

Key Questions about Clinical Genetic Testing for Dilated Cardiomyopathy

Clinical Genetic Testing for Dilated Cardiomyopathy *Information for patients – what you need to know.*

Why clinical genetic testing? You may be offered clinical genetic testing because you or a family member has been diagnosed with dilated cardiomyopathy (DCM), which is a weakening of the heart muscle and enlargement of its pumping chambers. DCM that occurs in families is called familial dilated cardiomyopathy (FDC). Causes of DCM/FDC include mutations in several different genes. DCM is commonly accompanied by conduction system disease which can cause heart rhythm disturbances (arrhythmias), such as atrial flutter or atrial fibrillation, heart block, and other atrial or ventricular arrhythmias, some of which may require treatment with a cardiac pacemaker or implantable cardiac defibrillator. Mutations in some DCM genes (e.g., lamin A/C) may cause prominent conduction system disease before or as the heart muscle weakens.

What is the chance that I carry a DCM gene mutation? This depends on 1) if you have DCM, 2) If you have a family member with known or suspected DCM, and 3) if a DCM gene mutation has been identified in your family. Almost all mutations in DCM genes are transmitted in an autosomal dominant manner. This means that a person with a gene mutation has a 50% chance of passing it on to his or her children. Therefore each first degree relative (parent, child, sibling) of a person with a mutation has a 50% chance of also having the mutation. It also means that only one of the two copies of the gene needs to be mutated to cause disease.

Why consider clinical genetic testing for dilated cardiomyopathy or other heart issues? Genetic testing may be helpful in determining the cause of a patient's dilated cardiomyopathy. Obtaining a clear diagnosis can help your doctor know how to care for you and your heart. If you don't have dilated cardiomyopathy but are experiencing another heart problem (such as an arrhythmia), finding a DCM gene mutation may provide the context to more clearly understand what's wrong. Such information could greatly assist in deciding upon the best treatment.

What if my results are positive for a DCM gene mutation? If you are found to have a mutation in a DCM gene and you have dilated cardiomyopathy and/or an arrhythmia, the gene mutation is a likely cause of or plays a major role in your heart problems. If you have no evidence of cardiovascular disease but test positive for a mutation already identified in your family, this means you are at increased risk to develop cardiomyopathy and/or arrhythmia sometime in the future. Regular clinical cardiovascular screening (echocardiogram, ECG) would be recommended to detect the first signs of disease that may be diminished by early treatment. For a person who is found to carry his or her family's gene mutation but who is not yet showing symptoms, it is important to remember that each of his or her children has a 50% chance of inheriting the same mutation, putting the next generation at risk for future heart problems.

If I test positive for a DCM gene mutation, will the test tell me when I will develop heart problems? No, it can't predict timing or onset of clinical disease. The symptoms, age of onset, and severity of the disease can be very different, even among members of the same family. While some gene mutation carriers may have severe, earlier onset disease, others may have only minor heart muscle and/or rhythm problems. In addition, some individuals carry the gene mutation but have no cardiac symptoms or signs of heart problems. These "unaffected" gene mutation carriers still have a 50/50 chance of passing on the gene mutation to each of their offspring, who again could fall anywhere in the disease spectrum.

What if my results are negative? If you have heart problems and the DCM genetic testing results are negative, either you have a genetic change that could not be detected by the currently available technology or your heart problems are due to some other unrelated cause. There are approximately 30 genes that when mutated can cause DCM. Genetic testing only examines one or a few genes for mutations, usually the one(s) most likely to be involved. If you are a family member of a person with a known DCM gene mutation and your test result for the same mutation is negative, your risk to develop heart problems like that of your relative is dramatically reduced.

Can I still get heart disease even if my genetic testing was negative? Yes, you remain at risk for DCM, just like the general population. In this case, DCM can be caused by other genetic and non-genetic causes that were not tested for – such as a myocardial infarction (heart attack) or coronary artery disease. Like everyone else, if you experience symptoms of chest pain, tightness, etc, suggestive of a myocardial infarction or other heart problems, you should seek emergent medical care regardless of a negative gene mutation test result.

In a family with a known DCM mutation, why might family members without heart problems consider genetic testing for that mutation? Asymptomatic first-degree family members of a person with a known DCM gene mutation are at risk for carrying the DCM gene, and if they carry it, of developing cardiomyopathy in the future. Genetic testing for that specific DCM gene mutation will reveal who carries it. This knowledge can direct clinical screening activities (ECGs, echocardiograms) to family members at risk who carry the disease gene, and can reduce anxiety and uncertainty for those who do not carry it.

Is genetic testing helpful for family members with no known heart problems and no known DCM gene mutation in the family? In almost all cases clinical genetic testing for DCM is only helpful with some history of cardiomyopathy in the family. It is usually most helpful if the first family member tested has dilated cardiomyopathy and/or conduction system disease. However, in some families the most affected family member is deceased and no genetic material is available for testing, and based on the affected person's family health history the testing of at-risk first-degree relatives may be indicated.

How good is the test at finding a mutation in a gene that may cause DCM? Currently, we know of 30 genes that when mutated, can cause DCM. However, these 30 genes only explain about 30% of DCM cases. Therefore, because there yet to discover genes for which genetic testing is not available, the chance that a test will identify a mutation in any given case is about 30%.

How good is the test at finding a mutation, if I have one in a gene that is being tested? If there is a mutation in the coding portion of the gene(s) being tested (the portion that is the blueprint for the protein), the likelihood that testing will identify the mutation is approximately 99%. The chance that a mutation exists outside of the coding region of a gene or spans a large section of the gene is currently unknown.

Are my children at risk for a mutation in a specific DCM gene if my gene test results are negative? If you do not carry a specific DCM gene mutation that runs in your family, then your children would not be at risk of inheriting that mutation from you.

Do problems other than heart disease result from these DCM gene mutations? Occasionally DCM gene mutations have also been associated with other problems. For example, muscular dystrophy or other neuromuscular conditions occasionally accompany DCM

resulting from lamin A/C mutations.

What are some other considerations to think about with DCM gene testing? People may sometimes experience unexpected emotions after learning their genetic status, whether results are negative or positive. Emotions can range from reassurance or relief to anxiety or guilt. Because genetic test results impact risks for other family members such as children, such information has additional medical and emotional impact. With much to be learned about genetic testing for DCM, finding out one's gene mutation status can still raise questions about screening, management, and treatment for which answers remain unknown.

What about confidentiality? Some people also have concerns about the privacy and confidentiality of genetic test results and how these results may affect their health or life insurance coverage. The Genetics Information Non Discrimination Act (GINA) was signed into law and is now on effect. This means that medical insurance companies and employers are prohibited from raising premiums, firing or in any way discriminating against a person based on their family history or genetic testing results. Our newsletter from November 2008 (Volume IX, Issue 3) is available on our website and contains additional information about GINA. Some states have also enacted additional laws to protect people from such discrimination. While each person has the right to decide individually whether to learn their DCM gene mutation status or not, such testing at times may have an impact on the family and family relationships. If you seek medical treatments or make lifestyle changes based on what you learn from testing, you may decide to share your results with others. Should you pursue clinical genetic testing for DCM, your results will be sent to your ordering health provider, thus you may wish to discuss with him/her who will have access to such test results.

Further questions about clinical genetic testing? If you have further questions, we encourage you to talk with your provider and/or a genetic counselor [www.nsgc.org/resourcelink.asp]. He/She can help you understand your risk for a DCM gene mutation, discuss the risks, benefits, and limitations of such testing, and explain what any genetic test results mean for you and your family. If you are an enrolled research subject in the FDC research program, you are welcome to email or call us with your questions.

If you are interested in genetic counseling services, you can make an appointment at the University of Miami Cardiovascular Genetic Medicine Clinic. The goal of our clinic is to provide care to patients and their families who are known or suspected to have cardiovascular genetic disease, including DCM. The clinic is staffed by a multidisciplinary team led by Dr. Ray Hershberger. If you are interested, please contact us and we will help you make an appointment.

The above information is meant to facilitate a better understanding of clinical genetic testing for dilated cardiomyopathy. It is by no means comprehensive. We highly recommend genetic counseling for anyone considering testing.

Prepared by the Familial Dilated Cardiomyopathy Research Group
Further information is available at www.fdc.to.

2/8/2010