FRAGILE X INFO SERIES:
FEMALES AND FRAGILE X

NATIONAL **FRAGILE X** FOUNDATION

Overview

Fragile X is a group of conditions associated with changes in the Fragile X gene – called FMR1 and located on the X chromosome. The FMR1 gene can undergo changes, when inherited, which affects a pattern of DNA called CGG repeats. Typically, the FMR1 gene has up to 54 CGG repeats, though the range between 45 – 54 repeats, is called the intermediate or gray zone. A premutation carrier has 55–200 CGG repeats, and someone with a full mutation has more than 200 CGG repeats.

When a premutation or full mutation is present, it can result in a Fragile X-associated Disorder (FXD). These include:

- Fragile X syndrome (FXS): A condition affecting intellectual, behavioral, and social development. It occurs in both males and females who have a *full mutation* of the FMR1 gene.
- Fragile X-associated tremor/ataxia syndrome (FXTAS): An adult onset (over 50 years of age) neurological condition, seen in males and females, but more common and more severe in some male *premutation carriers*. It can cause tremors, memory, and balance issues.
- Fragile X-associated primary ovarian insufficiency (FXPOI): A condition affecting ovarian function that can lead to infertility and early menopause in some female *premutation carriers*.
- Other issues may be present in *premutation carriers*, and this is an ongoing area of study for researchers.

Females with a Full Mutation

Females with a full mutation exhibit a wide range of characteristics, though they usually have milder symptoms than males with a full mutation. This is because females have two X chromosomes (males have only one), and the unaffected X chromosome can often compensate to varying degrees for the one with the Fragile X mutation.

Physical Characteristics

Girls are much less likely than boys to exhibit physical characteristics of Fragile X. Many have no noticeable physical differences. Of those who do, the most common features are:

- Slightly prominent ears
- Highly flexible finger joints, wrists, or elbows
- Flat feet

Cognitive Characteristics

Females with a full mutation range from having very mild to moderate learning difficulties.
The most common challenges are in:

- Visual-spatial abilities like reading maps and graphs
- Executive functioning (the ability to formulate, execute, and carry out a plan)
- Mathematics

Behavioral Characteristics

Females with a full mutation can exhibit behavioral or social challenges that include:

- Attention/concentration difficulties (or ADHD)
- Shyness or social anxiety
- Difficulty in picking up “social cues

Emotional Issues

Females with a full mutation are at increased risk to experience anxiety. Mood swings and depression may be present—often most acutely during adolescence. Medication, counseling, and other interventions may help address these issues. Consultations with family physicians and experts with experience in FXDs can be important in obtaining the assistance a person needs.

A small percentage of females who have the full mutation will have no apparent signs of the condition—physical, cognitive, behavioral, or emotional. These females are often identified only after another family member has been diagnosed.

For more information:
Uniqueness of Females with FXS
https://fragilex.org/fxs/uniqueness-females-fragile-x-syndrome/

Females with Premutation

Females with a premutation are at risk to have a child, male or female, with Fragile X syndrome. The magnitude of this risk is related to the number of CGG repeats identified in her FMR1 gene. The larger the number, the higher the risk for expansion from a premutation to a full mutation if it is passed on.

Approximately 20-25% of women with a premutation experience FXPOI, which is characterized by infertility, decreased ovarian function, early menopause, or irregular cycles.

FXTAS is another medical effect of the premutation. It is more common in male carriers, but has been reported in about 5-8% of female carriers over the age of 50.

Some women with a premutation have reported increased general anxiety, shyness, and social anxiety. In addition, there is evidence that women with the premutation are at increased risk for depression.

For more information:
What Defines a Carrier
https://fragilex.org/genetics/what-defines-a-carrier/

Other Considerations

- Women with a full mutation are not at risk for FXPOI and have no associated infertility.
- Genetic counseling is recommended for any woman with a Fragile X premutation or full mutation. This can allow for discussion of pregnancy issues, reproductive options including prenatal testing, use of egg donor or IVF, and other options.
- Some women with a full mutation have only mild or no effects and may not even know their status. Testing to determine whether a full mutation or premutation exists is recommended for any adult woman who may be at risk to be a premutation carrier. This includes women with a personal or family history of intellectual disability, FXS, FXTAS or infertility.

About the NFXF

The National Fragile X Foundation (NFXF) was founded in 1984 to support individuals with Fragile X syndrome (FXS), their families, and the professionals who work with them. Today, it is a comprehensive resource not only for FXS, but also for the conditions of Fragile X-associated tremor/ataxia syndrome (FXTAS), Fragile X-associated primary ovarian insufficiency (FXPOI), and other premutation carrier conditions and disorders. The NFXF is dedicated to serving the entire Fragile X community to live their best lives by providing the knowledge, resources, and tools, until, and even after more effective treatments and a cure are achieved. Learn more at and more at *https://fragilex.org/welcome*

If you have questions please reach out to us at **treatment@fragilex.org** or call **(800) 688-8765**.