one Y chromosome.

A female who carries the Fra X gene on one of her X chromosomes has a 50% chance of passing the abnormal gene to her baby with each pregnancy. Some females who inherit the Fra X gene on one of the X chromosomes are affected while some other females are protected from the harmful effects of the abnormal gene by the normal gene on the other X chromosome.

A male who has the Fra X gene on his single X chromosome will pass it to each of his daughters but none of his sons. Most males who inherit the Fra X gene are affected and show a Fragile X chromosome site (Xq27.3).

Some males who inherit the premutation Fra X gene from their mothers do not have signs of Fra X or the Xq27.3 fragile site. These males are said to be "non-penetrant normal transmitting males". These males will pass the abnormal gene to each of their daughters but none of their sons.

WHO SHOULD BE TESTED FOR FRAGILE X?

- Children and adults who have unexplained mental retardation or developmental delay should be tested for chromosomal abnormalities and Fra X.
- Women with a family history of unexplained mental retardation.

- Relatives of a diagnosed Fra X carrier or Fra X affected should have counseling and be tested to determine whether they also carry the Fra X gene.
- A pregnant woman who is a possible or known Fra X carrier may elect to have prenatal testing performed.
- Women with premature ovarian failure / infertility.

WHAT TESTS ARE RECOMMENDED?

Individuals who have clinical signs of Fra X should have a

Fragile X Checklist	Not Present (score 0)	Borderline or present in the past (score 1)	Definitely present (score 2)
Mental retardation			
Hyperactivity			
Short attention span			
Tactilely defensive			
Hand-flapping			
Hand-biting			
Poor eye-contact			
Perseverative speech			
Hyperextensible MP joints			
Large or prominent ears			
Large testicles			
Simian crease or Sydney line			
Family history of mental retardation			
Fragile X DNA test is indicated for scores 15+		Total Score: _____	
<small>Source: Fragile X Checklist: Hagerman, Amiri, and Cronister, American Journal of Medical Genetics 38:283-287 (1991)</small>			

standard chromosome analysis to identify chromosomal abnormalities and should have a DNA analysis to determine whether the Fra X gene mutation is present.

DNA analysis can very accurately differentiate Fra X affected males and normal non-penetrant transmitting males from normal males. DNA can also differentiate expressing female carriers and non-expressing female carriers from normal females.

Unaffected relatives should consider DNA testing.

HOW SOON CAN THESE TESTS BE COMPLETED?

The average turnaround time for the blood chromosome test is 7 days and the Fra X DNA test takes 1-2 weeks. Prenatal diagnosis takes about 3 weeks because the amniotic fluid cells must be grown in the laboratory before DNA analysis can begin.

HOW CAN A FRAGILE X EVALUATION BE ARRANGED?

Contact Dr. Buchanan and Dr. Laundon for consultations. Blood specimens may be sent or drawn at GeneCare when testing is indicated.

Individuals who are concerned about the possibility of a family member being affected with Fra X are encouraged to discuss genetic testing with their physician and consider having genetic counseling. During counseling, a detailed family history will be reviewed

and appropriate testing determined for each individual situation.

GENETIC COUNSELING:

A genetic counselor can offer extensive information and support regarding testing, inheritance patterns, and advice concerning the family planning options that are available. Genetic counselors can also help families cope with a positive diagnosis.

TREATMENT:

At this time there is no cure for Fra X syndrome, however, many treatments are available. Treatment is provided through various forms of therapy including special education, speech and language therapy, occupational therapy, and physical therapies. The use of medications is often helpful in managing hyperactivity, poor attention span, aggression, anxiety, and depression.

SPECIMEN COLLECTION:

- Call GeneCare to discuss clinical indications, appropriate testing, current fees, and method of payment. Supplies and transport are free.
- Complete Laboratory Request Form.
- Label each tube with patient's name, date of birth, and collection date.
- Specimen: For chromosome analysis and DNA tests, obtain blood from adults and children: 10cc NaHeparin green top and 10cc EDTA purple tubes. For infants: 2cc NaHeparin and 2cc EDTA tubes.

SPECIMEN TRANSPORT:

- Include Lab Request Form
- **SHIP AT ROOM TEMPERATURE** in our kit to:

GeneCare Medical Genetics Center
201 Sage Road, Suite 300
Chapel Hill, NC 27514

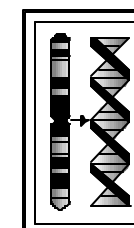
- DHL/Airborne (800) 247-2676 **priority overnight** or by our courier to reach GeneCare Monday - Thursday. 24 hour delivery required.
- Notify GeneCare of shipment date and DHL/Airborne airbill/tracking number

GeneCare Medical Genetics Centers

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Fragile X Syndrome

DNA and Chromosome Testing



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