Fragile *WHAT?*

By Mary Beth Langan and Sally Nantais

Although Fragile X Syndrome is the most common known cause of inherited cognitive impairment, the up-to-date name for mental retardation, the average person has not heard of Fragile X Syndrome. The average health professional has very little knowledge, or dated knowledge, of Fragile X Syndrome. Until our children were diagnosed, we were average people asking, "Fragile *what*?"

Cognitive impairment related to Fragile X Syndrome affects probably one in 4,000. However, because more milder learning difficulties are probably much more common, it is estimated that one in 2,000 are affected.

Approximately 1 in 100 to 200 women and 1 in 800 men are carriers of Fragile X Syndrome.**

It's critical to remember these numbers are only estimates because it is also estimated that 80-90% of people with FXS are not yet correctly diagnosed.

Fragile X Syndrome is a genetic condition caused by a mutation of the FMR1 gene on the X chromosome. The mutation can differ from person to person, typically a boy with a full-mutation's genetic material does not produce FMR1 protein, or not enough of it. Through research, it has been determined that the FMR1 protein is critical for typical brain development. Boys only have one X chromosome, therefore they are typically more affected than girls. Girls have an advantage because they have two X chromosomes; an unaffected chromosome may produce enough FMR1 limiting the affect.

What does this really mean?

Unless a parent already knew they were a carrier of Fragile X Syndrome (FXS), they wouldn't know their child might have FXS until they began to see developmental delays. There are minor physical traits noted in many persons with FXS, but not in all. These are traits which may also be present within the typical population, nothing unique which would necessarily indicate FXS testing is necessary for your child.

Fragile X Syndrome may cause:

- Mild learning problems to severe cognitive impairment
- Behavior issues such as ADHD and ADD
- Autistic-like features such as poor social skills, poor eye contact, hand-biting and hand-flapping
- Shyness and social anxiety

The majority of persons with FXS have autistic-like features (estimated at 50–90%); a smaller percentage (approximately 30%) have a true dual diagnosis of autism.

Within the first few years in the life of a child with undiagnosed FXS, two of the most common things parents often notice are language delays and sensory issues. Even after a diagnosis of FXS, many parents believe working on these issues are the most important methods to help their child be the best they can be.

In recent years, research has also discovered that Fragile X Syndrome (FXS) not only affects children with a full mutation, but also male and female carriers of FXS.

- Fragile X-associated Tremor/Ataxia Syndrome (FXTAS), discovered in 2001, is a neurological disorder that can involve tremors, balance irregularities, difficulty walking and dementia which sadly is often misdiagnosed as Parkinson's and/or Alzheimer's. This condition is present in some older FXS carriers (typically after the age of fifty), usually in males but FXTAS can also affect female carriers.
- Premature Ovarian Failure, more commonly known as early menopause, is a condition that affects 20-28% of the female FXS carrier population.

Who should test for Fragile X Syndrome?

According to the American College of Medical Genetics (revised 2005), individuals for whom testing should be considered:

Fragile X Syndrome:

Individuals of either sex with mental retardation, developmental delay, or autism, especially if they have (a) any physical or behavioral characteristics of fragile X syndrome, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation. Individuals seeking reproductive counseling who have (a) a family history of fragile X syndrome or (b) a family history of undiagnosed mental retardation.

Ovarian dysfunction:

Women who are experiencing reproductive or fertility problems associated with elevated follicle stimulating hormone (FSH) levels, especially if they have (a) a family history of premature ovarian failure, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.

Tremor/ataxia syndrome:

Men and women who are experiencing late onset intention tremor and cerebellar ataxia of unknown origin, especially if they have (a) a family history of movement disorders, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.

Testing criteria is specific, yet as parents of first generation children with Fragile X Syndrome, we often question statements like "male or female relatives with undiagnosed mental retardation." Until our children were born, no one in our families fit this description.

What is the most important reason for testing for Fragile X Syndrome?

Test for Fragile X Syndrome (FXS) to obtain a diagnosis or to rule it out. If you don't have what may be the correct diagnosis of FXS, then you will never be aware of improved treatments or the cure when it's found.

Within our lifetime, quite possibly within the next 10-20 years, we believe there will be a cure. With a diagnosis of Fragile X Syndrome, there is hope. After all, they are just one gene away from a cure.

When testing for Fragile X Syndrome, it is critical that the correct blood tests are ordered – the Fragile X DNA (Southern Blot) and Polymerase Chain Reaction (PCR) tests. Inaccurate results occur far too often with the generic chromosomal panel.

If you would like to learn more about Fragile X Syndrome, go to fragilex.org for the National Fragile X Foundation or fraxa.org for the FRAXA Research Foundation.

July 22 is Fragile X Awareness Day. Our hope is that this time, next year, we won't hear "Fragile *what*?" as often, at least we'll know you won't be asking "Fragile *what*?"

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