

Drugs used in

Congestive Cardiac Failure

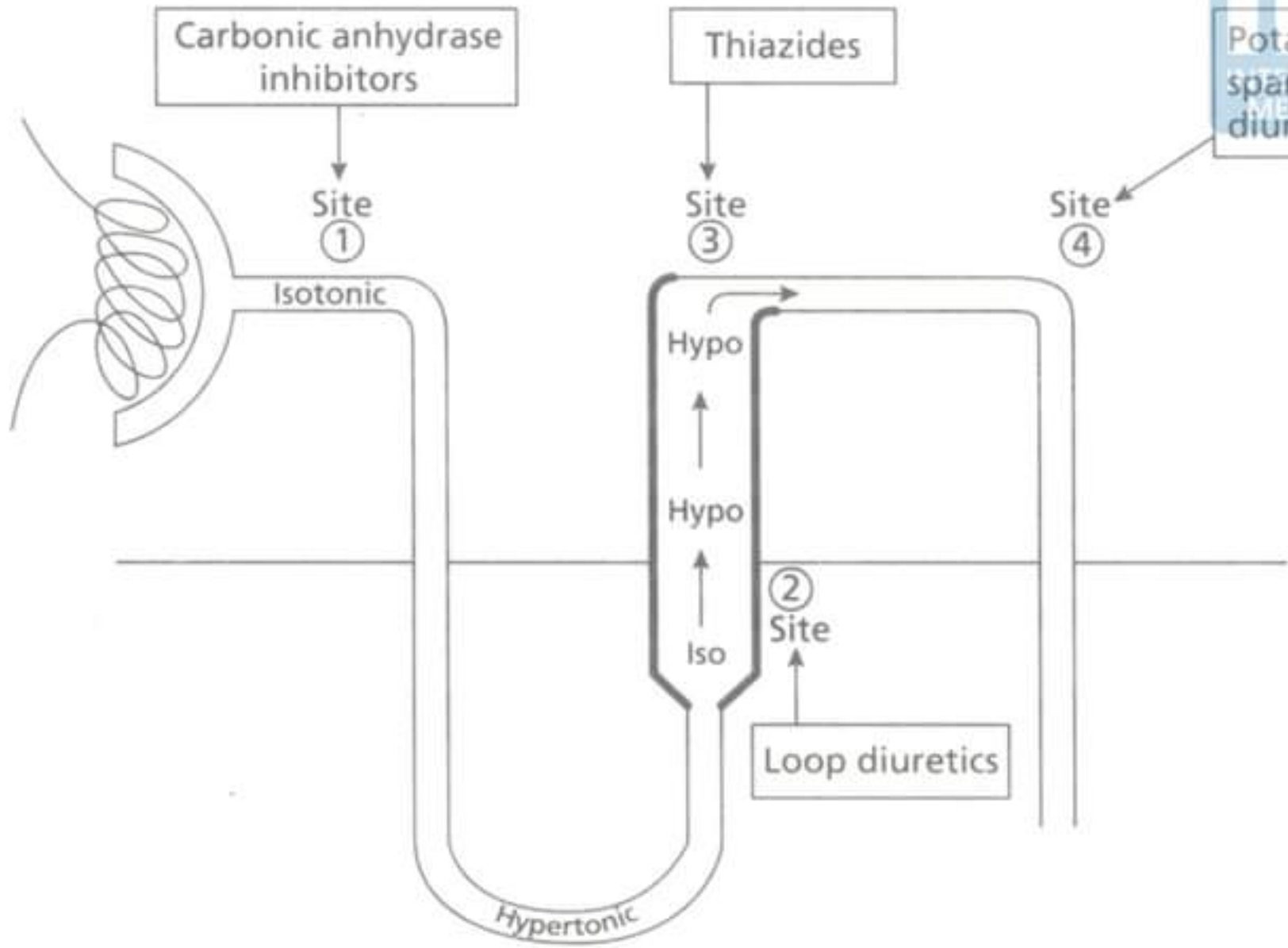
- Reduction of preload
 - Diuretics
 - Nitrates
- Reduction of afterload
 - hydralazine
- Reduction of preload and afterload
 - ACE inhibitors and angiotensin receptor blockers
 - β -adrenoceptor blocker
- Stimulation of myocardium
 - Digoxin

- Diuretics
- Cardiac glycosides
- Vasodilators
- β - blockers
- Sympathomimetic amines
- Phosphodiesterase inhibitors

Diuretics

- Loop diuretics : Frusemide, Bumetanide
- Thiazide : hydrochlorothiazide
- K⁺ sparing diuretics : Spiranolactone, amiloride, tramterene

- Loop diuretics
 - thick ascending limb
 - inhibit Na^+ - K^+ - 2Cl^- co-transport
 - used in severe cardiac failure
- Thiazide diuretics
 - cortical diluting segment
 - inhibit Na^+ - K^+
 - used in mild to moderate cardiac failure
 - Not effective if GFT <30 ml/min



Promote Na^+ and water excretion



Reduce ECF volume



Decrease preload



Improve ventricular efficiency

Cardiac Glycosides

Aglycone (steroid nucleus with an attached lactone ring) with one or more sugar moieties attached to it.

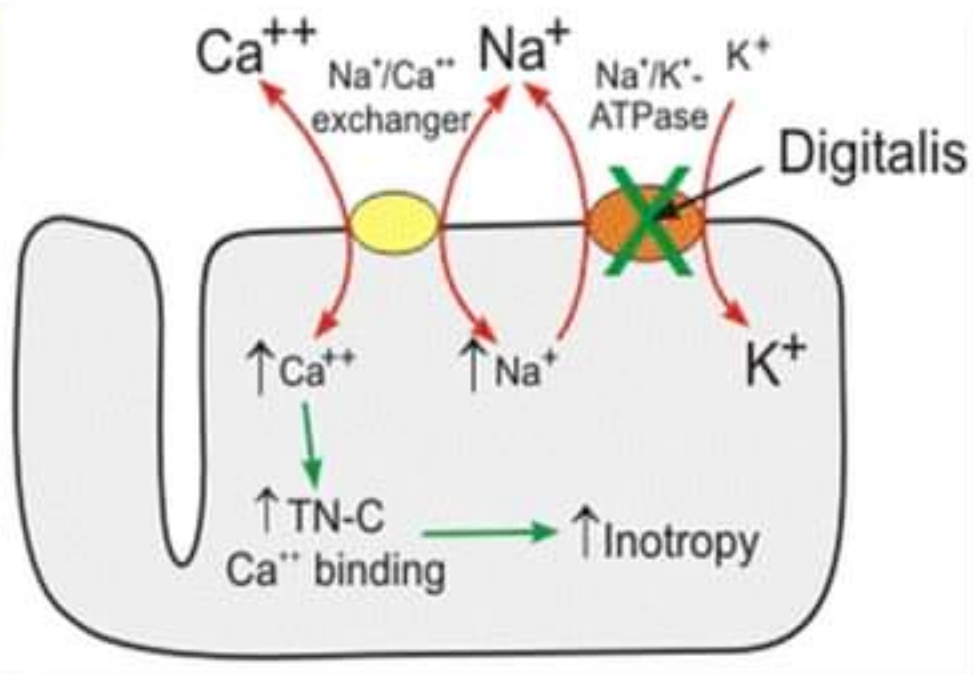
Potent action on the heart , hence referred to as cardiac glycosides

- *Digitalis pupurea* : Digitoxin
- *Digitalis lanata* : Digoxin, Digitoxin

The utility of digitalis in the treatment of heart failure was shown by William Withering.

Mechanism of Action

Direct



Indirect

Enhance vagal activity

Reduced SA and AV node activity

- Cardiac glycosides bind to and inactivate the Na^+/K^+ ATPase pump on the cytoplasmic membrane of cardiac cells
- As a result intracellular Na^+ concentration increases
- This affects the Na^+/Ca^+ exchange channels resulting in an increase in intracellular Ca^+ that leads to increased force of contraction

- Atrial fibrillation
- Atrial flutter
- Heart failure
 - benefit chiefly by direct action

- Digoxin is eliminated 85% unchanged in the kidney
- Remainder is metabolized in the liver
- $T_{1/2}$ is 36 hours
- Usually administered orally
- Hypokalaemia and hypomagnesaemia potentiate adverse effects of digoxin

- Ventricular arrhythmias
- Heart block
- Anorexia and vomiting
- Disturbance in colour vision
- Gynaecomastia
- Mental effects

Yellow Oleander Poisoning

iM
INTERESTING
MEDICINE



Treatment of Digoxin Toxicity

IM
INTERESTING
MEDICINE

- Atropine for bradycardia
- Iv phenytoin for ventricular arrhythmia
- Fab fragment of the antibody to digoxin (Digibind)
- Temporary pacing
- DC shock for ventricular fibrillation

- Verapamil, nifedipine, Quinidine and amiodarone increase plasma concentration of digoxin
- Increased likelihood of AV blocking with verapamil and β -blockers.

Vasodilators

- Predominant venodilatory → reduce preload
eg; Nitrates
some effect on arterioles
- Predominant arteriolar dilating effect
→ reduce afterload
eg; hydralazine, minoxidil, nicorandil
causes reflex tachycardia and fluid retention
- Mixed arteriolar and venodilators
→ reduce both pre and afterload
eg; ACE inhibitors, ARBs, sodium nitroprusside
Tachycardia is rare

ACE inhibitors

- First line drugs in the treatment of Chronic heart failure
- Action
 - inhibit conversion of angiotensin I to II
 - retard or reverse cardiac remodelling or hypertrophy
- Side effects;
 - Cough, angioedema and neutropenia

Angiotensin-receptor blockers (ARBs)

INTERESTING
MEDICINE

- Eg; Losartan, Candesartan
- Competitively block AT-receptors on the heart, peripheral vasculature and kidneys
- As effective as ACE inhibitors
- Mainly used for those who cannot tolerate ACE inhibitors

IV sodium nitroprusside and nitroglycerin are used for severe heart failure.

- Metoprolol, bisoprolol and carvedilol
- Useful in mild to moderate heart failure
- Acts through β -adrenergic blocking effect on the heart
- Therapy should be carefully supervised

Sympathomimetic amines : Dopamine

INTERESTING
MEDICINE

- Catecholamine with conc. dependent haemodynamic effects
 - Low conc.** Selectively dilates renal, mesenteric and coronary blood vessels by acting on D_1 receptors → increases GFR and UOP
 - Moderate doses** stimulates β_1 - receptors → increase myocardial contractility and cardiac output
tachycardia is less prominent

Useful in heart failure with renal impairment

At high concentration ($>10 \mu\text{g}/\text{kg}/\text{min}$)

- generalized vasoconstriction
- increases afterload and reduces blood flow to renal and other vital organs

Sympathomimetic Amines: Dobutamine

IM
INTERESTING
MEDICINE

- Synthetic catecholamine
- Act on $\beta_1\beta_2$ and α_1 receptors
- has selective inotropic effect and increases cardiac output
- In therapeutic doses, it has little effect on BP and heart rate.
- TPR is generally not affected (counterbalancing of α and β effects)

Selective Phosphodiesterase Inhibitors

IM
INTERESTING
MEDICINE

- Amrinone and milrinone
- Increase cAMP level
- Exert both positive inotropic and vasodilator actions
- Administered intravenously
- Used for short-term treatment of severe heart failure
- Side effects; nausea, vomiting, arrhythmias, thrombocytopenia and hepatotoxicity
- Milrinone is more potent than amrinone and does not produce thrombocytopenia

- Given as i.v. infusion in short-term treatment of acute heart failure due to MI or cardiac surgery
- Side effects;
 - tachycardia, rise in BP and tolerance