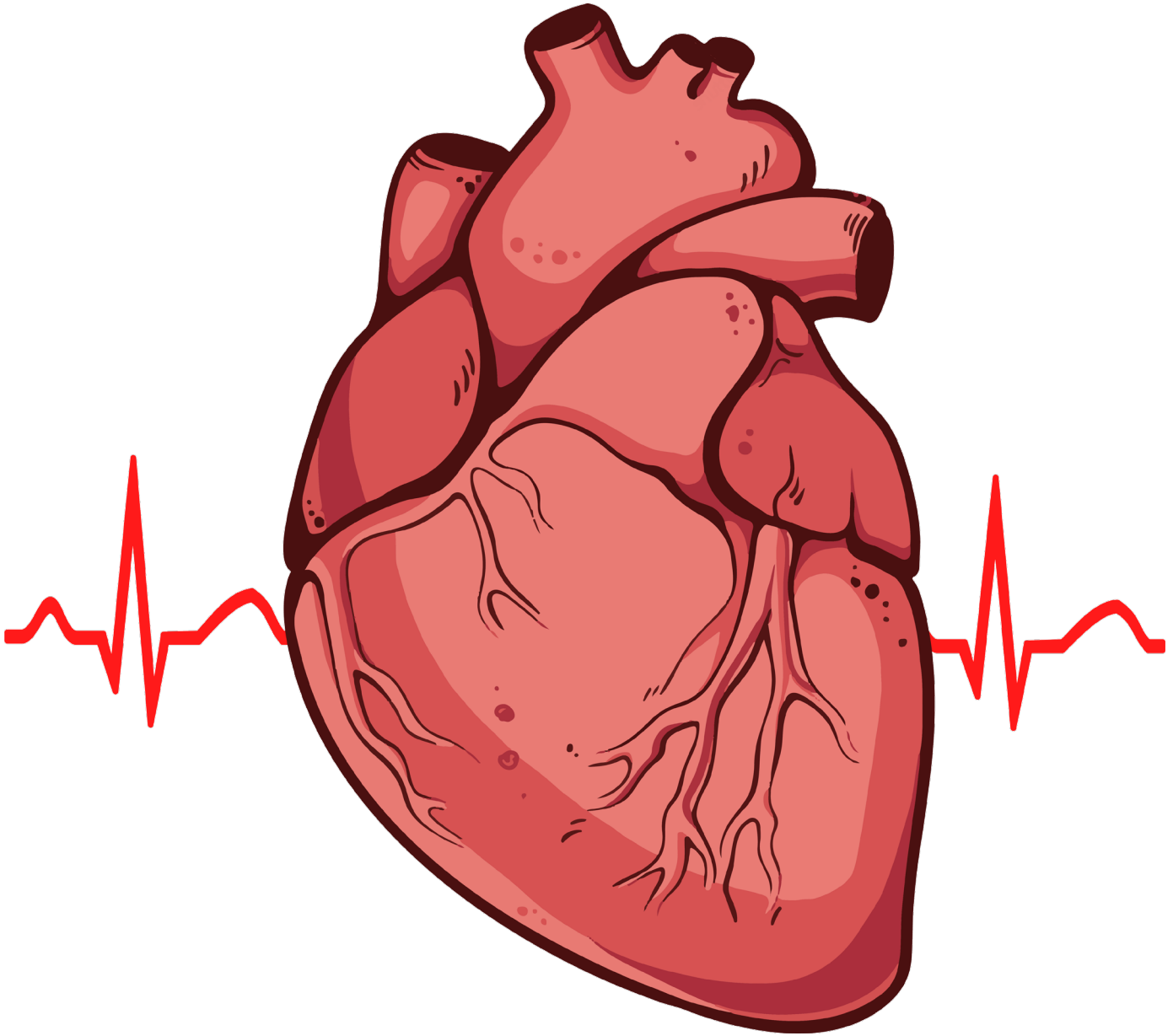
Heart Failure

Michigan Center for Clinical Systems Improvement (Mi-CCSI)

Disease State Management Module



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Objectives

At the conclusion of this presentation, the participant will be able to:

1. Describe the epidemiology, pathophysiology, and risk factors for heart failure.
2. Define diagnostic and classification criteria for heart failure.
3. Explain key aspects of the management of heart failure, including medications commonly used for treatment.
4. List medications that may precipitate or worsen heart failure symptoms.

Heart Failure (HF) Overview

- Complex clinical syndrome
- Can result from structural or functional cardiac disorder
- Impairs the ability of the ventricle to fill with or eject blood
- Characterized by specific signs and symptoms related to fluid retention and reduced perfusion
- Leading hospital discharge diagnosis in patients ≥ 65 years of age

Colucci S. Evaluation of the patient with suspected heart failure. In: UpToDate, Gottlief SS (Ed), UpToDate, Waltham, MA, 2019.
Page RL, et al. Drugs That May Cause or Exacerbate Heart Failure. A Scientific Statement From the American Heart Association. Circulation 2016;134:e32-69.

Epidemiology, Pathophysiology, and Risk Factors

Epidemiology

- 5.1 million people with HF in the United States in 2006
- Lifetime risk is approximately 20% at all ages above 40
- Prevalence increases dramatically with age
  - Incidence approximately doubles over each successive decade of life, rising more steeply with age in women than in men
- 25% higher prevalence for black patients
- Increase in the prevalence in the population over time
  - Patient population is getting older – people are living longer
- Trends for HF may be impacted by new diagnostic methodology, changes in hospital admission and reimbursement practices, increased awareness of the problem, and changes in the prevalence of comorbidities

Vasan RS, Wilson PWF. Epidemiology and causes of heart failure. In: UpToDate, Colucci WS (Ed), UpToDate, Waltham, MA, 2019.
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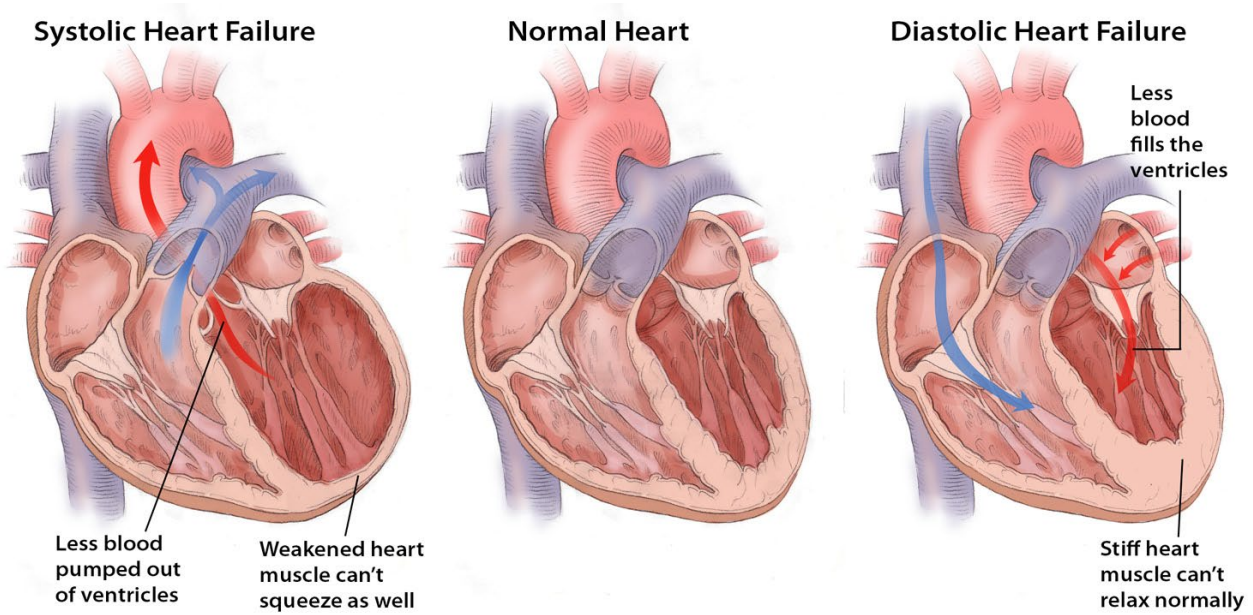
Pathophysiology



- Ventricular dysfunction resulting from:
  - Systolic dysfunction (problem with pushing blood out of the heart)
  - Diastolic dysfunction (problem with the heart filling with blood)

Colucci WS, Cohn JN. Pathophysiology of heart failure with reduced ejection fraction: Hemodynamic alterations and remodeling. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.
Image available from: https://www.emsworld.com/206842/ce-article-diagnosis-and-treatment-patient-heart-failure.

Pathophysiology

- Two distinct syndromes with unique management approaches

HF with preserved ejection fraction (HFpEF)	HF with reduced ejection fraction (HFrEF)

- Studies have identified a third group of patients with mid-range ejection fraction (HFmrEF)
  - Some experts treat these patients like HFrEF, while others treat these patients as borderline HFpEF.

Colucci WS, Cohn JN. Pathophysiology of heart failure with reduced ejection fraction: Hemodynamic alterations and remodeling. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.

Pathophysiology

HFpEF

- Normal LVEF (≥ 50%)
- Evidence of diastolic dysfunction
- Often a diagnosis of exclusion

HFmrEF

- LVEF 41-49%
- Share features of both HFrEF and HFpEF
- Limited data available
- Treat as HFrEF or as borderline HFpEF

HFrEF

- LVEF ≤ 40%
- More profound abnormalities in systolic function

LVEF = left ventricular ejection fraction

Vasan RS, Wilson PWF. Epidemiology and causes of heart failure. In: UpToDate, Colucci WS (Ed), UpToDate, Waltham, MA, 2019.

Risk Factors

- Coronary heart disease
- Cigarette smoking
- Hypertension
- Obesity
- Diabetes
- Valvular heart disease
- Socioeconomic deprivation

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Diagnosis and Classification

Diagnosis

- There is no single or specific diagnostic test for HF
  - The role of diagnostic tests is to help establish or confirm the diagnosis, assess the acuity/severity, and initiate an assessment of the potential cause
- Approach to diagnosis
  - History
  - Physical examination
  - Non-specific diagnostic tests

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History

- The history alone does not provide enough information to make a diagnosis of HF, but can provide information about acuity, cause, and rate of progression
- An assessment of past and present symptoms, especially variations with exertion, may point to root causes associated with heart failure

Reduced Cardiac Output	Excess Fluid Accumulation
• Fatigue • Weakness	• Shortness of breath (including while laying flat) • Swelling • Pain from hepatic congestion • Abdominal discomfort due to distention from ascites

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Physical Exam

- Assess for
  - Vital signs and appearance
  - Volume assessment
  - Heart sounds
- Finding may indicate evidence of the presence and extent of cardiac filling pressure elevation, volume overload, ventricular enlargement, pulmonary hypertension and reduction in cardiac output
- Presentation may vary by age

Colucci S. Evaluation of the patient with suspected heart failure. In: UpToDate, Gottlief SS (Ed), UpToDate, Waltham, MA, 2019.

Diagnostic Testing

- Electrocardiogram (ECG)
  - Most patients with HFrEF have a significant abnormality on ECG
  - May point to a specific factor that is causing or exacerbating HF
- Initial blood tests
  - Cardiac troponin T or I
  - Complete blood count (CBC)
  - Serum electrolytes, blood urea nitrogen, and creatinine
  - Liver function tests
  - Fasting blood glucose
  - BNP and NT-proBNP
  - Chest radiograph

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Differential Diagnosis

- Many of the symptoms and signs of heart failure are non-specific, so other potential causes should be considered.
  - Myocardial ischemia
  - Pulmonary disease
  - Sleep apnea
  - Depression
  - COPD
  - Venous thrombosis or insufficiency
  - Renal sodium retention
  - Drug side effects
  - Cirrhosis

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Modified Framingham Clinical Criteria for the Diagnosis of Heart Failure

Diagnosis requires that **two major OR one major and two minor** criteria cannot be attributed to another medical condition

Major	Minor
Paroxysmal nocturnal dyspnea	Bilateral leg edema
Orthopnea	Nocturnal cough
Elevated jugular venous pressure	Dyspnea on ordinary exertion
Pulmonary rales	Hepatomegaly
Third heart sound	Pleural effusion
Cardiomegaly on chest x-ray	Tachycardia (HR ≥ 120 beats/min)
Pulmonary edema on chest x-ray	Weight loss ≥ 4.5 kg in five days
Weight loss ≥ 4.5 kg in five days in response to treatment of presumed HF	

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Classification

- New York Heart Association (NYHA) Functional Class
  - Used to quantify the degree of functional limitation (e.g., impact on physical activity) imposed by HF
  - Places patients into one of four functional classes based on the degree of physical effort required to elicit symptoms
- American College of Cardiology Foundation/American Heart Association Guidelines
  - Emphasizes how far the disease has progressed
  - Defines approach to treatment based on current disease severity

Colucci WS. Determining the etiology and severity of heart failure or cardiomyopathy. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.

NYHA Functional Class

1

Patients with heart disease without resulting limitation of physical activity. Ordinary physical activity does not cause HF symptoms such as fatigue or dyspnea.

2

Patients with heart disease resulting in slight limitation of physical activity. Symptoms of HF develop with ordinary activity but there are no symptoms at rest.

3

Patients with heart disease resulting in marked limitation of physical activity. Symptoms of HF develop with less than ordinary physical activity but there are no symptoms at rest.

4

Patients with heart disease resulting in inability to carry on any physical activity without discomfort. Symptoms of HF may occur even at rest.

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American College of Cardiology Foundation/American Heart Association Guidelines

Stage A	• At high risk for HF but without structural heart disease or symptoms of HF.
Stage B	• Structural heart disease but without signs or symptoms of HF. This stage includes patients in NYHA functional class I with no prior or current symptoms or signs of HF.
Stage C	• Structural heart disease with prior or current symptoms of HF. This stage includes patients in any NYHA functional class (including class I with prior symptoms).
Stage D	• Refractory HF requiring specialized interventions. This stage includes patients in NYHA functional class IV with refractory HF.

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Pharmacologic Management

Approach to Management

- Differs based on the clinical scenario:
  - HFpEF – focus is on management of underlying conditions
  - HFmrEF – some experts treat these patients like they would treat HFrEF while other treat them as borderline HFpEF
  - HFrEF – specific pharmacologic therapy aimed at reducing symptom severity, improving health-related quality of life, and decreased rates of hospitalization and mortality
  - Acute decompensation – maintenance of oxygen status and management of volume overload and/or hemodynamic stability

Borlaug BA, Colucci WS. Treatment and prognosis of heart failure with preserved ejection fraction. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.
Vasan RS, Wilson PWF. Epidemiology and causes of heart failure. In: UpToDate, Colucci WS (Ed), UpToDate, Waltham, MA, 2019.
Colucci WS. Overview of the management of heart failure with reduced ejection fraction in adults. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.
Colucci WS. Treatment of acute decompensated heart failure: Components of therapy. In: UpToDate, Gottlieb SS, Hoekstra J (Ed), UpToDate, Waltham, MA, 2019.

HFpEF – Approach to Therapy

- Management of underlying conditions is the cornerstone of therapy
  - Hypertension, coronary artery disease, diabetes, kidney disease, etc.
- General principles
  - Control of pulmonary congestion and peripheral edema with diuretics
  - Treatment of systolic hypertension
  - Prevention of rapid heart rates
  - Coronary revascularization
- **Therapies typically used specifically in the management of HFrEF (e.g., beta blockers, angiotensin system blocking agents) have not been shown to decrease morbidity and mortality in HFpEF**

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HFrEF – Goals of Therapy / Approach to Care

- Goals
  - Reduce morbidity (e.g., reduce symptoms, improve health-related quality of life and functional status, and reduce hospitalizations)
  - Slow or reverse deterioration in myocardial function
  - Reduce mortality
  - Address the underlying cause and associated conditions
- Key components of care
  - Promotion of HF self-management
  - Appropriate and timely referrals
  - Appropriate systems of care (may include HF team)
  - Close coordination of ambulatory care following admissions

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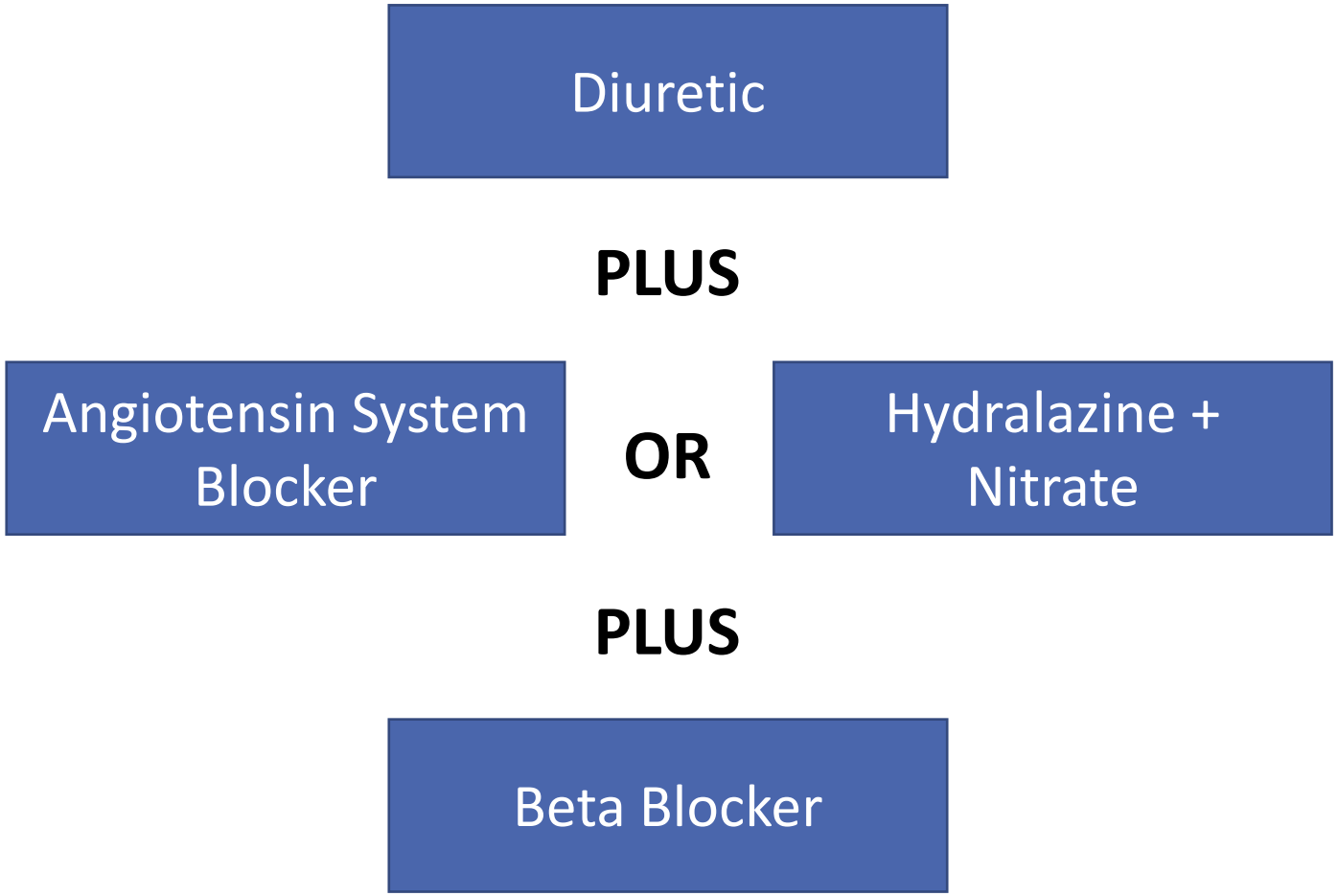
Meyer TE. Initial pharmacologic therapy of heart failure with reduced ejection fraction in adults. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.

HFrEF – **Initial** Pharmacologic Therapy



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HFrEF – Diuretic Therapy

- Utility
  - Management of volume status (e.g., overload)
  - Symptom relief
- Loop diuretics (furosemide, torsemide, bumetanide) are the agents of first choice
  - It is common to start with furosemide and switch to torsemide or bumetanide if the response is inadequate
  - Caution: hypokalemia
- Aldosterone antagonism (spironolactone or eplerenone) can be added to loop diuretics
  - Additional (modest) diuresis and minimization of potassium loss
  - Survival benefit (patients with systolic HF)

Meyer TE. Initial pharmacologic therapy of heart failure with reduced ejection fraction in adults. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.
Colucci WS, Sterns RH. Use of diuretics in patients with heart failure. In: UpToDate, Gottlieb SS, Emmett M (Ed), UpToDate, Waltham, MA, 2019.

HFrEF – Angiotensin System Blockers

Angiotensin System Blocker Type	Products	Efficacy	Notes on Dosing	Precautions
Angiotensin Receptor-Neprilysin Inhibitor (ARNI)	Sacubitril-valsartan (Entresto®)	Strongest	• Initial dose is based on whether the patient is already taking an ACEI or ARB (NOTE: The valsartan in this product is more bioavailable than the mono product) • Double the dose at 2-4 week intervals	Contraindications: • Pregnancy (all) • History of angioedema (sacubitril-valsartan or ACE)) • Severe hepatic impairment (sacubitril-valsartan only) Do not duplicate therapy with more than one angiotensin system blocker (observe 36 hour washout period when switching between agents) Avoid in combination with aliskiren (Tekturna)
Angiotensin Converting Enzyme Inhibitor (ACEI)	Captopil, enalopril, lisinopril, ramipril	Intermediate	• Start low and titrate to target maximum dose by doubling the dose at 1-2 week intervals	
Angiotensin Receptor Blocker (ARB)	Candesartan or valsartan usually preferred (may consider losartan)	Weakest		

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HFrEF – Beta Blockers

- For patients with no or minimal current evidence of volume overload
- Products that have been studied and proven efficacious
  - Carvedilol
  - Extended release metoprolol succinate
  - Bisoprolol
- Commonly initiated soon after the patient has started an angiotensin system blocker
- Very low doses to start – double every 2 weeks or more until target dose is achieved or side effects become limiting
- Benefit of therapy is dose dependent, so every effort should be made to achieve target doses

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HFrEF – Hydralazine + Nitrate

- Concurrent use of any form of phosphodiesterase-5 inhibitor therapy (e.g., sildenafil, vardenafil, tadalafil) with a nitrate is contraindicated
- Isosorbide dinitrate is preferred, but some clinicians use mononitrate formulation for compliance purposes

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HFrEF – **Secondary** Pharmacologic Therapy

- Indicated **in addition to** continuation of initial pharmacologic therapy
- In contrast to initial therapy (which includes three types of drugs in almost all cases), second therapy is recommended for patients who meet agent-specific criteria
  - Number and type of secondary agents prescribed depends on patient characteristics and response to initial pharmacologic therapy

Colucci WS. Secondary pharmacologic therapy in heart failure with reduced ejection fraction (HRfEF) in adults. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA, 2019.

HFrEF – **Secondary** Pharmacologic Therapy

If…	Then consider:
• Persistent symptoms on initial therapy (at maximum tolerate doses) and LVEF ≤ 35% • The patient is post MI with LVEF ≤ 40%, is already receiving therapeutic doses of an an ARB and has symptomatic HF or DM	Aldosterone antagonism (spironolactone preferred over eplerenone due to cost)
• LVEF ≤ 35%, resting HR ≥ 70 bpm, and on maximum tolerated dose of a beta blocker (or beta blocker contraindication)	Ivabradine (Corlanor)
• Persistent symptoms despite initial therapy plus aldosterone antagonism plus cardiac resynchronization therapy	Dapagliflozin* (Farxiga) or hydralazine plus nitrate (if not already prescribed) *check for contraindications prior to initiation of dapagliflozin
• Persistent moderate to severe symptoms on initial therapy plus all other indicated secondary therapies	Digoxin

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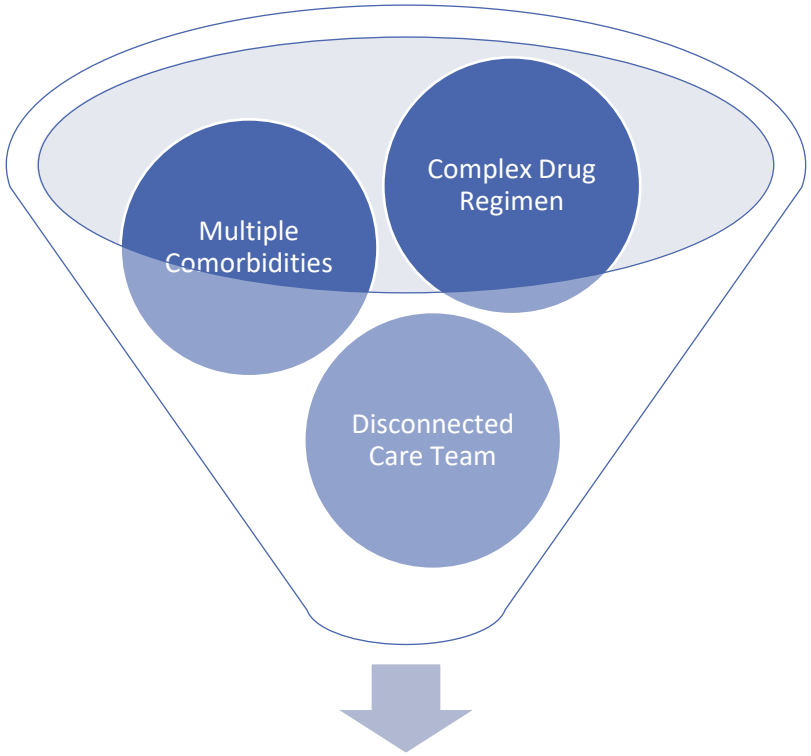
Medications to Avoid

Drug-Induced HF Exacerbation



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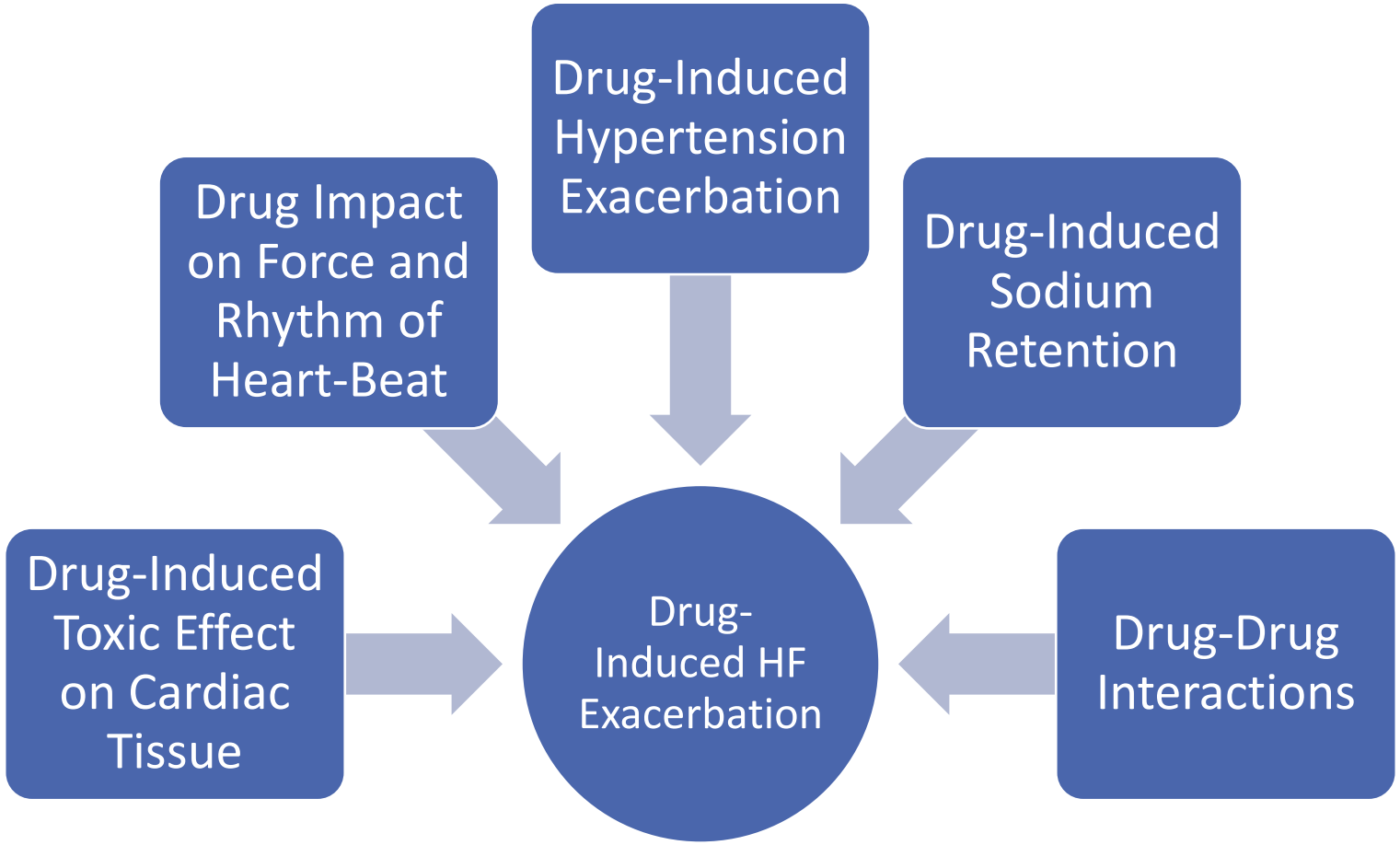

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NSAIDs

- May trigger HF by:
  - Facilitating sodium and water retention
  - Blunting response to diuretics
  - Increasing systemic vascular resistance
- One study showed a 10-fold increase in the risk of HF recurrence in patients that had filled at least one prescription for an NSAID since their HF diagnosis
- The American College of Cardiology Foundation/American Heart Association guidelines recommend NSAIDs be avoided or withdrawn whenever possible

Page RL, et al. Drugs That May Cause or Exacerbate Heart Failure. A Scientific Statement From the American Heart Association. Circulation 2016;134:e32-69.

Medications for the Treatment of Diabetes

- Metformin
  - Current ADA standards allow for use in patients with normal renal function
  - Avoid in patients with unstable HF or in patients hospitalized with HF
- Thiazolidinedione drug class
  - Rosiglitazone (Avandia) and pioglitazone (Actos)
  - Avoid in patients with symptomatic HF
- Dipeptidyl Peptidase-4 (DPP4) Inhibitors
  - Sitagliptin (Januvia), saxagliptin (Onglyza), alogliptin (Nesina), linagliptin (Tradjenta)
  - Potential for increased risk of HF hospitalization

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Medications for the Treatment of Hypertension (HTN)

- α-blockers
  - Prazosin and doxazosin
  - Increased risk for HF
- Calcium channel blockers
  - Dihydropyridine (DHP) – amlodipine and nifedipine
    - Negative inotropic effects offset by vasodilation
    - Some studies have shown negative effects in patients with HF receiving nifedipine
    - Amlodipine appears to be safe patients with HF and can be used if treatment is necessary for an indication other than HF
  - Non-DHP – diltiazem and verapamil
    - Negative inotropic effects only

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Miscellaneous

Anesthesia Medications

- Most anesthesia medications interfere with cardiovascular performance in some way
- Studies show an increase in the risk of operative mortality and greater risk of 30-day all-cause readmission for patients with HF compared to patients without HF or coronary artery disease

Antiarrhythmic Medications

- Most medications in this class have some negative inotropic activity as a component of their mechanism of action and thus, have the potential to precipitate HF
- Patients with HF may also be more likely to develop side effects (e.g., Torsades de Pointes) or drug toxicity due to impaired elimination with these agents
- Amiodarone is generally considered the preferred treatment for arrhythmia in patients with HF

Antifungals

- Itraconazole may cause cardiotoxicity and should be avoided in patients with a history of HF

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Miscellaneous

Trimethoprim-Sulfamethoxazole (TMP-SMX)

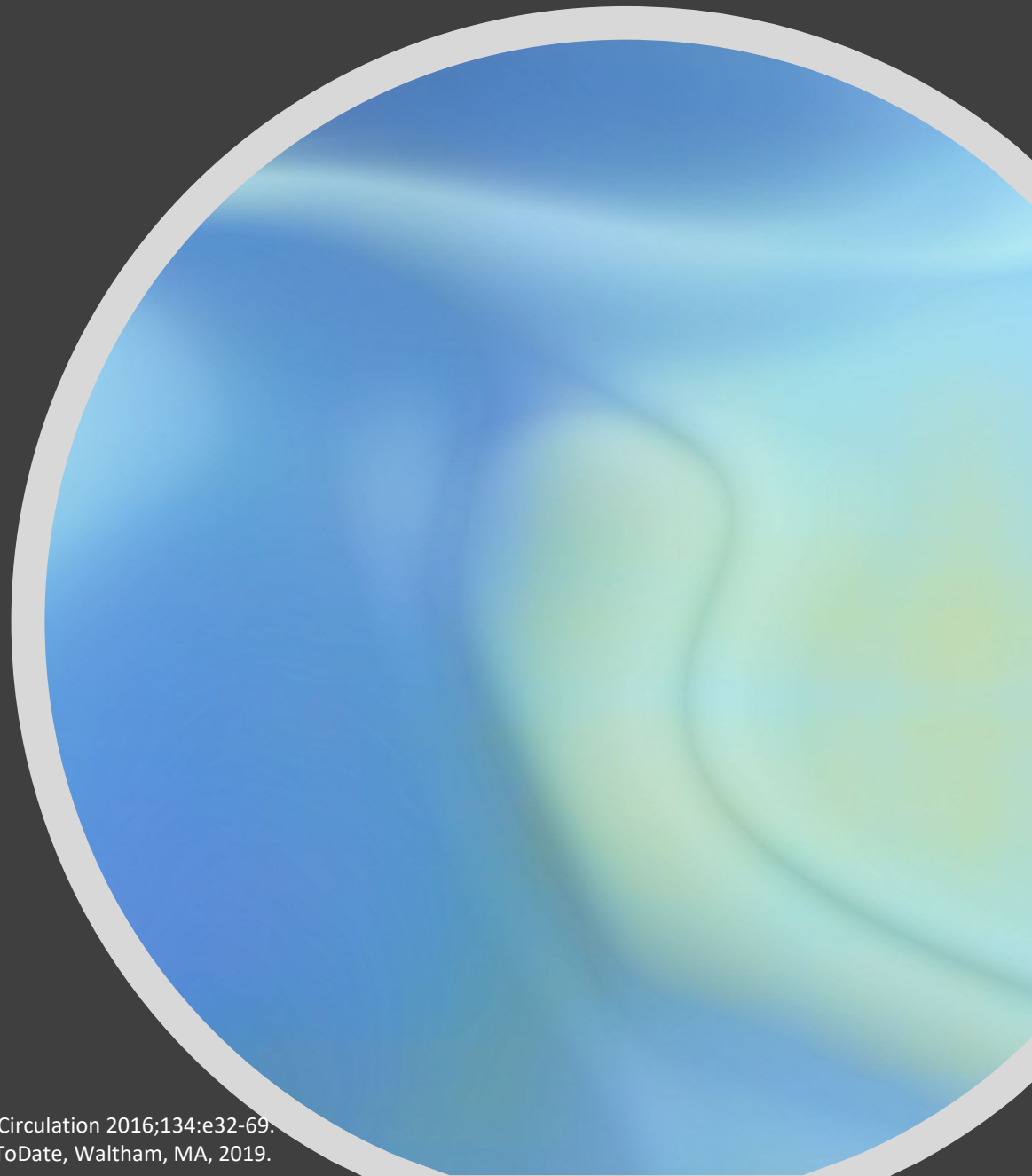
- Should be avoided or used with caution in patients taking an ACEI, ARB, or androgen antagonist due to an elevated risk of hyperkalemia, acute kidney injury, and death

Anti-Cancer Therapy

- Cardiotoxic chemotherapy agents (e.g., anthracyclines [doxorubicin], alkylating agents [cyclophosphamide], etc) are of particular concern

Stimulants

- Generally not used in patients with HF due to case reports of sudden death, acute coronary syndrome, MI, stroke, and cardiomyopathy in addition to the well-established risk of stimulation



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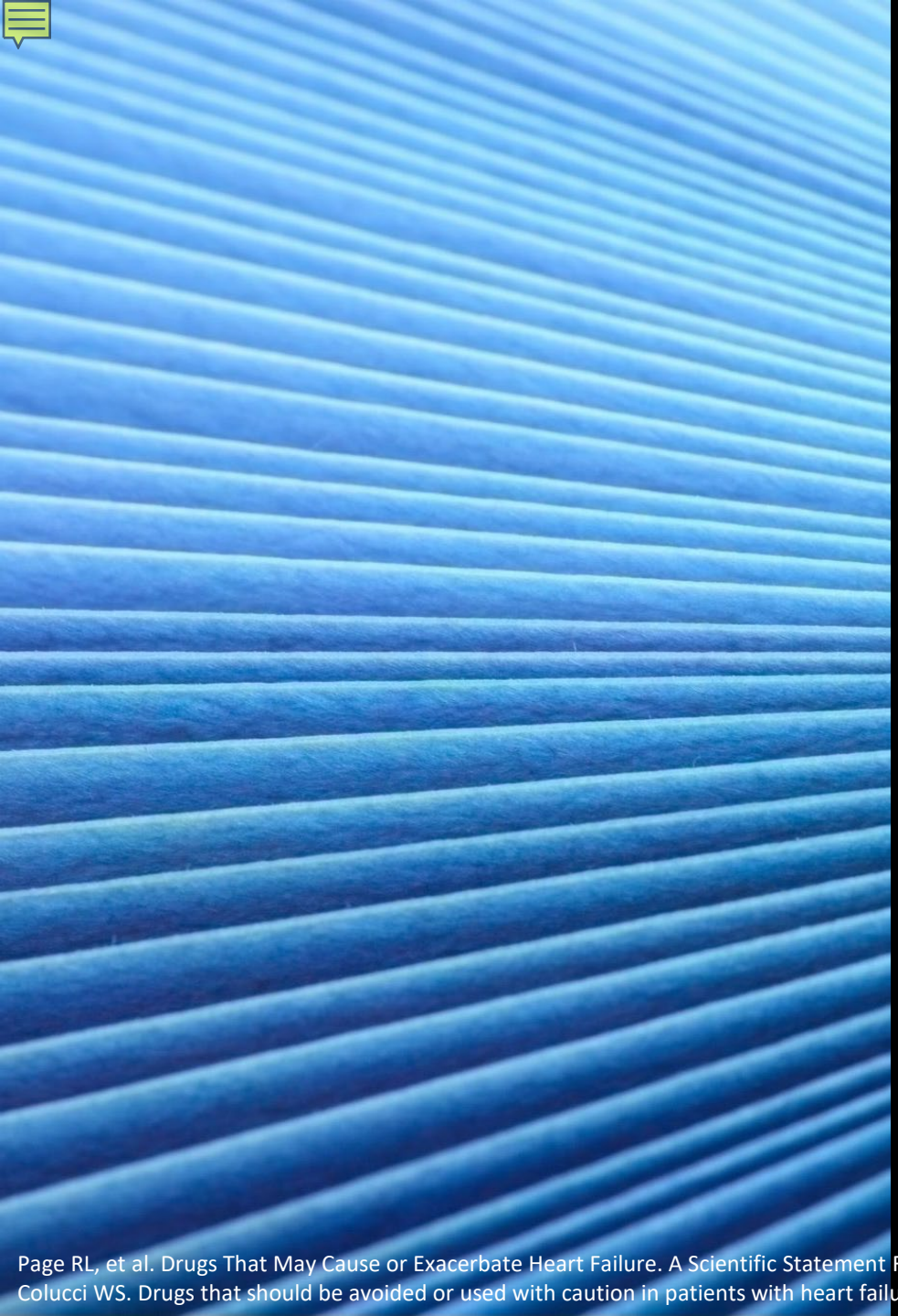

Miscellaneous

Phosphodiesterase (PDE)-5 Inhibitors	Sildenafil, vardenafil, and tadalafil are all contraindicated with any form of nitrate therapy and are potentially hazardous in patients with HF who have borderline low blood pressure and/or low volume status Lower pulmonary and systemic arterial pressure through vasodilation.
Androgens	FDA-approved labeling for the testosterone patch includes a warning about the potential for edema in patients with pre-existing cardiac, renal, or hepatic disease The 2010 Endocrine Society guidelines recommended against testosterone therapy in patients with uncontrolled or poorly controlled HF
Tumor Necrosis Factor (TNF)-α Inhibitors	May be associated with new onset or worsening of pre-existing HF
"Natural" Products	Potential that products may include substances known to be harmful to patients with HF (e.g., ephedra) Risk/benefit profiles are not always clear

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A Note on Medication Reconciliation

- Sometimes referred to as “medication history”
- Collection of accurate information about all medications (prescription and non-prescription) the patient is taking and how they are taking them
  - Name
  - Dosage
  - Frequency
  - Route
- As many as 50% of medication errors and up to 20% of adverse drug events in the hospital setting are due to poor communication of medical information at transition points

Midelfort L. Medication Reconciliation Review. Institute for Healthcare Improvement. Available from: http://www.ihi.org/resources/Pages/Tools/MedicationReconciliationReview.aspx. Accessed March31, 2020.

Tips for an Impactful Medication Reconciliation

- Invest the time to ensure understanding and take advantage of a teaching opportunity
- Let the patient take the lead on information sharing
  - Instead of “Is furosemide your diuretic?”
    - Ask: ”What do you take furosemide for?”
  - Instead of: “Still taking 20 mg of furosemide in the morning?”
    - Ask: ”What dose of furosemide are you taking?” Followed by: “When do you take it?”
- Fill in knowledge gaps as they present themselves
  - “The name of your diuretic is furosemide. The brand name is Lasix.”
- Use the medication reconciliation as an opportunity to optimize care
  - “You said you’re taking two furosemide tablets every morning. The directions I have here say it’s prescribed as one tablet once a day. Can you help me understand why you’re taking two tablets at a time?
- Encourage patients to keep an accurate and up-to-date list of medications with them at all times

Summary

Final Thoughts

- HF is a complex clinical syndrome.
- History, physical examination, and non-specific diagnostic tests can guide diagnosis of HF.
- The approach to management of HF differs based on the clinical scenario.
- An accurate medication history is essential to ensuring patients do not experience adverse drug reactions that precipitate HF or worsen symptoms.

Questions?