



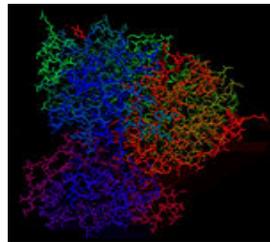
## The Learning Curve

*“Enhancing the Knowledge of DDDS Professionals”*

### Facts About Fragile X Syndrome ...

(Article adopted from Child Development Institute, LLC).

Fragile X syndrome is the most common genetically-inherited form of mental retardation currently known. In addition to intellectual disability, some individuals with Fragile X display common physical traits and characteristic facial features, such as prominent ears. Children with Fragile X often appear normal in infancy but develop typical physical characteristics during their lifetime. Mental impairment may range from mild learning disability and hyperactivity to severe mental retardation and autism. This genetic syndrome is caused by a defect on the X chromosome. Because of scientific advances, improvements in genetic



testing, and increased awareness, the number of children diagnosed with Fragile X has increased significantly over the last decade.

A substantial research effort led to the 1991 discovery of FMR-1 (Fragile X mental retardation), the gene that when damaged causes Fragile X. Although the normal function of the FMR-1 gene is not fully understood, it appears to be important early in development. The mechanism by which the normal FMR-1 gene is converted into an altered, or mutant, gene capable of causing disease symptoms involves an increase in the length of the gene. A small region of the gene, CGG, undergoes repeated duplications, forming deoxyribo-

nucleic acid (DNA) repeats that result in a longer gene. The lengthened DNA region is susceptible to a chemical modification process called DNA methylation. When the number of repeats is small (less than 200) the individual often has no signs of the disorder. However, in individuals with a larger number of repeats, the characteristics that are typical of Fragile X are observed. In families that exhibit Fragile X, both the number of repeats and the length of the chromosome increase with succeeding generations. The severity of the symptoms increases with the increasing length of the repeated region.

Fragile X exhibits X-linkage. The effect of X-linkage is that the frequency of the syndrome is greater in males than in females. To understand the mechanism of X-linkage some background information on the organization of human chromosomes is needed. Human females typically have two X chromosomes, and human males have one X and one Y chromosome. A female who inherits a chromosome carrying the Fragile X gene from either parent is likely to inherit a normal X chromosome from the other parent. The normal X chromosome could provide the normal gene function and mask the presence of the Fragile X gene in a female. In that case, the female would still possess the Fragile X gene and be capable of passing it on to her offspring, but she would not exhibit symptoms. She would be a "carrier." On the other hand, a male who inherits the Fragile X gene from his mother would inherit a Y chromosome and not a normal X chromosome from his father, and therefore a male with one copy of the gene is likely to show symptoms.

#### Inheritance

In normal individuals the FMR-1 gene is passed on, in stable fashion, from the parent to the offspring. In Fragile X individuals, the repeated sequences not only expand abnormally, but are unstable and the degree of impairment in offspring may vary. The Fragile X mutation appears to increase in length as it is inherited by succeeding generations. This phenomenon is known as "genetic anticipation." Eventually, the mutation reaches a critical number of repeats and causes Fragile X

syndrome. For example, a male may have normal IQ, no Fragile X symptoms, and a short region of DNA repeats at the Fragile X region of his X chromosome. This individual, called a "transmitting" male, may have a daughter with 50 to 200 repeats. At that stage the condition is considered a "premutation," as there still may be no apparent symptoms. This daughter, a "carrier," might have a son with 1,000 repeats and the full blown Fragile X syndrome. If a woman is a carrier, each of her children has a 50 percent chance of inheriting her Fragile X gene. Each time her Fragile X gene is inherited, it is likely to have expanded in length. A daughter who inherits the gene will be a carrier with some chance of impairment; a son who inherits the gene has an 80 percent likelihood of developing Fragile X syndrome.

#### Testing for Fragile X Carrier

A simple test is now available that can determine if a woman is carrier of the Fragile X gene. A drop of blood can be taken from the woman's finger and analyzed quickly

Volume 2, Issue 2  
September 8, 2008

A Publication of the Office of  
Training and Professional  
Development

#### Did you know that...

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#### Fragile X Syndrome (FXS) Facts

- Fragile X can be passed on in a family by individuals who have no apparent signs of this genetic condition.
- The observable characteristics of Fragile X occur in approximately 1 in 1,000 male births and 1 in 2,500 female births.
- FXS, the most common cause of inherited mental impairment. This impairment can range from learning disabilities to more severe cognitive or intellectual disabilities.
- FXS is the most common known cause of autism or "autistic-like" behaviors.
- Fragile X-associated tremor/ataxia syndrome (FXTAS), a condition which affects balance, tremor and memory in some older male gene carriers.
- Fragile X-associated primary ovarian insufficiency (FXPOI), a problem with ovarian function which can lead to infertility and early menopause in



The National Fragile X Foundation

The National Fragile X Foundation (NFXF) has been helping individuals with Fragile X, their families, and the professionals who work with them, since 1984. The NFXF is committed to keeping the Fragile X community well informed. To find a genetic counselor in your area log on to [www.NSGC.org](http://www.NSGC.org) or call the genetic specialist at the National Fragile X Foundation at 1-800-688-8765.

and inexpensively. If a woman who is found to be a carrier is pregnant, she can arrange for testing of the fetus, as described below. For a woman with a family history of retardation, testing before pregnancy will help determine if she is at risk.

### Prenatal Testing

Three prenatal tests can determine if Fragile X is present in the fetus. Chorionic villi sampling (CVS) involves extracting a tiny amount of fetal tissue at 9 to 11 weeks of pregnancy. CVS is not widely used and carries a 1-2 percent risk of miscarriage following the procedure.

Amniocentesis is the removal and analysis of a small sample of fetal cells from the amniotic fluid. Amniocentesis is widely available and involves a lower risk of miscarriage. However, amniocentesis cannot be done until the 15th to 18th week of pregnancy and it usually takes an additional 2 to 4 weeks for the cells to grow and be analyzed. So a woman may have to wait until the 17th to 22nd week of her pregnancy to have the results of this test.

The third method, percutaneous umbilical blood sampling (PUBS), is the most accurate method and can be used to confirm the results of CVS or amniocentesis. However, PUBS is not done until the 18th to 22nd week and carries the greatest risk of miscarriage.



### Diagnosing and Treating Fragile X Syndrome

Individuals with Fragile X may have a cluster of physical, behavioral, mental, and other characteristics. These symptoms may vary in number and degree among affected children. In the best of circumstances, early identification of a child with Fragile X and subsequent treatment involves a team of professionals. These might include a speech and language pathologist, an occupational therapist (perhaps even a specialist in sensory integration), a physical therapist, a special education teacher, a genetics counselor, and a psychologist.

### Physical Characteristics

Males with Fragile X have some common physical characteristics: a long narrow face; large or prominent ears; and macroorchidism (enlarged testicles). More than 80 percent of males with

Fragile X develop at least one of these features, but often not until after puberty. Other physical characteristics of males with Fragile X are double-jointed fingers, flat feet, puffy eyelids, and "hollow chest." These physical features may indicate an underlying abnormality of the connective tissue.

Females with Fragile X syndrome do not exhibit most of the physical characteristics found in males with Fragile X, although they often have large or prominent ears.

### Behavioral Characteristics

The most prevalent behavioral characteristics of children with Fragile X are attention problems and hyperactivity, known as attention-deficit hyperactivity disorder (ADHD). ADHD is frequently treated with medication, generally central nervous system stimulants such as Ritalin®, Cylert® and Dexedrine®. Because these drugs have side effects that include irritability and poor appetite, alternatives such as amantadine and clonidine may be appropriate. Amantadine has been used with surprising success to treat hyperactivity and attention difficulties in children with low IQs, for whom stimulants are generally less effective.

Fragile X children with ADHD may benefit from the addition of tricyclic antidepressants or a major tranquilizer such as Mellaril®. Because mood swings and temper tantrums present major difficulties for children with Fragile X, psychotherapeutic medications such as Lithium and more recently Prozac® have helped control aggression and outbursts. Anticonvulsants are used if seizures are present, can also help treat behavior problems, including aggression in males with Fragile X.

Children with Fragile X have strong reactions to changes in their environment, and their heightened anxiety can compound their behavioral difficulties. They appear to have an underlying disability related to processing external stimuli, called sensory integration. Extreme hypersensitivity to their environment makes it difficult for them to screen out stimuli such as noise, lights, or odors. This, in turn, often provokes emotional outbursts or tantrums.

Some of the other behaviors associated with Fragile X are similar to those of autism, including hand flapping, hand biting, poor eye contact, and tactile defensiveness (responding negatively to being touched). However, one strength of males with Fragile X is their great sociability and friendliness, in contrast to autistic children, who appear unable to relate to others. Researchers recommend that autistic children be screened for Fragile X.

### Mental Impairment

Mental retardation associated with Fragile X is similar to that of Down syndrome in that most of those affected fall somewhere in the middle range of impairment. There are differences between males and females with Fragile X with respect to their mental impairment. There are differences between males and females with Fragile X with respect to their mental impairment.

Many females with Fragile X syndrome are learning disabled in math, but perform exceptionally well in reading and spelling. In addition, one-third of females with Fragile X have mental disabilities similar to those associated with schizophrenia, such as dependence on odd forms of communication and preference for social isolation. Males with Fragile X appear to differ in mental development from both females with Fragile X and children with other kinds of developmental delays who exhibit learning disabilities. Males with Fragile X may actually achieve more than some other developmentally disabled children with higher IQ scores. It is important for educators to understand the particular difficulties of males with Fragile X. They appear to process information in simultaneous fashion; this causes difficulty when they are taught skills that require sequential processing of information, such as reading. For males with Fragile X, learning often involves seeing the whole in order to understand the parts.

### Speech, Language, and Learning Disabilities

Speech and language present special difficulties. Children with Fragile X often speak in rapid bursts or repeat words (called echolalia). For males with Fragile X, the primary language difficulty is perseveration. Perseveration is the inability to complete a sentence because of continuous repetition of words at the end of a phrase. Another language-based behavior displayed by males with Fragile X is talking inappropriately and incessantly about one topic. This particular difficulty distinguishes males with Fragile X from individuals with other forms of mental retardation or autism. Speech problems are made worse in situations where the child must have eye contact with another person or when the child becomes anxious, leading researchers to suspect some underlying relationship between difficulties with language and difficulties with sensory processing.

### Medical Problems

Although most children with Fragile X do not have serious physical problems, they are at greater risk for certain types of moderate medical problems than are normal children. For example, they often suffer recurrent otitis media (inner ear infections), which should be treated as early as possible to prevent it from becoming a source of language difficulties. Common eye problems include myopia (nearsightedness) and

a high incidence of "lazy eye." Orthopedic difficulties related to flat feet and joint laxity may occur. Twenty percent of males with Fragile X are prone to seizures. In addition, many children with Fragile X have digestive disorders, such as gastroesophageal reflux, that causes gagging, regurgitation, and discomfort.



### Education of Children with Fragile X

Even at a young age, children with Fragile X tend to be good at imitation and to be very social. Consequently, they can benefit immensely from early intervention programs and prolonged contact with children who are developing normally. Congressional legislation (Public Law 99-457) mandates early intervention services for children with developmental delays, ages 3 to 5 years; in some states this includes younger children.

Parents and educators should be aware that many children with Fragile X achieve above the level that would have been predicted from measured IQ, and it is important for parents and educators to help these children reach their maximum potential. Children with Fragile X with an IQ above 70 generally do best when mainstreamed into a well-organized classroom environment with individualized help from special education experts and other professionals. Cooperative instruction, using peers to help teach, often relieves some of the stress of the classroom environment and the teacher-child relationship.

### Additional Therapies

To counter the sensory integration difficulties of children with Fragile X, a wide range of strategies has been employed. Minimizing exposure to noise and odors may prevent over stimulation. Therapeutic calming techniques, such as music therapy, can also be used. It may be helpful to make special efforts to provide structure in the immediate environment and in day-to-day activities. Children with Fragile X often develop their own routines. Occupational therapists specializing in sensory integration therapy can work with

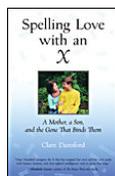
children with Fragile X to help them organize environmental stimuli and to improve their response to formal education.

The strength of their visual memory means that children with Fragile X process information better when they are presented with whole pictures rather than when information is presented orally or sequentially, as in normal reading. As a result, use of pictures, message boards, calculators, and other visual devices may be helpful. Some children with Fragile X learn sign language, a visual system. Computer software is now available for learning basic concepts in language and math using high-interest visual themes.

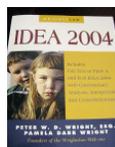
Psychology professionals warn against the tendency to assume that all characteristics of a child with Fragile X stem directly from the Fragile X syndrome. The emotional difficulties of an individual with Fragile X may include insecurity and anxiety related to having a disability.

These strategies are only a few that specialists have developed to help children with Fragile X. Parents and other individuals working with these children should make use of their assets, such as their positive outlook on life and love of other people. Children with Fragile X should be encouraged to express their feelings openly even when they have difficulty using words.

### FRAGILE X RESOURCES— Books, Videos, and Websites:



**Spelling Love with an X: A Mother, a Son, and the Gene That Binds Them** (2007) Clare Dunsford draws on poetry and science to reflect on her life with J.P. and to illuminate his metaphoric way of communicating.



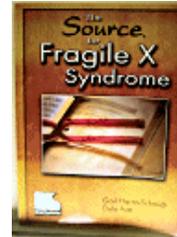
**Wrightslaw: 2004** (2006) Peter and Pamela Wright, founders of the Wrightslaw Web site. This is an invaluable resource for every parent that has a child in special education.



**Educating Children with Fragile X Syndrome** (2004) Edited by Denise Dew-Hughes in Association with the Fragile X Society, UK. This book benefits from the expertise of an international field of researchers, whose variety of perspectives contribute to their unique, multi-professional approach.



**X Stories: The Personal Side of fragile X syndrome** (2006) Charles Luckmann and Paul Piper have added greatly to the growing body of literature about living with fragile X.



**The Source® for Fragile X Syndrome** (2004) by Gail Harris-Schmidt, Ph.D. and Dale Fast, Ph.D. An excellent book for explaining the nature of fragile X, its effect on speech-language development and related issues.

### Online Video to Understanding Fragile X syndrome...

*Please see this Centers for Disease Control Prevention (CDC) brief video about what causes Fragile X syndrome (FXS).*

[Click here to view a video about what causes fragile X syndrome](#) (Press CTL + Click on Mouse to view) [\[transcript of video\]](#)

### HELPFUL WEBSITES RESOURCES:

[Conquer Fragile X Foundation \(CFXF\)](#) Promotes the development of international fragile X research collaborations to increase the capacity and skills of fragile X labs and researchers around the world.

[Fragile X Research Foundation \(FRAXA\)](#) The Fragile X Research Foundation supports families affected by fragile X and raises awareness of the disease.

[National Fragile X Foundation \(NFXF\)](#) The National Fragile X Foundation is an organization that unites the fragile X community through educational and emotional support and referral networks. NFXF promotes public and professional awareness.

[National Institute of Child Health and Development - Families and Fragile X Syndrome](#) (NICHD) is a research agency that is part of the National Institutes of Health. This site provides some general information about fragile X syndrome, its causes, its features, and its treatments.

[Univ. of Calif., Davis - Medical Investigation of Neurodevelopmental Disorders \(MIND\) Institute - Fragile X Research and Treatment Center](#) An international research organization focusing on neurodevelopmental disorders. The Fragile X Research and Treatment Center was established at the M.I.N.D. Institute in 2001.