

The logo of Galgotias University is a stylized circular emblem composed of several overlapping, curved segments in shades of yellow, blue, and pink, creating a sense of motion or a spiral.

## Drugs for Congestive Heart Failure

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# Disclaimer

All the content material provided here is only made for teaching purpose.

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# Compensatory responses during heart failure

Heart failure

↓ FOC ↓ COP

↓ Renal perfusion

↑ Sympathetic discharge

Ventricular dilation

↑ Renin release

↓ GFR

• Vasoconstriction  
•  $\beta_1$  activation

Cardiac remodelling

↑ AT-1

Na & water retention (Edema)

↑ preload  
↑ afterload

↑ FOC  
↑ HR

Back pressure

↑ AT-II

Initially ↑ CO Later ↓ CO

Oedema

↑ Aldosterone

Inotropics

$\beta$ -blockers

Drugs Used in  
Heart Failure

Diuretics

Aldosterone  
Antagonists

Vasodilators

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# Inotropic drugs

- Cardiac glycosides:  
Digoxin, digitoxin
- Sympathomimetic amines:  
Dopamine, dobutamine
- Phosphodiesterase inhibitors:  
Amrinone, milrinone

# Vasodilators

- Arteriolar: hydralazine , minoxidil, nicorandil
- Venodilators: nitrates
- Arteriolar and venodilators: ACE inhibitors, angiotensin receptor blockers

# Diuretics

- Loop diuretics: furosemide, torsemide
- Thiazide diuretics: hydrochlorothiazide
- K<sup>+</sup> Sparing diuretics:
  - Spironolactone (Also is aldosterone antagonist)
  - Amiloride

# Beta Blockers

- Metoprolol,
- bisoprolol,
- carvedilol

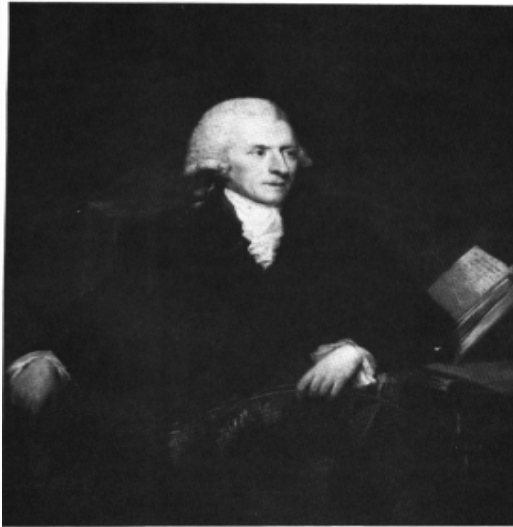
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# Inotropic Agents

- Cardiac glycosides: Digoxin



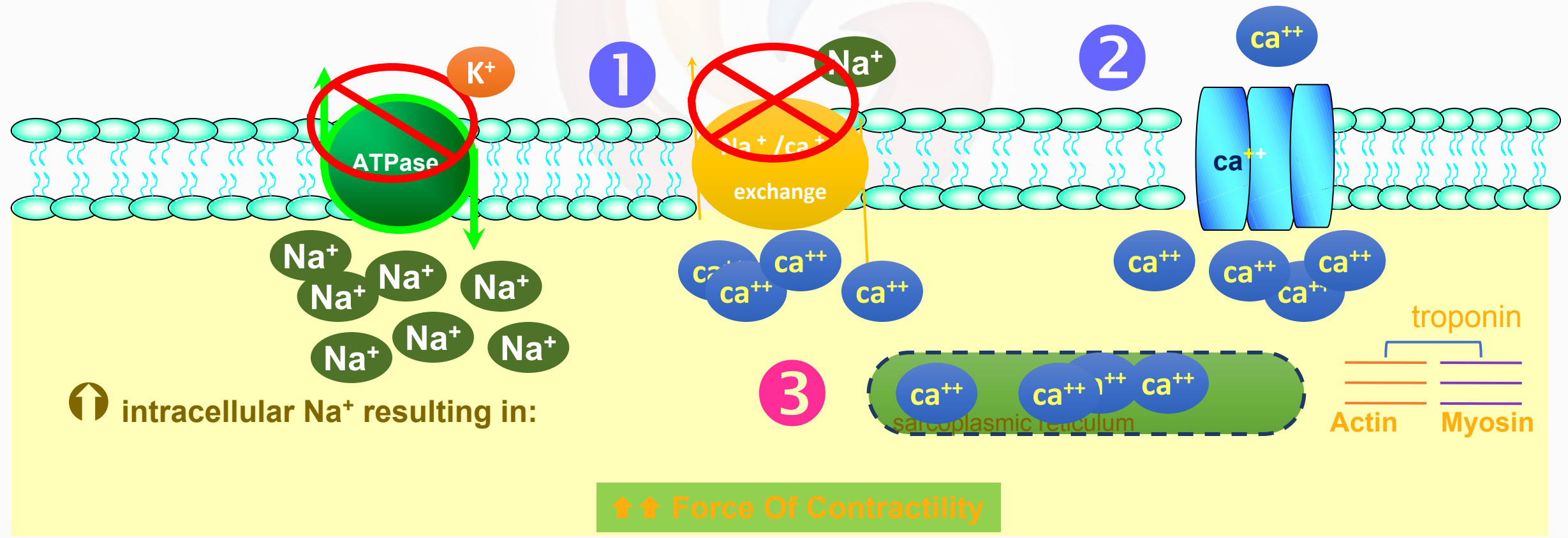
William Withering 1785



Foxglove plant

# MOA of Digitalis

In therapeutic dose leads to partial inhibition of  $\text{Na}^+/\text{K}^+$  ATPase enzyme



# Pharmacological actions

## CARDIAC

- ↑ force of contraction & Cardiac Output
- ↓ Heart rate
- ↓ Refractory period (RP) & ↑ Conduction velocity (CV) in atria/ventricles
- ↑ RP & ↓ CV in AV node
- Increased automaticity
- ECG: ↑ PR interval, ↓ QT interval

## EXTRA CARDIAC

- Kidney:
  - Due to improvement in circulation and renal perfusion
  - Retained salt and water is gradually excreted
- CNS:
  - Nausea, vomiting

# Pharmacokinetic properties

Property	Digoxin
Oral absorption	60 -80 %
Plasma protein binding	25 %
Onset of action	15 -30 min
Duration of action	2-6 days
Plasma $t_{1/2}$	40 hrs
Route of elimination	Renal excretion
Time for digitalization	5-7 days
Daily maintenance dose	0.125 – 0.5 mg
Administration	Oral / IV

# Cardiac Glycosides (Digitalis)

- Two glycosides:
  - Short acting Digoxin ( $t_{1/2}$ : 1.5 days)
  - Long acting Digitoxin ( $t_{1/2}$ : 5 days)

# Uses of digoxin

- Congestive heart failure
- Cardiac arrhythmias
  - Atrial fibrillation
  - Atrial flutter
  - Paroxysmal supraventricular tachycardia

# Adverse effects of digoxin

## Extra-Cardiac

- GIT: Nausea & vomiting (first to appear)
- CNS: Vomiting Restlessness, Disorientation, Visual disturbance
- Endocrine: Gynaecomastia

## Cardiac

- Bradycardia (first cardiac toxic sign)
- Pulsus bigemini
- Atrial extra-systole → flutter → fibrillation
- Ventricular extra-systole → tachycardia → fibrillation
- Partial heart block → complete block

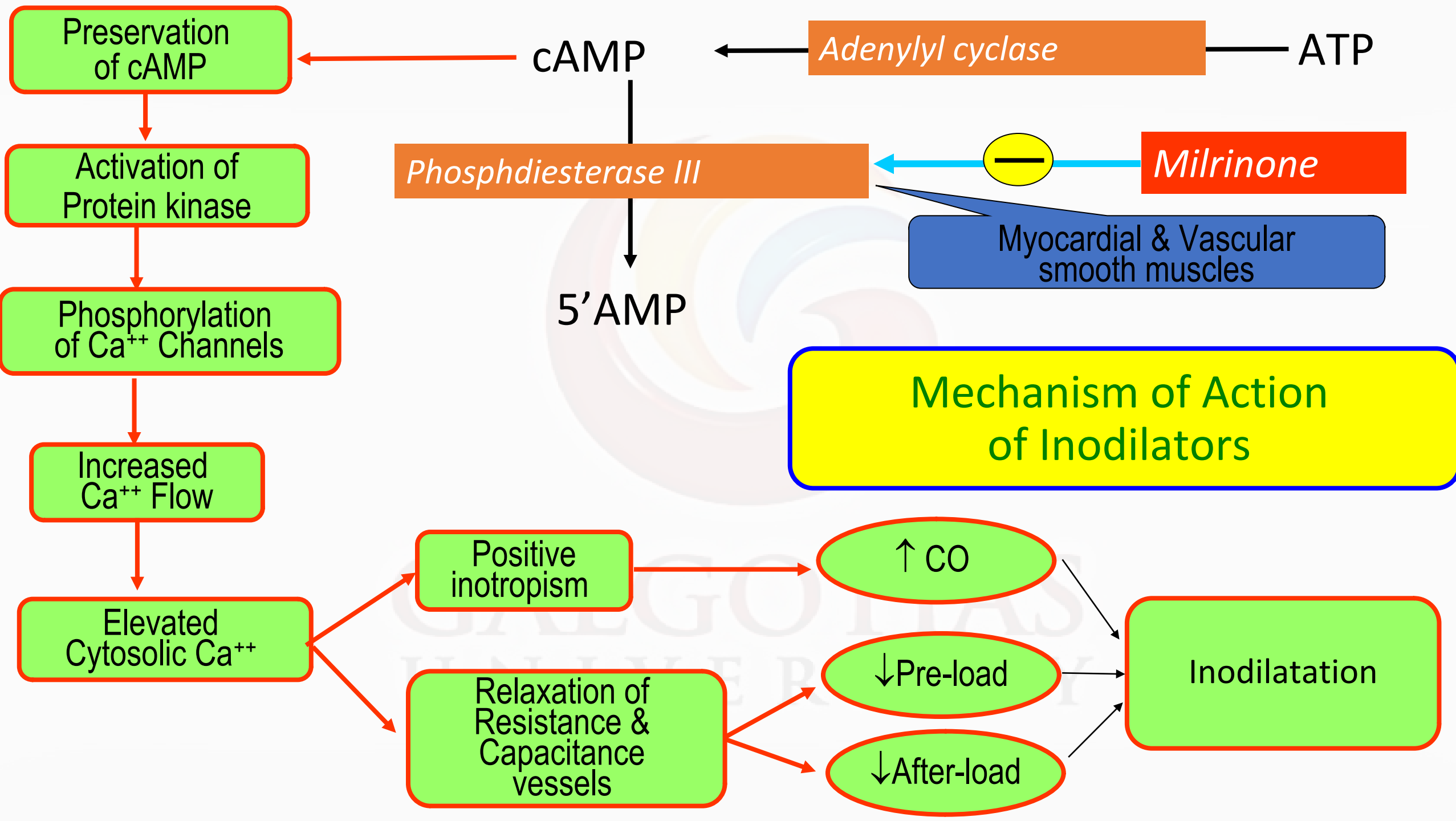
# Treatment of toxicity

- Stop digitalis
- Oral or parenteral potassium supplements
- For ventricular arrhythmias:
  - Lidocaine IV drug of choice
- For supraventricular arrhythmia:
  - Propranolol may be given IV or orally
- For AV block and bradycardia
  - Atropine 0.6 -1.2 mg IM
- Digoxin antibody



# Phosphodiesterase inhibitors in heart failure

- Amrinone & milrinone are selective phosphodiesterase III inhibitors
- ↑ cAMP levels
- The PDE III isoenzyme is specific for intracellular degradation of cAMP in heart, blood vessels and bronchial smooth muscles.
- Inodilators
- IV administration for short term treatment of severe heart failure
- Milrinone is more potent than amrinone and does not produce thrombocytopenia



# Other inotropic drugs

- Dopamine
- Dobutamine

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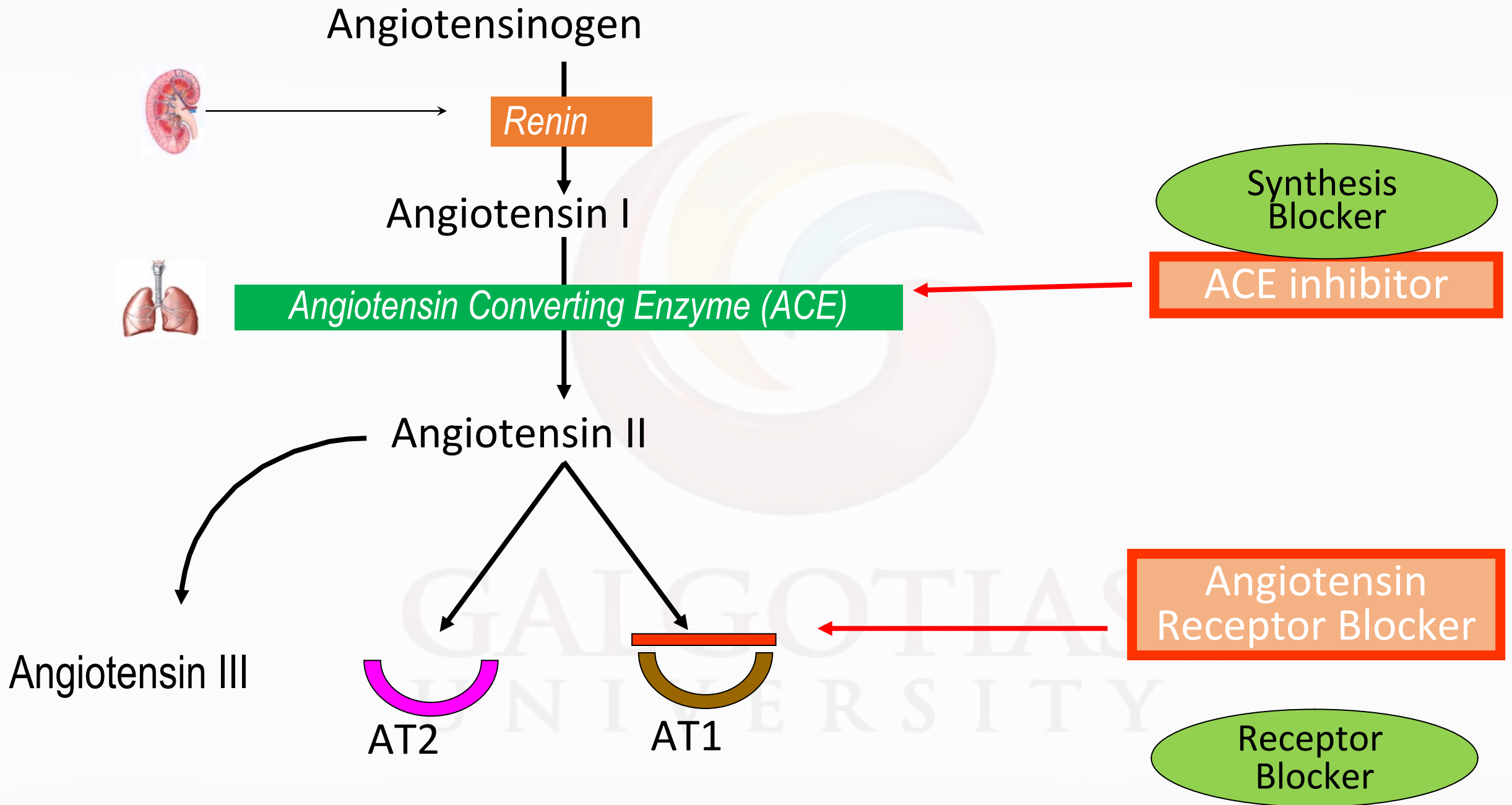
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# Role of diuretics in heart failure

- Almost all symptomatic Patients treated with a diuretic
- High ceiling diuretics (loop diuretics) preferred
  - Low dose therapy for maintenance
- They increase salt and water excretion & reduce blood volume
  - Reduce preload & venous pressure
  - Improve cardiac performance & relieve edema

# ACE Inhibitors in heart failure

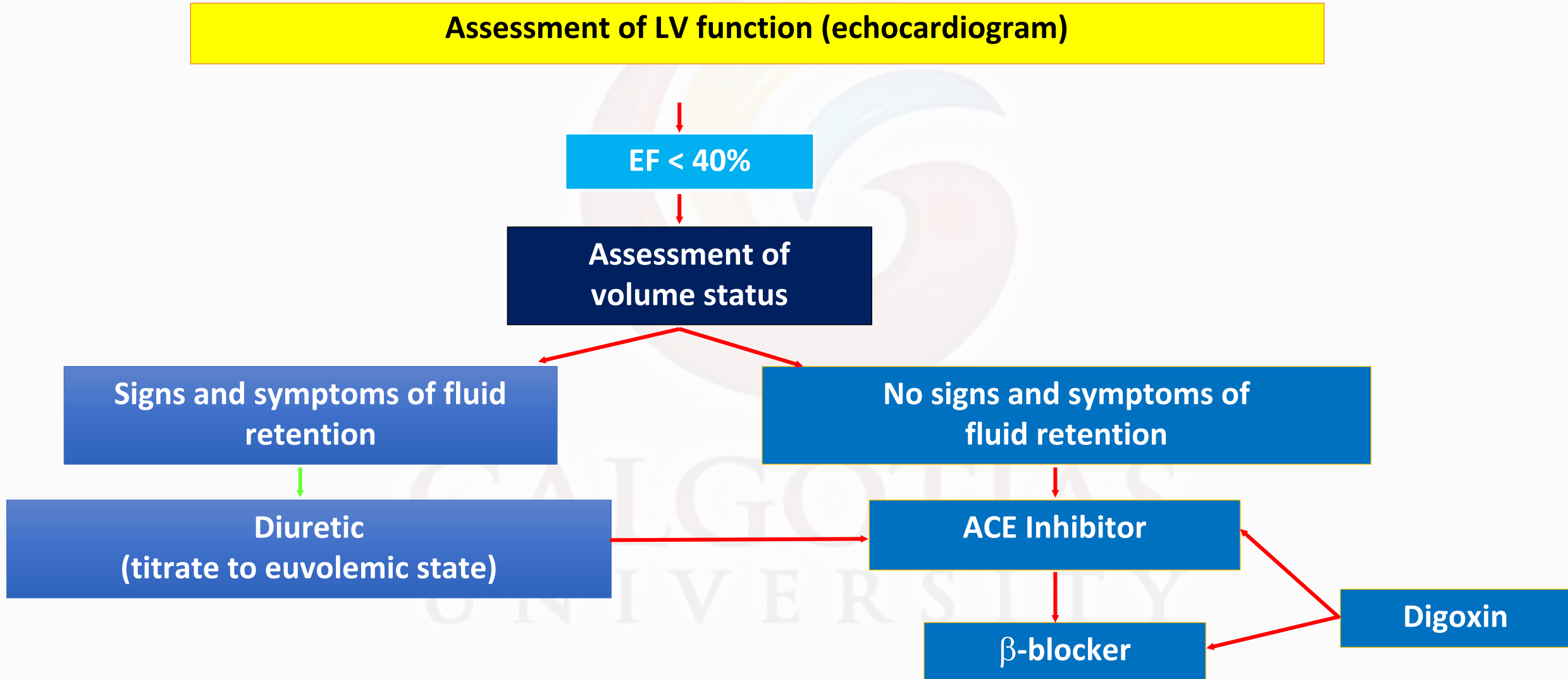
- Angiotensin converting enzyme inhibitors
  - Captopril, enalapril, ramipril, lisinopril
- Act by
  - Reduction of after load
  - Reduction of preload
  - Reversing the compensatory changes
- ACE inhibitors are the most preferred drugs for treatment of Congestive cardiac failure



# Angiotensin receptor blockers in heart failure

- Losartan , candesartan, valsartan, telmisartan
- Block AT<sub>1</sub> receptor on the heart, peripheral vasculature and kidney
- As effective as ACE inhibitors
- Used mainly in patients who cannot tolerate ACE inhibitors because of cough, angioedema, neutropenia

# Approach to the Patient with Heart Failure





# Drugs used in heart failure

## Chronic heart failure

- Diuretics
- Aldosterone receptor antagonist
- ACE inhibitors
- Angiotensin receptor blockers
- Cardiac glycosides
- Vasodilators

## Acute heart failure

- Diuretics
- Vasodilators
- Dopamine, dobutamine
- Amrinone

## References

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