

# HEART FAILURE



- Heart Failure (HF) is a complex progressive disorder in which the heart is unable to pump sufficient blood to meet the needs of the body
- Main symptoms:
  - ▣ Dyspnea
  - ▣ Fatigue
  - ▣ Fluid retention
- HF is caused by inability of the heart to adequately fill with and/or eject blood
- HF is accompanied by abnormal increases in blood volume and interstitial fluid



- Causes of HF:

- ▣ Arteriosclerotic heart disease

- ▣ Myocardial infarction

- ▣ Hypertensive heart disease

- ▣ Valvular heart disease

- ▣ Congenital heart disease

- ▣ Left systolic dysfunction secondary to coronary artery disease is the most common cause of HF

# HF

- Physiologic compensatory mechanisms in HF
  - Chronic activation of the sympathetic nervous system and renin angiotensin-aldosterone system is associated with remodeling of cardiac tissue
    - Loss of myocytes, hypertrophy, fibrosis.

# Pharmacological treatment of HF

- Goals of HF therapy
  - ▣ Alleviate symptoms
  - ▣ Slow the disease progression
  - ▣ Improve survival
- Drug classes
  1. Inhibitors of renin-angiotensin system
  2.  $\beta$ -Blockers
  3. Diuretics
  4. Direct vasodilators
  5. Inotropic agents
  6. Aldosterone antagonists

# Pharmacological treatment of HF

- Individuals might have one or more of the drug classes used for HF depending on the severity of the disease
- Beneficial effects of HF treatment
  - ▣ Reduction of the load on the heart
  - ▣ Decrease in extracellular volume
  - ▣ Improved cardiac contractility
  - ▣ Slowing the rate of cardiac remodeling

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- Non-pharmacological strategies for HF
    - ▣ Reduction in physical activity
    - ▣ Low dietary intake of sodium
  
  - Drugs that may exacerbate HF
    - ▣ Nonsteroidal anti-inflammatory drugs
    - ▣ Alcohol
  
    - ▣ Cardioselective calcium channel blockers like verapamil and diltiazem are contraindicated in heart failure because of their negative inotropic effect

# Renin-Angiotensin Aldosterone system

- HF activates the renin-angiotensin system by:
  - ▣ Promoting renin release in response to lower renal perfusion pressure caused by the failing heart
  - ▣ Sympathetic stimulation and activation of  $\beta$  receptors in the kidney leading to renin release
- Consequent to renin release, the potent vasoconstrictor angiotensin II is produced
- The resulting stimulation of Aldosterone release causes salt and water retention increasing the preload and afterload that are characteristic of the failing heart

# Inhibitors of the renin angiotensin aldosterone system

- Angiotensin converting enzyme inhibitors
- Angiotensin receptors blockers

# Angiotensin converting enzyme inhibitors

- Drugs of choice for HF
- Mechanism of action
  - ▣ Block the enzyme that converts angiotensin I to the potent vasoconstrictor angiotensin II
  - ▣ Cause vasodilation
  - ▣ Decrease aldosterone secretion decreasing sodium and water retention

# Angiotensin converting enzymes inhibitors



- Captopril
- Enalapril
- Fosinopril
- Ramipril

# Angiotensin converting enzyme inhibitors

- Beneficial effects on heart
  - ▣ Reduce vascular resistance and blood pressure
  - ▣ Increase cardiac output

# Angiotensin converting enzymes inhibitors

- Adverse effects
  - ▣ Postural hypotension
  - ▣ Renal insufficiency
  - ▣ Hyperkalemia
  - ▣ Persistent dry cough
  - ▣ Angioedema
- Contraindicated in pregnancy

# Angiotensin receptor blockers

- Losartan and valsartan
- Competitive antagonists of angiotensin receptor
- Used for HF in patients who can not tolerate angiotensin converting enzyme inhibitors
- Lower blood pressure
- Adverse effects: similar to ACE inhibitors, but do not cause dry cough and angioedema
- Contraindicated in pregnancy

# $\beta$ -blockers

- $\beta$ -blockers used in HF
  - ▣ Metoprolol ( $\beta$ 1 antagonist)
  - ▣ Bisoprolol ( $\beta$ 1 antagonist)
  - ▣ Carvediol (blocks  $\alpha$  and  $\beta$ )
- Block the changes caused by chronic activation of the sympathetic nervous system
- Decrease heart rate and inhibit the release of renin
- Decrease remodeling of cardiac muscle fibers caused by norepinephrine, reduce hypertrophy and cell death
- Beneficial if HF is accompanied by hypertension in the patient

# Diuretics

- Thiazide and loop diuretics
- Hydrochlorothiazide, Furosemide
- Relieve pulmonary congestion and peripheral edema
- Decrease plasma volume and venous return to the heart (preload)
- Can decrease afterload by reducing plasma volume, and so reduce blood pressure
- Side effects: (Loop and Thiazide)
  - ▣ Hypotension, hypokalemia, hyperuricemia

# Direct acting vasodilators

- Hydralazine, Isosorbide dinitrate, Isosorbide mononitrate
- Cause vasodilation leading to reduced cardiac preload
- Used if patient is intolerant to ACE inhibitors or  $\beta$ -blockers

# Inotropic drugs

- Digoxin, increase cardiac muscle contractility by influencing sodium and calcium flow in the cardiac muscle
  - ▣ Inhibits Na/K ATPase pump, which increases intracellular calcium increasing the force of contractility within myocytes
- Dobutamine ( $\beta$ -agonist)
- Enhance cardiac muscle contractility and thus increase cardiac output
- Digoxin has a narrow therapeutic index (shows a small difference between the therapeutic and toxic doses and can be fatal)

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- Digoxin adverse effects
    - ▣ Arrhythmia
    - ▣ Anorexia, nausea, vomiting
    - ▣ CNS effects headache, fatigue, confusion

# Aldosterone antagonists

Spirolactone

Eplerenone

- Mechanism of action
  - ▣ Direct antagonist of aldosterone
  - ▣ Prevents salt retention, myocardial hypertrophy
- Used for the most advanced stages of HF
- Adverse effects
  - ▣ Hyperkalemia
  - ▣ GI disturbances (ulcer)
  - ▣ CNS abnormalities (confusion, lethargy)
  - ▣ Endocrine abnormalities

# Order of therapy

