Congestive Cardiac Failure-1

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What is Congestive Cardiac Failure (CCF)?

- Heart failure does not mean the heart has stopped working
- Heart's pumping power is weaker than normal
- In Heart failure:
  - blood moves through the heart and body at a slower rate
  - pressure in the heart increases
  - heart cannot pump enough oxygen and nutrients to meet the body's needs

What is Congestive Cardiac Failure (CCF)?

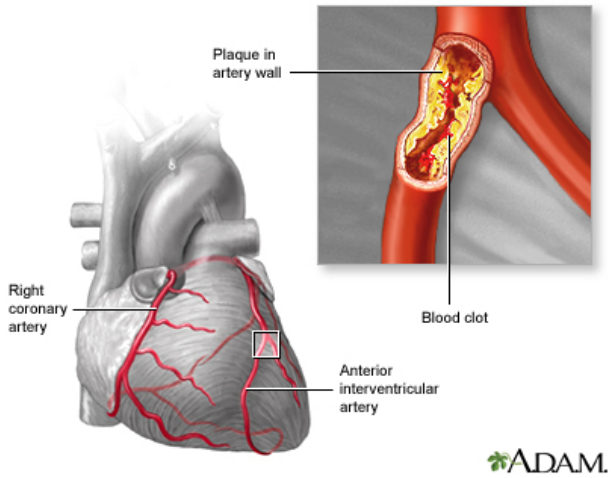
- In Heart failure:
  - The chambers of the heart respond by stretching
  - Heart muscle walls weaken and become unable to pump as efficiently
  - kidneys may respond by causing the body to retain fluid
  - Leads to Edema (congestion), hence the name Congestive Cardiac Failure (CCF)

What are symptoms of Congestive Cardiac Failure (CCF)?

- Symptoms in Heart failure:
  - Shortness of breath (dyspnea) when you exert yourself or when you lie down
  - Fatigue and weakness
  - Swelling (edema) in your legs, ankles and feet
  - Rapid or irregular heartbeat
  - Swelling of your abdomen (ascites)
  - Sudden weight gain from fluid retention
  - Difficulty concentrating or decreased alertness
  - Sudden, severe shortness of breath and coughing up pink, foamy mucus
  - Elevated blood pressure
  - Chest pain, if your heart failure is caused by a heart attack

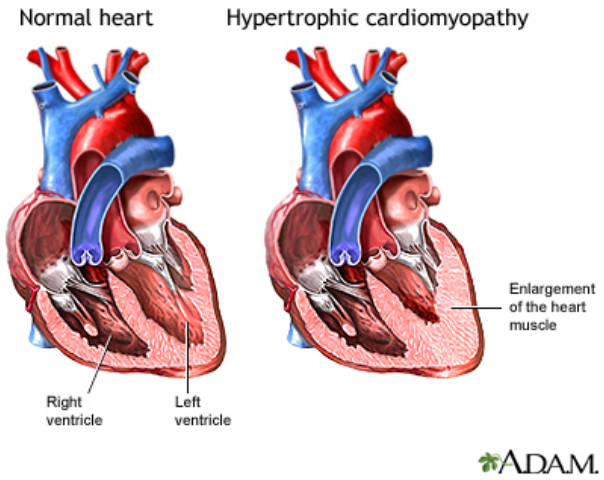
What causes Congestive Cardiac Failure (CCF)?

- Coronary artery disease:
  - Disease of the arteries that supply blood and oxygen to the heart
  - If arteries become blocked or severely narrowed, the heart becomes starved for oxygen and nutrients
- Heart attack:
  - Coronary artery becomes suddenly blocked, stopping the flow of blood to the heart muscle



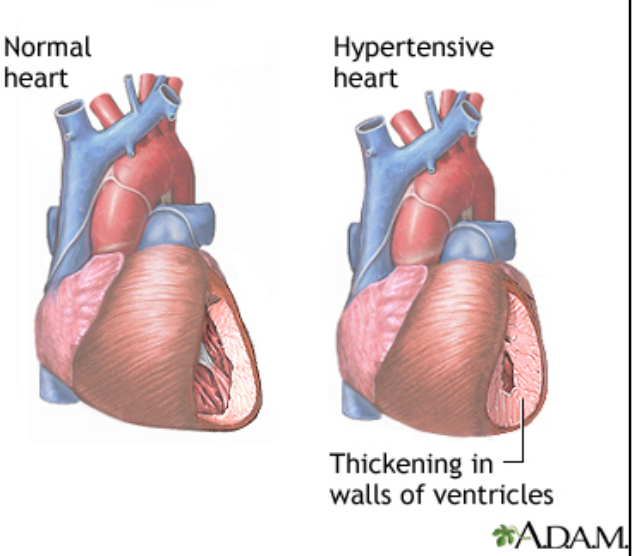
What causes Congestive Cardiac Failure (CCF)?

- Cardiomyopathy:
  - Damage to the heart muscle from causes other than artery or blood flow problems



What causes Congestive Cardiac Failure (CCF)?

- Hypertension:
  - **High blood pressure (75% cases)**
    - The heart muscles thicken to make up for increased blood pressure
    - The force of the heart muscle contractions become weak over time
    - muscles have difficulty relaxing
    - This prevents the normal filling of the heart with blood



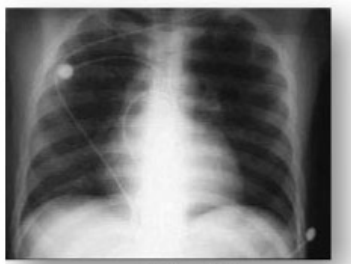
What causes Congestive Cardiac Failure (CCF)?

- Conditions that overwork the heart:
  - valve disease
  - thyroid disease
  - kidney disease
  - diabetes, or
  - heart defects present at birth

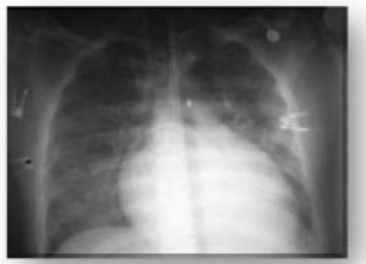
How do you Diagnose Heart Failure?

- Echocardiography
  - Use of Ultrasound to determine
    - Stroke volume (Volume of blood pumped with each beat)
    - End diastolic volume (volume of blood in the right and/or left ventricle at end load)
    - Ejection fraction (Fraction of blood leaving ventricles)

- Chest X-ray
  - Visible enlargement of heart in acute cases



normal sized heart



abnormally large heart (cardiomegaly)

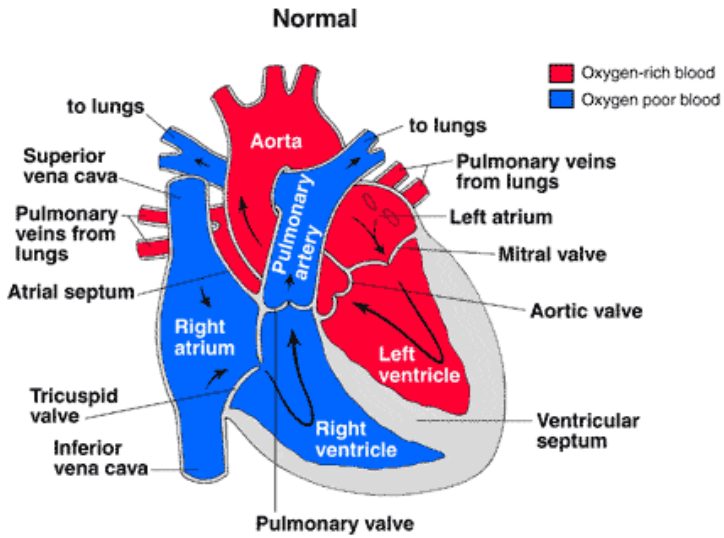
How do you Diagnose Heart Failure?

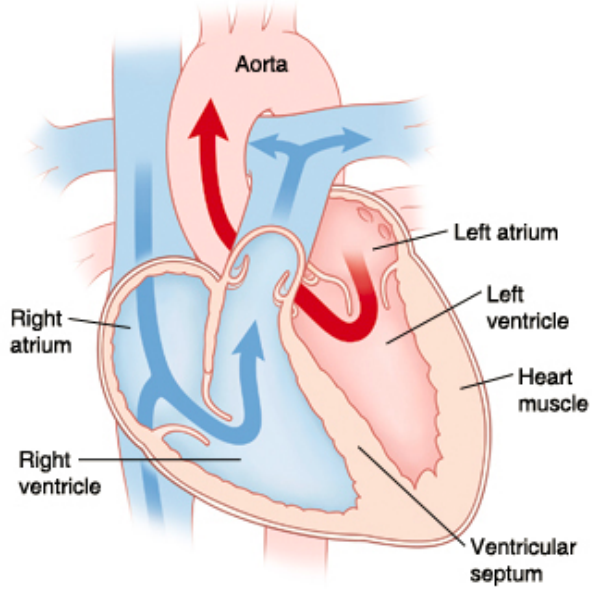
- Blood test
  - Electrolytes
  - Measures of renal, liver, thyroid function
  - B-type natriuretic peptide (BNP) is a specific test indicative of heart failure

Treatment Strategy

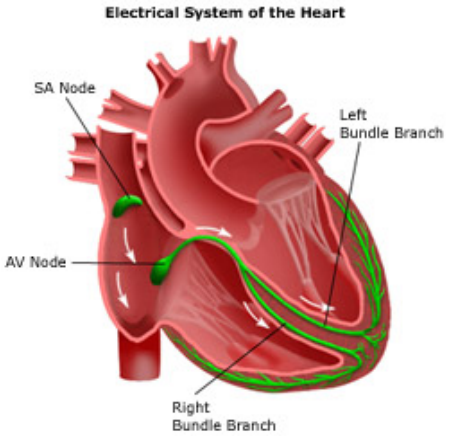
- Cardiac targets: traditional positive ionotropic agents
  - Preferred in acute systolic failures
- Non-cardiac targets: ACE inhib, angiotensin receptor blockers, b-blockers, Diuretics
  - These agents are more useful in reducing long term mortality rates

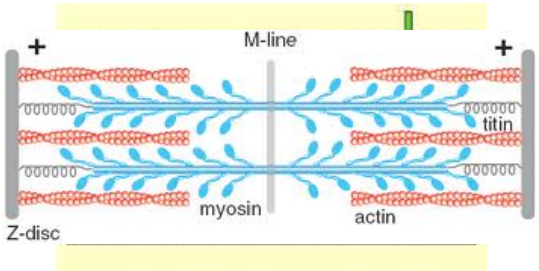
Normal Functioning of Heart

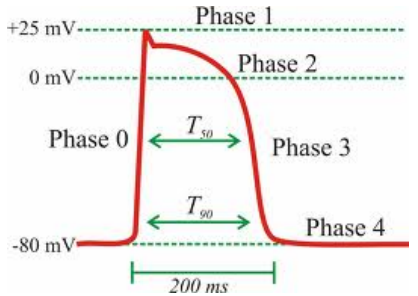




Cardiac electro-conduction



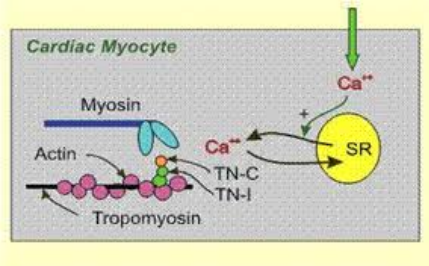


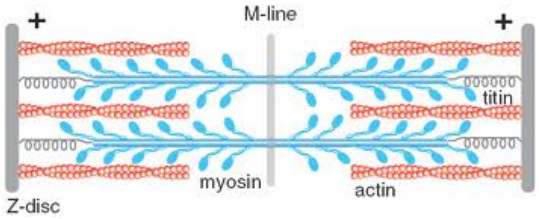


Action Potential

Cardiac contractility

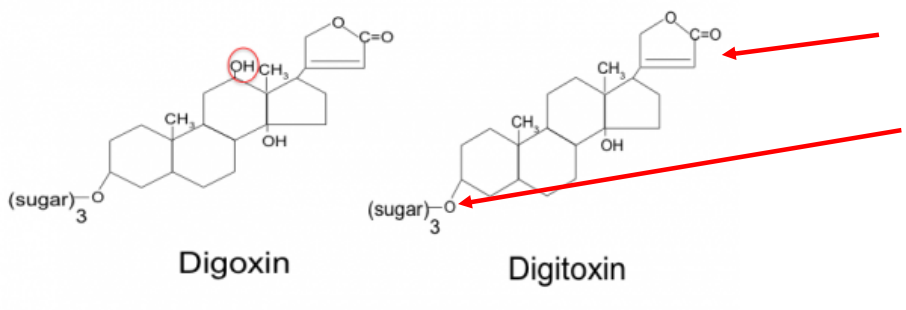
- Slow Ca^{+} entry acts as a triggers
- Releases large amounts of Ca^{+} from SR





Ionotropic Drugs
Cardiac glycosides

- Group of compounds that affect cardiac contractility
- Several ; Digoxin, digitoxin, digitalis and ouabain

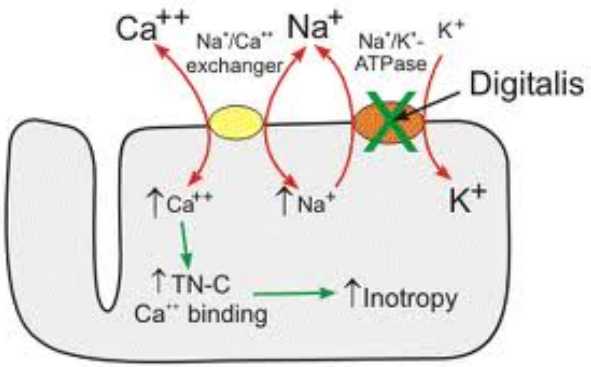


- Steroid nucleus linked to lactone ring at C-17
- Series of sugar at C-3

Pharmacodynamic effect of Digoxin

- Na^+/K^+ ATPase is membrane bound transport (Na pump)
- At molecular level digoxin inhibits Na^+/K^+ ATPase

- <u>Inhibition leads to</u>
  1. Increase in Na^+ conc in cell
  2. Reduction in Ca^{++} exchange by Na^+/Ca^{++} exchanger
  3. High conc of Ca^{++} increases contractility of heart



Digoxin Pharmacokinetics

- Following oral administration, peak serum concentrations of digoxin occur at 1 to 3 hours
- After absorption, Digoxin is extensively distributed in tissues
- Very little metabolism, mostly excretion in urine
- Half life is 1-2 days

Clinical uses of Digoxin

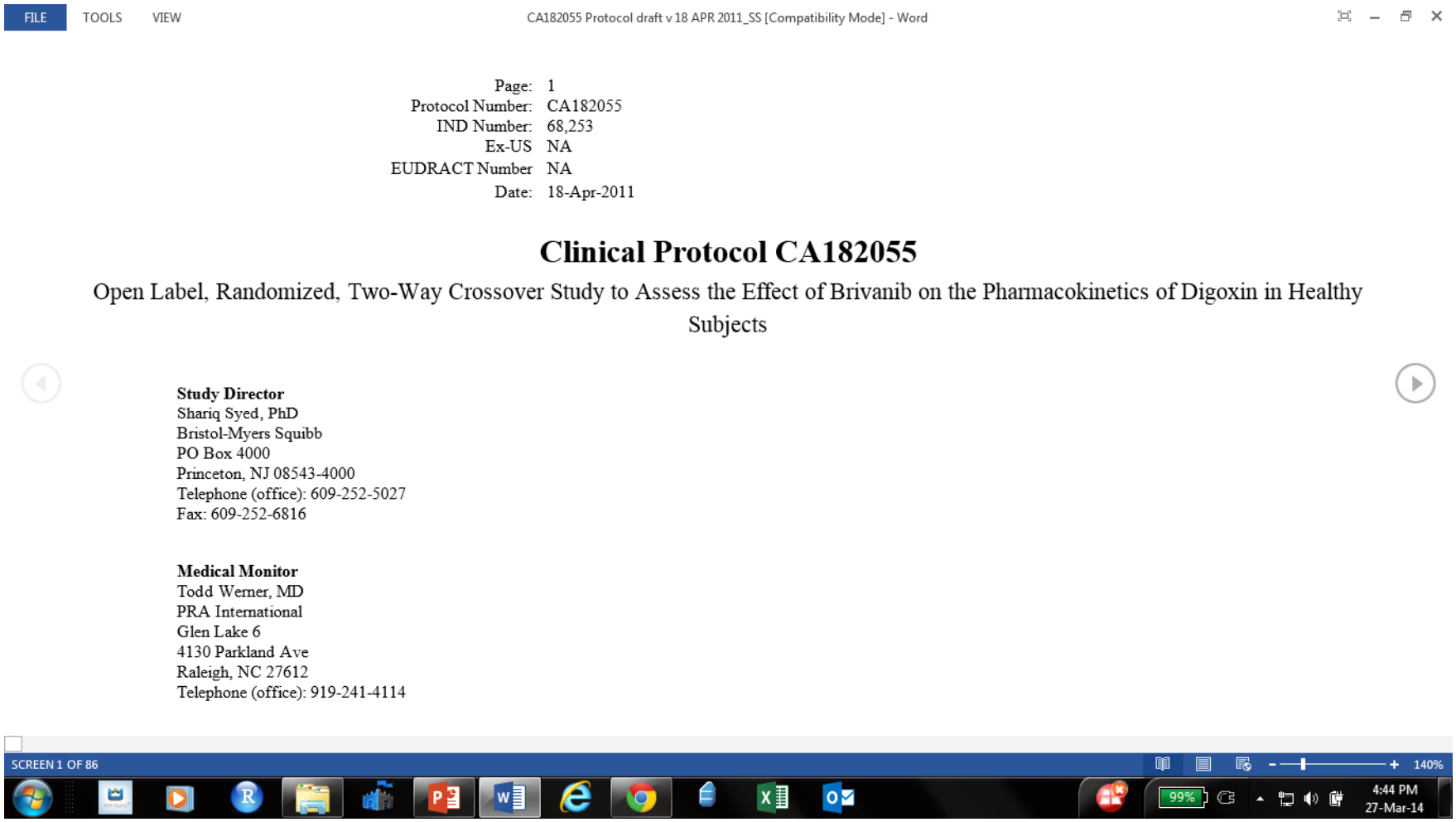
- Indicated for patients with heart failure & Atrial fibrillation
- Only administered when Diuretics, ACE inhibitors have failed to control symptoms
- Used in systolic dysfunction
- Needs to be carefully monitored
- When symptoms mild
  - Slow loading dose 0.125 – 0.25 mg/day is safe
  - Same effect as 0.5 – 0.75 mg/8 hrs for three dose, followed by 0.125 – 0.25 mg/day

Digoxin Toxicity

- Mild toxicity:
- visual changes
- GI disturbances generally require lowering of dose

- Serum levels of digitalis, K^+ have to be carefully monitored
- Monitoring of K^+ especially dialysis patients

- In severe intoxication, K^+ levels elevated
- In this case prompt treatment by cardiac pacemaker catheter, digitalis antibodies



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Clinical Protocol CA182055

Open Label, Randomized, Two-Way Crossover Study to Assess the Effect of Brivanib on the Pharmacokinetics of Digoxin in Healthy Subjects

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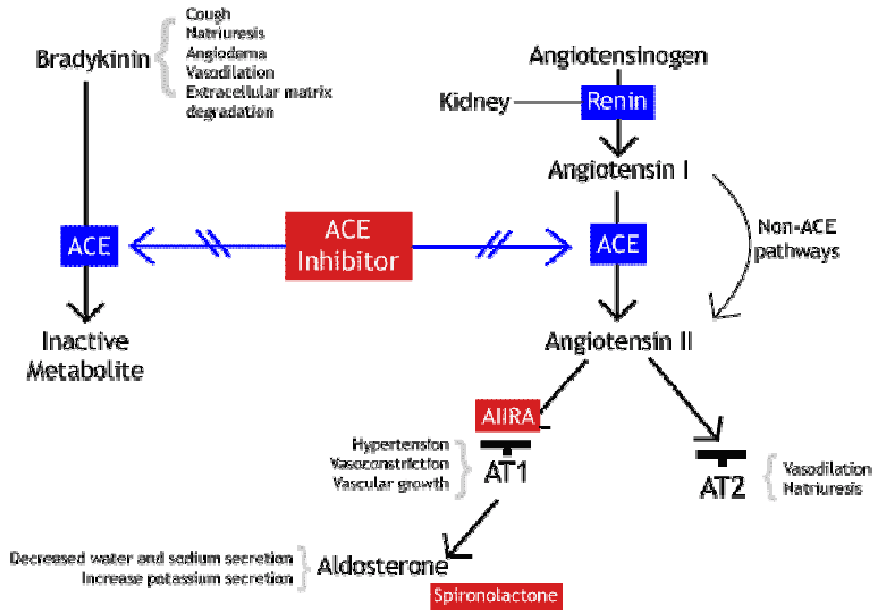
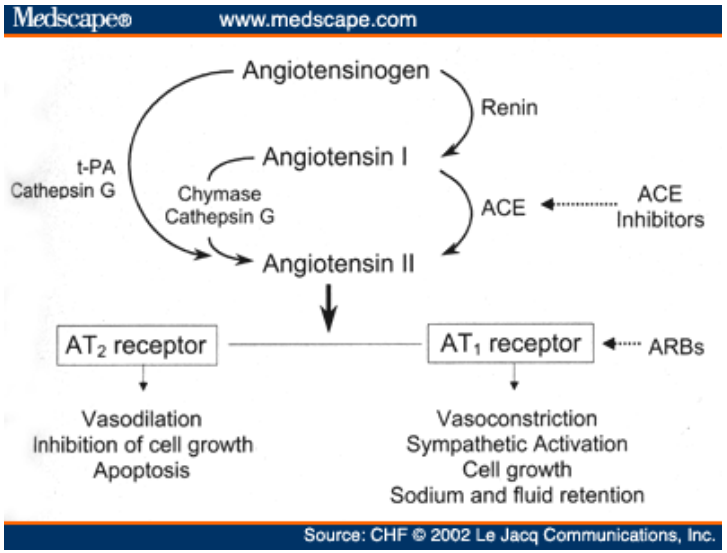
ACE inhibitors

- First line of treatment for patients with left ventricular dysfunction & no edema
- In asymptomatic patients, reduces preload & afterload, slows progression of ventricular dilation
- Beneficial in both non-symptomatic , severe heart failure
- Captopril, Ramipril, Enalopril



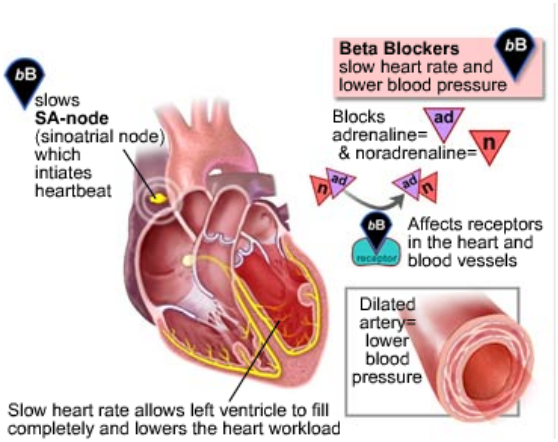
Angiotensin Receptor blockers

- Blockers of Angiotensin II type I (AT_1) receptor
- More selective blockers of Angiotensin system compared to ACE inhibitors
- Similar hemodynamic effects as ACE inhibitors
- Reserved for patients that do not tolerate ACE inhibitors
- Losartan, olmesartan, Telmisartan, Azilsartan



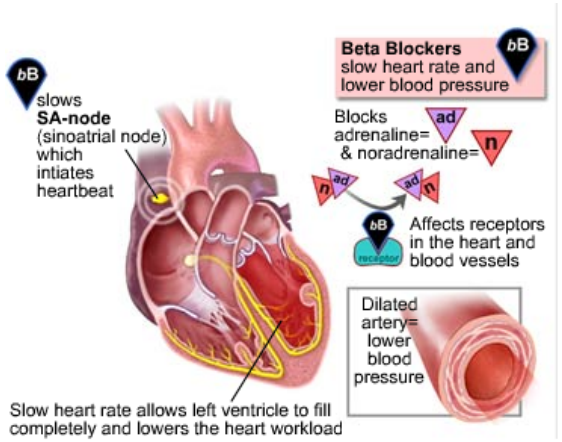
Beta-blockers

- Beta blockers block the effect of sympathetic nervous system on heart
- Beta blockers prevent binding of catecholamines (adrenaline) on beta receptors (b1) on heart
  1. resulting is slow heart rate
  2. This leads to increasing the ejection fraction of the heart



Beta-blockers

- Beta blockers cause a decrease in renin secretion,
- which in turn reduces the heart oxygen demand by
  - lowering extracellular volume and
  - increasing the oxygen-carrying capacity of blood



- Non-selective beta-blockers:
  - Carvedilol
  - Nebivolol
- Selective beta-blockers:
  - Bisoprolol, metaprolol

Diuretics

- Diuretics are used in heart failure where there are symptoms of Edema (Fluid build up in body)
- Typically used along with ACE inhibitors
- Class of Diuretics used:
  - Loop Diuretics
  - Thiazide Diuretics
  - K-Sparing Diuretics