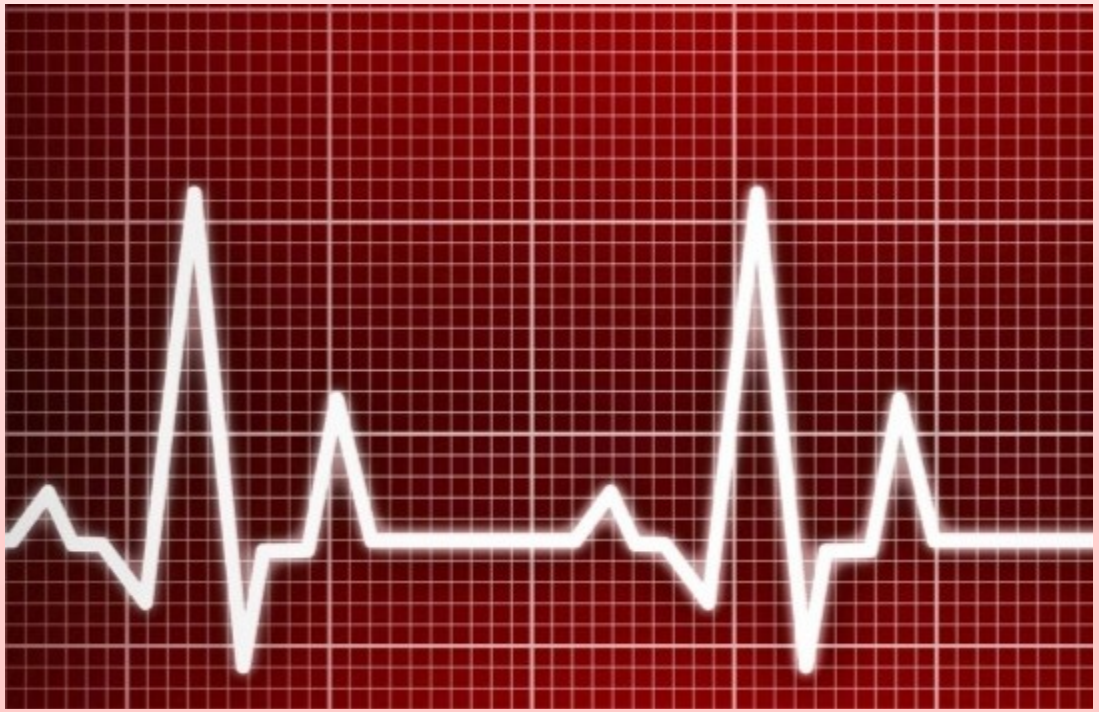
Drugs acting in Congestive Heart Failure (CHF)



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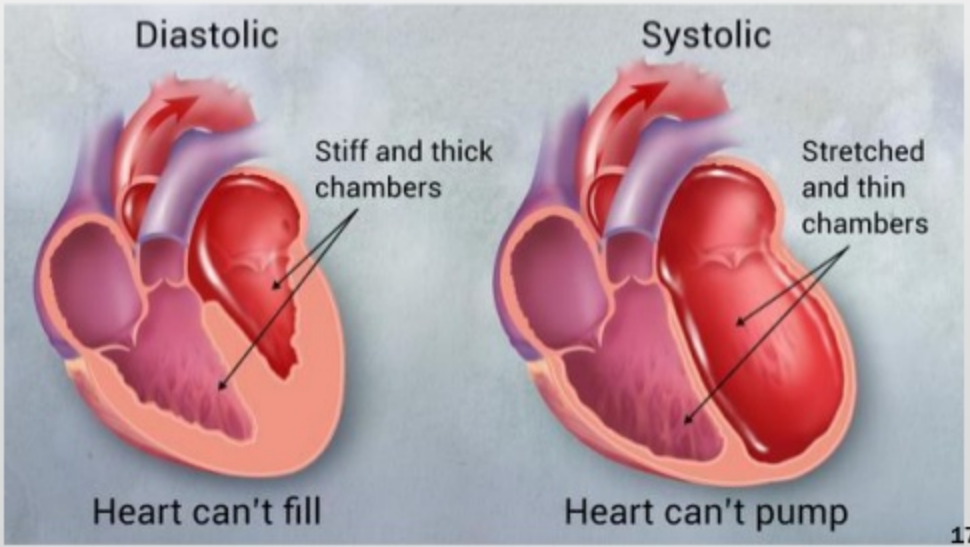
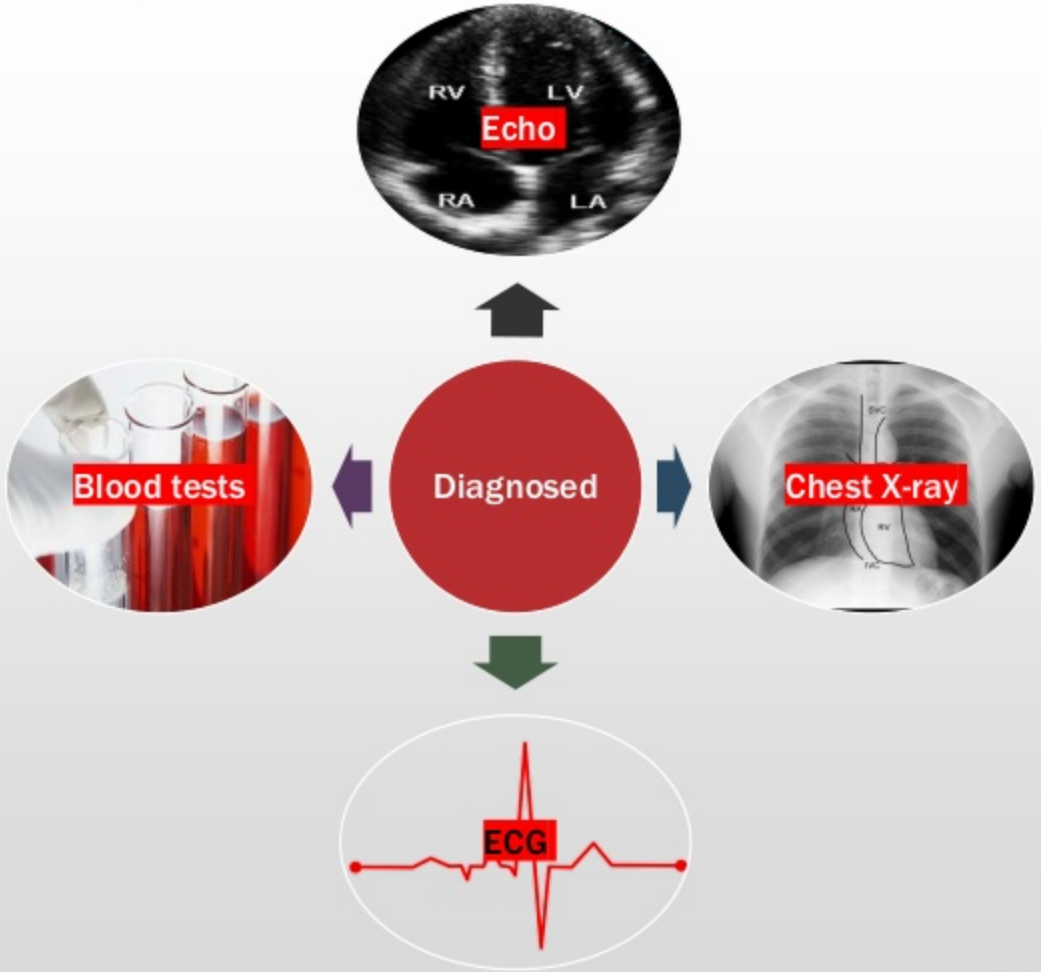
Introduction

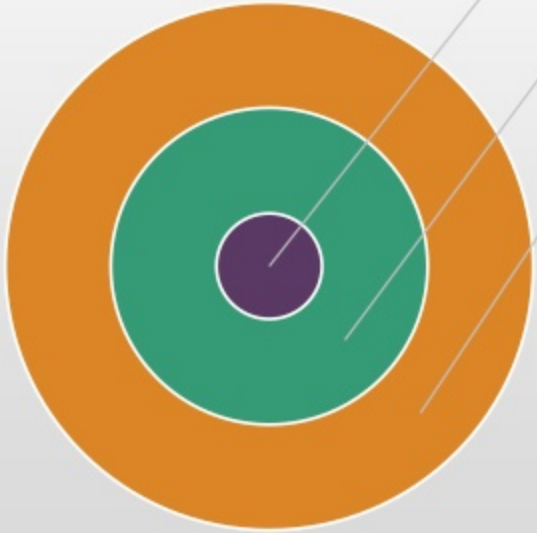
A condition in which the heart is *unable to pump sufficient blood* to meet the metabolic demand of the body and also unable to receive it back because every time after a systole.



How Heart Failure Is Diagnosed



Treatment strategies of CHF GOAL



Increase cardiac output

Reduce preload and afterload

increase myocardial contractility.

- Inotropic agents
- β adrenergic agonist
- β adrenergic antagonist
- Vasodilators: Ca^{2+} Channel Blocker
- Diuretic agents

Classification..

1. Inotropic drugs:

(a)Cardiac glycosides: Digoxin, Digitoxin

(b)Sympathomimetics: Dobutamine, Dopamine

(c) Phosphodiesterase III inhibitors: Amrinone

IDIA-V

2. Diuretics:

(a) High ceiling diuretics: Furosemide, Bumetanide

(b) Thiazide like diuretics: Hydrochlorothiazide, Metolazone.

3. Inhibitors of Renin-Angiotensin system-

(a) ACE-inhibitors: Enalapril, Ramipril

(b) Angiotensin (AT receptor) antagonists: Losartan

4. Aldosterone antagonist- Spironolactone, Eplerenone

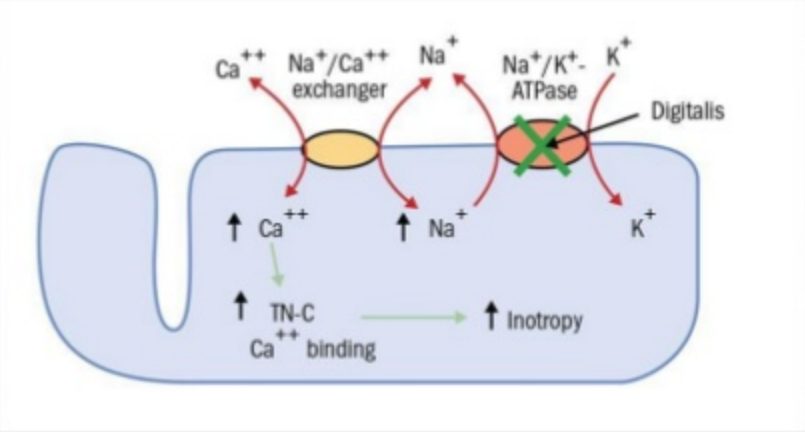
5. Vasodilators-

(a) Venodilators: Glyceryl trinitrate

(b) Arteriolar dilator: Hydralazine

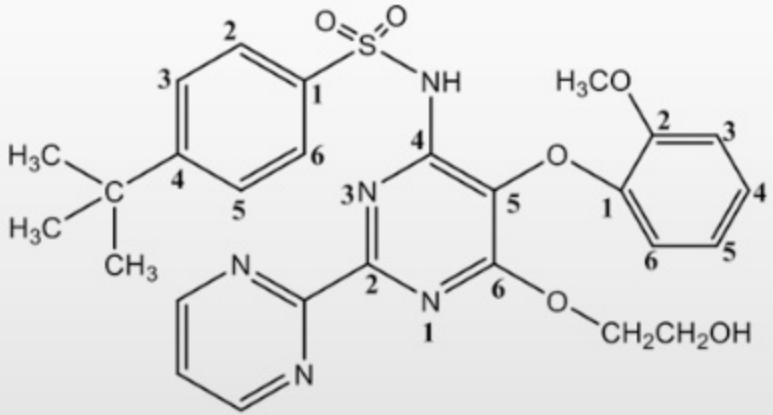
(c) Arteriolar + Venodilator: Sod. Nitroprusside

Mechanism of Action of Digoxin



- Inhibition of Na+/K ATPase pimp by Digitalis
- Increases Na+ concentration inside the cell
- Increases exchanges Na+ for ca++
- Incresed intracellular Ca++
- Incresed influx of Ca++ from sarcoplasmic reticulum
- Increases contractility of cardiac muscles.

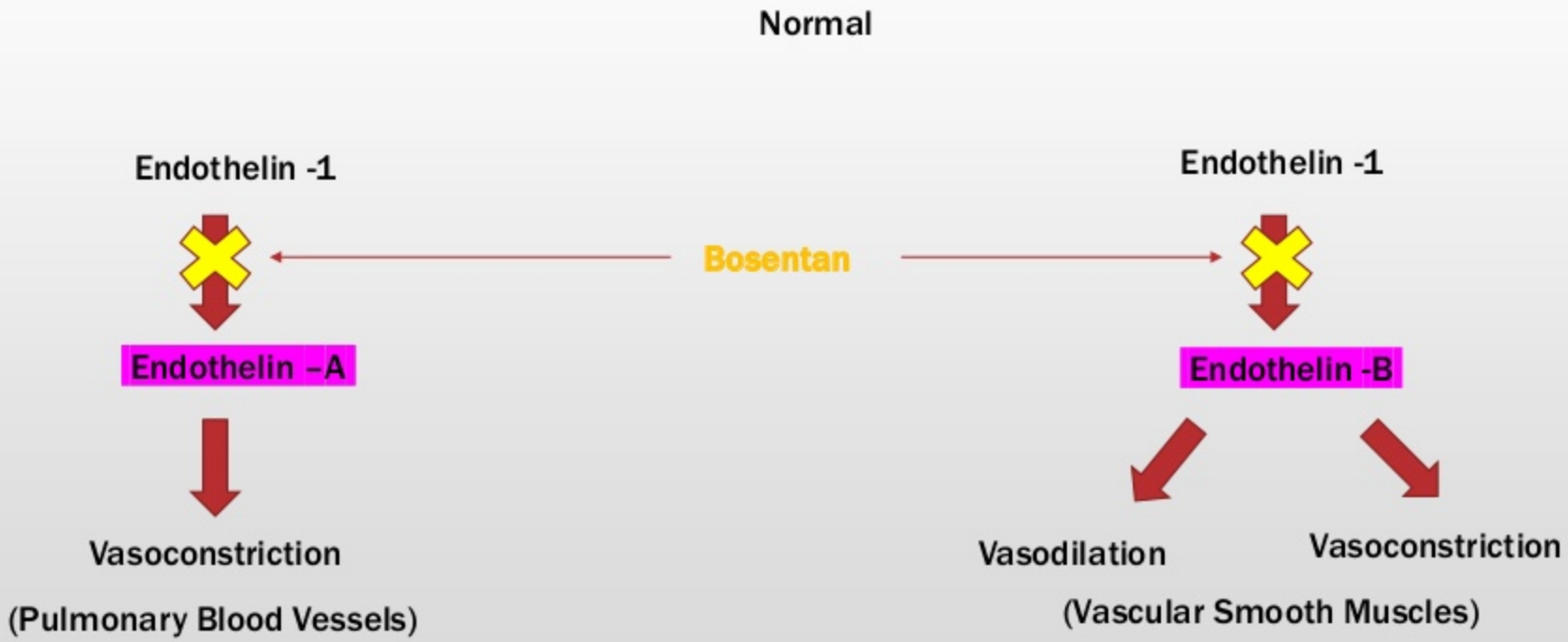
Bosentan



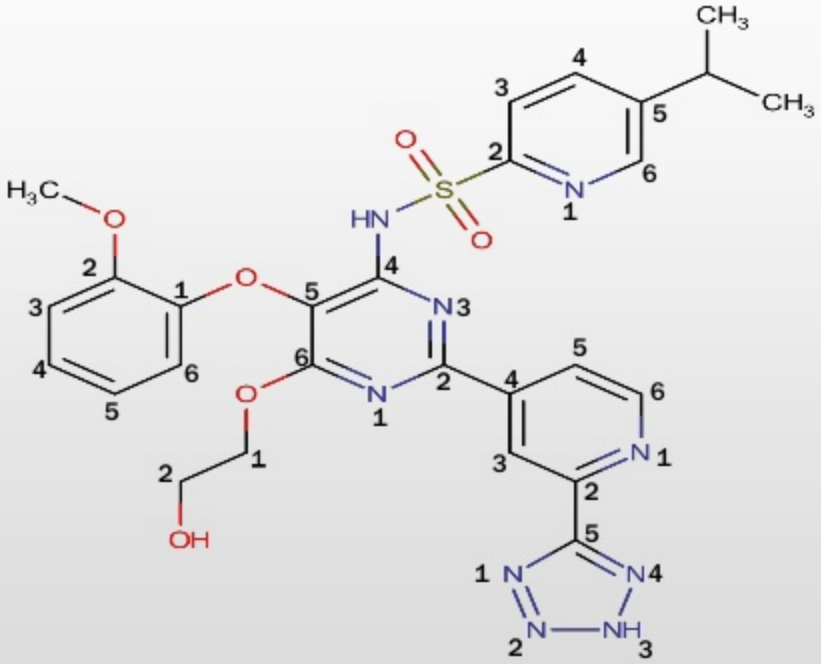
4-*tert*-butyl-*N*-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-(pyrimidin-2- yl)pyrimidin-4-yl]benzene-1-sulfonamide

- Bosentan is a competitive antagonist of endothelin-1 at the endothelin-A (ET-A) and endothelin-B (ET-B) receptors.
- Under normal conditions, endothelin-1 binding of ET-A receptors causes constriction of the pulmonary blood vessels.
- Conversely, binding of endothelin-1 to ET-B receptors has been associated with both vasodilation and vasoconstriction of vascular smooth muscle, depending on the ET-B subtype (ET-B1 or ET-B2) and tissue.
- Bosentan blocks both ET-A and ET-B receptors, but is thought to exert a greater effect on ET-A receptors, causing a total decrease in pulmonary vascular resistance

Mechanism of Action...



Tezosentan



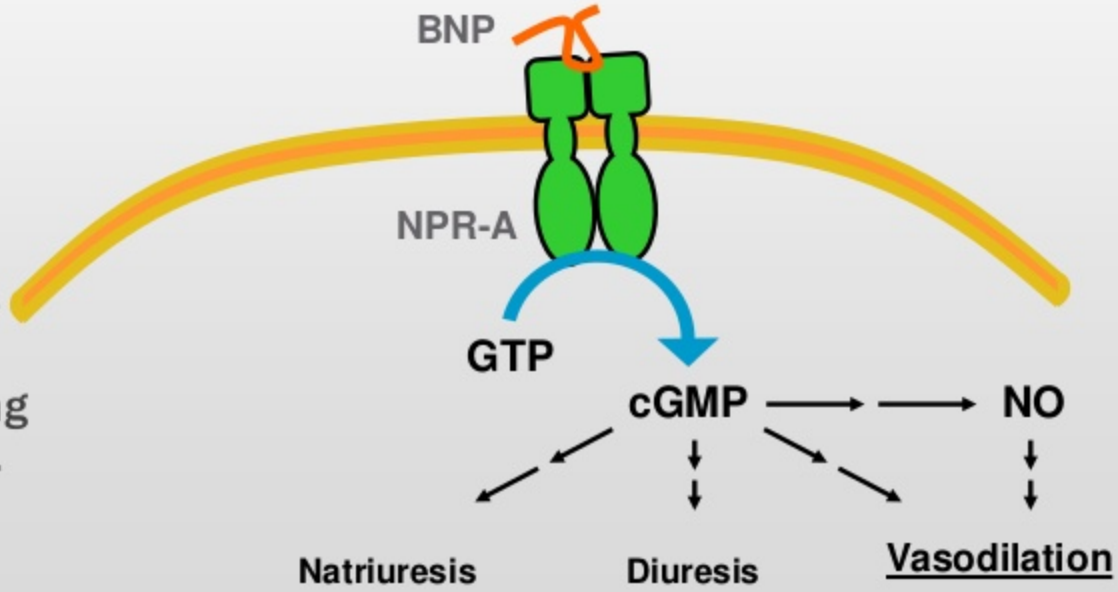
- Tezosentan is a non-selective ETA and ETB receptor antagonist.
- It acts as a vasodilator and was designed as a therapy for patients with acute heart failure.

N-(2-(2-(2H-tetrazol-5-yl)pyridin-4-yl)-6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy) pyrimidin-4-yl)-5-isopropylpyridine-2-sulfonamide

Nesiritide

- Nesiritide (Natrecor) is the recombinant form of the 32 amino acid human B-type natriuretic peptide(BNP), which is normally produced by the ventricular myocardium.
- Nesiritide works to facilitate cardiovascular fluid homeostasis through counter regulation of the renin–angiotensin–aldosterone system, stimulating cGMP, leading to smooth muscle cell relaxation.

- Recombinant human B-type natriuretic peptide (BNP)



“Thank You”