Congestive Heart Failure in Children

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Education Gaps

1. The signs and symptoms of heart failure in children are frequently mistaken for other more common childhood illnesses.
2. Standard-of-care medications are commonly underprescribed in children who are discharged after hospitalization for heart failure. (1)

Objectives

After completing this article, readers should be able to:

1. Recognize the signs and symptoms of heart failure in children of various ages.
2. Identify the causes of heart failure in children of various ages.
3. Plan the initial diagnostic evaluation of heart failure in children.
4. Plan the initial treatment of heart failure in children.

Abstract

Congestive heart failure is a final common clinical pathway for several diseases in childhood, such as familial cardiomyopathy, viral myocarditis, inborn errors of metabolism, and autoimmune disorders. Early identification and treatment can reduce symptom severity and may affect outcomes. In this review, the clinical characteristics of pediatric heart failure are described, and the initial diagnostic evaluation is outlined. Evidence-based heart failure treatment strategies at various clinical stages are discussed in detail, including the management of acute decompensated heart failure.

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ABBREVIATIONS

ACC	American College of Cardiology
ACE	angiotensin-converting enzyme
AHA	American Heart Association
ALCAPA	anomalous left coronary artery from the pulmonary artery
BNP	B-type natriuretic peptide
CCS	Canadian Cardiovascular Society
DCM	dilated cardiomyopathy
HF	heart failure
ISHLT	International Society for Heart and Lung Transplantation
MCS	mechanical circulatory support

INTRODUCTION

A good definition of congestive heart failure (HF) is elusive and has changed over time with our understanding of the pathophysiology of the failing heart. This is especially true in pediatrics because the etiology and symptoms of HF may differ by age group. Dr Arnold Katz has proposed a popular definition of HF in adults that acknowledges a clinical pattern of myocardial disease and a neurohormonal paradigm responsible for its progression: "a clinical syndrome in which heart disease reduces cardiac output, increases venous pressures, and is accompanied

by molecular abnormalities that cause progressive deterioration of the failing heart and premature myocardial cell death." (2) Most pediatric HF specialists would agree that pulmonary overcirculation that results from a large left-to-right intracardiac shunt (eg, ventricular septal defect) is not HF. For the purposes of this review, the term *heart failure* is limited to children whose signs and symptoms are attributable to ventricular dysfunction.

CLASSIFICATION OF HF

The American College of Cardiology (ACC) and the American Heart Association (AHA) staging classification of HF is a useful tool for categorizing patients across populations. (3) The staging system emphasizes the onset and progression of the disease, unlike the New York Heart Association functional classification system, which emphasizes exercise capacity. (4) The International Society for Heart and Lung Transplantation (ISHLT) published guidelines and recommendations for the evaluation and treatment of HF in children in 2004 and proposed a staging classification (Table 1). (5)

ETIOLOGY OF NEW-ONSET HF

The etiology of new-onset HF varies by age (Table 2). In newborns and infants, structural heart disease commonly leads to ventricular dysfunction and HF. Congenital abnormalities such as anomalous left coronary artery from the pulmonary artery (ALCAPA), critical aortic stenosis, coarctation of the aorta, and single-ventricle congenital heart disease are frequently associated with ventricular chamber enlargement, abnormal ventricular systolic and/or diastolic function, and signs of HF. Although rare, inborn errors of metabolism may also cause HF in infancy. Diseases such as fatty acid oxidation disorder and other mitochondrial disorders may lead to hypertrophic or dilated forms of cardiomyopathy with impaired ventricular function.

Dilated cardiomyopathy (DCM) is the most common myopathic process leading to HF in children. The annual incidence of DCM in US children is 0.57 cases per 100,000. (6) In children, DCM may be caused by genetic mutations, autoimmune diseases, infectious diseases, drug exposures, and endocrine disorders (Table 3). Familial forms of DCM occur in approximately 20% to 50% of affected children. The most common inheritance pattern of DCM is autosomal dominant, although X-linked and autosomal recessive patterns also occur. Spontaneous, or de novo, mutations have been described as well.

The most common cause of acquired DCM in children is myocarditis. Acute myocarditis is usually attributed to a virus or other infectious agent. Viruses such as enterovirus, parvovirus, and adenovirus are frequently implicated. Infection with human immunodeficiency virus may also lead to HF. The prevalence of cardiac involvement is high among human immunodeficiency virus–positive children and includes ventricular chamber enlargement (DCM), increased ventricular mass, arrhythmias, and pericardial effusion. Noninfectious agents, such as drugs or toxins, can also cause myocarditis and a dilated form of cardiomyopathy.

Beyond infancy, other causes of HF are encountered. Kawasaki disease may cause large coronary artery aneurysms that can lead to vascular thrombosis and myocardial ischemia with ventricular dysfunction early in the disease

TABLE 1. **Proposed HF Classification for Infants and Children**

STAGE	DEFINITION	EXAMPLES
A	Patients with increased risk of developing HF but who have normal cardiac function and no evidence of cardiac chamber volume overload.	Previous exposure to cardiotoxic agents, family history of heritable cardiomyopathy, univentricular heart, congenitally corrected transposition of the great arteries.
B	Patients with abnormal cardiac morphology or cardiac function, with no symptoms of HF, past or present.	Aortic insufficiency with LV enlargement, history of anthracycline with decreased LV systolic function.
C	Patients with underlying structural or functional heart disease, and past or current symptoms of HF.	Dilated cardiomyopathy with chronic HF due to decreased LV systolic function.
D	Patients with end-stage HF requiring continuous infusion of inotropic agents, mechanical circulatory support, cardiac transplant, or hospice care.	Acute decompensated HF due to viral myocarditis.

HF=heart failure, LV=left ventricular.
From Rosenthal D, Chrisant MR, Edens E, et al. International Society for Heart and Lung Transplantation: practice guidelines for management of heart failure in children. J Heart Lung Transplant. *2004;23(12):1313.*

TABLE 2. **Etiology of New-Onset Heart Failure by Age**

Newborns and infants	Acute viral myocarditis Idiopathic dilated cardiomyopathy Familial cardiomyopathy Anomalous left coronary artery origin from the pulmonary artery Tachycardia-induced cardiomyopathy Inborn error of metabolism Hypertrophic cardiomyopathy Coarctation of the aorta Critical aortic stenosis Single-ventricle congenital heart disease
Age 2-5 y	Acute viral myocarditis Idiopathic dilated cardiomyopathy Familial cardiomyopathy Single-ventricle congenital heart disease Tachycardia-induced cardiomyopathy Kawasaki disease
Age >5 y	Acute viral myocarditis Idiopathic dilated cardiomyopathy Familial cardiomyopathy Tachycardia-induced cardiomyopathy Single-ventricle congenital heart disease Rheumatic heart disease Anemia Hypothyroidism Systemic lupus erythematosus

process. Over several years, the coronary arteries may develop stenoses and occlusion. Autoimmune disorders, such as systemic lupus erythematosus and rheumatic heart disease, may occur in older children and adolescents. These disorders cause myocardial inflammation with vascular stenosis, valvulitis, myocardial fibrosis, and ventricular dysfunction.

Neuromuscular disorders such as Duchenne and Becker muscular dystrophies are also associated with DCM and HF in children. Boys with Duchenne muscular dystrophy commonly develop DCM, usually in puberty or early adolescence. Although they are living longer due to advances in respiratory therapies, death from HF and sudden death is increasing in frequency.

Abnormal and sustained heart rhythms, usually tachyarrhythmias, may also lead to DCM and HF. Atrial ectopic tachycardia is the most common cause of tachycardia-induced cardiomyopathy. Fortunately, cardiac function usually normalizes within a few months of rhythm control with either medication or an ablation procedure.

CLINICAL FEATURES OF HF

Children with HF caused by DCM may present with clinical features that mimic many other diseases of childhood, such as bronchitis and gastrointestinal disease. Most children with HF complain of fatigue or lack of energy, labored breathing (either at rest or with exertion), abdominal pain, and nausea or vomiting (Table 4). Other symptoms may include chest pain and wheezing.

In children, the clinical signs of HF may not be obvious on physical examination. (7) Resting tachycardia and tachypnea are commonly present in all ages. Blood pressure, however, is usually normal except in patients with cardiogenic shock or impending shock. Signs of fluid overload, such as hepatomegaly and a gallop rhythm, are common in children; however, other findings of congestion, such as edema of the lower extremities, abdominal ascites, rales, and jugular venous distention, are identified less frequently. Signs of poor perfusion may be present, including delayed capillary refill and cool distal extremities. A blowing holosystolic murmur at the apex may be appreciated in patients with a dilated left ventricular chamber and an incompetent mitral valve.

CLINICAL EVALUATION OF HF

Diagnostic tools such as chest radiography and electrocardiography can help determine whether a child's signs or symptoms are attributable to HF. On chest radiography, the cardiac silhouette is usually enlarged (Figs 1 and 2). Severe mitral regurgitation can lead to left atrial enlargement, which may be appreciated on a lateral projection. Children with HF frequently have normal lung markings on chest radiographs. Increased pulmonary vascular markings, alveolar edema, and pleural effusions may be seen on radiographs, but the absence of these findings does not rule out HF.

The electrocardiogram commonly demonstrates nonspecific abnormalities such as ventricular hypertrophy by voltage criteria and ST-segment or T-wave changes. Sometimes it will reveal electrical conduction disturbances, especially in patients with advanced disease. Rhythm disturbances are also common in patients with HF and may include supraventricular tachycardia, atrial fibrillation/flutter, atrioventricular block, and ventricular tachycardia.

Laboratory biomarkers of heart failure may help establish a diagnosis. B-type natriuretic peptide (BNP) and N-terminal proBNP concentrations are almost always elevated in children with HF and may portend a poor prognosis in the outpatient setting. Serum electrolytes and markers of kidney function may be abnormal, especially in patients with decompensated HF. Hyponatremia is frequently identified in patients with advanced disease and is associated with

TABLE 3. **Etiology of Dilated Cardiomyopathy in Childhood**

FACTOR	EXAMPLES
Genetic mutations	Lamin A-C, myosin binding protein-C, tropinin I, taffazin (Barth syndrome), dystrophin, LAMP2 (Danon disease), mitochondrial disorders, limb-girdle dystrophy, titin, desmin
Myocarditis	Enteroviruses, parvovirus, adenovirus, influenza, Epstein-Barr virus, human immunodeficiency virus, cytomegalovirus, varicella, mumps, Giant cell disease, Lyme disease, mycoplasma
Ischemia	Anomalous origin of left coronary artery from pulmonary artery, Kawasaki disease with coronary aneurysms
Metabolic disorders	Disorders of fatty acid oxidation, glycogen storage disorders (eg, Pompe), carnitine deficiency
Structural heart disease	Valvular disease, congenital heart disease
Endocrine disorders	Hypothyroidism, parathyroid disease, pheochromocytoma
Hematologic disorders	Iron deficiency, sickle cell anemia, hemochromacytosis, thalassemia
Autoimmune/collagen vascular diseases	Systemic lupus erythematosus, dermatomyositis, rheumatic heart disease
Toxins	Anthracycline, radiation, cyclophosphamide

worse outcomes in hospitalized patients. (8) Kidney function should be evaluated and monitored in children with HF because low cardiac output and venous congestion may lead to kidney injury and further progression of the disease and exacerbation of symptoms.

An echocardiogram should be performed in any child with suspected ventricular dysfunction or HF. It can reveal important information about ventricular chamber size and systolic/diastolic function. In children younger than 1 year with newly diagnosed DCM with HF, it is compulsory to determine the origins of the coronary arteries to rule out ALCAPA. In left ventricular noncompaction cardiomyopathy, the myocardium will appear heavily trabeculated, with fingerlike projections and recesses along the left ventricular apex and free wall. Left atrial enlargement is frequently seen on echocardiograms in the presence of severe mitral regurgitation. Bi-atrial enlargement should raise suspicion for restrictive cardiomyopathy.

TREATMENT OF HF

Only 1 large randomized controlled trial has ever been conducted to assess the efficacy and safety of oral HF therapy in children. (9) Most of our understanding of the management of HF comes from studies performed in adults with HF resulting from ischemic heart disease. Until more therapies are studied in children, the pediatrician must rely on evidence from large trials in adults, familiarizing oneself with the societal guidelines and cautiously applying those recommendations to the pediatric HF population.

In 1995, the ACC and the AHA formed a task force to recommend practice guidelines for the evaluation and management of HF in adults. The guidelines were reassessed and expanded in 2013 with collaboration from the ISHLT, the American College of Chest Physicians, and the Heart Rhythm Society. (3) An updated version has been endorsed

TABLE 4. **Clinical Features of Decompensated Pediatric Heart Failure**

AGE	SIGNS OF HEART FAILURE	SYMPTOMS OF HEART FAILURE[a]
Newborns, infants, and toddlers	Tachycardia, tachypnea, diaphoresis, grunting, nasal flaring, crackles, wheezing, gallop rhythm, displaced point of maximal impulse, pallor, hepatomegaly, poor perfusion	Poor weight gain, decreased oral intake, increased work of breathing, fussiness, diaphoresis
Age ≥5 y	Tachycardia, tachypnea, peripheral edema, jugular venous distention, wheezing, gallop, hepatomegaly	Abdominal pain, nausea and vomiting, dyspnea at rest or with exercise, orthopnea, fatigue, poor appetite, cough

[a]*As reported by a parent or guardian in the youngest patients.*

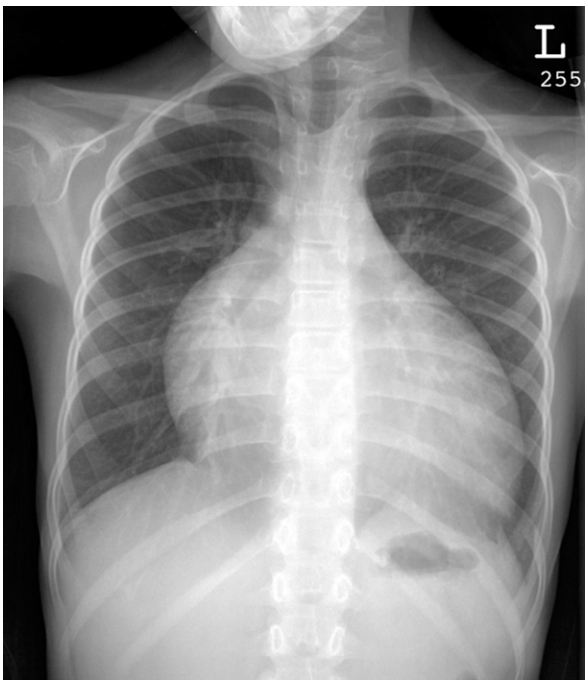

Figure 1. Anteroposterior chest radiograph of a child with dilated cardiomyopathy and new-onset heart failure. Marked cardiomegaly is present, but there is no evidence of pulmonary vascular congestion and only trace pleural effusion on the left.

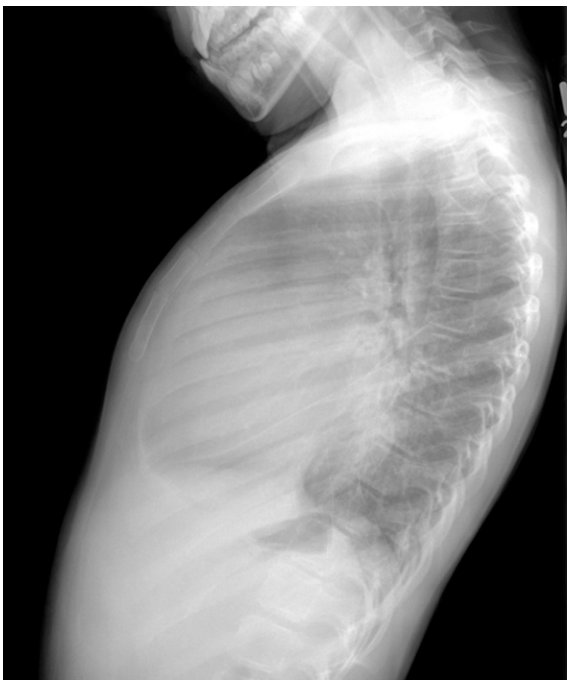

Figure 2. Lateral chest radiograph.

by the Heart Failure Society of America. (10) The Canadian Cardiovascular Society (CCS) and the ISHLT have both published guidelines for the evaluation and management of HF in children, relying heavily on published data in adults to make recommendations. (11)(12) See Fig 3 for graduated medical therapies based on HF clinical stage.

Stage A

In stage A, no particular HF medications are recommended; however, regular clinical surveillance and monitoring are important for patients who are at high risk for HF. For example, patients with cancer who have received cardiotoxic chemotherapeutic agents (eg, anthracyclines) should be considered for annual screening with echocardiography. Similarly, patients with chronic kidney disease, especially those who require dialysis, are at risk for ventricular dysfunction and HF and may benefit from routine cardiac follow-up.

Stage B

The ACC Foundation/AHA HF guidelines recommend the use of angiotensin-converting enzyme (ACE) inhibitors in asymptomatic adults with impaired systolic function to prevent the development of symptomatic HF. Inhibition of the ACE has been widely studied in adults with congestive HF. Landmark investigations have demonstrated improved functional capacity, fewer hospitalizations, and decreased mortality in adult patients with HF. There is strong evidence for the benefits of ACE inhibition in both ischemic and nonischemic forms of heart disease and even in asymptomatic patients. (13)(14)(15)(16)(17)(18)(19)

The Studies of Left Ventricular Dysfunction evaluated the impact of enalapril on mortality in asymptomatic adults with decreased left ventricular systolic function and in patients with symptomatic HF. (18)(19) Patients with asymptomatic left ventricular dysfunction were randomized to either enalapril or placebo and were followed for a mean of just over 3 years. No reduction in mortality was observed; however, when patients who died were combined with those who progressed to symptomatic HF, a risk reduction of 29% was identified in those treated with enalapril. In addition, patients treated with enalapril were less likely to require hospitalization for HF.

The evidence is less robust for children, however, and we understand little about the efficacy of ACE inhibition in children with myocardial dysfunction. Retrospective data have shown a survival benefit for children with DCM, but these findings have not been duplicated in subsequent studies. (20)(21) Enalapril may reduce left ventricular wall stress and improve function in children treated with chemotherapeutic agents.

The CCS give a strong recommendation for the use of ACE inhibitors in children with HF. It also recommends

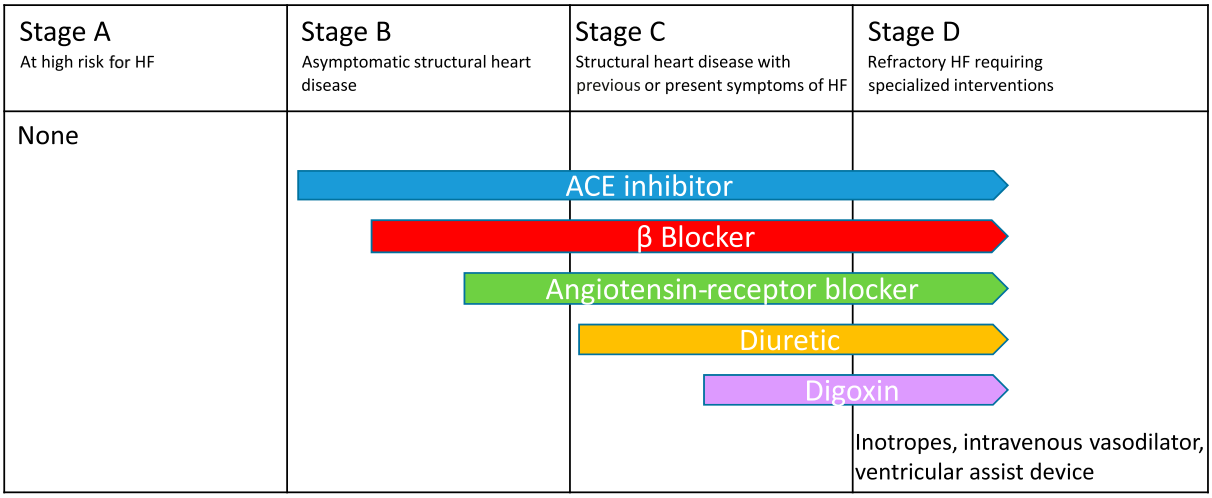

Figure 3. Medical therapy for heart failure (HF) by stage. Angiotensin-converting enzyme (ACE) inhibitors and β-blockers may by initiated in asymptomatic individuals with ventricular dysfunction at a low dose and uptitrated to the target dosage based on tolerance of the medication. (Modified with permission from Kantor PF, Lougheed J, Dancea A, et al; Children's Heart Failure Study Group. Presentation, diagnosis, and medical management of heart failure in children: Canadian Cardiovascular Society guidelines. *Can J Cardiol.* 2013;29(12):1535–1552.)

caution when initiating and uptitrating ACE inhibitors during the first 4 months after birth due to the risk of renal dysfunction. (11) Captopril is more often prescribed to newborns and infants, whereas longer-acting lisinopril and enalapril are prescribed to older children. See Table 5 for suggested target dosages.

β-Blockers are also recommended by the ACC Foundation/AHA in asymptomatic patients with ventricular systolic dysfunction. (3) Several years ago, β-blocker therapy in patients with left ventricular dysfunction was viewed with skepticism. It has since become the established standard of care and is very frequently used in conjunction with an ACE inhibitor. Several decades ago, numerous small trials signaled potential hemodynamic and clinical benefits of β-blocker treatment. Subsequent large-scale studies have demonstrated the safety and efficacy of β-blocker use for treating symptoms and reducing morbidity and mortality. (22)(23)(24)(25)(26)(27) (28)(29)(30)(31) Accordingly, β-blockers are now a mainstay of HF therapy in adult patients.

Among the β-blockers, carvedilol is the most thoroughly investigated and prescribed. It attenuates the effects of high

TABLE 5. **Heart Failure Medication Target Dosing**

β-BLOCKERS	ACE INHIBITORS	DIURETIC/ALDOSTERONE ANTAGONISTS
Carvedilol	**Captopril**	**Furosemide**
Infants and young children: 0.8–1 mg/kg per day	Infants: 1–4 mg/kg per day	Infants and young children: 1–2 mg/kg per dose every 6–24 h
Children (<50 kg): 25 mg/day	Children (>50 kg): 150 mg/day	Children (>50 kg): 20–80 mg/day
Children (>50 kg): 50 mg/day		
Metoprolol	**Enalapril**	**Spironolactone**
Infants and young children: 2 mg/kg per day	Infants and young children: 0.4–0.5 mg/kg per day	Infants and young children: 1–3.3 mg/kg per day divided doses every 6–24 h
Children (<50 kg): 100 mg/day	Children (<50 kg): 10 mg/day	May increase to 5–6 mg/kg per day
Children (>50 kg): 200 mg/day	Children (>50 kg): 20 mg/day	Maximum dose: 100 mg/day

ACE=angiotensin-converting enzyme.
From the Texas Children's Hospital Cardiomyopathy and Heart Failure Service, Houston, TX.

circulating concentrations of norepinephrine and upregulates β-receptor density in HF, leading to improved chamber remodeling and function. In one study of asymptomatic patients with stage B HF and low ejection fraction, administration of carvedilol resulted in a 31% reduction in the risk of deleterious long-term outcomes. (32) The ISHLT guidelines state that "following adult heart failure guidelines, it is reasonable to consider β-blockers in asymptomatic children with systemic LV [left ventricular] systolic dysfunction." Therapy should start at a small dose and slowly uptitrate. The CCS recommends starting at a dose of 0.05 mg/kg every 12 hours and uptitrating to the target dose over several weeks.

Stage C

Patients with stage C HF have "functional heart disease with prior or current symptoms of heart failure." (3) In this population, the goals of therapy are to provide symptomatic relief and limit progression of the disease. Both ACE inhibitors and β-blockers are recommended in children with stage C HF. Generally, if these medications are being introduced at this stage, they are added sequentially, and ACE inhibitors are started first.

The Cooperative North Scandinavian Enalapril Survival Study was a randomized study of adults with severe HF who received either enalapril or placebo. (17) Mortality was reduced by 31% at 1 year in patients who received enalapril compared with patients who received placebo.

β-Blockers reduce morbidity and mortality in patients with chronic HF. A study evaluating the efficacy of carvedilol in patients with chronic HF (26) found a beneficial effect of carvedilol on survival. The mortality risk in patients treated with carvedilol was significantly lower compared with placebo (3.2% carvedilol vs 7.8% placebo; $P < .001$). In addition, there was a 27% reduction in the risk of cardiac hospitalization (14.1% vs 19.6%; $P = .036$).

Only 1 multicenter, randomized study has been performed of the effects of β-blockers in children with HF. (9) Symptomatic children and adolescents were randomized to receive either carvedilol or placebo and were treated for 6 months. The investigators found no significant improvement in clinical outcomes in children who received carvedilol compared with placebo. This may be due to the fact that the study was underpowered or that 56% of patients who received placebo had significant clinical improvements.

Despite the paucity of controlled studies in children, the consensus opinion among HF specialists is that ACE inhibitors and β-blockers should be prescribed to eligible pediatric patients with HF. It is safe and advisable to prescribe these medications before discharge in hospitalized patients. The prescription rate in discharged children is quite low, however. Moffett and Price (1) found wide variation in the use of ACE inhibitors and β-blockers in children at hospital discharge, with most centers prescribing at rates less than 50%. Furthermore, only 40% to 60% of eligible patients were prescribed these medications at hospital discharge.

In patients who exhibit signs or symptoms of congestion due to fluid overload, diuretics can be administered for symptomatic relief. Loop diuretics, such as furosemide, are the preferred first-line agents for most children with HF. Diuretics can reduce body weight and edema in patients with HF with mild-to-moderate symptoms and may improve stroke volume and ventricular performance in certain patients. The effects of diuretics on mortality are not known; however, a Cochrane analysis of several small studies in adult patients with chronic HF showed that conventional diuretics may decrease the incidence of death and worsening HF. (33)

Aldosterone antagonists are relatively weak diuretics but have other features (antifibrotic) that benefit patients with HF. There is strong evidence in adults that aldosterone antagonists reduce mortality and alleviate HF symptoms. In the Randomized Aldactone Evaluation Study of adults with severe HF, randomization to receive spironolactone was associated with a 30% reduction in the risk of death and a decreased frequency of hospitalization for worsening HF. (34) In addition, HF symptoms significantly improved in patients treated with spironolactone. Spironolactone is the most common aldosterone antagonist used in children. It is reasonable to consider its use in children with ventricular dysfunction and mild-to-moderate symptoms. Spironolactone is generally prescribed after an ACE inhibitor and a β-blocker have been initiated and uptitrated to target dosing. Renal function and serum potassium should be monitored closely, especially if co-administered with an ACE inhibitor. Spironolactone should be avoided in patients with a creatinine clearance less than 30 mL/min/1.72 m^2 (0.50 mL/s/m^2).

Historically, digoxin was prescribed commonly in children with HF. This therapy seems sensible given the potential beneficial effects of digoxin, including increased inotropic response, attenuated neurohormonal response, and enhanced control of heart rate in adult patients with atrial fibrillation. Digoxin seems to ameliorate symptoms of advanced HF and improve quality of life, but there are no data showing improved survival. It may be prescribed in children with symptomatic HF attributable to ventricular

dysfunction but at a low dose (5–10 μg/kg per day). (35) Serum digoxin concentrations should be measured in follow-up with a goal value of 0.5 to 0.8 ng/mL (0.64–1.02 nmol/L).

Stage D

In stage D, patients have developed symptomatic HF that is refractory to optimized oral therapies, and they frequently require inpatient treatments. This stage may be characterized by frequent hospitalizations for fluid overload or low cardiac output and by development of comorbidities such as anemia, renal impairment, and hyponatremia. For some patients, their disease may progress to end-stage, at which point long-term survival requires cardiac transplant and/or mechanical circulatory support (MCS).

Diuretics, Fluid Restriction, and Nutrition

Intravenous loop diuretics should be considered first-line therapy for the initial treatment of decompensated HF. When patients present to the clinic or emergency department with symptomatic HF, diuretics should be administered without delay. Patients receiving chronic diuretic therapy may need higher doses than patients with new-onset HF. In situations of diuretic "resistance," the addition of metolazone or chlorothiazide may be helpful. Some patients with perceived diuretic resistance may respond to loop diuretic administered as a continuous infusion rather than as scheduled bolus dosing. The treating physician should frequently monitor for electrolyte disturbances (hypokalemia, hypomagnesemia), renal injury, and lowered blood pressure during treatment with intravenous diuretics.

Some patients with chronic recurrent fluid overload (or even acute congestion) may benefit from restriction of fluid intake, especially in the setting of diminished diuretic responsiveness. The degree of fluid restriction should vary depending on the severity of fluid overload, refractoriness of diuretics, nutritional status of the patient, and electrolyte abnormalities such as hyponatremia. However, there are no data that show a clinical benefit of fluid restriction in children. One must also practice caution in infants because limited fluid intake may also lead to calorie restriction and limited growth.

The metabolic demands of the body are usually increased during HF exacerbation and may lead to muscle wasting. As well, high concentrations of neurohormones such as tumor necrosis factor α can lead to cardiac cachexia. Malabsorption of nutrients in the gut due to bowel wall edema and decreased perfusion also plays a role. The most important therapy for malnutrition in HF is the administration of appropriate HF medications, such as ACE inhibitors and β-blockers. Dietary supplementation may be necessary for some patients, and a formal assessment by an experienced dietitian may be helpful. There are few data for appetite stimulants in adults with HF, and the cardiovascular societies have made no recommendation regarding their use.

Inotropes

The ACC Foundation and the AHA have recommended against the routine use of inotropes in the treatment of decompensated HF in adults. However, inotropes still play an important role in the management of patients with symptomatic HF and evidence of poor perfusion or low blood pressure. In these patients, inotropic agents may be necessary to maintain circulatory function, relieve symptoms, and improve end-organ function.

Milrinone is a phosphodiesterase inhibitor that enhances inotropy and reduces afterload by increasing cyclic adenosine monophosphate. Milrinone also reduces pulmonary vascular tone and is less likely to cause tachycardia than other inotropic agents. Only a few studies have evaluated milrinone for the treatment of decompensated HF in adults and have shown only little, if any, clinical benefit. (36) In fact, milrinone may pose a greater risk of arrhythmias and death in adults with advanced HF. In the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure study, adults with chronic HF were randomized to receive either an intravenous infusion of milrinone or placebo. There was no difference in length of stay between the patients taking milrinone and the placebo group, but arrhythmias and hypotension occurred at a greater frequency in patients randomized to receive milrinone.

Dobutamine

Dobutamine is an adrenergic agent frequently used to treat low cardiac output in adults with decompensated HF. The agent activates β-receptors in the heart and peripheral vasculature, increasing contractility of the myocardium and decreasing vascular tone. Although this physiologic effect might seem favorable, dobutamine infusions in patients with HF may cause more harm than good. (37) (38) The Flolan International Randomized Survival Trial showed that patients with symptomatic HF treated with dobutamine had a higher mortality rate than patients with HF who did not receive dobutamine. (38) Adverse effects of dobutamine include tachycardia, increased myocardial oxygen consumption, and increased incidence of atrial and

ventricular arrhythmias. No controlled dobutamine studies have been performed in children with HF.

Dopamine

Dopamine is an adrenergic therapy that stimulates α- and β-receptors and can be considered in situations of cardiogenic shock or low cardiac output. It also stimulates dopaminergic receptors on the renal vasculature. At doses of 3 μg/kg per minute and higher, stimulation of β-1 receptors in the heart may enhance ventricular contractility and increase heart rate. At doses of 5 μg/kg per minute and higher, the α-receptor activity increases peripheral vascular tone and negates any peripheral vasodilation caused by β-2 receptor stimulation. (39) Epinephrine may also be considered in this situation. Although it can stabilize blood pressure and heart rate, epinephrine may also result in ischemia, atrial and ventricular arrhythmias, and increased myocardial oxygen consumption.

Despite the most optimized medical therapy, some children develop worsening and advanced end-stage HF with low cardiac output syndrome; MCS may be the only treatment option remaining for patients being considered for cardiac transplant. It can be used as a bridge to cardiac transplant or as a bridge to recovery in patients with potentially reversable disease processes, such as myocarditis or acute graft rejection. Outcomes with MCS are most successful when application is early, that is, before the patient develops significant end-organ injury. Careful consideration must be given to cases on an individual basis before committing to long-term support because clinical experience with chronic MCS is still limited.

Summary

- Substantial research has demonstrated that heart failure (HF) can be caused by a variety of disease processes that lead to a final common clinical syndrome consisting of ventricular dysfunction, elevated filling pressures, neurohormonal activation, and clinical symptoms. (2)
- Based on clinical research, common clinical features of HF in children include abdominal pain, decreased appetite, labored breathing, wheezing, diaphoresis, poor weight gain, hepatomegaly, and gallop rhythm. (6)
- Clinical studies have shown that diagnostic testing in HF may reveal cardiomegaly on chest radiography, abnormal cardiac rhythm on electrocardiography, decreased ventricular function and ventricular chamber enlargement on echocardiography, and elevated B-type natriuretic peptide concentration. (5)(7)(10)(11)
- Strong evidence supports the use of an angiotensin-converting enzyme (ACE) inhibitor with or without a β-blocker for the initial treatment of asymptomatic ventricular systolic dysfunction. (13)(14)(15)(16)(17)(18)(19)(20)(21)
- Consensus opinion and limited evidence support the use of a loop diuretic in patients with symptomatic HF. (5)(34)
- Clinical evidence suggests that patients with advanced HF should be considered for an aldosterone antagonist co-administered with an ACE inhibitor and a β-blocker. (35)
- If disease progresses to refractory symptoms, inotropic support may improve cardiac output and end-organ perfusion. Mechanical circulatory support may be indicated if a patient is considered a good candidate for cardiac transplant.

References for this article are at http://pedsinreview.aappublications.org/content/40/2/60.

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1. A 2-year-old boy with recurrent respiratory issues and gastrointestinal concerns is brought to the clinic for evaluation. The parents report that he is napping more frequently than a few months ago. He is less interested in his food and seems tired during the day. On cardiac examination, S1 is normal. S2 is single. There are third and fourth gallop heart sounds in diastole. The patient is referred to cardiology. Which of the following is the best initial test for the cardiologist to perform in the evaluation of this patient?
    A. Echocardiogram.
    B. Feeding evaluation.
    C. Holter monitor for 1 week.
    D. Sleep study.
    E. Trial of β-blocker medication.
2. A 3-year-old girl is brought to the clinic for evaluation of progressive fatigue and recurrent respiratory concerns. She was previously seen in the emergency department and was treated for wheezing with good response. She is otherwise healthy. Her physical examination today is significant for hepatomegaly. An echocardiogram shows bi-atrial enlargement. Which of the following is the most likely diagnosis in this patient?
    A. Aortic stenosis.
    B. Hepatitis.
    C. Idiopathic atrial flutter.
    D. Restrictive cardiomyopathy.
    E. Sequelae of Kawasaki disease.
3. A 10-year-old boy is being followed in the cardiology clinic for history of heart failure associated with mitral valve regurgitation. He remains asymptomatic and has demonstrated appropriate growth and development for his age. The cardiologist following him shares that the boy has impaired systolic function. Which of the following is the most appropriate next step in the management in this patient?
    A. Addition of an angiotensin-converting enzyme (ACE) inhibitor.
    B. Emergency mitral valve surgery.
    C. Nutrition evaluation and review of sodium intake.
    D. Trial of digoxin.
    E. Trial of oral milrinone.
4. A 9-year-old girl with a history of cardiomyopathy is followed in the cardiology clinic. She has hepatomegaly on examination and fatigue with exercise. She is taking enalapril for treatment of congestive heart failure. Which of the following is the most appropriate medication to be added to her treatment regimen??
    A. Alprazolam.
    B. Carvedilol.
    C. Dobutamine.
    D. Milrinone.
    E. Trazodone.

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5. A 10-year-old boy with a history of complex congenital heart disease and congestive heart failure is brought to the cardiology clinic for follow-up. He is taking enalapril and propranolol. He is fatigued during the day, and his parents are concerned that he is not able to participate in school activities owing to his fatigue. Which of the following is the most appropriate medication to be added to the treatment regimen of this patient?

   A. Dobutamine.
   B. Dopamine.
   C. High-dose enalapril.
   D. Milrinone.
   E. Spironolactone.

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