

# **FRAGILE X SYNDROME — INFORMATION SHEET (SHEET 1)**

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.

Fragile X syndrome is the most common known inherited cause of intellectual disability and has a wide variety of presentations. Although caused by a mutation on the X chromosome, it may have clinical effects in both males and females.

## **Genetics**

Fragile X syndrome is caused by a gene mutation at the FMR1 (the “fragile X mental retardation 1” gene) on the long arm of the X chromosome. A premutation is the state of less extensive damage to the chromosome.

Either the man or the woman who carries the affected X chromosome transmits the fragile X premutation or full mutation.

- A man with the fragile X syndrome premutation will pass the premutation on to all of his daughters without it changing in size, but to none of his sons, as they receive their father's Y chromosome.
- A woman with the fragile X syndrome premutation will have a 50 % chance of passing the premutation on to her sons and daughters. The degree of expansion is dependent on its size. A woman with a full mutation will pass the full mutation on to 50% of her sons and daughters.

Once an individual is identified with Fragile X syndrome, a large proportion of the extended family across the generations will be found to carry the premutation, and there may or may not be other affected members in the family. Genetic counselling is important and allows families to make informed decisions about family planning.

## **Fragile X Syndrome Carriers (ie Premutations)**

Carriers of the Fragile X syndrome are generally considered to be unaffected and will only be detected following DNA testing. However, some individuals do demonstrate some features of the full mutation.

### **Full Mutation Individuals**

Individuals with the full mutation of the Fragile X gene demonstrate developmental, physical, behavioural and emotional characteristics but typical features may not always be present. Females may also be affected but usually less so than males because one of their X chromosomes is unaffected.

## **Typical Features of Fragile X Syndrome**

### **Developmental Disability**

- Speech delay or disturbance
- Intellectual disability — most males and one third of affected females, mostly mild to moderate but can be severe.
- Learning disabilities
- Co-ordination and motor problems, low muscle tone

### **Physical Characteristics** (often subtle and can be overlooked and less evident in women)

- Large or prominent ears, long face and large testes – may not be evident until puberty
- High broad forehead, high palate, prominent jaw

### **Associated Medical conditions**

- Epilepsy – up to 20%, usually tonic-clonic or partial complex
- Elastin disorder resulting in heart, eye, ear, joint and bone problems in some individuals

## Behavioural and Emotional Characteristics

- Attention-deficit disorders, often with hyperactivity, distractibility, impulsiveness and poor concentration
- Hand mannerisms – hand or wrist biting, hand flapping
- Speech pattern disturbances
- Shyness, social avoidance, poor eye contact
- Autistic-like stereotyped behaviours, pre-occupation with objects, echolalia
- Sensory defensiveness - aversion to touch, bright lights, loud noises, strong smells
- Emotional instability – outbursts of anger and aggression , especially in post-pubertal males
- Social anxiety, hyperarousal

## TESTING FOR FRAGILE X SYNDROME

Testing for fragile X syndrome using DNA studies has been available since 1991 and, unlike previous tests, is highly sensitive and specific and will also reliably detect carriers. When ordering, specify ‘DNA studies for Fragile X syndrome. Cytogenetic testing (karyotyping) should also be requested initially when trying to establish the cause of developmental delay as other chromosomal explanations may be identified

### Who should be tested for fragile X syndrome?

Any individual with significant developmental delay should be tested as, occasionally, Fragile X can occur concomitantly with any other syndrome or disability e.g. Down syndrome, cerebral palsy.

There are guidelines in Australia for who should be tested and a Medicare rebate applies to such tests. These cover anyone with ID of unknown cause, people with previous negative or inconclusive results, susceptible people with a confirmed family history, people with learning difficulties of unknown cause and emotional or behavioural features of fragile X, women with premature menopause (<40 years) and males over 50 years with unexplained ataxia.

Testing can be offered to intending or pregnant mothers with referral for genetic counselling.

**Note:** *Detection of carriers allows families to make informed decisions regarding family planning.*

In cases where a male is suspected of having fragile X syndrome, an alternative option is to test the mother of the male in question. If the mother is not a carrier, then Fragile X syndrome can be excluded from her male children. If she is, relevant members of her entire extended family need to be tested and offered genetic counselling.

If an individual tests positive for the fragile X mutation or premutation the family should be referred to a genetic centre for counselling. If the affected person is male, genetic testing focuses on his mother and her relatives. However, it is important to remember that normal brothers may carry premutations.

## MANAGEMENT

Specific treatment and intervention strategies are now available and are of great benefit to affected individuals and their families. These include educational, behavioural, pharmacological and medical strategies which integrate multiple professionals as well as the parents and carers.

It needs to be recognised that families cope well if given sufficient information and support, and that all individuals have an important place in society. Families need to be referred for genetic counselling.

Information may be obtained from genetic counsellors and developmental paediatricians. A wide range of resource material for professionals and parents is available from the **Fragile X Alliance**

## Early Intervention

Early intervention is vital for children especially if they are to take their place in society. Although most males and some females will require life long supervision, most will achieve good functional life skills.

## Support for Families

The family may need the assistance of a community worker or social worker not only for personal support but also to access financial assistance such as pensions and disability allowances. The demands and stresses placed on families that include a person with Fragile X syndrome can be immense, especially where that person exhibits problem behaviours. Families should be treated with an understanding of the difficulties they may face and be respected for their ability to manage what may be an extremely difficult situation.

## Behavioural Issues

Understanding behavioural features such as hyperarousal and attention problems is necessary in order to coordinate behavioural and pharmacological management strategies. Referral to a practitioner familiar with these issues for early implementation of these strategies is vital in order to optimise the lives of these individuals and their families. The most effective approach is one that integrates the following disciplines, all of which need to be considered for referral.

- Speech and language therapy
- Special education
- Occupational Therapist
- Clinical and educational psychology
- Developmental paediatrician
- Psychiatrist

## Medical Issues

Regular review is recommended in order to detect and manage the wide range of issues associated with Fragile X syndrome.

### Pharmacological Treatment of:

- **Epilepsy** –Carbamazepine is commonly used in Fragile X syndrome perhaps because of the additional effects on behaviour.
- **Attention disorders** –Methylphenidate or dexamphetamine will produce improvement in the majority. Pharmacological management and behavioural interventions are both important.
- **Aggression** - tends to be more common after puberty and also requires behavioural intervention. In addition, pharmacological interventions including SSRIs, mood stabilisers and risperidone may be useful.
- **Mood disorders** (especially post puberty) – depression may occur either by itself or as a result of the individual developing insight into their condition. The newer range of SSRIs may be effective.

There are no controlled studies of the use of psychotropic medication in the Fragile X population, but these medications are widely used in clinical practice and less rigorous studies provide some evidence to support their use.

## **Educational Strategies**

Education is one of the most important needs for any child. Good educational outcomes can be achieved ideally in an inclusive setting where the child interacts along with his/her peers and with a syllabus modified for each individual's circumstances. Regular education support group meetings between educators and all those involved in the child's care are necessary to delineate appropriate goals and monitor progress.

Poor short term memory, difficulty with auditory processing, abstract concepts, poor attention span and difficulty with initiation all contribute to the academic difficulties experienced by affected individuals. However, there are a number of strengths that may be utilised to optimise learning and the development of 'real-life' performance skills (see next).

## **Maximising Strengths**

These individuals generally exhibit many strengths such as a marvellous sense of humour, socially engaging nature, strong imitation skills, excellent visual skills, visual memory and intense interests. Affected individuals are strong visual learners who do well with pictures, logos and in particular learn well with interactive multimedia computer programs. Using drama takes advantage of their imitation skills and good long-term memory. They do best with concrete relevant tasks such as shopping or cooking.

In general, individuals with Fragile X syndrome thrive in an environment which:

- is highly structured and follows routines
- preparations for changes are clearly emphasised
- written and visual schedules outline the day's activities
- has minimal auditory and visual distractions
- utilises maximum visual input (such as pictures or drama)
- utilises calculators and computers with interactive multimedia as teaching tools
- involves regular communication between parent and school/ day placement

## **Support Groups**

The Fragile X Association of Australia: <http://www.fragilex.org.au>

Fragile X Research Foundation: <http://www.fraxa.org>