

Hereditary Heart Health Test

Genes covered and recommended screening guidelines



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Gene	Cardiomyopathies	Arrhythmias	Arteriopathies	Familial Hypercholesterolemia
<i>ACTA2</i>			•	
<i>ACTC1</i>	•			
<i>APOB*</i>				•
<i>COL3A1</i>			•	
<i>DSC2</i>	•			
<i>DSG2</i>	•			
<i>DSP</i>	•			
<i>FBN1</i>			•	
<i>GLA</i>	•			
<i>KCNH2*</i>		•		
<i>KCNQ1*</i>		•		
<i>LDLR**</i>				•
<i>LMNA</i>	•			
<i>MYBPC3</i>	•			
<i>MYH7</i>	•			
<i>MYH11</i>			•	
<i>MYL2</i>	•			
<i>MYL3</i>	•			
<i>PCSK9</i>				•
<i>PKP2</i>	•			
<i>PRKAG2</i>	•			
<i>RYR2</i>		•		
<i>SCN5A</i>		•		
<i>SMAD3</i>			•	
<i>TGFBR1*</i>			•	
<i>TGFBR2</i>			•	
<i>TMEM43</i>	•			
<i>TNNI3</i>	•			
<i>TNNT2</i>	•			
<i>TPM1</i>	•			

* These regions are not analyzed: *APOB* exon 1, *KCNH2* exon 4, *KCNQ1* exon 1, *TGFBR1* exon 1.

** For the *LDLR* promoter region, the detection of deletions, duplications, and complex structural rearrangements may be limited.

ACTA2

The ACTA2 gene is one of many genes that helps provide strength and stability to tissues in the body. The ACTA2 gene makes a protein which prevents arteries from stretching out as blood is pumped through them. When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of ACTA2 mutations

Individuals with a mutation in the ACTA2 gene are at an increased risk for developing familial thoracic aortic aneurysm and dissection (FTAAD), a hereditary cardiovascular (heart and blood vessel) called an arteriopathy. This disorder can cause weakness, enlargement, and tears of the walls of the arteries.

Disorders associated with the ACTA2 gene

Mutations in the ACTA2 gene have been associated with familial thoracic aortic aneurysm and dissection (FTAAD).

Familial thoracic aortic aneurysm and dissection (FTAAD)

FTAAD is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

<http://www.heart.org>

The John Ritter Foundation for Aortic Health

Dedicated to improving the identification of individuals at risk for aortic dissections and the treatment of thoracic aortic disease through medical research.

<http://johnritterfoundation.org>

TAD Coalition

Committed to increasing public awareness of the factors that put people at risk for aortic aneurysm and dissection, and to improving the diagnosis and management of these life-threatening conditions.

<http://www.tadcoalition.org>

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ACTC1

The *ACTC1* gene is one of many genes that helps muscles tense up (contract). The *ACTC1* gene makes a protein that plays a key role in allowing muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *ACTC1* mutations

Individuals with a mutation in the *ACTC1* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include dilated cardiomyopathy, hypertrophic cardiomyopathy, left ventricular noncompaction cardiomyopathy, and restrictive cardiomyopathy.

Disorders associated with the *ACTC1* gene

Mutations in the *ACTC1* gene have been associated with the following disorders:

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical

procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Left Ventricular Noncompaction Cardiomyopathy

Left ventricular noncompaction cardiomyopathy (LVNC) is associated with a problem with the heart muscle that can affect the heart's ability to pump blood and disrupt the normal electrical

signalling of the heart.

LVNC is a disorder of the heart where the walls of the major pumping chamber of the heart, called the left ventricle, do not develop properly. Abnormal pieces of muscle (trabeculations) extend into the left ventricle, resulting in a spongy appearance in this part of the heart, which is normally smooth. This affects the heart's ability to pump blood and can disrupt the normal electrical signalling of the heart. In some cases, the minor pumping chamber of the heart, called the right ventricle, can also be affected. People with LVNC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals may experience shortness of breath, strong or irregular heartbeats (heart palpitations), tiredness or dizziness, fainting due to a fall in blood pressure (syncope), chest pain, or buildup of fluid in the body (edema), due to heart failure. Some individuals with LVNC experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest. Individuals with LVNC are also at increased risk for certain types of heart muscle disease (cardiomyopathy).

Diagnosing LVNC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications such as anticoagulants to reduce the risk of blood clots which can lead to a stroke. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in LVNC are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally, which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a

fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

<http://www.heart.org>

Hypertrophic Cardiomyopathy Association

Provides support, education, and advocacy as well as advancing research, understanding and care to those with hypertrophic cardiomyopathy.

<http://www.4hcm.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

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APOB

The *APOB* gene makes a type of protein called apolipoprotein B that transports fats and cholesterol in the blood.

Impact of *APOB* mutations

Like most genes, each person has two copies of the *APOB* gene: one inherited from each parent. A mutation in a single copy of the *APOB* gene inherited from either parent is known to cause Familial Hypercholesterolemia (FH), which is a hereditary disorder associated with very high levels of cholesterol at an early age, specifically LDL-C. High cholesterol levels can increase the risk of developing coronary heart disease (CHD), which is the most common type of heart disease and can lead to heart attack and stroke.

Other than increasing the risk of heart disease, elevated levels of LDL-C can lead to deposits of cholesterol in other parts of the body, such as around the eyelids (xanthelasma) and within tendons of the elbows, hands, knees and feet (xanthomas). This may worsen with age.

In very rare cases, a person can inherit two *APOB* mutations, one from each parent. This causes a more severe form of FH called Homozygous Familial Hypercholesterolemia (HoFH), which is associated with high levels of cholesterol from birth and an increased risk of heart attack in childhood or adolescence.

How common are mutations in the *APOB* gene?

Mutations that cause Familial Hypercholesterolemia are rare—found in approximately 1 in 250 individuals.¹ Mutations in *APOB* account for about 5% of cases of FH where there is a known genetic mutation.²

¹ Khera AV, Won HH, Peloso GM, et al. Diagnostic Yield and Clinical Utility of Sequencing Familial Hypercholesterolemia Genes in Patients With Severe Hypercholesterolemia. *J Am Coll Cardiol*. 2016;67(22):2578-89.

² Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34(45):3478-90a.

How mutations in this gene impact risk

Risk with FH caused by an *APOB* mutation

Risk among US individuals to develop coronary heart disease. Risk may vary based on age, diet, exercise, and other factors.

Coronary Heart Disease¹

FH + high cholesterol	No FH + high cholesterol	No FH + normal cholesterol
22x average	6x average	Average

Screening guidelines

Below is a summary of current screening guidelines from the International FH Foundation. These guidelines are for individuals who have Familial Hypercholesterolemia. Your healthcare provider may use these guidelines to help create a customized screening plan for you.

Coronary heart disease (CHD)^{3,4}

Starting at age 8-10 or at diagnosis of FH:

- Speak to your provider to learn whether your cholesterol levels have already been checked and how often testing should be repeated.
- Discuss ways to reduce your cholesterol with your provider. This may include certain medications as well as lifestyle modifications such as diet, exercise and quitting smoking.
- Consider completing a baseline electrocardiogram, a test that checks the electrical activity of the heart.

Women who are pregnant or are planning to become pregnant are recommended to speak with their healthcare provider about how to best manage their cholesterol before and during pregnancy.⁵

General heart health recommendations for all individuals:⁶

- Don't smoke and avoid second-hand smoke
- Treat high blood pressure if you have it
- Eat foods that are low in saturated fat, trans fat, sodium (salt) and added sugars

³ Watts GF, Gidding S, Wierzbicki AS, et al. Integrated guidance on the care of familial hypercholesterolaemia from the International FH Foundation. *Int J Cardiol.* 2014;171(3):309-25.

⁴ Wiegman A, Gidding SS, Watts GF, et al. Familial hypercholesterolaemia in children and adolescents: gaining decades of life by optimizing detection and treatment. *Eur Heart J.* 2015;36(36):2425-37.

⁵ Christensen JJ, Retterstøl K, Godang K, et al. LDL cholesterol in early pregnancy and offspring cardiovascular disease risk factors. *J Clin Lipidol.* 2016;10(6):1369-1378.e7.

⁶ Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;129(25 Suppl 2):S76-99.

- Be physically active
- Reach and maintain a healthy weight
- Control your blood sugar if you have diabetes
- Get regular medical check-ups
- Take medicine as prescribed

Useful resources

The FH Foundation

The FH Foundation is a patient-centered non-profit dedicated to research, advocacy, and education of all forms of familial hypercholesterolemia.

www.thefhfoundation.org

National Heart, Lung, and Blood Institute

Provides leadership for a research, training and education program to promote the prevention and treatment of heart, lung, and blood diseases.

www.nhlbi.nih.gov

American Heart Association

Focused on building healthier lives free of heart disease by promoting heart healthy lifestyle choices, providing accessible education, and funding innovative research.

www.heart.org

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COL3A1

The *COL3A1* gene is one of many genes that helps provide strength and stability to tissues in the body. The *COL3A1* gene makes a protein which is found in the skin, lungs, and the blood vessels. When this protein doesn't work properly, these tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *COL3A1* mutations

Individuals with a mutation in the *COL3A1* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called arteriopathies, which can cause weakness, enlargement, and tears of the walls of the arteries. These include familial thoracic aortic aneurysm and dissection and vascular Ehlers Danlos syndrome.

Disorders associated with the *COL3A1* gene

Mutations in the *COL3A1* gene have been associated with the following disorders:

Familial thoracic aortic aneurysm and dissection

Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Vascular Ehlers-Danlos syndrome

Vascular Ehlers-Danlos syndrome (vEDS) is a hereditary disorder associated with problems with the structure of connective tissue in many parts of the body, which can cause weakness of the blood vessel walls and other organs, fragile skin, and easy bruising and bleeding.

vEDS is a connective tissue disorder. Connective tissue supports, binds, or connects other tissues or organs in the body. Individuals with vEDS commonly have problems with the heart and the surrounding blood vessels, especially the large blood vessels that carry blood away from the heart to the rest of the body (arteries). The walls of the arteries can become weakened and stretch (dilation). This can lead to a bulge in the wall of the artery (aneurysm) or a sudden tearing of the artery (dissection). In individuals with vEDS, dissections commonly occur in the aorta, the largest artery in the body, but may occur in other arteries. Arterial dissections are life threatening, and are the major cause of death in individuals with vEDS .

Other common features of vEDS include easy bruising and bleeding, enlarged veins, and very flexible joints (joint hypermobility). Some individuals may have specific facial features, as well as thin, clear skin that wrinkles on the hands and feet. Besides dissection of the arteries, vEDS is associated with other major complications, including ruptures in the gastrointestinal tract, spleen, or liver, as well as collapsed lung (pneumothorax). This can lead to internal bleeding, stroke, and shock. Women with vEDS are at increased risk for serious and possibly life-threatening complications during pregnancy, such as rupture of the uterus, and may require special care.

Diagnosing vEDS typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose vEDS.

Treatment for vEDS is typically focused on preventing complications. Individuals are recommended to have a heart exam that includes an echocardiogram. They may also benefit from wearing protective pads or bandages to prevent bruising and bleeding. It is usually recommended that individuals with vEDS avoid contact sports and strenuous exercise, as well as certain medications that keep the blood from clotting. Surgery and other invasive procedures are generally discouraged, except if necessary and with special precaution.¹

Useful resources

EDS Network Cares

Improves the quality of life for people who have Ehlers-Danlos Syndrome through research, education, and support.

<http://www.ehlersdanlosnetwork.org>

The Ehlers-Danlos Society

Guides both patients and medical professionals to information, resources, support, and education.

<https://ehlers-danlos.com>

The Marfan Foundation

Provides information and support to healthcare providers, caregivers, and families affected by Marfan syndrome and related disorders, including FTAAD and Ehlers-Danlos syndrome.

<http://www.marfan.org>

Last updated April 4, 2018

¹ Malfait F, De paepe A. The Ehlers-Danlos syndrome. Adv Exp Med Biol. 2014;802:129-43.

DSC2

The *DSC2* gene is one of many genes that helps provide strength and stability to tissues in the body. The *DSC2* gene makes a protein which is found in the heart muscle and skin. When this protein doesn't work properly, the tissues can be weakened, especially the heart.

Impact of *DSC2* mutations

Individuals with a mutation in the *DSC2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include and arrhythmogenic cardiomyopathy and dilated cardiomyopathy.

Disorders associated with the *DSC2* gene

Mutations in the *DSC2* gene have been associated with the following disorders:

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), lightheadedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other

surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

<http://www.heart.org>

ARVD/C Patient Registry (The Johns Hopkins Hospital)

The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

<https://www.hopkinsmedicine.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

DSG2

The *DSG2* gene is one of many genes that helps provide strength and stability to tissues in the body. The *DSG2* gene makes a protein which is found in the heart muscle and skin. When this protein doesn't work properly, the tissues can be weakened, especially the heart.

Impact of *DSG2* mutations

Individuals with a mutation in the *DSG2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include arrhythmogenic cardiomyopathy and dilated cardiomyopathy.

Disorders associated with the *DSG2* gene

Mutations in the *DSG2* gene have been associated with the following disorders:

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), lightheadedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other

surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

<http://www.heart.org>

ARVD/C Patient Registry (The Johns Hopkins Hospital)

The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

<https://www.hopkinsmedicine.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

DSP

The *DSP* gene is one of many genes that helps provide strength and stability to tissues in the body. The *DSP* gene makes a protein which is found in the heart muscle and skin. When this protein doesn't work properly, the tissues can be weakened, especially the heart.

Impact of *DSP* mutations

Individuals with a mutation in the *DSP* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include arrhythmogenic cardiomyopathy and dilated cardiomyopathy.

Disorders associated with the *DSP* gene

Mutations in the *DSP* gene have been associated with the following disorders:

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), lightheadedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other

surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

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The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

<https://www.hopkinsmedicine.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

FBN1

The *FBN1* gene is one of many genes that helps provide strength and stability to tissues in the body. The *FBN1* gene makes a protein which is used to form elastic fibers that allow the skin, ligaments, and blood vessels to stretch. When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *FBN1* mutations

Individuals with a mutation in the *FBN1* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called arteriopathies, which can cause weakness, enlargement, and tears of the walls of the arteries. These include familial thoracic aortic aneurysm and dissection and Marfan syndrome.

Disorders associated with the *FBN1* gene

Mutations in the *FBN1* gene have been associated with the following disorders:

Familial Thoracic Aortic Aneurysm and Dissection

Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Marfan Syndrome

Marfan syndrome is a hereditary disorder associated with problems with the structure of connective tissue in many parts of the body, which can cause weakness of the blood vessel walls, dislocation of the lens in the eye (ectopia lentis), and increased flexibility in the joints.

Marfan syndrome is a connective tissue disorder. Connective tissue supports, binds, or connects other tissues or organs in the body. Individuals with Marfan syndrome commonly have problems with the heart and the surrounding blood vessels, especially the large blood vessel that carries blood away from the heart to the rest of the body (aorta). The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening. Other heart problems may include leaks in the valves that connect the chambers of the heart, which can cause fatigue, shortness of breath, and strong or irregular heartbeats (heart palpitations).

Individuals may have problems with the eyes, such as dislocation of the lenses in one or both eyes (ectopia lentis), nearsightedness, cataracts, or glaucoma. They may have a tall and slender body type with long fingers and toes (arachnodactyly). Other symptoms may include increased flexibility in joints, a curved spine (scoliosis), back pain, flat feet, collapsed lung (pneumothorax), and a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum). The features of Marfan syndrome may appear at any age. Women with Marfan syndrome are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing Marfan syndrome typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose Marfan syndrome.

Treatment for individuals with Marfan syndrome may include medications that help control blood pressure to reduce stress on the walls of the aorta, as well as frequent echocardiograms to identify aneurysms that develop. If aneurysms develop, surgery may be required. Some individuals may also need surgeries to correct a curved spine or a dislocated lens in the eye. It is also recommended that individuals avoid contact sports or strenuous exercise and substances that stimulate the heart, such as certain cold medicines and caffeine.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

<http://www.heart.org>

The John Ritter Foundation for Aortic Health

Dedicated to improving the identification of individuals at risk for aortic dissections and the treatment of thoracic aortic disease through medical research.

<http://johnritterfoundation.org>

The Marfan Foundation

Provides information and support to healthcare providers, caregivers, and families affected by Marfan syndrome and related disorders, including FTAAD.

<http://www.marfan.org>

Last updated April 4, 2018

GLA

The *GLA* gene is one of many genes that helps cells to break down substances they no longer need. The *GLA* gene makes a protein which breaks down a fatty substance in the cell called globotriaosylceramide. When this protein doesn't work properly, this fatty substance can build up in the cell, which can affect organs such as the heart, kidneys, and skin.

Impact of *GLA* mutations

Individuals with a mutation in the *GLA* gene are at increased risk of developing a disorder called Fabry disease. Fabry disease typically only affects males, however females may also develop symptoms. Having Fabry disease can cause problems throughout the body, including the heart, kidney, and nervous system.

Disorders associated with the *GLA* gene

Mutations in the *GLA* gene have been associated with the following disorders:

Fabry Disease

Individuals with Fabry disease are unable to break down a type of fat called globotriaosylceramide (GL-3) in the body. Beginning in childhood, GL-3 builds up and accumulates throughout the body, which can cause problems in the heart, skin, eye, kidneys, brain and nervous system. While Fabry disease typically only affects males, females may develop symptoms ranging from mild to severe.

Common symptoms in childhood or adolescence include dark red or blue patches on the skin (angiokeratomas), abdominal pain, and visual impairment caused by clouding of the eye (corneal whorling and opacity). Other common symptoms of Fabry disease include episodes of severe, burning pain in the hands and feet (acroparesthesias), and reduced sweating (hypohidrosis). In adulthood, individuals with Fabry disease may also experience life-threatening complications such as kidney damage, heart attack, and stroke. The lifespan of an individual with Fabry disease is variable and primarily depends on the severity of heart and kidney problems.

Many individuals with Fabry disease develop a cardiac condition called left ventricular hypertrophy, caused by heart muscle cells that become filled with GL-3, that has symptoms that resemble hypertrophic cardiomyopathy (HCM). HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting. When untreated, HCM can lead to heart failure, sudden cardiac arrest, or sudden cardiac death. Individuals may experience other problems with the heart, such as problems with

the valves that allow blood to flow through the heart, chest pain, irregular heartbeat, and others.

Diagnosing Fabry disease typically involves a blood test that measures the breakdown of GL-3 in white blood cells, as well as evaluation of an individual's medical and family histories, physical exam, hearing assessment, and examination of the skin, eyes, brain, heart, and kidneys. These evaluations may be combined with genetic testing to diagnose Fabry disease.

Treatment for individuals with Fabry disease may include enzyme replacement therapy, which helps breakdown GL-3. Pain medications may be used to help reduce the frequency and severity of pain episodes. Other medications, hemodialysis, or kidney transplant may be required by individuals with renal involvement. Ongoing evaluation of the brain, eyes, heart, and hearing may be recommended.

Interesting information about the *GLA* gene

Fabry disease is an X-linked disorder. This means that having a mutation in a single copy of the *GLA* gene causes Fabry disease in males and does not typically cause Fabry disease in females. This is because the *GLA* gene is located on the X chromosome, and males only have one copy of the X chromosome, while females have two copies. Even if a female has one mutation, the extra copy can usually make up for the impact of the mutation on the other.

Certain mutations in the *GLA* gene have a milder impact than others. Some specific mutations are known to cause symptoms that only affect the heart or kidneys and appear later in life.

Useful resources

Fabry International Network

Promotes collaboration between organizations to support those affected by Fabry disease by enabling communication and advocating for good practices.

<http://www.fabrynetwork.org>

Fabry Support and Information Group

Raises awareness of Fabry disease and its symptoms by connecting patients, family members, and caregivers.

<http://www.fabry.org/>

National Fabry Disease Foundation

Supports the Fabry disease community by promoting education, awareness, advocacy and research dedicated to Fabry disease.

<http://www.fabrydisease.org>

Last updated May 25, 2018

KCNH2

The *KCNH2* gene is one of many genes that helps maintain a regular heartbeat. The *KCNH2* gene makes a protein whose primary role is to form a potassium channel which generates and transmits electrical charges in the body when needed, such as when the heart beats. When this protein doesn't work properly the heartbeat can be abnormal.

Impact of *KCNH2* mutations

Individuals with a mutation in the *KCNH2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called arrhythmias, which can affect the heartbeat's regular rhythm. These include long QT syndrome and short QT syndrome.

Disorders associated with the *KCNH2* gene

Mutations in the *KCNH2* gene have been associated with the following disorders:

Long QT Syndrome

Long QT syndrome (LQTS) is a hereditary disorder associated with a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia). LQTS may increase risk of sudden cardiac arrest or sudden cardiac death at young ages.

LQTS is associated with problems in the heart's electrical system in which there is a dangerously fast heart beat in the lower pumping chambers of the heart (torsade de pointes). Symptoms of LQTS may include fainting, seizures, or sudden cardiac arrest. Exercise and heightened or intense emotions may be a trigger for sudden cardiac arrest, which can happen from infancy through middle age. An individual's risk depends on their sex, age, and previous symptoms. The severity of the electrical problem in the heart and the specific gene that causes LQTS also play a role. Some individuals with LQTS experience no noticeable symptoms, but are still at risk for sudden cardiac arrest and death.

Women with LQTS have an increased risk of cardiac arrest or death in the first nine months after giving birth.

Diagnosing LQTS typically involves evaluating an individual's medical and family histories as well as results of a test of the heart's electrical system called an electrocardiogram (EKG or ECG). These evaluations may be combined with genetic testing to diagnose the type of LQTS an individual has.

Treatment is recommended for everyone since there is no way to predict who may have symptoms and who may not. Treatment typically involves taking medications that help moderate your heart's rhythm. Some individuals may also need a device that detects a

dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. Individuals are recommended to avoid certain medications and drugs. Some individuals are advised to avoid strenuous exercise, competitive sports, or exposure to loud noises.

Regular visits to a cardiologist specializing in LQTS are recommended in order to check that treatment is effective.

Short QT Syndrome

Short QT syndrome (SQTS) is a hereditary disorder associated with a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia). SQTS may increase risk of sudden cardiac arrest or death at young ages.

SQTS is associated with problems in the heart's electrical system that can cause one of two rhythm problems. The first is called atrial fibrillation, in which there is an irregular heartbeat starting in the upper pumping chambers of the heart (atria). This can cause shortness of breath, dizziness, chest tightness, fatigue, and fainting. The second is called ventricular tachycardia or fibrillation, in which there is a very fast heartbeat starting in the lower pumping chambers of the heart (ventricles). This can cause fainting and sudden cardiac death. An individual's risk depends on their sex, age, and previous symptoms. Some individuals with SQTS experience no noticeable symptoms, but are still at risk for sudden cardiac arrest and death.

Diagnosing SQTS typically involves evaluating an individual's medical and family histories as well as results of a test of the heart's electrical system called an electrocardiogram (EKG or ECG). These evaluations may be combined with genetic testing to diagnose SQTS.

Treatment may involve use of a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD). Medication can also be used for treatment.

Regular visits to a cardiologist specializing in SQTS are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Heart Rhythm Society

Provides information sheets on types of arrhythmias and associated treatments, risk factors, signs and symptoms.

<http://resources.hrsonline.org>

Sudden Arrhythmia Death syndromes (SADS)

SADS advocates for nondiscriminatory treatment for people who are diagnosed with a SADS disorder. SADS is committed to supporting efforts that will improve the quality of life for patients with heart rhythm abnormalities.

www.sads.org

Last updated April 4, 2018

KCNQ1

The *KCNQ1* gene is one of many genes that helps maintain a regular heartbeat. The *KCNQ1* gene makes a protein whose primary role is to form a potassium channel which generates and transmits electrical charges in the body when needed, such as when the heart beats. When this protein doesn't work properly the heartbeat can be abnormal.

Impact of *KCNQ1* mutations

Individuals with a mutation in the *KCNQ1* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called arrhythmias, which can affect the heartbeat's regular rhythm. These include long QT syndrome and short QT syndrome.

Disorders associated with the *KCNQ1* gene

Mutations in the *KCNQ1* gene have been associated with the following disorders:

Long QT Syndrome

Long QT syndrome (LQTS) is a hereditary disorder associated with a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia). LQTS may increase risk of sudden cardiac arrest or sudden cardiac death at young ages.

LQTS is associated with problems in the heart's electrical system in which there is a dangerously fast heart beat in the lower pumping chambers of the heart (torsade de pointes). Symptoms of LQTS may include fainting, seizures, or sudden cardiac arrest. Exercise and heightened or intense emotions may be a trigger for sudden cardiac arrest, which can happen from infancy through middle age. An individual's risk depends on their sex, age, and previous symptoms. The severity of the electrical problem in the heart and the specific gene that causes LQTS also play a role. Some individuals with LQTS experience no noticeable symptoms, but are still at risk for sudden cardiac arrest and death.

Women with LQTS have an increased risk of cardiac arrest or death in the first nine months after giving birth.

Diagnosing LQTS typically involves evaluating an individual's medical and family histories as well as results of a test of the heart's electrical system called an electrocardiogram (EKG or ECG). These evaluations may be combined with genetic testing to diagnose the type of LQTS an individual has.

Treatment is recommended for everyone since there is no way to predict who may have symptoms and who may not. Treatment typically involves taking medications that help moderate your heart's rhythm. Some individuals may also need a device that detects a

dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. Individuals are recommended to avoid certain medications and drugs. Some individuals are advised to avoid strenuous exercise, competitive sports, or exposure to loud noises.

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Treatment may involve use of a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD). Medication can also be used for treatment.

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www.sads.org

Last updated April 4, 2018

LDLR

The *LDLR* gene makes a protein called LDL receptor protein. These proteins are mainly found in the liver, which is responsible for removing most excess cholesterol from the body.

Impact of *LDLR* mutations

Like most genes, each person has two copies of the *LDLR* gene: one inherited from each parent. A mutation in a single copy of the *LDLR* gene inherited from either parent is known to cause Familial Hypercholesterolemia (FH), which is a hereditary disorder associated with very high levels of cholesterol at an early age, specifically LDL-C. High cholesterol levels can increase the risk of developing coronary heart disease (CHD), which is the most common type of heart disease and can lead to heart attack and stroke.

Other than increasing the risk of heart disease, elevated levels of LDL-C can lead to deposits of cholesterol in other parts of the body, such as around the eyelids (xanthelasma) and within tendons of the elbows, hands, knees and feet (xanthomas). This may worsen with age.

In very rare cases, a person can inherit two *LDLR* mutations, one from each parent. This causes a more severe form of FH called Homozygous Familial Hypercholesterolemia (HoFH), which is associated with high levels of cholesterol from birth and an increased risk of heart attack in childhood or adolescence.

How common are mutations in the *LDLR* gene?

Mutations that cause Familial Hypercholesterolemia are rare—found in approximately 1 in 250 individuals.¹ Mutations in *LDLR* account for >90% of cases of FH where there is a known genetic mutation.²

¹ Khera AV, Won HH, Peloso GM, et al. Diagnostic Yield and Clinical Utility of Sequencing Familial Hypercholesterolemia Genes in Patients With Severe Hypercholesterolemia. *J Am Coll Cardiol*. 2016;67(22):2578-89.

² Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34(45):3478-90a.

How mutations in this gene impact risk

Risk with FH caused by an *LDLR* mutation

Risk among US individuals to develop coronary heart disease. Risk may vary based on age, diet, exercise, and other factors.

Coronary Heart Disease¹

FH + high cholesterol	No FH + high cholesterol	No FH + normal cholesterol
22x average	6x average	Average

Screening guidelines

Below is a summary of current screening guidelines from the International FH Foundation. These guidelines are for individuals who have Familial Hypercholesterolemia. Your healthcare provider may use these guidelines to help create a customized screening plan for you.

Coronary heart disease (CHD)^{3,4}

- Starting at age 8-10 or at diagnosis of FH:
 - Speak to your provider to learn whether your cholesterol levels have already been checked and how often testing should be repeated.
 - Discuss ways to reduce your cholesterol with your provider. This may include certain medications as well as lifestyle modifications such as diet, exercise and quitting smoking.
 - Consider completing a baseline electrocardiogram, a test that checks the electrical activity of the heart.
- Women who are pregnant or are planning to become pregnant are recommended to speak with their healthcare provider about how to best manage their cholesterol before and during pregnancy.⁵

General heart health recommendations for all individuals:⁶

- Don't smoke and avoid second-hand smoke
- Treat high blood pressure if you have it
- Eat foods that are low in saturated fat, trans fat, sodium (salt) and added sugars
- Be physically active

³ Watts GF, Gidding S, Wierzbicki AS, et al. Integrated guidance on the care of familial hypercholesterolaemia from the International FH Foundation. *Int J Cardiol.* 2014;171(3):309-25.

⁴ Wiegman A, Gidding SS, Watts GF, et al. Familial hypercholesterolaemia in children and adolescents: gaining decades of life by optimizing detection and treatment. *Eur Heart J.* 2015;36(36):2425-37.

⁵ Christensen JJ, Retterstøl K, Godang K, et al. LDL cholesterol in early pregnancy and offspring cardiovascular disease risk factors. *J Clin Lipidol.* 2016;10(6):1369-1378.e7.

⁶ Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;129(25 Suppl 2):S76-99.

- Reach and maintain a healthy weight
- Control your blood sugar if you have diabetes
- Get regular medical check-ups
- Take medicine as prescribed

Useful resources

The FH Foundation

The FH Foundation is a patient-centered non-profit dedicated to research, advocacy, and education of all forms of familial hypercholesterolemia.

www.thefhfoundation.org

National Heart, Lung, and Blood Institute

Provides leadership for a research, training and education program to promote the prevention and treatment of heart, lung, and blood diseases.

www.nhlbi.nih.gov

American Heart Association

Focused on building healthier lives free of heart disease by promoting heart healthy lifestyle choices, providing accessible education, and funding innovative research.

www.heart.org

Last updated July 18, 2017

LMNA

The *LMNA* gene is one of many genes that helps provide strength and stability to tissues in the body. The *LMNA* gene makes structural proteins that support cell components. When these proteins don't work properly, tissues can be weakened, especially heart muscle tissue.

Impact of *LMNA* mutations

Individuals with a mutation in the *LMNA* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include arrhythmogenic cardiomyopathy, dilated cardiomyopathy, and left ventricular noncompaction cardiomyopathy.

Disorders associated with the *LMNA* gene

Mutations in the *LMNA* gene have been associated with the following disorders:

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), lightheadedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other

surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Left Ventricular Noncompaction Cardiomyopathy

Left ventricular noncompaction cardiomyopathy (LVNC) is associated with a problem with the heart muscle that can affect the heart's ability to pump blood and disrupt the normal electrical signalling of the heart.

LVNC is a disorder of the heart where the walls of the major pumping chamber of the heart, called the left ventricle, do not develop properly. Abnormal pieces of muscle (trabeculations) extend into the left ventricle, resulting in a spongy appearance in this part of the heart, which is normally smooth. This affects the heart's ability to pump blood and can disrupt the normal electrical signalling of the heart. In some cases, the minor pumping chamber of the heart, called the right ventricle, can also be affected. People with LVNC can have a problem with the electrical

system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals may experience shortness of breath, strong or irregular heartbeats (heart palpitations), tiredness or dizziness, fainting due to a fall in blood pressure (syncope), chest pain, or buildup of fluid in the body (edema), due to heart failure. Some individuals with LVNC experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest. Individuals with LVNC are also at increased risk for certain types of heart muscle disease (cardiomyopathy).

Diagnosing LVNC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications such as anticoagulants to reduce the risk of blood clots which can lead to a stroke. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in LVNC are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

ARVD/C Patient Registry (The Johns Hopkins Hospital)

The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

<https://www.hopkinsmedicine.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

MYBPC3

The *MYBPC3* gene is one of many genes that helps muscles tense up (contract). The *MYBPC3* gene makes a protein which is found in heart muscle tissue and plays a key role in allowing muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *MYBPC3* mutations

Individuals with a mutation in the *MYBPC3* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include dilated cardiomyopathy, hypertrophic cardiomyopathy, left ventricular noncompaction cardiomyopathy and restrictive cardiomyopathy.

Disorders associated with the *MYBPC3* gene

Mutations in the *MYBPC3* gene have been associated with the following disorders:

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical

procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Left Ventricular Noncompaction Cardiomyopathy

Left ventricular noncompaction cardiomyopathy (LVNC) is associated with a problem with the heart muscle that can affect the heart's ability to pump blood and disrupt the normal electrical

signalling of the heart.

LVNC is a disorder of the heart where the walls of the major pumping chamber of the heart, called the left ventricle, do not develop properly. Abnormal pieces of muscle (trabeculations) extend into the left ventricle, resulting in a spongy appearance in this part of the heart, which is normally smooth. This affects the heart's ability to pump blood and can disrupt the normal electrical signalling of the heart. In some cases, the minor pumping chamber of the heart, called the right ventricle, can also be affected. People with LVNC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals may experience shortness of breath, strong or irregular heartbeats (heart palpitations), tiredness or dizziness, fainting due to a fall in blood pressure (syncope), chest pain, or buildup of fluid in the body (edema), due to heart failure. Some individuals with LVNC experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest. Individuals with LVNC are also at increased risk for certain types of heart muscle disease (cardiomyopathy).

Diagnosing LVNC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications such as anticoagulants to reduce the risk of blood clots which can lead to a stroke. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in LVNC are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally, which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a

fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, and advocacy as well as advancing research, understanding and care to those with hypertrophic cardiomyopathy.

www.4hcm.org

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

MYH7

The *MYH7* gene is one of many genes that helps muscles tense up (contract). The *MYH7* gene makes a protein which is found in heart muscles and in the muscles that allow the body to move (skeletal muscles). The *MYH7* protein plays a key role in allowing the muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *MYH7* mutations

Individuals with a mutation in the *MYH7* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include dilated cardiomyopathy, hypertrophic cardiomyopathy, left ventricular noncompaction cardiomyopathy and restrictive cardiomyopathy.

Disorders associated with the *MYH7* gene

Mutations in the *MYH7* gene have been associated with the following disorders.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a

shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Left Ventricular Noncompaction Cardiomyopathy

Left ventricular noncompaction cardiomyopathy (LVNC) is associated with a problem with the heart muscle that can affect the heart's ability to pump blood and disrupt the normal electrical signalling of the heart.

LVNC is a disorder of the heart where the walls of the major pumping chamber of the heart, called the left ventricle, do not develop properly. Abnormal pieces of muscle (trabeculations) extend into the left ventricle, resulting in a spongy appearance in this part of the heart, which is normally smooth. This affects the heart's ability to pump blood and can disrupt the normal electrical signalling of the heart. In some cases, the minor pumping chamber of the heart, called the right ventricle, can also be affected. People with LVNC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals may experience shortness of breath, strong or irregular heartbeats (heart palpitations), tiredness or dizziness, fainting due to a fall in blood pressure (syncope), chest pain, or buildup of fluid in the body (edema), due to heart failure. Some individuals with LVNC experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest. Individuals with LVNC are also at increased risk for certain types of heart muscle disease (cardiomyopathy).

Diagnosing LVNC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications such as anticoagulants to reduce the risk of blood clots which can lead to a stroke. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in LVNC are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally, which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart

that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, and advocacy as well as advancing research, understanding and care to those with hypertrophic cardiomyopathy.

www.4hcm.org

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

MYH11

The *MYH11* gene is one of many genes that helps provide strength and stability to tissues in the body. The *MYH11* gene makes a protein which is found in smooth muscle, such as the blood vessels, stomach, and intestines. The *MYH11* protein plays a key role in allowing smooth muscles to tense up (contract). When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *MYH11* mutations

Individuals with a mutation in the *MYH11* gene are at an increased risk for developing familial thoracic aortic aneurysm and dissection, a hereditary cardiovascular (heart and blood vessel) disorder called an arteriopathy which can cause weakness, enlargement, and tears of the walls of the arteries.

Disorders associated with the *MYH11* gene

Mutations in the *MYH11* gene have been associated with the following disorders:

Familial Thoracic Aortic Aneurysm and Dissection

Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

The John Ritter Foundation for Aortic Health

Dedicated to improving the identification of individuals at risk for aortic dissections and the treatment of thoracic aortic disease through medical research.

<http://johnritterfoundation.org>

TAD Coalition

Committed to increasing public awareness of the factors that put people at risk for aortic aneurysm and dissection, and to improving the diagnosis and management of these life-threatening conditions.

www.tadcoalition.org

Last updated April 4, 2018

MYL2

The *MYL2* gene is one of many genes that helps muscles tense up (contract). The *MYL2* gene makes a protein which plays a key role in allowing muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *MYL2* mutations

Individuals with a mutation in the *MYL2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include hypertrophic cardiomyopathy and restrictive cardiomyopathy.

Disorders associated with the *MYL2* gene

Mutations in the *MYL2* gene have been associated with the following disorders:

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether

HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally, which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

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Last updated April 4, 2018

MYL3

The *MYL3* gene is one of many genes that helps muscles tense up (contract). The *MYL3* gene makes a protein which plays a key role in allowing muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *MYL3* mutations

Individuals with a mutation in the *MYL3* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood (cardiomyopathy). These include hypertrophic cardiomyopathy and restrictive cardiomyopathy.

Disorders associated with the *MYL3* gene

Mutations in the *MYL2* gene have been associated with the following disorders:

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether

HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally, which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, and advocacy as well as advancing research, understanding and care to those with hypertrophic cardiomyopathy.

www.4hcm.org

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

PCSK9

The *PCSK9* gene makes a protein called proprotein convertase, subtilisin/kexin-type 9. These proteins help maintain a normal amount of cholesterol in the bloodstream.

Impact of *PCSK9* mutations

Like most genes, each person has two copies of the *PCSK9* gene: one inherited from each parent. A mutation in a single copy of the *PCSK9* gene inherited from either parent is known to cause Familial Hypercholesterolemia (FH), which is a hereditary disorder associated with very high levels of cholesterol at an early age, specifically LDL-C. High cholesterol levels can increase the risk of developing coronary heart disease (CHD), which is the most common type of heart disease and can lead to heart attack and stroke.

Other than increasing the risk of heart disease, elevated levels of LDL-C can lead to deposits of cholesterol in other parts of the body, such as around the eyelids (xanthelasma) and within tendons of the elbows, hands, knees and feet (xanthomas). This may worsen with age.

In very rare cases, a person can inherit two *PCSK9* mutations, one from each parent. This causes a more severe form of FH called Homozygous Familial Hypercholesterolemia (HoFH), which is associated with high levels of cholesterol from birth and an increased risk of heart attack in childhood or adolescence.

How common are mutations in the *PCSK9* gene?

Mutations that cause Familial Hypercholesterolemia are rare—found in approximately 1 in 250 individuals.¹ Mutations in *PCSK9* account for about 1% of cases of FH where there is a known genetic mutation.²

¹ Khera AV, Won HH, Peloso GM, et al. Diagnostic Yield and Clinical Utility of Sequencing Familial Hypercholesterolemia Genes in Patients With Severe Hypercholesterolemia. *J Am Coll Cardiol*. 2016;67(22):2578-89.

² Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34(45):3478-90a.

How mutations in this gene impact risk

Risk with FH caused by an *PCSK9* mutation

Risk among US individuals to develop coronary heart disease. Risk may vary based on age, diet, exercise, and other factors.

Coronary Heart Disease¹

FH + high cholesterol	No FH + high cholesterol	No FH + normal cholesterol
22x average	6x average	Average

Additional information

Thanks to the discovery of *PCSK9* as an FH-causing gene, new medications called PCSK9 inhibitors have been developed that have the ability to treat high cholesterol caused by FH. Prior to PCSK9 inhibitors, there was no specific medication for high cholesterol due to FH. However, PCSK9 inhibitors can target the problems in cells caused by mutations in FH genes that lead to high LDL-C levels, allowing for specialized and effective treatment of the high cholesterol levels caused by FH.

Screening guidelines

Below is a summary of current screening guidelines from the International FH Foundation. These guidelines are for individuals who have Familial Hypercholesterolemia. Your healthcare provider may use these guidelines to help create a customized screening plan for you.

Coronary Heart Disease (CHD)^{3,4}

Starting at age 8-10 or at diagnosis of FH:

- Speak to your provider to learn whether your cholesterol levels have already been checked and how often testing should be repeated.
- Discuss ways to reduce your cholesterol with your provider. This may include certain medications as well as lifestyle modifications such as diet, exercise and quitting smoking.
- Consider completing a baseline electrocardiogram, a test that checks the electrical activity of the heart.

³ Watts GF, Gidding S, Wierzbicki AS, et al. Integrated guidance on the care of familial hypercholesterolaemia from the International FH Foundation. *Int J Cardiol.* 2014;171(3):309-25.

⁴ Wiegman A, Gidding SS, Watts GF, et al. Familial hypercholesterolaemia in children and adolescents: gaining decades of life by optimizing detection and treatment. *Eur Heart J.* 2015;36(36):2425-37.

Women who are pregnant or are planning to become pregnant are recommended to speak with their healthcare provider about how to best manage their cholesterol before and during pregnancy.⁵

General heart health recommendations for all individuals:⁶

- Don't smoke and avoid second-hand smoke
- Treat high blood pressure if you have it
- Eat foods that are low in saturated fat, trans fat, sodium (salt) and added sugars
- Be physically active
- Reach and maintain a healthy weight
- Control your blood sugar if you have diabetes
- Get regular medical check-ups
- Take medicine as prescribed

Useful resources

The FH Foundation

The FH Foundation is a patient-centered non-profit dedicated to research, advocacy, and education of all forms of familial hypercholesterolemia.

www.thefhfoundation.org

National Heart, Lung, and Blood Institute

Provides leadership for a research, training and education program to promote the prevention and treatment of heart, lung, and blood diseases.

www.nhlbi.nih.gov

American Heart Association

Focused on building healthier lives free of heart disease by promoting heart healthy lifestyle choices, providing accessible education, and funding innovative research.

www.heart.org

Last updated July 18, 2017

⁵ Christensen JJ, Retterstøl K, Godang K, et al. LDL cholesterol in early pregnancy and offspring cardiovascular disease risk factors. *J Clin Lipidol*. 2016;10(6):1369-1378.e7.

⁶ Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(25 Suppl 2):S76-99.

PKP2

The *PKP2* gene is one of many genes that helps provide strength and stability to tissues in the body. The *PKP2* gene makes a protein which is found in the heart muscle. When this protein doesn't work properly, the heart can be weakened.

Impact of *PKP2* mutations

Individuals with a mutation in the *PKP2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include arrhythmogenic cardiomyopathy and dilated cardiomyopathy.

Disorders associated with the *PKP2* gene

Mutations in the *PKP2* gene have been associated with the following disorders:

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), light-headedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart

failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in AC are recommended in order to check that treatment is effective.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

ARVD/C Patient Registry (The Johns Hopkins Hospital)

The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

<https://www.hopkinsmedicine.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

PRKAG2

The *PRKAG2* gene is one of many genes that helps muscles tense up (contract). The *PRKAG2* gene makes a protein that works with other proteins to help sense and respond to energy demands within cells, especially in the heart muscle and in the muscles that allow the body to move (skeletal muscle). When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *PRKAG2* mutations

Individuals with a mutation in the *PRKAG2* gene are at an increased risk for developing hypertrophic cardiomyopathy, a hereditary cardiovascular (heart and blood vessel) disorder, which can affect the heart's ability to pump blood.

Disorders associated with the *PRKAG2* gene

Mutations in the *PRKAG2* gene have been associated with the following disorder:

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether

HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, advocacy and advancing research, understanding and care to those with hypertrophic cardiomyopathy.

<http://www.4hcm.org>

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

RYR2

The *RYR2* gene is one of many genes that helps maintain a regular heartbeat. The *RYR2* gene makes a protein whose primary role is to form a calcium channel which generates and transmits electrical charges in the body when needed, such as when the heart beats. When this protein doesn't work properly the heartbeat can be abnormal.

Impact of *RYR2* mutations

Individuals with a mutation in the *RYR2* gene are at an increased risk for developing catecholaminergic polymorphic ventricular tachycardia (CPVT), a hereditary cardiovascular (heart and blood vessel) disorder, called an arrhythmia, which can affect the heartbeat's regular rhythm.

Disorders associated with the *RYR2* gene

Mutations in the *RYR2* gene have been associated with the following disorder:

Catecholaminergic polymorphic ventricular tachycardia

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a hereditary disorder associated with a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia). CPVT typically occurs in response to strenuous physical activity or heightened emotions and may increase risk of sudden cardiac arrest or death at young ages.

CPVT is associated with problems in the heart's electrical system in which there is a dangerously fast heartbeat in the lower pumping chambers of the heart (ventricles). Symptoms of CPVT may include fainting or sudden cardiac arrest. Sudden cardiac death can occur, even in individuals who have no other symptoms. Exercise, heightened or intense emotions, or other activities that cause an increase in adrenaline are typically a trigger for sudden cardiac arrest, which can happen from childhood through middle age. An individual's risk depends on their sex, age, and previous symptoms. Some individuals with CPVT experience no noticeable symptoms, but are still at risk for sudden cardiac arrest and death.

Diagnosing CPVT typically involves evaluating an individual's medical and family histories as well as results of a test that evaluates your heart's function during exercise (stress test). These evaluations may be combined with genetic testing to diagnose CPVT.

Treatment typically involves taking medication that helps moderate your heart's rhythm. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. Individuals are advised to avoid certain medications, strenuous exercise, competitive sports and stressful environments.

Regular visits to a cardiologist specializing in CPVT are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Heart Rhythm Society

Provides information sheets on types of arrhythmias and associated treatments, risk factors, signs and symptoms.

<http://resources.hrsonline.org>

Sudden Arrhythmia Death syndromes (SADS)

SADS advocates for nondiscriminatory treatment for people who are diagnosed with a SADS disorder. SADS is committed to supporting efforts that will improve the quality of life for patients with heart rhythm abnormalities.

www.sads.org

Last updated April 4, 2018

SCN5A

The SCN5A gene is one of many genes that helps maintain a regular heartbeat. The SCN5A gene makes a protein whose primary role is to form a sodium channel which generates and transmits electrical charges in the body when needed, such as when the heart beats. When this protein doesn't work properly the heartbeat can be abnormal.

Impact of SCN5A mutations

Individuals with a mutation in the SCN5A gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called arrhythmias, which can affect the heartbeat's regular rhythm. These include Brugada syndrome and long QT syndrome.

Disorders associated with the SCN5A gene

Mutations in the SCN5A gene have been associated with the following disorders:

Brugada Syndrome

Brugada syndrome is a hereditary disorder associated with a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia). Brugada syndrome may increase risk of sudden cardiac arrest or sudden cardiac death at young ages.

Brugada syndrome is associated with problems in the heart's electrical system in which there is a dangerously fast and chaotic heartbeat called ventricular fibrillation (VFib). Symptoms of Brugada syndrome may include fainting or sudden cardiac arrest. These can happen from infancy through middle age. An individual's risk depends on their sex, age, and previous symptoms. Some individuals with Brugada syndrome experience no noticeable symptoms, but are still at risk for sudden cardiac arrest and death.

Diagnosing Brugada syndrome typically involves evaluating an individual's medical and family histories as well as results of a test of the heart's electrical system called an electrocardiogram (EKG or ECG), and a test that evaluates your heart's function during exercise (stress test). These evaluations may be combined with genetic testing to diagnose Brugada syndrome.

Treatment for people with symptoms may involve use of a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. Medication can also be used for treatment. Individuals are advised to avoid certain medications and drugs. Illnesses that include fever and electrolyte imbalance caused by dehydration are recommended to be treated promptly as they can increase risk. Individuals are advised to avoid excessive alcohol consumption and large meals.

Regular visits to a cardiologist specializing in Brugada syndrome are recommended in order to check that treatment is effective.

Long QT Syndrome

Long QT syndrome (LQTS) is a hereditary disorder associated with a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia). LQTS may increase risk of sudden cardiac arrest or sudden cardiac death at young ages.

LQTS is associated with problems in the heart's electrical system in which there is a dangerously fast heart beat in the lower pumping chambers of the heart (torsade de pointes). Symptoms of LQTS may include fainting, seizures, or sudden cardiac arrest. Exercise and heightened or intense emotions may be a trigger for sudden cardiac arrest, which can happen from infancy through middle age. An individual's risk depends on their sex, age, and previous symptoms. The severity of the electrical problem in the heart and the specific gene that causes LQTS also play a role. Some individuals with LQTS experience no noticeable symptoms, but are still at risk for sudden cardiac arrest and death.

Women with LQTS have an increased risk of cardiac arrest or death in the first nine months after giving birth.

Diagnosing LQTS typically involves evaluating an individual's medical and family histories as well as results of a test of the heart's electrical system called an electrocardiogram (EKG or ECG). These evaluations may be combined with genetic testing to diagnose the type of LQTS an individual has.

Treatment is recommended for everyone since there is no way to predict who may have symptoms and who may not. Treatment typically involves taking medications that help control blood pressure. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. Individuals are recommended to avoid certain medications and drugs. Some individuals are advised to avoid strenuous exercise, competitive sports, or exposure to loud noises.

Regular visits to a cardiologist specializing in LQTS are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Heart Rhythm Society

Provides information sheets on types of arrhythmias and associated treatments, risk factors, signs and symptoms.

<http://resources.hrsonline.org>

Sudden Arrhythmia Death syndromes (SADS)

SADS advocates for nondiscriminatory treatment for people who are diagnosed with a SADS disorder. SADS is committed to supporting efforts that will improve the quality of life for patients with heart rhythm abnormalities.

www.sads.org

Last updated April 4, 2018

SMAD3

The *SMAD3* gene is one of many genes that helps provide strength and stability to tissues in the body. The *SMAD3* gene regulates proteins that maintain the structure of the wall of the aorta and other blood vessels. When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *SMAD3* mutations

Individuals with a mutation in the *SMAD3* gene are at an increased risk for developing hereditary cardiovascular (heart and blood vessel) disorders called arteriopathies, which can cause weakness, enlargement, and tears of the walls of the arteries. These include familial thoracic aortic aneurysm and dissection and Loeys-Dietz syndrome.

Disorders associated with the *SMAD3* gene

Mutations in the *SMAD3* gene have been associated with the following disorders:

Familial Thoracic Aortic Aneurysm and Dissection

Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Loeys-Dietz Syndrome

Loeys-Dietz syndrome (LDS) is a hereditary disorder associated with problems with the structure of connective tissue in many parts of the body, which can cause weakness of the blood vessel walls, skeletal problems, and abnormal bruising and scarring of the skin.

LDS is a connective tissue disorder. Connective tissue supports, binds, or connects other tissues or organs in the body. Individuals with LDS commonly have problems with the heart and the surrounding blood vessels, especially the large artery that carries blood away from the heart to the rest of the body (aorta). The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening, and are the major cause of death in individuals with LDS. Individuals can also have aneurysms or dissections in other arteries throughout the body and have arteries with abnormal twists and turns (arterial tortuosity).

Individuals may also have skeletal problems such as an abnormal skull shape (craniosynostosis), curved spine (scoliosis) or abnormal spinal bones, a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum), and long limbs whose joints have restricted movement (contractures). They often have a split in the flap of tissue that hangs down in the back of the mouth (bifid uvula) or an opening in the roof of the mouth (cleft palate). Infants and children with LDS may have trouble gaining weight (failure to thrive). Other symptoms may include easy bruising, abnormal scarring, stretch marks in the skin, and collapsed lung (pneumothorax). Symptoms and severity of the symptoms may vary between individuals. Women with LDS are at risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing LDS typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the blood vessels between the head and the pelvis (angiogram). These evaluations may be combined with genetic testing to diagnose LDS.

Treatment for LDS is focused on the prevention of complications and management of symptoms. Individuals are recommended to have an imaging test used to see the heart and aorta (echocardiogram) at least every year. An examination of the blood vessels (angiography) may also be performed to identify aneurysms in other areas. Medication to lower blood pressure may also be used to reduce the risk of dissection. Surgery may be required to fix any aneurysms that develop to prevent dissection. Failure to thrive can be treated with a feeding tube or high-calorie diet. Many problems with the bones, such as scoliosis and cleft palate, can be surgically repaired. In general, it is recommended that individuals with LDS avoid contact or

competitive sports, strenuous exercise, and certain medications that can affect the heart.

Useful resources

Loeys-Dietz Syndrome Foundation

Encourages education about Loeys-Dietz syndrome and provides a support network for individuals, parents, and families affected by Loeys-Dietz syndrome.

www.loeysdietz.org

The Marfan Foundation

Provides information and support to healthcare providers, caregivers, and families affected by Marfan syndrome and related disorders, including FTAAD and Loeys-Dietz syndrome.

www.marfan.org

TAD Coalition

Committed to increasing public awareness of the factors that put people at risk for aortic aneurysm and dissection, and to improving the diagnosis and management of these life-threatening conditions.

www.tadcoalition.org

Last updated April 4, 2018

TGFB1

The *TGFB1* gene is one of many genes that helps provide strength and stability to tissues in the body. The *TGFB1* gene regulates proteins that maintain the structure of the wall of the aorta and other blood vessels. When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *TGFB1* mutations

Individuals with a mutation in the *TGFB1* gene are at an increased risk for developing hereditary cardiovascular (heart and blood vessel) disorders called arteriopathies, which can cause weakness, enlargement, and tears of the walls of the arteries. These include familial thoracic aortic aneurysm and dissection and Loeys-Dietz syndrome.

Disorders associated with the *TGFB1* gene

Mutations in the *TGFB1* gene have been associated with the following disorders:

Familial Thoracic Aortic Aneurysm and Dissection

Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Loeys-Dietz Syndrome

Loeys-Dietz syndrome (LDS) is a hereditary disorder associated with problems with the structure of connective tissue in many parts of the body, which can cause weakness of the blood vessel walls, skeletal problems, and abnormal bruising and scarring of the skin.

LDS is a connective tissue disorder. Connective tissue supports, binds, or connects other tissues or organs in the body. Individuals with LDS commonly have problems with the heart and the surrounding blood vessels, especially the large artery that carries blood away from the heart to the rest of the body (aorta). The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening, and are the major cause of death in individuals with LDS. Individuals can also have aneurysms or dissections in other arteries throughout the body and have arteries with abnormal twists and turns (arterial tortuosity).

Individuals may also have skeletal problems such as an abnormal skull shape (craniosynostosis), curved spine (scoliosis) or abnormal spinal bones, a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum), and long limbs whose joints have restricted movement (contractures). They often have a split in the flap of tissue that hangs down in the back of the mouth (bifid uvula) or an opening in the roof of the mouth (cleft palate). Infants and children with LDS may have trouble gaining weight (failure to thrive). Other symptoms may include easy bruising, abnormal scarring, stretch marks in the skin, and collapsed lung (pneumothorax). Symptoms and severity of the symptoms may vary between individuals. Women with LDS are at risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing LDS typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the blood vessels between the head and the pelvis (angiogram). These evaluations may be combined with genetic testing to diagnose LDS.

Treatment for LDS is focused on the prevention of complications and management of symptoms. Individuals are recommended to have an imaging test used to see the heart and aorta (echocardiogram) at least every year. An examination of the blood vessels (angiography) may also be performed to identify aneurysms in other areas. Medication to lower blood pressure may also be used to reduce the risk of dissection. Surgery may be required to fix any aneurysms that develop to prevent dissection. Failure to thrive can be treated with a feeding tube or high-calorie diet. Many problems with the bones, such as scoliosis and cleft palate, can be surgically repaired. In general, it is recommended that individuals with LDS avoid contact or

competitive sports, strenuous exercise, and certain medications that can affect the heart.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Loeys-Dietz Syndrome Foundation

Encourages education about Loeys-Dietz syndrome and provides a support network for individuals, parents, and families affected by Loeys-Dietz syndrome.

www.loeysdietz.org

The Marfan Foundation

Provides information and support to healthcare providers, caregivers, and families affected by Marfan syndrome and related disorders, including FTAAD and Loeys-Dietz syndrome.

www.marfan.org

Last updated April 4, 2018

TGFB2

The *TGFB2* gene is one of many genes that helps provide strength and stability to tissues in the body. The *TGFB2* gene regulates proteins that maintain the structure of the wall of the aorta and other blood vessels. When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *TGFB2* mutations

Individuals with a mutation in the *TGFB2* gene are at an increased risk for developing hereditary cardiovascular (heart and blood vessel) disorders called arteriopathies, which can cause weakness, enlargement, and tears of the walls of the arteries. These include familial thoracic aortic aneurysm and dissection and Loeys-Dietz syndrome.

Disorders associated with the *TGFB2* gene

Mutations in the *TGFB2* gene have been associated with the following disorders:

Familial Thoracic Aortic Aneurysm and Dissection

Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Loeys-Dietz Syndrome

Loeys-Dietz syndrome (LDS) is a hereditary disorder associated with problems with the structure of connective tissue in many parts of the body, which can cause weakness of the blood vessel walls, skeletal problems, and abnormal bruising and scarring of the skin.

LDS is a connective tissue disorder. Connective tissue supports, binds, or connects other tissues or organs in the body. Individuals with LDS commonly have problems with the heart and the surrounding blood vessels, especially the large artery that carries blood away from the heart to the rest of the body (aorta). The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening, and are the major cause of death in individuals with LDS. Individuals can also have aneurysms or dissections in other arteries throughout the body and have arteries with abnormal twists and turns (arterial tortuosity).

Individuals may also have skeletal problems such as an abnormal skull shape (craniosynostosis), curved spine (scoliosis) or abnormal spinal bones, a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum), and long limbs whose joints have restricted movement (contractures). They often have a split in the flap of tissue that hangs down in the back of the mouth (bifid uvula) or an opening in the roof of the mouth (cleft palate). Infants and children with LDS may have trouble gaining weight (failure to thrive). Other symptoms may include easy bruising, abnormal scarring, stretch marks in the skin, and collapsed lung (pneumothorax). Symptoms and severity of the symptoms may vary between individuals. Women with LDS are at risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing LDS typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the blood vessels between the head and the pelvis (angiogram). These evaluations may be combined with genetic testing to diagnose LDS.

Treatment for LDS is focused on the prevention of complications and management of symptoms. Individuals are recommended to have an imaging test used to see the heart and aorta (echocardiogram) at least every year. An examination of the blood vessels (angiography) may also be performed to identify aneurysms in other areas. Medication to lower blood pressure may also be used to reduce the risk of dissection. Surgery may be required to fix any aneurysms that develop to prevent dissection. Failure to thrive can be treated with a feeding tube or high-calorie diet. Many problems with the bones, such as scoliosis and cleft palate, can be surgically repaired. In general, it is recommended that individuals with LDS avoid contact or

competitive sports, strenuous exercise, and certain medications that can affect the heart.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Loeys-Dietz Syndrome Foundation

Encourages education about Loeys-Dietz syndrome and provides a support network for individuals, parents, and families affected by Loeys-Dietz syndrome.

www.loeysdietz.org

The Marfan Foundation

Provides information and support to healthcare providers, caregivers, and families affected by Marfan syndrome and related disorders, including FTAAD and Loeys-Dietz syndrome.

www.marfan.org

Last updated April 4, 2018

TMEM43

The *TMEM43* gene is one of many genes that helps provide strength and stability to tissues in the body. The *TMEM43* gene makes a protein which is found in the heart muscle. When this protein doesn't work properly, the heart can be weakened.

Impact of *TMEM43* mutations

Individuals with a mutation in the *TMEM43* gene are at an increased risk for developing arrhythmogenic cardiomyopathy, a hereditary cardiovascular (heart and blood vessel) disorder, which can affect the heart's ability to pump blood.

Disorders associated with the *TMEM43* gene

Mutations in the *TMEM43* gene have been associated with the following disorder:

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), lightheadedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

ARVD/C Patient Registry (The Johns Hopkins Hospital)

The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

www.hopkinsmedicine.org

Sudden Arrhythmia Death syndromes (SADS)

SADS advocates for nondiscriminatory treatment for people who are diagnosed with a SADS disorder. SADS is committed to supporting efforts that will improve the quality of life for patients with heart rhythm abnormalities.

www.sads.org

Last updated April 4, 2018

TNNI3

The *TNNI3* gene is one of many genes that helps muscles tense up (contract). The *TNNI3* gene makes a protein which is found in heart muscle tissue and plays a key role in allowing muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *TNNI3* mutations

Individuals with a mutation in the *TNNI3* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include dilated cardiomyopathy, hypertrophic cardiomyopathy, and restrictive cardiomyopathy.

Disorders associated with the *TNNI3* gene

Mutations in the *TNNI3* gene have been associated with the following disorders:

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a

heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally, which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, advocacy and advancing research, understanding and care to those with hypertrophic cardiomyopathy.

www.4hcm.org

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

TNNT2

The *TNNT2* gene is one of many genes that helps muscles tense up (contract). The *TNNT2* gene makes a protein which is found in heart muscle tissue and plays a key role in allowing muscles in the heart to tense up (contract). When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *TNNT2* mutations

Individuals with a mutation in the *TNNT2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include dilated cardiomyopathy, hypertrophic cardiomyopathy, left ventricular noncompaction cardiomyopathy, and restrictive cardiomyopathy.

Disorders associated with the *TNNT2* gene

Mutations in the *TNNT2* gene have been associated with the following disorders:

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical

procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether HCM symptoms are present, medications that help control blood pressure may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Left Ventricular Noncompaction Cardiomyopathy

Left ventricular noncompaction cardiomyopathy (LVNC) is associated with a problem with the heart muscle that can affect the heart's ability to pump blood and disrupt the normal electrical signalling of the heart.

LVNC is a disorder of the heart where the walls of the major pumping chamber of the heart, called the left ventricle, do not develop properly. Abnormal pieces of muscle (trabeculations) extend into the left ventricle, resulting in a spongy appearance in this part of the heart, which is normally smooth. This affects the heart's ability to pump blood and can disrupt the normal electrical signalling of the heart. In some cases, the minor pumping chamber of the heart, called the right ventricle, can also be affected. People with LVNC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals may experience shortness of breath, strong or irregular heartbeats (heart palpitations), tiredness or dizziness, fainting due to a fall in blood pressure (syncope), chest pain, or buildup of fluid in the body (edema), due to heart failure. Some individuals with LVNC experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest. Individuals with LVNC are also at increased risk for certain types of heart muscle disease (cardiomyopathy).

Diagnosing LVNC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications such as anticoagulants to reduce the risk of blood clots which can lead to a stroke. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in LVNC are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally,

which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, advocacy and advancing research, understanding and care to those with hypertrophic cardiomyopathy.

www.4hcm.org

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

Last updated April 4, 2018

TPM1

The *TPM1* gene is one of many genes that helps muscles tense up (contract). The *TPM1* gene makes a protein found in heart muscle tissue that plays a key role in allowing muscles in the heart to contract. When this protein doesn't work properly, it decreases the heart's ability to pump blood to the rest of the body.

Impact of *TPM1* mutations

Individuals with a mutation in the *TPM1* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include dilated cardiomyopathy, hypertrophic cardiomyopathy, left ventricular noncompaction cardiomyopathy, and restrictive cardiomyopathy.

Disorders associated with the *TPM1* gene

Mutations in the *TPM1* gene have been associated with the following disorders:

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical

procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is associated with an abnormal thickening of the heart muscle, which can make it hard for the heart to pump blood.

HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting.

The majority of people with HCM will have mild symptoms and a normal life expectancy. However, in some cases, symptoms of HCM can be life-threatening. People with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals can also develop heart failure that is potentially fatal if untreated. Age of onset and severity of symptoms may vary, even within the same family.

Diagnosing HCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with HCM are advised to make certain lifestyle changes, such as staying well-hydrated and avoiding strenuous exercise and certain medications. Depending on whether HCM symptoms are present, medications that help control blood pressure, and other medications may be prescribed. Antibiotics may be prescribed before certain medical and dental procedures to guard against infections in the heart. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in HCM are recommended in order to check that treatment is effective.

Left Ventricular Noncompaction Cardiomyopathy

Left ventricular noncompaction cardiomyopathy (LVNC) is associated with a problem with the heart muscle that can affect the heart's ability to pump blood and disrupt the normal electrical signalling of the heart.

LVNC is a disorder of the heart where the walls of the major pumping chamber of the heart, called the left ventricle, do not develop properly. Abnormal pieces of muscle (trabeculations) extend into the left ventricle, resulting in a spongy appearance in this part of the heart, which is normally smooth. This affects the heart's ability to pump blood and can disrupt the normal electrical signalling of the heart. In some cases, the minor pumping chamber of the heart, called the right ventricle, can also be affected. People with LVNC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Individuals may experience shortness of breath, strong or irregular heartbeats (heart palpitations), tiredness or dizziness, fainting due to a fall in blood pressure (syncope), chest pain, or buildup of fluid in the body (edema), due to heart failure. Some individuals with LVNC experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest. Individuals with LVNC are also at increased risk for certain types of heart muscle disease (cardiomyopathy).

Diagnosing LVNC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications such as anticoagulants to reduce the risk of blood clots which can lead to a stroke. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in LVNC are recommended in order to check that treatment is effective.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is associated with an abnormal stiffness of the heart muscle, which can affect the heart's ability to pump blood.

RCM is associated with a replacement of normal tissue with scar tissue in the heart's pumping chambers (ventricles). When this happens, the ventricles are not able to fill with blood normally,

which reduces the blood flow in the heart. This can lead to problems such as heart failure and sudden cardiac death. People can also have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), including a type called heart block which causes the heart to beat too slowly. Symptoms include shortness of breath, persistent cough, strong or irregular heartbeats (heart palpitations), tiredness, dizziness, fainting due to a fall in blood pressure (syncope), chest pain, buildup of fluid in the body (edema), or nausea, bloating, and poor appetite. Blood clots may also occur. Age of onset and severity of symptoms may vary, even within the same family. Some individuals with RCM experience no noticeable symptoms, but may still be at risk for heart failure or sudden cardiac arrest.

Diagnosing RCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG) with an experienced cardiologist. Additional screening and diagnostic tests may be ordered, including an MRI.

Treatment typically involves taking medications to reduce the risk of blood clots. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in RCM are recommended in order to check that treatment is effective.

Useful resources

American Heart Association

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

www.heart.org

Hypertrophic Cardiomyopathy Association

Provides support, education, advocacy and advancing research, understanding and care to those with hypertrophic cardiomyopathy.

www.4hcm.org

SHARE Registry

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

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About Color

Color is a health service that helps people better understand their risk of hereditary conditions, such as cancer and heart disease. By partnering with Color, healthcare providers can offer their patients improved access to genetic health information that can drive personalized patient care and lead to improved health outcomes.

Your patients' privacy is our priority

Color takes privacy very seriously and only collects the information that is needed to provide a high-quality experience. We comply with HIPAA requirements regarding protected health information. To learn more, you can review our privacy policy at color.com/privacy or contact us to request a copy.

color.com/providers

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