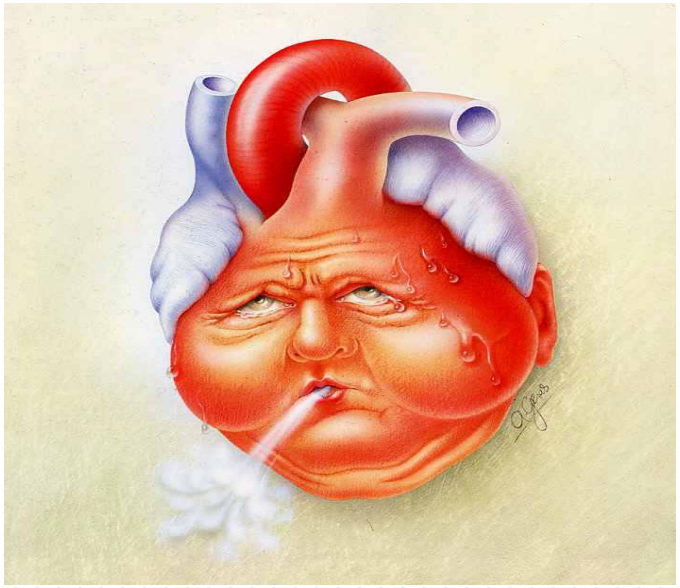
HEART FAILURE



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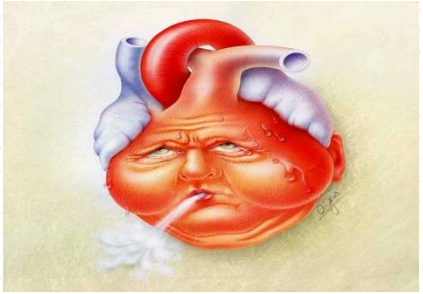
DEFINITION & EPIDEMIOLOGY

- **Def.:**
  - Inability of the heart to pump sufficient blood to meet the metabolic needs of the body.

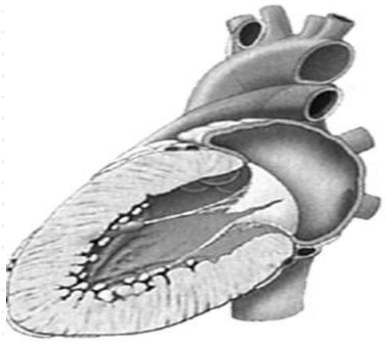


  - HF can result from any disorder that reduces
    1. Ventricular filling **(diastolic)** and/or
    2. Myocardial contractility **(systolic)**.

- **Epidemiology:**
  - 0.3- 2% of general population & increase with age:
    - 3–5% in > 65 years old,
    - 8 - 16% in > 75 years.
  - More in men, elderly, and black
  - Mortality is high (8-year survival rate 15%)

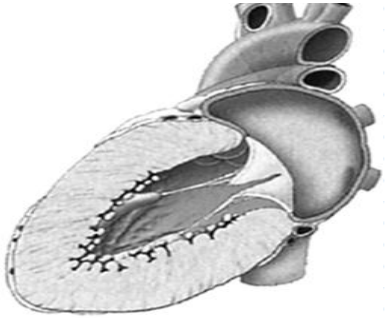
Pathogenesis & Compensatory mechanisms in HF

- **Structural changes:**
  - Remodeling (Dilatation, Hypertrophy)



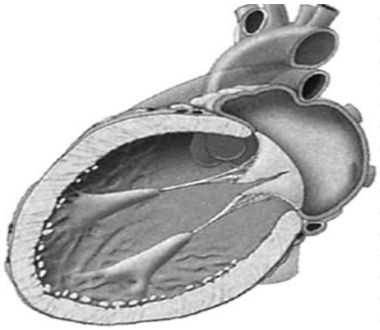
Normal heart

- **Neurohumoral changes:**
  1. ↑ **Sympathetic nervous system**. Leading to:
     - ↑ H.R & Contractility
     - VC:
       - Arterio- constriction ➔ maintains arterial Bl Pr
       - Veno- constriction ➔ maintain venous return
     - remodeling



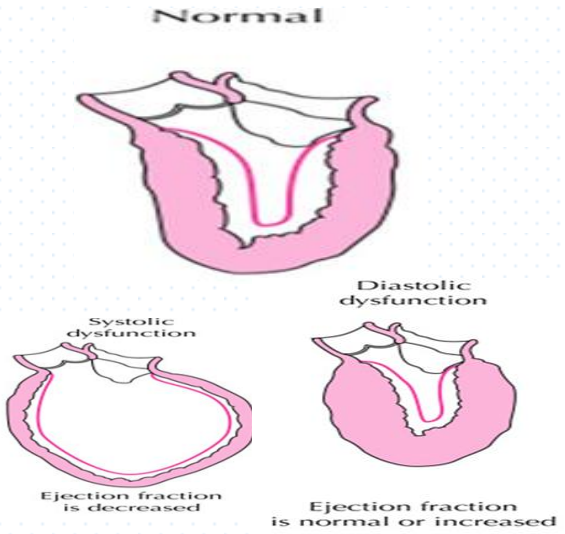
Hypertrophied heart
(diastolic heart failure)

  2. ↑ **RAAS** leading to:
     - VC
     - ↑ Aldosterone ➔ salt & H_2O retention ➔ ↑ blood volume
     - Remodeling
     - ↑ Endothelin secretion ➔ VC
  3. ↑ **Natriuretic peptides** (esp. BNP)
     - VD, natriuretc & diuretic effect
     - antagonize sympathetic outflow, RAAS & endothelin
     - Metabolized by Nebrilysin



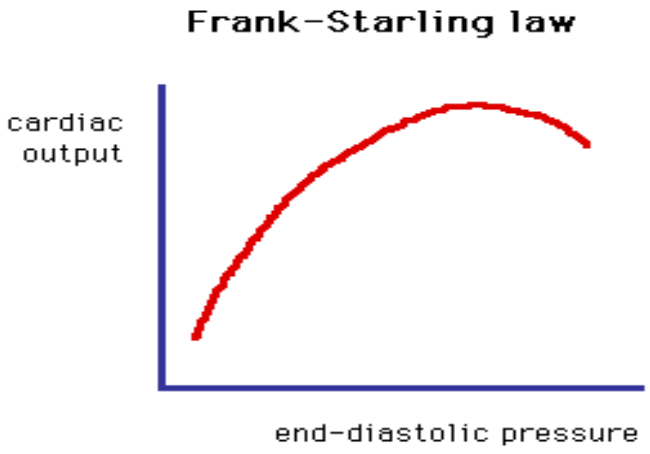
Dilated heart
(systolic heart failure)

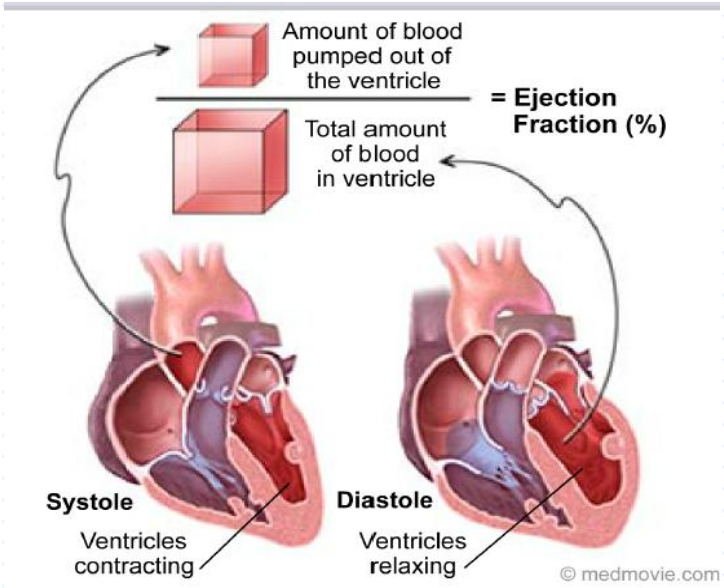
Classification of HF



- **Which <u>side</u> of heart is affected**
  - Left (more common)
  - Right (right-sided MI, pulmonary HTN)

- **Which heart <u>function</u> is affected**
  - Systolic (HF with reduced LVEF): ↓ contraction & EF (below 40%), dilated LV
  - Diastolic (HFPEF): ↓ relaxation ➔ Failure of LV filling (but contractile function & EF usually normal 50-70%)





Classification of Heart Failure
ACC/AHA Staging v/s NYHA Functional Class

ACC/AHA HF Stage	NYHA Functional Class
A At high risk for HF but without structural heart disease or symptoms of HF (eg, patients with HTN, CAD, obesity, diabetes, dyslipidemia)	None
B Structural heart disease but without symptoms of HF	**I** Asymptomatic
C Structural heart disease with prior or current symptoms of HF	**II** Symptomatic with moderate exertion
	III Symptomatic with minimal exertion
D Refractory HF requiring specialized interventions	**IV** Symptomatic at rest

Causes of heart failure

↑Preload

1- Volume overload
- rapid infusion
- Drugs: eg cortisone, licorice ..

2- Aortic or mitral valve defects

Disease affecting heart

1- Cardiomyopathy

2- **IHD**

3- Arrhythmia

3- Infection

4- Drugs (cardiotoxic & -ve inotropic drugs)

↑Afterload

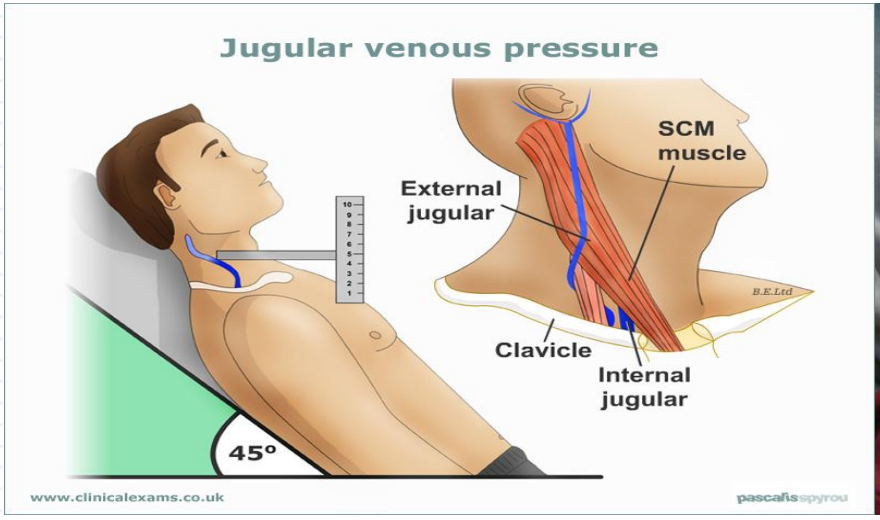
1- **Hypertension**

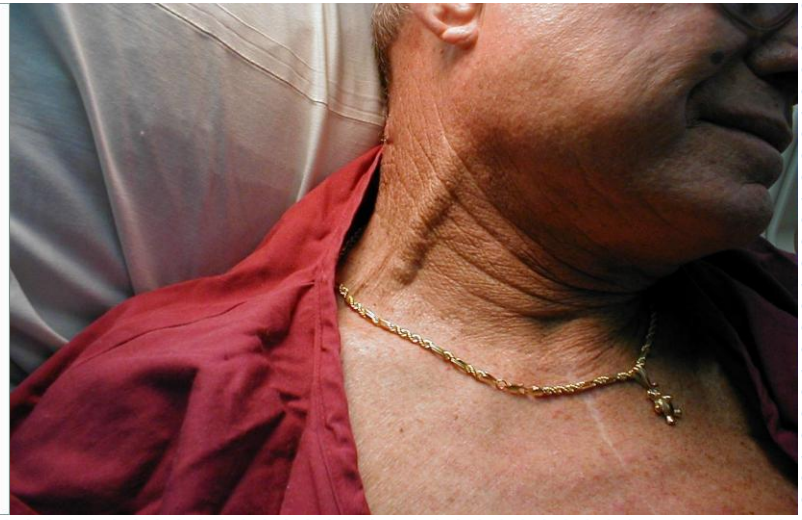
2- Aortic stenosis

- **Hypertension & IHD are the major causes**
- **Anemia & hyperthyroidism may cause high-output HF (uncommon)**

Manifestations of HF

Symptoms	Signs
• **Related to ↓ CO** 1. Fatigue 2. Confusion 3. Angina • **Related to fluid overload (congestion)** 1. DOE (shortness of breath) 2. Orthopnea 3. Cough 4. peripheral edema 5. weight gain	• **Related to ↓ CO** 1. Confusion 2. Sinus tachycardia 3. Peripheral VC (cool, pale) • **Related to fluid overload** 1. Pulmonary edema 2. Ascites 3. Peripheral edema **4. Elevated JVP**





Diagnosis of HF

1. **Clinically:** **symptoms & signs**

2. **Immaging:**
    1. Chest X-ray &
    2. Echocardiogram (THE MOST USEFUL)
3. **ECG**

4. **Laboratory:** **BNP (more than 200 pcg/L)**

5. **Invasive:** **Cardiac catheterization**

Treatment of HF

- **Goal of therapy:**
  1. Ameliorate symptoms,
  2. Avoid complications such as arrhythmias,
  3. Improve the quality of life
  4. Prolong survival.

- **Treatment lines:**
  1. **Life style changes:**
     - ↓ 1- Fluid intake, 2- ↓ Dietary sodium, 3- ↓ weight
     - Moderate exercise
  2. **Pharmacological:**
     - **ACEi, Diuretics, BB, digitalis & spironolactone**
  3. Devices:
     - CRT (Cardiac resynchronization therapy)
  4. Surgical:
     - cardiac transplant

Drug treatment in heart failure

Drug treatment in heart failure

- **Drugs that decrease the load on heart:**
  1. **Vasodilators**
     1. mainly ACE inhibitors
     2. Others: Nitrates, Hydralazine & Nitroprusside
     3. **Nesiritide (Natrecor):**
        - it is a recombinant form of BNP
        - used IV in acute HF with dyspnea
     4. **Sacubitril**:
        - Nebrilysin inhibitor used with Valsartan ***(Enteresto)*** in ttt of CHF
     5. **Bosentan:** endothelin receptor antagonist
  2. **Diuretics** (Loop - Thiazide)
  3. **Aldosterone antagonist:** Spironolactone
  4. **BB**

- **Inotropic drugs:**
  1. **A**minophylline
  2. **B**ipyridine [Inamrinone & Milrinone]
  3. **B** -agonist [Dopamine & Dobutamine]
  4. **C**ardiac glycosides (digitalis)

	Stage A	Stage B	Stage C	Stage D
Manifestation	High risk pt.with no structural disease or symptoms	Structural heart disease with no symptoms	Structural heart disease with symptoms	Refractory heart failure
Therapy	• Treat predisposing factors • Use ACE.I in appropriate pt. (DM, atherosclerosis)	• ACE.I + • BB	• ACE.I + • BB + • Diuretics ± • Digitalis • Aldosterone antagonist • CRT	• All previous measures+ • Continuous IV inotropics+ • Heart transplantation

ACE Inhibitors

- **Indication:** **Should be used in all stages of HF**
- **benefits:**
  1. Improve symptoms & decrease mortality (25%)
  2. Slow disease progression
  3. Reduce remodeling

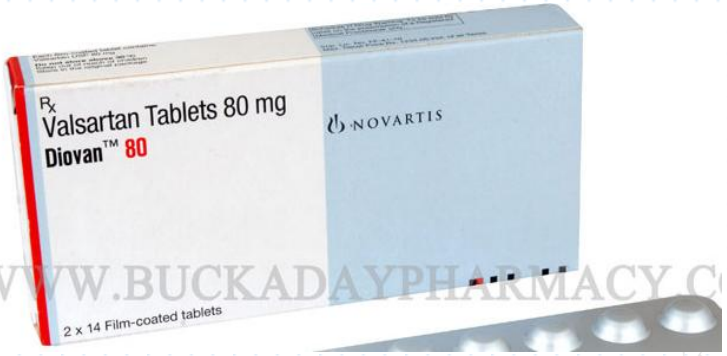
- **ACE-i Dosing Guidelines**

	Initial	Target
Captopril	**6.25 / 8h**	**50 / 8h**
Enalapril	**2.5 / 12 h**	**10 / 12h**
Fosinopril	**5 to 10 / day**	**40 / day**
Lisinopril	**2.5 to 5.0 / day**	**20 - 40 / day**
Quinapril	**10 / 12 h**	**20 - 40 / 12 h**
Ramipril	**1.25 to 2.5 / day**	**5 / 12 h**

ARBs

- **Indications:**
  - In patients who are intolerant of ACE inhibitors

  - ✓ **Candesartan**, 4- 8 mg once daily initially; target dose, 32 mg once daily.
  - ✓ **Valsartan**, 20- 40 mg twice daily initially; target dose, 160 mg twice daily.
  - ✓ Losartan: 25-50 mg once daily; target 100 mg once daily



β-Blockers

- **Beneficial effects may result from:**
  1. Improve symptoms & ↓ mortality (35%)
  2. ↓ arrhythmic,
  3. ↓ heart rate ➔ ↓ myocardial O_2 demand,
  4. ↓ ventricular remodeling,
  5. ↓ renin release.
  6. ↓ myocyte death from catecholamine-induced necrosis

- **Indication:**
  - **All stable patients** with HF (at least 2 w.) & ↓ LVEF in the absence of C.I
    - **NB.:** stable: - Not receiving **IV** inotropic or **IV** diuretic therapy,
      - without significant peripheral & pulmonary cong.

- **NB.: addition of βB is likely to be of greater benefit than↑ ACEI dose**
- **βB may cause acute ↓ in LVEF & short-term worsening of HF symptoms on initiation & at each dosage titration.**

βB Dosing

- **βB should be started in very low doses with slow titration**
- **Doses is doubled every 2-4 weeks**

	Starting Dosage	Target Dosage
Carvedilol	3.125 mg BID	25 mg BID
Bisoprolol	1.25 mg/day	10 mg/day
Metoprolol succinate XL	12.5–25 mg/day	200 mg/day

- **NB.:**
  - higher βB doses are associated with ↑ reduction in mortality. Therefore, if hypotension alone is the problem, try reducing the dose of the ACEI first.
  - Carvedilol may be preferred esp if associated with hypertension??, but not preferred if EF less than 20

Diuretics in HF

- **Indications:**
  - Symptomatic HF with evidence of fluid retention (edema)
- **Benefits:**
  - Improve symptoms (No benefit on mortality)
  - ***NB.:*** *Never use as the only therapy for HF (no effect on progression or mortality)*

	Furosemide (lassix)	Bumetanide	Torsemide
Usual daily dose (oral)	20–160 mg/day	0.5–4 mg/day	10–80 mg/day
Maximum daily dose	600	10	200
Ceiling dose*:			
Normal renal function	80–160 mg	1–2 mg	20–40 mg
CL_{cr}: 20–50 mL/min	160 mg	2 mg	40 mg
CL_{cr}: <20 mL/min	400 mg	8–10 mg	100 mg

***Ceiling dose:** single dose above which additional response is unlikely to be observed.

- Thus, once reached, more frequent dosing should be used for additional effect, rather than giving higher doses.

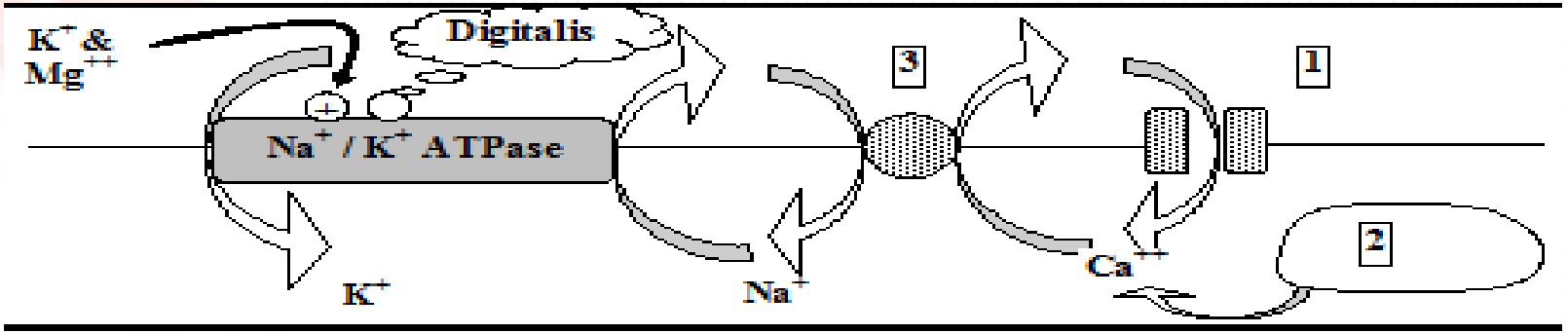
- **Choosing diuretic:**
  - **Loop diuretic is usually preferred over THZ** (why???)
  - **THZ is indicated in:**
    - Combination with loop to enhance the effect of loop
    - Mild fluid retention with HTN (THZ is preferred)
    - NB.: **Metolazone** is often used in
      - Compromised renal function (Cl_{Cr} **<** 30 mL/min) instead of Hydrochlorthiazide
      - Combination with loop diuretics when patients exhibit *diuretic resistance* (edema unresponsive to loop diuretics alone).

Aldosterone Antagonists

- **Include: Spironolactone & eplerenone**
- **Benefit: comes from aldosterone antagonist rather than diuretic effect**
  - Improve symptoms & decrease mortality (30%)
- **Indications:**
  - patients with moderate to severe HF **(class III and IV)** who are receiving standard therapy
- **Dosing:**
  - Initial doses should be low (spironolactone 12.5 mg/day; eplerenone 25 mg/day), especially:
    - Elderly
    - Diabetes
    - Creatinine clearance <50 mL/min.
- **Side effects:**
  - Hyperkalemia & Gynecomastia (see HT)

Digitalis

- **Indications**
  1. When no adequate response to ACE-i + BB + diuretics
  2. Supraventricular arrhythmia, to slow AV conduction
- **Benefits:** **Improve symptoms (No benefit on mortality)**
- **Dose** **0.125 to 0.250 mg / day**
- **Mechanism:**

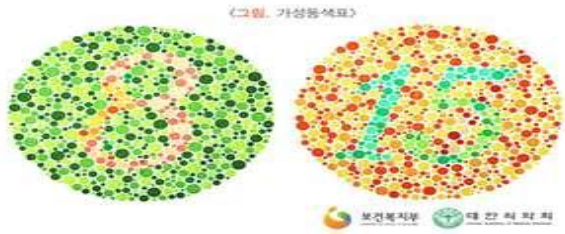


SE of digitalis

1. **Narrow safety margin (Low therapeutic index):**
   1. Therapeutic level for digoxin: 0.5-2 ng/ml
   2. Toxic level: more than 2 ng/ml

2. **Early manifestation of toxicity:**
   1. Anorexia – nausea – vomiting
   2. Bradycardia < 60 beat /min.

3. **Late manifiatation of toxicity:**
   1. C.V.S: Bradycardia – HB – Ventricular arrhythmia
   2. G.I.T: Anorexia – Nausea – Vomiting – Colic – Diarrhea
   3. C.N.S: - Headache - Hallucination – Delirium - Confusion - Convulsions
   4. Eye: visual disturbance & colored vision [yellow or green] *(Chromatopsia)*
   5. Skin: Allergy
   6. Hormonal: Gynecomastia (rare)



4) Treatment of digitalis toxicity

1. ***Stop*** **digitalis & K^+- depleting diuretics**
2. ***KCl*** **➔ Oral or I.V infusion with ECG monitoring, IF plasma K^+ is low or normal & provided no HB or RF**
   - **NB.:** In severe digitalis toxicity, serum K^+ will be already elevated (due its loss from tissues)

3. ***Digitalis antibodies*** **(digoxin immune fab IV)** ***(digibind, digifab)***
4. ***Treatment of arrhythmia:***
   1. - O_2 [as ischemia favors arrhythmia]
   2. - *If bradycardia or H.B only* ➔ Atropine
   3. - *If arrhythmia ± H.B* ➔ **Phenytoin** [Drug of choice] or **Lidocain**

N.B.: *No need* for stomach wash

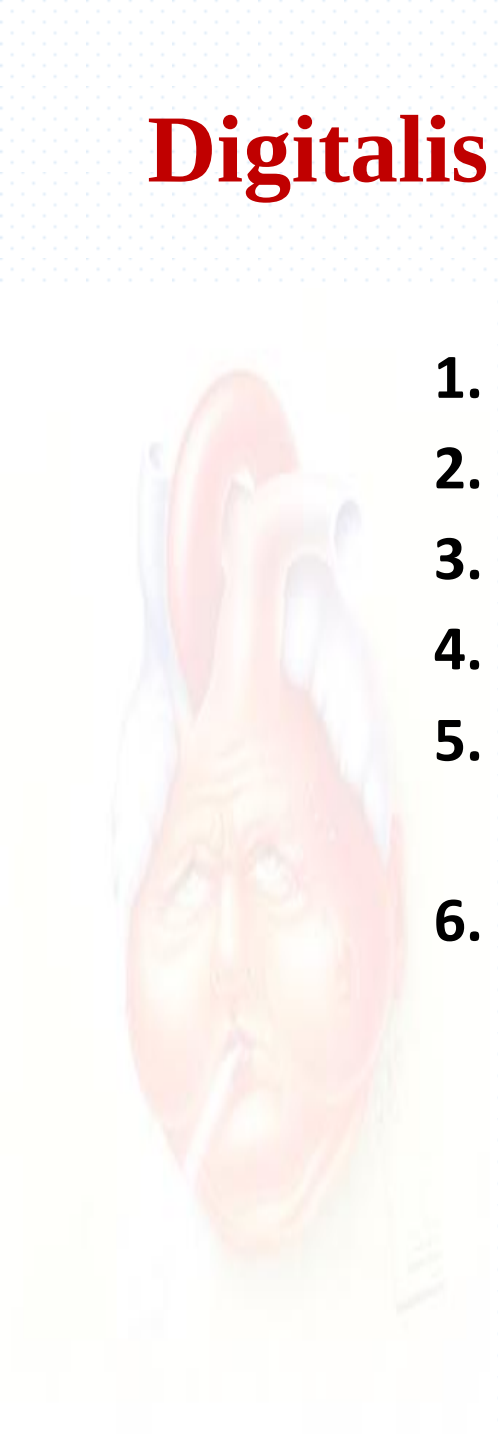
Drugs that may increase Digitalis toxicity

1. Sympathomimetic B_1 agonist: [Adr. – Isoprenaline-Ephedrine] ➔ Arrhythmia
2. Sympatholytic BB: [Propranolol] ➔ severe H.B
3. Parasympatholytic [Atropine] ➔ ↓ gastric emptying ➔ ↑ absorp. & toxicity

4. Calcium I.V
5. Calcium channel blockers: [Verapamil] ➔ severe H.B
6. Quinidine ➔displaces Digitalis & ↓ Excretion

7. Thyroxin ➔ arrhythmia
8. Hypokalemia induced by some drugs as: K^+ depleting diuretic [Thiazide & Loop] – Cortisone – Carbenoxolone

Digitalis Contraindications



1. Hypersensitive carotid sinus or bradycardia
2. Advanced A-V block
3. Ventricular arrhythmia
4. W-P-W with atrial fibrillation
5. Obstructive cardiomyopathy ➔ ↓CO

6. Marked Hypokalemia

Acute pulmonary edema (acute HF)

1- Asses/treat arrhythmia or acute coronary syndrome

2- O2

3- IV diuretic (furosemide 50 mg)

4- IV opiate + antiemetic (4-8 mg morphine + 10 mg metoclopromide)

If hypotension or shock

5- IV inotrpics (milrinon, dobutamine, dopamine)

If inadequate response

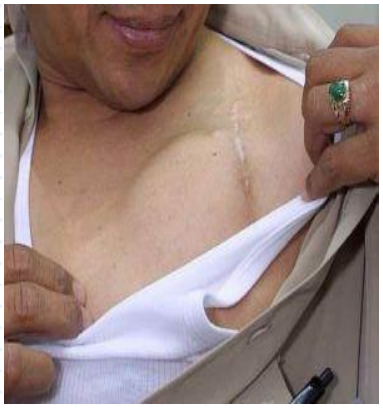
6- IV vasodilators (NTG, Nitroprusside, Nesiretide)

Inamrinone & Milrinone

- **Mechanism of action:** ↓ PDE enzyme type 3 ➔ ↑ c.AMP ➔ inodilators:
  - +ve inotropic effect
  - Mixed V.D [artery & Vein] ➔ ↓ preload & after load
- **Side effects:**
  1. Bone marrow toxicity ➔ Thrombocytopenia
  2. Hepatotoxicity
  3. ↑ O_2 consumption ➔ worsens angina
- **Uses:**
  - I.V as short term therapy in acute heart failure

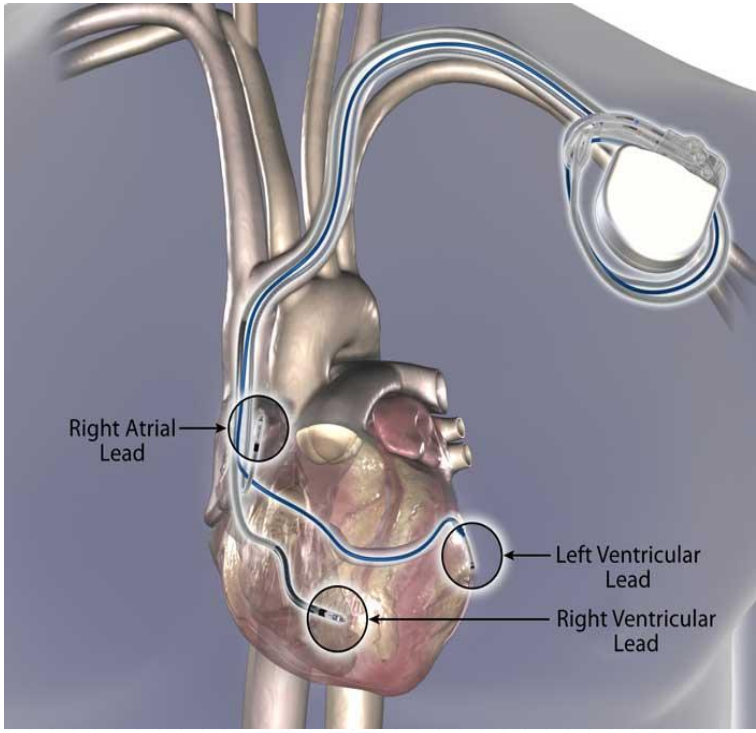
- ***N.B:*** **Milrinone as Inamrinone but differs in:**
  1. Less side bone marrow depression & hepatotoxicity, but
  2. More liable to cause arrhythmia

Cardiac resynchronization therapy (CRT)



- **CRT**
  - is the use of cardiac pacing to coordinate the contraction of the left & right ventricles.

- **Indicated in patients:**
  1. Receiving optimal HF standard medical therapy +
  2. LVEF ≤35% +
  3. electric asynchrony shown by wide QRS (>120 milliseconds)



Animation New therapy prevents heart failure.flv

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