



Fragile X

For Healthcare Providers

This is a customized health care provider version of our website. Please visit the main website to find more comprehensive information for families and schools (www.negenetics.org).

Fragile X syndrome occurs in both males and females. It is caused by a change or mutation in the FMR1 gene located on the X chromosome. The FMR1 gene produces a protein important for normal brain development. Fragile X syndrome is caused by what is termed a trinucleotide repeat expansion (an increase in a CGG repetitive sequence) in the FMR1 gene. There is a range of normal number of CGG repeats (5-44 repeats), in which there is no known instability and will not lead to an expansion; an intermediate range (45-54 repeats) in which about 14% of the time can expand to premutation size; a premutation range (55-200 repeats) and a full mutation (>200 repeats). Intellectual disability may be found in up to 50% of females and virtually all males with a full mutation.

NOTE: This document only reviews the features found in males and females with a full mutation.

Physical characteristics and/or symptoms

Note: not all people with Fragile X will have all of these features.

MALES - The clinical findings in males with a full mutation may include the following:

- Intellectual disability (IQ may range from 22-65).
- Behavioral differences *may* include:
 - Autism spectrum disorder
 - Hyperactivity
 - Shyness
 - Gaze aversion
 - Hand flapping
 - Hand biting
 - Temper tantrums

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- Specific facial appearance and physical findings which may include:
 - Large head
 - Long face
 - Large forehead and chin
 - Ears that stick out
 - High arched palate or sometimes cleft palate
- Macroorchidism - not apparent until after puberty
- Joint hypermobility
- Cardiac findings include mitral valve prolapse and aortic root dilatation.
- Strabismus
- Other findings may include:
 - Hypotonia
 - Reflux
 - Recurrent otitis media
 - High blood pressure
 - Seizures.

FEMALES - Clinical finding in females who have a full mutation:

- Females may have some of the same physical features as males.
- Mild intellectual disability in up to 50% of females (IQ may range from 74-91).
- Other learning difficulties or subtle cognitive features, such as difficulty with math
- Behavioral differences **may** include the following:
 - Social anxiety
 - Selective mutism
 - Excessive shyness
 - Poor eye contact
 - Hyperactivity, and/or impulsive behavior.

Recommended Routine Surveillance

- Assessment of feeding/eating, digestive problems (including constipation and gastroesophageal reflux)
- Surveillance for cardiac abnormalities
- Assessment for hypertension
- Ophthalmologic evaluation
- Monitor recurrent otitis media
- Evaluate hypotonia and/or connective tissue findings
- Monitor for seizures

Emergency Protocols

There are no specific emergency protocols for this particular condition as it is not typically associated with episodes of sudden and serious medical decompensation.

- Emergencies should be handled as with any child.
- If seizures are present, the following seizure action plan may be useful:
<https://www.epilepsy.com/learn/managing-your-epilepsy/seizure-action-plans>

Specialists Who May Be Involved

Follow up is need on a case-by-case basis. A multidisciplinary team approach to best meet the child's individual needs is recommended.

- Cardiologist
 - Screening for mitral valve prolapse
 - Aortic root dilatation
- Developmental specialist
 - Speech therapy
 - Physical therapy
 - Occupational therapy
 - Autism spectrum disorder /autistic signs
- Gastroenterologist
 - Gastroesophageal reflex
 - Constipation
- Geneticist /Genetic Counselor:
 - Diagnosis
 - Coordination of care
 - Genetic risk for family

- Clinical trials
- Neurology
 - Monitor seizures
- Ophthalmologist
 - Strabismus
- Orthopedists
 - Gait ataxia
 - Joint laxity
 - Pes planus
 - Hypotonia
- Ophthalmologist
 - Strabismus

Sample Forms

- Sample paragraph to be used for Letters of Medical Necessity or Letters to the school:

My patient _____ has been diagnosed with Fragile X. This condition is characterized by hypotonia, autism, behavioral differences, and developmental delays/intellectual disability. Medical complications with Fragile may seizures and gastrointestinal symptoms. Because of these, _____ needs the following accommodations.

Seven Important Aspects of School Life

“[Fragile X at a Glance](#)” will help you talk with parents and schools about:

- Medical / Dietary Needs
- Education Supports
- Behavior & Sensory Supports
- Physical Activity, Trips, Events
- School Absences & Fatigue
- Emergency Planning
- Transitions



Resources

Fragile X Syndrome: Diagnosis, Treatment and Research

This book published in 2002 by John Hopkins University Press is a good resource. It was edited by Randi Jenssen Hagerman, M.D. and Paul J. Hagerman, M.D., Ph.D.

National Center for Biotechnology Information (NCBI) Bookshelf – Fragile X

<http://www.ncbi.nlm.nih.gov/books/NBK22189/>

American Academy of Pediatrics (AAP) – Health Supervision Guidelines

<http://pediatrics.aappublications.org/content/127/5/994.full.pdf%20html>

FMR1 Disorders

<https://www.ncbi.nlm.nih.gov/books/NBK1384/>

AAP: Fragile X Syndrome: Resources for Pediatric Clinicians

<https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Pages/Fragile-X-Syndrome.aspx>

National Fragile X Foundation – Find a Clinic

<https://fragilex.org/our-research/fragile-x-clinics/>