

## **Heart Failure: Diagnosis and Treatment**

Approximately 5 million people—about 2 percent of the U.S. population—are affected by heart failure. Diabetes affects 20.8 million Americans and 65 million Americans have hypertension. Although a relatively small number of people suffer from it, heart failure accounts for 12 to 15 million office visits and 6.5 million hospital admissions each year. In fact, more Medicare dollars are spent on the treatment of heart failure than on any other diagnosed medical condition. Heart failure is a very common disease that can have a high death rate. Despite advancements in treatment, the death rate has been increasing. It is, therefore, important to understand the disease mechanism and its progression, common causes, risk factors, signs and symptoms, and treatments.

Heart failure results when the heart cannot efficiently supply the body with blood. Arteries deliver blood and oxygen to the body. If the blood supply decreases, the body's requirement for oxygen may not be met. Diastolic and systolic are the two basic types of heart failure. Diastolic heart failure happens when the heart cannot properly fill with blood. Systolic heart failure, the more common of the two, occurs when the heart does not efficiently pump blood from the ventricles to the body. The result of either type of heart failure is decreased cardiac output. Less blood is pumped from the heart to the body. Decreased cardiac output also can lead to decreased blood pressure.

Many things can lead to heart failure. Systolic heart failure is commonly caused by a heart attack and/or persistent high blood pressure. Diastolic heart failure may be a result of systolic heart failure, dysfunctional heart valves, or a diseased heart lining.

Hypertension, also called high blood pressure, is one of the most common causes. Other major risk factors are diabetes mellitus, high cholesterol, obesity, and smoking.

Once heart failure has developed, the body will try to compensate for the decrease in cardiac output. The body releases hormones that increase the heart rate and strength of heart contractions and that cause narrowing of the blood vessels to maintain blood pressure. The body will retain sodium and water in an attempt to increase the volume of blood available to pump to the body.

Changes may also occur in the heart itself. Hypertrophy (enlargement) and remodeling (changes in heart muscle) are evident by a thickening in the ventricle wall and a change in the geometry of the heart. All of these mechanisms will initially help the failing heart but over time will become detrimental and the condition will worsen.

The signs and symptoms of heart failure depend on which side of the heart is affected. Heart failure can be left-sided, right-sided, or a combination of both. Right-sided heart failure results in fluid backing up in the body causing edema (swelling) in the lower extremities. Left-sided heart failure results in fluid backing up in the lungs. Common symptoms are difficulty breathing while lying down and shortness of breath with minimal activity. Exercise intolerance and fatigue or tiredness are common symptoms of both left- and right-sided heart failure.

Once a diagnosis of heart failure has been made, one of two different methods is used to classify the failure. The first method is the New York Heart Association Function Class Summary, which assigns classification based on the amount of activity it takes to evoke symptoms. Class I in the NYHA System represents no limitation of activity. Class II is the diagnosis when symptoms appear beyond mild exertion. Class III is characterized

by no symptoms only when the person is resting. Class IV diagnosis is made when symptoms are present even at complete rest.

The second classification scheme was developed by the American College of Cardiology and the American Heart Association and is based on clinically measurable findings in the heart. It has four stages and is known as the ACC/AHA Staging Classification.

Stage A represents a patient at high risk for developing heart failure but who does not yet have changes in the heart. Stage B is also considered an at-risk stage, but some changes have begun to occur. Stage C is the first stage when the actual diagnosis of heart failure is made. Because this is the first time symptoms appear, it is usually when patients go to a physician for diagnosis and treatment. Stage D is end-stage heart failure when patients are no longer responding to conventional therapy.

Specific treatment is linked to each ACC/AHA stage. All patients with heart failure should begin treatment with an angiotensin converting enzyme inhibitor (ACE inhibitor). One side effect of these drugs is a persistent cough that cannot be treated with cough medications. The drugs also have a more serious side effect called angioedema, which is characterized by severe swelling of the lips and mouth. Seek emergency treatment at the first sign of this reaction because angioedema can become life-threatening if the swelling causes breathing difficulty.

Beta-blockers are the next class of drugs that should be included in the treatment. They help decrease the hypertrophy and remodeling associated with the compensatory mechanisms of the heart. Beta-blockers should only be prescribed for a patient who is stable. Start in low doses, gradually increasing to the recommended dose. A few common

side effects associated with these medications include fluid retention, fatigue, bradycardia (slow heart rate), and hypotension (low blood pressure).

An aldosterone antagonist such as spironolactone or eplerenone can be added to the therapy of a patient with severe heart failure (NYHA III-IV). The drugs require careful monitoring. Although both have relatively good side effect profiles, spironolactone may cause men to experience gynecomastia, or the development of breasts. The odds of breast development occurring are about 1 in 10 so this should be considered and carefully weighed against its benefits.

A diuretic (water pill) can also be prescribed to treat fluid overload, a common problem in heart failure patients. Fluid can backup in the lungs leading to breathing difficulty at night and exercise intolerance. The fluid back up most commonly causes swelling in the legs and feet. Because many of these symptoms lead to a decrease in the patient's quality of life, this is an important drug for most patients with symptomatic heart failure.

Digoxin is another agent that may be added to a heart failure regimen. Its use was very common in the past, but it is now typically reserved for patients who continue to have symptoms even though they are on all of the other recommended agents. Digoxin can either be added before or after an aldosterone antagonist, but physicians prefer to prescribe it as a last resort.

Heart failure is a very prevalent disease associated with high death rates if the condition is not appropriately managed. The most common symptoms are edema, exercise intolerance, difficulty breathing while lying down, and fatigue. The first symptoms appear and a diagnosis of heart failure is made in Stage C. Patients begin

taking a diuretic if they have fluid overload, an ACE inhibitor, and a beta-blocker if they are in stable condition. An aldosterone antagonist is added to the treatment if the patient is classified as severe, with digoxin following if the patient is still experiencing symptoms and not responding well to other therapy.

Table 1: NYHA Function Class Summary

Class I	No limitation of activities
Class II	Slight, mild limitation of activity
Class III	Marked limitation of activity
Class IV	Activity severely limited

Table 2: ACC/AHA Staging Classification

Stage A	High Risk
Stage B	Structural abnormalities without the development of symptoms
Stage C	Current or prior symptoms of heart failure with normal or decreased ejection fraction (blood output)
Stage D	End-stage, refractory heart failure

Table 3: Drugs Used in the Management of Heart Failure

Medication Class	Commonly Used Agents	Trade Name (examples)	Adverse Effects	Monitoring Parameters
Angiotensin Converting Enzyme Inhibitors (ACEI)	ramipril lisinopril captopril fosinopril	Altace Zestril Capoten Monopril	cough, angioedema	serum creatinine and potassium
Beta-blockers (BB)	carvedilol metoprolol bisoprolol	Coreg Lopressor Zebeta	fatigue, slow heart rate, low blood pressure	heart rate, blood pressure
Aldosterone Antagonists	spironolactone eplerenone	Aldactone Inspra	gynecomastia, high potassium levels	serum creatinine and potassium
Loop Diuretics	furosemide	Lasix	electrolyte imbalance, fluid depletion, low blood pressure	serum potassium, blood pressure, symptoms of

				dehydration
Glycoside	Digoxin	Lanoxin	nausea, vomiting, arrhythmias	serum potassium and magnesium, serum digoxin levels

References:

1. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). American College of Cardiology Web site. Available at: <http://www.acc.org/clinical/guidelines/failure//index.pdf>.
2. American Heart Association [homepage on the Internet]. Texas: American Heart Association, Inc.; c2005 [cited 2005 August 20]. Diagnosing heart disease; [about 2 screens]. Available from: <http://www.americanheart.org/presenter.jhtml?identifier=330>
3. American Heart Association. *Heart Disease and Stroke Statistics—2005 Update*. Dallas, Texas: American Heart Association, 2004.
4. Johnson JA, Parker RB, Patterson JH. Heart Failure. In: Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. *Pharmacotherapy: A Pathophysiologic Approach*. 5th ed. New York. McGraw-Hill; 2002. p. 185-217.
5. DiBianco R. Update on therapy for heart failure. *Am J Med* 2003;115:480-88.
6. Jessup M, Brozena S. Heart failure. *N Engl J Med* 2003;348:2007-18.
7. Pitt B, Williams G, Remme W, et al. The EPHEsus trial: eplerenone in patients with heart failure due to systolic dysfunction complicating acute myocardial infarction: Eplerenone Post-AMI Heart Failure Efficacy and Survival Study. *Cardiovasc Drugs Ther* 2001;15:79-87.
8. Pitt B, Zannad F, Remme WJ, et al, for the Randomized Aldactone Evaluation Study Investigators. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med* 1999;341:709-17.

Julie Rafferty, Pharm.D. Candidate  
Auburn University, Harrison School of Pharmacy

M. Michelle Ducharme, Pharm.D.

Drug Information Resident  
Columbus Regional Medical Center

Bernie R. Olin, Pharm.D.  
Clinical Associate Professor and Director, Drug Information  
Auburn University, Harrison School of Pharmacy