

Fragile X Syndrome

Definition of Fragile X Syndrome

Fragile X Syndrome (FXS) is a genetic disorder caused by a mutation (a change in the DNA structure) in the X chromosome. It results in a wide range of developmental, physical and behavioural problems and is the most common known cause of inherited developmental disability worldwide. One in 2,500 males and one in 5,000 females are affected. One in 250 females carries the premutation and will pass the gene on to 50% of her offspring, male or female.

Causes of Fragile X Syndrome

The genetic disorder is a mutation in a gene on the 'X' chromosome called FMR1 (fragile X mental retardation gene 1). This gene normally contains a repeat code of 6 – 50 'CGG' triplet repeats. Premutation carriers have a small change in the FMR1 gene (a repeat code of 50 –200), whereas the full mutation tends to be affected individuals with a large change in the gene (more than 200 repeats). The mutation turns the gene off, thus causing the problems associated with the syndrome.

Presentation

Physical

Boys and girls may have prominent ears, high forehead, high palate, hyperflexible joints, soft skin and flat feet. After puberty, the face may gradually become longer and boys may develop testicular enlargement. Medical complications do not generally develop, however, ear infections are common and there is an increased risk of epilepsy (seizures), strabismus (squint), mitral valve prolapse, hernia and joint dislocations. Physical features may not always be present, especially in children.

Developmental

Intellectual disability occurs in 80% of males and 65% of females. Global problems tend to occur with learning disabilities and delays in speech, fine and gross motor movements and co-ordination difficulties.

Behavioural and Emotional

Common features include attention deficit disorders with or without hyperactivity, anxiety (hyperarousal), extreme reaction or aversion to sensory stimuli (loud noise, touch, strong smells or tastes, eye contact) and difficulties with expressive language. Autism-like features include hand flapping and biting (or chewing on clothes), poor eye contact and resistance to changes in routine. A diagnosis of autism spectrum disorder, pervasive developmental delay or Asperger's may have been made. Girls may appear less affected and may present with shyness, social anxiety and moodiness.

Fragile X Syndrome Carriers (Pre-mutation)

Carriers are generally considered to be unaffected and will only be detected following DNA testing. However a number of subgroups may demonstrate some features of the full mutation.

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Diagnosis of Fragile X Syndrome

DNA studies for Fragile X Syndrome should be requested. They are highly sensitive and specific and will reliably detect carriers. Cytogenetic testing (karyotyping) should also be requested initially when trying to establish the cause of developmental delay as other chromosomal explanations may be identified.

Early detection allows the implementation of effective treatment and intervention strategies thus optimising outcome. As this is an inherited condition, diagnosis also allows families to make informed choices regarding both treatment and family planning.

Who should be tested for Fragile X Syndrome? (see also FXS sheet 2)

Testing should be considered for:

- Any male or female with intellectual disability, developmental delay, learning disabilities, or autism-like features.
- Individuals who have only had a cytogenetic test previously, or who were tested prior to 1991.
- Pre-conceptual: women or their partners with a personal or an extended family history as above, or who wishes to be tested.
- Obstetric: Pregnant women or their partners with a family history of fragile X syndrome, or intellectual disability of unknown cause; foetuses of a parent known to be a fragile X carrier; couples with a personal or family history of premature menopause; if undergoing IVF, CVS or amniocentesis.

Management

Counselling

Families will cope better if given sufficient information and support.

Early Intervention

Early intervention is vital. Most males and some females will require lifelong supervision, most will achieve good functional life skills if they are able to achieve an optimal outcome.

Behavioural Issues

The 3 main behavioural issues will be:

- Sensory defensiveness.
- Hyperarousal.
- Attention problems.

Medical Issues

Regular review is recommended in order to detect and manage a range of issues:

- Epilepsy.
- Attention disorders.
- Aggression.
- Mood disorders.

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Fact Sheet

Strengths

- Learn visually eg pictures, computers.
- Whole word, number and pattern recognition, ‘gestalt’ learning.
- Long term and incidental memory.
- Concrete, relevant tasks.
- Strong imitation skills, drama.
- Good functional life skills.
- Friendly, good sense of humour.

Weaknesses

- Short-term memory.
- Auditory-only processing.
- Abstract concepts.
- Sequencing, praxis and planning.
- Fine and gross motor skills.
- Perceptual, visual motor skills.
- Social, language, semantic-pragmatic.
- Attention and initiation.

Treatment

- Speech and language therapy.
- Occupational therapy with sensory integration.
- Special education.
- Psychological therapies.
- Medical and pharmacological.

Strategies

- Prepare for transitions with highly structured routines.
- Maximise visual input (use pictures, timetables).
- Minimise auditory and visual distractions.
- Utilise calming strategies and distractors.
- Positively reinforce good behaviour.

The material in this sheet has been adapted from the Therapeutic Guidelines book ‘Management Guidelines for People with Developmental and Intellectual Disabilities’ and updated from the 2005 version, Management Guidelines – Developmental Disability’ which can be consulted for more detailed information.

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