



## SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

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# What is Heart Failure?

- A disorder in which the heart **loses its ability to pump blood efficiently** throughout the body.

## ↓ Cardiac Output

- Heart failure occurs when CO is inadequate to provide the oxygen needed by the body.



## ***Definition***

Congestive heart failure (CHF) is a clinical syndrome in which the heart is unable to pump enough blood to the body to meet its needs, to dispose of systemic or pulmonary venous return adequately, or a combination of the two.

### **DRUGS USED IN CONGESTIVE CARDIAC FAILURE**

## Drugs for Heart Failure: Classification



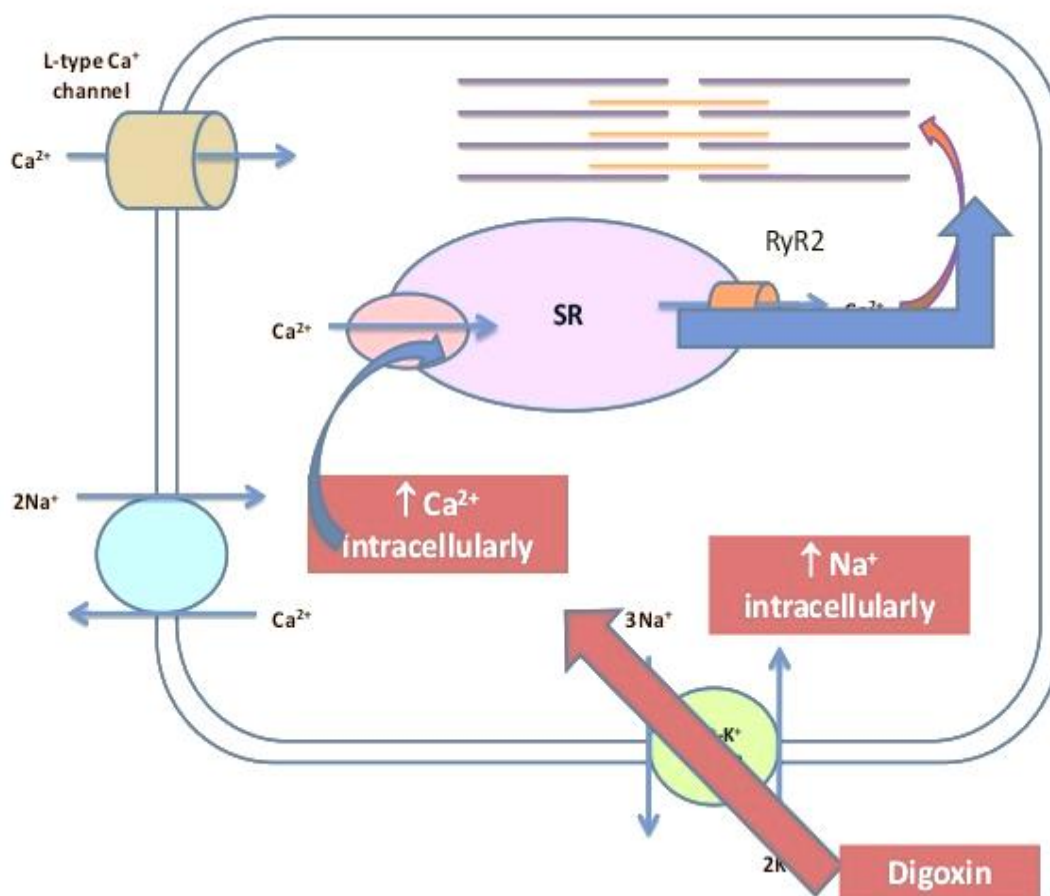
- **Inotropic drugs:** Digoxin, Dobutamine, Dopamine, Amrinone/Milrinone
- **Diuretics:** Furosemide, Thiazides
- **RAS inhibitors:** ACE inhibitors, ARBs
- **Aldosterone Antagonists:** Spironolactone, Eplerenone
- **Vasodilators:** Hydralazine, Nitrate, Nitroprusside
- **β- blockers:** Metoprolol, Bisoprolol, Carvedilol, Nebivolol

# DRUG THERAPY

- **To increase force of contraction**
  - Digoxin
  - $\beta$  agoists (dobutamine, dopamine)
  - Bipyridines (milrinone)
- **To reduce cardiac workload**
  - To decrease preload (venodilators) (diuretics, nitrates)
  - To decrease afterload (arterial vasodilators)
  - To decrease preload and afterload (ACEI, ARB) (nitrates, sodium nitroprusside)
- **To prolong the survival**
  - $\beta$  adrenoreceptor blockers

## (a) Mechanism of action of digoxin

- cardiac glycosides increases intracellular  $\text{Ca}^{2+}$  concentration.
- It is the result of 2 step process.
- **First**, inhibit  $\text{Na}^+/\text{K}^+$  pump by binding on  $\text{K}^+$ - binding site  $\text{Na}^+/\text{K}^+$ - ATPase on the cell membrane which causes a rise in intracellular sodium.
- **Secondly**, a rise in intracellular sodium can slow down the extrusion of calcium
- because extrusion of calcium is by a  $\text{Na}^+/\text{Ca}^{2+}$  exchange mechanism.
- Increased cytoplasmic calcium is transported to sarcoplasmic reticulum,
- Finally, increases the amount of calcium released by the action potential.



## How digoxin corrects heart failure?

- Due to  $\uparrow \text{FOC} \rightarrow \uparrow \text{CO} \rightarrow \uparrow \text{RBF}$  (relieve oliguria)
- Due to better tissue perfusion  $\rightarrow$  relieve cyanosis
- Due to blockage of AV node, conducting tissues  $\rightarrow$  slow ventricular rate  $\rightarrow$  relieve tachycardia [stronger, slower heartbeat (increased efficiency) without increased demand]
- Due to  $\uparrow \text{CO} \rightarrow$  better emptying of the ventricles  $\rightarrow$  increased venous return  $\rightarrow$  better drainage from the tissues with relief of congestion in the lungs and liver and reduction of oedema, relief of dyspnoea,
- Better results are obtained in patients with atrial fibrillation than with normal rhythm
- narrow Therapeutic Index (safety margin)  $\rightarrow$  side-effects common

## (b) Pharmacological action of digoxin

- Can be generally divided into two portions
  - Cardiac effect
  - Effect on other organs

### 1. Cardiac effect

#### At therapeutic dose

- Direct - increased FOC of heart
- Indirect - decreased HR ( d/t vagal stimulation & decreased sympathetic activity ) may lead to AV block, sinus bradycardia, cardiac arrest.

#### At higher concentration,

- Direct - increase automaticity of heart
- Indirect - sympathetic activation
- Both may lead to ventricular arrhythmias

### 2. Effects on other organs

- CNS
  - through vagal and CTZ stimulation:
  - disorientation, hallucination, visual disturbances (aberration of color perception)
- GIT
  - by direct and through CNS (chemoreceptor trigger zone) effect.
  - ANVD (anorexia, nausea, vomiting, diarrhoea)
  - gastrointestinal tract is most common site of digitalis toxicity outside the heart
- d/t sterold structure - gynaecomastia (rare)



## (c) Therapeutic Uses of digoxin

1. Heart failure with atrial fibrillation (use only when diuretics and ACEI have failed to control the symptoms)
  - Mild symptoms - slow loading dose
  - Acute heart failure - rapid digitalization
2. Treatment of atrial arrhythmia (atrial fibrillation & flutter)

## (d) Adverse effects of digoxin

- **CNS** - disorientation, hallucination, visual disturbances (aberration of color perception)
- **GIT** - ANVD (anorexia, nausea, vomiting, diarrhoea)
  - gastrointestinal tract is most common site of digitalis toxicity outside the heart
- **d/t steroid structure** - gynaecomastia (rare)
- **CVS** - ventricular arrhythmia.
- **interaction with electrolytes:** hypokalaemia, hypercalcaemia can worsen the toxicity.
- **Narrow therapeutic index drug.**