Drug therapy of congestive heart failure (Part I)

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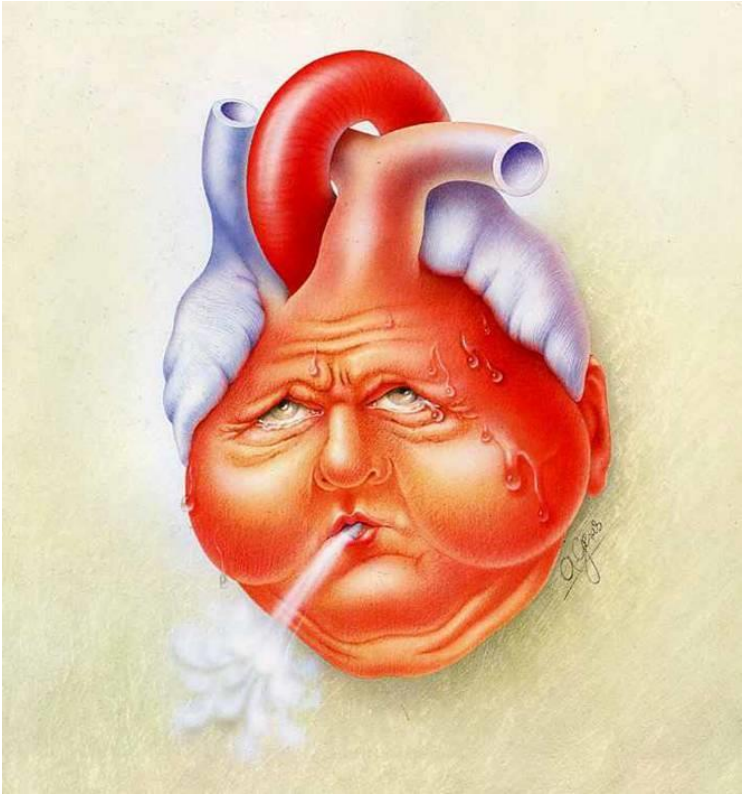
Jordan 2024/ 2025



Objectives

- 1- List major drug groups used in treatment of heart failure
- 2- Describe the clinical implications of diuretics, vasodilators, ACE inhibitors and other drugs that lack positive inotropic effects in heart failure
- 3- Explain mechanism of action of digitalis and its major effects
- 4- Explain the nature and mechanism of digitalis toxic effects
- 5- Ivabredine and ARNIs
- 6- Describe the strategies used in the treatment of heart failure

What is heart failure?

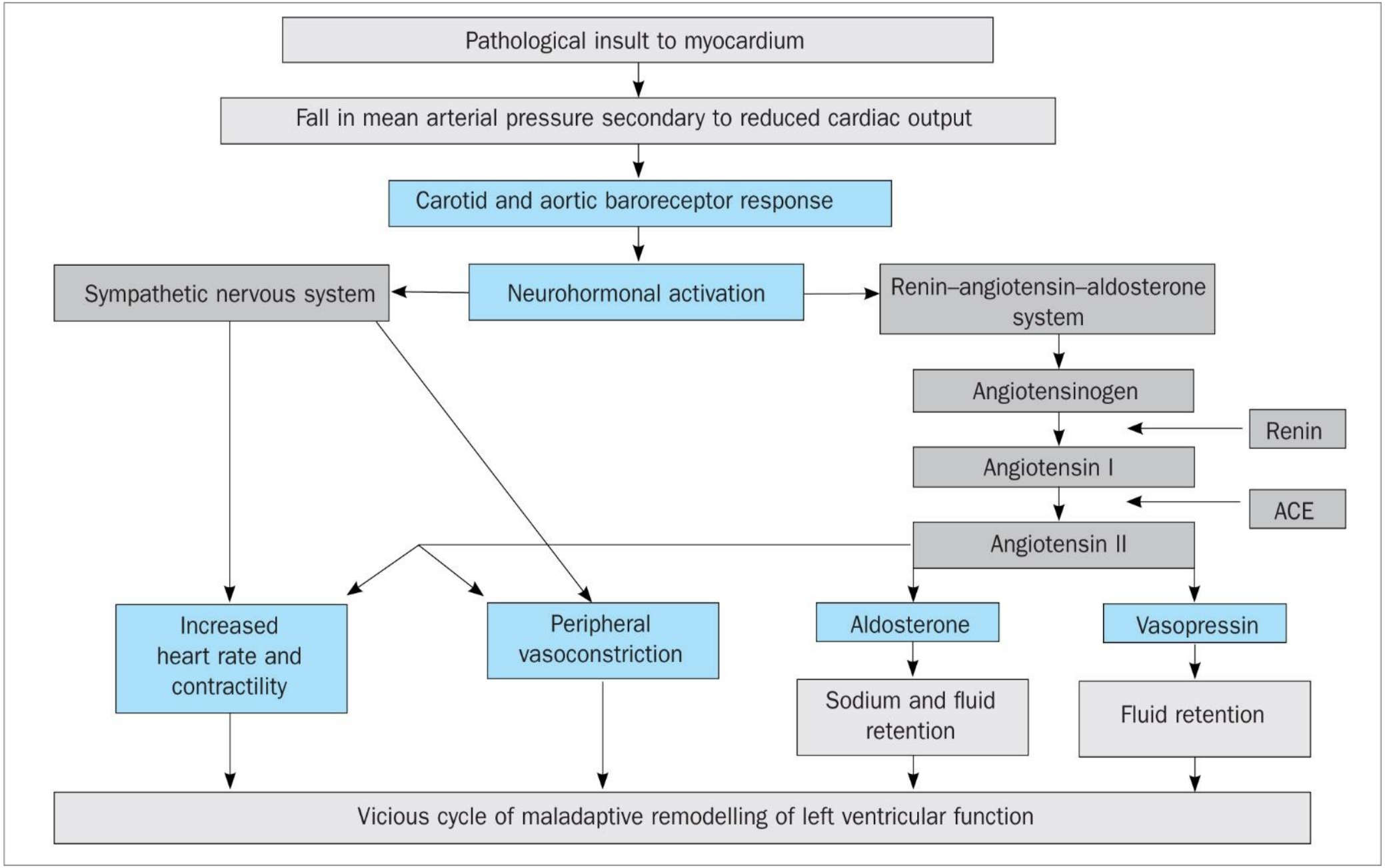
- **Inability of the heart to maintain sufficient cardiac output inspite of good venous return.**
- Heart failure (HF) is a **complex clinical syndrome (not a disease)** that can result from any **structural** or **functional** cardiac disorder that impairs the ability of the ventricle to **fill** with or **eject** blood.
- **Types of HF according to ejection fraction (EF = SV/EDV):**
- **Systolic HF: HFrEF**
- **Diastolic HF: HFpEF**

Causes of HF (classification)

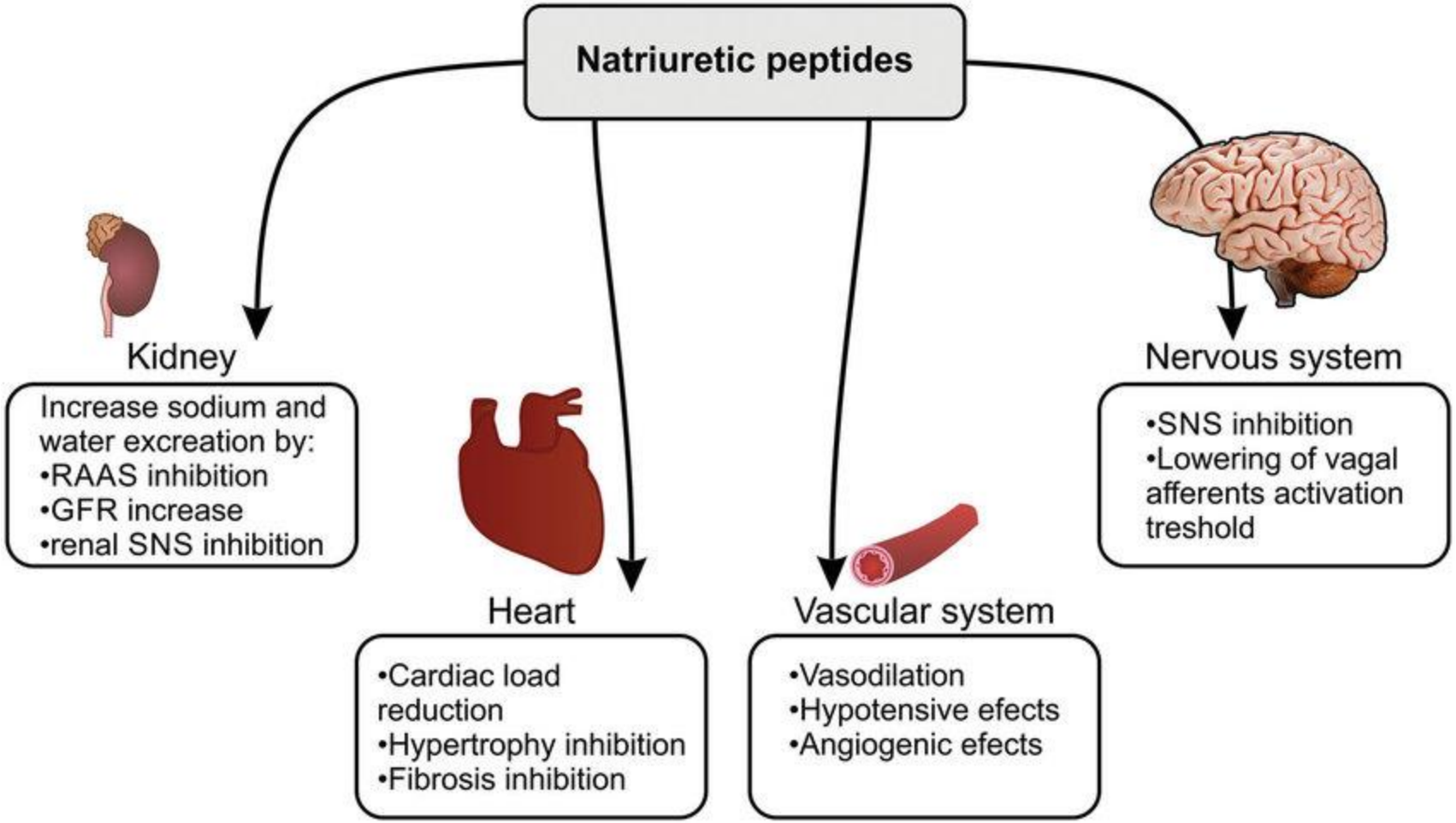
Etiology	Left-sided HF	Right-sised HF
Increased preload	AR, MR, VSD, hyperdynamic circulation	TR, PR, VSD, hyperdynamic circulation
Increased afterload	AS, Aortic cortication, systemic hypertension	PS, Pulmonary hypertension, COPD
Decreased contractility	Coronary ischemia, cardiomyopathy, myocarditis	

Drug-induced HF

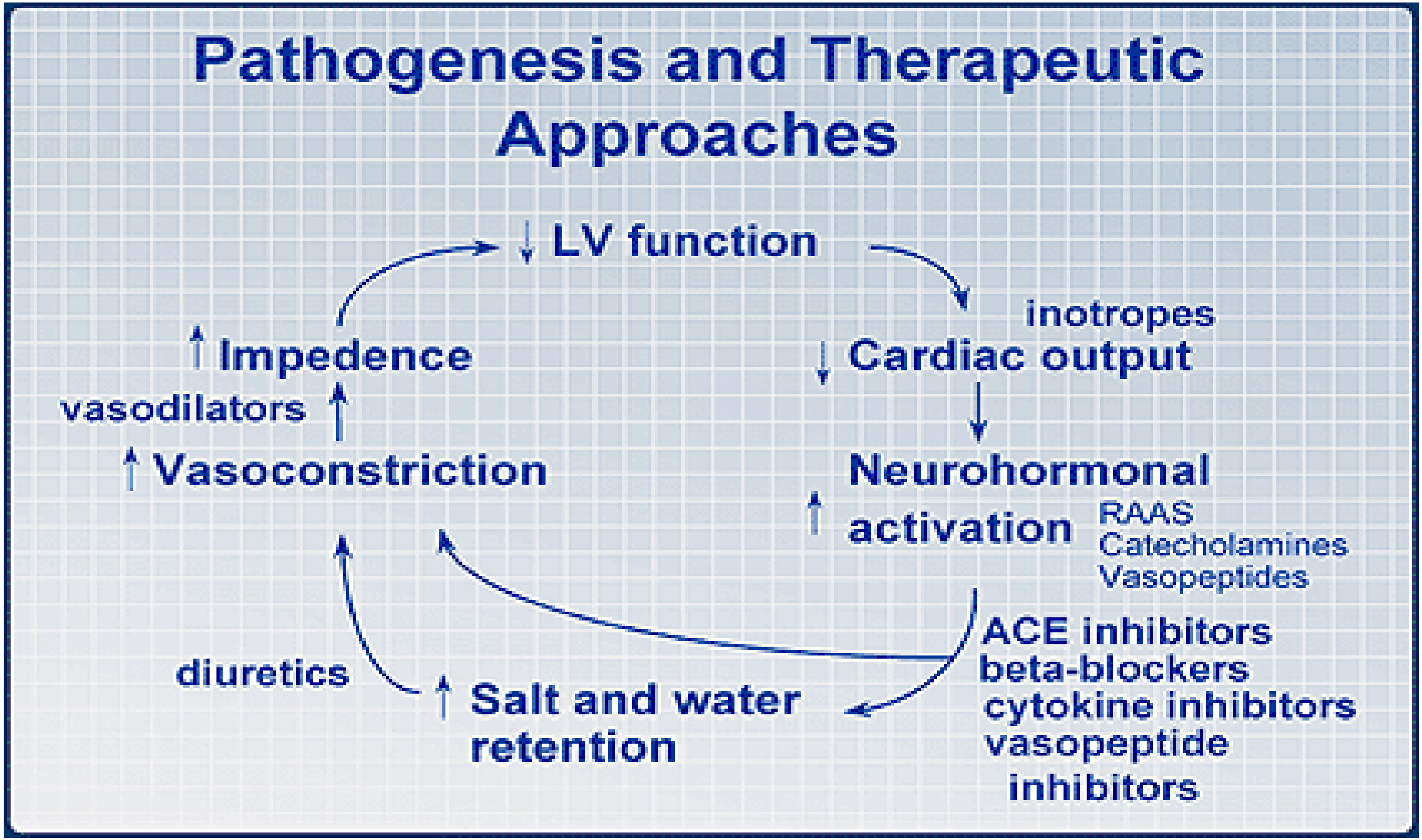
- Alcoholism and drug abuse
- Calcium channel blockers
- Potassium supplements and other drugs associated with hyperkalemia
- Antiarrhythmic agents
- Androgens
- Sodium-containing preparations
- TNF-alpha inhibitors


Pathological insult to myocardium
Fall in mean arterial pressure secondary to reduced cardiac output
Carotid and aortic baroreceptor response
Sympathetic nervous system
Neurohormonal activation
Renin–angiotensin–aldosterone system
Angiotensinogen
Renin
Angiotensin I
ACE
Angiotensin II
Increased heart rate and contractility
Peripheral vasoconstriction
Aldosterone
Vasopressin
Sodium and fluid retention
Fluid retention
Vicious cycle of maladaptive remodelling of left ventricular function

Activation of natriuretic peptide system in HF

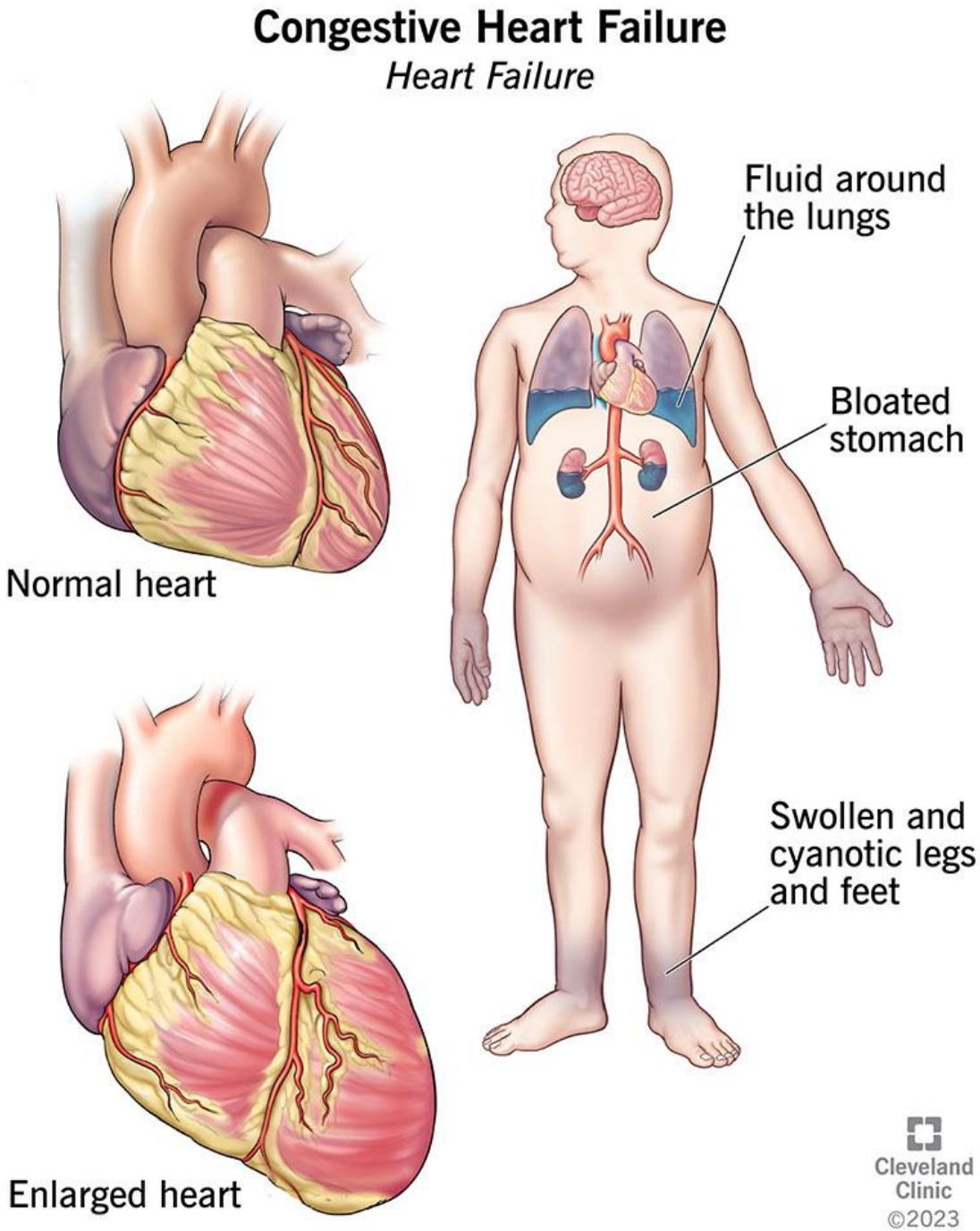


Pathogenesis and Therapeutic Approaches



Diagnostic Criteria Of HF

- **Triade of:**
- **Symptoms: shortness of breath, physical fatigue**
- **Signs: tachycardia, tachypnea, edema**
- **Evidence of structural or functional abnormality of heart, example: cardiomegaly**


Congestive Heart Failure
Heart Failure
Normal heart
Fluid around the lungs
Bloated stomach
Swollen and cyanotic legs and feet
Enlarged heart
Cleveland Clinic
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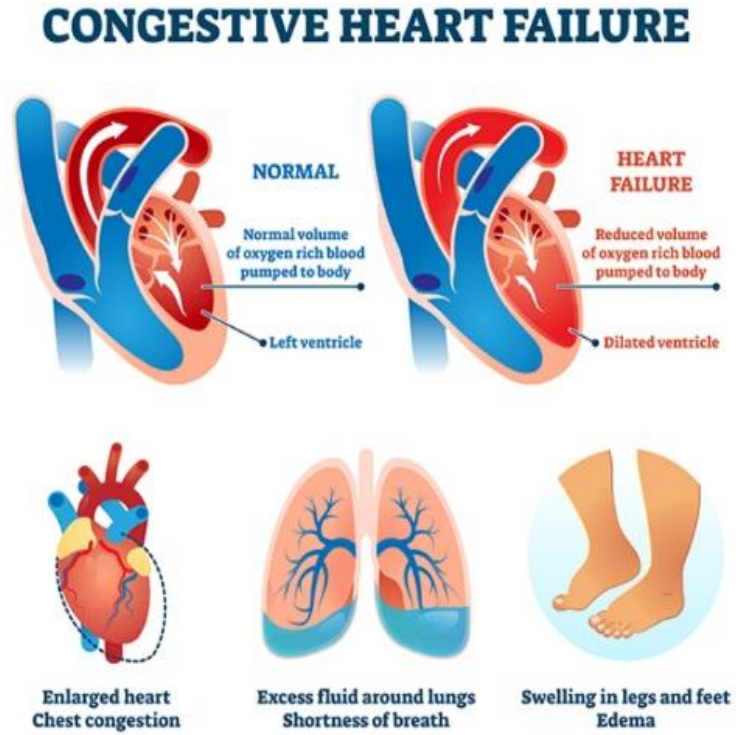
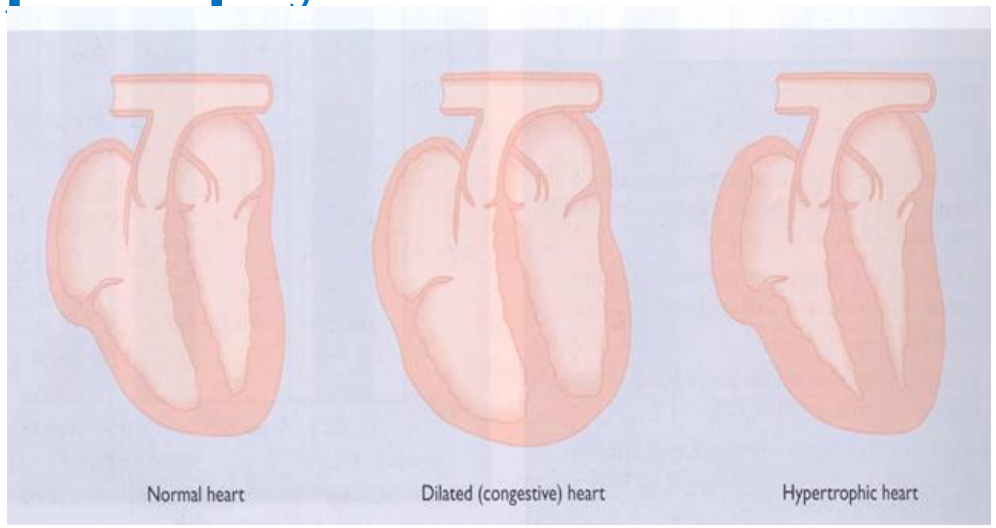
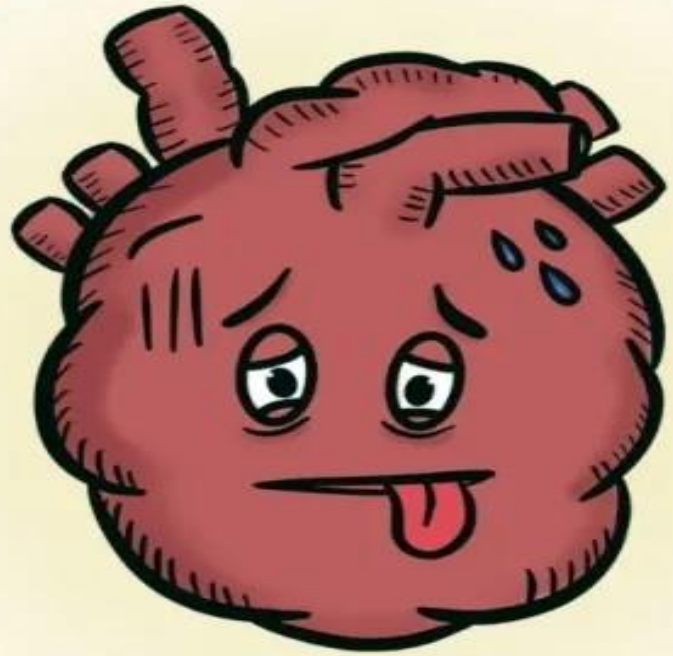

CONGESTIVE HEART FAILURE
NORMAL
Normal volume of oxygen rich blood pumped to body
Left ventricle
HEART FAILURE
Reduced volume of oxygen rich blood pumped to body
Dilated ventricle
Enlarged heart
Chest congestion
Excess fluid around lungs
Shortness of breath
Swelling in legs and feet
Edema

Factors Affecting Cardiac Output And Heart Failure

- Cardiac contractility
- Preload: volume overload: cardiac dilatation
- Afterload: tension overload: cardiac hypertrophy
- Heart rate: tachycardia

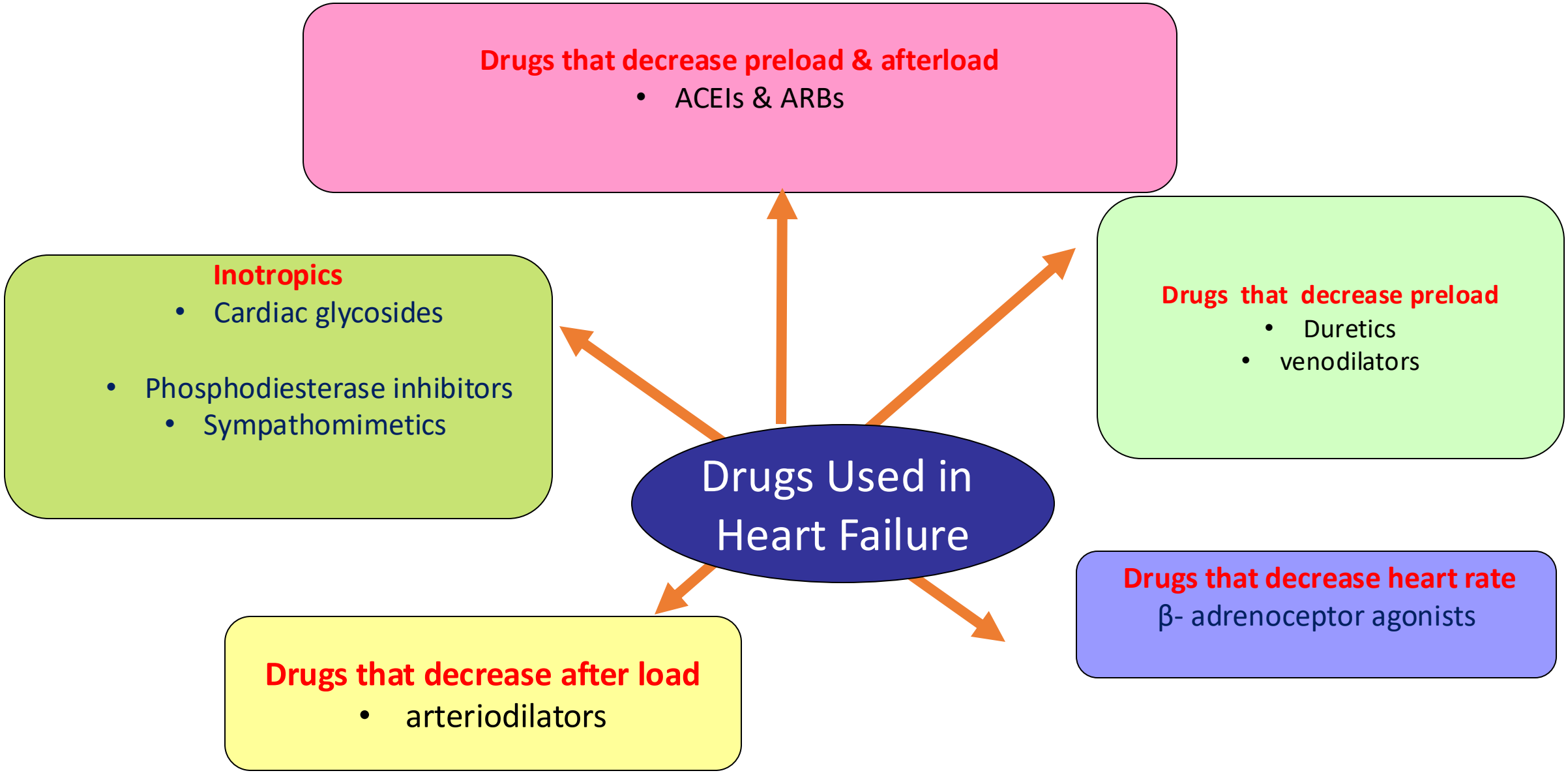


HEART FAILURE



DRUGS

@MEMORYPHARMSTUDY


Drugs that decrease preload & afterload
• ACEIs & ARBs
Inotropics
• Cardiac glycosides
• Phosphodiesterase inhibitors
• Sympathomimetics
Drugs that decrease preload
• Duretics
• venodilators
Drugs Used in Heart Failure
Drugs that decrease after load
• arteriodilators
Drugs that decrease heart rate
β- adrenoceptor agonists

Drug therapy of HF

- **First line drugs for HF with reduced ejection fraction (HFrEF): ACEIs (ARBs), ARNI and B-blockers**

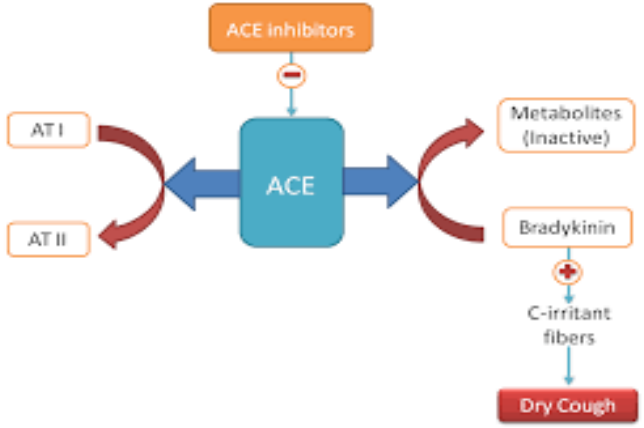
- **First line drugs for HF with volume overload (edema and congestion):**
- **Diuretics and positive inotropic drugs**

ACE Inhibitors & Angiotensin Receptor Blockers

- **Are now considered as first –line drugs for heart failure therapy**
- **ACEIs**: Captopril, enalapril, ramipril, lisinopril
- **AT1 receptor blockers**: Losartan , candesartan, valsartan, telmisartan
- **Effects of converting enzyme inhibitors (ACEIs)**
- **↓angiotensin II and aldosterone leading to (inhibition of RAAS):**
- **1- ↓Peripheral resistance (Afterload)**
- **2- ↓Venous return (Preload)**
- **3- ↓cardiac remodeling →↓mortality rate**

Adverse effects of ACEIs

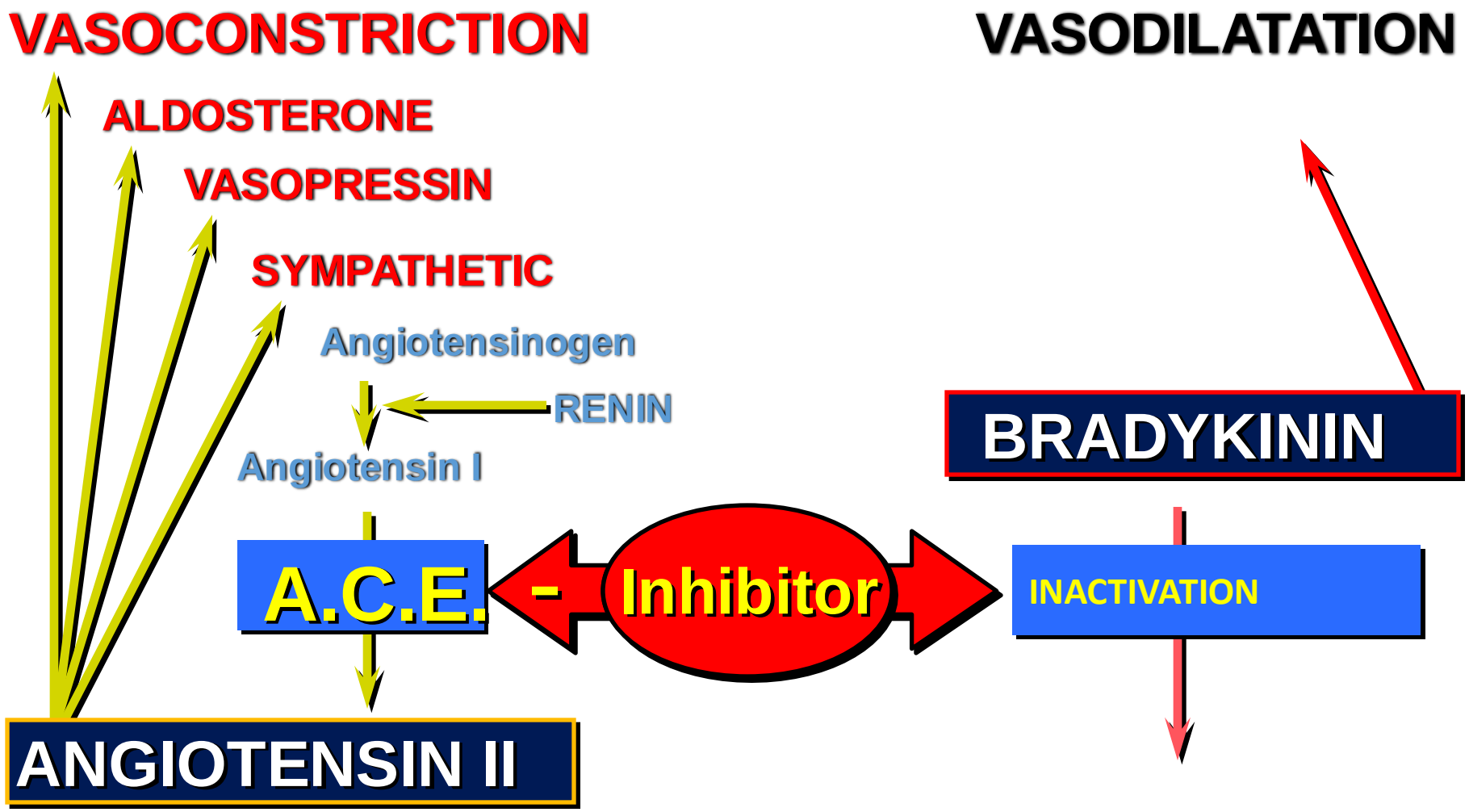
- 1- Dry cough: 10%
- 2- Headach
- 3- Hypotension
- 4- Angioedema: rare



- Dry cough and angioedema are due to elevated plasma bradykinins.
- **ARBs**: less effective and typically used in patients who can not tolerate ACEIs.

Angiotensin converting enzyme inhibitors

MECHANISM OF ACTION



B-adrenoceptor Blockers In Heart Failure

- **Benefits in HF:**
- **Reduce catecholamine myocyte toxicity (remodeling)**
- **Inhibit renin release**
- **Decrease heart rate**
- **Decrease mortality rate**
- **Adverse effects:**
- **1- Hypotension 2- Rare but sever: bradycardia, A-V block**
- **Contraindications in HF:**
- **1- Beta blockers in large dose**
- **2- Acute HF**
- **Beta blockers approved in HF (stable cases, in small doses):**

1- Bisoprolol

2- Metoprolol

3- Carvedilol (additional VD)

Vasodilators

- **Indications of vasodilators in HF:**
- **patients who can not tolerate ACEIs, ARBs**
- **Arteriolodilators**: hydralazine , minoxidil, nicorandil
- **Hydralazine:**
- Direct acting vasodilator
- Reduces both right and left ventricular **afterload** by reducing pulmonary and systemic vascular resistance
- **Results in increased cardiac output**
- Reduces renal vascular resistance and increases renal blood flow
- Increases renal blood flow more than any other vasodilator except ACE inhibitors
- **Preferred drug in CHF (ACE intolerant) with renal impairment**

Venodilators: nitrates

- **How nitrates are helpful in CHF?**
- Reduce preload
- Coronary artery dilatation- reperfusion
- **Given alone their efficacy is limited due to**:

✓limited effect on systemic resistance

✓Nitrate tolerance

- **Often combined with other vasodilators for better results:**
- **Hydralazine/isosorbide dinitrate(Bidil)** is a fixed-dose combination: improve motrality in some cases of HF.

Diuretics

- **Among First-line therapy of heart failure**
- **Role in HF:**
- 1- Remove the signs and symptoms of volume overload (pulmonary congestion/ peripheral edema).
- 2- Reduce salt and water retention (Natriuresis)→↓ventricular preload and venous pressure.
- 3- Reduction of cardiac size →improve cardiac performance
- Loop diuretics – **furosemide:** most powerful and used for most patients
- Thiazide Diuretics- less effective but indicated in patients with hypertension and mild fluid retention: chlorthiazide, hydrochlorthiazide
- **Side effects of diuretics**: metabolic alkalosis, electrolyte imbalance (hypokalemia) and hypovolemia
- **N.B. Diuretics do not improve the mortality rate in patients**

K^+ Sparing Diuretics (aldosterone antagonists)

•Spironolactone, triamterene, amiloride are weak diuretics-for achieving volume reduction with minimal K^+ loss

•**Advantages of spironolactone**:

•1- Preserve K: prevents hypokalemia

•2- Decreases mortality in cases of sever HF

•3- Reverse aldosterone-induced remodeling

•Dose: one tablet lasilactone 50 mg in the morning 5 days a week.

To be continued 💚