Myocarditis, Viral

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Synonyms and related keywords: viral myocarditis, myocardium, adenovirus, enterovirus, coxsackievirus, active myocarditis, borderline myocarditis

INTRODUCTION

Background: Myocarditis is an inflammatory disorder of the myocardium with necrosis of the myocytes and associated inflammatory infiltrate. It is usually caused by a viral infection, particularly adenovirus and enterovirus infections (eg, coxsackievirus), although many infectious organisms commonly seen in infants and children have been implicated. Occasionally, myocarditis may be a manifestation of drug hypersensitivity or toxicity. Although the utility of myocardial biopsy is debated, suspected myocarditis can be classified into the following 3 types based on pathologic findings as defined in the Dallas Criteria (1987):

- Active myocarditis - Characterized by abundant inflammatory cells and myocardial necrosis

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Borderline myocarditis - Characterized by an inflammatory response that is too sparse for this type to be labeled as active myocarditis; degeneration of myocytes not demonstrated with light microscopy

Nonmyocarditis

If an active or borderline inflammatory process is found, follow-up biopsies can be subclassified into ongoing, resolving, or resolved myocarditis.

Pathophysiology: Myocarditis generally results in a decrease in myocardial function, with concomitant enlargement of the heart and an increase in the end-diastolic volume caused by increased preload. Normally, the heart compensates for dilation with an increase in contractility (Starling law), but because of inflammation and muscle damage, a heart affected with myocarditis is unable to respond to the increase in volume. In addition, inflammatory mediators, such as cytokines and adhesion molecules, as well as apoptotic mechanisms are activated. The progressive increase in left ventricular end-diastolic volume increases left atrial, pulmonary venous, and arterial pressures, resulting in increasing hydrostatic forces. These increased forces lead to both pulmonary edema and congestive heart failure. Without treatment, this process may progress to end-stage cardiac failure and death.

Frequency:

Internationally: Myocarditis is a rare disease. The World Health Organization reports that incidence of cardiovascular involvement after enteroviral infection is 1-4%, depending on the causative organism. Incidence varies greatly among countries and is related to hygiene and socioeconomic conditions. Availability of medical services and immunizations also affect incidence. Occasional epidemics of viral infections have been reported with an associated higher incidence of myocarditis. Enteroviruses, such as coxsackievirus and echovirus, and adenoviruses, particularly types 2 and 5, are the most commonly involved organisms.

Mortality/Morbidity: Studies give a wide spectrum of mortality and morbidity statistics. With suspected coxsackievirus B, the mortality rate is higher in newborns (75%) than in older infants and children (10-25%). Complete recovery of ventricular function has been reported in as many as 50% of patients. Some patients develop chronic myocarditis (ongoing or resolving) and/or dilated cardiomyopathy and may eventually require cardiac transplantation.

Race: No racial predilection exists.

Sex: No sex predilection exists in humans, but some research in laboratory animals suggests that the disease may be more aggressive in males than in females. Certain strains of female mice had a reduced inflammatory process when treated with estradiol. In other studies, testosterone appeared to increase cytolytic activity of T lymphocytes in male mice.

Age: No age predilection exists. Younger patients, especially newborns and infants, and immunocompromised patients may have increased susceptibility to myocarditis.

History:

Clinical presentation varies considerably. In mild forms, there are few or no symptoms. In severe cases, patients may present with acute cardiac decompensation and progress to death.

- Heart failure: This is the most common presenting picture in all ages. The condition of patients who present with heart failure may rapidly deteriorate even with supportive care. Neonates and young children have higher mortality rates than older patients. Rapid supportive care with blood pressure support, afterload reduction, and control of arrhythmia may prevent early death.
- Chest pain: Although rare in young children, this may be the initial presentation for older children, adolescents, and adults. Chest pain may be due to myocardial ischemia or concurrent pericarditis.

- Arrhythmia: Patients can present with any type of dysrhythmia, including atrioventricular conduction disturbances. Sinus tachycardia is typical and the rate is faster than expected for the degree of fever present, which is typically low-grade. Junctional tachycardia is also seen and can be difficult to control medically.

- Dilated cardiomyopathy: The debate continues over whether myocarditis progresses to dilated cardiomyopathy. Many investigators believe that dilated cardiomyopathy is a direct result of a previously burned-out myocarditis episode.

- Initial symptoms in infants include the following:
  - Irritability
  - Lethargy
  - Periodic episodes of pallor
  - Fever
  - Hypothermia
  - Tachypnea
  - Anorexia
  - Failure to thrive

- Older children present with similar symptoms and may experience lack of energy and general malaise.

- Parents may refer to a recent, nonspecific, flulike illness, gastrointestinal symptoms, poor feeding, or rapid breathing.

**Physical:**

- Signs of diminished cardiac output, such as tachycardia, weak pulse, cool extremities, decreased capillary refill, and pale or mottled skin may be present.

- Heart sounds may be muffled, especially in the presence of pericarditis. An S₃ may be present, and a heart murmur caused by atrioventricular valve regurgitation may be heard.

- Hepatomegaly may be present in younger children.

- Rales may be heard in older children.

- Jugular venous distention and edema of the lower extremities may be present.

**Neonates**

- Neonates may seem irritable, be in respiratory distress, and exhibit signs of sepsis.

- Somnolence, hypotonia, and seizures can be associated if the CNS is involved.

- Hypothermia or hyperthermia, oliguria, elevated liver enzymes and elevated blood urea nitrogen and creatinine caused by direct viral damage and/or low
cardiac output may be present.

- **Infants**
  - Signs include failure to thrive, anorexia, tachypnea, tachycardia, wheezing, and diaphoresis with feeding.
  - In severe cases, low cardiac output may progress to acidosis and death.
  - End organ damage may develop because of direct viral infestation or because of low cardiac output.
  - CNS involvement may also develop.

- **Adolescents**
  - Presentation may be similar to that of younger children but with a more prominent decrease in exercise tolerance, lack of energy, malaise, chest pain, low-grade fever, arrhythmia, and cough.
  - End-organ damage and low cardiac output may be present.

**Causes:**

- Infecting organisms include the following:
  - Coxsackievirus types A and B, especially type B, are the most common viral causes of myocarditis.
  - Adenovirus (types 2 and 5 most common)
  - Cytomegalovirus
  - Echovirus
  - Epstein-Barr virus
  - Hepatitis C virus
  - Herpes virus
  - Human immunodeficiency virus
  - Influenza and parainfluenza
  - Measles
  - Mumps, associated with endocardial fibroelastosis (EFE)
  - Parvovirus B19
  - Poliomyelitis virus
  - Rubella
  - Varicella

- **Murine model**
  - The coxsackievirus and adenovirus receptor acts as the receptor for the four most common viruses causing human myocarditis: type C (type 2 and type 5) adenovirus and coxsackievirus B3 and B4.
  - Coxsackievirus B serotypes 1-6 have been associated with human
myocarditis, but the most serious cases have been attributed to types 3 and 4.

- In 1973, Lerner and Wilson developed an animal model of myocarditis using mice inoculated with coxsackievirus B3. This model was characterized by an early and a late phase. Following inoculation of the mice with the virus, there was initial replication of the virus with maximum replication within 3-5 days. By day 5, focal myocyte necrosis was evident. On day 7, most mice showed no further inflammation and no organisms could be recovered; however, some mice showed ongoing worsening inflammation similar to that seen in humans.

- The primary response to the early phase of viral infection is the release of natural killer (NK) cells, which lyse infected myocytes. This helps clear the virus from the system.

- NK cells also induce expression of major histocompatibility complex antigens on myocytes by releasing cytokines, which prepare the NK cells to interact with T lymphocytes. Animal models depleted of NK cells develop a more severe form of myocarditis.

- The late phase or second wave of T lymphocytes (CD4, CD8) begins approximately 1 week after the mouse has been inoculated with the virus. T lymphocytes can injure cells in the following 3 ways:
  - Stimulation of cytotoxic T cells
  - Production of antibody and antibody-dependent myotoxicity
  - Direct antibody and complement formation

- These ongoing processes are considered genetically mediated autoimmune processes. Two different strains of cytolytic T cells have been recognized; one strain attacks virus-infected myocytes and the other strain attacks uninfected cells.

- Enzymatic cleavage by viral proteins of cytoskeletal proteins appears to play a role in development of dilated cardiomyopathy.

- Apoptosis appears to play a role in the development of dilated cardiomyopathy.

- Various kinds of autoantibodies have been found in as many as 60% of patients with myocarditis. These include complement-fixing antimyolemmal antibodies, complement-fixing antisarcolemmal antibodies, antmyosin heavy chain antibodies, and anti–alpha myosin antibodies. Although their role in the disease is not completely understood, their presence may serve as a marker for diagnosing myocarditis in the future.
Other Problems to be Considered:

Medial necrosis of the coronary arteries
Shock

Lab Studies:

- Complete blood count with differential
  - Acute anemia of any origin may cause heart failure, and chronic anemia exacerbates heart failure; both respond to blood transfusion.
  - The presence of lymphocytosis or neutropenia supports diagnosis of a viral infection.
- Blood cultures: Ruling out any bacterial infection is important.
- Sedimentation rate and C-reactive protein: These nonspecific markers of inflammation usually are elevated. However, a normal value does not rule out myocarditis, particularly in the presence of congestive heart failure, which may lower the sedimentation rate.
- Viral cultures: Nasopharyngeal and rectal swabs may help identify etiology.
- Viral titers: A 4-fold increase in a specific titer from the acute to convalescent phase is strong evidence of infection.
- In situ hybridization
  - This process identifies viral RNA in myocardial tissue of patients believed to have myocarditis.
  - The incidence of false-negative results is high.
- Polymerase chain reaction (PCR)
  - PCR is used to find the viral genome in myocardial cells.
  - It is rapid, sensitive, and may become the test of choice for the diagnosis of viral myocarditis.
- Creatinine kinase–MB isoenzyme (CK-MB): These markers of myocardial damage are elevated most commonly when associated elevation of the ST segment on the ECG is present.
- Lactate dehydrogenase isoenzyme 1: This may be elevated in idiopathic myocarditis.
- Troponin I
  - This is another indicator of myocardial damage.
  - It is usually elevated up to a month after infection but is not specific for this disease.

Imaging Studies:

- Echocardiography
  - This is the most cost-effective test used for evaluation of myocardial function.
  - It is sensitive but not specific.
  - Findings include the following:
    - Global hypokinesis (the most common finding)
- Increased left ventricular end diastolic and systolic dimensions
- Left ventricular dysfunction, primarily systolic with decreased ejection fraction and shortening fraction
- Segmental wall motion abnormalities
- Pericardial effusion

- Chest radiography
  - Cardiomegaly and pulmonary edema may be depicted.
  - Incidentally noted cardiomegaly on chest radiograph may be the initial presentation.

- Radionuclide imaging
  - This may be helpful as a screening tool.
  - Gallium citrate Ga 67 myocardial scintigraphy is useful to reveal chronic inflammatory processes. It is a sensitive test but is limited by its low specificity and predictive value.
  - Indium In 111 antmyosin antibody imaging is highly sensitive for myocardial necrosis, but has a high incidence of false-positive results. However, absence of antmyosin uptake is highly predictive of a negative biopsy (92-98%).
  - Myocardial perfusion imaging with technetium Tc 99m–labeled labeled methoxyisobutyl isonitrile single-photon emission computed tomography (99mTc-MIBI SPECT) is usually a tool used to evaluate the severity of myocardial ischemia. Because the uptake and clearance of 99mTc-MIBI is affected by cell viability and membrane integrity, clinicians have recently used it as a marker for the severity of myocardial necrosis and inflammation in patients with myocarditis, with results comparable to those obtained with enzymatic cell damage markers.

**Other Tests:**

- Electrocardiography (ECG)
  - In some patients with mild cardiac involvement, ECG changes may be the only abnormal findings suggestive of myocarditis.
  - Low-voltage QRS (<5 mm throughout the limb leads) is the classic pattern. Pseudoinfarction patterns with pathologic Q waves and poor progression of R waves in the precordial leads may also be present.
  - T-wave flattening or inversion is a common finding associated with small or absent Q waves in V₅ and V₆.
  - Left ventricular hypertrophy with strain may be present.
  - Other nonspecific findings include prolonged PR segment and prolonged QT interval.
  - Sinus tachycardia is the most common finding. Premature ventricular contractions and atrial tachycardias have been reported. Junctional tachycardia is common and may worsen congestive heart failure. Occasional second- and third-degree atrioventricular block may be present, requiring temporary pacing.
  - Ventricular tachycardia is commonly associated and may be the initial presentation.

- Other techniques are under investigation to determine a specific viral etiology of myocarditis, such as immunohistochemical stains, inflammatory mediators, and autoantibody measurements.

**Procedures:**

- Endomyocardial biopsy
Biopsy is the criterion standard for the diagnosis of myocarditis. Myocardial biopsy establishes diagnosis and classifies disease stage.

- Biopsy is a relatively safe and effective way to sample heart muscle in older children; however, a risk of perforation in sick or younger infants exists.
- The utility of endomyocardial biopsy is controversial because of the possibility of a high false-negative result rate and because no proven therapy exists, even when a positive biopsy is obtained.
- Some advocate using radionuclide imaging techniques as screening tools before considering endomyocardial biopsy.

- Biopsy specimens may be useful for PCR diagnosis of viral etiology.

**Histologic Findings:** Gross evaluation of the heart reveals flabby and pale muscle with petechiae. Ventricular muscle is usually thin and may be hypertrophied. Heart valves and the endocardium are not usually involved, but in cases of chronic myocarditis, they might appear as they appear in endocardial fibroelastosis. Some experts believe that endocardial fibroelastosis is a result of viral myocarditis.

The microscopic hallmark of acute myocarditis is focal or diffuse interstitial infiltrate of mononuclear cells, lymphocytes, plasma cells, and eosinophils. Viral particles are rarely seen unless searched with special techniques (ie, PCR). Necrosis and disarrangement of the myocytes are typical and often are seen with coxsackievirus infection. In the chronic and healing stages, myocytes are replaced by fibroblasts (scar tissue).

In adenoviral myocarditis, less severe infiltrate can be seen histologically than is seen in cases of enteroviral infection.

**Medical Care:**

- General care

  - In the acute phase, the patient should be admitted to the hospital even if only mild signs of respiratory distress or congestive heart failure are present. Rapid progression to overt heart failure and/or hemodynamic collapse may occur.

  - Medical care is aimed at minimizing hemodynamic demands of the body. No specific proven therapy is available to prevent the myocardial damage, but maintenance of tissue perfusion is the goal to avoid further complications. Normal arterial blood oxygen levels should be maintained with supplemental oxygen as needed.

**Consultations:** Cardiologist

**Diet:** A low-salt diet is recommended for patients with congestive heart failure.

**Activity:**

- Bed rest is necessary during the acute phase of the illness and may slow the intramyocardial replication of the virus.

- Activity is permitted as partial or complete recovery is achieved.

If congestive heart failure is present, digitalis may be useful in maintaining adequate function. Diuretics can be given concomitantly to remove excess extracellular fluid and to decrease preload. Caution should be exercised since removal of fluid may cause low cardiac output and shock. It may be necessary to keep a higher venous-filling pressure to maintain an adequate cardiac output. Intracardiac pressure monitoring can facilitate...
maintenance of adequate filling pressures.

Inotropic agents are used when cardiac output cannot be maintained by less invasive measures. Dopamine, dobutamine, inamrinone (formerly amrinone), and milrinone are the most commonly used vasopressors.

Afterload reduction is most important in treating acute myocarditis and is used when hypotension is not present. This decreases the workload for the compromised myocardium and can allow patients to recover from the acute phase of illness. Agents that reduce afterload improve cardiac output by decreasing systemic arterial resistance. Intravenous medications such as nitroprusside, inamrinone, and milrinone can be replaced with oral ACE inhibitors when the patient stabilizes.

The use of immunosuppressive agents for the treatment of viral myocarditis is still controversial. Some animal studies revealed an exacerbation of viral cytotoxicity when treated with immunosuppressive agents. Other small series in humans have shown that the conditions of patients improve when the patients are treated with these agents. The Multicenter Myocarditis Treatment Trial aimed to establish differences in outcome among 3 treatment modalities. A total of 111 patients were randomized into 1 of the 3 following groups:

1. Prednisone/azathioprine
2. Prednisone/cyclosporine
3. Conventional therapy without immunosuppression

Findings revealed left ventricular function and survival were not significantly different among the 3 groups.

Intravenous gamma globulin may be important in the treatment of acute myocarditis. It has been associated with improved left ventricular function and improved survival.

New therapeutic agents are being studied as candidates for the treatment of myocarditis. These include agents that inhibit the virus entrance to the cells; antiviral agents that inhibit translation, transcription, or both; and interferon, among others. However, these strategies are still in early stages and, although they have promising results, some time may go by before they are widely accepted. Pleconaril, an investigational agent that inhibits viral attachment to host cell receptors, has a broad antienteroviral activity and, in clinical trials, has demonstrated benefit in children with enteroviral meningitis. This medicine is being tested in children with myocarditis.

Conventional management includes digoxin, diuretics, and afterload reduction. Severe cases with hemodynamic compromise may require intravenous inotropic agents, afterload reduction, vasodilators, and anticoagulation.

Drug Category: **Cardiac glycosides** -- These may improve left ventricular function by increasing myocardial contraction by inhibiting the sodium/potassium adenosine triphosphatase (ATPase) pump. This leads to sodium accumulation within the myocyte, which stimulates the sodium-calcium exchange. The increased intracellular calcium increases the force of contraction.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Digoxin (Lanoxin) -- Cardiac glycoside with direct inotropic effects in addition to indirect effects on the cardiovascular system. Acts directly on cardiac muscle, increasing myocardial systolic contractions. Its indirect actions result in increased carotid sinus nerve activity and enhanced sympathetic withdrawal for any given increase in mean arterial pressure.</th>
</tr>
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<tr>
<td>Adult Dose</td>
<td>Total digitalizing dose (TDD): 0.75-1.5 mg PO; 0.5-1 mg IV/IM. Divide TDD: Initially give 50% of TDD, and then give the remaining two 25% portions at 6- to 12-h intervals (1/2, 1/4, 1/4). Maintenance dose: 0.125-0.5 mg PO; 0.1-0.4 mg IV/IM. Individualize dose based on levels.</td>
</tr>
<tr>
<td>TDD PO:</td>
<td>Preterm infant: 20-30 mcg/kg, Term infant: 25-35 mcg/kg, 1 month to 2 years: 35-60 mcg/kg, 2-5 years: 30-40 mcg/kg, 5-10 years: 20-35 mcg/kg</td>
</tr>
</tbody>
</table>
Drug Category: Diuretics -- Hypoperfusion of the kidneys causes retention of sodium and water, which produces peripheral and pulmonary edema. Diuretics decrease the intravascular volume overload.

**Drug Name**
Furosemide (Lasix) -- This loop diuretic is the diuretic of choice in pediatric patients. Increases excretion of water by interfering with chloride-binding cotransport system which in turn inhibits sodium and chloride reabsorption in ascending loop of Henle and distal renal tubule.

**Adult Dose**
20-80 mg/d PO/IV/IM divided q6-12h

**Pediatric Dose**
0.5-2 mg/kg/dose PO/IV/IM up to tid

**Contraindications**
Documented hypersensitivity; hypokalemia; renal failure

**Interactions**
Pay special attention if given with aminoglycosides, cephalosporins, lithium, salicylates, ethacrynic acid, or indomethacin as concomitant administration with these medications may produce or worsen renal insufficiency; ototoxicity may be increased with concomitant
Drug Category: **Angiotensin-converting enzyme (ACE) inhibitors** -- Cardiac output and systemic resistance determine blood pressure. When systemic resistance is decreased with afterload reduction, myocardial shortening and stroke volume improve. Therefore, cardiac output can be maintained at a lower heart rate with lower myocardial oxygen demand. ACE inhibitors decrease production of angiotensin II, a potent vasoconstrictor. High levels of angiotensin II have also been associated with cellular damage in patients

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**Pregnancy**

C - Safety for use during pregnancy has not been established.

**Precautions**

Potent diuretic that may cause profound diuresis and electrolyte loss; metabolic alkalosis is a common complication; should not be given in the same intravenous line with inamrinone since it may cause precipitation of the compounds; may cause renal stones, especially in premature newborns; concomitant administration of chlorothiazide may decrease the hypercalciuria; administer oral dose with food or milk to decrease stomach upset

**Drug Name**

Chlorothiazide (Diuril) -- This is a thiazide diuretic. If given with furosemide, it may decrease hypercalciuria. Inhibits sodium reabsorption at the distal tubule in the kidney.

**Adult Dose**

500 mg to 2 g/d PO qd or divided bid  
100-500 mg/d IV qd or divided bid

**Pediatric Dose**

<6 months: 20-40 mg/kg/d PO divided bid; 2-8 mg/kg/d IV divided bid  
>6 months: 20 mg/kg/d PO divided bid; 4 mg/kg/d IV divided bid

**Contraindications**

Documented hypersensitivity; anuria

**Interactions**

Thiazide diuretics may decrease the effectiveness of anticoagulants, antigenot agents, and sulfonlyureas; effectiveness may be decreased by bile acid sequestrants, methenamine, and NSAIDs; thiazide diuretics may increase the toxicity of allopurinol, anesthetics, antineoplastics, calcium salts, diazoxide, digitalis, lithium, loop diuretics, methylodopa, muscle relaxants, and vitamin D; amphotericin B and anticholinergics may increase the toxicity of thiazide diuretics.

**Pregnancy**

B - Usually safe but benefits must outweigh the risks.

**Precautions**

Safety of IV use in children has not been established; this drug can produce electrolyte imbalance; not to be given SC or IM

**Drug Name**


**Adult Dose**

100-200 mg/d PO qd or divided bid

**Pediatric Dose**

2-3 mg/kg/d PO divided bid/tid

**Contraindications**

Documented hypersensitivity; hyperkalemia; hyponatremia; severe renal impairment; Addison disease

**Interactions**

ACE inhibitors, cyclosporine, or potassium supplements increase risk of hyperkalemia; may increase the risk of digoxin toxicity; avoid salt substitutes or natural licorice

**Pregnancy**

D - Unsafe in pregnancy

**Precautions**

May cause electrolyte imbalance, especially hyperkalemia; concomitant use with indomethacin or ACE inhibitors may cause hyperkalemia; main adverse effects are GI upset, hyponatremia, hyperkalemia, hepatotoxicity, lethargy, confusion, impotence and gynecomastia; spironolactone is carcinogenic in rodents

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administration of aminoglycosides
Drug Category: Adrenergic agonist agents (inotropic agents) -- Dopamine is a precursor to epinephrine, thus augmenting endogenous release of catecholamines. Also stimulates specific dopamine receptors. Dobutamine does not promote release of endogenous epinephrine. Dobutamine predominantly augments myocardial contractility via beta1 stimulation.

<table>
<thead>
<tr>
<th>Drug Name</th>
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<tbody>
<tr>
<td>Captopril (Capoten) -- Reduces afterload and myocyte necrosis. Beneficial in all stages of chronic heart failure. Pharmacologic effects result in a decrease in systemic vascular resistance, reducing blood pressure, preload, and afterload. Dyspnea and exercise tolerance are improved.</td>
<td>Dopamine (Intropin) -- At lower doses, this drug stimulates beta1-adrenergic and dopaminergic receptors (renal vasodilation, positive inotropism); at higher doses, it stimulates alpha-adrenergic receptors (renal vasoconstriction).</td>
<td>Dobutamine (Dobutrex) -- Stimulates beta1-adrenergic receptors. It has less alpha1 stimulation than dopamine; therefore, it produces less increase in systemic vascular resistance.</td>
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<tr>
<td>12.5-25 mg PO q8-12h; increase dose by 25 mg pm; not to exceed 450 mg/d divided tid</td>
<td>&lt;6 months: 0.05-0.5 mg/kg/dose PO up to tid &gt;6 months: 0.5-2 mg/kg/dose PO up to tid Test dose: 0.1 mg/kg/dose</td>
<td>Documented hypersensitivity; pregnancy; unilateral renal artery stenosis is a relative contraindication</td>
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<td>NSAIDs may reduce hypotensive effects of captopril; ACE inhibitors may increase digoxin, lithium, and allopurinol levels; rifampin decreases captopril levels; probenecid may increase captopril levels; the hypotensive effects of ACE inhibitors may be enhanced when given concurrently with diuretics</td>
<td>D - Unsafe in pregnancy</td>
<td>Titrate to patient’s tolerance and to effectiveness; decrease dose in renally impaired or volume depleted patients; may cause idiosyncratic hypotension after the first dose in children; test dose should be given and blood pressure monitored frequently after administration</td>
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<td>Dobutamine (Dobutrex) -- Stimulates beta1-adrenergic receptors. It has less alpha1 stimulation than dopamine; therefore, it produces less increase in systemic vascular resistance.</td>
<td>Administer as in adults</td>
<td>Documented hypersensitivity; subaortic stenosis</td>
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<td>Effects are prolonged and intensified by MAOIs, alpha- and beta-blockers, general anesthetics, and phenytoin</td>
<td>C - Safety for use during pregnancy has not been established.</td>
<td>Hypovolemia should be treated before infusion of this drug; extravasation should be treated promptly with SC administration of phentolamine (Regitine); administration through a central vein is recommended; do not use umbilical artery for infusion; if dosages &gt;20 mcg/kg/min are required, a different agent should be considered (eg, epinephrine, dobutamine)</td>
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<td>Beta-adrenergic blockers antagonize effects of dobutamine; general anesthetics may increase toxicity</td>
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</table>
Drug Category: **Cyclic adenosine monophosphate (c-AMP) phosphodiesterase inhibitors** --
Inotropic effects occur by inhibiting c-AMP phosphodiesterase, which increases the cellular levels of c-AMP. The sodium-potassium pump is not affected, as with digitalis. Vasodilatory activity is related to the direct relaxation effect on vascular smooth muscle.

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<th>Drug Name</th>
<th>Inamrinone - formerly amrinone (Inocor) -- Produces vasodilation and increases inotropic state. More likely to cause tachycardia than dobutamine; may exacerbate myocardial ischemia.</th>
</tr>
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<tbody>
<tr>
<td>Adult Dose</td>
<td>Loading dose: 0.75 mg/kg (undiluted) IV over 2-3 min Maintenance dose: 5-10 mcg/kg/min IV; titrate to effect</td>
</tr>
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<td>Pediatric Dose</td>
<td>Administer as in adults</td>
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<td>Contraindications</td>
<td>Documented hypersensitivity</td>
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<td>Interactions</td>
<td>Furosemide should not be given in the same IV line as inamrinone since it may cause precipitation of the compounds; do not dilute in solutions containing glucose Coadministration with diuretics, may result in hypovolemia and decrease in filling pressure; cardiac glycosides have additive effects on amrinone</td>
</tr>
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<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
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<td>Precautions</td>
<td>Like other inotropic agents, this drug may aggravate outflow tract obstructions; inamrinone should be monitored for hypotension, thrombocytopenia, and hepatotoxicity; GI symptoms, including nausea, vomiting, abdominal pain, and anorexia, are some of the more common adverse drug reactions</td>
</tr>
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</table>

Drug Category: **Immunomodulatory agents** -- Immune globulin is a purified preparation of gamma globulin. It is derived from large pools of human plasma and is comprised of 4 subclasses of antibodies, approximating the distribution of human serum.

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<tr>
<th>Drug Name</th>
<th>Immune globulin (Gamimune, Sandoglobulin, Gammagard SD) -- Use of these agents in myocarditis is not widely accepted. Clinical studies have shown IVIG may improve left ventricular function and survival in children.</th>
</tr>
</thead>
</table>

**Pregnancy**

- B - Usually safe but benefits must outweigh the risks.

**Precautions**

- Treat hypovolemia before infusion; treat extravasation promptly with SC administration of phentolamine (Regitine); administration through a central vein is recommended; do not use umbilical artery for infusion; may decrease central venous pressure (CVP) and wedge pressure.
Further Inpatient Care:
- Discharge when stable on oral medications.

Further Outpatient Care:
- Monitor medication doses and adverse effects.
- Serial echocardiograms are useful to follow ventricular function.

In/Out Patient Meds:
- Medications include the following, when indicated:
  - Digitalis
  - Afterload reduction agents
  - Diuretics
  - Antiarrhythmics
  - Anticoagulants

Transfer:
- Transfer to a facility with intensive and cardiology care may be required.

Deterrence/Prevention:
- Limit patient activity until recovered.
- Avoid negative inotropes.
- Be aware of the possibility of further decrease in ventricular function.

Complications:
- Arrhythmia
- Congestive heart failure
• Thromboembolism
• Further decrease in ventricular function
• Dilated cardiomyopathy

Prognosis:
• Studies give a wide spectrum of mortality and morbidity statistics.
• With suspected coxsackievirus B, mortality rate is higher in newborns (75%) than in older infants and children (10-25%).
• Complete recovery of ventricular function has been reported in as many as 50% of patients.
• Some patients develop chronic myocarditis (ongoing or resolving) and/or dilated cardiomyopathy. Those who develop dilated cardiomyopathy may require a heart transplant.

Patient Education:
• Restrict activity based on performance after the acute phase.

Medical/Legal Pitfalls:
• Failure to make a diagnosis

Special Concerns:
• Viral myocarditis may be a fatal disease during pregnancy; however, pregnant women are not at a higher risk of developing viral myocarditis compared with the general population.

Karjalainen J: Clinical diagnosis of myocarditis and dilated cardiomyopathy. Scand J Infect Dis Suppl...
Myocarditis, Viral excerpt


NOTE:
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