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Idiopathic dilated cardiomyopathy (DCM) refers to congestive cardiac failure secondary to systemic disease known to cause myocardial dysfunction. DCM is the most common type of (predominantly left) in the absence of congenital, valvular, or coronary artery disease or any systemic disease known to cause myocardial dysfunction. DCM is the most common type of cardiomyopathy, dilated (DCM).

**Background**

Idiopathic dilated cardiomyopathy (DCM) refers to congestive cardiac failure secondary to dilatation and systolic dysfunction (with or without diastolic dysfunction) of the ventricles (predominantly left) in the absence of congenital, valvular, or coronary artery disease or any systemic disease known to cause myocardial dysfunction. DCM is the most common type of cardiomyopathy, dilated (DCM).
heart muscle disease in children.

All 4 cardiac chambers are dilated and are sometimes hypertrophied. Dilation is more pronounced than hypertrophy, and the left ventricle is affected more often than the right ventricle. The cardiac valves are intrinsically normal, although the mitral and tricuspid valve rings are dilated, and the valve leaflets do not appose each other in systole, giving rise to varying degrees of mitral regurgitation, tricuspid regurgitation, or both. Persistent mitral regurgitation leads to thickening of the mitral valve leaflets, and, at times, distinguishing this thickening from other causes of mitral regurgitation is difficult. Thrombus formation (secondary to the low-flow cardiac output state) is often seen in the left ventricular apex and, at times, is seen in the atria. Occasionally, the right ventricle is preferentially involved in the cardiomyopathic process; this often indicates a familial basis.

Pathophysiology

Injury to the myocardial cell is the initiating factor that leads to cell death. If considerable cell loss occurs, the myocardium fails to generate enough contractile force to produce adequate cardiac output. This results in the activation of compensatory mechanisms, including the renin-angiotensin-aldosterone system, sympathetic stimulation, anti-diuretic hormone production, release of atrial natriuretic peptide, tumor necrosis factor (TNF)-α, and mechanical factors, such as increased end-diastolic stretch on the ventricle. These compensatory mechanisms help to maintain cardiac output in the initial phase; however, as myocardial damage progresses, persistent and excessive activation can be detrimental to cardiac function, leading to overt congestive heart failure.

Over-stretching of the ventricles causes myocardial thinning, cavity dilation, secondary valvular regurgitation, and compromised myocardial perfusion. The resulting subendocardial ischemia perpetuates myocyte damage.

Myocardial remodeling is an important contributor to worsening heart failure. Lost myocyte cells are replaced with fibrous tissue, thereby decreasing the compliance of one or more ventricles and adversely affecting performance. Aldosterone, angiotensin II, catecholamines, endothelins, and mechanical factors, such as excessive myocardial stretch and ischemia, have been identified as mediators of remodeling.

Apoptosis is a process of programmed cell death and is now believed to play a role in the continuing loss of myocardial cells in chronic heart failure. Overloading of myocytes possibly triggers apoptosis without fibrosis.

Heightened peripheral vasoconstriction, abnormal and excessive remodeling of the peripheral vasculature, and abnormalities in endothelium-dependent vasodilatation contribute to the progression of heart failure. Abnormal responses to muscarinic stimulation along with a defect in the endothelial nitric oxide pathway have been suggested as the potential underlying mechanisms.

Altered gene expressions resulting in calcium-handling abnormalities, downregulation of myosin or conversion to the less-active beta isoform, and abnormal beta-receptor signal transduction have all been identified at the molecular level in the chronically failing heart.

Frequency

United States

The reported incidence rate is 0.57 cases per 100,000 children.¹

International

- The incidence rate in Finland is 2.6 cases per 100,000 children.² No reliable figures are available for the rest of the world.
- Genetic causes account for more than 30% of DCM.

Mortality/Morbidity

- Mortality and morbidity have greatly decreased because of advances in medical management. Studies from 1975-1990 reported 70% survival at 2 years and 52% survival at 11.5 years of follow-up.³⁻⁶⁻⁷⁻⁸ Studies
from 1992-1997 document more than 85% survival at 5 years.

- In general, approximately one third of patients die from the disease, one third of patients continue to have chronic heart failure requiring therapy, and one third of patients experience improvement in their condition.

- Causes of death include heart failure, ventricular arrhythmias, and transplantation-related complications (less common).

Sex

DCM is reportedly more common in boys than in girls, and some forms are clearly X-linked.1

Age

All age groups are affected. However, studies suggest that DCM is more common in infancy (age <1 y) than in children.2 Fetal presentation is uncommon.

History

- Onset is usually insidious but may be acute in as many as 25% of patients, especially if exacerbated by a complicating lower respiratory infection.

- Cough, poor feeding, irritability, and shortness of breath are usually the initial presenting symptoms.

- Pallor, sweating, easy fatigability, failure to gain weight, and decreased urine output may be observed.

- Wheezing may be an important clinical sign, suggesting congestive heart failure manifestation in infants.

- Chest pain, palpitations, orthopnea, hemoptysis, frothy sputum, sudden death, abdominal pain, syncope, and neurologic deficit are other symptoms at presentation (20%).

- Cardiomegaly that is incidentally detected on a chest radiograph or an arrhythmia that is incidentally detected on an ECG may be the basis for initial cardiac referral.

- Approximately 50% of patients with dilated cardiomyopathy (DCM) have a history of preceding viral illness. A detailed family history for familial cardiomyopathy is revealing in as many as 25% of cases.

Physical

- In a patient with established disease, features of congestive heart failure are dominant.

- The infant or young child with the disease is often tachypneic, tachycardic with weak peripheral pulses, and has cool extremities and hepatomegaly. Blood pressure is low with a decreased pulse pressure. In extreme cases, patients may present in shock.

- Older children may show dependent edema, elevated jugular venous pulses, and fine basal crepitations in the lungs.

- Major cardiac findings include cardiomegaly, quiet precordium, tachycardia, gallop rhythm (S₃ and/or S₄), accentuated P-2, and murmurs of mitral and tricuspid regurgitation. Murmurs may be inconspicuous initially if the patient presents with acute heart failure.

- Infants often present with predominantly respiratory signs and, in the absence of a precordial heave or prominent murmur, the underlying cardiac disease may remain undiagnosed until cardiomegaly is detected on a chest radiograph.

Causes

- Various factors have been identified as causes of myocardial damage. These are presented in Table 1. However, in the vast majority of patients, no specific etiology is demonstrable (idiopathic). Systemic carnitine
deficiency and anthracycline-induced cardiomyopathy are notable exceptions.

### Table 1. Factors Identified as Causes of Myocardial Damage

<table>
<thead>
<tr>
<th>Category Of Factors</th>
<th>Specific Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral infections (myocarditis)</td>
<td>Coxsackievirus B, human immunodeficiency, echovirus, rubella, varicella, mumps, Ebstein-Barr virus, cytomegalovirus, measles, polio</td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>Diphtheria, Mycoplasma, tuberculosis, lyme disease, septicemia</td>
</tr>
<tr>
<td>Rickettsia</td>
<td>Psittacosis, Rocky Mountain spotted fever</td>
</tr>
<tr>
<td>Parasites</td>
<td>Toxoplasma, Toxocara, Cysticercus</td>
</tr>
<tr>
<td>Fungi</td>
<td>Histoplasma, coccidioidomycoses, Actinomycetes</td>
</tr>
<tr>
<td>Neuromuscular disorders</td>
<td>Duchenne or Becker muscular dystrophies, Friedreich ataxia, Kearns-Sayre syndrome, other muscular dystrophies</td>
</tr>
<tr>
<td>Nutritional factors</td>
<td>Kwashiorkor, pellagra, thiamine deficiency, selenium deficiency</td>
</tr>
<tr>
<td>Collagen vascular diseases</td>
<td>Rheumatic fever, rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, Kawasaki disease</td>
</tr>
<tr>
<td>Hematological diseases</td>
<td>Thalassemia, sickle cell disease, iron deficiency anemia</td>
</tr>
<tr>
<td>Coronary artery diseases</td>
<td>Anomalous left coronary artery from pulmonary artery, infarction</td>
</tr>
<tr>
<td>Drugs</td>
<td>Anthracycline, cyclophosphamide, chloroquine, iron overload</td>
</tr>
<tr>
<td>Endocrine diseases</td>
<td>Hypothyroidism, hyperthyroidism, hypoparathyroidism, pheochromocytoma, hypoglycemia</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>Glycogen storage diseases, carnitine deficiency, fatty acid oxidation defects, mucopolysaccharidoses</td>
</tr>
<tr>
<td>Malformation syndromes</td>
<td>Cat-cry syndrome (5p-)</td>
</tr>
</tbody>
</table>

- Three major factors have been implicated in the pathogenesis of myocardial damage in DCM: preceding viral myocarditis, autoimmunity, and underlying genetic predisposition.
  - **Viral myocarditis**
    - Epidemiologic, serologic, and molecular studies have detected evidence of enteroviral infection, in particular coxsackievirus B, in 20-25% of patients. Recent evidence implicates various other viruses. In fact, the most common associated viruses appear to vary over time.\(^8\)\(^9\) Currently, coxsackievirus B is likely a less common cause of DCM than in the past.
    - Currently, no methods can be used to distinguish cardiovirulent strains of enteroviruses from those that are not virulent. Furthermore, the presence of a virus a patient with DCM does not necessarily establish a causal relationship. Demonstration of viral DNA or RNA by polymerase chain reaction (PCR) is a more reliable method for revealing viral myocarditis. Unfortunately, obtaining myocardial tissue is invasive.
    - The exact mechanism of myocardial damage (rapid destruction or a long-term slowing of cardiomyocyte function) also remains unclear.
  - **Autoimmunity**
    - Animal studies have shown that DCM is an autoimmune disease in genetically predisposed strains of mice.
    - Approximately 30-40% of adult patients with DCM have organ-specific and disease-specific autoantibodies. The absence of these antibodies in the remaining patients may be related to the
The notion that an insult such as viral myocarditis initiates an autoimmune process with superantigen-triggered immune responses, resulting in massive T-lymphocyte activation and myocardial damage, has been postulated.

- Genetic predisposition
  - Genetic causes account for 25-50% of DCM cases.
  - The role of genetic factors is exemplified by the studies on familial DCM.\textsuperscript{10,11}
  - Patients with familial DCM have an increased frequency of human leukocyte antigen (HLA)-DR4. The frequency of HLA-DQA1 0501 alleles has been reported to be significantly higher in patients with idiopathic DCM.\textsuperscript{12}
  - Autosomal dominant and recessive inheritance, X-linked transmission, and polygenic and mitochondrial inheritance have all been documented. Presently known DCM genetic loci are summarized in Table 2.

Table 2. Summary of Genetic Loci and Disease Genes for Familial Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th>Clinical Pattern</th>
<th>Identified Genetic Loci</th>
<th>Identified Disease Genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant (AD)</td>
<td>10q21-10q23, 9q13-q22, 1q32, 15q14, 2q31, 1q11-21</td>
<td>Actin, desmin, lamin A/C</td>
</tr>
<tr>
<td>AD with conduction defect</td>
<td>1p1-1q1, 3p22-3p25</td>
<td></td>
</tr>
<tr>
<td>X-linked (XL)</td>
<td>Xp21</td>
<td>Dystrophin</td>
</tr>
<tr>
<td>XL cardio-skeletal (Barth syndrome)</td>
<td>Xq28 (gene G4.5)</td>
<td>Tafazzin</td>
</tr>
</tbody>
</table>

- Mutation analysis: Mutation screening of the exons that code for actin, β myosin heavy chain (\textit{MYH7} gene), cardiac troponin T (\textit{TNNT2} gene), phospholamban (\textit{PLN} gene), titin, αβ-crystallin, and the cardio-specific exon of metavinculin (\textit{VCL} gene) could be helpful in detecting some forms of familial DCM.

- Anthracyclines and cardiomyopathy
  - Anthracyclines, which are widely used in the management of childhood malignancies, account for as many as 30% of cases of DCM in the United States and a lesser percentage in other countries. Besides DCM, the other manifestations of anthracycline cardiotoxicity include restrictive cardiomyopathy (symptomatic and asymptomatic), asymptomatic left ventricular enlargement, and more subtle changes of cardiac function.
  - Early diagnosis requires periodic Doppler echocardiography studies during therapy and for several years after cessation of treatment. It also requires more widespread use of load-independent measurements of cardiac contractility (like stress velocity index), which incorporate measurements of contractility, afterload, and preload.
  - Cardiotoxicity has 2 types: early onset and late onset. The early onset type may be acute nonprogressive or chronically progressive.
    - Acute-onset type is defined as left ventricular dysfunction during or immediately following infusion of anthracycline and is attenuated by discontinuation of therapy. With use of low-dose regimens, this type is becoming rare. ECG changes include nonspecific ST segment and T wave changes, decreased QRS voltage, prolonged QT interval, and sinus tachycardia. Less commonly, ventricular, junctional, or supraventricular tachycardia or atrioventricular and bundle branch blocks. Blood levels of cardiac troponin T (cTnT) are a specific marker of this type of injury.
    - Early onset chronically progressive toxicity presents within one year of completion of therapy and persists or progresses even after discontinuation of therapy. Clinical features are similar to any
other type of cardiomyopathy and include ECG changes, left ventricular dysfunction, arrhythmias, reduced exercise-stress capacity, and even overt signs of heart failure. Blood levels of cTnT are elevated. Presence of early onset cardiotoxicity is believed to be a harbinger of poor patient outcome.

- Late-onset toxicity clinically manifests after a latent period of one or more years following completion of therapy. This type of manifestation is presumably due to diminished left ventricular contractility and an inappropriately thin left ventricular wall, resulting in elevated wall stress and progressive left ventricular dysfunction. Myocyte loss underlies all these sequelae, and alteration of myocellular protein transcription by anthracyclines may contribute. Thus, the latent period is not latent at all, and more sensitive markers may be able to detect the changes earlier. Late-onset asymptomatic toxicity has also been reported, but more detailed questioning often reveals easy fatigability or dyspnea in many of these patients.

- Risk factors contributing to the development of cardiotoxicity include the following: (1) the total cumulative dose of the drug received (20% mortality with cumulative dose >550 mg/m², 65% frequency of subtle Echo changes with dose >400 mg/m², and histologic evidence of toxicity with >240 mg/m²), (2) female sex (higher cellular concentrations because of higher body fat percentage), (3) young children, (4) rate of drug administration (maximum risk with doses >50 mg/m²/dose), (5) concomitant cardiac radiation exposure or use of amsacrine, (6) black race, and (7) trisomy 21.

### Lab Studies

- Full blood counts, erythrocyte sedimentation rate, and C-reactive proteins may show evidence of acute inflammation in the presence of active myocarditis.

- Similarly, creatine kinase–myocardial fraction may be elevated.
  
  - Rising titers of specific viral-neutralizing antibodies in the serum and positive viral cultures from nasopharyngeal or stool swabs may suggest a viral etiology; however, this does not necessarily mean a cause-and-effect relationship.
  
  - Serum carnitine levels (total and free) are low when the disease is due to systemic carnitine deficiency.

- Arterial blood gas (ABG) analysis reveals early stages of mild respiratory alkalosis and, later, mild hypoxemia secondary to pulmonary edema. In advanced disease, mixed acid-base disturbances with metabolic acidosis indicate the need for intravenous inotropes and ventilatory assistance.

### Imaging Studies

- Chest radiography
  
  - Chest radiography reveals cardiomegaly with a prominent left ventricular apex and prominent pulmonary artery segment.
  
  - Elevation of left main bronchus reflects dilation of the left atrium. This can result in compression of the left lower lobe bronchus when combined with a dilated pulmonary artery, leading to collapse of the left
lower lobe of the lung.

- Pulmonary venous congestion and frank pulmonary edema are often evident. When present, pleural effusion is better appreciated in the erect and lateral decubitus films.

- Massive cardiomegaly resembling pericardial effusion is the hallmark of established disease.

- Rarely, in fulminant cases, cardiomegaly may not be prominent because the ventricle has not had time to dilate despite the presence of features of pulmonary edema.

- **Echocardiography and Doppler studies**

  - These form the basis for the diagnosis of dilated cardiomyopathy (DCM) in most patients. Marked dilation of the left ventricle with global hypokinesia is the hallmark of the disease. Left ventricular fractional shortening is usually less than 25% (ejection fraction <50%). Left ventricular walls are thin and areas of dyskinesis may be observed. The left atrium is also dilated, and mitral valve leaflets show sluggish movement; the anterior leaflet does not appose to the interventricular septum, giving an increased E point septal separation on the M-mode pictures. The M-mode also clearly reveals the limited excursions of the anterior and posterior leaflets during diastole.

  - Doppler studies show varying degrees of mitral regurgitation secondary to left ventricular dilation and possible papillary muscle dysfunction. Mitral regurgitation is more prominent in follow-up studies after commencing therapy when the cardiac output has improved. Left ventricular ejection parameters show decrease in peak velocity and peak acceleration, prolongation of the pre-ejection period, and decrease in ejection time. These flow measurements are dependent on loading conditions. The dilatation of the mitral valve ring and the altered shape of the left ventricle cavity, which leads to change in the direction of the papillary muscles, are used to explain the secondary mitral regurgitation seen in a large proportion of children with DCM. Tissue Doppler studies have recently been reported in children with DCM.

  - Parameters of diastolic dysfunction are not reliable in the presence of established systolic dysfunction and mitral regurgitation; however, they may be useful in the early stages of the disease. Diastolic dysfunction is not as typical or as pronounced as it is in hypertrophic cardiomyopathy.

  - Long-standing cases show evidence of pulmonary hypertension in the form of right ventricular dilation and hypertrophy and tricuspid regurgitation. Tricuspid regurgitation and pulmonary regurgitation velocities give an estimate of the pulmonary artery systolic and diastolic pressures respectively. In severe cases, swirling echodensity (smoke or spontaneous echocardiographic contrast) can be observed along the outer ventricular wall, moving from the mitral valve towards the aortic valve. Occasionally, thrombi can be visualized in the left ventricular apex and in the left atrium. Pericardial effusion also may be present.

  - Echocardiography can exclude other heart diseases, both congenital and acquired. Cardiomyopathy secondary to severe aortic stenosis, coarctation of aorta or congenital mitral valve dysplasia, and anomalous left coronary artery arising from pulmonary artery (ALCAPA) are the major differential diagnoses. At times, identifying cardiomyopathy secondary to congenital mitral regurgitation (dysplastic mitral valve without stenosis) is difficult, but the abnormal anatomy of the mitral valve leaflets should help. The echo-dense papillary muscles and the dilated proximal right coronary artery and continuous retrograde flow of blood into the origin of pulmonary artery all direct the attention of the cardiologist to ALCAPA, a potentially treatable condition that mimics DCM.

- **Radionuclide imaging**

  - First-pass test and multiple gated acquisition (MUGA) scans help to measure the left and right ventricular stroke volumes and cardiac outputs. They are also helpful in documenting dyskinetic segments in the ventricular walls. Although theoretically superior to echocardiographic measurements, their practical application is limited because of a lack of standardization and because of nonreproducibility, especially in children.

  - Thallium studies can identify areas of decreased myocardial perfusion, although this is seldom required.

  - Gallium citrate Ga 67 scintigraphy and indium In-111 altumomab pentetate antimyosin antibody cardiac imaging have been suggested to help identify ongoing inflammation noninvasively. They may be used to identify patients who might benefit from myocardial biopsy.

### Other Tests
Electrocardiography

- ECG changes are usually nonspecific.
- Some patients have sinus tachycardia, downward frontal plane QRS axis, left atrial enlargement, left ventricular hypertrophy, deep Q waves with ST segment depression, and tall T waves in leads I, aVL, V₅, V₆ (the latter reflect left ventricular volume overload).
- In more advanced disease, right axis deviation, right atrial enlargement, and right ventricular hypertrophy are seen (because of pulmonary hypertension).
- The main role of ECG is to detect evidence of myocardial ischemia (pathologic Q waves with ST elevation and T-wave inversion in leads I, aVL, V₅, V₆) that might point to anomalous coronary artery as the etiology of the cardiomyopathy. A segmental myocarditis may result in ECG features of myocardial infarction.
- Cardiac arrhythmias, such as supraventricular/ventricular ectopy or tachycardia, may be revealed. These might indicate an underlying myocarditis or cardiomyopathy; however, if sustained, the arrhythmia may be the cause of the cardiomyopathy rather than the result (ie, tachycardia-mediated cardiomyopathy).

Procedures

- Cardiac catheterization and angiography
  - Children with DCM are at a particular risk for complications during cardiac catheter studies and angiography. Procedures should be performed by experienced pediatric cardiologists and only when absolutely essential.
  - At present, preparation for cardiac transplant and need for myocardial biopsy are the main indications for performing the procedure.
  - Patients should be under optimum medical therapy and kept hemodynamically stable before and after catheterization. Careful observation is required during the procedure for ventricular arrhythmias and hemodynamic deterioration.
  - Echocardiography should be considered after catheterization to identify any pericardial effusion secondary to subclinical perforation of the myocardium, especially if a biopsy has also been performed.
  - Aortography may be performed to identify a coronary artery anatomy, and left ventricular angiography may be performed to assess mitral valve function. The number of biopsy specimens collected should be limited to the minimum required (usually 4-8).
  - Usual findings include elevated filling pressures in all the cardiac chambers (especially the left ventricle), elevated pulmonary wedge pressure, and reduced cardiac output and stroke volume. Mixed venous oxygen saturation and reduced arterial saturation reflect low cardiac output and pulmonary edema. Pulmonary and systemic vascular resistances are elevated. With end-stage disease, the peak systolic left ventricular and aortic pressures drop.

- Myocardial biopsy
  - At present, preparation for cardiac transplant and post-transplant follow-up monitoring for rejection are the main indications for biopsy. If facilities are available, molecular or metabolic studies can be additional indications for academic and research purposes. Rarely, suspected metabolic diseases (isolated myocardial carnitine deficiency, rare forms of glycogen storage disease, fatty acid oxidation defects) or persistent myocarditis might require biopsy for confirmation.
  - Specimens should be subjected to both light and electron microscopy. PCR and metabolic studies should be performed when indicated.
  - The most important aspect is the availability of a sufficient level of expertise for interpretation of the findings.
  - PCR has been used to aid the detection of viral antigens in myocardial tissue in patients with DCM. Studies have revealed an association between viral antigens and DCM. However, a proportion of the
studies gave negative results. A recently published meta-analysis of the studies on DCM gave an odds ratio of 3.8 to the association between presence of viral antigens in DCM. The results are influenced by factors like contamination from the reference strain used in the laboratory and choice of the controls. It also is not clear whether these positive cases among DCM actually represented acute myocarditis rather than DCM.

- Diagnostic evaluation: Flow charts (Tables 3 and 4) guide evaluation of children with suspected DCM to arrive at a firm diagnosis.

Table 3. Diagnosis of Dilated Cardiomyopathy in Children - Step I: Diagnosis

<table>
<thead>
<tr>
<th>Approach</th>
<th>Findings</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical suspicion</td>
<td>Infants and young children: Shortness of breath, feeding difficulties, wheezing, failure to thrive, recurrent chest infections, hepatomegaly, cardiomegaly</td>
<td>Probable heart disease with heart failure</td>
</tr>
<tr>
<td>Chest radiography</td>
<td>Cardiomegaly, pulmonary plethora, prominent upper lobe veins, pulmonary edema, pleural effusion, collapsed left lower lobe</td>
<td>High probability of heart failure with or without chest infection</td>
</tr>
<tr>
<td>Electrocardiography</td>
<td>Low-voltage complexes, Presence of Q waves and inversion of T waves in leads I, II, aVL, and V₆ through V₆ (anterolateral infarction pattern)</td>
<td>Pericardial effusion, Anomalous left coronary artery from pulmonary artery</td>
</tr>
<tr>
<td>Doppler echocardiographic studies</td>
<td>Significant arrhythmia, Left ventricular or biventricular hypertrophy with or without left ventricular strain pattern</td>
<td>Dilated cardiomyopathy secondary to arrhythmia, Often unhelpful</td>
</tr>
</tbody>
</table>

Table 4. Diagnosis of Dilated Cardiomyopathy in Children - Step II: Identification of Any Underlying Etiology

<table>
<thead>
<tr>
<th>Approach</th>
<th>Findings</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>Positive family history, Acute or chronic encephalopathy, muscle weakness, hypotonia, growth retardation, recurrent vomiting, lethargy</td>
<td>Genetic cause for dilated cardiomyopathy, Inborn error of metabolism involving energy production</td>
</tr>
<tr>
<td></td>
<td>Coarse or dysmorphic features, organomegaly, skeletal abnormalities,</td>
<td>Storage diseases</td>
</tr>
</tbody>
</table>
**Histologic Findings**

Histologic features are nonspecific in most patients and include myocardial cell loss with varying degree of necrosis and fibrosis. In presence of myocarditis, lymphocytic infiltration of varying degree is also present (Dallas criteria).

<table>
<thead>
<tr>
<th>Blood investigations</th>
<th>TREATMENT</th>
<th>Section 6 of 11</th>
<th>Back</th>
<th>Top</th>
<th>Next</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood urea nitrogen and creatinine levels, low calcium and magnesium levels, electrolyte disturbances</td>
<td>Neurorheumatology disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Medical Care

- Perform general supportive measures during acute-stage management, including endotracheal intubation and mechanical ventilation, vasoactive infusions, and fluid/acid-base management. Treat chest infections appropriately. Treat anemia appropriately.

- Oxygen inhalation is of benefit only in the presence of hypoxia (as with pneumonia or pulmonary edema).

- Carnitine supplements (100 mg/kg IV infusion over 30 min, followed by 100 mg/kg/d as continuous infusion for 24-72 h; 25-50 mg/kg/dose PO bid/tid, not to exceed 200 mg/kg/d) reverse the myocardial dysfunction in most patients affected by systemic carnitine deficiency.

- Coenzyme Q10 has also been used in children with dilated cardiomyopathy (DCM), with variable results.

- Decreased serum levels of growth hormone (GH), which acts on cardiac myocytes primarily through insulinlike growth factor (IGF)-1, are associated with impaired myocardial growth and function, which can be improved with the restoration of GH/IGF-1 homeostasis. Based on this hypothesis and on observation of benefits in animal models, GH therapy has been used in children with DCM, but the results have not been conclusive.

Surgical Care

Cardiac transplantation is currently the optimal treatment for DCM-induced resistant chronic congestive heart failure in children.

- Limiting factors include availability of a suitable donor, complications of rejection, and lifelong immunosuppression. Survival rates of as much as 92% at 5 years have been reported.¹³

- Palliative surgical measures are associated with significant mortality and morbidity rates despite advances. Resection of a large segment of the hypertrophied ventricular muscle (Batista procedure) and repair or replacement of mitral valve to minimize volume overload of left ventricle have been used as palliative measures. Cardiomyoplasty is the transposition of electrically transformed skeletal muscle to provide systolic and diastolic augmentation to the native heart.

- Implantable mechanical support devices, modified for use in infants and children, have been introduced to support the failing heart until a suitable donor is available for transplantation (bridge to transplant). Major limitations include infection, thromboembolism, disturbance from noise, and the need to recharge batteries frequently.

- Cardiac resynchronization therapy using a biventricular pacemaker has been shown to be effective in adults with DCM. In addition, these devices are available with defibrillator backup for patients at risk for ventricular arrhythmias. They are being used in children with DCM, with early favorable results.

- Prolonged support of left ventricular function with these devices has shown restoration of the native cardiac function, enabling removal of the device in a few cases. This raises the possibility that mechanical intervention at an earlier stage in viral myocarditis and DCM might prevent the deterioration of cardiac function. Recent adult studies have documented myocardial recovery and successful explantation of the left ventricular assist system, even after they were on the device for a year. A lesser degree of fibrotic changes in the left ventricle could predict better chances of recovery.

Consultations

- A multidisciplinary approach is a must for optimum management and should include the following:
  - Pediatric cardiologist
  - Pediatric cardiothoracic surgeon
  - Pharmacist
  - Dietitian and nutritionist
  - Pediatrician or family physician
Occupational therapist
Psychologist
School teacher
Specialist nurse

Diet
- Dietary requirements are high because of the catabolic state, recurrent infections, increased muscle activity, and need for rapid growth.
- Dietary intake may be inadequate consequent to the anorexia, dietary restrictions, malabsorption, diarrhea, and frequent exacerbations of heart failure.
- Ensuring an appropriate and palatable diet is a challenge.
- Temporary nasogastric tube feedings may be required for sick and severely anorectic children.
- Powerful diuretics have largely obviated the need for stringent restrictions on salt and fluid intake.

Activity
- Enforced bed rest is impractical and probably unnecessary.
- Often, restriction of physical activity is self-enforced.
- Infants might need intravenous alimentation for relief from feeding activity.
- Apart from the above, activity to the limit of tolerance should be allowed and encouraged.
- In patients with chronic illness, regular graded exercise has been shown to improve effort tolerance and quality of life.
- All feasible support should be provided for peer interaction and participation in normal life activities. Restricted life activities, frequent diagnostic and therapeutic interventions, and an uncertain prognosis make these children prone to psychological problems that may significantly influence prognosis and outcome. Among the described abnormalities are inhibition of emotions, marked anxiety, depressive reaction with loneliness, low self-esteem, feelings of inadequacy, emotional lability, impulsiveness, and weakness of self-identity.
Medical therapy is largely directed at the symptoms and is aimed at the underlying heart failure. Diuretics, angiotensin-converting enzyme (ACE) inhibitors, and beta-blockers form the initial therapy. Diuretics may provide an improvement in symptoms, whereas ACE inhibitors appear to prolong survival. Beta-blockers also have a long-term positive effect on outcome. Intravenous infusions of vasoactive agents may be required in patients with resistant heart failure. Recently, the use of beta-blockers has become more extensive in childhood dilated cardiomyopathy (DCM) drug therapy.

Antibiotics for endocarditis prophylaxis are administered to patients with certain cardiac conditions, such as DCM, before performing procedures that may cause bacteremia. For more information, see Antibiotic Prophylactic Regimens for Endocarditis.

**Drug Category: Diuretics**

These agents are used to eliminate retained fluid and preload reduction.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Furosemide (Lasix)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>This is the DOC. Inhibits reabsorption of fluid from the ascending loop of Henle in the renal tubule. With IV administration, has venodilator action and lowers preload even before diuresis sets in. DOC in acute heart failure and in exacerbations of chronic heart failure. Also used for long-term management of chronic heart failure.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>40 mg PO bid</td>
</tr>
<tr>
<td></td>
<td>20-50 mg IV; repeat q6-8h</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>1-4 mg/kg PO qd or bid</td>
</tr>
<tr>
<td></td>
<td>1-4 mg/kg IV q8h</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; hepatic coma; anuria; state of severe electrolyte depletion</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Metformin decreases concentrations; interferes with hypoglycemic effect of antidiabetic agents and antagonizes muscle relaxing effect of tubocurarine; auditory toxicity appears to be increased with coadministration of amino- glycosides (hearing loss of varying degrees may occur); anticoagulant activity of warfarin may be enhanced when concurrently administered; increased plasma lithium levels and toxicity are possible; risk of hypokalemia with concurrent administration of amiodarone and flecainide; sotalol enhances hypotension and risk of cardiac arrhythmia</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus</td>
</tr>
</tbody>
</table>
Drug Category: Angiotensin -converting enzyme inhibitors

These drugs reduce afterload and decrease myocardial remodeling that worsens chronic heart failure.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Captopril (Capoten)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Accepted as an essential part of any antifailure therapy; provides symptomatic improvement and prolonged survival; prevents conversion of angiotensin I to angiotensin II, a potent vasoconstrictor, resulting in lower aldosterone secretion.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>6.25-25 mg PO tid; not to exceed 150 mg tid</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>0.1-1 mg/kg PO tid</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; renal impairment; renal artery stenosis</td>
</tr>
<tr>
<td>Interactions</td>
<td>NSAIDs may reduce hypotensive effects; ACE inhibitors may increase digoxin, lithium, and allopurinol levels; rifampin decreases levels; probenecid may increase levels; the hypotensive effects of ACE inhibitors may be enhanced when given concurrently with diuretics</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus</td>
</tr>
<tr>
<td>Precautions</td>
<td>Caution in renal impairment, valvular stenosis, or severe congestive heart failure; hypotension; tachycardia; renal failure; persistent dry cough has been reported in 5-20% of children</td>
</tr>
</tbody>
</table>

Drug Category: Cardiac glycosides

These drugs provide improvement of symptoms with chronic administration. The role of cardiac glycosides is currently less clear than in an earlier era.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Digoxin (Lanoxin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Improves myocardial contractility, reduces heart rate, and lowers sympathetic stimulation in chronic heart failure. Digoxin inhibits Na⁺-K⁺ ATPase pump. Sodium preferentially exchanges with calcium, increasing the intracellular calcium and resulting in an increase in contractility.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>Total digitalizing dose (TDD): 0.75-1.5 mg PO 50% of TDD initially; remaining 2 doses at 25% TDD q6-12h (1/2, 1/4, 1/4) Maintenance dose: 0.125-0.5 mg PO qd</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Total digitalizing dose (TDD): Preterm infant: 20-30 mcg/kg PO Term infant: 25-35 mcg/kg PO 1 month to 2 years: 35-60 mcg/kg PO 2-5 years: 30-40 mcg/kg PO 5-10 years: 20-35 mcg/kg PO &gt;10 years: Administer as in adults 50% of TDD initially; remaining 2 doses at 25% TDD q6-12h (1/2, 1/4, 1/4) Maintenance dose: Preterm infant: 5-7.5 mcg/kg PO divided bid Term infant: 6-10 mcg/kg PO divided bid 1 month to 2 years: 10-15 mcg/kg PO divided bid 2-5 years: 7.5-10 mcg/kg PO divided bid 5-10 years: 5-10 mcg/kg divided bid &gt;10 years: Administer as in adults</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus</td>
</tr>
<tr>
<td>Precautions</td>
<td>Caution in renal impairment, valvular stenosis, or severe congestive heart failure; hypotension; tachycardia; renal failure; persistent dry cough has been reported in 5-20% of children</td>
</tr>
</tbody>
</table>

Pregnancy
- established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions
- GI upset; hyponatremia; hyperkalemia; hepatotoxicity; lethargy; confusion; impotence; gynecomastia; avoid salt substitutes or natural licorice

Drug Name
- Captopril (Capoten)
- Digoxin (Lanoxin)
Drug Category: **Oral anticoagulant**

These agents are administered to prevent recurrence of thromboembolic episodes of cardiac origin.

<table>
<thead>
<tr>
<th><strong>Drug Name</strong></th>
<th>Warfarin (Coumadin)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Interferes with hepatic synthesis of vitamin K-dependent coagulation factors. Prevents thrombus formation within cardiac chambers and venous circulation. Tailor dose to maintain an INR of 2-3.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>5-15 mg/d PO qd for 2-5 d; adjust dose according to desired INR</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>0.05-0.34 mg/kg/d PO; adjust dose according to desired INR</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; severe liver or kidney disease; open wounds or GI ulcers</td>
</tr>
</tbody>
</table>

**Interactions**

Drugs that may decrease anticoagulant effects include griseofulvin, carbamazepine, glutethimide, estrogens, nafcillin, phenytoin, rifampin, barbiturates, cholestyramine, colestipol, vitamin K, spironolactone, oral contraceptives, and sucralfate; medications that may increase anticoagulant effects include oral antibiotics, phenylbutazone, salicylates, sulfonamides, chloral hydrate, clofibrate, diazoxide, anabolic steroids, ketoconazole, ethacrynic acid, miconazole, nalidixic acid, sulfonyleureas, allopurinol, chloramphenicol, cimetidine, disulfiram, metronidazole, phenylbutazone, phenytoin, propoxyphene, sulfonamides, gemfibrozil, acetaminophen, and sulindac.

**Pregnancy**

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

**Precautions**

Hypokalemia may reduce positive inotropic effect of digitalis; once digitalized, rapid administration of IV calcium may produce serious arrhythmias; hypercalcemia predisposes patient to digitalis toxicity, and hypocalcemia can make digoxin ineffective until serum calcium levels are normal; magnesium replacement therapy must be instituted in patients with hypomagnesemia to prevent digitalis toxicity; patients diagnosed with incomplete AV block may progress to complete block when treated with digoxin; exercise caution in hypothyroidism, hypoxia, and acute myocarditis

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Drug Category: **Beta-adrenergic blocking agents**

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Contraindications

<table>
<thead>
<tr>
<th><strong>Contraindications</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications that may increase levels include alprazolam, benzodiazepines, bepridil, captopril, cyclosporine, propafenone, propantheline, quinidine, diltiazem, aminoglycosides, oral amiodarone, anticholinergics, diphenoxylate, erythromycin, felodipine, flecainide, hydroxychloroquine, itraconazole, nifedipine, omeprazole, quinine, ibuprofen, indomethacin, esmolol, tetracycline, tolbutamide, and verapamil; medications that may decrease serum digoxin levels include aminogluthethimide, antihistamines, cholestyramine, neomycin, penicillamine, aminoglycosides, oral colestipol, hydantoin, hypoglycemic agents, antineoplastic treatment combinations (including carbamazepine, bleomycin, methotrexate, cytarabine, doxorubicin, cyclophosphamide, vincristine, procarbazine), aluminum or magnesium antacids, rifampin, sucralfate, sulfasalazine, barbiturates, kaolin/pectin, and aminosalicylic acid</td>
</tr>
</tbody>
</table>

Pregnancy

<table>
<thead>
<tr>
<th><strong>Pregnancy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus</td>
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Interactions

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Drugs that may decrease anticoagulant effects include griseofulvin, carbamazepine, glutethimide, estrogens, nafcillin, phenytoin, rifampin, barbiturates, cholestyramine, colestipol, vitamin K, spironolactone, oral contraceptives, and sucralfate; medications that may increase anticoagulant effects include oral antibiotics, phenylbutazone, salicylates, sulfonamides, chloral hydrate, clofibrate, diazoxide, anabolic steroids, ketoconazole, ethacrynic acid, miconazole, nalidixic acid, sulfonyleureas, allopurinol, chloramphenicol, cimetidine, disulfiram, metronidazole, phenylbutazone, phenytoin, propoxyphene, sulfonamides, gemfibrozil, acetaminophen, and sulindac</td>
</tr>
</tbody>
</table>

Precautions

<table>
<thead>
<tr>
<th><strong>Precautions</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not switch brands after achieving therapeutic response; caution in active tuberculosis or diabetes; patients with protein C or protein S deficiency are at risk of developing skin necrosis</td>
</tr>
</tbody>
</table>
These agents block the beta-adrenergic receptor and are modulators of the autonomic system.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Propranolol (Inderal)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Inhibits both beta1- and beta2-adrenergic receptors. Nonselective adrenergic antagonist.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>40-80 mg PO bid initially; increase to 160-320 mg/d (some patients require up to 640 mg/d)</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>1-4 mg/kg/d PO divided bid/tid</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; uncompensated congestive heart failure; bradycardia; cardiogenic shock; AV conduction abnormalities</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Coadministration with aluminum salts, barbiturates, NSAIDs, penicillins, calcium salts, cholestyramine, and rifampin may decrease effects; calcium channel blockers, cimetidine, loop diuretics, and MAOIs may increase toxicity; toxicity of hydralazine, haloperidol, benzodiazepines, and phenothiazines may increase</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Beta-adrenergic blockade may decrease signs of acute hypoglycemia and hyperthyroidism; abrupt withdrawal may exacerbate symptoms of hyperthyroidism, including thyroid storm; withdraw drug slowly and closely monitor; gradually taper over 1-2 wk when discontinuing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Carvedilol (Coreg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Nonselective beta-blocker with additional direct vasodilator action.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>25 mg PO bid; not to exceed 50 mg bid</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>0.08 mg/kg PO qd initially; increase as tolerated over 12 wk; not to exceed 0.5 mg/kg/d</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; uncompensated congestive heart failure; bradycardia; cardiogenic shock; AV conduction abnormalities</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Coadministration with rifampin may decrease effects; calcium channel blockers, cimetidine, loop diuretics, and MAOIs may increase toxicity</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Beta-adrenergic blockade may decrease signs of acute hypoglycemia and hyperthyroidism; abrupt withdrawal may exacerbate symptoms of hyperthyroidism, including thyroid storm; withdraw drug slowly and closely monitor; gradually taper over 1-2 wk when discontinuing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Metoprolol (Lopressor, Toprol XL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Selective beta-1 adrenergic receptor blocker that decreases automaticity of contractions.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>Extended release tablets (Toprol XL): NYHA Class II heart failure: 25 mg PO qd initially More severe heart failure: 12.5 mg PO qd May double the dose q2wk as tolerated; not to exceed 200 mg/d</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>0.1 mg/kg/dose PO bid; dose may be increased as patient tolerates</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; uncompensated congestive heart failure, bradycardia, asthma, cardiogenic shock, and AV conduction abnormalities</td>
</tr>
<tr>
<td></td>
<td>Aluminum salts, barbiturates, NSAIDs, penicillins, calcium salts, cholestyramine, and rifampin may decrease</td>
</tr>
</tbody>
</table>
**Drug Category: Vasoactive infusions**

These agents are used in resistant cases as intravenous infusions and are stimulators of beta1-adrenergic receptors in the myocardium. They are also useful for periodic home inotropic therapy in end-stage disease, in which cardiac transplant is not feasible, to improve the quality of life. However, studies have shown increased mortality related to arrhythmogenic potential.

### Interactions

Bioavailability and plasma levels of metoprolol, possibly resulting in decreased pharmacologic effects; toxicity of metoprolol may increase with coadministration of sparfloxacin, phenothiazines, astemizole, calcium channel blockers, quinidine, flecainide, and contraceptives; metoprolol may increase toxicity of digoxin, flecainide, clonidine, epinephrine, nifedipine, prazosin, verapamil, and lidocaine.

### Pregnancy

- **C**: Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus
- **D**: Fetal risk shown in humans; use only if benefits outweigh risk to fetus

### Precautions

Beta-adrenergic blockade may reduce signs and symptoms of acute hypoglycemia and may decrease clinical signs of hyperthyroidism; abrupt withdrawal may exacerbate symptoms of hyperthyroidism, including thyroid storm; monitor patient closely and slowly withdraw the drug; during IV administration, carefully monitor blood pressure, heart rate, and ECG.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dobutamine hydrochloride (Dobutrex)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Synthetic catecholamine with potent cardiac-stimulating properties; in addition, has direct vasodilating action on peripheral blood vessels; infusion with or without additional dopamine infusion in renal dose would be appropriate therapy for cardiogenic shock secondary to dilated cardiomyopathy.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>0.5 mcg/kg/min IV infusion initially; titrate to effect; not to exceed 40 mcg/kg/min</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Administer as in adults</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; idiopathic hypertrophic subaortic stenosis; atrial fibrillation or flutter</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Beta-adrenergic blockers antagonize effects; general anesthetics may increase toxicity</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Close monitoring of heart rate, blood pressure and ECG are advisable during infusion; hypovolemic state should be corrected before use</td>
</tr>
</tbody>
</table>

**Drug Category: Phosphodiesterase enzyme inhibitors**

These agents elicit positive inotropic and vasodilatory effects.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Milrinone (Primacor)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Bipyridine with positive inotrope and vasodilator activity. Little chronotropic activity observed. Different in mode of action from both digitalis glycosides and catecholamines. Selectively inhibits phosphodiesterase type III (PDE III) in cardiac and smooth vascular muscle, resulting in reduced afterload, reduced preload, and increased inotropy. Not FDA-approved for pediatric patients, although often considered DOC in pediatric patients in ICU setting.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>50 mcg/kg IV loading dose over 10 min followed by continuous IV infusion at 0.375-0.75 mcg/kg/min</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Limited data exist; administer as in adults</td>
</tr>
</tbody>
</table>
### Drug Category: Angiotensin-converting enzyme inhibitors

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Enalapril (Vasotec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>ACE Inhibitor with prolonged duration of action PO; competitive inhibitor of ACE; reduces angiotensin II levels, decreasing aldosterone secretion.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>20-40 mg PO qd or divided bid</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>0.1-1 mg/kg/d PO; not to exceed 40 mg</td>
</tr>
</tbody>
</table>

### Contraindications
- Documented hypersensitivity to milrinone, any component, or inamrinone

### Interactions
- NSAIDs may reduce hypotensive effects; ACE inhibitors may increase digoxin, lithium, and allopurinol levels; rifampin decreases levels; probenecid may increase levels; the hypotensive effects of ACE inhibitors may be enhanced when given concurrently with diuretics

### Pregnancy
- C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus
- D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

### Precautions
- Caution in renal impairment, valvular stenosis, or severe congestive heart failure

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### Further Inpatient Care

- Admission is necessitated for patients with exacerbations of heart failure often precipitated by chest infection. Admission may also be necessary for reevaluation if first-line medications fail to provide significant relief of symptoms (resistant heart failure). During terminal illness, patients and parents might opt to stay in the hospital.

- In addition to taking aggressive steps to treat the precipitating factor (infection, anemia), compliance to therapy has to be evaluated when symptoms persist.

- Diminished absorption and waning action of diuretics can be partially overcome by parenteral administration of furosemide or by sequential segmental nephron blockade achieved by combining metolazone, a thiazide diuretic, with furosemide.

- Intravenous infusions of beta agonists, such as dopamine and dobutamine, temporarily improve myocardial function and partly reverse the abnormal neuro-endocrine profile of chronic congestive heart failure. However, in the long-term, they increase myocardial irritability, leading to arrhythmia.

- Recently, use of beta-blocker therapy in children with chronic congestive heart failure due to dilated...
Cardiomyopathy (DCM) was shown to improve symptoms and left ventricular ejection fraction. Carvedilol is a beta-adrenergic blocker with additional vasodilating action. Carvedilol, in addition to standard therapy for dilated cardiomyopathy in children, improves cardiac function and symptoms; it is well tolerated, with minimal adverse effects, but close monitoring is necessary because it might worsen congestive heart failure and precipitate asthma.

- Anticoagulants and antiarrhythmic agents, particularly amiodarone, are often used in patients with low myocardial contractility and symptomatic arrhythmias, respectively. Results are encouraging.

- Cardiac resynchronization therapy with AV synchronous biventricular pacing has been successful in some children with DCM and left bundle branch block (LBBB). Optimization of resynchronization for children with DCM is still in the early stages.

- Automatic implantable cardioverter-defibrillators (ICDs) reduce sudden death, and their efficacy has been clearly demonstrated in adults with chronic congestive heart failure. However, their use in children has been limited. Recent studies have reported on the efficacy of ICDs in children with DCM and other cardiomyopathies.14

- Studies in adults who died from heart failure report significant fatigue, dyspnea, and pain in the days before death. Concluding that similar problems in children is logical.

Further Outpatient Care

- See Heart Failure, Congestive.

In/Out Patient Meds

- See Heart Failure, Congestive.

Transfer

- Transfer may be required for further diagnostic evaluation and surgical intervention (cardiac transplantation).

Complications

- Congestive heart failure
- Pneumonia
- Cardiac arrhythmias (supraventricular and ventricular)
- Infective endocarditis
- Thromboembolism
- Venous thrombosis
- Cardiac cirrhosis
- Post-transplant complications
- Sudden, unexplained death

Prognosis

- If a treatable cause is discovered, prognosis is better.
- Prognosis is worst for cardiomyopathy secondary to storage diseases that do not have effective therapy.
- History of viral illness in the 3 months before onset may suggest a better prognosis.
- In DCM with no obvious detectable etiology, outcome depends on severity of myocardial dysfunction,
improvement during the first year after onset, compliance to therapy, and availability of timely transplant.

- Degree of depression of fractional shortening or ejection fraction at time of initial echocardiography, elevation of left ventricular end diastolic pressure, and cardiothoracic ratio have all been applied as predictors of outcome, although they are not often predictive. Other possible prognostic factors include age at onset (better for infants), presence of symptomatic arrhythmias, and thromboembolic episodes.

- Arrhythmic death can occur even after the left ventricular ejection fraction has returned to normal.

- Following cardiac transplant, survival rates of as much as 77% at 1 year and as much as 65% at 5 years have been reported in children.

**Patient Education**

- Education is a continuous process from the time of diagnosis. Explain the disease process, management, and prognosis to parents and older patients.

- Compliance to medication is an important factor in the success of therapy. Compliance is affected by complexity of the dosing regime, perceptions of illness, benefits of treatment, and family dynamics.
  
  - Increased dosage frequency, timing of drug administration during school hours, and unpalatability increase noncompliance. Young children may not understand the benefits of treatment, whereas adolescents may exhibit independence or denial.
  
  - Family dynamics can include parental anxiety, parental preoccupation, and unstable marital relationships.
  
  - Effective communication is a confounding problem when a family member who is not the primary care provider accompanies the child to the hospital.
  
  - Educating and counseling parents and caretakers, with the help of models, diagrams, and written instructions, lessen the problem.
  
  - Concordance, in which the pediatrician forms a therapeutic alliance with the caretaker and the child, and negotiation with the family to choose the best-fit regime have been found to improve compliance.

- Patients should avoid competitive sports.

- Patients should avoid activity beyond tolerance.

- In patients with chronic illness, regular graded exercise has been shown to improve effort tolerance and quality of life.

- For excellent patient education resources, visit eMedicine's [Heart Center](#). Also, see eMedicine's patient education article [Heart and Lung Transplant](#).

**Medical/Legal Pitfalls**

- Failure to identify a treatable cause (including congenital aortic stenosis, coarctation of aorta, ALCAPA, and congenital mitral regurgitation) of dilated cardiomyopathy (DCM)

- Failure to diagnose the disease in infants who present with predominantly respiratory symptoms

- Failure to inform patients and parents of the diagnosis, prognosis, and treatment options

- Failure to inform patients of the complications of cardiac transplantation

- Failure to discuss potential interventional treatment options such as cardiac resynchronization therapy, implantable defibrillators, or ventricular assist devices
Special Concerns

- Schoolteachers should be informed of the child's condition. Teachers and other caregivers should be adequately trained for first aid and cardiopulmonary resuscitation (CPR).

- Family members should be screened with ECG and echocardiography to detect asymptomatic cases.

- Pregnancy imposes special demands on the cardiac reserve, and the decision to have children has to be individualized, depending mainly on the degree of exercise tolerance and the severity of ventricular dysfunction and cardiomyopathy.


27. Diogenes MS, Carvalho AC, Succi RC. Reversible cardiomyopathy subsequent to perinatal infection with the


Privacy Policy Changes

Important Announcement:

WebMD, Inc. ("WebMD Health"), a leader in online health information services to the medical professional community has acquired eMedicine. This acquisition was completed January 18, 2006. As we become more fully integrated, eMedicine users are now eligible to utilize the services available to physicians through WebMD Health's professional portals, including Medscape.com, theheart.org and Medsite.com. Your eMedicine account information will now be accessible to WebMD Health where it will be maintained in accordance with the WebMD Professional Services Privacy Policy. Click here to view the WebMD Professional Services Privacy Policy.

If you desire to remove your account information from WebMD Health, please send an email to PrivacyPolicyNotice@emedicine.com.