Heart Failure and Its Symptoms, Risk Factors and Treatment

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LEARNING OBJECTIVES
Upon completion of this module, the subscriber will be able to:
1. Recognize who is affected by heart failure (HF) along with the risk factors and disease process for HF.
2. Describe the common signs and symptoms of heart failure.
3. Define the different types of heart failure.
4. Outline different treatment strategies for the management of heart failure and its symptoms.
5. List the generic and brand name, route of administration, common side effects and monitoring parameters associated with medications used in the management of heart failure.

ACCREDITATION
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This module will provide 2.5 contact hours of continuing pharmacy education credit for pharmacy technicians.
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MEET THE AUTHOR

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Heart Failure and Its Symptoms, Risk Factors and Treatment

**INTRODUCTION**

**Incidence and Prevalence**

Heart failure (HF) is a common disease affecting over 5.7 million Americans over the age of 21 years old. The prevalence of HF continues to increase, and is estimated to affect more than 8 million people over 18 years old by 2030. There are currently 870,000 new patients diagnosed with HF every year. At the age of 40 years old, both men and women have a 1 in 5 risk of developing HF over their lifetime. The risk of HF increases as a patient ages and is more common after the age of 65 years old. Gender plays a role in the time of HF onset. It is more common in men under the age of 80 years old but after the age of 80 years old, more women have HF. The increasing number of HF patients makes it likely pharmacy technicians will come into contact with these patients regardless of their practice setting (hospital, retail or specialty).

The economic burden of HF on the medical system is high, with an estimated total cost for HF in 2012 of $30.7 billion, with over $20 billion in direct medical costs. Patients with HF spend a lot of time in contact with the healthcare system. In 2010, HF was listed as the discharge diagnosis (the reason for hospitalization) for over 1 million patients. Patients with HF required over 1.8 million physician visits and over 650,000 emergency room visits. There continues to be a high mortality (death) rate linked to HF. Heart failure is listed as the cause of death on 1 in 9 death certificates. In 2011, nearly 60,000 people died from heart failure. The high cost and frequency of contact with the healthcare system gives pharmacy technicians ample opportunity to positively impact the care HF patients receive.

A patient’s risk of developing HF is influenced by many factors. As mentioned above, age and male gender are strong risk factors for a patient developing HF. Race is also considered a risk factor for heart failure with African American patients presenting with HF at a higher rate at an age less than 75 years old. In addition, other established risk factors include high blood pressure, coronary artery disease (i.e. a history of a heart attack), diabetes, and a family history of HF. Treating high blood pressure (hypertension) can decrease a patient’s risk of developing HF by up to 50%. A complete list of heart failure risk factors can be found in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Risk Factors for the Development of Heart Failure$^{1,2,3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (especially greater than 65 years old)</strong></td>
</tr>
<tr>
<td><strong>Gender (men more than women until age 80 years old)</strong></td>
</tr>
<tr>
<td><strong>African American race</strong></td>
</tr>
<tr>
<td><strong>High blood pressure</strong></td>
</tr>
<tr>
<td><strong>Coronary artery disease (i.e. history of heart attack)</strong></td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
</tr>
<tr>
<td><strong>Family history of heart failure</strong></td>
</tr>
</tbody>
</table>

**DISEASE STATE**

**Pathophysiology**

When heart failure starts, there is initially a drop in the amount of blood pumped by the heart (specifically the left ventricle), which can be caused by damage (i.e. heart attack) or decreased filling of the heart. The amount of blood pumped by the heart is measured in terms of liters/minute and referred to as cardiac output (CO). A normal cardiac output is between 5-6 liters/minute and is higher for men than women. Another important measure of heart function is the ejection fraction (EF). The EF is determined by dividing the amount of blood pumped out during contraction (“ejected” from the left ventricle) by the amount at the beginning of the heartbeat. A typical ejection fraction is greater than 60% and is considered abnormal when below 40%.

**Example Calculation of Ejection Fraction**

Blood volume in ventricle at the beginning of contraction: 200 ml  
Blood volume in ventricle at the end of contraction: 75 ml  
Amount of blood ejected during contraction: 200 ml - 75 ml = 125 ml  
Ejection fraction = 125 ml/200 ml = 0.625 x 100% = 62.5%
As a patient’s heart function declines there is a complex interplay of multiple hormone systems in the body. The two more prominent of these systems are the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system. The RAAS works to maintain adequate blood pressure and blood volume. In patients with HF the RAAS is over stimulated. Higher levels of two hormones in the RAAS, angiotensin II and aldosterone, have detrimental long-term effects. Angiotensin II causes contraction of the blood vessels increasing blood pressure and the work of the heart. Aldosterone causes salt and water retention. Both angiotensin II and aldosterone cause structural changes in the heart termed “cardiac remodeling”. These long term changes cause the heart to get bigger and the walls to get thinner resulting in a decreased pumping ability. Fortunately, there are medication therapies that can minimize the detrimental effects of the RAAS.

The second important hormone system involved in HF is the sympathetic nervous system (SNS). The SNS is part of the autonomic nervous system and functions in the “fight or flight” response. When the brain senses a threat to the body it uses the SNS to increase cardiac output (makes the heart beat harder and faster), constrict the blood vessels to increase blood pressure, and open up the lungs to take in more oxygen. Initially this change is good for patients with HF, but over time, over stimulation of the SNS leads to worsening heart function and may cause dangerous heart rhythms and death. The main hormones involved in this process are norepinephrine and epinephrine. These hormones bind to the beta-receptors on the heart acting to increase heart rate and squeezing power of the heart muscle. Over time, the higher levels of these hormones in patients with HF damage the heart muscle, resulting in worsening heart function. Also, over stimulation of the beta-receptors contributes to an abnormal heart rhythm called ventricular fibrillation which is fatal. This is also called sudden cardiac death. Thankfully, there are medications available that inhibit the over activation of the SNS and protect patients from these bad outcomes. The pathophysiology (process of disease) of HF is depicted in Figure 1.

Signs and Symptoms of Heart Failure

Patients with heart failure may have many different findings associated with their disease. In general, a sign is something seen during physical examination or diagnostic testing indicative of the disease and a symptom

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**Test Your Knowledge #1**

List the risk factors for heart failure:

1) _____________________________________________________________________
2) _____________________________________________________________________
3) _____________________________________________________________________
4) _____________________________________________________________________
5) _____________________________________________________________________
6) _____________________________________________________________________
7) _____________________________________________________________________

*Answers on page 23.*

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**Figure 1. Pathophysiology of Heart Failure**

- **Initial Damage to the Heart** (i.e. heart attack)
- **Decreased Heart Function** (decreased Ejection Fraction, decreased Cardiac Output)
- **Activation of Sympathetic Nervous System (SNS)**
  - Increased levels of norepinephrine and epinephrine
  - Dangerous rhythms in the heart and possibly sudden cardiac death
- **Activation of Renin-Angiotensin-Aldosterone System (RAAS)**
  - Increased levels of Angiotensin II and Aldosterone
  - Fluid accumulation (symptoms) and Cardiac remodeling leading to worsening heart function
- **DEATH FROM HEART FAILURE** ("pump failure"—the heart gives out)
is something the patient feels due to their condition. Patients will most likely have some but not all the signs or symptoms of the disease. The signs and symptoms of heart failure are the result of the heart not moving blood around the body properly. Patients may have signs of fluid overload, such as swelling of the feet and legs and fluid buildup in their lungs as seen on a chest x-ray. The extra fluid is called edema; the presence of edema is an important measure of a patient's control of heart failure. Fluid accumulation occurs due to poor blood flow to the kidneys resulting in the activation of RAAS which causes the body to retain salt and water. The combination of dietary restrictions and medication therapy are key to controlling edema. Patients also often report feelings of shortness of breath; this is also related to excess fluid around the lungs. A list of the most common signs and symptoms of HF is given in Table 2 and depicted in Figure 2 (refer to page 20).

It is helpful to assess patients with heart failure symptoms and disease progression in a systematic way. The American College of Cardiology Foundation (ACCF) and American Heart Association (AHA) have jointly developed a staging system for HF, going from Stage A (patients at risk of HF) through Stage D (patients with end-stage HF), to determine a patient's disease progression. Once a patient advances in HF stage they cannot go back to the previous stage. A patient's symptom control is measured with the New York Heart Association Functional Class (NYHA-FC). This rating system contains four levels with Class I indicating no symptoms and Class IV indicating symptoms at rest. Patients can move back and forth in functional class depending on symptom control. Complete lists of ACCF/AHA HF stages and NYHA-FC are provided in Table 3 (refer to page 6). When HF stage and functional class are both used to assess a patient, this provides a clear measure of the disease progression and current symptom control of a patient.

Ejection fraction (EF) less than 40% has been commonly used as a sign of heart failure. However, patients with an EF less than 40% may not always have HF symptoms. Conversely, patients may have HF symptoms with an EF greater than 40%. The guidelines differentiate patients that have symptoms of HF and a normal EF, referring to those patients as having heart failure with preserved ejection fraction (HFpEF). Typically, HFpEF results from dysfunction of the filling of the heart, referred to as diastolic dysfunction rather than the pumping function of the heart referred to as systolic dysfunction. Patients with symptoms of HF and an EF less than 40% are referred to as having heart failure with reduced ejection fraction (HFrEF). The management of HFpEF is different and not as well defined yet. The remainder of this chapter will deal specifically with HFrEF management.

**TREATMENT**

**Goals of Therapy**

Heart failure is a complex chronic disease and patients may be on as many as seven different medications to control this disease state. In that situation it is important to understand the goals of therapy to ensure the treatment is achieving those goals. The goals of therapy vary depending on ACCF/AHA HF Stage. Patients in Stage A are essentially asymptomatic (without symptoms) but at high risk for developing HF, therefore the goals focus on slowing the progression of their disease.

<table>
<thead>
<tr>
<th>Table 2. Signs and Symptoms of Heart Failure $^{3,7}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signs (seen during examination or testing)</strong></td>
</tr>
<tr>
<td>Edema (swelling in the legs and arms, or fluid buildup in the lungs)</td>
</tr>
<tr>
<td>Low ejection fraction (less than 40%)</td>
</tr>
<tr>
<td>Fast heart rate (body trying to move more blood by making heart beat faster)</td>
</tr>
<tr>
<td>Abnormal breath sounds (crackles or rales - sign of fluid in the lungs)</td>
</tr>
<tr>
<td>Enlarged heart (seen on a chest x-ray - sign of cardiac remodeling)</td>
</tr>
<tr>
<td><strong>Symptoms (felt by the patient)</strong></td>
</tr>
<tr>
<td>Exercise intolerance (unable to do usual activity)</td>
</tr>
<tr>
<td>Shortness of breath with exercise (this is called dyspnea on exertion)</td>
</tr>
<tr>
<td>Shortness of breath when lying down (this is called orthopnea)</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Cough (constant, non-productive - related to fluid in the lungs)</td>
</tr>
</tbody>
</table>

Goals for Stage A Heart Failure
1) encourage a heart healthy lifestyle, and
2) prevent heart disease by treating risk factors such as high blood pressure or diabetes mellitus.$^{5}$
### Table 3. Classification of Heart Failure Patients (ACCF/AHA Stages and NYHA-FC)³

<table>
<thead>
<tr>
<th>ACCF/AHA Stages</th>
<th>NYHA-FC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage A</strong></td>
<td>At high risk for HF but without structural heart disease or symptoms of HF</td>
</tr>
<tr>
<td><strong>Stage B</strong></td>
<td>Structural heart disease but without signs or symptoms of HF</td>
</tr>
<tr>
<td><strong>Stage C</strong></td>
<td>Structural heart disease with prior or current symptoms of HF</td>
</tr>
<tr>
<td><strong>Stage D</strong></td>
<td>Refractory HF requiring specialized interventions</td>
</tr>
</tbody>
</table>

**NYHA-FC**

<table>
<thead>
<tr>
<th>Class I</th>
<th>No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class II</td>
<td>Ordinary physical activity results in symptoms of HF.</td>
</tr>
<tr>
<td>Class III</td>
<td>Less than ordinary activity causes symptoms of HF.</td>
</tr>
<tr>
<td>Class IV</td>
<td>Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.</td>
</tr>
</tbody>
</table>

ACCF= American College of Cardiology Foundation; AHA= American Heart Association; NYHA-FC= New York Heart Association Functional Class; HF= heart failure

Patients with Stage B heart failure have had some damage to their hearts (perhaps from a heart attack) but have not yet had symptoms of HF.

**Goals for Stage B Heart Failure**

1) preventing the development of symptoms, and 2) preventing any further heart damage (termed cardiac remodeling).³

Stage C HF patients are the prototypical HF patients with known heart damage and symptoms of the disease. The majority of clinical trials and guideline recommendations focus on this stage of HF. These patients have a high risk of dying, are limited in daily activities, and spend a lot of time in contact with the healthcare system due to their disease.

**Goals for Stage C Heart Failure**

1) control symptoms, 2) improve quality of life, 3) prevent mortality (help the patient live longer), 4) prevent hospitalizations, and 5) increase the patient’s understanding of their disease through education.³

### Test Your Knowledge #2

Name three signs of heart failure:

1. ______________________
2. ______________________
3. ______________________

Name three symptoms of heart failure:

4. ______________________
5. ______________________
6. ______________________
7. ______________________

*Answers on page 23*

The NYHA-FC is used to track and monitor patients’ symptoms over time, allowing for changes in medication therapy based on the symptom control. There are numerous scales used to determine a patient’s quality of life (e.g., The Minnesota Living with Heart Failure Questionnaire and Kansas City Cardiomyopathy Questionnaire).²⁹ Scales ask various questions to determine how HF is affecting the patient’s daily activities. Scales can be repeated over time to determine if treatments are improving the patient’s quality of life. As noted above, patients with HF have a high mortality rate. Mortality is reported as both heart failure related (meaning death was a direct result of worsening HF) and all-cause mortality.
(may or may not be related to HF). Many of the medications discussed later have been shown to reduce the risk of both HF related and all-cause mortality. Hospitalizations are also frequent for patients with HF. The goal is to reduce the overall number, and increase the time between, hospital admissions. A key performance measure, which will be discussed in more detail later, is the rate of 30 day readmission in patients with HF. This is the number of patients with HF readmitted within 30 days after discharge regardless of cause. This is presented as a percentage (i.e. 100 patients discharged and 20 patients readmitted = 20% readmission rate). There are government programs that link hospital reimbursement to HF readmission rate, therefore a lot of attention is given to reducing the number of readmissions. Managing HF is a complicated process and patients need to be invested in this process. The goal for patient education attempts to ensure patients have adequate information to make appropriate decisions. As will be discussed below, there are many non-pharmacological (non-medication) therapies for HF that patients need to implement at home to successfully control their disease. Later in this module various resources that are available to patients to attain this education will be listed.

Patients in Stage D HF are at the end of their disease process. There are no longer medication therapies that will significantly change their long-term outcome. The goals are somewhat similar to stage C with the exception of preventing mortality because in this stage that has become inevitable. The patient will either need advanced heart failure treatment (i.e. heart transplant or left ventricular assist device) or they will not live much longer.

Goals for Stage D Heart Failure
1) control symptoms,
2) improve quality of life,
3) reduce hospital admissions, and
4) establish end-of-life-goals.³

Care for patients with stage D HF usually involves palliative care. Palliative care involves multiple disciplines (i.e. medical, pharmacy, nursing, social work, and spiritual care) focusing on managing the patient and family as a whole and making them comfortable rather than treating their disease.³⁰ Treatment at the end-of-life may change to include stopping some long-term therapies that do not affect symptoms. Hospice care may be involved when patients are in stage D HF and forego, or are not eligible, for more aggressive therapies such as heart transplant. Generally patients on hospice care are expected to live less than 6 months and are provided extra services to allow them to pass away in the place of their choosing, such as at home.¹⁰

**Non-Medication Management of Heart Failure**

Medication therapy is key to heart failure management, however there are non-medication approaches that patients with HF should be educated on that will improve control of their disease. Non-medication treatments work in concert with medication treatment to achieve the goals stated above. The following text will touch on the key non-medication therapies for HF. A complete listing of the recommended non-medication therapies can be found in Table 4 (refer to page 8).

**Sodium Restriction**

Patients should be educated to limit the amount of sodium (salt) they consume in their diet daily. The rationale behind limiting sodium is that higher levels of sodium results in fluid retention causing symptoms of heart failure such as shortness of breath and edema. It is estimated that the average sodium intake is between 3.3-3.5 grams (3300-3500mg) per day and less than 10% of adults take in less than 2.3 grams (2300mg) per day of sodium.¹ Both major HF guidelines contain a statement regarding sodium restriction, however it is unclear what the optimal level should be.³¹ There have been numerous studies to determine the “best” level for sodium limitations.¹² Unfortunately, the results have been mixed with no clear answer. Generally the recommendations range from 1.5gm (1500mg) to less than 2.3gm (2300mg) per day, with the lower end being reserved for patients with significant symptoms of fluid overload. Patients need to be educated on the importance of limiting salt and the impact it could have on their disease. Most patients incorrectly assume that the majority of the salt in their diet comes from adding table salt to their meals. The Centers for Disease Control (CDC) estimates that more than 75% of daily sodium intake comes from processed food or restaurant meals.¹³ Therefore, for patients to successfully limit their daily sodium, they must be educated on how to read a food label. The American Heart Association (AHA) provides a great resource for patients on “Understanding Food Nutrition Labels”.¹⁴ Foods that are known to be high in sodium include: processed meats (e.g. bacon, lunchmeat), canned soups or vegetables, sauces (e.g. barbeque sauce or salad dressing), and some cheeses. Patients with HF need to cut their salt consumption almost in half from approxi-
approximately 3.5gm/day to less than 2gm/day. For many this is a big change and is not easy. Patients should receive positive reinforcement for every positive change in their dietary salt intake. Pharmacy technicians are in the position to ask about these changes and praise the results.

Fluid Restriction

Similar to sodium restriction, patients should be educated to limit the amount of fluid they consume in a day. The rationale is that since the patient's heart is not working as well (reduced cardiac output) there is less blood going to the kidneys to remove excess fluid. Therefore lowering the amount of fluid taken in daily will reduce symptoms of fluid overload, such as shortness of breath and edema. Both the major medical guidelines support fluid restriction as a non-medication approach to the management of heart failure. The most common fluid restriction level is less than 2 liters (2000mL) of fluid daily. Occasionally, if a patient continues to struggle with fluid overload, they may be asked to reduce fluid intake to less than 1.5 liters (1500mL) per day. Patients should be educated on the importance of fluid restriction and given tools and tricks to measure fluid. Patients struggle changing between units of measurement like ounces or milliliters. During a hospital stay patients are usually provided a large cup with measurements on the side and can be encouraged to keep that at home as a measuring tool. If patients have access to an empty 2 liter soda bottle, it can be used to measure fluid at home. Patients should be instructed to add equal amounts of fluid to that bottle for all the fluids they drink throughout the day. For example, the patient has a glass of tea. When they are finished they fill the glass to the same level and pour it into the empty two liter bottle. Once the two liter bottle is full they have reached their fluid restriction for the day.

Attention also needs to be given to identifying all fluids taken in throughout the day. Anything that is liquid at room temperature should be included in the daily fluid intake. Items that are commonly omitted but should be counted include: 1) milk when used with cereal, 2) gravy or other toppings with meals (e.g. salad dressing), 3) ice and ice cubes, 4) ice cream and popsicles, and 5) coffee and tea. Restricting fluids can be a cumbersome task and patients should be congratulated for efforts in this regard.

Weight Monitoring

As a complement to sodium and fluid restriction, patients should be instructed to weigh themselves daily and monitor for changes in their weight. The rationale being that weight gain is the first sign of fluid accumulation and shows up before shortness of breath or edema. This is a key step to avoid unnecessary hospitalizations for patients with heart failure. It is estimated that less than half of patients with HF weigh themselves daily at home. Patients should be instructed to weigh themselves at the same time each day using the same scale and to keep a log. The exact amount of weight gain that indicates a problem is unknown, but generally the recommendation is to contact the provider if a patient gains more than 3 pounds in a day or 5 pounds in total over their “dry weight”. A patient’s dry weight is the weight at which they have no symptoms of fluid overload. This weight is determined by the provider and should be shared with the patient. The call to the provider will typically result in additional medications to reduce fluid accumulation in an effort to prevent a hospitalization. This usually involves the addition of a diuretic or water pill. Depending on the patient's other symptoms, the patient may also be asked to see the provider to be evaluated.

Table 4. Non-Medication Interventions for Heart Failure

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium restriction (&lt; 1.5-2.3 grams of sodium daily)</td>
<td>lowers risk of fluid retention</td>
</tr>
<tr>
<td>Fluid restriction (&lt; 1.5-2 liters of fluid daily)</td>
<td>lowers risk of fluid retention</td>
</tr>
<tr>
<td>Education on HF self-care including:</td>
<td></td>
</tr>
<tr>
<td>Adherence to medication therapy (take medicine continually for long-term benefit)</td>
<td></td>
</tr>
<tr>
<td>Weight monitoring (call provider if gain &gt; 3lbs/day or 5lbs/over dry weight)</td>
<td></td>
</tr>
<tr>
<td>Symptom monitoring (when to call the provider due to symptoms)</td>
<td></td>
</tr>
<tr>
<td>Exercise training - 30 minutes a day most days of the week (will improve functional capacity)</td>
<td></td>
</tr>
<tr>
<td>Possibly continuous positive airway pressure (CPAP) if also have sleep apnea</td>
<td></td>
</tr>
</tbody>
</table>

lbs= pounds; HF= heart failure; < = less than; > = greater than
Example of Monitoring Dry Weight

Dry weight = 175 lbs.
Weight day one = 177 lbs.
  (less than 3 lbs. weight gain in one day does NOT need to call provider)
Weight day two = 179 lbs.
  (less than 3 lbs. weight gain in one day does NOT need to call provider)
Weight day three = 178 lbs
  (no weight gain)
Weight day four = 180 lbs
  (less than 3 lbs. weight gain in one day but 5 lbs. gained over dry weight patient needs to call provider)

Exercise Training

Patients with HF typically have a decreased exercise tolerance, meaning that they are unable to perform the same levels of activity they did prior to their disease (i.e. they used to be able to walk two miles before getting short of breath, now they have that feeling walking to the mailbox). A patient’s exercise tolerance and functional capacity can be measured and tracked over time using a 6-minute walk test. This test simply involves a patient walking on a flat surface for 6 minutes and measuring how far they walk. Patients walking less than 300 meters (about 3 football fields) have a higher risk of death from HF. Therefore patients benefit from exercise training to improve their tolerance for physical exertion, resulting in improved quality of life and survival. Guidelines recommend a gradual increase in activity with a goal of 30 minutes of moderate activity up to 5 days a week.

Chronic heart failure is also an indication for cardiac rehabilitation, which involves monitored exercise training for up to 36 sessions with nurses and exercise physiologists. Pharmacy technicians are positioned to frequently encourage patients with HF to continue working to improve exercise tolerance, understanding that the goal is not for the patient to run a marathon, but to regain enough functional capacity to do the things they enjoy.

Medication Treatment of Heart Failure

Medication therapy is the cornerstone of treatment for heart failure. As mentioned earlier, many patients may require up to seven different medications to treat their disease. Medication therapy can be broadly divided into two main categories: 1) medications that improve survival and lower hospitalizations, and 2) medications that improve symptoms but not survival. The medications that improve survival generally inhibit the two main hormone systems discussed earlier involved in the pathophysiology of HF: the RAAS or the SNS. The medication classes that inhibit the RAAS are angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and aldosterone antagonists (AAs). The medication class used to inhibit the SNS is beta-blockers (BBS). One other combination of medications, hydralazine and isosorbide dinitrate, has been shown to improve survival. There are two types of medications that have been proven to improve symptoms of HF but do not improve survival, these are diuretics and digoxin. These medication classes and examples of medications in each class are listed in Table 5 (refer to page 10). Figure 3 (refer to page 11) gives an overview of how these medications are used to treat HF. The following section will describe each class of medication, briefly detail how it treats HF, discuss the major side effects, and cover important patient education points.

Test Your Knowledge #3

List four non-medication treatments for heart failure:

1) ______________________________________
2) ______________________________________
3) ______________________________________
4) ______________________________________

Answers on page 23.

Medications that Improve Survival and Lower Hospitalizations

Angiotensin Converting Enzyme Inhibitors

The renin angiotensin aldosterone system plays a vital role in the disease process of HF. High levels of two hormones, angiotensin II and aldosterone, cause elevations in blood pressure and “cardiac remodeling” long term. ACE inhibitors block the formation of angiotensin II, which results in lower blood pressures and slows the pro-
In many different clinical studies, ACE inhibitors have been shown to increase survival and decrease hospitalizations for patients with NYHA-FC II (mild), III (moderate), or IV (severe) HF symptoms. ACE inhibitors should be given early in the disease to most patients. These medications are started at low doses and titrated up at 2-4 week intervals to the “maximum tolerated dose” or in other words the highest dose the patient can take without having side effects. Patients should not take ACE inhibitors if they have a severe side effect called angioedema (swelling of the eyes, tongue, lips and throat that can be life threatening), or if they are pregnant or plan to become pregnant. Other major side effects include: 1) low blood pressure or dizziness (ACE inhibitors

### Table 5. Medication Therapy for Heart Failure

<table>
<thead>
<tr>
<th>Medications that improve survival and reduce hospitalizations</th>
<th>Route of administration</th>
<th>Side effects and monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lisinopril (Prinivil/Zestril)</td>
<td>PO</td>
<td>low blood pressure/dizziness</td>
</tr>
<tr>
<td>Enalapril (Vasotec)</td>
<td>PO/IV</td>
<td>cough (up to 20% of patients)</td>
</tr>
<tr>
<td>Fosinopril (Monopril)</td>
<td>PO</td>
<td>angioedema (&lt;1% of patients)</td>
</tr>
<tr>
<td>Quinapril (Accupril)</td>
<td>PO</td>
<td>increased potassium in blood</td>
</tr>
<tr>
<td><strong>Angiotensin Receptor Blockers (ARBs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valsartan ( Diovan)</td>
<td>PO</td>
<td>similar side effects to ACE inhibitors, except DO NOT cause cough</td>
</tr>
<tr>
<td>Losartan (Cozaar)</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Candesartan (Atacand)</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td><strong>Beta-Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol Succinate (Toprol XL)†</td>
<td>PO</td>
<td>low blood pressure and heart rate</td>
</tr>
<tr>
<td>Carvedilol (Coreg/Coreg CR)</td>
<td>PO</td>
<td>dizziness</td>
</tr>
<tr>
<td>Bisoprolol (Zebeta)</td>
<td>PO</td>
<td>fatigue (usually lasts ~ 2weeks)</td>
</tr>
<tr>
<td><strong>Aldosterone Antagonists</strong></td>
<td></td>
<td>worsen the HF (when starting medication)</td>
</tr>
<tr>
<td>Spironolactone (Aldactone)</td>
<td>PO</td>
<td>increased potassium in blood</td>
</tr>
<tr>
<td>Eplerenone (Inspra)</td>
<td>PO</td>
<td>worsening kidney function</td>
</tr>
<tr>
<td><strong>Hydralazine and Isosorbide dinitrate</strong></td>
<td></td>
<td>gynecomastia (breast pain in men)</td>
</tr>
<tr>
<td>Hydralazine/Isosorbide dinitrate (BiDil)</td>
<td>PO</td>
<td>[eplerenone has less gynecomastia]</td>
</tr>
<tr>
<td><strong>Diuretics‡</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide (Lasix)</td>
<td>PO/IV</td>
<td>electrolyte disturbances (i.e. low potassium or magnesium in blood)</td>
</tr>
<tr>
<td>Bumetanide (Bumex)</td>
<td>PO/IV</td>
<td>damage to ears (ototoxicity) at higher doses</td>
</tr>
<tr>
<td>Torsemide (Demadex)</td>
<td>PO/IV</td>
<td>kidney damage</td>
</tr>
<tr>
<td>Metolazone (Zaroxolyn)</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide (Microzide)</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Chlorothiazide (Diuril)</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td><strong>Digoxin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin (Lanoxin)</td>
<td>PO/IV</td>
<td>dangerous heart rhythms</td>
</tr>
</tbody>
</table>

*All ACE inhibitors are considered appropriate for HF treatment examples which are provided.
†Only Toprol XL is considered appropriate for HF; Lopressor (metoprolol tartrate) is not.
‡There are many options for diuretics, examples are given. Loop diuretics are preferred because of more robust urine production.
PO= oral, IV= intravenous, < = less than
should be used with caution if a patient’s systolic blood pressure is less than 90mmHg), 2) kidney dysfunction (these medications may cause an increase in potassium in the blood or a decrease in renal function in select patients and must be used cautiously), and 3) cough (up to 20% of patients will get a dry cough with this class of medicines). Overall, ACE inhibitors are considered a highly effective and safe treatment for HF and the guidelines recommend this treatment in all patients who do not have a contraindication (refer to Figure 3). Patients should be educated that ACE inhibitors are a long-term treatment for HF that allow them to live longer with their disease and stay out of the hospital. ACE inhibitors do improve symptoms as well and patients should continue taking them even once they feel better.

**Angiotensin Receptor Blockers**

Angiotensin receptor blockers (ARBs) work in the same RAAS pathway as ACE inhibitors. The difference is that ARBs block where angiotensin II works instead of blocking the formation of it. This medication class has also been shown to lower mortality and hospitalizations for patients with HF. However, when an ARB was compared to an ACE inhibitor the benefits were similar; therefore, ACE inhibitors are preferred due to a larger amount of clinical data and lower cost. The main advantage of ARBs is that these medications do not cause a cough like ACE inhibitors. In general, ARBs are considered in patients who cannot take ACE inhibitors. ARBs are also started at low doses and increased slowly over time. Patients who have had angioedema (the life threatening reaction) on an ACE inhibitor may have the same reaction to an ARB; therefore, they should be monitored closely if they are started on an ARB. Other side effects of ARBs are similar to ACE inhibitors such as low blood pressure and renal function changes. It is important to note that ACE inhibitors and ARBs are not generally used together to treat HF, except in rare cases. Patients on both of these types of medications have a higher chance of adverse reactions. If a patient is on both an ACE inhibitor and an ARB, the pharmacist should be notified. Patient education for ARBs is similar to that of ACE inhibitors and should focus on the long-term benefits of these medications. Patients should continue taking these medications even after feeling better.

**Aldosterone Antagonists**

The last group of medications used to block the RAAS for patients with HF is the aldosterone antagonists. When angiotensin II binds to its receptor it causes the release of aldosterone. Aldosterone is a hormone that controls
sodium and potassium balance in the body. High levels of aldosterone cause negative changes long-term in the heart of patients with HF including “cardiac remodeling”. There are two medications in this group, spironolactone and eplerenone, which work by blocking aldosterone at its site of action. Treatment with aldosterone antagonists resulted in lower rates of death and hospitalizations in patients with HF. The evidence for benefit with these medications is limited to selected patients; namely those with NYHA–FC II-IV HF symptoms, adequate kidney function, and normal potassium levels in the blood (see Figure 3 refer to page 11). These medications have a risk of causing a decline in kidney function and increase in potassium levels. Doses range from 12.5mg-50mg daily for both spironolactone and eplerenone, are started at the lower end of the range, and are increased if potassium levels stay normal. Other side effects include: 1) diarrhea which can worsen the changes in potassium, and 2) breast pain or tenderness in about 10% of men taking spironolactone (referred to as gynecomastia). Eplerenone causes less gynecomastia and may be used as an alternative to spironolactone if this develops. Patients taking aldosterone antagonists should be educated on the importance of keeping good follow-up with their doctors and getting all required laboratory tests. Elevations in potassium levels in the blood can have serious consequences and is difficult to find without appropriate follow-up testing.

**Beta-Blockers**

The other hormone system that is over stimulated in patients with HF is the sympathetic nervous system (SNS). This stimulation of the SNS results in high levels of norepinephrine (NE) and epinephrine in the blood stream which then bind to beta-receptors on the heart. Beta-receptors act like an on-switch telling the heart to beat faster and harder. High levels of NE lead to many bad effects in HF patients over time: 1) NE can directly damage the heart tissue causing a drop in ejection fraction over time; 2) cause faster heart rates (more beats per minute) leaving less time for the heart to fill with blood; 3) result in exercise intolerance (the patient’s heart is already going faster than usual so when they try to walk up a flight of stairs there is no more reserve); and 4) cause dangerous rhythms in the heart (the weakened heart muscle and heart tissue damage increase the patients’ risks of going into a life threatening rhythm such as ventricular fibrillation and dying suddenly). Beta-blockers (BBs) are used to block the action of NE on the heart thereby slowing down the heart rate and lowering the chances of the dangerous rhythm. There are many different BBs available, but only three BBs have been shown to have benefit in patients with HF. These BBs are bisoprolol (Zebeta), carvedilol (Coreg), and metoprolol succinate (Toprol XL). Clinical trials have shown that these medications lower the risk of death and hospitalization and improve symptoms in patients with HF and should be used in all patients with current or prior symptoms (see Figure 3 refer to page 11). BBs should be started at very low doses and slowly increased over time, due to the risk of lowering the squeezing function (i.e. contractility) of the heart when these medications are started, making HF worse initially.

**Other risks of BB treatment include:**

1) slow heart rate (bradycardia) - caution should be used if a patient’s heart rate is less than 50 beats per minute,
2) tiredness or fatigue - this generally happens at the beginning of treatment and gets better after 2 weeks, but can happen again when the dose is increased,
3) low blood pressure (hypotension) - since BB are also used to treat high blood pressure, patients have a risk of their blood pressure going too low. Caution should be used if the patient’s blood pressure is less than 90mmHg before starting treatment, and
4) sexual dysfunction - there is a risk that some patients may experience impotence or decreased libido - if this occurs a change to one of the other three BBs may resolve this side effect.

Certain other diseases put patients at risk for adverse reactions to BBs. Patients with asthma may get more symptoms because there are beta-receptors in the lungs, which may bronchospasm (constrict the bronchioles) when blocked by a BB. Patients with diabetes mellitus may not have the same feeling when their blood sugar is low because BBs prevent the racing heart feeling. Patients being started on BBs need a lot of education to understand the benefits of this treatment and management of side effects. Education should focus on slow and steady improvement, it may feel worse initially (due to fatigue), but the lower risk of death and improved exercise tolerance in the future is worth it.

**Hydralazine and Isosorbide Dinitrate Combination**

The last combination of medications that has been shown to improve survival and symptoms is hydralazine (Apsoline) and isosorbide dinitrate (Isordil). These medica-
tions are offered in a combination product called BiDil. This combination does not directly affect either the RAAS or the SNS, but causes dilation of the veins and arteries, similar to ACE inhibitors. BiDil lowered hospitalizations and death when added to an ACE inhibitor and BB in African American patients with HF and NYHA–FC III or IV. This combination can also be used in place of an ACE inhibitor or ARB if a patient cannot take those medications due to renal function or angioedema (refer to Figure 3 on page 11).3 These medications are reserved for later in HF treatment because they are difficult to take. Both hydralazine and isosorbide dinitrate need to be taken 3-4 times a day. This presents challenges for patients to be compliant with treatment. There are also numerous side effects with this treatment. About one-half of the patients get a headache while taking this treatment. Patients also frequently get upset stomach and dizziness. Patient education for these medications should include the importance of taking these medications as directed and the need to monitor for side effects.3

Medications That Improve Symptoms But NOT Survival

Lowering the risk of death is a key goal for HF management, but controlling a patient’s symptoms can significantly impact their quality of life. The medications that improve survival may also improve symptoms, but occasionally patients will need additional treatment specifically directed at treating symptoms, improving quality of life, and reducing hospitalizations.

Diuretics

Diuretics or “water pills” are an important class of medications used to control symptoms in patients with HF. There are four main sub-types of diuretics: 1) carbonic anhydrase inhibitors, 2) loop diuretics, 3) thiazide and related diuretics, and 4) potassium sparing diuretics.19 All diuretics work slightly differently but in general work in the kidneys to block the reabsorption of sodium plus or minus chloride to make the patient put out more urine. The subtype most frequently used in the treatment of HF are loop diuretics such as furosemide (Lasix) because of a larger effect on urine output. Occasionally a thiazide type diuretic such as metolazone (Zaroxolyn) will be added to a loop diuretic to increase the urine output. The use of diuretics in patients with HF has been proven to relieve symptoms and increase functional capacity (i.e. NYHA-FC).3 The effects of diuretics on long-term outcomes like hospitalization and survival is unknown, but is generally thought to be neutral. Patients who have signs of fluid overload who are on treatment with an ACE inhibitor or ARB and a BB should be treated with a diuretic (refer to Figure 3 on page 11).3 Diuretics are usually started at a low dose to see how a patient responds. Patients who have never taken a diuretic before are called “diuretic naive” and will usually have a large urine output with small doses. Over time patients can develop “diuretic resistance” which means they are getting less response to that same dose of diuretic.3 This can be just a normal sign of the progression of the patient’s HF or a sign that they are in an exacerbation, which is an acute worsening of symptoms. Patients with diuretic resistance may need higher doses, addition of a second diuretic, or admission to the hospital for intravenous administration of diuretics.3

While a patient is taking a diuretic, it is important that they monitor their fluid status. In the hospital this is accomplished by taking the total fluid intake compared to the fluid output (i.e. I/O). Patients who are fluid overloaded (carrying extra water weight) will have a goal of one to two liters of fluid loss daily.

Example of Fluid Intake/Output
Goal I/O= net -2000ml
Total fluid intake= 1900ml
Total fluid output= 4000ml
Net I/O= 4000-1900= -2100ml (goal met)

Another essential measure of fluid status that patients can use inside or outside the hospital is the daily weight. As was discussed earlier, a patient’s weight every day in relation to their “dry weight” gives a good indication of how much extra fluid they have gained. Patients taking a diuretic should be reminded to weigh themselves every day on the same scale and contact their provider if they gain more than 3 pounds in one day or 5 pounds over their “dry weight”. The major side effects of diuretics are: 1) electrolyte changes (potassium and magnesium can get too low which increases the risk of arrhythmias [dangerous heart rhythm]); 2) kidney damage (if too much fluid is removed there is a risk of the diuretic causing damage to the kidneys); and 3) damage to the ears also called ototoxicity (patients will report “ringing in the ears” which generally happens when high doses are used for long periods of time).3 Patients taking diuretics should be educated not to take these medications too
close to bedtime because they will be going to the bath
toom frequently after taking their dose. Also, this is an
portunity to emphasize salt (less than 2gm/day) and
uid restrictions (less than 2 liters/day) because diuretic
treatment works in concert with these non-medication
treatments to improve symptoms, regardless if a patient
takes their diuretics. If they do not follow these recom-
dendations it will not be as effective.

Digoxin

Digoxin (Lanoxin) is a medication that has been proven
to improve symptoms, quality of life, and reduce hospital-
izations for patients with HF, but does not have an effect
on survival. Digoxin works by raising the amount of cal-
cium in the heart cells which makes the heart beat harder
(i.e. increasing EF). Digoxin is generally reserved for
patients who continue to have symptoms and hospitaliza-
tions while on maximum tolerated doses of ACE inhibi-
tors or ARBs, BBs, and aldosterone antagonists. Digoxin
is used at doses of 0.125mg-0.25mg daily, with the lower
dose being preferred. Digoxin is removed from the body
by the kidneys and builds up in patients with poor kidney
function. Occasionally the dosing may be changed to ev-
ery other day to prevent build up. It also has a number of
side effects that make this treatment harder for patients
to tolerate. The major side effects for digoxin include: 1)
abnormal heart rhythms (arrhythmias) - patients may
experience slower heart rates and skipped beats; 2) gas-
trointestinal effects - usually nausea, vomiting or diar-
three; and 3) neurological complaints - patients get disor-
iented, confused and have visual disturbances described
as a green-yellow halo around objects. These side effects
can occur at any time but are more common if the pa-
tient’s dose is too high for their kidney function result-
ing in high blood levels. Patients taking digoxin should
be educated on watching for side effects and the need to
continue taking the medication even after HF symptoms
resolve to keep them from coming back.

Medications That Should Be Avoided in
Patients With Heart Failure

Certain medication treatments can worsen the condition
of a patient with HF and should not be given (contra-
indicated). These classes of medications either make the
symptoms of HF worse leading to more hospitalizations
or can increase the risk of death. This sec-
tion will describe these four classes of medi-
cations and their negative effects in HF pa-
tients. Table 6 (refer to page 16) summarizes
the classes of medications and their adverse
effects. Pharmacy technicians can contribute
to the care of patients with HF by screening
for these medications. If any of these medica-
tions are found on a profile of a patient with
HF, it should be brought to the attention of
the pharmacist.

Class I and Class III Antiarrhythmic
Medications

Antiarrhythmic medications are used to lower
the risk of patients having an unsafe heart
rhythm (arrhythmia). Class I antiarrhythmic
medications change impulse conduction in
heart muscles by blocking sodium channels,
and class III antiarrhythmic medications do
the same thing by blocking potassium chan-
nels. Most antiarrhythmic medications have a cardiode-
pressant effect, meaning that they lower the pumping
strength of the heart thereby lowering ejection fraction.
This is called a negative inotropic effect, with inotrope
meaning pumping function. While these medications
are used to treat certain types of arrhythmias, they can
increase the risk of another different type of more seri-
ous arrhythmia called ventricular fibrillation and tors-
ade de pointes which can lead to death. The increased
risk of bad rhythms (ventricular fibrillation) is higher in

Test Your Knowledge #4

Write the letter for the benefit provided in the space for each
medication: (note: each benefit will be used more than once, most
medications have multiple benefits)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Answer</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1)Quinapril</td>
<td>______</td>
<td>a) death</td>
</tr>
<tr>
<td>2)Losartan</td>
<td>______</td>
<td>b) symptoms of HF</td>
</tr>
<tr>
<td>3)Carvedilol</td>
<td>______</td>
<td>c) hospitalizations for HF</td>
</tr>
<tr>
<td>4)Digoxin</td>
<td>______</td>
<td></td>
</tr>
<tr>
<td>5)Bumetanide</td>
<td>______</td>
<td></td>
</tr>
<tr>
<td>6)Hydralazine/Isosorbide dinitrate</td>
<td>______</td>
<td></td>
</tr>
<tr>
<td>7)Eplerenone</td>
<td>______</td>
<td></td>
</tr>
</tbody>
</table>

Answers on page 23.
patients with HF making these medications unsafe. Two antiarrhythmic medications, amiodarone (Cordarone) and dofetilide (Tikosyn), are considered safe in patients with HF because, in trials, these medications have not increased the rate of death.³

**Calcium Channel Blockers**

Calcium channel blockers have many different uses ranging from high blood pressure to migraines. As the name suggests, these medications work by blocking calcium channels in various types of cells in the body. For example, blocking calcium channels in the peripheral arteries causes dilation and lowering of blood pressure. Blocking calcium channels in the heart cells causes a slower heart rate and a decrease in pumping function (negative inotropic). There are two subtypes of calcium channel blockers based on chemical structure: dihydropyridine and nondihydropyridine.²² The dihydropyridine (e.g. felodipine or Plendil) subtype exerts more action on the peripheral tissues while the nondihydropyridine (e.g. diltiazem or Tiazacand and Cardizem) work more on the heart. The negative effects in patients with HF are slightly different for each sub-type of calcium channel blocker. The dihydropyridine medications have more of a risk to cause swelling in the legs (called peripheral edema) thereby worsening HF symptoms with a minor effect of lowering heart pumping function. The nondihydropyridine medications have a significant effect on heart pumping function resulting in decreased ejection fraction, worsening symptoms, and increasing hospitalizations.²² Of note, one calcium channel blocker, amlodipine (Norvasc), has been shown to be well tolerated in patients with HF and has a neutral effect on survival.³ Amlodipine is a dihydropyridine calcium channel blocker.

**Nonsteroidal Anti-inflammatory Medications**

Nonsteroidal anti-inflammatory medications (NSAIDs) are used to treat many different conditions including arthritis and minor pain. There are many different NSAIDs with quite a few available over the counter, therefore patients with HF have easy access to these medications. NSAIDs work by blocking the action of an enzyme called cyclo-oxygenase (COX).²³ There are multiple sub-types of COX. NSAIDs are divided into subgroups based on whether they block COX-1 or COX-2. The effects in patients with HF are the same whether a NSAID blocks COX-1 or COX-2. NSAIDs cause a drop in kidney function and also sodium and water retention. In patients with HF, this change in kidney function leads to more HF symptoms and ultimately more hospitalizations. Several studies have shown that when patients with HF are started on a NSAID, they have a higher chance of being admitted to the hospital.²³

**Thiazolidinediones**

Thiazolidinediones are a class of medications used to treat diabetes mellitus. There are two medications in this class: pioglitazone (Actos) and rosiglitazone (Avandia). These medications may also be referred to as the glitazones or TZDs. These medications work by making the body more sensitive to insulin and thereby lowering the amount of glucose (sugar) in the blood.²⁴ The concern for patients with HF is that there is a higher risk of swelling in the legs (peripheral edema) and HF symptoms in patients treated with these medications.²⁴ Generally this class of medications should be avoided in patients with HF.

**Patient Education and Resources for Heart Failure**

Patient education is a crucial part of the management of HF. Patients with HF are confronted with a complex medication regimen as well as dietary restrictions. Patients need consistent and frequent reinforcement of HF self-care principles to successfully manage their disease state. Pharmacy technicians are in a good position to remind patients about key concepts and connect patients with the pharmacist for more detailed education. Routine education is important enough that the American Heart Association tracks a performance metric of the percentage of patients provided with education on three or more elements of self-care on a yearly basis.²⁵ The vital self-care behaviors of patients with HF are: 1) medication taking, 2) symptom monitoring, 3) dietary compliance, 4) fluid restriction, 5) alcohol restriction (two or less drinks/day for men and 1 or less drinks/day for women), 6) weight loss, 7) exercise, 8) smoking cessation, 9) preventive behaviors (patient should be up-to-date on all immunizations and get influenza vaccine yearly), and 10) nonprescription medications (patients should talk to the pharmacist or their physician before starting any over the counter medications).²⁶

Weight loss is an interesting self-care behavior that deserves further discussion. Weight monitoring is a critical part of
Table 6. Medications That Should Be Avoided in Patients with HF

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples (Generic (Brand))</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiarrhythmics</strong></td>
<td>Class I (sodium channel blockers)</td>
<td>Lower pumping function of the heart – leading to more HF symptoms</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Disopyramide (Norpace)</td>
<td>More risk of abnormal rhythms in the heart - raising risk of death</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Flecainide (Tambocor)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Lidocaine (Xylocaine)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Mexiletine (Mexitil)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Procainamide (Pronestyl)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Propafenone (Rythmol)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Quinidine (Quinaglute)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Class III (potassium channel blockers)*</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Sotalol (Betapace)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Ibutilide (Corvert)</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Dronedarone (Multaq)</td>
<td></td>
</tr>
<tr>
<td><strong>Calcium channel-blockers</strong></td>
<td>Dihydropyridine type†</td>
<td>Fluid accumulation in the lower legs - leading to more HF symptoms</td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Felodipine (Plendil)</td>
<td>Decreased pumping function of the heart - may lead to more hospitalization or death</td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Isradipine (DynaCirc)</td>
<td></td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Nicardipine (Cardene)</td>
<td></td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Nifedipine (Procardia)</td>
<td></td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Non-Dihydropyridine type</td>
<td></td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Diltiazem (Cardizem, Tiazac)</td>
<td></td>
</tr>
<tr>
<td>Calcium channel-blockers</td>
<td>Verapamil (Calan, Verlan)</td>
<td></td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Celecoxib (Celebrex)</td>
<td>More fluid accumulation leading to more HF symptoms and higher risk of hospitalizations and death</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Etodolac (Lodine)</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Ibuprofen (Motrin, Advil)</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Indomethacin (Indocin)</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Naproxen (Naprosyn, Aleve)</td>
<td></td>
</tr>
<tr>
<td><strong>Thiazolidinediones</strong></td>
<td>Pioglitazone (Actos)</td>
<td>Swelling in the lower legs - more HF symptoms and hospitalizations</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Rosiglitazone (Avandia)</td>
<td></td>
</tr>
</tbody>
</table>

HF = Heart failure; NSAID = nonsteroidal anti-inflammatory drug

*Amiodarone (Cordarone) and dofetilide (Tikosyn) are considered safe in patients with heart failure because they do not increase mortality; †Amlodipine (Norvasc) is considered safe in patients with heart failure due to no effect on mortality

fluid management as discussed above, however patients also need to monitor for loss of appetite and progressive weight loss due to “cardiac cachexia”. As a patient’s HF progresses, they either do not absorb adequate nutrition or just do not have the energy to take in enough calories. This can be a bad prognostic finding. National organizations such as the American Heart Association and the Heart Failure Society of America have patient education materials available on their websites. Table 7 (refer to page 18) provides links to various patient education materials that can be found online. Many institutions provide patients with heart failure resources kits. These kits can contain many different items to improve self-care such as: 1) measuring cups (for portion size); 2) a large cup with volumes marked on the side (for measuring fluids); 3) a pillbox (improving compliance); 4) a pedometer (measuring exercise); and 5) a scale (for weight
Heart Failure and Its Symptoms, Risk Factors and Treatment

**Test Your Knowledge #5**

Complete the crossword puzzle below:

**Across**
1. A medication that may be used in place of an ACE inhibitor, if the patient has a cough
2. Shortness of breath when a patient lies down
3. A hormone that increases salt and water retention and is inhibited by spironolactone
4. A NSAID medication that is contraindicated in patients with HF due to fluid retention
5. A combination medication that has shown benefit in reducing death in African American patients with HF
6. A medication that blocks the conversion of angiotensin I to angiotensin II, slowing the progression of HF
7. A medication that increases the pumping function of the heart, lowering symptoms of HF
8. A medication that blocks beta-receptors and lowers the chance of arrhythmias in patients with HF
9. Patients with HF should limit themselves to less than 2 grams per day of this
10. A measure of the symptom control for patients with HF
11. A medication that encourages salt and water excretion, lowering the symptoms of HF
12. A calcium-channel blocker medication contraindicated in patients with HF because it lowers the pumping function of the heart

**Down**
1. A medication that may be used in place of an ACE inhibitor, if the patient has a cough
3. A hormone that increases salt and water retention and is inhibited by spironolactone
4. A NSAID medication that is contraindicated in patients with HF due to fluid retention
5. A combination medication that has shown benefit in reducing death in African American patients with HF
6. A medication that blocks the conversion of angiotensin I to angiotensin II, slowing the progression of HF
9. Patients with HF should limit themselves to less than 2 grams per day of this

Answers on page 23.
monitoring). Patients newly diagnosed with HF should be seen in clinic as often as every 1-2 weeks for medication titration and education. This means that they will frequently have new prescriptions and will be coming to the pharmacy, offering pharmacy staff opportunities to reinforce their self-care activities.

**HEALTH-CARE REFORM AND HEART FAILURE**

Since patients with HF account for a significant portion of healthcare expenditures and are frequently readmitted to the hospital, many regulatory agencies focus on HF management and outcomes. The American Heart Association includes nine performance metrics within its guideline for healthcare organizations to track to ensure quality HF care.\(^3\) Two pharmacy related measures are the percentage of patients treated with beta-blocker therapy within the last year as an outpatient or at hospital discharge; and the percentage of patients treated with ACE inhibitors or ARBs in the same timeframe.\(^3\) Heart failure outcomes have also become the focus of changes in insurance reimbursement referred to as “pay for performance”. The Centers for Medicare & Medicaid Services (CMS), the federal agency that runs Medicare, is changing the way it reimburses hospitals for caring for patients with heart failure. The Affordable Care Act allows Medicare to alter payments for hospitals that have excessive readmissions for heart failure. Simply put, if the readmission rate is above a threshold, the reimbursement is reduced. However, if the readmission rate is below a threshold, the reimbursement is increased. This program was designed to reward institutions providing above average care and compel institutions with subpar outcomes to focus on improving quality.\(^27\) The outcomes examined for this program related to HF are: 1) rate of 30-day unplanned readmission for heart failure patients and 2) 30-day death rate for heart failure patients. A website is available to see how different hospitals perform in relation to these metrics (http://www.medicare.gov/hospitalcompare/search.html#). While care of the patient with HF is paramount, it is important to acknowledge that there are outside forces monitoring the performance of the institution regarding the outcomes of these patients.

**CONCLUSION**

Heart failure is a common disease affecting a large number of adults. Patients with HF generally have many different signs or symptoms of their disease such as shortness of breath and swelling in their legs. The goals of treatment for HF are to increase survival, lower hospitalizations and relieve symptoms. Heart failure requires complex treatment with many different medications and non-medication therapies. Certain medications (ACE inhibitors, ARBs or beta blockers) have been shown to lower death rate and should be used in all patients. If a patient with HF is not taking one of these medications, this is an opportunity to alert the pharmacist to review their profile. Other medications such as aldosterone antagonists and the combination of hydralazine and isosorbide dinitrate increase survival in certain patients. Some medications are used mainly to control the symptoms of heart failure (i.e. diuretics and digoxin). The use of some medications should raise concern because of the risk of worse outcomes in patients with HF. These medications are 1) most antiarrhythmics, 2) calcium channel blockers,

<table>
<thead>
<tr>
<th>Table 7. Patient Education Resources</th>
<th>Organization</th>
<th>Resource</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Heart Association</td>
<td>Heart Hub</td>
<td><a href="http://www.hearthub.org/hc-heart-failure.html">http://www.hearthub.org/hc-heart-failure.html</a></td>
</tr>
<tr>
<td>Heart Failure Society of America</td>
<td>Education Modules</td>
<td><a href="http://www.hfsa.org/hfsa-wp/wp/patient/education-modules/">http://www.hfsa.org/hfsa-wp/wp/patient/education-modules/</a></td>
</tr>
<tr>
<td>National Institutes of Health</td>
<td>Patient Education</td>
<td></td>
</tr>
</tbody>
</table>
3) NSAIDs, and 4) thiazolidinediones. Patient education is key to improved outcomes in HF. Patients need consistent education and reinforcement on concepts such as fluid and salt restrictions, symptom management, medication adherence, and exercise. The frequent contact that patients have with the healthcare system give ample opportunity for pharmacy technicians, either in an inpatient setting through medication reconciliation or outpatient setting through new prescriptions, to identify HF patients and apply the concepts discussed in this chapter to improve their care.
Figure 2. Most Common Symptoms of Heart Failure

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In: Clivir Learning Community, Symptoms Congestive Heart Failure is Worsening. June 1, 2009.
References


Heart Failure and Its Symptoms, Risk Factors and Treatment

ANSWER KEY: TEST YOUR KNOWLEDGE
EXERCISES

Exercise #1:
1) Male gender
2) African American race
3) Age
4) Coronary artery disease
5) High blood pressure
6) Diabetes mellitus
7) Family history

Exercise #2:
Signs of heart failure
1) Edema
2) Low ejection fraction (<40%)
3) Fast heart rate
4) Abnormal breath sounds
5) Enlarged heart

Symptoms of heart failure
1) Exercise intolerance
2) Dyspnea on exertion
3) Orthopnea
4) Fatigue
5) Cough

Exercise #3:
1) Salt restriction
2) Fluid restriction
3) Education of self-care
4) Exercise training
5) CPAP

Exercise #4:
1) Quinapril A,C
2) Losartan A,C
3) Carvedilol A,B,C
4) Digoxin B,C
5) Bumetanide B
6) Hydralazine/isosorbide dinitrate A,C
7) Eplerenone A,C

Exercise #5:
Across
2) Orthopnea
7) Digoxin
8) Metoprolol
10) NYHAFC
11) Furosemide
12) Diltiazem

Down
1) Valsartan
3) Aldosterone
4) Ibuprofen
5) Bidil
6) Lisinopril
9) Salt
SELF ASSESSMENT QUESTIONS

1. Which of the following is TRUE about heart failure?
   A. Heart failure costs the healthcare system under $20 million dollars per year
   B. Heart failure is listed as the cause of death on 1 in 9 death certificates
   C. There are about 500,000 heart failure related physician visits each year
   D. There are over 1 million new patients diagnosed each year

2. Which of the following is NOT a risk factor for heart failure?
   A. African American race
   B. Age less than 65 years old
   C. Family history
   D. High blood pressure

3. The amount of blood pumped by the heart measured in liters/minute is called?
   A. Cardiac output
   B. Contractility
   C. Ejection fraction
   D. Heart rate

4. Name the hormone that causes salt and water retention and “cardiac remodeling”.
   A. Aldosterone
   B. Salt
   C. Calcium
   D. Norepinephrine

5. This hormone system, which controls the “fight or flight” response, is over-stimulated in patients with heart failure.
   A. Cortisol system
   B. Endocrine system
   C. Renin-angiotensin-aldosterone system (RAAS)
   D. Sympathetic nervous system (SNS)

6. Which of the following is a SIGN of heart failure?
   A. Cough
   B. Edema (swelling in the legs and arms)
   C. Exercise intolerance
   D. Shortness of breath while lying down (orthopnea)

7. A patient with heart failure symptoms and a left ventricular ejection fraction of 55% would be classified as having what type of heart failure?
   A. Coronary artery disease
   B. Heart failure with preserved ejection fraction (HFpEF)
   C. Heart failure with reduced ejection fraction (HFrEF)
   D. No heart failure because ejection fraction is normal

8. What is the correct NYHA-FC for a patient if they have symptoms with less than ordinary activity?
   A. Class I
   B. Class II
   C. Class III
   D. Class IV

9. Which of the following is NOT a treatment goal for patients with ACCF/AHA Stage D heart failure?
   A. Control symptoms
   B. Improve quality of life
   C. Prolong life
   D. Reduce hospital admissions

10. What is an appropriate non-medication treatment for heart failure?
    A. Increase alcohol consumption to more than 2 drinks per day
    B. Maintain fluid intake to 2 liters or less per day
    C. Sodium restriction to less than 3.5 grams per day
    D. Weigh yourself at least once a week and report changes of 10 pounds or greater
11. A patient’s “dry weight” is their weight:
   A. After they dry off after taking a shower
   B. When they are sent home from the hospital
   C. When they see the doctor in the clinic
   D. When they have no symptoms of fluid overload

12. Which of the following medication classes blocks the formation of angiotensin II?
   A. Angiotensin Converting Enzyme (ACE) Inhibitors
   B. Angiotensin Receptor Blockers (ARBs)
   C. Beta-Blockers
   D. Diuretics

13. Patients should not take an ACE inhibitor if they have had this life threatening reaction which involves swelling of the eyes, tongue, and lips?
   A. Alopecia
   B. Angioedema
   C. Ataxia
   D. Visual disturbances

14. Which of the following medications lowers death and hospitalizations for patients with heart failure by blocking the action of aldosterone but can cause gynecomastia (breast pain or tenderness in men)?
   A. Furosemide (Lasix)
   B. Lisinopril (Prinivil)
   C. Spironolactone (Aldactone)
   D. Valsartan (Diovan)

15. Which of the following medications has been shown to reduce hospitalizations and death, and improve symptoms by blocking the negative effects of norepinephrine and epinephrine on the heart?
   A. Eplerenone (Inspra)
   B. Hydralazine/Isosorbide dinitrate (BiDil)
   C. Metolazone (Zaroxolyn)
   D. Metoprolol Succinate (Toprol XL)

16. Which medication improves symptoms and reduces hospitalizations, but does not improve survival?
   A. Bisoprolol (Zebeta)
   B. Enalapril (Vasotec)
   C. Digoxin (Lanoxin)
   D. Losartan (Cozaar)

17. All of the following are major side effects of digoxin EXCEPT:
   A. Abnormal heart rhythm (arrhythmia)
   B. Low blood pressure
   C. Nausea, vomiting, or diarrhea
   D. Visual disturbances (green-yellow halo)

18. Which of the following medications should be avoided in patients with heart failure due to a risk of a drop in kidney function leading to sodium and water retention and ultimately hospitalizations?
   A. Amlodipine (Norvasc)
   B. Dofetilide (Tikosyn)
   C. Ibuprofen (Motrin, Advil)
   D. Pioglitazone (Actos)

19. Which of the following is NOT a vital self-care behavior of patients with heart failure?
   A. Alcohol restriction
   B. Monitoring symptoms
   C. Exercise
   D. Weight gain

20. What is the outcome measure associated with the Centers for Medicare & Medicaid Services’ “pay for performance” reimbursement structure?
   A. 30-day unplanned readmission for heart failure patients
   B. ACE inhibitor prescription given at discharge from the hospital
   C. Goal ejection fraction
   D. Improved quality of life