Medicine

Pharmacology Team

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Heart Failure

BY:

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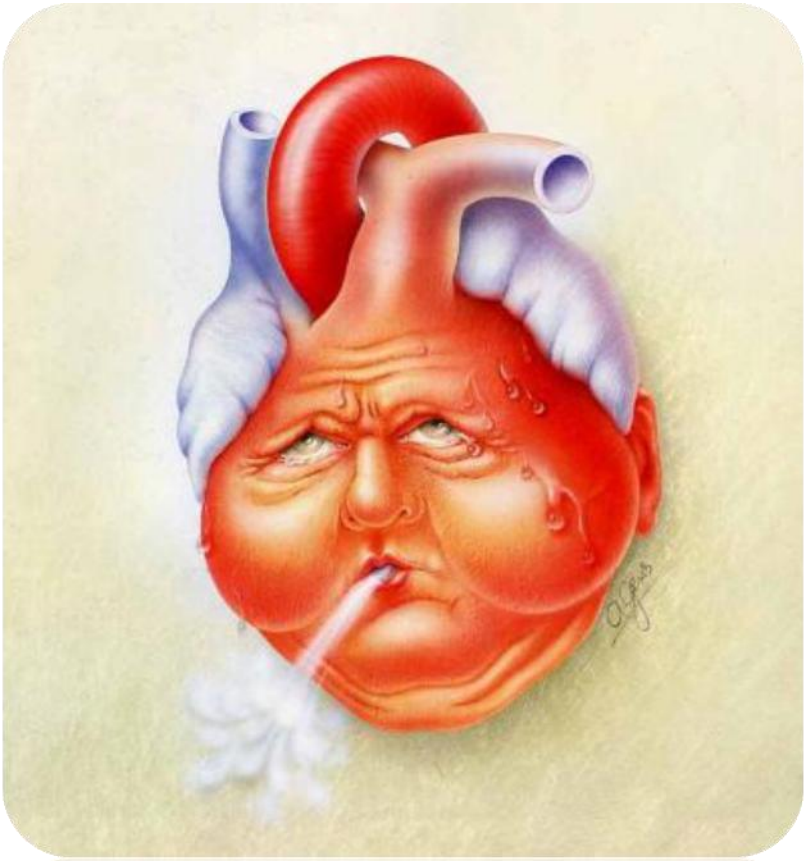

Heart Failure

- Result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood to meet the body's metabolic needs at rest or during exercise.

Team Note

If the blood that ejected to the body is not enough to meet the body's metabolic needs..there will be Heart Failure
So, that means there is something wrong in the heart "in function or in structure"

Clinical manifestation of heart failure:

<u>According to the pathology of the heart</u>

- Tachycardia → Increased heart rate, above 100 beats/min.
- Decreased exercise tolerance (rapid fatigue)
- Dyspnea →Breathlessness due to (pulmonary congestion).
- Peripheral edema → Water retention.
  These are the **symptoms** of heart failure noticed by patients
- Cardiomegaly → A **sign** of heart failure.

Types of heart failure :

- **Low Out Put Heart Failure:**

the amount of ejected blood is not enough to meat the body demands (common type).

- **High Out Put Heart Failure:**

A state where the output is normal or slightily high and, also, can not satisfy the body demands (rare).
Especially when the patient has:

- hyperthyroidism
- type of anemia

High output failure :

- The increase in output is not sufficient as in hyperthyroidism, and anemia.

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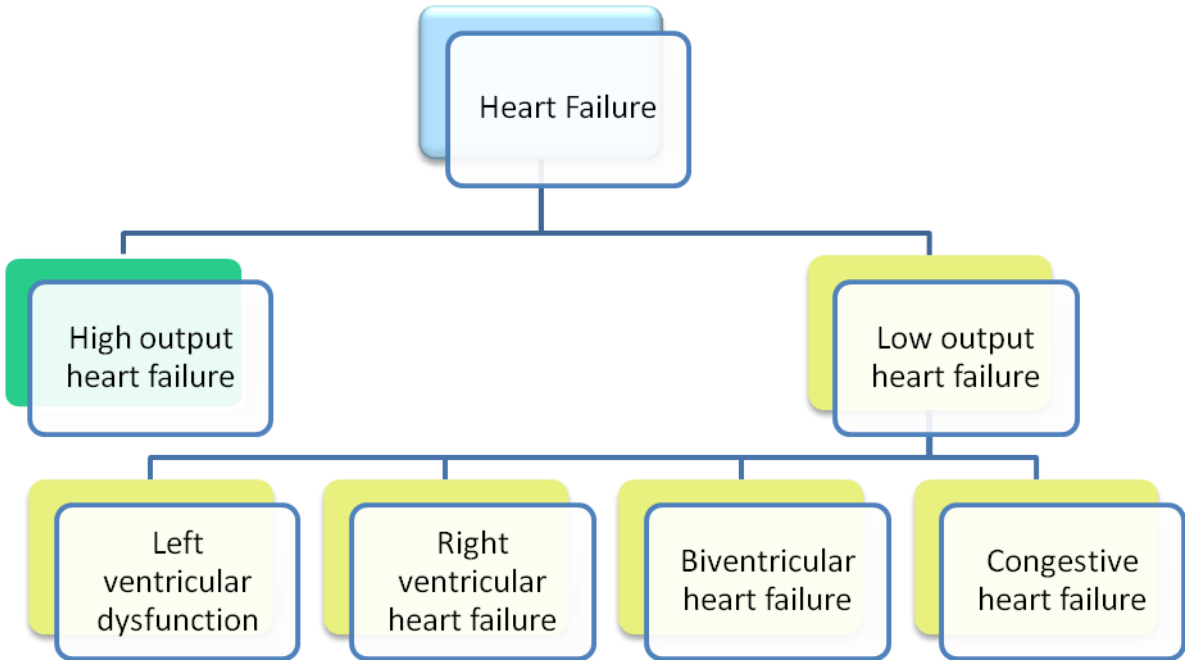


Team Note

Types of Low Output Heart Failure:

1.Left Ventricular dysfunction:

the most common type because the left ventricle is responsible for pumping blood to the whole body.

so the LV failure either →Systole: pumping

→Distole : filling

2.Right Heart Failure:

rare, e.g: (pulmonary arterial hypertension). When the pressure in the Pulmonary artery increase, the pressure in the right ventricle increases, too.

3. Biventricular Heart Failure:

Right and left ventricles failure

Common, it happens in two condition:

-When having ischemia or angina which leads to infarction

-when having a left heart failure but without taking care of it, may leads to right heart failure

4. Congestive heart failure:

the same as left heart failure, but here, the heart is dilated and congested (the blood is trapped inside). Manifestation: swelling of the neck because of congestion of blood vessels.

Factors affect cardiac output :

-Cardiac contractility:

Less. affects the ability of pumping blood efficiently.

-Preload:

increase in preload = (increase in venous return) lead to :

1- Blood volume.→ increases due to salt and water retention in the body,

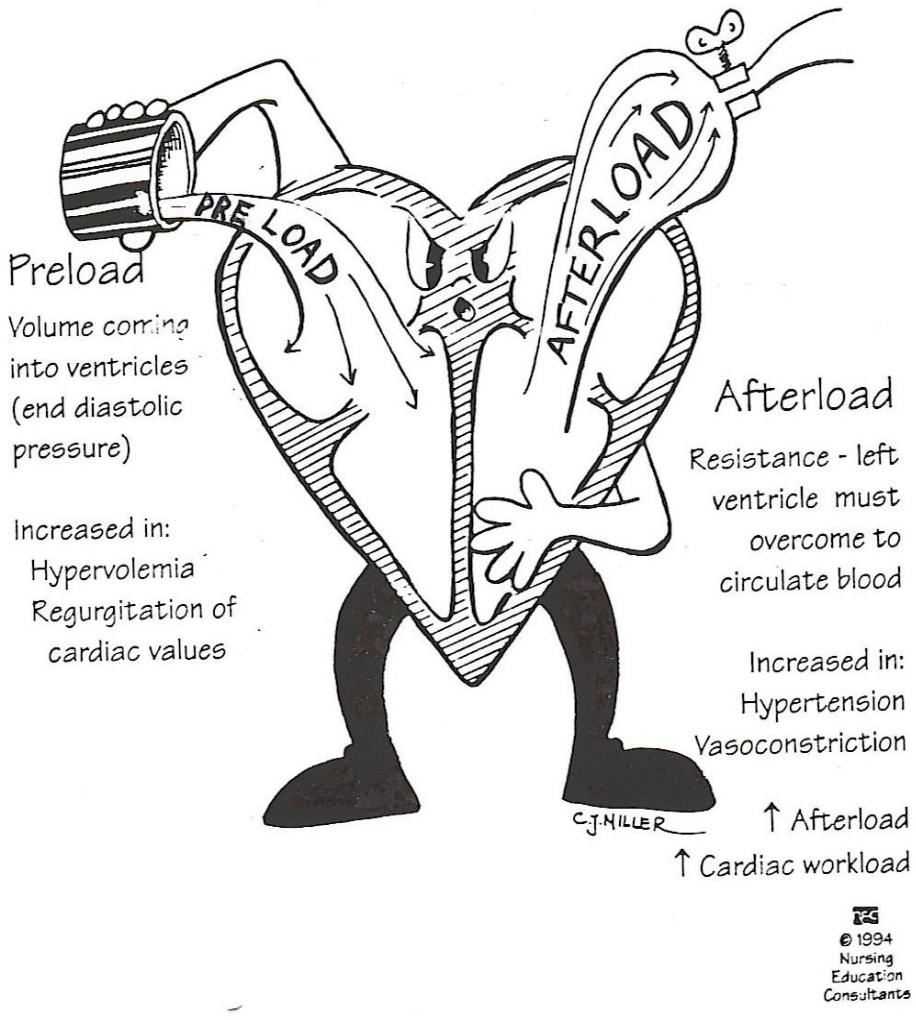
2- Venous tone.→ venous tone increases (vasodilation of veins)

-Afterload:

peripheral systemic resistance of arteries . It increases in HF.

-Heart rate:

In HF, stimulated sympathetic activity causes heart rate to increase in an attempt to overcome the decrease in cardiac output (to increase contractility and output) = tachycardia



CARDIAC SYSTEM
Memory Notebook of Nursing

http://www.mac.edu/faculty/ChristineStaake/Nursing%20420/pictures/Nursing%20420/Preload-Afterload.JPG

Team Note

Cardiac performance in heart failure:

Compensatory mechanism

Intrinsic change
Extrinsic change

Intrinsic changes :

Myocardial hypertrophy (cardiomegaly) to maintain cardiac performance in the face of a decrease in myocardial contractility.

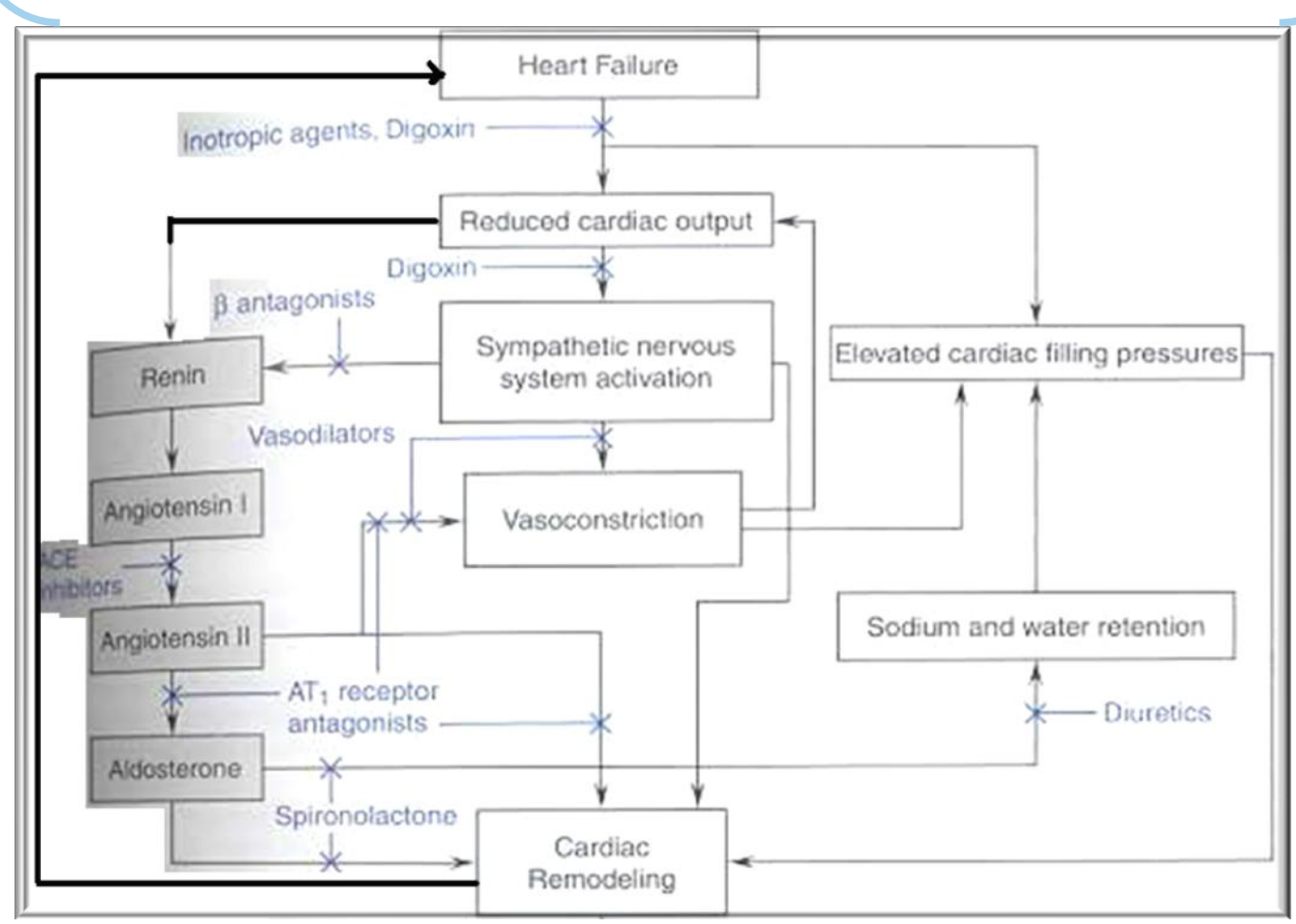
Extrinsic changes

↓ cardiac output → ↓renal blood flow → ↑ renin release → ↑angiotensin11

- ↓ cardiac output → low cardiac output means that the blood reaching the body decrease
- ↓renal blood flow → ↑ renin release → ↑angiotensin11 → secreted by the kidneys

↑in peripheral resistance (↑afterload) + ↑venous return + ↑sympathetic activity →↑cardiac output

Also cause Remodeling = Proliferation of connective tissue cells, abnormal myocardial cells.(hypertrophy)



Classification of heart failure

- **According to NYHA (New York Heart Association)**

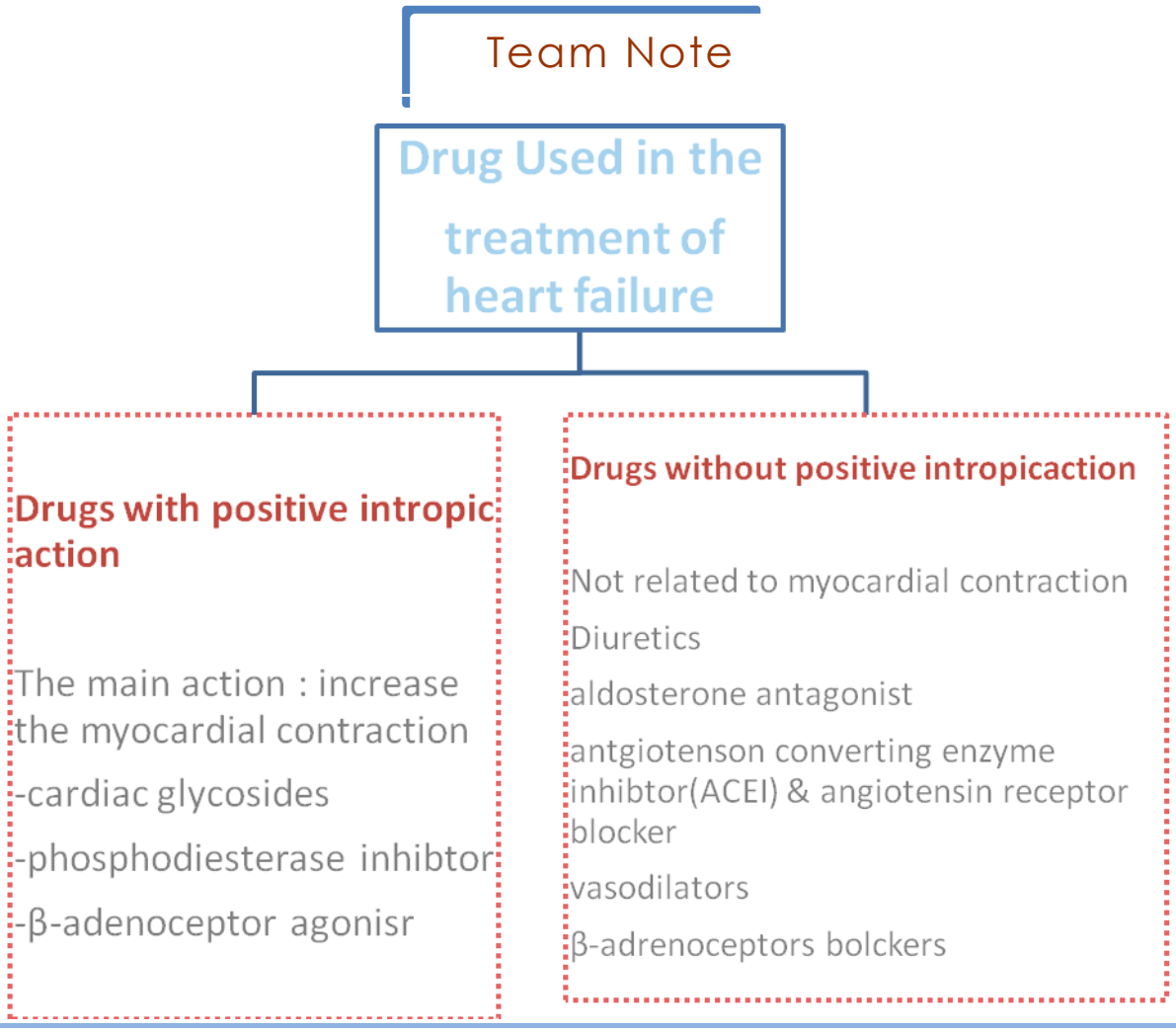
Class I: Symptoms of fatigue occur only with greater than ordinary activity when doing extra activity.

Class II: Slight limitation of ordinary activities , that result in fatigue & palpitation

Class III: fatigue occur with less than ordinary physical activity

Class IV : Is associated with symptoms even at rest.

Team Note



Drugs used in the treatment of heart failure

Drugs with positive inotropic effect :

Associated with myocardial contractility (intrinsic changes).

- Cardiac glycosides
- Phosphodiesterase inhibitors
- β- adrenoceptor agonist

Team Note

Drugs without positive inotropic effect:

Main work on pre &after load.

- Diuretics
- Aldosterone antagonists
  aldosterone causes:
  1-retention of salt and water.
  2- hypertrophy of cardiac muscle.
  3- hypocalemia (cause arrhythmias).
- Angiotensin converting enzyme inhibitors (ACEI) prevent production of angiotension II & Angiotensin receptor blockers prevent angiotension II from binding to receprtros.
- Vasodilators
- β- adrenoceptor blockers

Vasodilators

Drugs which dilate blood vessels:
We choose vasodilators according to signs, symptoms and hemodynamic changes :

- Selective venodilators as **nitrate group** is used when the main symptoms is **dyspnea** due to pulmonary congestion

Venodilators decrease preload, blood volume, venous return and venous tone.

- Selective arteriodilators as **hydralazine** is used when the main complain is **rapid fatigue** due to low cardiac output.

and that lead to increase in peripheral resistance, and increase in afterload.

- Non-selective vasodilators as **ACEI** (angiotension-converting enzyme inhibitors) **or blockers:** dilate arteries and veins.

Clinical uses of vasodilators
Acute heart failure : given through the parenteral route.
Chronic heart failure: The long use of vasodilators decrease remodeling.
The routes of administration differ.

Angiotensin converting enzyme inhibitors & angiotensin receptor blockers :

- **↓Peripheral resistance (After load)** → by reducing sympathetic activity.
- **↓Venous return (Preload)** → because angiotension II stimulate aldosterone production which cause salt and water retention and increase blood volume).
- **↓sympathetic activity and that ↓ heart rate.**
- **↓remodeling** →↓mortality rate (hypertrophy)
- **Angiotensin** يقلل الافترلود والبريلود وتضخم القلب

من اسمها نستنتج عملها
-تمنع عمل الأدرينالين المسؤول عن زيادة الـ tachycardiaالمؤدي إلى heart failure
sympathetic
اللي هو اهم علامات

β-adrenoceptor blockers:

- → Used to treat chronic heart failure
- (class 2 or 3) only, and the HF should be
- stable i.e. still not decompensate.
- Antagonism for the enhancing action of sympathetic over activity.
- → Reduce sympathetic over activity and thus reduce remodeling process caused by the release of catecholamine: adrenaline and noradrenaline, which are secreted by the sympathetic nervous system, and lead to the formation of abnormal myocardial cells.
- Reduce mortality → by reducing remodeling
- Inhibit renin release
- Some of them have antioxidant activity →reduce free radicals

Diuretics

- Reduce salt and water retention→ reduce edema, pulmonary edema (congestion) → ↓ventricular preload and venous pressure.
- Reduction of edema and its symptoms.
- Reduction of cardiac size→ improve cardiac performance→ reduce blood volume → reduce venous return

Team Note

Drugs with positive Inotropic effects

β-Adrenoceptor agonist

intravenous I.V. route in acute heart failure (emergency).

*** True or False:**

In chronic HF, β-Adrenoceptor agonist drugs are given intravenously(X).
Oral route.

Dopamine : Acts on a ,β_1 and dopamine receptors
Used in acute L.H.F. mainly in patients with impaired renal blood flow.

Activation of dopamine receptors lead to vasodilatation in renal blood vessels, and that lead to improved renal function.

Dobutamine : commonly used, Selective β_1 agonist,
Used in the treatment of acute heart failure ..

- **Both of them are given intravenously.**
- **Their adverse effects :**

-Tachycardia
-Angina
-Tachyphylaxis

Phosphodiesterase Inhibitors:

- Bipyridines :(Amrinone ,Milrinone)
- They are only available in parenteral form.
- Half-life 3-6hrs.
- Excreted in urine.

Mechanism of action:

- Inhibit phosphodiesterase enzyme in cardiac & smooth muscles resulting in :

Increase in cAMP

In the heart : Increase in myocardial contraction
In the peripheral vasculature : Dilation in both arterial & venous vessels leading in reduction in both after load & preload.

Therapeutic uses

- Used only intravenously for:
  1- acute heart failure
  2-an exacerbation of chronic heart failure.

Team Note

"**Acute HF on top of chronic**"
Used for short-term treatment. Not used in chronic HF because of its side effects.
Adverse effects:

- Nausea ,vomiting
- Arrhythmias (less than digitalis)
- Thrombocytopenia → (bone marrow depression).
- Liver toxicity
- Milrinone less hepatotoxic and less bone marrow depression than amrinone. → That's why it's used more

Cardiac glycosides (Digitalis):
Prototype Digoxin

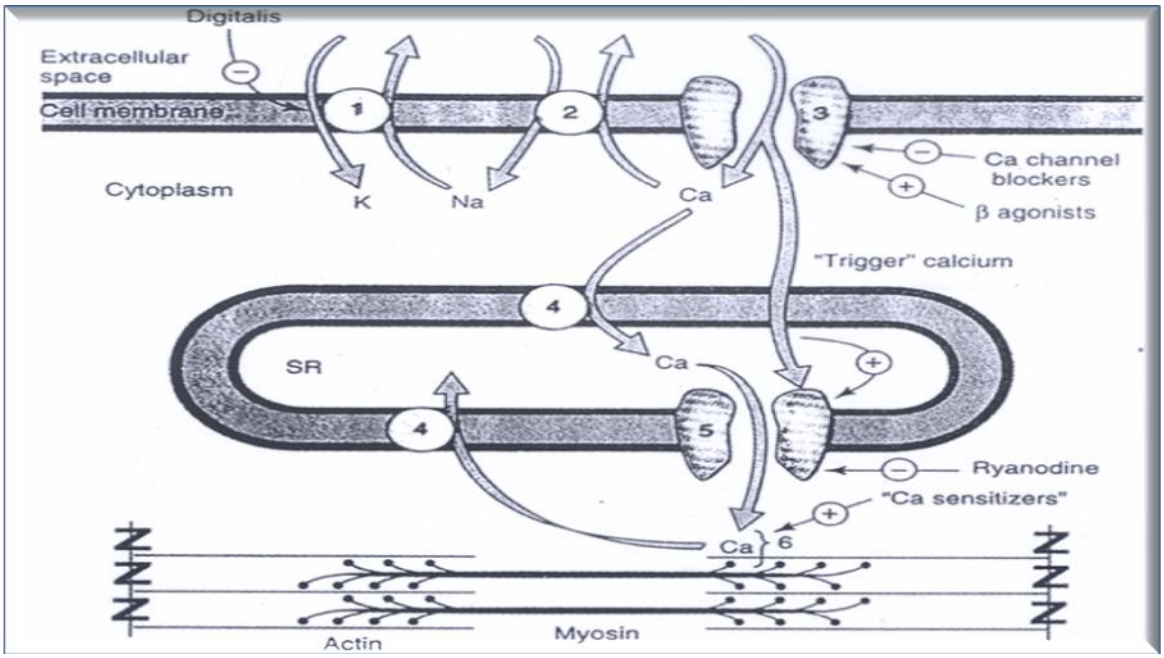
- Origin .. Plant extracted from a herb (foxglove)
- Chemistry
- Preparations
- Pharmacokinetics

Prototype = digoxin → (أفضل أنواع الأدوية البوستف اللي يُعطى عن طريق الفم)

Pharmacodynamics:

- At the molecular level cardiac glycosides inhibit Na^+ / K^+ ATPase (sodium pump).
- Cardiac effects :
  A) Mechanical
  B) Electrical

Mechanism of action:



Mechanical effects:

- Increased contractility of the cardiac muscles
- The resulting improved circulation leads
- To reduced sympathetic activity & reduction in heart rate.
- Vagal tone is enhanced causing decrease in heart rate & oxygen requirement

Electrical effects:

- Slow conduction through S.A.N. & A.V.N.
- → prolong conduction time between atrium and ventricles (prolong P-R interval in ECG.) .
- Short duration of action potential & refractory periods of both atrium & ventricles (↑ entry of calcium during plateau phase) .

Extracardiac adverse effects:

- **GIT :**Anorexia, nausea,vomiting, diarrhea
- **C.N.S. :**Hallucination,visual disturbances, convulsions.
- **Gynecomastia**
- **Skin rash**

Contraindications:

- Toxic myocarditis
- Constrictive pericarditis
- Cardioversion : في حالات علاجهم بالصدمات الكهربائية

Team Note

Therapeutic uses of digoxin:

- Treatment of severe left ventricular systolic dysfunction due to hypertension , atherosclerosis or ischemic heart disease .

Factors increase digitalis toxicity

- Small Lean body mass
- Renal disease
- Hypothyroidism
- Hypokalemia
- Hypomagnesemia
- Hypercalemia
- Drugs

فكرة الهايبو إنه القلب كتعويض للنقص يزيد نشاط ATPs sodium pump فهذا يؤدي إلى زيادة نشاط الديجوكسن لأنه بدل مايشتغل على نسبة طبيعية قاعد يشتغل على نسبة مضاعفة من ATPs

كما هو معلوم إنه الديجوكسين يزيد نسبة الكالسيوم فلما يكون فيه زيادة من الأساس فكأني ضاعفت الجرعة

Treatment of digitalis toxicity:

- Stop drug
- Potassium therapy
- Cholestyramine → the drug which decrease the absorption of **digitalis**
- Atropine (A-V block) >>↓vigal stimulation >> ↓parasympathetic
  :: كما هو معلوم الديجوكسين يزيد البارا فزيادة جرعته يعني زيادة البارا عن المطلوب ::
- Lidocaine: antiarrythmia drug
- Fab antibodies in life-threating or severe cases.

Drug interactions:

- **Diuretics**→ hypokalemia (arrhythmia)
- **Quinidine** : ↑plasma level of digitalis
- **Antibiotics** that alter intestinal flora ↑digoxin bioavailability
- **Agents that release catecholamines** sensitize myocardium to digitalis to induce arrhythmias.

Management of chronic heart failure:

- Reduce work load of the heart
  - Limits the activity
  - Reduce weight
  - Control hypertension
- Restrict sodium
- Diuretics
- ACEI or receptor blockers
- Digitalis
- β- blockers
- Vasodilators

Management of acute heart failure:

- Volume replacement
- Diuretics
- Positive inotropic drugs
- Vasodilators
- Antiarrhythmic drugs
- Treatment of myocardial infarction