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.gemssforschools.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

- 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.aap.org/en-us/Documents/Seizure_Action_Plan_for%20School.pdf

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

Gene Reviews: FMR1 Related 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