VITEBSK STATE MEDICAL UNIVERSITY

CHAIR OF THE FACULTY THERAPY

**FACULTY THERAPY**

(Methodics work out for foreign students, studying the course of faculty therapy)

Part 1

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**HEART FAILURE**

Synonyms: congestive heart failure, CHF, myocardial failure, circulatory failure

Heart failure is the pathophysiologic state in which the heart, via an abnormality of cardiac function (detectable or not), fails to pump blood at a rate commensurate with the requirements of the metabolizing tissues and/or pumps only from an abnormally elevated diastolic filling pressure.

Heart failure may be caused by myocardial failure but may also occur in the presence of near-normal cardiac function under conditions of high demand. Heart failure always causes circulatory failure, but the converse is not necessarily the case because various noncardiac conditions (eg, hypovolemic shock, septic shock) can produce circulatory failure in the presence of normal, modestly impaired, or even supranormal cardiac function.

**Frequency**

CHF is a worldwide problem, but few accurate financial data are available. CHF is the fastest-growing clinical cardiac disease entity in the United States, affecting 2% of the population. As discussed elsewhere, the most common cause of CHF in industrialized countries is ischemic cardiomyopathy. Other causes, including Chagas disease, assume a more important role in underdeveloped countries than in the United States.

Despite recent advances in the management of patients with heart failure, morbidity and mortality rates remain high, with an estimated 5-year mortality rate of 50%.

Assigning figures for inpatient mortality rates is difficult because the causes and the severity of heart failure vary considerably. The most recent estimates of inpatient mortality rates indicate that death occurs in up to 5-20% of patients.

Hypoxemia that occurs in decompensated CHF, which may be severe, may result in myocardial ischemia or infarction.

*Race*: The incidence and prevalence of CHF are higher in African Americans, Hispanic persons, Native Americans, and recent immigrants from nonindustrialized nations, Russia, and the former Soviet republics.

The higher prevalence of CHF in African Americans, Hispanic persons, and Native Americans is directly related to the higher incidence and prevalence of hypertension and diabetes. This problem is particularly exacerbated by a lack of access to health care and to substandard preventive health care of the most indigent of these and other groups; many persons within these groups are without adequate health insurance coverage.

The higher incidence and prevalence of CHF among recent immigrants from nonindustrialized nations is largely due to a lack of prior preventive health care and to a lack of treatment or to substandard treatment for common conditions such as hypertension, diabetes, rheumatic fever, and ischemic heart disease.

*Sex*: Men and women have equivalent incidence and prevalence of CHF. CHF in women tends to occur later in life compared to men.

*Age*: The prevalence of CHF increases with age, being most common in individuals older than 65 years. Nonetheless, CHF can occur at any age, depending on the cause.

**Causes**

 From a clinical standpoint, it is useful to classify the causes of heart failure into 3 broad categories:

1) underlying causes, comprising structural abnormalities (congenital or acquired) that affect the peripheral and coronary arterial circulation, pericardium, myocardium, or cardiac valves, thus leading to the increased hemodynamic burden or myocardial or coronary insufficiency responsible for heart failure;

2) fundamental causes, comprising the biochemical and physiological mechanisms, through which either an increased hemodynamic burden or a reduction in oxygen delivery to the myocardium results in impairment of myocardial contraction;

3) precipitating causes, including the specific causes or incidents that precipitate heart failure in most episodes of heart failure.

Note that most patients who present with significant heart failure do so because of an inability to provide adequate cardiac output in that setting. This is often a combination of the causes listed above in the setting of an abnormal myocardium. The list of causes responsible for presentation of a patient with a CHF exacerbation is very long, and it is important to search for the proximate cause in order to optimize therapeutic interventions.

Overt heart failure may be precipitated by progression of the underlying heart disease. A previously stable compensated patient may develop heart failure that is clinically apparent for the first time when the intrinsic process has advanced to a critical point, such as with further narrowing of a stenotic aortic valve or mitral valve. Alternatively, decompensation may occur as a result of failure or exhaustion of the compensatory mechanisms but without any change in the load on the heart in patients with persistent severe pressure or volume overload.

Precipitating causes of heart failure

Inappropriate reduction of therapy: The most common cause of decompensation in a previously compensated patient with heart failure is inappropriate reduction in the intensity of treatment, whether dietary sodium restriction, physical activity reduction, drug regimen reduction, or, most commonly, a combination of these measures.

* Arrhythmias
* Tachyarrhythmias, most commonly atrial fibrillation
* Marked bradycardia
* Atrioventricular dissociation
* Abnormal intraventricular conduction
* Systemic infection or development of unrelated illness
* Pulmonary embolism
* Cardiac infection and inflammation
* Myocarditis or infective endocarditis may directly impair myocardial function and exacerbate existing heart disease. The anemia, fever, and tachycardia that frequently accompany these processes are also deleterious.
* In the case of infective endocarditis, the additional valvular damage that ensues may precipitate cardiac decompensation.
* Excessive intake of water and/or sodium
* Administration of cardiac depressants or drugs that cause salt retention
* Development of a second form of heart disease

Patients with one form of underlying heart disease that may be well compensated can develop heart failure when a second form of heart disease ensues.

For example, a patient with chronic hypertension and asymptomatic LV hypertrophy may be asymptomatic until a myocardial infarction develops and precipitates heart failure.

**Pathophysiology**

 Inadequate adaptation of the cardiac myocytes to increased wall stress in order to maintain adequate cardiac output following myocardial injury (whether of acute onset or over several months to years, whether a primary disturbance in myocardial contractility or an excessive hemodynamic burden placed on the ventricle, or both), is the inciting event in CHF.

Most important among these adaptations are the

1) Frank-Starling mechanism, in which an increased preload helps to sustain cardiac performance;

2) myocardial hypertrophy with or without cardiac chamber dilatation, in which the mass of contractile tissue is augmented;

3) activation of neurohumoral systems, especially the release of norepinephrine (NE) by adrenergic cardiac nerves, which augments myocardial contractility and the activation of the renin-angiotensin-aldosterone system (RAAS) and other neurohumoral adjustments that act to maintain arterial pressure and perfusion of vital organs.

 In acute heart failure, the finite adaptive mechanisms that may be adequate to maintain the overall contractile performance of the heart at relatively normal levels become maladaptive when trying to sustain adequate cardiac performance.

* The primary myocardial response to chronic increased wall stress includes myocyte hypertrophy and remodeling, usually of the eccentric type.
* The reduction of cardiac output following myocardial injury sets into motion a cascade of hemodynamic and neurohormonal derangements that provoke activation of neuroendocrine systems, most notably the above-mentioned adrenergic systems and RAAS. The release of epinephrine (E) and nor epinephrine (NE), along with the vasoactive substances endothelin-1 (ET-1) and vasopressin (V), causes vasoconstriction, which increases afterload, and, via an increase in cyclic adenosine monophosphate (cAMP), causes an increase in cytosolic calcium entry. The increased calcium entry into the myocytes augments myocardial contractility and impairs myocardial relaxation (lusitropy).
* The calcium overload may also induce arrhythmias and lead to sudden death. The increase in afterload and myocardial contractility (known as inotropy) and the impairment in myocardial lusitropy lead to an increase in myocardial energy expenditure and a further decrease in cardiac output. The increase in myocardial energy expenditure leads to myocardial cell death, resulting in heart failure and further reduction in cardiac output, thus starting an accelerating cycle of further increased neurohumoral stimulation and further adverse hemodynamic and myocardial responses as described above.
* In addition, the activation of the RAAS leads to salt and water retention, resulting in increased preload and further increases in myocardial energy expenditure. Increases in renin, mediated by decreased stretch of the glomerular afferent arteriole, reduced delivery of chloride to the macula densa, and increased beta1-adrenergic activity as a response to decreased cardiac output, results in an increase in angiotensin II (Ang II) levels and, in turn, aldosterone levels. This results in stimulation of release of aldosterone. Ang II, along with ET-1, is crucial in maintaining effective intravascular homeostasis mediated by vasoconstriction and aldosterone-induced salt and water retention.

**CLINICAL**

1. History

 Breathlessness, a cardinal sign of LV failure, may manifest with progressively increasing severity as

1) exertional dyspnea,

2) orthopnea,

3) paroxysmal nocturnal dyspnea,

4) dyspnea at rest,

5) acute pulmonary edema.

The New York Heart Association (NYHA) Classification of Heart Failure, which varies slightly from the above categorization of CHF symptoms, is widely used in practice and in clinical studies to quantify clinical assessment of CHF.

***1. Exertional dyspnea***

The principal difference between exertional dyspnea in subjects who are healthy and exertional dyspnea in patients with heart failure is the degree of activity necessary to induce the symptom. As heart failure first develops, exertional dyspnea may simply appear to be an aggravation of the breathlessness that occurs in healthy persons during activity.

As LV failure advances, the intensity of exercise resulting in breathlessness progressively declines; however, subjective exercise capacity and objective measures of LV performance at rest in patients with heart failure are not closely correlated. Exertional dyspnea, in fact, may be absent in sedentary patients.

***2. Orthopnea***

This early symptom of CHF may be defined as dyspnea that develops in the recumbent position and is relieved with elevation of the head with pillows. As in the case of exertional dyspnea, the change in the number of pillows required is important.

In the recumbent position, decreased pooling of blood in the lower extremities and abdomen occurs. Blood is displaced from the extrathoracic to the thoracic compartment. The failing LV, operating on the flat portion of the Starling curve, cannot accept and pump out the extra volume of blood delivered to it without dilating. As a result, pulmonary venous and capillary pressures rise further, causing interstitial pulmonary edema, reduced pulmonary compliance, increased airway resistance, and dyspnea.

***3. Paroxysmal nocturnal dyspnea***

Attacks of paroxysmal nocturnal dyspnea usually occur at night. This symptom of CHF is defined by a sudden awakening of the patient, after a couple hours of sleep, with a feeling of severe anxiety, breathlessness, and suffocation. The patient may bolt upright in bed and gasp for breath. Bronchospasm increases ventilatory difficulty and the work of breathing and is a common complicating factor of paroxysmal nocturnal dyspnea. On chest auscultation, the bronchospasm associated with a CHF exacerbation can be difficult to distinguish from an acute asthma exacerbation, although other clues from the cardiovascular examination should lead the examiner to the correct diagnosis. Both types of bronchospasm can be present in the same individual.

In contrast to orthopnea, which may be relieved by immediately sitting up in bed, attacks of paroxysmal nocturnal dyspnea may require 30 minutes or longer in this position for relief. Episodes of this may be so frightening that the patient may be afraid to resume sleeping, even after the symptoms have abated.

***4. Dyspnea at rest - Mechanisms of dyspnea in heart failure***

Decreased pulmonary function

Decreased compliance

Increased airway resistance

Increased ventilatory drive

Hypoxemia due to increased pulmonary capillary wedge pressure (PCWP)

Ventilation/perfusion (V/Q) mismatching due to increased PCWP and cardiac output

Increased carbon dioxide production

Respiratory muscle dysfunction

Decreased respiratory muscle strength

Decreased endurance

Ischemia

Fatigue and weakness

These symptoms are often accompanied by a feeling of heaviness in the limbs.

Fatigue and weakness are generally related to poor perfusion of the skeletal muscles in patients with a lowered cardiac output. Although generally a constant feature of advanced CHF, episodic fatigue and weakness are common in earlier stages.

* ***Nocturia***

Nocturia may occur relatively early in the course of heart failure. Recumbency reduces the deficit in cardiac output in relation to oxygen demand; renal vasoconstriction diminishes and urine formation increases. This may be troublesome for the patient with heart failure because it may prevent the patient from obtaining much-needed rest.

Oliguria is a late finding in CHF and is found in patients with markedly reduced cardiac output from severely reduced LV function.

* **Cerebral symptoms**

 Cerebral symptoms: Confusion, memory impairment, anxiety, headaches, insomnia, bad dreams or nightmares, and rarely, psychosis with disorientation, delirium, or hallucinations may occur in elderly patients with advanced heart failure, particularly in those with cerebrovascular atherosclerosis.

* **Predominant right-sided heart failure**

Ascites,

congestive hepatomegaly,

anasarca

due to elevated right-sided heart pressures transmitted backward into the portal vein circulation may result in increased abdominal girth and epigastric and right upper quadrant (RUQ) abdominal pain. Other gastrointestinal symptoms, owing to congestion of the hepatic and gastrointestinal venous circulation, include anorexia, bloating, nausea, and constipation. In preterminal heart failure, inadequate bowel perfusion can cause abdominal pain, distention, and bloody stools. Distinguishing right-sided CHF from hepatic failure is often clinically difficult.

Dyspnea, prominent in LV failure, becomes less prominent in isolated right-sided heart failure because of the absence of pulmonary congestion. On the other hand, when cardiac output becomes markedly reduced in patients with terminal right-sided heart failure (as may occur in isolated RV infarction and in the late stages of primary pulmonary hypertension and pulmonary thromboembolic disease), severe dyspnea may occur as a consequence of the reduced cardiac output, poor perfusion of respiratory muscles, hypoxemia, and metabolic acidosis.

**Physical**

General appearance

* Patients with mild heart failure appear to be in no distress after a few minutes of rest, but they may be obviously dyspneic during and immediately after moderate activity. Patients with LV failure may be dyspneic when lying flat without elevation of the head for more than a few minutes. Those with severe heart failure appear anxious and may exhibit signs of air hunger in this position.
* Patients with recent onset of heart failure are generally well nourished, but those with chronic severe heart failure are often malnourished and sometimes even cachectic.
* Chronic marked elevation of systemic venous pressure may produce severe tricuspid regurgitation and may lead to visible pulsation of the eyes and of the neck veins.
* Central cyanosis, icterus, and malar flush may be evident in patients with severe heart failure.
* In mild or moderate heart failure, stroke volume is normal at rest; in severe heart failure, it is reduced, as reflected by a diminished pulse pressure and a dusky discoloration of the skin.

With very severe heart failure, particularly if cardiac output has declined acutely, systolic arterial pressure may be reduced. The pulse may be weak, rapid, and thready; the proportional pulse pressure (pulse pressure/systolic pressure) may be markedly reduced. The proportional pulse pressure correlates reasonably well with cardiac output. In one study, when pulse pressure was less than 25%, it usually reflected a cardiac index of less than 2.2 L/min/m2.

Evidence of increased adrenergic activity

Increased adrenergic activity is manifested by tachycardia, diaphoresis, pallor, peripheral cyanosis with pallor and coldness of the extremities, and obvious distention of the peripheral veins secondary to venoconstriction.

Diastolic arterial pressure may be slightly elevated.

Pulmonary rales

Rales heard over the lung bases are characteristic of CHF of at least moderate severity. With acute pulmonary edema, rales are frequently accompanied by wheezing and expectoration of frothy, blood-tinged sputum.

* Edema

Although a cardinal manifestation of CHF, edema does not correlate well with the level of systemic venous pressure. In patients with chronic LV failure and low cardiac output, extracellular fluid volume may be sufficiently expanded to cause edema in the presence of only slight elevations in systemic venous pressure.

Edema, in the absence of dyspnea or other signs of LV or RV failure, is not solely indicative of heart failure and can be observed in many other conditions, including chronic venous insufficiency, nephrotic syndrome, or other syndromes of hypoproteinemia or osmotic imbalance.

* Hepatomegaly

Hepatomegaly is prominent in patients with chronic right-sided heart failure, but it may occur rapidly in acute heart failure.

* Hydrothorax (pleural effusion)

Hydrothorax is most commonly observed in patients with hypertension involving both systemic and pulmonary systems. Hydrothorax is usually bilateral, although when unilateral, it is usually confined to the right side of the chest.

When hydrothorax develops, dyspnea usually intensifies because of further reductions in vital capacity.

* Ascites

This finding occurs in patients with increased pressure in the hepatic veins and in the veins draining into the peritoneum.

Ascites usually reflects long-standing systemic venous hypertension.

Protodiastolic (S3) gallop: This is the earliest cardiac physical finding in decompensated heart failure in the absence of severe mitral or tricuspid regurgitation or left-to-right shunts.

* Cardiomegaly

A nonspecific finding, cardiomegaly nonetheless occurs in most patients with chronic heart failure.

Notable exceptions include heart failure from acute myocardial infarction, constrictive pericarditis, restrictive cardiomyopathy, valve or chordae tendineae rupture, or heart failure due to tachyarrhythmias or bradyarrhythmias.

* Cardiac cachexia

Cardiac cachexia is found in long-standing heart failure, particularly of the RV, because of anorexia from hepatic and intestinal congestion and sometimes because of digitalis toxicity. Occasionally, impaired intestinal absorption of fat and (rarely) protein-losing enteropathy occur.

Patients with heart failure may also exhibit increased total metabolism secondary to augmentation of myocardial oxygen consumption, excessive work of breathing, low-grade fever, and elevated levels of circulating TNF.

 **Lab Studies**

CBC count: This study aids in the assessment of severe anemia, which may cause or aggravate heart failure. Leukocytosis may signal underlying infection. Otherwise, CBC counts are usually of little diagnostic help.

Electrolytes

* Serum electrolyte values are generally within reference ranges in patients with mild-to-moderate heart failure before treatment. However, in severe heart failure, prolonged, rigid sodium restriction, coupled with intensive diuretic therapy and the inability to excrete water, may lead to dilutional hyponatremia, which occurs because of a substantial expansion of extracellular fluid volume and a normal or increased level of total body sodium.
* Potassium levels are usually within reference ranges, although the prolonged administration of diuretics may result in hypokalemia. Hyperkalemia may occur in patients with severe heart failure who show marked reductions in GFR and inadequate delivery of sodium to the distal tubular sodium-potassium exchange sites of the kidney, particularly if they are receiving potassium-sparing diuretics and/or ACE inhibitors.

Renal function tests

* BUN and creatinine levels can be within reference ranges in patients with mild-to-moderate heart failure and normal renal function, although elevated BUN and BUN/creatinine ratios may also be present.
* Patients with severe heart failure, particularly those on large doses of diuretics for long periods, may have elevated BUN and creatinine levels indicative of renal insufficiency because of chronic reductions of renal blood flow from reduced cardiac output. Diuretics may aggravate renal insufficiency when these patients are overmedicated with diuretics and become volume depleted.

Liver function tests

* Congestive hepatomegaly and cardiac cirrhosis are often associated with impaired hepatic function, which is characterized by abnormal values of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactic dehydrogenase (LDH), and other liver enzymes.
* Hyperbilirubinemia, secondary to an increase in both the directly and indirectly reacting bilirubin, is common. In severe cases of acute RV or LV failure, frank jaundice may occur.
* Acute hepatic venous congestion can result in severe jaundice, with a bilirubin level as high as 15-20 mg/dL, elevation of AST to more than 10 times the upper reference range limit, elevation of the serum alkaline phosphatase level, and prolongation of the prothrombin time. Both the clinical and the laboratory pictures may resemble viral hepatitis, but the impairment of hepatic function is rapidly resolved by successful treatment of heart failure. In patients with long-standing heart failure, albumin synthesis may be impaired, leading to hypoalbuminemia and intensifying the accumulation of fluid.
* Fulminant hepatic failure is an uncommon, late, and sometimes terminal complication of cardiac cirrhosis.

B-type natriuretic peptide

* BNP is a 32-amino acid polypeptide containing a 17-amino acid ring structure common to all natriuretic peptides. Unlike ANP, whose major storage sites are in both the atria and ventricles, the major source of plasma BNP is the cardiac ventricles, suggesting that BNP may be a more sensitive and specific indicator of ventricular disorders than other natriuretic peptides. The release of BNP appears to be in direct proportion to ventricular volume expansion and pressure overload. BNP is an independent predictor of high LV end-diastolic pressure and is more useful than ANP or NE levels for assessing mortality risk in patients with CHF.
* BNP levels correlate closely with the NYHA Classification of Heart Failure as well as the Goldman Activity Classification of Heart Failure.

**Imaging Studies**

* Chest radiography

Chest radiographs are very helpful in distinguishing cardiogenic pulmonary edema (CPE) from other pulmonary causes of severe dyspnea.

Classic radiographic findings demonstrate cardiomegaly (in patients with underlying CHF) and alveolar edema with pleural effusions and bilateral infiltrates in a butterfly pattern. The other signs are loss of sharp definition of pulmonary vasculature, haziness of hilar shadows, and thickening of interlobular septa (Kerley B lines).

Chest radiographs in patients with abrupt onset are usually helpful but can be limited because a delay of as long as 12 hours is possible from the onset of dyspnea due to acute heart failure to the development of classic abnormal findings on x-ray films.

* Echocardiography

This is the easiest and least-expensive method of determining LV function, both systolic and diastolic. Echocardiography is also the easiest and least-expensive method of determining the presence of valvular heart disease, LV wall thickness, chamber sizes, presence of pericardial disease, and regional wall motion abnormalities that may suggest ischemic coronary artery disease as the cause. Echocardiography is very reliable in diagnosing the cause or causes of heart failure.

Transesophageal echocardiography is particularly useful in patients who are on mechanical ventilation or morbidly obese and in patients whose transthoracic echocardiogram was suboptimal in its imaging. It is an easy and safe alternative to conventional transthoracic echocardiography and provides superior imaging quality compared to conventional transthoracic echocardiography.

* Radionuclide multiple gated acquisition scan

Radionuclide multiple gated acquisition (MUGA) scan is a very reliable imaging technique for determining global heart function. LV ejection fraction, as determined by MUGA scanning, is often used for serial assessment of LV function because of its reliability.

However, this study is limited in its assessment of valvular heart disease and pericardial disease.

**Other Tests**

* Arterial blood gases

ABGs usually reveal mild hypoxemia in patients who have mild-to-moderate heart failure. ABGs are more accurate than pulse oximetry for measuring oxygen saturation. Patients with severe heart failure may have signs and symptoms ranging from severe hypoxemia, or even hypoxia, along with hypercapnia, to decreased vital capacity and poor ventilation.

* Pulse oximetry

Pulse oximetry is highly accurate at assessing the presence of hypoxemia and, therefore, the severity of heart failure.

Patients with mild-to-moderate heart failure show modest reductions in oxygen saturation, whereas patients with severe heart failure may have severe oxygen desaturation, even at rest.

Pulse oximetry is useful for monitoring the patient's response to supplemental oxygen and other therapies.

* **Electrocardiography**

The presence of left atrial enlargement and LV hypertrophy is sensitive (although nonspecific) for chronic LV dysfunction.

ECG may suggest an acute tachyarrhythmia or bradyarrhythmia as the cause of heart failure.

ECG may aid in the diagnosis of acute myocardial ischemia or infarction as the cause of heart failure or may suggest the likelihood of prior myocardial infarction or presence of coronary artery disease as the cause of heart failure.

ECG is of limited help when an acute valvular abnormality or LV systolic dysfunction is considered to be the cause of heart failure; however, the presence of left bundle branch block (LBBB) on an ECG is a strong marker for diminished LV systolic function.

**Procedures**

* Right-sided heart catheterization

PCWP can be measured by using a pulmonary arterial catheter (Swan-Ganz catheter), and this helps differentiate cardiogenic causes of decompensated heart failure from noncardiogenic causes such as ARDS, which occurs secondary to injury to the alveolar-capillary membrane rather than to alteration in Starling forces. A PCWP exceeding 18 mm Hg in a patient not known to have chronically elevated left atrial pressure is indicative of cardiogenic decompensated heart failure. In patients with chronic pulmonary capillary hypertension, capillary wedge pressures exceeding 30 mm Hg are generally required to overcome the pumping capacity of the lymphatics and produce pulmonary edema.

* Left-sided heart catheterization and coronary angiography

Left-sided heart catheterization and coronary angiography should be undertaken when the etiology of heart failure cannot be determined by clinical or noninvasive imaging methods or when the etiology is likely to be due to acute myocardial ischemia or myocardial infarction. Coronary angiography is particularly helpful in patients with LV systolic dysfunction and known or suspected coronary artery disease in whom myocardial ischemia is thought to play a dominant role in the reduction of LV systolic function and the worsening of heart failure. As a general rule, most patients with clinically significant CHF should undergo cardiac catheterization to exclude the reversible causes listed above.

Specific rationales for right- and left-sided heart catheterization include the need to determine the etiologic significance and severity of mitral and/or aortic valvular disease in patients with heart failure in whom the cause-effect relationship of valvular heart disease with regard to heart failure is unclear. Furthermore, right- and left-sided heart catheterization should be performed in patients in whom constrictive pericarditis is considered a likely cause of heart failure.

**Staging**

A classification of patients with heart disease based on the relation between symptoms and the amount of effort required to provoke them has been developed by the NYHA.

Class I: No limitations. Ordinary physical activity does not cause undue fatigue, dyspnea, or palpitations.

Class II: Slight limitation of physical activity. Such patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitations, dyspnea, or angina.

Class III: Marked limitation of physical activity. Although patients are comfortable at rest, less-than-ordinary activity leads to fatigue, dyspnea, palpitations, or angina.

Class IV: Symptomatic at rest. Symptoms of CHF are present at rest; discomfort increases with any physical activity.

The Goldman Activity Classification of Heart Failure is based on estimated metabolic cost of various activities, and classes correlate to NYHA classes.

Class I: Patients can perform to completion any activity up to 7 metabolic equivalents (METS).

Class II: Patients can perform to completion any activity up to 5 METS of activity but cannot perform to completion any activities equal to or more than 7 METS.

Class III: Patients can perform to completion any activity up to 2 METS of activity but cannot perform to completion any activities equal to or more than 5 METS.

Class IV: Patients cannot perform to completion activities equal to or more than 2 METS.

**TREATMENT**

Medical Care: Medical therapy of heart failure focuses on 3 main goals:

(1) preload reduction,

(2) reduction of systemic vascular resistance (afterload reduction),

(3) inhibition of both the RAAS systems and vasoconstrictor neurohumoral factors produced by the sympathetic nervous system in patients with heart failure.

The first 2 goals provide symptomatic relief. While reducing symptoms, inhibition of the RAAS and neurohumoral factors also results in significant reductions in morbidity and mortality rates.

Preload reduction results in decreased pulmonary capillary hydrostatic pressure and reduction of fluid transudation into the pulmonary interstitium and alveoli. Afterload reduction results in increased cardiac output and improved renal perfusion, which allows for diuresis in the patient with fluid overload. Inhibition of the RAAS and sympathetic nervous system results in favored vasodilation and reduction of neurohumoral vasoconstrictors, thereby increasing cardiac output and reducing blood volume and myocardial oxygen demand.

Patients with severe LV dysfunction or acute valvular disorders may present with hypotension. These patients may not tolerate medications to reduce their preload and afterload and may require inotropic support to maintain adequate blood pressure.

Patients who remain hypoxic despite supplemental oxygen or who demonstrate severe respiratory distress require mechanical ventilation, in addition to maximal medical therapy.

Preload reduction

* Nitroglycerin

Nitroglycerine (NTG) is the most effective, predictable, and rapid-acting medication available for preload reduction.

Multiple studies comparing NTG to furosemide or morphine sulfate have demonstrated greater efficacy and safety and a faster onset of action for NTG.

Use of sublingual NTG is associated with preload reduction within 5 minutes and some afterload reduction.

Topical NTG may be as effective as sublingual NTG in most patients with heart failure, but it should be avoided in patients with severe LV failure because of poor skin perfusion (manifesting as skin pallor or mottling) and resultant poor absorption.

Intravenous NTG at higher dosages provides rapid and titratable preload and afterload reduction and has been demonstrated to be an excellent single-agent therapy for patients with severe decompensated CHF.

* Loop diuretics

Loop diuretics are the cornerstone of heart failure treatment and have been considered as such for many decades. Furosemide is most commonly used. Bumetanide has a higher bioavailability and may be more effective in patients with severe CHF.

Loop diuretics are presumed to decrease preload through 2 mechanisms: diuresis and direct pulmonary artery vasodilation and venodilation.

In most patients, diuresis does not occur for at least 20-90 minutes; thus, the effect is delayed.

In some patients with heart failure, particularly those with diastolic heart failure who are minimally fluid overloaded, continued diuretic use after resolution of acute symptoms may be associated with adverse outcomes, including electrolyte derangements and hypotension.

Use of medications that decrease preload (eg, NTG) and afterload (eg, ACE inhibitors), either concomitantly or before the administration of loop diuretics, can prevent potential adverse hemodynamic changes.

* Potassium-sparing diuretics

Numerous studies have shown spironolactone to be as beneficial in the management of CHF as loop diuretics.

Some of the beneficial effects of spironolactone may be due to its neurohormonal actions.

* Morphine sulfate

Morphine sulfate use in acute CHF for preload reduction has been commonplace for many years.

Use should be weighed against potential adverse effects (eg, nausea/vomiting, local or systemic allergic reactions, respiratory depression) that may outweigh any potential benefit, especially given the availability of much more effective medications for preload reduction (eg, NTG).

Any beneficial hemodynamic effect probably is due to anxiolysis, with a resulting decrease in catecholamine production and systemic vascular resistance.

Vasodilators (combined afterload and preload reducers)

* ACE inhibitors

Although initial studies focused on the efficacy of ACE inhibitors in the treatment of chronic CHF, recent studies have demonstrated excellent results for treatment of acute decompensated CHF.

Studies demonstrate that the use of ACE inhibitors in acute heart failure is associated with reduced admission rates to ICUs and decreased endotracheal intubation rates.

Hemodynamic effects of ACE inhibitors include reduced afterload, improved stroke volume and cardiac output, and reduced preload.

ACE inhibitors must be initiated with extreme care in individuals presenting with borderline hemodynamic parameters.

When administered by intravenous (enalapril 1.25 mg) or sublingual routes, hemodynamic and subjective improvements are noted within 10 minutes; improvements occur more slowly with the oral route.

ACE inhibitors prolong survival in heart failure. Furthermore, compared to the combination of hydralazine and long-acting nitrates, ACE inhibitors showed a trend to a greater prolongation of survival, had improved hemodynamics, and were better tolerated.

* Ang II receptor inhibitors

Ang receptor inhibitors, such as losartan and candesartan, are highly recommended alternatives to ACE inhibitors in patients who cannot tolerate ACE inhibitors because of adverse effects, most notably, coughing.

Furthermore, these agents have gained wider use based on their low adverse effect profile and early study findings, which indicated that combined ACE inhibition and Ang II receptor inhibition is beneficial.

* Hydralazine

Hydralazine was the first oral balanced (afterload and preload reduction) vasodilator and was popular before the availability of ACE inhibitors. It is a direct vasodilator, unlike ACE inhibitors or Ang receptor inhibitors, which are vasodilators through inhibition of the RAAS system.

When combined with long-acting nitrates, hydralazine was shown, in the Veterans Administration Heart Failure Trial (VHEFT) studies, to prolong survival in patients with CHF.

Hydralazine has one main advantage over ACE inhibitors in that it is safe in pregnancy. It also is not known to worsen renal function in patients with heart failure who have reduced renal function and is not associated with the risk of hyperkalemia. Additionally, hydralazine use is recommended in patients who cannot tolerate ACE inhibitors.

Hydralazine, as a single agent, has less reduction in myocardial oxygen demand than ACE inhibitors because of a slight increase in heart rate that usually results from its use.

* Nitroprusside

Nitroprusside results in simultaneous preload and afterload reduction through direct smooth muscle relaxation, although it has a greater effect on afterload.

Afterload reduction is associated with increased cardiac output.

Potency and rapidity of onset and offset of effect make this an ideal medication for patients who are critically ill.

It may induce precipitous falls in blood pressure; intraarterial blood pressure monitoring often is recommended.

Use nitroprusside cautiously in the setting of acute myocardial infarction because of its potential to induce hypotension.

If nitroprusside is used, convert patients to oral or alternative intravenous vasodilator therapy as soon as possible because prolonged use is associated with thiocyanate toxicity.

Use in pregnancy is associated with fetal thiocyanate toxicity.

* Inotropic support

Digoxin (cardiac glycoside)

Digoxin has been a cornerstone for the treatment of heart failure for decades and is the only oral inotropic support agent currently used in clinical practice.

Digoxin acts by inhibiting the Na+/K+–ATPase transport pump and inhibits sodium and potassium transport across cell membranes. This increases the velocity and shortening of cardiac muscle, resulting in a shift upward and to the left of the ventricular function (Frank-Starling) curve relating stroke volume to filling volume or pressure. This occurs in healthy as well as failing myocardium and in atrial as well as ventricular muscle. The positive inotropic effect is due to an increase in the availability of cytosolic calcium during systole, thus increasing the velocity and extent of myocardial sarcomere shortening.

No evidence indicates that digoxin affects peripheral vascular resistance or systemic blood pressure.

All evidence suggests that digoxin provides, even in the short term, a moderate and metabolically efficient positive inotropic effect, an important consideration in ischemic cardiomyopathies.

Although the incidence and severity of digitalis intoxication is decreasing, vigilance for this important complication of therapy is essential. Drugs that interact with digoxin are numerous and include amiodarone, propafenone, quinidine, verapamil, nifedipine, diltiazem, levothyroxine, cyclosporine, flecainide, disopyramide, omeprazole, tetracycline, and erythromycin. These agents affect clearance or absorption of digoxin, thus necessitating dose alteration of digoxin in patients taking these medications. Furthermore, patients with renal insufficiency may need to have their digoxin dose adjusted downward to avoid digitalis intoxication.

Numerous studies confirm that digoxin does not prolong survival in patients with systolic heart failure, but it is associated with reduced hospital admissions, improved functional class, reduced symptoms of heart failure, and improved quality of life.

Digoxin is also an effective agent against atrial tachyarrhythmias at rest in patients with LV dysfunction, but it has limited efficacy in controlling the ventricular rate of atrial arrhythmias during exertion.

Dobutamine (sympathomimetic agent)

Dobutamine mainly serves as a beta1-receptor agonist, although it has some beta2-receptor and minimal alpha-receptor activity.

Intravenous dobutamine induces significant positive inotropic effects with mild chronotropic effects. It also induces mild peripheral vasodilation (decrease in afterload).

The combination effect of increased inotropy with decreased afterload results in a significant increase in cardiac output.

Combination use with intravenous NTG may be ideal for patients with myocardial infarction and decompensated heart failure and mild hypotension in order to provide simultaneous preload reduction with increased cardiac output. In the setting of acute myocardial infarction, dobutamine use could increase infarct size because of the increase in myocardial oxygen consumption that may ensue.

In general, avoid dobutamine in patients with moderate or severe hypotension (eg, systolic blood pressure <80 mm Hg) because of the peripheral vasodilation.

Dopamine (sympathomimetic agent)

Vascular and myocardial receptor effects are dose dependent.

Low dosages (0.5-3 mcg/kg/min) cause stimulation of dopaminergic receptors within the renal and splanchnic vascular beds, causing vasodilation and increased diuresis.

Moderate dosages (3-10 mcg/kg/min) cause stimulation of beta-receptors in the myocardium, resulting in increased cardiac contractility and heart rate.

High dosages (10-20 mcg/kg/min) cause stimulation of alpha-receptors, resulting in peripheral vasoconstriction (increased afterload), increased blood pressure, and no further improvement in cardiac output.

As with other inotropic agents, moderate and high dosages are arrhythmogenic and also result in increased myocardial oxygen demand (potential for myocardial ischemia); therefore, use dopamine only in patients with heart failure who cannot tolerate the use of dobutamine because of severe hypotension (eg, systolic blood pressure <60-80 mm Hg).

* Phosphodiesterase inhibitors (milrinone, amrinone)

Phosphodiesterase inhibitors (PDIs) increase intracellular cAMP, which results in a positive inotropic effect on the myocardium and peripheral vasodilation (decreased afterload) and a reduction in pulmonary vascular resistance (decreased preload).

PDIs, unlike catecholamine inotropes, are not dependent on adrenoreceptor activity; therefore, patients are less likely to develop tolerance to these medications. Tolerance to catecholamine inotropes can develop rapidly through down-regulation of the adrenoreceptors.

PDIs are less likely than catecholamine inotropes to cause adverse effects that are typically associated with adrenoreceptor activity (eg, increased myocardial oxygen demand, myocardial ischemia).

Several studies directly comparing the use of PDIs (milrinone, amrinone) to dobutamine in patients with heart failure have demonstrated that milrinone produced equal or greater improvements in stroke volume, cardiac output, PCWPs (preload), and systemic vascular resistance (afterload). They are also associated with less tachycardia and myocardial oxygen consumption. However, PDIs have been associated with a significantly greater incidence of adverse events (eg, tachyarrhythmias) than has dobutamine.

At present, oral PDIs have no role. Their use was associated with a 53% increase in mortality rates in patients with NYHA Class IV heart failure in the Prospective Randomized Milrinone Survival Evaluation (PROMISE) trial, prompting an early termination of that study.

Unfavorable results were also evident in a smaller trial that compared oral milrinone to digoxin or placebo. Furthermore, sustained hemodynamic improvement with oral milrinone was lacking, and the incidence of adverse events, particularly cardiac arrhythmias, was greater.

* Beta-adrenergic blocking agents (metoprolol, carvedilol)

A large and increasing body of evidence indicates that these agents improve symptoms, exercise tolerance, cardiac hemodynamics, and LV ejection fraction and that they decrease mortality rates in patients with heart failure, particularly those with both ischemic and idiopathic cardiomyopathy.

A growing body of evidence suggests that long-term beta-adrenergic antagonist administration improves cardiac function, reduces myocardial ischemia, improves ventricular-arterial coupling, and decreases myocardial oxygen consumption. These agents may also reduce the incidence of sudden death due to primary ventricular arrhythmias in patients with heart failure, although this latter benefit has yet to be definitively proven.

Detectable improvements in ventricular function are usually not apparent for a minimum of 1-3 months, and longer-term structural changes, such as a decline in ventricular volume or mass, may take 12-18 months.

Beta-adrenergic antagonists with vasodilator activity, such as carvedilol and labetalol, have the added benefit of further afterload reduction because of arterial vasodilation from alpha1-receptor blockade.

Treatment of heart failure with predominant diastolic dysfunction: The therapeutic approach to diastolic dysfunction has 2 major components. The first involves attempts to reverse the abnormal cardiac diastolic properties. The second is directed toward reducing LV filling pressure and thereby venous congestion.

Surgical Care

 Kantrowitz initially described intraaortic balloon pumping (IABP) in 1953, but the procedure was first used clinically in 1969 in a patient with cardiogenic shock. Since the 1980s, IABP has been increasingly used in various clinical situations as a lifesaving intervention to obtain hemodynamic stabilization prior to definite therapy.

The intraaortic balloon pump is inserted percutaneously via the femoral artery using a modified Seldinger technique. The distal end of the pump is placed just distal to the aortic knob and the origin of left subclavian artery.

Fluoroscopy may be used for correct positioning of the balloon, and a subsequent chest radiograph should be obtained to document satisfactory balloon placement.

Proper timing of IABP for optimal hemodynamic support

Proper timing of counterpulsation is necessary for maximum hemodynamic support. The timings of balloon inflation and deflation are best evaluated and adjusted at a pump frequency of 1:2.

* Cardiac transplantation

Diet

Patients admitted with heart failure or pulmonary edema should maintain a low-salt diet in order to minimize fluid overload. Monitor fluid balance closely.

Activity

Patients with decompensated heart failure should be placed on complete bed rest until their decompensation is resolved. This is necessary to maximally reduce myocardial oxygen demand and to avoid exacerbation of the abnormal hemodynamics and symptoms of heart failure.

Once the patient with heart failure has been stabilized, activity should be gradually and progressively increased. Emphasize the importance of cardiac rehabilitation to all patients with heart failure who require improved cardiac fitness. Encourage patients to exercise daily for at least 20-30 minutes in a low-intensity, endurance-enhancing activity such as walking, biking, or swimming. Regular exercise improves the quality of life for these patients and improves efficiency of oxygen utilization at the tissue level, thus reducing the workload of the heart in the role of oxygen delivery to end organs and muscles.

**Further Inpatient Care**

After the patient has been initially stabilized and the decompensation of heart failure has been resolved, further inpatient care depends on the underlying cause of CHF.

Place patients with heart failure in a monitored bed to watch for acute dysrhythmias. Pay strict attention to the patient's fluid balance by closely monitoring fluid input and output. Maintain patients who are fluid-overloaded in negative fluid balance through the use of diuretics, or, if necessary in patients with renal failure, hemodialysis with ultrafiltration.

Check cardiac enzymes to evaluate for myocardial infarction. Slight elevations in cardiac enzymes can occur with decompensated heart failure in the absence of myocardial infarction because of coronary thrombosis.

Perform coronary angiography on patients whose decompensated heart failure resulted from an acute coronary syndrome, either unstable angina or myocardial infarction. Stress testing can also be performed later during hospitalization to evaluate for reversible ischemia in patients without acute coronary syndromes but who have prior symptoms of angina or who have a high likelihood of coronary artery disease as the cause of LV dysfunction.

Order echocardiography at the earliest possible moment to evaluate for evidence of acute valvular dysfunction and wall motion abnormalities and to assess the patient's systolic and diastolic function. Since the long-term therapy of patients with heart failure differs significantly between those with predominantly systolic dysfunction and those with predominantly diastolic dysfunction, it is absolutely essential that all patients with heart failure have echocardiographic evaluation of cardiac function, chamber size, and valve function.

In most patients with decompensated heart failure, oral vasodilator therapy, most commonly ACE inhibitors, can be used as first-line therapy to reverse the cardiac decompensation and to restore optimal cardiac function. The clinician must be extremely cautious with vasodilator therapy only in patients with severe aortic or mitral stenosis or in those with obstructive cardiomyopathy. Patients who required intravenous inotropic support should be weaned off as quickly as possible and should have their vasodilator therapy maximized quickly in order to avoid the risk of adverse cardiac events from increased myocardial oxygen consumption leading to ischemia.

Patients in whom pulmonary edema was caused by dietary factors or medication noncompliance need strict counseling and education to help prevent recurrence.

**Further Outpatient Care**

Focus further outpatient care of patients with heart failure on maximizing some or all of the medical modalities used in their treatment. Undertake further assessment of the clinical and hemodynamic effects of that therapy fairly soon after discharge and at regular intervals.

Precise definition and aggressive treatment of all reversible causes for heart failure is absolutely essential. For instance, patients with myocardial ischemia (particularly those with reduced systolic function) should be promptly evaluated with noninvasive and/or invasive evaluations of coronary perfusion, and they should be promptly referred for revascularization if they are suitable candidates for such revascularization. Similarly, patients with severe valvular disease, assessed clinically and echocardiographically, should be promptly referred for cardiac catheterization. If a patient is a suitable candidate for valve replacement or repair, he or she should undergo prompt surgical therapy.

Patients with nonreversible NYHA class IV heart failure who are younger than 65 years and facing the likely prospect of death within the next 6-24 months, despite maximal medical therapy, and who are not candidates for beneficial surgical therapy, should be promptly referred to a cardiac transplant center for consideration of cardiac transplantation.

Screen patients with cardiomyopathy and heart failure for candidacy for cardioverter/defibrillator implantation because the risk of sudden death in these patients is considerable.

**Complications**

The major complications associated with heart failure are sudden cardiac death from ventricular tachyarrhythmias or bradyarrhythmias and pump failure with cardiovascular collapse. Approximately half of patients with heart failure eventually die from fatal ventricular arrhythmias. Prompt diagnosis and treatment usually prevent this complication in the acute setting. Prompt diagnosis of CHF and prompt treatment to reduce pulmonary venous congestion, reduce afterload, and improve cardiac output is essential in preventing cardiovascular and respiratory failure.

**Prognosis**

In general, the inpatient mortality rate for patients with heart failure is 5-20%.

Heart failure associated with acute myocardial infarction is associated with an inpatient mortality rate of 20-40%; mortality approaches 80% in patients who are also hypotensive (eg, cardiogenic shock).