4.2.4

Heart Failure

Heart failure (HF) is the failure of the heart to pump blood efficiently, and as a result tissues do not receive enough oxygen and nutrients. Heart failure is classified in two general ways. The first is by looking at the ejection fraction (EF) and determining if it is reduced or preserved. The second is by determining if the heart failure is because of dysfunction of the left or right side of the heart (it can involve both). Generally, left-sided HF proceeds and eventually causes right-sided HF.

Ejection Fraction Classification of HF

The **ejection fraction (EF)** is the amount of blood pumped out of the left ventricle (known as the stroke volume or SV) divided by the amount of blood left in the heart (known as the end diastolic volume or EDV) multiplied by 100.

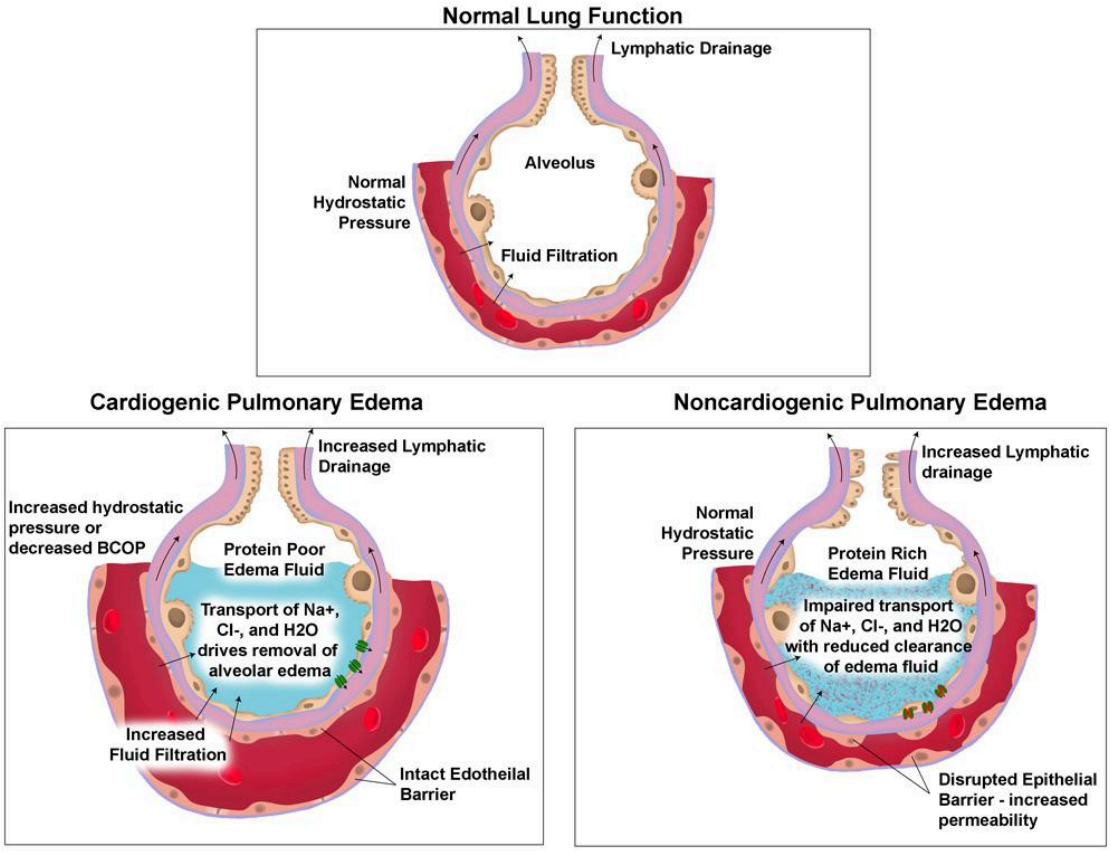
As stated previously, a normal EF is 50-70%. This means that ordinarily, the heart should eject half or almost 3/4ths of the blood in the left ventricle. There are two classifications of heart failure depending on the status of the EF: systolic and diastolic. For your understanding, it is important to recall that “systolic” refers to heart contraction (systole) while “diastolic” refers to the heart filling with blood (diastole).

- **Systolic heart failure** also called Heart Failure with Reduced Ejection Fraction (HFrEF) is defined as an ejection fraction of ≤40%. This reduced ejection fraction occurs when the heart is failing to pump out enough blood. Systolic failure may result from conditions that impair the contractile action of the heart like coronary artery disease and cardiomyopathy. It also may be caused by conditions that produce volume overload like anemia and aortic valvular insufficiency. It can also be caused by conditions that generate a pressure overload on the heart like valvular stenosis (narrowing of the semilunar valves). In systolic HF, the end systolic volume (ESV is the volume in the ventricle after contraction) is increased due to the reduced EF. This increased ESV plus a normal or increased venous return leads to an overall increase in ventricular preload. Increased preload can lead to an accumulation of blood in the atria and congestion/backup of blood in circulation (pulmonary congestion if left side failure and systemic venous congestion if right side failure).
- **Diastolic heart failure** also called Heart Failure with preserved ejection fraction (HFpEF) is heart failure with a preserved ejection fraction of ≥50%. Instead of the HF being due to issues with contraction, it is due to failure of the heart to fill with blood correctly. With diastolic failure, cardiac output is decreased because of a decrease in end diastolic volume (EDV) and stroke volume. If the heart can’t fill enough, it can’t pump enough (even though the EF may look normal, we are talking about less blood in general). Hypertension is the leading cause of diastolic failure because over time, the increased work the heart must do to pump against an increased pressure causes it to stiffen. As mentioned previously, hypertrophic cardiomyopathy reduces ventricle chamber size and can also cause diastolic dysfunction. A pericardial effusion can also cause decreased filling of the heart. Pericardial effusion is the acute or chronic accumulation of fluid in the pericardial space around the heart. If this fluid buildup begins to compress the heart enough, shortness of breath, lightheadedness, and even cardiogenic shock can occur. This uncontrolled pericardial effusion is called **cardiac tamponade**.

Left Ventricular Dysfunction

Left ventricular dysfunction is when the left side of the heart is underperforming. There is decreased cardiac output which results in a subsequent decrease in peripheral blood flow (remember the left side of the heart supplies systemic circulation). If the left ventricle isn't pumping blood downstream as it should, the blood will back up into pulmonary circulation. This process is somewhat similar to building a dam in a river. While the dam may have an outlet for some of the water to continue on, it blocks most of it from flowing downstream and as a result, the water pools and backs up. Similarly, if the left ventricle isn't pushing blood forward to the rest of the body, blood will back up into the lungs. As the extra blood increases hydrostatic pressure, more fluids are pushed into the lungs and **pulmonary congestion/edema** results. **Pleural effusions** (fluid between the visceral and parietal pleura) will take place because of the fluid that builds in the interstitial space of the lung crosses the very permeable visceral membrane. The lymphatic system of the lung is unable to remove the fluid fast enough and the pleural effusion progresses. **Cardiac asthma** can also occur due to bronchospasms because of the fluid congestion and irritation in the bronchial mucous membranes.

Throughout the day while left-sided HF patients are standing or sitting, excess fluid will accumulate in the lower extremities. When they assume a recumbent position (like sleeping at night), the excess fluid that reaches the heart from the now gravity-independent legs will cause more congestion in the lungs. This can result in **paroxysmal nocturnal dyspnea**, which is difficulty breathing at night.



Types of Pulmonary Edema *Image by Becky T F19*

Left sided heart failure can be caused by various conditions, a few of which are listed here:

- Ischemic heart diseases like coronary artery disease (CAD) and the aftermath of a myocardial infarction (MIs cause death of some of the cardiac myocytes and stress remaining cells).
- Hypertension increases the workload on the heart and can weaken it over time.
- Aortic and mitral valve diseases make the heart work harder because blood can move the wrong direction and the heart is less efficient.
- Congenital heart defects
- Hypertrophic cardiomyopathy
- Left semilunar valve stenosis
- Narrowing/coarctation of the aorta that causes extra pumping strain and can lead to left-sided hypertrophy.

Right Ventricular Dysfunction

Right ventricular dysfunction is when the right side of the heart is underperforming and there is decreased cardiac output. It is most often caused by left ventricular dysfunction because an increase in pulmonary blood volume eventually produces an increased burden on the right side of the heart.

Isolated right side heart failure is called **cor pulmonale**. Cor pulmonale is abnormal hypertrophy of the right side of the heart, most often due to issues with the lungs. It can be due to the following conditions:

- Primary pulmonary hypertension is the most common cause.
- Parenchymal diseases caused by inhaling contaminants such as silica, asbestos, or moldy hay that increase vasoconstriction in the lungs and cause pulmonary HTN.
- Recurrent pulmonary thromboembolisms that cause blockage of vessels in lungs and increase the pressure the right side of the heart must pump against.
- Conditions of hypoxia (like anemia, high altitude, or sleep apnea) reflexively stimulate the heart via the sympathetic nervous system to increase pulmonary vessel vasoconstriction. This may exacerbate or even cause ventricular hypertrophy.
- Right semilunar valve stenosis
- Narrowing/coarctation of the pulmonary trunk that causes extra pumping strain.

Because the right side of the heart receives deoxygenated blood from the veins, right-sided HF can result in the backup of blood in venous circulation throughout the body. Because of this, edema in right-sided heart failure occurs in the lower extremities (legs, feet, pitting edema in ankles) when the person is in the upright position and in the area over the sacrum when the person is supine. Patients will often get **ascites**, which is a swollen abdomen and enlarged abdominal veins because of fluid buildup in the peritoneal cavity. Patients may also develop **jugular vein distention (JVD)** because of congestion and increased hydrostatic pressure in venous circulation. Hepatomegaly and splenomegaly can also occur due to pooling of blood and fluids. In a way, the body becomes oversaturated with fluid and that is why all of these symptoms occur.

This table summarizes the key information presented above about the two different methods used to classify HF.

TYPE OF HEART FAILURE:	DESCRIPTION
Systolic Heart Failure: (HF with reduced EF)	Indicates a pumping problem where the left ventricle can't contract adequately. Manifests as an EF of ≤40%.

Diastolic Heart Failure: (HF with preserved EF)	Indicates a filling problem where the left ventricle can't fill or relax fully. Manifests as an EF of ≥50% combined with symptoms of diastolic dysfunction.
Left-Sided Heart Failure:	Inadequate action of the left ventricle leads to fluid backup in the lungs. The left ventricle is filled with oxygenated blood from the lungs. If it isn't pumping this blood to the body efficiently, the lungs eventually become congested. Pulmonary edema can develop and pulmonary symptoms such as dyspnea, orthopnea, and paroxysmal nocturnal dyspnea.
Right-Sided Heart Failure:	Inadequate action of the right ventricle leads to fluid backup in systemic circulation. The right ventricle receives deoxygenated blood from body. If it isn't pumping efficiently, the blood will back up in systemic circulation. This can cause swelling of abdomen, legs, and feet. Hepatomegaly, splenomegaly, jugular vein distension and ascites (blood pooling in peritoneal cavity) can all also arise due to blood congestion.

Table by Kaylie S. BYU-I S-21

Additional Complications/Indications of HF

Decreased ability to exercise and increased **tiredness** are common symptoms of HF. This is because if the circulatory system is not functioning properly, tissues do not get the oxygen and nutrients they need.

Central cyanosis is a blue or greyish coloring that can be seen on the tongue, skin, lips, or around the eyes. Central cyanosis is caused by a circulatory or ventilatory problem that leads to poor blood oxygenation in the lungs. It can be seen in those with heart failure because of impaired pulmonary gas exchange causing lower levels of oxygen. Central cyanosis is best monitored by assessing the lips and mucous membranes because they are not affected as much by environmental conditions like temperature.

Peripheral cyanosis occurs when the blood is properly oxygenated but it can't circulate properly because of inadequate flow or obstruction. It can be seen with heart failure due to weakness of the heart limiting its ability to provide adequate blood perfusion of tissues. The hands, fingertips, or feet can turn blue because they are not getting enough oxygen-rich blood.

Cardiac cachexia is a condition that happens to people with heart failure and it is characterized by the loss of serious amounts of body fat, muscle and bone. The cause is largely unknown.

Nocturia is a nightly increase in urine output that occurs rather early in the progression of heart failure. Heart failure results in a decreased cardiac output and thus decreased blood pressure. As a result, the body attempts to increase blood volume to increase blood pressure. During the day, the kidneys will reduce urine flow, ADH release will increase, and sodium will be retained. However, at night when a person lays down to sleep, venous return is much improved because gravity is now longer drawing blood downward to the lower extremities. As a result, extra blood volume returns to the heart, blood pressure increases, and the heart must work harder to pump the extra blood. An increased perfusion of the kidney due to the increased blood pressure puts the brakes on homeostatic mechanisms trying to raise blood pressure. This causes decreased ADH release, decreased sodium retention, and increased urinary output. The increased urine causes a need to void during the night that is called nocturia.

Oliguria is a decrease in urine output that is seen in the later stages of heart failure. Oliguria is a result of such a low cardiac output that the kidney is simply not perfused well enough to make adequate urine volume. This low perfusion of the kidney also results in kidney disease and kidney failure, further limiting the ability of the kidneys to make urine.

Liver damage can arise from HF because of a buildup of fluids that put too much pressure on the liver. This can lead to scarring and decrease liver functionality.

The development of **atrial and ventricular arrhythmias** is more common in those with any type of heart failure. Arrhythmias can further worsen heart failure because they can interfere with the chambers of the heart contracting in the right rhythm and the heart working together as a whole.

Cheyne-Stokes respiration is an abnormal breathing pattern found in many left-sided congestive heart failure patients. It can be found in other patients as well, but it is one of the symptoms that a clinician might look for when assessing how bad the congestion is in HF. Cheyne Stokes is a periodic breathing pattern characterized by a gradual increase in the depth and sometimes in the rate of breathing to a maximum followed by a decrease that results in apnea. This abnormal breathing pattern appears to be related to a decreased cardiac output and the inability to adequately move CO_2 out of the body through the lung.

Treatment for Chronic Heart Failure

Treatment for chronic heart failure (CHF) can be divided into two broad categories: Lifestyle modifications and pharmaceutical therapy.

1. **Lifestyle modification** like exercise and diet changes can be effective in the treatment of heart failure. Lack of exercise is typical in persons who develop chronic heart failure. However, exercise does put a strain on the heart, so it becomes difficult to increase exercise once heart problems have started. On one hand, exercise is important to stimulate improvement in cardiovascular health. On the other hand, exercise may strain and worsen the dysfunction of the heart. Individuals with heart failure should work very carefully with a professional to develop an individualized exercise program that can maximize benefit and minimize risk. A patient may also be advised in sodium and fluid restriction as well as weight loss programs.
2. **Pharmaceuticals** are also used to treat heart failure. The goals of pharmacologic therapy include improving symptoms (such as shortness of breath, fatigue, rapid heartbeat, and pulmonary and peripheral edema), slowing or reversing deterioration in myocardial function, and reducing mortality (instances of death).

In previous physiology classes, you have learned about the **renin-angiotensin-aldosterone system (RAAS)**. When it comes to heart health and treatment, it is important to understand this system in detail. Please review the image below.

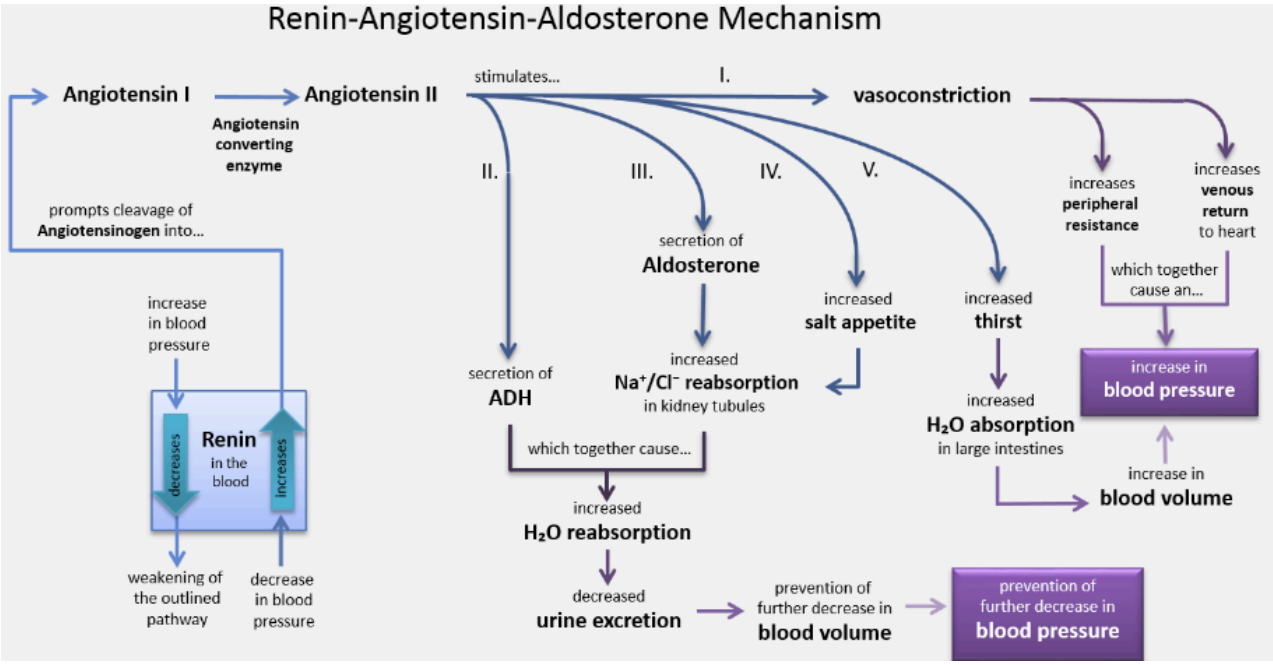


Image by BYU-I Biology Department

Drug Categories Used for HF

Beta blockers are a very important and very common drug treatment used for heart failure. Treatment with beta-blockers has been shown in clinical trials to reduce the morbidity and mortality of heart failure. Beta-1 blockers such as **carvedilol** are especially useful because they preferentially block beta-1 receptors and don't block beta-2 receptors. This is helpful in the management of HF because they decrease BP and the workload on the heart while not influencing the beta-2 receptors of the lungs. Beta blockers are especially beneficial with combating the reflex tachycardia that can occur due to the heart trying to compensate for decreased cardiac output and oxygen delivery. Reduction in tachycardia can reduce strain on the ventricles and help to halt strain-induced cardiac remodeling (hypertrophy). Beta-1 receptors are also found in the kidney where they increase renin release when stimulated by the sympathetic nervous system. Beta-1 blockers will therefore also work to reduce renin release and cause a resulting reduction in all the effects of angiotensin II.

Renin inhibitors inhibit the first step of the RAAS system. These drugs prevent the conversion of angiotensinogen into angiotensin I by renin. This leads to decreased angiotensin II and prevents an increase in BP overall. This effect is desirable because many people with HF have HTN, which stresses the heart.

ACE inhibitors like **benazepril** inhibit the effects of the RAAS by inhibiting angiotensin converting enzyme (ACE) from making angiotensin II. This reduction in the levels and effects of angiotensin II helps to reduce blood pressure, blood volume, and vasoconstriction. Angiotensin II also appears to bind AT-1 receptors in the heart and contribute to cardiomyocyte remodeling and pathogenic hypertrophy. Decreasing the stimulation of **AT-1 receptors** is therefore another beneficial effect of ACE inhibitors because they can help prevent cardiac remodeling.

Angiotensin II receptor blockers (ARBs) like **irbesartan** prevent angiotensin II from binding AT1 receptors. By doing this, they block the ability of angiotensin II to cause vasoconstriction, salt and water retention (via aldosterone), and cardiac myocyte remodeling.

Vasodilators work to prevent vasoconstriction and therefore help lower mean arterial pressure. This effect reduces the work that the ventricle must do to overcome the ventricular afterload in order to pump blood. This reduction allows a weak heart to continue perfusion of tissue.

Diuretics are useful in the treatment of CHF because they decrease the excess fluid and edema caused by heart failure. The three main diuretic classes used for heart failure include **loop diuretics (furosemide), thiazide diuretics,** and **potassium sparing diuretics (spironolactone)**.

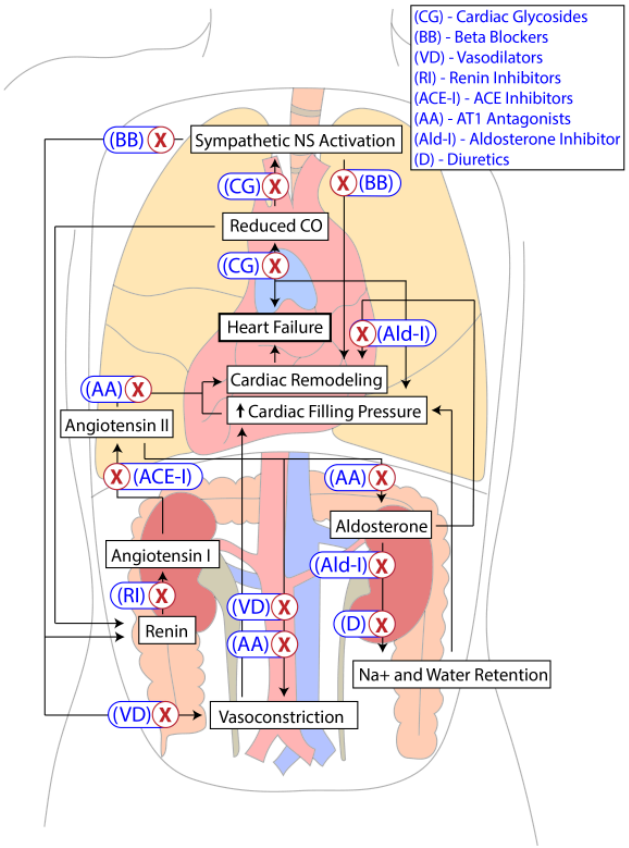
Aldosterone antagonists like **spironolactone** block the effects of aldosterone on aldosterone receptors. This reduces sodium and water retention and directly decreases blood volume. A reduced blood volume will diminish venous return and preload and decrease strain on the ventricles of the heart.

Oxygen therapy is often used in patients that have heart failure. Because heart failure results in decreased cardiac output, it is common for tissues to receive inadequate oxygen supply. This generally causes a reflex tachycardia which puts even further demand on the heart. Breathing extra oxygen can reduce the demand on the heart to pump faster to get oxygen to tissues.

The **cardiac glycoside** called **digoxin** (otherwise known as **digitalis**) is used for heart failure with atrial fibrillation when other drugs haven't worked. Overall, digoxin causes increased force of contraction and decreased heart rate. It inhibits the Na^+/K^+ ATPase on cardiac myocytes, which results in a decrease in the activity of the Na^+/Ca^{2+} exchange pump. This leads to increased levels of Ca^{2+} in the cell that cause a positive inotropic effect (increased force of contraction) and improve cardiac output. The cardiac glycosides (digoxin) also decrease heart rate (negative chronotropic effect), so it's important not to administer the drug if the patient's heart rate is less than 60 beats per minute.

While not a drug therapy, **left ventricular assist devices (LVAD)** are used in extreme cases of ventricular dysfunction. This treatment may extend the life of a patient, but its effects are limited because the left ventricle will continue to deteriorate. A patient on a ventricular assist device should receive a heart transplant as soon as possible.

Watch the Left Ventricular Assist Device | LVAD to understand the basics of how LVADs work.



Drug Categories for CHF *Image by Becky T F19*