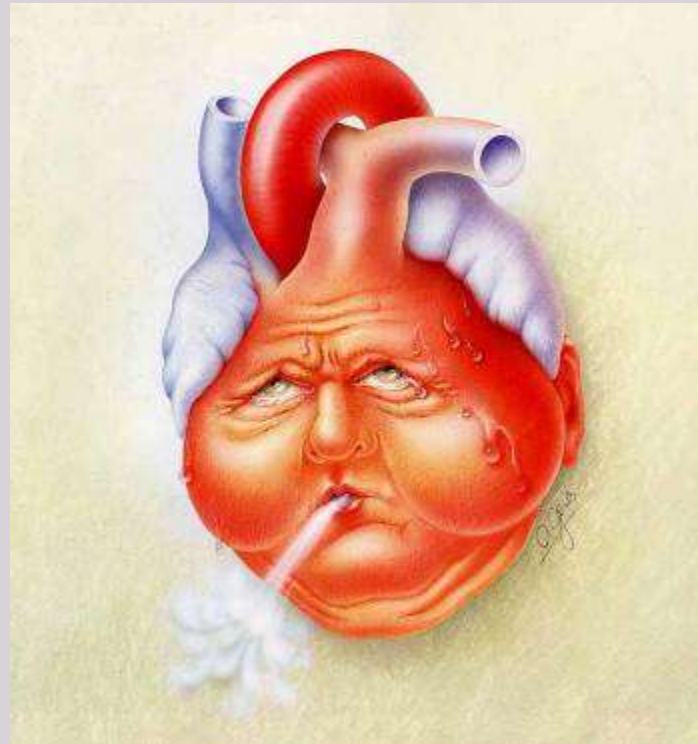


Pharmacological management of Heart Failure

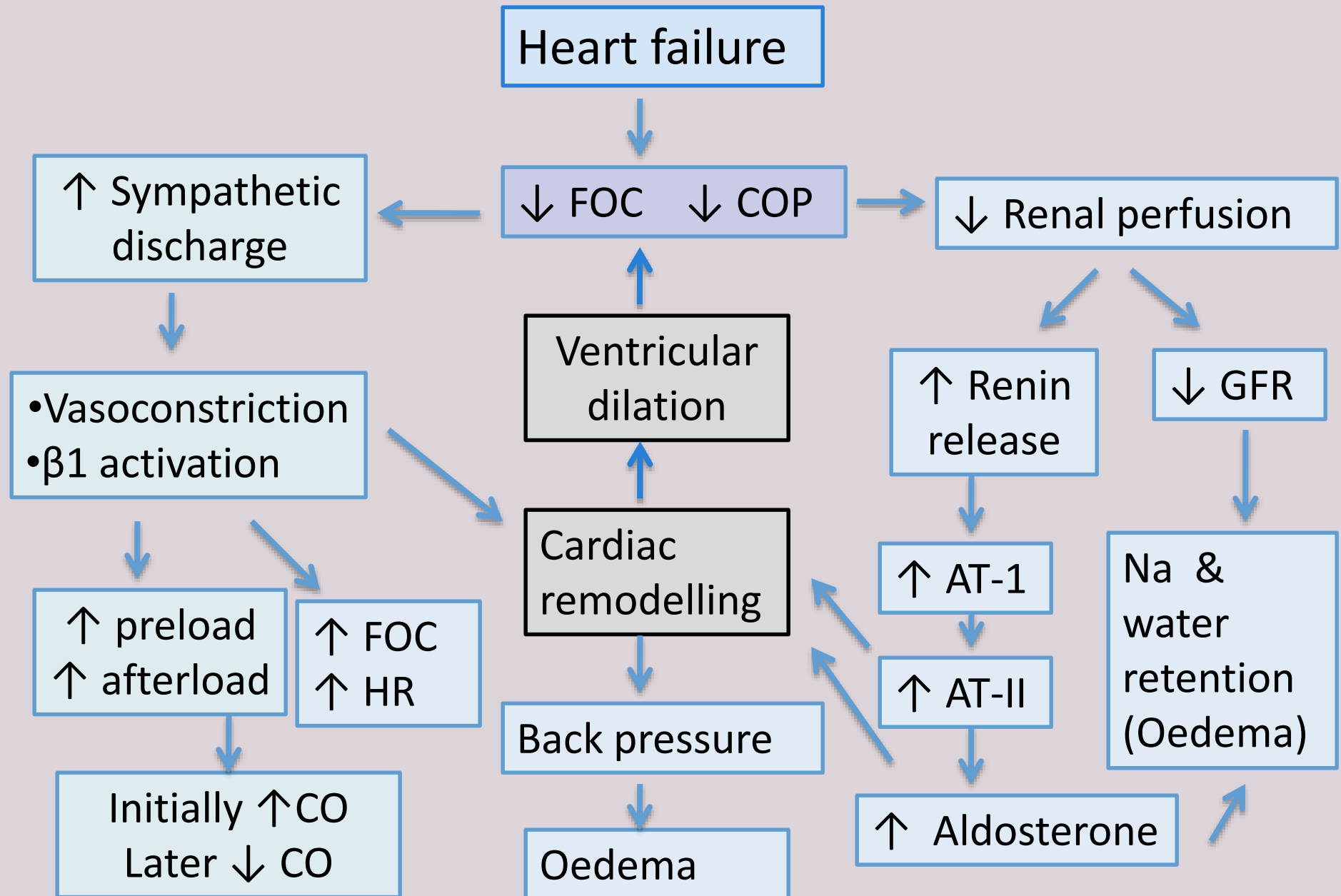
Dr Naser Ashraf Tadvi



What is heart failure



Pathophysiology of heart failure



Objectives

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

Major drug groups used in heart failure

Chronic Heart Failure

- Diuretics
- Aldosterone receptor antagonists
- Angiotensin converting enzyme inhibitors
- Angiotensin receptor blockers
- Beta blockers
- Cardiac glycosides
- Vasodilators

Acute Heart failure

- Diuretics
- Vasodilators
- Oxygen
- Morphine
- Bipyridines
- Beta receptor agonist: Dobutamine

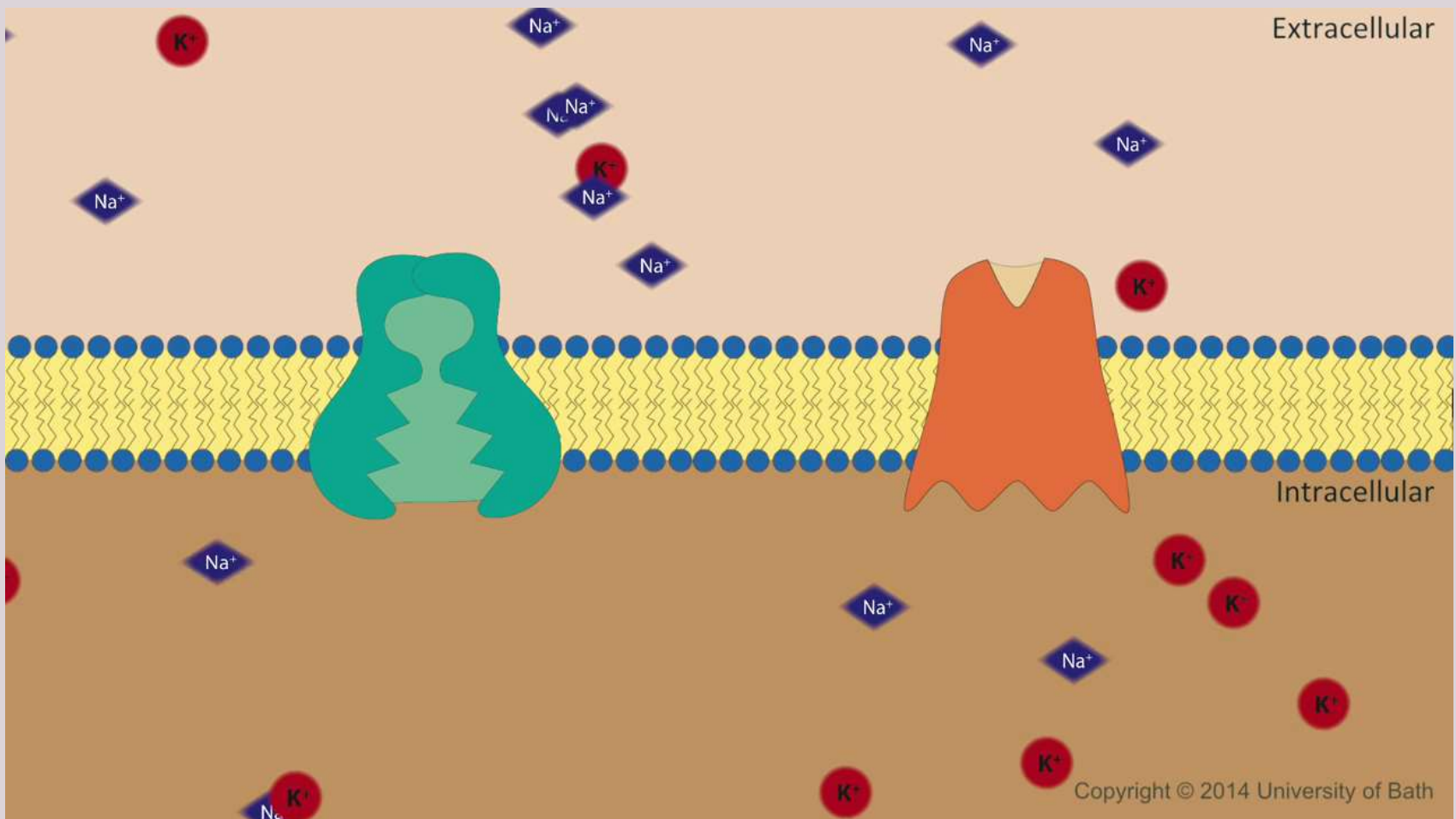
Drugs used in heart failure

- Diuretics:
 - Loop diuretic: Furosemide
 - Thiazide diuretic: Hydrochlorothiazide
 - Spironolactone: Potassium sparing diuretic and aldosterone antagonist
- Angiotensin converting enzyme inhibitors
 - Enalapril, lisinopril, captopril
- Angiotensin receptor blockers
 - Losartan, telmisartan

Drugs used in heart failure

- Beta blockers
 - Bisoprolol, Carvedilol, Metoprolol, Nebivolol
- Vasodilators
 - Hydralazine, Isosorbide dinitrate, Nesiritide
- Drugs which increase cardiac contractility:
(Inotropic drugs)
 - Cardiac glycosides: Digoxin
 - Beta agonist: Dobutamine
 - Bipyridines (Phosphodiesterase inhibitors) : Milrinone

Mechanism of action of Digoxin



Major effects of digoxin (Pharmacological actions)

CARDIAC

- ↑ force of contraction & Cardiac Output
- ↓ Heart rate
- ↑ Refractory period & ↓ conduction velocity in AV node
- Increased automaticity
- ECG: ↑ PR interval , ↓ QT interval , Flattening or inversion of T wave

EXTRA CARDIAC

- Kidney:
 - Increased renal perfusion
 - Retained salt and water is gradually excreted
- CNS:
 - Nausea, vomiting

Uses of Digoxin

- Congestive heart failure
- Atrial fibrillation
- Atrial flutter
- Paroxysmal atrial tachycardia

Digoxin adverse effects (Toxicity)

- Visual changes:(Visual disturbance, disturbance in color vision, blurring, photophobia)
- Gastrointestinal toxicity: anorexia, nausea, vomiting
- Cardiac adverse effects:
 - Bradycardia
 - Extrasystoles
 - A-V Block
 - Paroxysmal atrial Tachycardia
 - Sino Atrial arrest
 - Ventricular tachycardia
- Miscellaneous toxicity
 - Gynaecomastia, Skin Rashes

Contraindication to digoxin therapy is digoxin toxicity

Treatment of digoxin toxicity

- Prompt insertion of a temporary cardiac pacemaker & administration of digitalis antibodies (**digoxin immune fab**)
- These antibodies recognize cardiac glycosides from many plants in addition to digoxin. They are extremely useful in reversing severe intoxication with most glycosides
- Oral or parenteral potassium supplements :
 - contraindicated in presence of hyperkalemia
- 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

Phosphodiesterase inhibitors in heart failure

- Amrinone & milrinone : 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.
- Inodilator action: Inotropic effect with vasodilation
- IV administration for short term treatment of severe heart failure
- Common adverse effect of amrinone is thrombocytopenia
- Milrinone is more potent & doesn't cause thrombocytopenia

Role of diuretics in heart failure

- Diuretics, especially furosemide, are drugs of choice 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

Role of spironolactone in heart failure

- Aldosterone antagonist & potassium sparing diuretic
- ↓ mortality by 30% when added to in patients receiving ACE inhibitors and other standard therapy.
- Possible mechanism for this benefit is prevention of aldosterone induced myocardial and vascular fibrosis and baroreceptor dysfunction in addition to its renal effects.

ACE Inhibitors in heart failure

- ↓ peripheral resistance (↓ afterload)
- ↓ reduce salt and water retention by ↓ aldosterone secretion (↓ preload).
- ↓ long-term remodeling of the heart and vessels an effect that may be responsible for the observed reduction in mortality and morbidity
- Drug of first choice in left ventricular dysfunction without edema

Angiotensin receptor blockers in heart failure

- Losartan , telmisartan
- Block AT_1 receptor on the heart, peripheral vasculature and kidney
- Produce beneficial hemodynamic effects similar to those of ACE inhibitors.
- large clinical trials suggest that angiotensin receptor blockers are best reserved for patients who cannot tolerate ACE inhibitors (usually because of cough)

Role of vasodilators in heart failure

- The combination of hydralazine and isosorbide dinitrate should be used if intolerant of ACE-i and ARBS as it reduces mortality.
- It also reduces mortality when added to standard therapy.

Role of Beta blockers in heart failure

- Not all β blockers have proved useful, but **bisoprolol, carvedilol, metoprolol, and nebivolol** have been shown to reduce mortality.
- The beneficial effect may be due attenuation (\downarrow) of adverse effects of activated sympathetic drive
- Useful even though they have negative inotropic action

Approach to the Patient with Heart Failure

Assessment of LV function (echocardiogram)

EF < 40%

Assessment of volume status

Signs and symptoms of fluid retention

No signs and symptoms of fluid retention

Diuretic
(titrate to euvolemic state)

ACE Inhibitor

β -blocker

Digoxin

Management of acute LVF with pulmonary edema

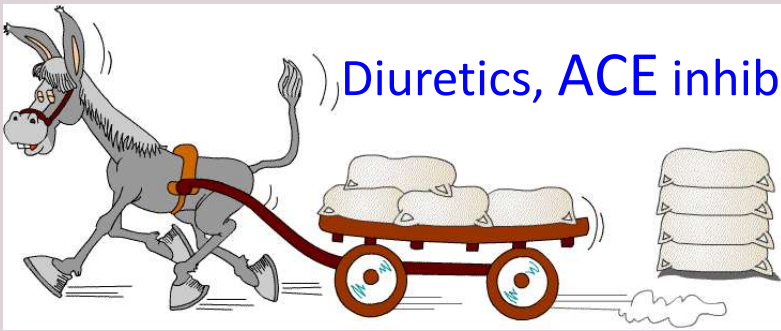
- Semi-upright posture
- Oxygen : 6-8 litres/min
- Furosemide: 40-80 mg IV
- Morphine
- Aminophylline: if associated bronchospasm
- Sublingual nitroglycerine
- Digoxin IV in patients with Atrial fibrillation/SVT/
Heart failure
- Continued management of heart failure /heart disease after resolution of acute heart failure

Newer drugs for heart failure

- Vasopeptidase inhibitors:
 - Omapatrilat
 - Nesiritide
- Omecamtiv mecarbil: selective cardiac myosin activator

Summary

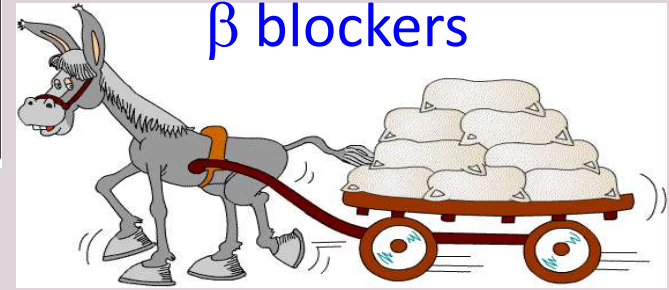
Diuretics, ACE inhibitors



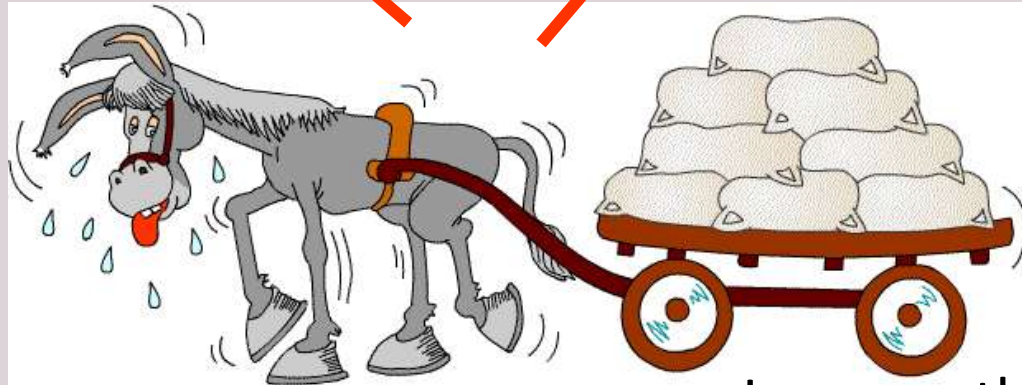
Reduce the number of sacks on the wagon

β blockers

SPEED LIMIT
35
MINIMUM
15



Limit the speed, thus saving energy



Increase the efficiency

Vasodilators



Like the carrot placed in front



Inotropes

references

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PHARMACOLOGY 13TH EDITION**