

University of Anbar  
College of Medicine  
Department of Pharmacology



# Heart Failure

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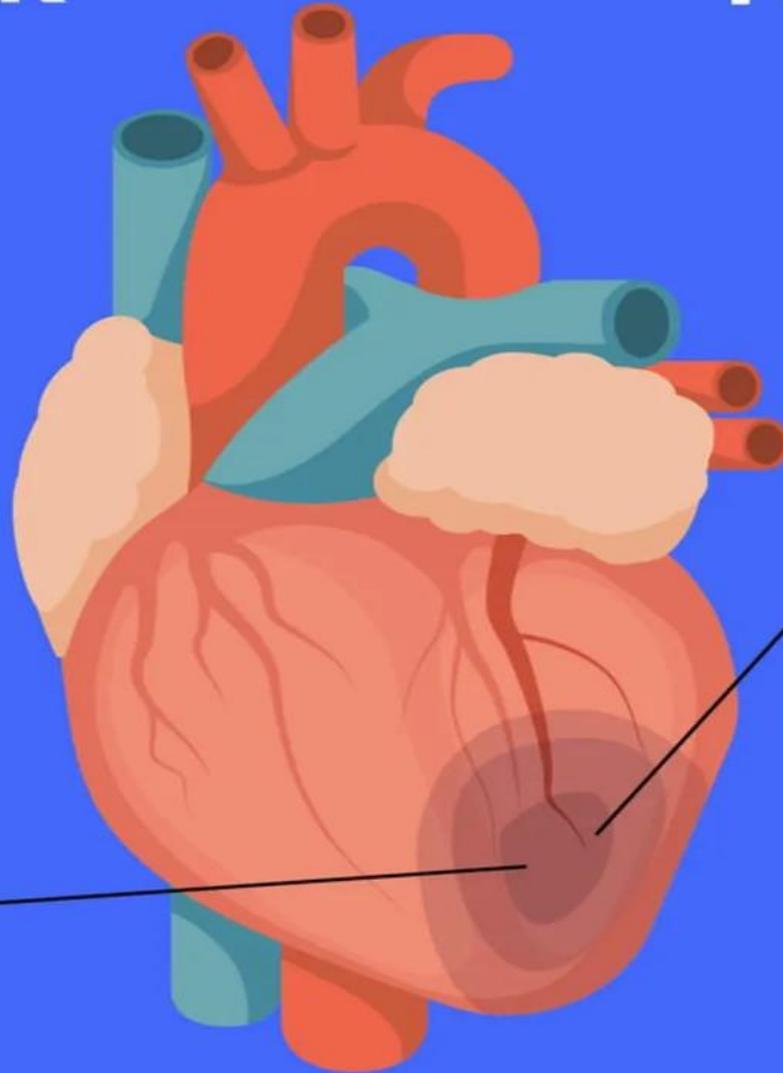
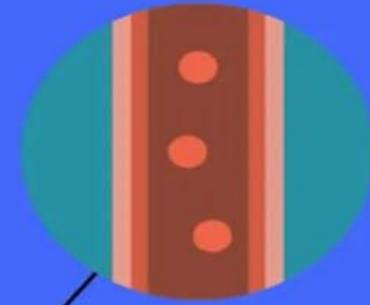
# Heart Attack

Blood flow to the heart gets cut off due to coronary artery blockage



# Heart Failure

Chronic, progressive disease in which the heart can't pump enough blood



# Heart Failure

The inability of the heart to maintain an adequate cardiac output sufficient to meet the metabolic demands of the body.

*The most common reason for hospitalization in adults >65 years old*

## Risk Factors for Heart Failure

- ✓ Coronary artery disease
- ✓ Hypertension (LVH)
- ✓ Valvular heart disease
- ✓ Alcoholism
- ✓ Infection (viral)
- ✓ Diabetes
- ✓ Congenital heart defects

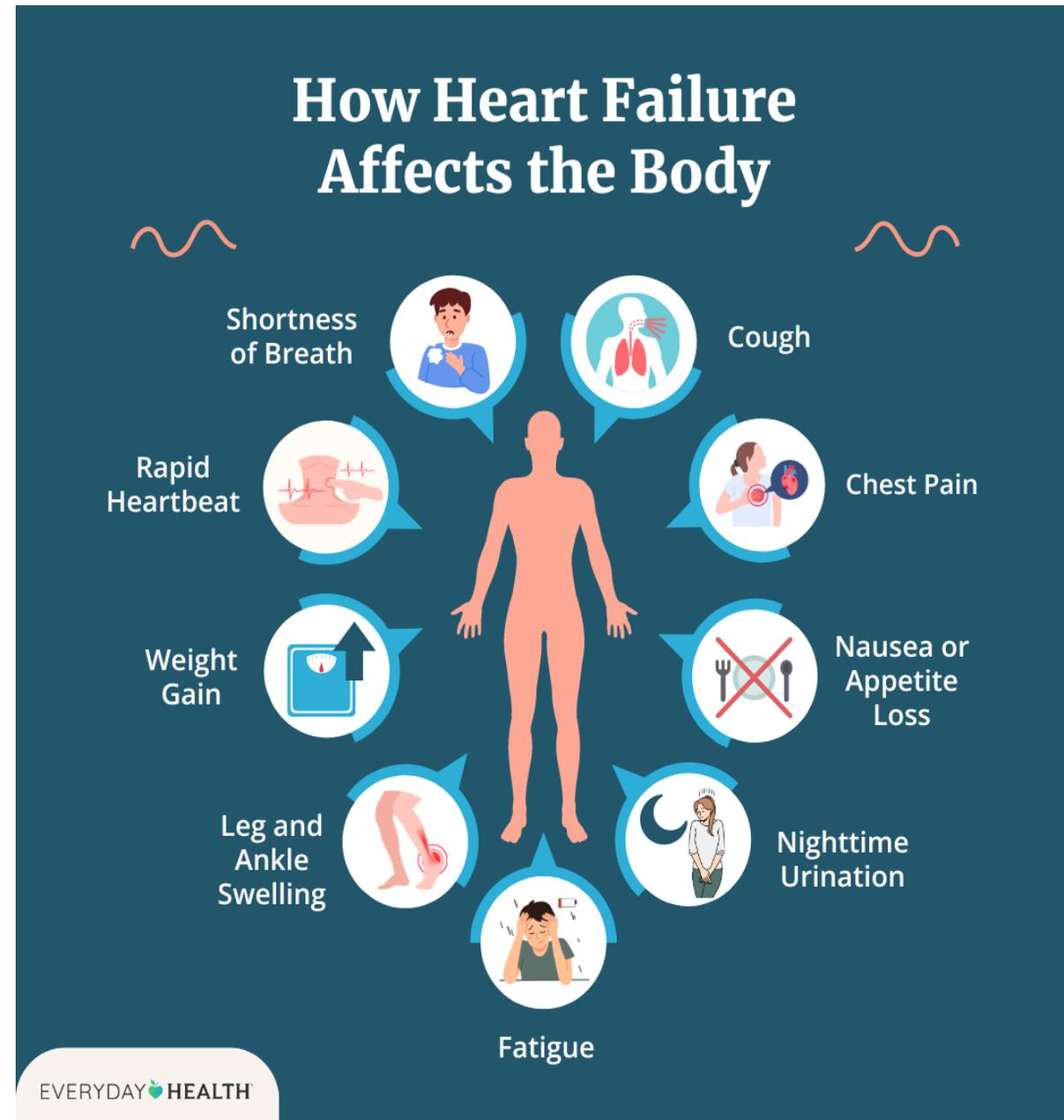
### Other:

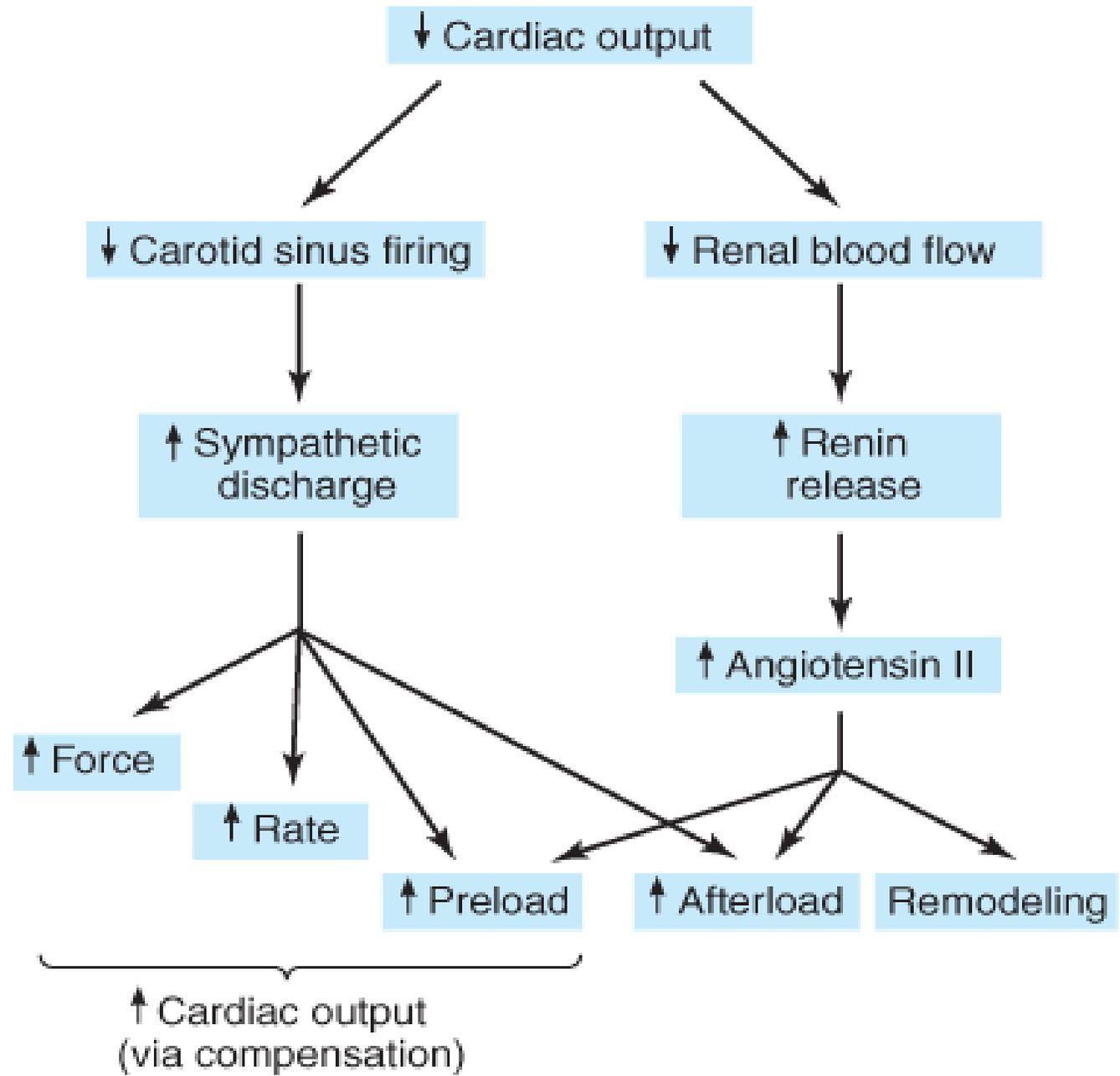
- Obesity
- Age
- Smoking
- High or low hematocrit level (HB)

# Symptoms of Heart Failure

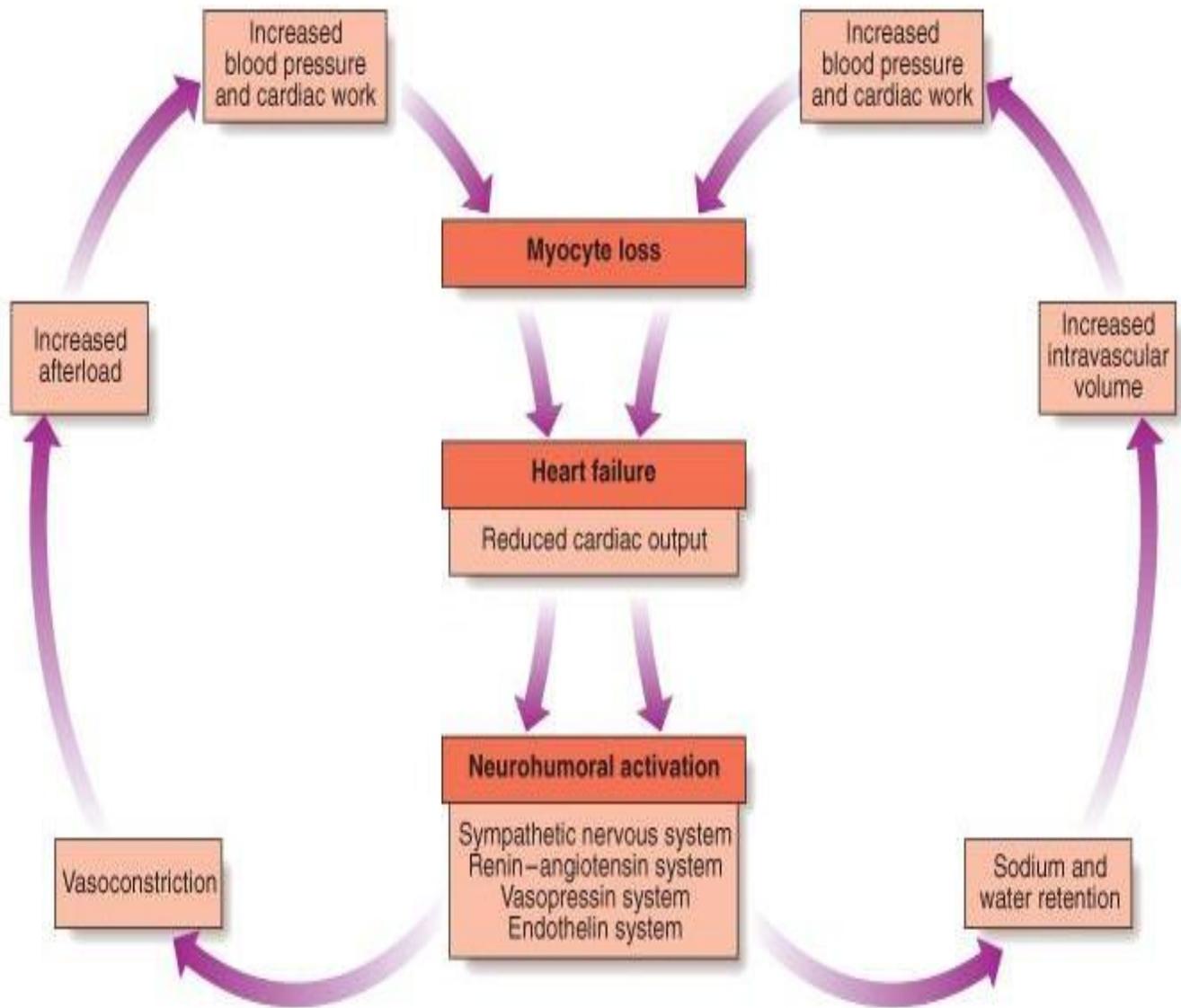
Think FACES...

- Fatigue
- Activities limited
- Chest congestion
- Edema or ankle swelling
- Shortness of breath





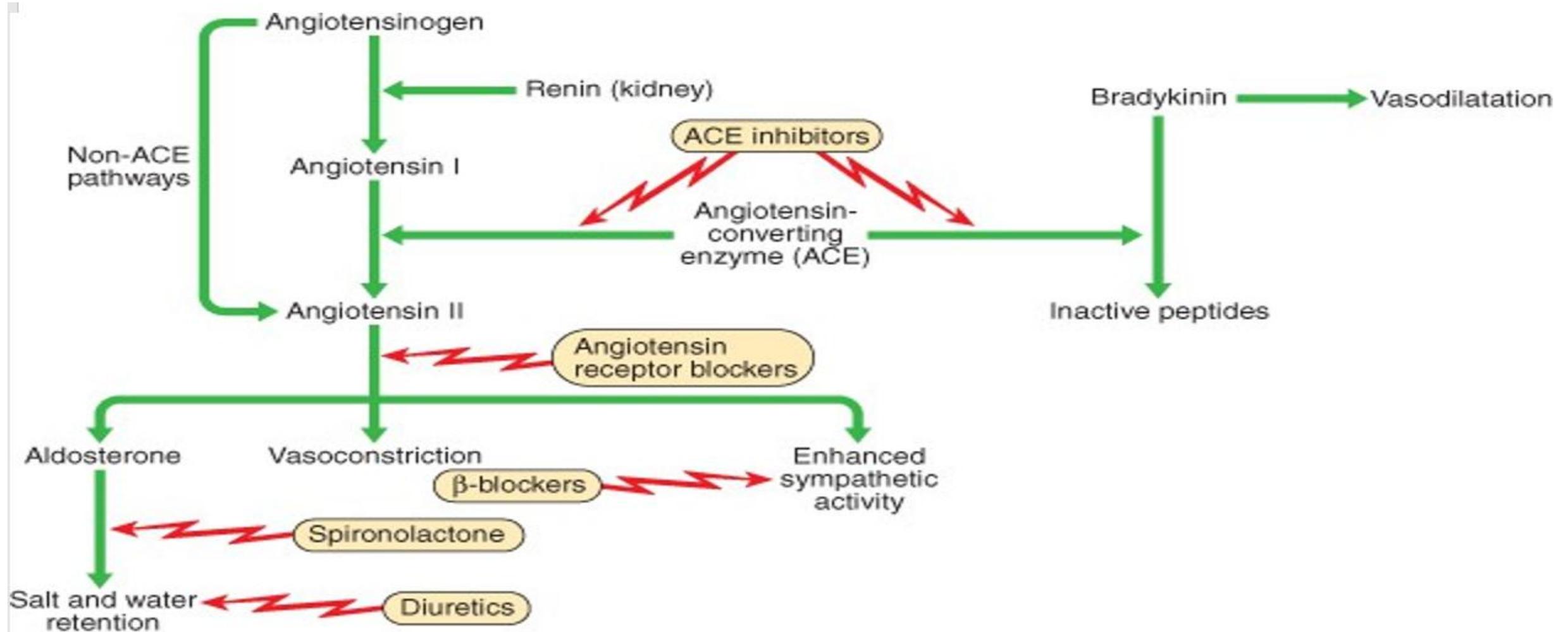
# COMPENSATORY MECHANISMS



***maladaptive changes***

# Principles of Treatment

↓ Preload    ↓ Afterload    ↑ Inotropy    ↓ Neurohumoral activity



1897 TW Engelmann described:

- **Inotropy:** Contractility
- **Chronotropy:** Rate (SA node)
- **Dromotropy:** Conduction (AV node)
- **Bathmotropy:** Excitability

1982 described:

- **Lusitropy:** Relaxation (active)

**D**

**D**igoxin



**D**

**D**opamine



**D**

**D**obutamine



**IN**otropic

“**IN**creased cardiac contractility”  
 “**IN**creased forceful contraction”

3 Ds for DEEP contraction

- D - Digoxin
- D - Dopamine
- D - Dobutamine

**Chronos**

Clock

- Neg. Chronos - Neg time
- Positive Chronos - Positive time
- Faster HR - Positive Chronotropic
- Lower HR - Negative Chronotropic

**Dromo**

Drums

- Neg. Dromotropic - stable heart rhythm




Drug	Inotropic Force of Heartbeat	Chronotropic Rate of Heartbeat	Dromotropic Rhythm of Heartbeat
<b>A</b> amiodarone	+ Pos.	- Neg.	- Neg.
<b>B</b> beta blockers Atenolol	- Neg.	- Neg.	- Neg.
<b>C</b> calcium CB	- Neg.	- Neg.	- Neg.
<b>C</b> cardiac glycosides Digoxin	+ Pos.	- Neg.	- Neg.
<b>D</b> dobutamine	+ Pos.	X	X
<b>D</b> dopamine	+ Pos.	+ Pos.	X
<b>E</b> epinephrine	+ Pos.	+ Pos.	X

# Drug Groups Commonly Used in Heart Failure

- Diuretics
- Aldosterone receptor antagonists
- Angiotensin-converting enzyme (ACE) inhibitors
- Angiotensin receptor blockers (ARBs)
- $\beta$  blockers
- Cardiac glycosides
- Vasodilators
- $\beta$  agonists
- Bipyridines
- Natriuretic peptide

# Treatment of Heart Failure

## ACE Inhibitors

- ✓ Works to inhibit the over stimulation of the RAS that leads to myocardial hypertrophy and fibrosis
- ✓ Causes balanced vasodilation
- ✓ Decrease the rate of morbidity & mortality in all patient with systolic heart failure

# Cardiac Inotropic Drugs

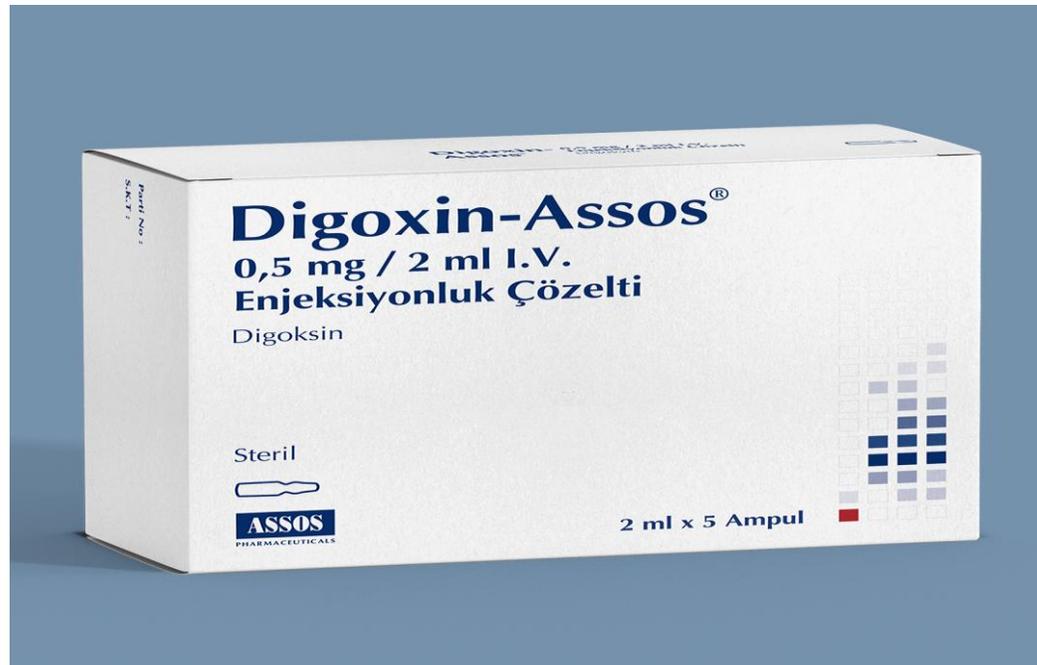
## Cardiac Inotropic Drugs (Cardiac Glycosides)

Cardiac glycosides are mainly derived from plant products such as

- purple foxglove (*digitalis purpurea*: digitoxin)
- white foxglove (*digitalis lanata*: digoxin)
- *Strophantus gratus*: ouabain.

# DIGOXIN

1. Inhibits Na/**K** ATP pump
2. Increases intracellular  $\text{Ca}^{++}$
3. Increases contractility
4. Decreases AV conduction velocity



# Indications

1. Atrial fibrillation (vagal effect on the AV-node)
2. Paroxysmal supraventricular tachycardia (vagal effect on the SA and AV-nodes)
3. Cardiac failure

**Digoxin is used as a first-line drug in patients with congestive heart failure who are in atrial fibrillation.**

## Adverse effects

- Abnormal cardiac rhythm (e.g. ventricular ectopic beats, Bradycardia, Heart block)
- GI effects (e.g. anorexia, vomiting, and diarrhoea)
- Visual effects (e.g. disturbances of colour vision, photophobia and blurring)
- Gynaecomastia
- Mental effects (e.g. confusion, agitation, nightmare and acute psychoses)

Contraindicatin

## ***Treatment of Digitalis Toxicity:***

- 1) Stop the responsible drug.
- 2) KCl syrup or slow release or I.V. with ECG monitoring if plasma potassium is low or normal.
- 3) If due to calcium injection give disodium edetate I.V. which is chelating agent for calcium.
- 4) **Cholestyramine binds** to digitalis in gut, thus inhibit absorption and decreases the toxicity especially of digitoxin.
- 5) In acute toxicity give specific **digitalis antibodies** (**Fab fragment**).

# Cautions/contraindications

1. Hypokalaemia
2. Hypercalcaemia
3. AV-block II – III (unless treated with pacemaker)
4. Impaired renal function (age-related)
5. Hypothyroidism
6. Conditions may lead to increased Na-influx (e.g. electrical cardioversion, acute myocardial infarction)

## Other Inotropic Drugs ----- Dopamine

### low doses

it stimulates **D1-receptors** causing renal, mesenteric and coronary vasodilatation. Hence, dopamine may lead to an increase in glomerular filtration rate and urine production.

### higher doses

dopamine progressively **increases heart rate and force** by directly stimulating  **$\beta_1$ -adrenoceptors** and indirectly releasing neuronal noradrenaline, which in turn activates  $\beta_1$ -adrenoceptors.

### still higher doses

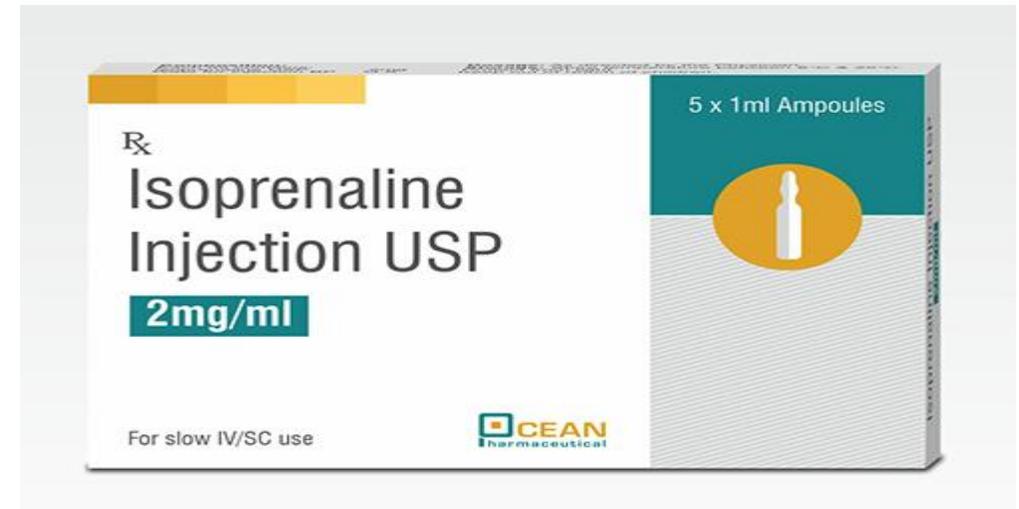
stimulate  **$\alpha$ -adrenoceptors**, causing a rise in blood pressure with a decrease in blood flow to vital organs including the kidneys.



## Isoprenaline

Potent non-selective  $\beta$ -receptor agonist with no or little  $\alpha$ -receptor actions.

- It reduces peripheral resistance, mean and diastolic blood pressure
- systolic blood pressure and renal blood flow may rise due to increased cardiac output.



## Dobutamine (synthetic drug)

- ❑  **$\beta_1$ -receptor** agonist showing greater inotropic than chronotropic effects on the heart.
- ❑ Has some  **$\alpha$ -receptor activity** (but less than that with dopamine).
- ❑ It may be useful in shock and in low output heart failure (in the absence of severe hypertension).

## Dopexamine (synthetic catecholamine)

- ❑ positive inotropic action (being a cardiac  **$\beta$ -receptor** agonist).
- ❑ some **D1-receptor** agonistic activity (thus, renal vasodilatation).
- ❑ inhibitory activity on noradrenaline reuptake, hence, increasing the synaptic availability of noradrenaline and thus, the stimulation of cardiac  $\beta_1$ -receptor.



# **Bipyridine Derivatives (Phosphodiesterase Inhibitors)**

*Milrinone and Inamrinone* (formerly known as amrinone, name change, July 1, 2000)

**They produce their inotropic activity by selectively inhibiting phosphodiesterase III (cAMP phosphodiesterase) resulting in an increase in tissue cAMP and presumably not cGMP.**

Catecholamines and xanthine derivatives [caffeine, theophylline ethylenediamine (aminophylline)], however, enhance the availability of both cAMP and cGMP.

Bipyridine derivatives appear to have a superior feature that they produce smaller positive chronotropic effects compared to catecholamines and xanthine derivatives and hence lower potential to cause arrhythmias.

## **Vasodilators (To be covered later on)**

## **Diuretics**

These are useful in reducing the symptoms of volume overload by  
decreasing the extra cellular volume  
decreasing the venous return

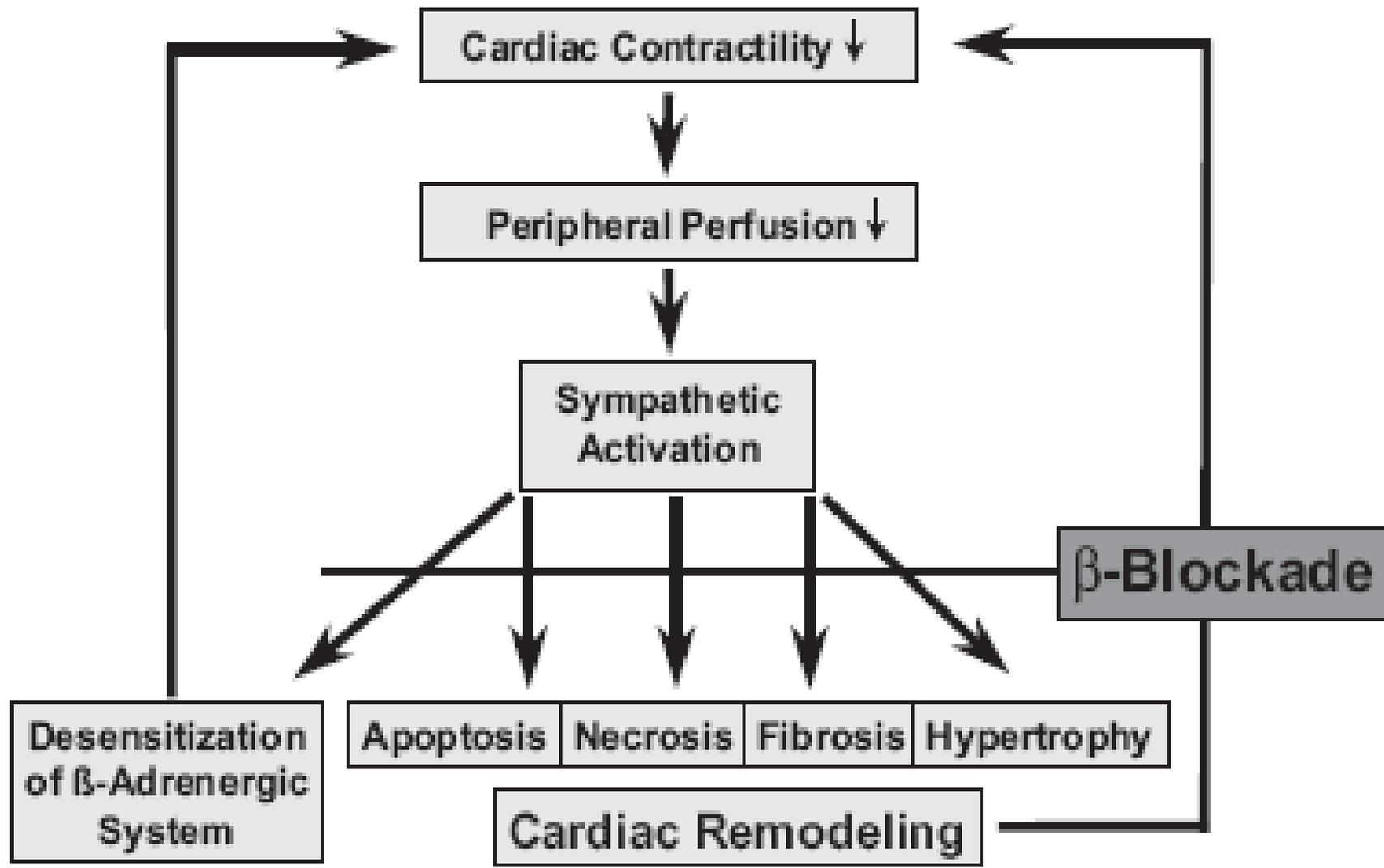
*Loop diuretics*

*Thiazide diuretics*

*Potassium sparing diuretics*

## **Beta blockers**

- Acts primarily by inhibiting the sympathetic nervous system.
- Increases beta receptor sensitivity (up regulation).
- Anti-arrhythmic properties.
- Anti-oxidant properties.



## **Beta blockers for CCF :**

- Start at low dose and monitor for bradycardia
- Carvedilol, bisoprolol and Metoprolol are the most commonly used for CCF among beta blockers

## **Natriuretic peptide Nesiritide**

- ✓ Produced by recombinant DNA technology
- ✓ Approved for clinical use by the FDA in August 2001.
- ✓ Nesiritide stimulates soluble guanylate cyclase and increases vascular levels of cyclic GMP
- ✓ Causes venous and arterial vasodilation (balanced vasodilator)
- ✓ Unlike the nitrates, tolerance does not develop with this drug.
- ✓ Given by intravenous administration.
- ✓ No benefit as an outpatient basis
- ✓ The major side effect is deleterious effect on renal function & prolonged hypotension.

A white card with a brown envelope, featuring various medical illustrations in a flat, colorful style. The illustrations include a syringe, a blue glove, a stethoscope, a bandage, a pair of scissors, a pill bottle, a blister pack, a pill tray, and a pill. There are also small red plus signs and blue starburst shapes scattered around the central text. The text 'Thank You' is written in a black, cursive font.

*Thank You*