If the number increases to more than 200, then the child has a full mutation. All sons with a full mutation will be affected with FRAX. Daughters with a full mutation have about a 1 in 2 (50%) chance of being affected, but usually with fewer problems than boys.

Women who carry a full mutation:
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Sources of further information
Fragile X Society
w: www.fragilex.org.uk/
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t: 020 7188 1364, f: 020 7188 1369
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Your comments and concerns
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t: 020 7188 8801 (PALS) e: pals@gstt.nhs.uk
t: 020 7188 3514 (complaints) e: complaints2@gstt.nhs.uk

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What is FRAX?
FRAX is the most common cause of inherited (from a parent) learning disability. It affects boys and girls, and causes a wide range of problems with learning and behaviour, from mild to severe. Boys are usually more seriously affected than girls. FRAX is caused by an alteration in the FRAX gene that is part of the X chromosome.

What are genes and chromosomes?
Genes are the ‘instructions’ that make each of us individual and are important for normal health, growth and development. A complete set of our genes is found in each cell of our body. Genes are packaged in structures called chromosomes. Each chromosome contains about a thousand genes.

Humans have 46 chromosomes in most of the cells in the body, you get half in the egg from your mum and half in the sperm from you dad. They are arranged in 23 pairs numbered 1-22 according to their size. The two remaining chromosomes, X and Y, are called the sex chromosomes. Females have two X chromosomes. Males have one X chromosome (from their mother) and a Y chromosome (from their father). Genes and chromosomes are made of DNA that is made of four letters C, T, A and G.

What causes FRAX?
Within the X chromosome is a gene called FMR1. If a person has FRAX the FMR1 gene has been altered so that it contains too many repeated sections of DNA. It is called a ‘triplet repeat’ as the section of code reads: ‘CGG CGG CGG CGG’ many times.

We all have a certain number of these triplet repeats at the beginning of our FMR1 gene. What matters is how many times the code, CGG, is repeated. If the code is repeated too many times, the FMR1 gene fails to work properly.

If there are more than 200 repeats in a boy, then he will be affected with FRAX, and will have learning and/or behavioural problems. More than 200 repeats of the code is called a full mutation.

If the code is repeated more than 200 times in a girl, she may also be affected with FRAX. However, girls have a second (“spare”) X chromosome with a normal FRAX gene. This means that girls are protected from some or all of the effects of the 200 or more repeats on their other X chromosome.

What happened if someone has fewer than 200 repeats?
If ‘CGG’ is repeated 60-200 times, then that person is a carrier of a premutation. Males and females can be carriers of a premutation. A carrier shouldn’t have the learning and behavioural problems seen in FRAX. Men with a premutation may develop problems with balance (ataxia) as they reach their 50s or 60s. Women with premutations may have an early menopause (described as premature ovarian failure).

How is FRAX inherited?
FRAX is inherited when a woman with a FRAX premutation passes this chromosome on to her child. When this happens, the number of CGG repeats can increase so that the child inherits more than 200 repeats. It is this unpredictable nature of the premutation repeat that leads to the condition occurring.

Will a parent who carries or is affected with FRAX have an affected child?
This depends on three things:
- which X chromosome is passed on
- how many CGG repeats the parent has
- the sex of the parent.

The easiest way of understanding this is to think of men and women separately as described below.

For men
Men only have one X chromosome, and this is passed to each of their daughters. Their sons inherit their Y chromosome.

Men who carry a premutation are called normal transmitting males. Each of their daughters will inherit their father’s premutation, so all their daughters will be carriers of FRAX.

Boys who inherit a full mutation are all affected with FRAX. As it is uncommon for boys affected with FRAX to have children, we don’t know whether their daughters would all inherit the full mutation.

For women
Women can also be divided into two different groups:

Women who carry a premutation:
- each of their children have a 1 in 2 (50%) chance of inheriting their mother’s X chromosome which carries the premutation. When this happens, the number of CGG repeats often increases in the child.
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Fragile X syndrome (FRAX)
This leaflet gives information about what FRAX is, what causes it, and how it is inherited.
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