FXPOI Q & A

How is the FMR1 gene inherited?

- Both males and females can be FMR1 carriers and can pass the premutation on to their offspring.
- Male premutation carriers will pass the premutation on to all their daughters and none of their sons.
- Female premutation carriers have a 50 per cent chance in each pregnancy of passing the premutation on to their children of either gender.
- Only premutations carried by women can expand to the full mutations that cause fragile X syndrome.

What if I have FXPOI and want to get pregnant?

Your doctor may suggest fertility treatments or refer you to a reproductive endocrinologist for consultation and treatment. Assisted reproductive technologies such as using egg donation may be available.

If I have ovarian insufficiency and have never had Fragile X testing, what is the chance I am a premutation carrier?

If you have ovarian insufficiency the chance is 2–15 per cent that you are a Fragile X carrier. This range includes women who have relatives with ovarian insufficiency as well as those with no family history of Fragile X, intellectual disability or ovarian insufficiency.

How do I get tested for Fragile X?

Request the Fragile X (FMR1) DNA test, which can be arranged by your GP/family doctor, any physician or genetic counsellor.

For more information about testing, visit www.fragilex.org.uk and then click on "Testing".

www.fragilex.org.uk

About the Fragile X Society

The Fragile X Society was founded in 1990 to provide support and information to fragile X families, to raise awareness of fragile X and to encourage research into all aspects of fragile X. The Society offers support and information through its family support workers, website, bi-monthly newsletters and other publications. It also organises annual conferences and supports research through the participation of its family members in fragile X studies.

For more information on FXPOI and other topics related to Fragile X, email: info@fragilex.org.uk or telephone 01371 875100

Other resources: The Daisy Network, a registered charity for women who have experienced a premature menopause/premature ovarian failure. www.daisynetwork.org.uk

Special thanks for assistance on this leaflet to: The National Fragile X Foundation

Photography by kind permission of the fragile X families whose photographs appear.

Additional copies of this leaflet available free of charge.

The FragileX Society
helping fragile X families

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FXPOI

Fragile X-Associated Primary Ovarian Insufficiency (FXPOI)

An Introduction for Individuals, Families and Healthcare Providers

The FragileX Society
helping fragile X families

What is Fragile X?

Fragile X is associated with changes in the Fragile X gene, which is on the X chromosome. The Fragile X gene (also known by its scientific name of "FMR1") can be normal, but it can also exhibit a "premutation" or "full mutation". When a premutation or full mutation is present, it can result in a Fragile X condition. These include:

- **Fragile X syndrome (FXS):**

  An inherited condition affecting intellectual, behavioural, language and social development. It occurs in both males and females who have a full mutation of the FMR1 gene.

- **Fragile X-associated primary ovarian insufficiency (FXPOI):**

  A condition affecting ovarian function that can lead to infertility and early menopause. It occurs in some adult females who have a premutation of the FMR1 gene. These individuals are also referred to as "carriers".

- **Fragile X-associated tremor/ataxia syndrome (FXTAS):**

  An adult onset (over 50 years of age) neurological condition causing tremor, memory difficulties and balance problems. It occurs in some older adult carriers (more commonly male) who have a premutation of the FMR1 gene.

The FMR1 Gene

The FMR1 gene can undergo changes which cause these fragile X conditions. These changes affect a pattern of DNA called CGG repeats. Typically, the FMR1 gene has up to about 54 CGG repeats. A premutation in the FMR1 gene results in approximately 60–200 CGG repeats, and a full mutation in 200 or more.

www.fragilex.org.uk

Fragile X-Associated Primary Ovarian Insufficiency (FXPOI) & Premature Ovarian Failure (POF)

FXPOI is a condition in which women have decreased or abnormal ovarian function. This can result in infertility or "subfertility", irregular or absent menstrual cycles, premature ovarian failure (POF) with associated early menopause or abnormal hormone (FSH) levels.

POF is defined as the cessation of menstrual periods before age 40. It is at the severe end of the FXPOI spectrum. Women who are not Fragile X carriers can also experience primary ovarian insufficiency (POI) or premature ovarian failure (POF) due to other causes.

FXPOI and Menopause

While FXPOI mimics menopause in some of its symptoms, such as "hot flushes" and vaginal dryness, it is not the same as menopause. It differs in at least two significant ways:

- Women with FXPOI occasionally do get pregnant, because their ovaries may function to release eggs. Women who have completed menopause cannot get pregnant because their egg production has ceased.
- Women with FXPOI can experience a return of menstrual periods. Women who have completed menopause do not.

Risk Factors

Studies show that approximately 20–25 percent of women with a Fragile X premutation experience FXPOI.
In addition:

- Women with a premutation often go through menopause an average of five years earlier than non-carriers.
- Because of the decrease in hormone levels that accompanies this condition, women with FXPOI are at risk for osteoporosis at an earlier age than non-carriers.
- Women with a premutation cannot assume a reduction or absence of fertility; therefore, those who don't wish to become pregnant should take steps to prevent it.
- Women with a premutation are at risk of having children with fragile X syndrome, which can cause varying degrees of intellectual disability, social and language issues and behavioural challenges (see www.fragilex.org.uk).
- Because of their risk of FXPOI, women with a premutation who want to use preimplantation genetic diagnosis (PGD) with in vitro fertilisation (IVF) to have a baby unaffected by fragile X syndrome are usually required to have an ovarian reserve test (known as the FSH test) to identify their suitability for PGD with IVF.
- Women with a premutation may be at risk of developing FXTAS, though it is more common in male carriers. To date, the risk in women appears relatively low.
- Relatives of carriers may also have the premutation. If so, they face the same risks listed here.