GENETIC COUNSELING: ISSUES AND INFORMATION

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When one is scheduled to meet with a genetic counselor, a number of questions may be raised:

- What does a genetic counselor do?
- Why do I need to meet with the genetic counselor?
- What do I do with the genetic counselor?
- What should I tell the genetic counselor?
- What can the genetic counselor tell me?

A genetic counselor is a professional who works with the family and the physician to obtain a detailed family history and to explain the genetic inheritance pattern, reproductive options, and genetic testing related to the diagnosis. The genetic counselor provides you, as a family member, with professional and emotional support as needed. Because of the role the genetic counselor plays with the physician in giving and receiving information, it is important for you and your family members to meet with a genetic counselor.
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When meeting with a genetic counselor, you will be asked to give information regarding the medical history of other family members (including children, parents, brothers and sisters, aunts and uncles, cousins, nieces and nephews, grandparents). Information will be shared regarding the genetic implications of the diagnosis such as identifying other family members who are at risk to have inherited the gene mutation and who may need to be contacted regarding testing. The genetic counselor will answer your questions and address your concerns.

A genetic counselor is a communicator and is trained to receive and give information in a way that can be understood by you. A genetic counselor is sensitive to you and is in a position to be of help to you. The information shared in a genetic counseling session is confidential.

GENETIC COUNSELING FOR FRAGILE X SYNDROME

When your child is diagnosed as carrying the gene mutation for fragile X syndrome, you will be referred to a genetic counselor. Often the first contact with the genetic counselor will be by telephone. In this initial contact, the discussion may center around an overview of the clinical findings associated with fragile X syndrome, a brief explanation of the testing procedure and result, and what the diagnosis means for you, your child and for other family members. A meeting with both the genetic counselor and a physician will be scheduled for you and your child. You may wish to have other concerned family members join you during this meeting.

The genetic counseling process for fragile X syndrome is one that touches on many different areas and the session is structured so that information can be shared between you and the genetic counselor. The session may begin with an overview of your understanding of fragile X syndrome, your concerns, and the questions you would like addressed during the genetic counseling session. Then, the genetic counseling session will proceed to cover several different areas. A detailed discussion regarding the clinical findings associated with fragile X syndrome will take place and information regarding the specific findings related to your child will be obtained. The genetic counselor will also review in depth with you the testing that was performed on your child and help you to understand the result and the implication of this testing. You will be introduced to such new concepts as: **chromosomes, fragile site, FMR-1 gene, CGG repeats, methylation, and FMRP.** You will be amazed at how quickly you will master these words and

concepts. Also at this time, information will be obtained from you about yourself and other family members. The emphasis will be upon identifying those in your family who carry the fragile X gene mutation and who may or may not be experiencing difficulties associated with it's presence. As you and the genetic counselor review the family information, you will be able to increase your knowledge regarding the X- linked inheritance pattern of the fragile X gene mutation. During the genetic counseling session, you will also learn about the prenatal testing options that are available to you and to other family members who also carry the gene mutation. Finding out that you carry the fragile X gene mutation does **NOT** mean that you cannot have children without the gene mutation. From your meeting with the genetic counselor, you may also obtain information regarding interventions that are available to enhance the developmental potential of your child. The information shared during the genetic counseling session is reviewed and used by the physician in the clinical evaluation of your child.

You may wish to stay in contact with the genetic counselor after the initial meeting as the genetic counselor can help you as you move through the various stages of coping with the diagnosis. The genetic counselor can also provide you with continuing information that will be of help to you and the professionals in your area who are working with your child. Additionally, the genetic counselor can work with you and other family members in explaining the fragile X syndrome diagnosis and coordinating testing throughout the family.

If you or a family member are planning a pregnancy or find that you are pregnant, then it is often the genetic counselor that is contacted. The genetic counselor has the resources to determine who is at risk to have a child affected with fragile X syndrome, to refer you or your family member to appropriate testing sites or to help arrange testing, to interpret and explain testing results, and to support you or your family member through the prenatal process.

FRAGILE X SYNDROME - GENETIC OVERVIEW

Fragile X syndrome derives its name from the presence of an unusual chromosomal finding called the **"fragile site"**. Specifically, the fragile site describes a portion of chromosomal material located on the bottom of the X chromosome, which when chromosomes are prepared for chromosome analysis using specific chemicals appears as though it is hanging by a thread from the main body of the chromosome. Chromosome testing was used in the past to diagnose an individual with fragile X syndrome. Chromosome testing for fragile X syndrome was an imprecise test and is no longer used to make the diagnosis of fragile X syndrome.

The fragile X gene is known as the **Fragile X M**ental **R**etardation-**1** (**FMR-1**) gene. Everyone has the **FMR-1** gene on his or her X chromosome. People who are unaffected with fragile X syndrome but are known to carry the gene mutation (mutation = change) are carriers of the FMR-1 gene **premutation.** People who are affected with fragile X syndrome have the FMR-1 **full mutation**.

Fragile X syndrome is inherited in an X-linked fashion. This means that the fragile X gene mutation is carried on one of the chromosomes called the X chromosome. A woman has two X chromosomes. One X chromosome is inherited from her mother and the other X chromosome is inherited from her father. A woman is considered to be a **carrier** if the FMR-1 premutation is present on one of her X chromosomes. Carriers usually do not have the characteristic features of the condition. However, if a woman has the FMR-1 full mutation on one of her X chromosomes, then she is at risk to have physical characteristics, as well as cognitive and emotional difficulties related to the presence of the FMR-1 full mutation. Women with the full mutation are often less affected than their male counterparts, as the effects of the FMR-1 gene are "covered up" by the FMR-1 gene on their other X chromosome. Children of women who carry the FMR-1 gene mutation are at a 50% risk to inherit the FMR-1 gene mutation from their mother. Since the gene mutation expands as it passes from mother to child, a woman carrying the FMR-1 gene mutation is at an increased risk to have an affected child.

Males have one X chromosome inherited from their mother and one Y chromosome inherited from their father. A male who inherits the FMR-1 full mutation on his X chromosome will be affected with fragile X syndrome. Approximately 20% of males inherit the FMR-1 premutation and are called normal transmitting males (NTM's) because they are intellectually normal. Importantly, all males who carry the FMR-1 gene mutation will pass the gene premutation onto **all** of their daughters, but **none** of their sons will inherit the gene mutation.

In May 1991, a new test using molecular DNA analysis became available to diagnose individuals who carry the FMR-1 gene mutation. This test is the FMR-1 gene test and is 99+ % accurate in revealing who does or does not carry the FMR-1 gene mutation. The FMR-1 gene test looks at two specific areas of the FMR-1 gene and is accurate in reporting the number of **CGG repeat** sequences within the gene and the **methylation** status. If an individual has 40 or less CGG repeat sequences, then that individual does not have the FMR-1 gene mutation. If an individual has 60 - 200 CGG repeat sequences, then that individual has the premutation. If an individual has more than 200 CGG repeat sequences, then that individual has the full mutation. Methylation refers to the process whereby the gene is turned on or off. If methylation is present, then the gene is turned off and no FMR-1 protein will be made.

The FMR-1 protein is known as **FMRP**. FMRP is not a protein that is found in one's diet, but is instead a specific protein product of the FMR-1 gene. FMRP has many important functions within the cell. These functions particularly impact the way the brain cells work and when FMRP is not present in the brain the result is mental retardation. Current research is focused on learning more about FMRP with the goal being one of specific medical treatment for fragile X syndrome. With any genetic diagnosis, it is important to remember that everyone has 6 to 8 genes that have the potential to cause problems. In some families, one of these genes is the FMR-1 gene. Identification of the FMR-1 gene mutation and diagnosis of fragile X syndrome leads to specific interventions and treatment for those affected with fragile X syndrome and gives other family members reproductive options that would not have been available to them had the diagnosis not been made.

If someone in your family is suspected of having, or has been diagnosed with fragile X syndrome, it is important for you to contact a genetic counselor in your geographic area for further information. Or you are welcome to contact the author at the UC Davis M.I.N.D. Institute Fragile X Care Program (916) 734-8266.ies with children. *Psychopharmacol Bull*, special issue. pp. 24-84, 219-222.

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