GENEReviews

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Dilated Cardiomyopathy Overview

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Summary

Disease characteristics. Hereditary dilated cardiomyopathy (DCM) is characterized by left ventricular enlargement and systolic dysfunction, a reduction in the myocardial force of contraction. DCM usually presents with any one of the following: heart failure with symptoms of congestion (edema, orthopnea, paroxysmal dyspnea) and/or reduced cardiac output (fatigue, dyspnea on exertion); arrhythmias and/or conduction system disease; thromboembolic disease (from left ventricular mural thrombus) including stroke.

Diagnosis/testing. Genetic forms of DCM must be distinguished from the many acquired (non-genetic) causes of DCM. After exclusion of all acquired identifiable causes, DCM is traditionally referred to as *idiopathic* dilated cardiomyopathy (IDC), which includes genetic forms of DCM. When two or more closely related family members meet a formal diagnostic standard for IDC, the diagnosis of familial dilated cardiomyopathy (FDC) is made. The genetic forms of DCM are diagnosed by family history and molecular genetic testing available in clinical laboratories.

Management. *Treatment of manifestations:* Treatment by physicians skilled in diagnosis and management of symptomatic and asymptomatic disease with pharmacologic therapy and pacemakers and implantable cardiac defibrillator devices improves survival and quality of life; cardiac transplantation remains the definitive treatment for progressive DCM and heart failure refractory to medical or device therapy. *Prevention of primary manifestations:* Treatment prior to the onset of symptoms may result in remission of DCM or delay onset of symptomatic disease. *Prevention of secondary complications:* All at-risk persons should understand the need to seek medical care when signs and symptoms of heart failure, syncope, sudden death, and stroke appear; training of relatives and/or caregivers in cardiopulmonary resuscitation (CPR) is advisable, particularly in those with a strong family history of sudden death and/or significant arrhythmias. *Surveillance:* Cardiovascular screening (physical examination, echocardiogram,

ECG), usually starting in adulthood, is recommended: every one to two years in an asymptomatic person with a known disease-causing mutation; every one to three years in an asymptomatic at-risk first-degree relative in a kindred with an established diagnosis of FDC; every three to five years in an asymptomatic first-degree relative of an individual with IDC that is not known to be sporadic or familial. *Testing of relatives at risk:* Offer molecular genetic testing when the disease-causing mutation has been identified in a family.

Genetic counseling. Genetic DCM can be inherited in an autosomal dominant, autosomal recessive, or X-linked manner. Genetic counseling and risk assessment depend on determination of the specific DCM subtype in an individual.

Definition

Clinical Manifestations of Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) usually presents with any one of the following:

- **Heart failure.** Symptoms include those of congestion (edema, orthopnea, paroxysmal dyspnea) and/or reduced cardiac output (fatigue, dyspnea on exertion).
- **Arrhythmias and/or conduction system disease.** These commonly accompany advanced cardiomyopathy and heart failure but may also precede heart failure in individuals with heritable cardiomyopathy.
- **Thromboembolic disease** (from left ventricular mural thrombus), including stroke

Dilated cardiomyopathy may also be asymptomatic.

Extensive additional background is available [Hunt 2005].

Establishing the Diagnosis of DCM

The diagnosis of DCM is established by the presence of both of the following findings:

- **Left ventricular enlargement,** most commonly assessed by M-mode and two-dimensional echocardiography
- **Systolic dysfunction,** a reduction in the myocardial force of contraction
  - The left ventricular ejection fraction is the most commonly used clinical measure of systolic dysfunction, and is usually estimated from a two-dimensional echocardiogram, from other noninvasive studies (e.g., cardiac nuclear or magnetic resonance imaging studies), or from a left ventricular angiogram. An ejection fraction of less than 50% is considered systolic dysfunction.
  - Fractional shortening is another clinical measure of systolic function. A fractional shortening of less than 25%-30% is considered systolic dysfunction.

Idiopathic dilated cardiomyopathy (IDC). After exclusion of all acquired identifiable causes, DCM is traditionally referred to as *idiopathic* dilated cardiomyopathy (IDC), which includes genetic forms of DCM.

Familial dilated cardiomyopathy (FDC). When each of two or more closely related family members meet a formal diagnostic standard for IDC (i.e., all detectable causes of DCM have been ruled out), the diagnosis of familial dilated cardiomyopathy (FDC) is made [Burkett & Hershberger 2005].

Differential Diagnosis of DCM

The term 'dilated cardiomyopathy' (DCM) has multiple meanings.

In the cardiovascular literature the most generic use of the term DCM describes the two key anatomic findings of the left ventricle: left ventricular enlargement and systolic dysfunction. Hence, such generic use includes all etiologies of DCM, of which the most common is ischemic injury to the myocardium from recent or remote myocardial ischemia and/or infarct from coronary artery disease. This is most commonly termed ischemic cardiomyopathy (or ischemic dilated cardiomyopathy). Potential genetic causes of coronary artery disease that may lead to ischemic injury and thus ischemic dilated cardiomyopathy are not addressed in this review. Other known causes of DCM include valvular or congenital heart disease, toxins, thyroid disease, inflammatory conditions, myocarditis, severe long-standing hypertension, radiation, and others.

Prevalence of DCM

The only formal estimate of IDC prevalence cited is by Codd et al (1989); an Olmsted County, Minnesota study conducted from 1975 to 1984 estimated IDC prevalence (as of 1-1-85) at 36.5:100,000 (~1:2,700). This was twice the prevalence of hypertrophic cardiomyopathy (HCM), which was estimated at 19.7:100,000 (~1:5,000) from the same cohort during this study period. Subsequently, multiple well-designed epidemiologic studies have shown an HCM prevalence of approximately 1:500. It is possible, if not likely, that the Olmsted County study also significantly underestimated the prevalence of IDC.

Causes

Environmental (Acquired) Causes

Ischemic injury from myocardial infarction and related coronary artery disease is considered the most common cause of dilated cardiomyopathy (DCM) (also known as ischemic cardiomyopathy or ischemic dilated cardiomyopathy) [Hunt 2005].

Other causes of DCM include valvular and congenital heart disease, toxins (most commonly anthracyclines), thyroid disease, inflammatory conditions, myocarditis, severe long-standing hypertension, and radiation — most of which are detected with a careful medical history.

Iron overload from hemochromatosis can also present as DCM, but more commonly presents as nondilated and/or infiltrative cardiomyopathy (see HFE-Associated Hereditary Hemochromatosis).

Heritable Causes

It is thought that approximately 20%-50% of IDC may have a genetic basis. Screening first-degree relatives of a proband with IDC by echocardiography and electrocardiography (ECG) reveals that 20%-48% of probands have affected relatives, consistent with a diagnosis of familial dilated cardiomyopathy (FDC) [Michels et al 1992, Baig et al 1998, Grünig et al 1998]. Numerous large kindreds with FDC have provided the foundation for establishing genetic causation, and mutations in multiple genes have been shown to cause FDC [Burkett & Hershberger 2005] (Table 1). Current estimates indicate that the 20-plus known FDC-causing genes account for a minority of cases of FDC (Table 1).

Locus heterogeneity and allellic heterogeneity are the rule.

FDC is largely an adult-onset disease, but has demonstrated a highly variable age of onset and reduced penetrance.

Table 1. Molecular Genetics of Familial Dilated Cardiomyopathy (FDC)

Gene Symbol	Protein Name	OMIM	% of FDC Caused by Mutations in This Gene [1]	Molecular Genetic Test Availability for FDC [2, 3]	Allelic Disorders [4]
Autosomal Dominant					
ACTC1	Actin, alpha cardiac muscle 1	102540	<1%	Clinical Testing	FHC [5]
DES	Desmin	125660	<1%	Clinical Testing	Desminopathy, Myofibrillar myopathy
LMNA	Lamin-A/C	150330	7%-8%	Clinical Testing	Partial lipodystrophy, CMT2B1, Emery-Dreifuss muscular dystrophy, Hutchinson-Gilford progeria syndrome, LGMD1B [6]
SGCD	Delta-sarcoglycan	601411	?	Clinical Testing	Delta sarcoglycanopathy (LGMD2F) [6]
MYH7	Myosin-7	160760	5%-8%	Clinical Testing	Laing distal myopathy, FHC
TNNT2	Troponin T, cardiac muscle	191045	2%-4%	Clinical Testing	FHC
TPM1	Tropomyosin alpha-1 chain	191010	?	Clinical Testing	FHC
TTN	Titin	188840	?	Clinical Testing	Udd distal myopathy
VCL	Vinculin	193065	?	Research only	
MYBPC3	Myosin-binding protein C, cardiac-type	600958	?	Clinical Testing	FHC
PLN	Cardiac phospholamban	172405	?	Clinical Testing	
LDB3	LIM domain-binding protein 3	605906	?	Clinical Testing	
ACTN2	Alpha-actinin-2	102573	?	Research only	
CSRP3	Cysteine and glycine-rich protein 3	600824	?		
MYH6	Myosin-6	160710	?	Research only [7]	FHC
ABCC9	ATP-binding cassette transporter sub-family C member 9	601439	?	Research only	
Gene Symbol	**Protein Name**	**OMIM**	**% of FDC Caused by Mutations in This Gene**	**Molecular Genetic Test Availability for FDC**	**Allelic Disorders**
TNNC1	Troponin C, slow skeletal and cardiac muscles	191040	?	Research only	
TCAP	Telethonin	604488	?	Research only [7]	LGMD2G [6]
SCN5A	Sodium channel protein type 5 subunit alpha	600163	2%-4%	Clinical Testing	Long QT syndrome type 3, Brugada syndrome, idiopathic ventricular fibrillation, sick sinus syndrome, cardiac conduction system disease
EYA4	Eyes absent homolog 4	603550	?	Research only	
TMPO	Thymopoietin	188380	?		

PSEN1	Presenilin-1	104311	<1%	Research only [7]	Early-onset Alzheimer disease
PSEN2	Presenilin-2	600759	<1%		Early- and late-onset Alzheimer disease
FCMD	Fukutin	607440	?		Fukuyama congenital muscular dystrophy
X-Linked					
DMD	Dystrophin	300377	?	Clinical Testing	Dystrophinopathies (Duchenne muscular dystrophy, Becker muscular dystrophy)
TAZ	Tafazzin	30094	?	Clinical Testing	Barth syndrome, endocardial fibroelastosis type 2, familial isolated non-compaction of the left ventricular myocardium
Autosomal Recessive					
TNNI3	Troponin I, cardiac muscle	191044	?	Clinical Testing	FHC, restrictive cardiomyopathy

1. The percentages provided (based upon two or more reports screening larger numbers of probands with IDC or FDC) should be interpreted as preliminary estimates.

2. Per the GeneTests Laboratory Directory

3. Data are only now emerging to justify the clinical use of molecular genetic testing in individuals with DCM; because mutations in the genes encoding lamin-A/C *(LMNA*) and myosin-7 *(MYH7*) appear to be more common than mutations in other genes, testing for mutations in these genes may be considered.

4. Allelic disorders = other phenotypes caused by mutation in the same gene

5. FHC = familial hypertrophic cardiomyopathy

6. See Limb-Girdle Muscular Dystrophy Overview.

7. Testing is available on a research basis only for this disorder; testing is available on a clinical basis for some of the allelic disorders per the GeneTests Laboratory Directory.

Unknown Causes

By definition, the pathogenesis of nonfamilial causes of idiopathic dilated cardiomyopathy is unknown.

The frequency of genetic causation in persons with simplex IDC (i.e., a single occurrence in a family) remains largely unknown.

Evaluation Strategy

Idiopathic Dilated Cardiomyopathy (IDC)

When IDC is established in an individual, the following approach can help determine if IDC may actually be familial dilated cardiomyopathy (FDC). This approach is particularly relevant because a person with dilated cardiomyopathy (DCM) may remain asymptomatic for years. Screening and identification of DCM before the onset of symptoms enables the initiation of medical therapy that may delay disease progression.

Family history. A detailed three- to four-generation family history (including heart failure, dilated cardiomyopathy, cardiac transplantation, unexplained sudden death, unexplained cardiac conduction system disease and/or arrhythmia, or unexplained stroke or other thromboembolic disease) should be obtained from relatives to assess the possibility of FDC.

Both sides of the family should be considered as possibly contributing to familial disease. Families with FDC in both maternal and paternal lineages have been noted, and experience has shown that regardless of an apparent inheritance pattern in a family, assumptions regarding maternal or paternal inheritance of mutations in genes causing FDC in a given family may be unreliable and potentially misleading [Author, personal observation].

Screening of first-degree relatives for dilated cardiomyopathy. Current evidence indicates that IDC may be familial (and therefore possibly genetic) in 20%-50% of cases. A medical history, physical examination, echocardiogram, and ECG can be used to evaluate a proband's first-degree relatives to determine if any have asymptomatic DCM, thus supporting the diagnosis of FDC. However, because the age of onset is variable and penetrance is reduced, a normal baseline echocardiogram and ECG in a first-degree relative does not rule out FDC in that individual or a potential genetic basis of IDC in the proband. Therefore, it is recommended that first-degree relatives with a normal echocardiogram and ECG be rescreened every three to five years to fully address their risk as well as the question of FDC in the family.

Note: Because most FDC is adult onset, screening is usually not recommended for children or adolescents unless onset of disease in the proband was in these age groups.

Any abnormal cardiovascular test results in a relative of a proband should be followed with a full cardiovascular assessment to evaluate for acquired causes of disease (e.g., coronary artery disease with history of myocardial infarction or history of exposure to cardiotoxic medications).

Screening results that do not meet criteria for DCM but do show some abnormality (e.g., left ventricular enlargement but normal function, decreased ejection fraction but normal-sized left ventricle, normal echocardiogram with ECG abnormality) may reflect variable expression of FDC in that relative.

Molecular genetic testing. The frequency of genetic causation in simplex cases of IDC (i.e., a single occurrence in a family) remains largely unknown. Thus, in such cases firm recommendations for molecular genetic testing cannot be made at this time.

- Molecular genetic testing for *LMNA*-related cardiomyopathy may be considered in an individual with a diagnosis of IDC accompanied by significant conduction system disease and/or arrhythmias regardless of family history or outcome of first-degree relative screening. It should be noted that although the analytical sensitivity for *LMNA* gene mutations is quite high, the clinical sensitivity (likelihood of identifying a mutation in a person with the disorder) is approximately 6% for all cases of IDC and 8% in FDC.
- Because mutations in *MYH7* (encoding myosin-7) may be as common, testing may be considered; clinical sensitivity in large cohorts has not yet been established.

Familial Dilated Cardiomyopathy (FDC)

A diagnosis of FDC is made when two or more closely related family members have each met a rigorous diagnostic standard for IDC. With a diagnosis of FDC, the following evaluation strategy is recommended.

Family history. The family history should be reviewed to evaluate possible patterns of inheritance. A genetic basis is more likely with multigenerational FDC. However, care should be taken to avoid assumptions regarding inheritance patterns prior to molecular genetic testing.

Molecular genetic testing

- Molecular genetic testing of the proband for an *LMNA* mutation is probably indicated, particularly if significant conduction system disease is present in the family. It should be noted that although the analytical sensitivity for detecting *LMNA* gene mutations is quite high, the clinical sensitivity (likelihood of identifying a mutation in a person with the disorder) is approximately 8% for FDC.
- Because molecular genetic testing for *MYH7* has comparable clinical sensitivity, testing for mutations in *MHY7* may also be considered.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members. This section is not meant to address all personal, cultural, or ethical issues that individuals may face or to substitute for consultation with a genetics professional. To find a genetics or prenatal diagnosis clinic, see the GeneTests Clinic Directory.

Mode of Inheritance

Familial dilated cardiomyopathy (FDC) may be inherited in an autosomal dominant, an autosomal recessive, or an X-linked manner. Mitochondrial inheritance has also been reported. Most FDC appears to be autosomal dominant (probably 80%-90%); X-linked and recessive forms are less common.

Risk to Family Members — Autosomal Dominant Hereditary Dilated Cardiomyopathies

Parents of a proband

- Some individuals diagnosed as having autosomal dominant DCM have an affected parent.
- A proband with autosomal dominant dilated cardiomyopathy may have the disorder as the result of a new gene mutation. The proportion of cases caused by *de novo* mutations is unknown.
- Recommendations for the evaluation of parents of a proband with an apparent *de novo* mutation are included in the evaluation strategy outlined in Evaluation Strategy, **Screening of first-degree relatives for dilated cardiomyopathy**. Evaluation of parents may determine that one is affected but has escaped previous diagnosis and/or has a milder phenotypic presentation, including evidence of DCM on echocardiogram without clinical heart failure symptoms (i.e., asymptomatic affected).
- Parental screening results that do not meet criteria for DCM but do show some abnormality (e.g., left ventricular enlargement but normal function, decreased ejection fraction but normal-sized left ventricle, normal echocardiogram with ECG abnormality) may be variable expression of FDC.
- Because of variable age of onset, a parent may have normal baseline echocardiogram and ECG results but develop abnormalities at a later time. Thus, negative screening does not rule out FDC and potential risk for DCM, and thus it is suggested that parents with normal tests be rescreened every three to five years.
- In an unknown proportion of cases, both parents may have evidence of DCM, with possible codominant expression of the parental genes in the proband.

Note: (1) Although many individuals diagnosed with autosomal dominant IDC/FDC have an affected parent, the family history may appear to be negative because of failure to recognize the disorder in family members, early death of the parent before the onset of symptoms, or late onset of the disease in the affected parent. (2) If the parent is the individual in whom the mutation first occurred it is possible that s/he may have somatic mosaicism for the mutation and may be mildly affected, although this has not yet been reported.

Sibs of a proband

- The risk to sibs depends upon the genetic status of the proband's parents.
- If a parent of the proband is affected and/or shown to have a disease-causing mutation, the risk to the sibs of inheriting the allele is 50%. However the degree of penetrance and age of onset cannot be predicted.
- For families in which both parents of a proband have an FDC allele, sibs have a 50% chance of inheriting each of the mutations, and a 25% chance of inheriting both, regardless of the degree of penetrance in the parents.
- When the parents have no signs of dilated cardiomyopathy, the risk to the sibs of a proband is increased over the general population risk but cannot be precisely calculated. Recommendations for sibs are included in the evaluation strategy outlined in Evaluation Strategy, **Screening of first-degree relatives for dilated cardiomyopathy**.
- If the disease-causing mutation found in the proband cannot be detected in the DNA of either parent, the risk to sibs is low but greater than that of the general population because of the possibility of germline mosaicism. When the mutation is known, the sib may be offered genetic testing to help clarify risk. However, the absence of a likely disease-causing mutation in an unaffected sib should be interpreted with caution, as it is possible that some families may have two or more pathogenic mutations.

Offspring of a proband. Each child of an individual with autosomal dominant DCM has a 50% chance of inheriting the parent's mutation. However, because of variable expression and reduced penetrance, no predictions can be made regarding age of onset or severity of disease.

Risk to Family Members — Autosomal Recessive Hereditary Dilated Cardiomyopathies

Parents of a proband

- The parents are obligate heterozygotes and therefore carry a single copy of a disease-causing mutation.
- Heterozygotes are asymptomatic.

Sibs of a proband

- Each sib of a proband has a 25% chance of being homozygous for the disease-causing mutation and thus at risk for disease, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. However, without a known mutation it is not possible to identify carriers.
- Recommendations for sibs are included in the evaluation strategy outlined in Evaluation Strategy, **Screening of first-degree relatives for dilated cardiomyopathy**.

Offspring of a proband. All offspring are obligate carriers.

Carrier Detection

Carrier testing for at-risk family members may be available on a clinical basis for mutations in some DCM-causing genes once the specific mutations have been identified in the proband.

Risk to Family Members — X-Linked DCM Caused by *DMD* Mutations

Parents of a proband

- The father of an affected male will not have the disease nor will he be a carrier of the mutation.
- Women who have an affected son and another affected male relative are obligate heterozygotes.
- If pedigree analysis reveals that an affected male represents a simplex case (a single case without a positive family history), several possibilities regarding his mother's carrier status need to be considered:
  - He has a *de novo* disease-causing mutation and his mother is not a carrier;
  - His mother has a *de novo* disease-causing mutation either (a) as a "germline mutation" (i.e., present at the time of her conception and therefore in every cell of her body; or (b) as "germline mosaicism" (i.e., present in only some of her germ cells);
  - His mother is a carrier of a family mutation that has not yet been inherited or expressed in other family members.
- Carrier mothers may be at some risk of developing disease, and therefore mothers of affected sons should follow the recommendations included in the evaluation strategy outlined in Evaluation Strategy, **Screening of first-degree relatives for dilated cardiomyopathy**.

Sibs of a proband

- The risk to sibs depends upon the genetic status of the proband's mother.
- A female who is heterozygous for a germline mutation (i.e., a carrier) has a 50% chance of transmitting the disease-causing mutation with each pregnancy. Sons who inherit the mutation will be at risk of developing disease; daughters who inherit the mutation are heterozygous for a germline mutation (i.e., carriers) and may or may not be affected.
- If the mother is not a carrier, the risk to sibs is low but greater than that of the general population because of the possibility of germline mosaicism, as mentioned above.

Offspring of a proband. Males with X-linked dilated cardiomyopathy will pass the disease-causing mutation to all of their daughters, who are heterozygotes (i.e., carriers), and to none of their sons.

Other family members of a proband. The proband's maternal aunts may be at risk of being carriers and the aunt's offspring, depending upon their gender, may be at risk of being carriers or being affected.

Related Genetic Counseling Issues

See Surveillance for information on testing at-risk relatives for the purpose of early diagnosis and treatment.

Ambiguous echocardiographic and/or ECG results in asymptomatic at-risk relatives who do not meet criteria for DCM but nevertheless have abnormal cardiac findings (e.g., left ventricular enlargement with normal systolic function, decreased ejection fraction but normal-sized left ventricle, normal echocardiogram but significant conduction system disease and/or arrhythmias), with other causes ruled out, may represent variable expression of FDC. Such results complicate family risk assessment and management/surveillance for the individual and other family members.

Molecular genetic testing of at-risk asymptomatic adult relatives of individuals with DCM is possible if molecular genetic testing has identified the specific mutation in an affected relative. Such testing should only be performed in the context of formal genetic counseling, and is not useful in predicting age of disease onset, severity, or rate of progression. Testing of asymptomatic at-risk individuals is predictive testing, not diagnostic testing.

Molecular genetic testing of asymptomatic individuals younger than age 18 years who are at risk for adult-onset disorders for which no treatment exists is not considered appropriate, primarily because it negates the autonomy of the child with no compelling benefit. Further, concern exists regarding the potential unhealthy adverse effects that such information may have on family dynamics, the risk of discrimination and stigmatization in the future, and the anxiety that such information may cause.

That said, early diagnosis of DCM may offer a benefit that outweighs the arguments against such testing. Treatment of early DCM may forestall the development of advanced disease and thus justify screening and genetic testing of asymptomatic minors in the setting of early onset and/or aggressive familial disease, where a positive molecular genetic test may guide more stringent clinical screening for asymptomatic but clinically detectable cardiovascular disease.

Genetic testing is always indicated in affected or symptomatic individuals in a family with established FDC regardless of age.

For more information, see the National Society of Genetic Counselors statement on genetic testing of children and the American Society of Human Genetics and American College of Medical Genetics points to consider: ethical, legal, and psychosocial implications of genetic testing in children and adolescents (see Genetic Testing; pdf).

DNA Banking. DNA banking is the storage of DNA (typically extracted from white blood cells) for possible future use. Because it is likely that testing methodology and our understanding of genes, mutations, and diseases will improve in the future, consideration should be given to banking DNA of affected individuals. See Testing for a list of laboratories offering DNA banking.

Prenatal Testing

Prenatal diagnosis for some of the hereditary dilated cardiomyopathies is technically possible by analyzing fetal DNA extracted from cells obtained by chorionic villus sampling (CVS) at about ten to 12 weeks' gestation or by amniocentesis, usually performed at about 15-18 weeks' gestation. The disease-causing allele(s) of an affected family member must be identified before prenatal testing can be performed.

Note: Gestational age is expressed as menstrual weeks calculated either from the first day of the last normal menstrual period or by ultrasound measurements.

For the hereditary dilated cardiomyopathies for which prenatal testing is not listed in the GeneTests Laboratory Directory, such testing may be available to families in which the disease-

causing mutations have been identified. For laboratories offering custom prenatal testing, see Testing.

Requests for prenatal testing for (typically) adult-onset diseases are not common. Differences in perspective exist among medical professionals and within families regarding the use of prenatal testing, particularly if the testing is being considered for the purpose of pregnancy termination rather than early diagnosis. Although most centers would consider decisions about prenatal testing to be the choice of the parents, discussion of these issues is appropriate.

Preimplantation genetic diagnosis (PGD) may be available for families in which the disease-causing mutation(s) has/have been identified. For laboratories offering PGD, see Testing.

Management

Treatment of Manifestations

Management of dilated cardiomyopathy (DCM) includes pharmacologic therapy, and pacemaker and implantable cardiac defibrillator device therapy for symptomatic and asymptomatic disease. Care should be provided by physicians skilled in the diagnosis and treatment of patients with heart failure and DCM.

Symptoms include those related to heart failure, arrhythmia, or stroke. Symptomatic DCM represents late disease. Full medical therapy (ACE inhibitors, beta blockers) with evaluation for antiarrhythmic therapy (e.g., pacemakers, implantable cardiac defibrillators) should be considered by cardiovascular specialists with expertise in the field [Hunt 2005].

Individuals with IDC/FDC should:

- Be counseled that IDC/FDC is treatable even prior to the onset of symptoms, that treatment may result in remission of DCM, that treatment may forestall symptomatic disease, and that treatment of symptomatic disease (heart failure, arrhythmias, or thromboembolic disease) improves survival and quality of life.
- Understand the symptoms of heart failure, arrhythmia (including presyncope and syncope), and thromboemoblic disease, and be counseled to urgently seek medical care with the new presentation of any of these symptoms.

Training of relatives and/or caregivers in cardiopulmonary resuscitation (CPR) may be suggested, particularly in families with a strong family history of sudden death and/or significant arrhythmias.

Cardiac transplantation remains the definitive treatment for progressive DCM and heart failure refractory to medical or device therapy.

Additional comprehensive guidelines are available [Hunt 2005].

Surveillance

An asymptomatic person with a known disease-causing mutation should understand the signs and symptoms of heart failure, syncope, sudden death, and stroke, and should seek medical assistance if any of these symptoms occur. Depending on age, cardiovascular screening (physical examination, echocardiogram, and ECG) should be performed every one to two years.

An asymptomatic at-risk first-degree relative in a kindred with an established diagnosis of FDC should understand the signs and symptoms of heart failure, syncope, sudden death, and stroke, and should seek medical assistance if any of these symptoms occur. Depending on age, cardiovascular screening (physical examination, echocardiogram, and ECG) is indicated every one to three years. Should a first-degree at-risk relative have evidence of IDC/FDC, the screening recommendations outlined in Evaluation Strategy should extend to that person's first-degree relatives (i.e., stepwise [or "cascade"] screening).

An asymptomatic first-degree relative of an individual with IDC in whom it is unknown if the IDC is sporadic or familial should undergo cardiovascular screening (physical examination, echocardiogram, and ECG) every three to five years starting in adulthood. If a first-degree at-risk relative shows evidence of IDC/FDC, the screening recommendations outlined in Evaluation Strategy should extend to that person's first-degree relatives (i.e., stepwise screening).

Testing of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Search ClinicalTrials.gov for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Other

Genetics clinics, staffed by genetics professionals, provide information for individuals and families regarding the natural history, treatment, mode of inheritance, and genetic risks to other family members as well as information about available consumer-oriented resources. See the GeneTests Clinic Directory.

Support groups have been established for individuals and families to provide information, support, and contact with other affected individuals. The Resources section may include disease-specific and/or umbrella support organizations.

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Resources

GeneReviews provides information about selected national organizations and resources for the benefit of the reader. GeneReviews is not responsible for information provided by other organizations. Information that appears in the Resources section of a GeneReview is current as of initial posting or most recent update of the GeneReview. Search GeneTests*for this disorder and select* Resources *for the most up-to-date Resources information.*—ED.

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Cardiomyopathy

References

Medical Genetic Searches: A specialized PubMed search designed for clinicians that is located on the PubMed Clinical Queries page. PubMed

Published Statements and Policies Regarding Genetic Testing

No specific guidelines regarding genetic testing for this disorder have been developed.

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Chapter Notes

Author Notes

Web site: Familial Dilated Cardiomyopathy Research Project

Revision History

- 10 July 2008 (cd) Revision: clinical testing available for *TTN* mutations as a cause of dilated cardiomyopathy

- 27 July 2007 (me) Review posted to live Web site
- 6 December 2006 (jdk) Original submission