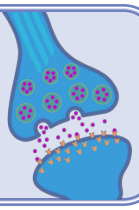
Fragile X Syndrome

X – linked dominant

CGG repeat expansion

A genetic disorder caused by a **CGG repeat expansion** in the **FMR1 gene**, leading to a lack of FMR protein and **abnormal synapse development**. It is the **most common inherited cause of intellectual disability**, primarily affecting **males**, with **X-linked dominant inheritance** and a prevalence of 1 in 4000.



CLINICAL FEATURES

Growth:
- **Macrocephaly**
- Accelerated linear growth in early childhood

Craniofacial:
- **Large protruding ears**
- Prominent forehead
- Prominent lower jaw
- Long narrow face
- Strabismus

Psychiatric:
- **Behavioral issues**
- Social avoidance
- **Poor impulse control**
- ADHD
- Anxiety
- Depression
- Sleep disorder

Learning challenges:
- **Intellectual disability**
- Speech delay

Connective tissues:
- Pectus excavatum
- Joint laxity
- Scoliosis
- **Mitral valve prolapse**

Genitourinary:
- **Macro-orchidism**
- Dilated ureters
- Vesicoureteral reflux

Gastrointestinal:
- Constipation
- Gastroesophageal reflux disease

DIAGNOSIS

Identification of key clinical features

Confirmatory Genetic Testing:
- FMR1 molecular genetic testing
- CGG allele repeat sizes

- **Normal:** 5 to 44 repeats
- **Intermediate**: 45 to 54 repeats
- **Premutation:** 55 to 200 repeats
- **Full mutation**: 200+ repeats

Fragile X–associated tremor ataxia syndrome:
- Late onset progressive cerebellar ataxia in **premutation-range males**

MANAGEMENT

Behavioral & Educational Support	Medication	Developmental Interventions	Medical Management
▪ **Behavioral therapy** ▪ Special education tailored to **learning needs** ▪ **Speech & occupational therapy** for communication and motor skills	***May include:*** ▪ **Stimulants** for ADHD ▪ **SSRIs** for anxiety and mood ▪ **Antipsychotics** for aggression	▪ **Early intervention** to address developmental delays ▪ **Physical & sensory therapy** to improve motor skills and sensory processing	▪ **Monitor** for seizures, sleep disorders, and connective tissue problems ▪ **Manage** gastro-intestinal issues (e.g., constipation, GERD)

Family Support: genetic counseling for families and respite care for caregivers

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Dr. Katharine V. Jensen (Pediatric Resident, University of Alberta) and Dr. Karen Forbes (Professor of Pediatrics, University of Alberta) for www.pedscases.com