Frequently Asked Questions

1. **If no members of my family are affected by FXS, can I still have a child with the condition?**
   Yes. Due to the way the disease is inherited, it is possible for the defective gene to be present in the family without anyone showing symptoms. Hence, you may not be aware of a family history. In addition to that, there is also a risk of spontaneous mutations occurring in families without a family history.

2. **Since FXS is a genetic condition, is it possible to have more than one child with the condition?**
   Yes. If a parent is a premutation carrier there is a risk associated with each pregnancy, depending on which parent carries the mutation.

3. **Why are girls usually less severely affected by FXS?**
   A girl has two copies of the X chromosome. Hence, when she inherits a flawed *FMR1* gene from one parent, she usually also gets a healthy *FMR1* gene from her other parent, giving her enough of the protein to protect her from the disease.

4. **What are the implications of FXPOI to female premutation carriers?**
   FXPOI may lead to early menopause (before the age of 40) in some females. This may result in some women wanting to start a family at an earlier age in anticipation of early menopause.

5. **If a woman is a premutation carrier, does that mean that her children will not have a full mutation?**
   No. The premutation may expand in subsequent generations and result in a full mutation. It is not possible to predict whether or not the mutation will expand or remain the same.

6. **Can a male who is a premutation carrier pass the mutation to his children?**
   Yes. A man who is a premutation carrier will pass down the mutation to all his daughters. He will not pass it to his sons as men do not pass on their X chromosome to their sons.

References

Fact Sheet 42: Fragile X Syndrome [online] Available from: http://www.genetics.com.au/pdf/factsheets/fs42.pdf [Accessed April 2010]

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The National Fragile X Foundation [online] Available from: http://www.fragilex.org/html/home.shtml [Accessed April 2010]

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MALAYSIAN RARE DISORDERS SOCIETY

Rare Disorders Series:

Fragile X Syndrome

What is Fragile X Syndrome (FXS)?

Fragile X Syndrome is the most common form of inherited intellectual disability in males. Females may also be affected by the condition, but usually to a lesser extent.

The condition is caused by a change (mutation) in the *FMR1* gene.

Genes are located on chromosomes and contain 'recipes' to make proteins.
The *FMR1* gene is located on the X chromosome.

The protein made by the *FMR1* gene has a role in the development of the brain.

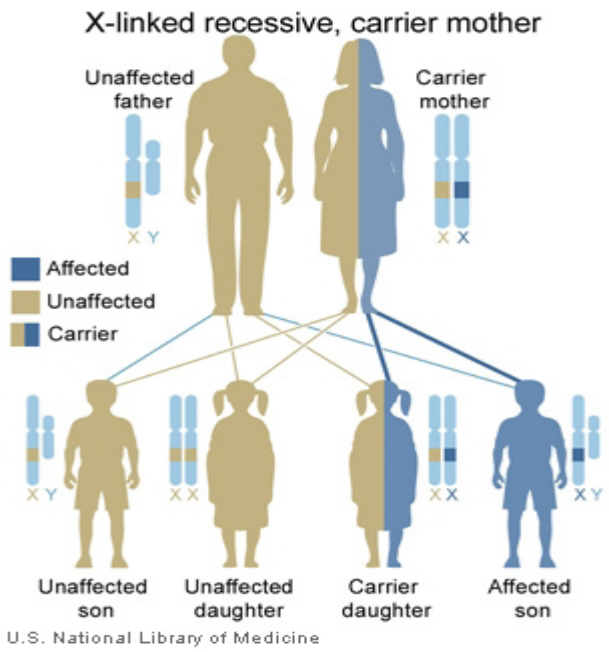
Mutations cause the protein to be produced in reduced amounts or not at all, resulting in learning disabilities and cognitive impairment.

Some individuals may have a milder type of gene change. This is known as a premutation.
No mental impairment is observed in those having this type of mutation.

Adults may develop a neurological condition called Fragile X Tremor/Ataxia Syndrome (FXTAS). Women may also experience early menopause due a condition known as Fragile X Premature Ovarian Insufficiency (FXPOI).

FXS may be inherited from either mother or father. The risk of having an affected child varies according to the gender of the parent carrying the mutation.

Patients are advised to consult a geneticist to obtain further information on reproductive risks and disease progression.



Inheritance pattern of Fragile X Syndrome

Signs and symptoms

- Large prominent ears and a long face (may be subtle in childhood)
- Intellectual disability
- Speech and language delay
- Behavioural issues such as hyperactivity, temper tantrums and hand flapping
- Emotional problems
- Loose joints and large testicles in males after puberty

Note that females with a full mutation may be affected less severely than males.

Signs and symptoms in premutation carriers

- Mild intellectual and behavioural issues
- Shy personality and selective lack of speech

Testing

Genetic counselling by qualified personnel is advised if there is a family history of the condition and before any genetic testing is done.

Genetic testing for Fragile X Syndrome is available for confirmation of diagnosis.

Testing can determine the length of the gene change which distinguishes whether one is a premutation or full mutation carrier.

The testing however does not reveal the severity of the disease and symptoms that will be manifested by the carrier.

Treatment

There is currently no known cure for Fragile X Syndrome.

Treatments and therapies are given to manage symptoms and to maximise the skills and potential of individuals with FXS.

Special education which incorporates speech, language, occupational and behavioural therapy may be helpful in addressing many of the behavioural and cognitive issues.

Medications may be administered to manage aggression, anxiety, hyperactivity and poor attention span.

Early intervention and continuous education as well as support are key factors in helping those affected achieve their maximum potential and live independently in the community.