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Educational Material*
Second Quarter, 2019

Heart Failure

Summary:

Nearly 5 million adults in the Unites States are currently living with heart failure. Heart failure is responsible for 11 million physician visits each year and more hospitalizations than all forms of cancers combined. Heart failure costs the nation an estimated $30.7 billion each year. The goal of this quarter's educational material* is to discuss heart failure treatment options.

Objective(s):

1. Review heart failure epidemiology
2. Provide heart failure definition
3. Review types of heart failure
4. Review classes of heart failure
5. Discuss common diagnostic tests/procedure
6. Review acute and chronic treatment options

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*As required by Medicaid Mega Reg

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Congestive Heart Failure

Overview

- Epidemiology
- Definition of Heart Failure (HF)
- Types of HF
- Classes of HF
- Common diagnostic tests/procedures
- Treatment options
  - Chronic
  - Acute

Impact of Heart Failure

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- Nearly 5 million adults in the U.S. are currently living with HF
- Approximately 550,000 new cases are **diagnosed** in the U.S. each year
- HF is responsible for 11 million physician visits each year, and more hospitalizations than all forms of cancer combined
- HF costs the nation an estimated $30.7 billion each year

Risk Factors

- Diseases that damage the heart, which increase the risk of HF Some of these diseases include:
  - Coronary heart disease and heart attacks
  - Hypertension
  - Diabetes
- In the U.S., most cases are due to damage from an MI (myocardia infarction) or from long-standing hypertension

Demographics

- HF affects people of all ages, from children and young adults to the middle-aged and the elderly
- Almost 1.4 million person with HF are under 60 years of age
- More than 5% of person age 60 to 69 have HF
- The incidence of HF is equally frequent in men and women
- African Americans are 1.5 times more likely to develop HF than Caucasians

Life expectancy

- Depends on many factors and there is no one answer for an individual patient
- For patients with severe or advanced HF
  - Only around 10 to 20% of patients will be alive after one year.

Heart Failure

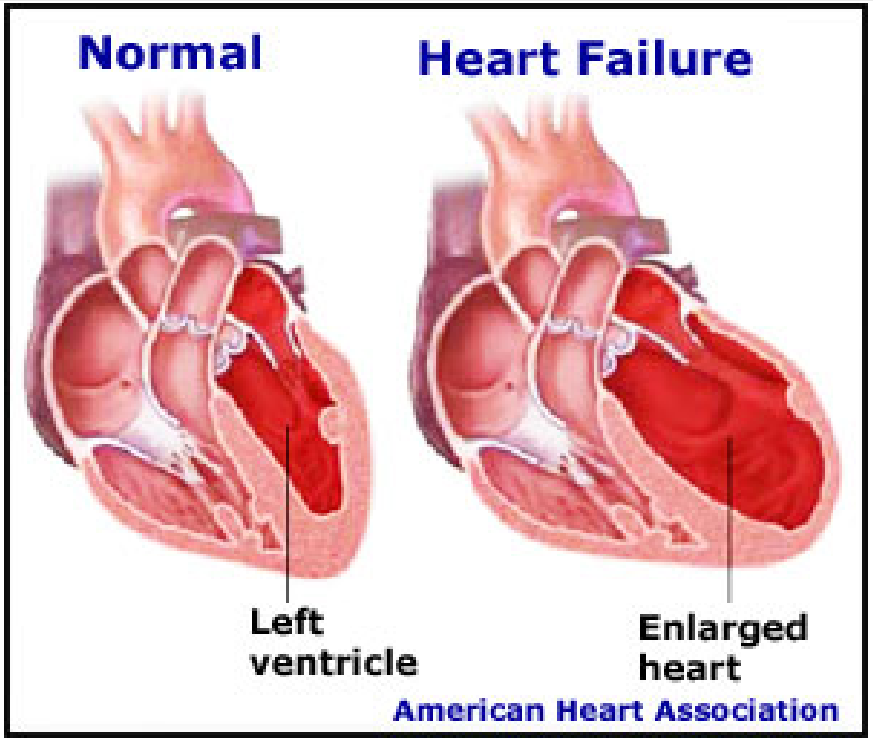
- The heart muscle is unable to pump enough blood to meet the body's needs for blood and oxygen

  - Not supplying the cells with enough blood
  - Cannot keep up with its workload
  - The body may not get the oxygen it needs

At first the heart tries to make up for this by:

1. **Enlarging**
    - The heart stretches to contract more strongly and keep up with the demand
2. **Developing more muscle mass**
    - Due to contracting cells of the heart get bigger, this allows for the heart pump more strongly
3. **Pumping faster**
    - This helps increase the output

Normal vs Heart Failure



Pathophysiology of HF

- Compensatory mechanisms
  - Renin angiotensin aldosterone system (RAAS)
  - Sympathetic nervous system (SNS)
  - Vasopressin

Diagnostic test for HF

- Echocardiography (ECHO)
  - An ultrasound of the heart
  - Provides an estimate of left ventricular ejection fraction (LVEF)
- LVEF
  - measurement of how much blood is pumped out of the left ventricle with each contraction

Ejection Fraction

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EF	Term	Primary Problem
55-70%	Normal	Normal
≥50%	Heart Failure with Preserved EF (HFpEF) Diastolic Dysfunction	Impaired ventricular relaxation and filling during diastole
40-49%	Heart Failure with mid-range HF (HFmrEF)	Likely mixed systolic and diastolic dysfunction
<40%	Heart Failure with Reduced EF (HFrEF) Systolic Dysfunction	Impaired ability to eject blood during systole

Preserved vs Reduced Ejection Fraction

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Preserved EF	Reduced EF
• EF ≥ 50% • Diastolic dysfunction (systolic function in tact) • Usually older women with a hx of hypertension, obesity, CAD, diabetes, atrial fibrillation and hyperlipidemia	• EF ≤ 40 % • Clinical diagnosis of HF • Systolic dysfunction

Signs & Symptoms of HF

- General Signs and symptoms
  - Dyspnea (shortness of breath at rest or upon exertion)
  - Cough
  - Swollen ankles
  - Fatigue, weakness
  - Reduction in exercise capacity

Labs

- B-type natriuretic peptide: normal is <100 pg/mL
- N-terminal pro B-type natriuretic peptide: normal is <300 pg/mL
- Both are increased in HF

Classification of Heart Failure

ACCF/AHA Stages of HF		NYHA Functional Classification	
A	At high risk for HF but without structural heart disease or symptoms of HF.	None	
B	Structural heart disease but without signs or symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.
D	Refractory HF requiring specialized interventions.		

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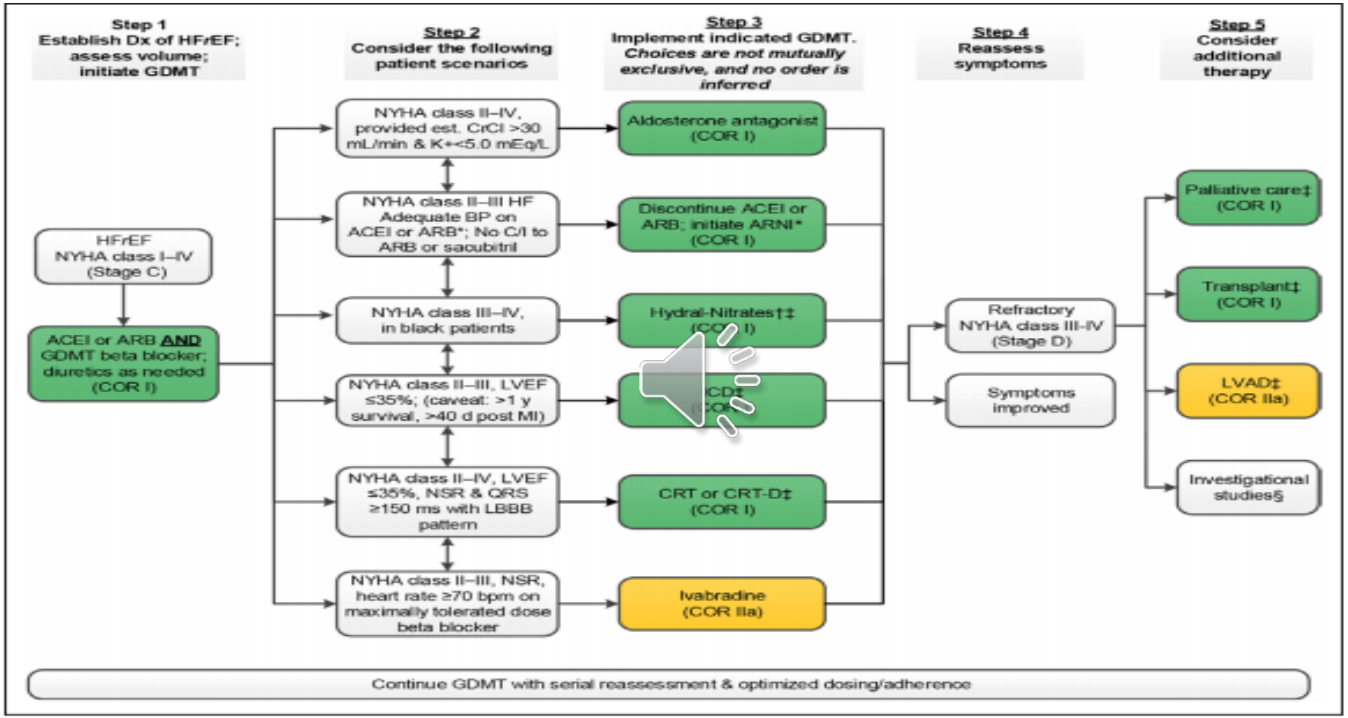
American Heart Association.

Treatment Options

Treatment of Chronic Systolic Heart Failure Overview

- First-line therapy
  - Angiotensin converting enzyme (ACE) inhibitors or Angiotensin receptor blocker (ARBs) or Angiotensin receptor and Neprilysin inhibitor (ARNI)
  - Beta blockers
  - Aldosterone receptor antagonists (ARAs)
- Alternative/Additive therapies
  - Hydralazine and nitrates
  - Loop diuretics
  - Digoxin
  - Ivabradine

Treatment of HFrEF Stage C and D



Yancy, Clyde, et al. ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. *American College of Cardiology/American Heart Association.* 2017; 136-161

Drug Treatment

Drug Therapy Targets	Mechanism of Action	Benefit with Drug Class
ACE inhibitors/ARB	Block neurohormonal activation of the RAAS, resulting in vasodilation and improved EF	***Reduces morbidity & mortality***, decreases cardiac remodeling, improves LVEF
ARNI	Counteract effects of RAAS activation and produce vasodilation	***Reduces morbidity & mortality***
Beta blockers	Block the activation of the SNS by blocking Epinephrine and Norepinephrine	***Reduces morbidity & mortality***, provides benefit in controlling heart rate and reducing arrhythmia risk
ARA	Reduces sodium and water retention	***Reduces morbidity & mortality,*** improve symptoms and ejection fraction
Hydralazine/Nitrate	A direct arterial vasodilator and venous vasodilation	Improves survival
Digoxin	Increases cardiac output and decrease heart rate through inhibition of the Na/K ATPase pump	Improves symptoms, exercise tolerance and quality of life, improves symptoms and reduces hospitalizations
Ivabradine	Reduces heart rate through inhibition of the “funny” current	Reduces hospitalizations
Loop Diuretics	Increase excretion of Na, K, Cl, Mg, Ca and H20	Improves symptoms

Potassium Oral Supplementation

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- Loop diuretics cause a decrease in potassium while other HF drugs (RAAS inhibitors, ARAs) increase potassium
- Maintenance of potassium levels is essential to reduce the pro-arrhythmic risk
- Range of potassium is 3.5-5 mEq/L

Digoxin

- Provides a small increase in cardiac output
  - Decreases HR
- Improves symptoms and decreases hospitalizations
- Added in patients who remain symptomatic despite receiving standard treatment of an ACE inhibitor or ARB with a beta blocker

Heart Failure with preserved ejection fraction of ≥50% (HFpEf)

- Systolic and diastolic blood pressure should be controlled
  - Less than 130/80 mm Hg
- *Diuretics* should be used for relief of symptoms due to volume overload
- *Aldosterone receptor antagonist* might be considered to decrease hospitalization
  - With HF admission within 1 yr, eGFR >30 ml/min, creatinine <2.5 mg/dL, potassium <5 mEq/L.

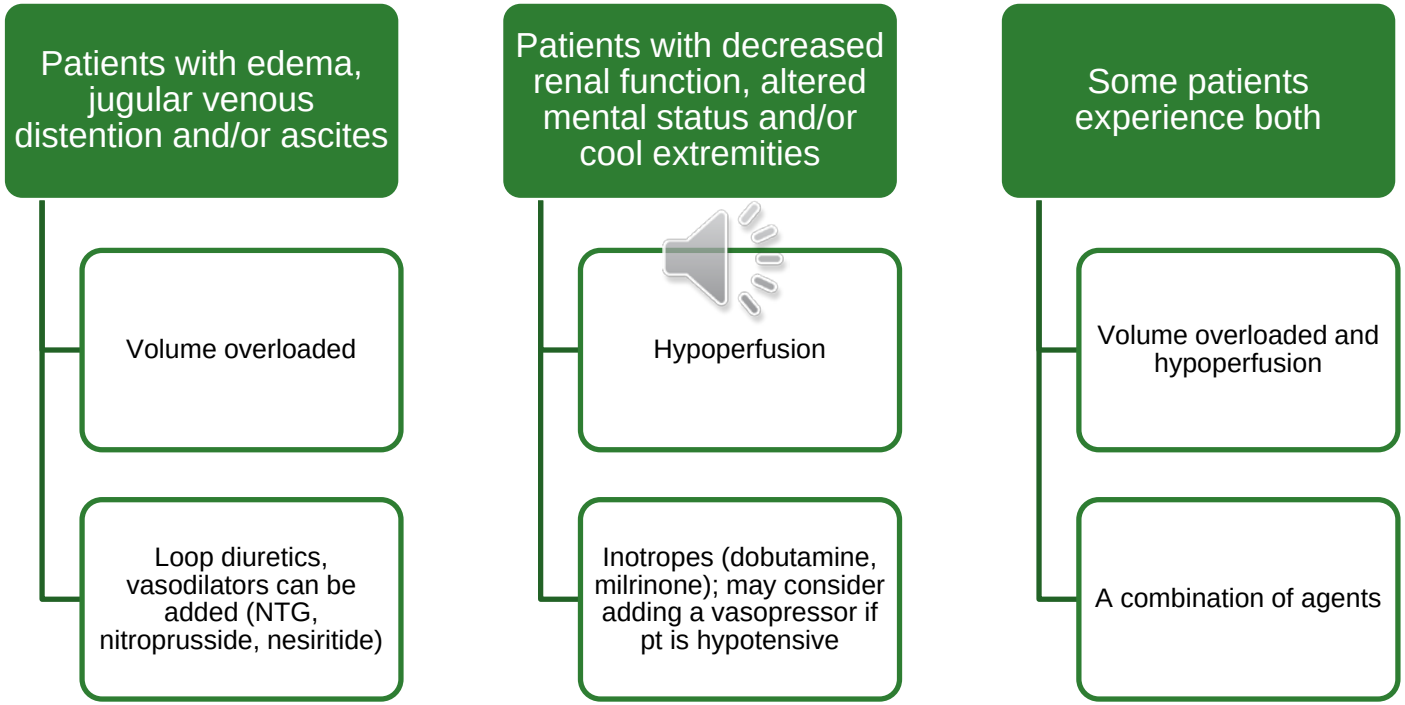
Lifestyle Management

- Body weight
- Sodium Restricted diet, <1500 mg/day
- Fluid restriction (1.5-2 L/day)
- Limit alcohol intake
- Avoid illicit drug use, stop smoking
- Exercise training or regular physical activity

Acute Decompensated Heart Failure

- Worsening symptoms
  - Sudden weight gain
    - Weight gain of more than 5 lbs in 1 week
  - Increasing shortness of breath and fatigue
  - Inability to lie flat without becoming short of breath
- Due to Nonadherence with medications and/or lifestyle recommendations

Treating Acute Decompensated Heart Failure



Clinical Pearls

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Drug class	Target Dosing	Black Box Warnings	Contraindications	Monitoring Parameters
ACE inhibitors	Lisinopril 20-40mg daily Enalapril 10-20mg bid	can cause injury and death to the developing fetus	History of angioedema, use with aliskiren in pts with diabetes, use within 36 hrs of Entresto	Potassium, renal function
ARBs	Candesartan 32mg daily Losartan 50-150 mg daily Valsartan 160mg bid	Same BBW as above	use with aliskiren in pts with diabetes 	Potassium, renal function
ARNI	Entresto 200mg bid	Same BBW as above	Use with ACE inhibitors or ARBs, hx of angioedema, use with aliskiren with diabetes	Potassium, renal function, requires renal adjustment
Beta Blockers	Zebeta 10 mg daily Toprol XL 200 mg daily Coreg IR 3.125 mg BID	Do not discontinue abruptly	Severe bradycardia, 2nd or 3rd degree heart block or sick sinus syndrome or cardiogenic shock	Heart rate (decrease dose if HR < 55 bpm), BP

Clinical Pearls

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Drug class	Target Dosing	Contraindications	Warnings	Monitoring Parameters
ARA	Spironolactone 25 mg daily Eplerenone 25 mg daily	Hyperkalemia, anuria, CrCl ≤ 30 mL/min, Addison's disease	Do not initiate tx in HF pts with K > 5 mEq/L or SCr > 2 mg/dL (females) or SCr > 2.5 mg/dL (males)	Potassium, renal function, fluid status
Hydralazine/Nitrate	Bidil 300 mg/day in divided doses Isosorbide mononitrate 120 mg in divided doses	Mitral valve rheumatic heart disease, CAD; for nitrates use with PDE-5 inhibitors and riociguat	Drug-Induced lupus erythematosus (hydralazine	Heart rate, Blood pressure
Digoxin	0.125-0.25 mg daily	Ventricular fibrillation	2nd/3rd degree heart block without a pacemaker, Wolff-Parkinson-White syndrome with Afib, electrolyte imbalances	Heart rate, ECG, electrolytes, renal function, dig level
Ivabradine	2.5-7.5 mg bid Target resting heart rate between 50-60 bpm	Acute decompensated HF, BP < 90/50 mmHg, sick sinus syndrome or 3rd degree AV block without pacemaker, resting heart rate <60 bpm, severe hepatic impairment	bradycardia, risk of QTc prolongation, fetal toxicity (females should use effective contraception	Heart rate, ECG
Loop Diuretics	Furosemide Bumetanide Ethacrynic Acid Torsemide	Anuria	Sulfa allergy (does not apply to ethacrynic acid), electrolyte abnormalities	Renal function, fluid status, electrolytes

References

1. Yancy, Clyde, et al. ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. *American College of Cardiology/American Heart Association.* 2017; 136-161.
2. Yancy, Clyde, et al. ACCF/AHA Guideline for the Management of Heart Failure. *American College of Cardiology/American Heart Association.* 2013; (62)147-239.
3. Heart Failure. *American Heart Association,* April 2019. www.heart.org/en/health-topics/heartfailure/
4. HFSA 2010 guideline on evaluation and management of patients with acute decompensated heart failure; 16(6): e134

Supplementary for HF medications

Drug	*Target Dosing*	*Safety/Side effects/Monitoring*
ACE inhibitors		**BBW:** can cause injury and death to the developing fetus **Contraindications:** History of angioedema, use with aliskiren in pts with diabetes, use within 36 hrs of Entresto **Warnings:** Angioedema, hyperkalemia, hypotension, renal impairment **Side effects:** Cough, dizziness, HA, rash **Monitoring:** BP, K, renal function, s/sx of HF and angioedema
Enalapril	10-20 mg PO BID	
Lisinopril	20-40 mg PO daily	
Quinapril	20 mg PO daily	
Ramipril	10 mg PO daily	
ARB		Same as above Less cough & angioedema, no washout period required with Entresto
Candesartan	32 mg PO daily	
Losartan	50-150 mg PO daily	
Valsartan	160 mg PO BID	
ARNI		
Sacubitril/Valsartan (Entresto), brand name only	200 mg PO BID = 97/103 mg sacubitril/valsartan	Same BBW as above **Contraindications:** Use with ACE inhibitors or ARBs, hx of angioedema, use with aliskiren with diabetes **Warnings**: Angioedema, hyperkalemia, hypotension, renal impairment **Side effects:** cough, dizziness **Monitoring:** requires renal adjustment*, BP, K, s/sx of HF
Beta Blockers		
Selective Beta Blocker		
Bisoprolol -not FDA approved for HF -benefit in clinical trials	10 mg PO daily	**BBW:** Do not discontinue abruptly **Contraindications:** Severe bradycardia, 2nd or 3rd degree heart block or sick sinus syndrome or cardiogenic shock **Warnings:** can worsen hyper or hypoglycemia and mask hypoglycemia symptoms, Use caution with asthma **Side effects:** decreases HR, hypotension, fatigue, dizziness,
Metoprolol Succinate extended release	200 mg PO daily	

		depression, increases triglycerides **Monitoring:** Heart rate (decrease dose if HR < 55 bpm), BP, s/sx of HF
Non-selective Beta Blocker and Alpha-1 blocker		
Carvedilol	Immediate release: ≤ 85 kg: 25 mg PO BID > 85 kg: 50 mg PO BID Controlled release: 80 mg PO BID	Same BBW as above **Contraindications:** Severe hepatic impairment **Warning:** Intraoperative floppy iris syndrome has occurred in cataract surgery patients who were on or were previously treated with an alpha-1 blocker **Notes:** Take with food (all forms) to decrease the risk of orthostatic hypotension, dosing conversions are not 1:1 (IR 3.125 mg BID = CR 10 mg daily)
Aldosterone Receptor Antagonist		
Spironolactone	25 mg PO daily or BID	**Contraindications:** Hyperkalemia, anuria, CrCl ≤ 30 mL/min, Addison's disease **Warnings:** Do not initiate tx in HF pts with K > 5 mEq/L or SCr > 2 mg/dL (females) or SCr > 2.5 mg/dL (males) **Side Effects:** Hyperkalemia, Increases SCr, dizziness, Spironolactone -> gynecomastia, breast tenderness, impotence Eplerenone -> Increases triglycerides **Monitoring:** BP, electrolytes (check K before starting & frequently thereafter), renal function, fluid status, s/sx of HF
Eplerenone	50 mg PO daily, titrate based on K level	
Hydralazine/Nitrate		
Hydralazine + isosorbide dinitrate (Bidil)	300 mg/day in divided doses	**Contraindications:** Mitral valve rheumatic heart disease, CAD; for nitrates use with PDE-5 inhibitors and riociguat

		Warnings: Drug-Induced lupus erythematotsus (hydralazine) **Side effects:** Headache, hypotension, reflex tachycardia, palpitations **Monitoring:** Heart rate, BP, s/sx of HF
Isosorbide mononitrate	120 mg daily in divided doses	**Contraindications:** Use with PDE-5 inhibitors and riociguat **Side effects:** Hypotension, headache, dizziness, flushing, tachyphylaxis (need 10-12 hour nitrate-free interval), syncope **Monitoring:** Heart rate, BP, s/sx of HF
Digoxin		
Digoxin	0.125-0.25 mg PO daily Therapeutic range for HF = 0.5-0.9 ng/mL Antidote: DigiFab	**Contraindication:** Ventricular fibrillation **Warnings:** 2nd/3rd degree heart block without pacemakers, Wolff-Parkinson-White syndrome **Side effects:** dizziness, mental disturbances, headache, N/V/D **Monitoring:** ECG, heart rate, BP, electrolytes, renal function, dig level **Toxicity:** Initial s/sx of toxicity are N/V, loss of appetite and bradycardia. Severe s/sx of toxicity include yellow/green vision, blurriness, halos (around lights/objects), abdominal pain, confusion, delirium, prolonged PR interval, arrhythmias
Ivabradine		
Ivabradine (Corlanor)	2.5-7.5 mg PO BID Target: resting heart rate between 50-60 bpm	**Contraindications:** Acute decompensated HF, BP < 90/50 mmHg, sick sinus syndrome or 3rd degree AV block without pacemaker, resting heart rate <60 bpm, severe hepatic impairment **Warnings:** bradycardia, risk of QTc prolongation, fetal toxicity (females should use effective contraception)

Supplementary for HF medications

		Side effects: Bradycardia, hypertension, Afib, luminous phenomena (seeing flashes of light) **Monitoring:** Heart rate, ECG, BP
Loop Diuretics		
Furosemide	20-40 mg PO daily or BID	**Contraindications:** Anuria **Warnings:** Sulfa allergy (does not apply to ethacrynic acid) **Side effects:** decrease in K, Na, Mg, Cl, Ca, Increase in HCO3, hyperuricemia, hyperglycemia, hypertriglyceridemia, orthostatic hypotension, photosensitivity, ototoxicity (more with ethacrynic acid) **Monitoring:** Renal function, fluid status, BP, electrolytes, audiology, s/sx of HF **Notes:** Take early in the day to avoid nocturia Oral equivalent dosing: furosemide 40mg = bumetanide 1 mg = torsemide 20mg = ethacrynic 50 mg
Bumetanide	0.5-1 mg PO daily or BID	
Torsemide	10-20 mg PO daily	
Ethacrynic Acid	50-200 mg PO daily or divided	