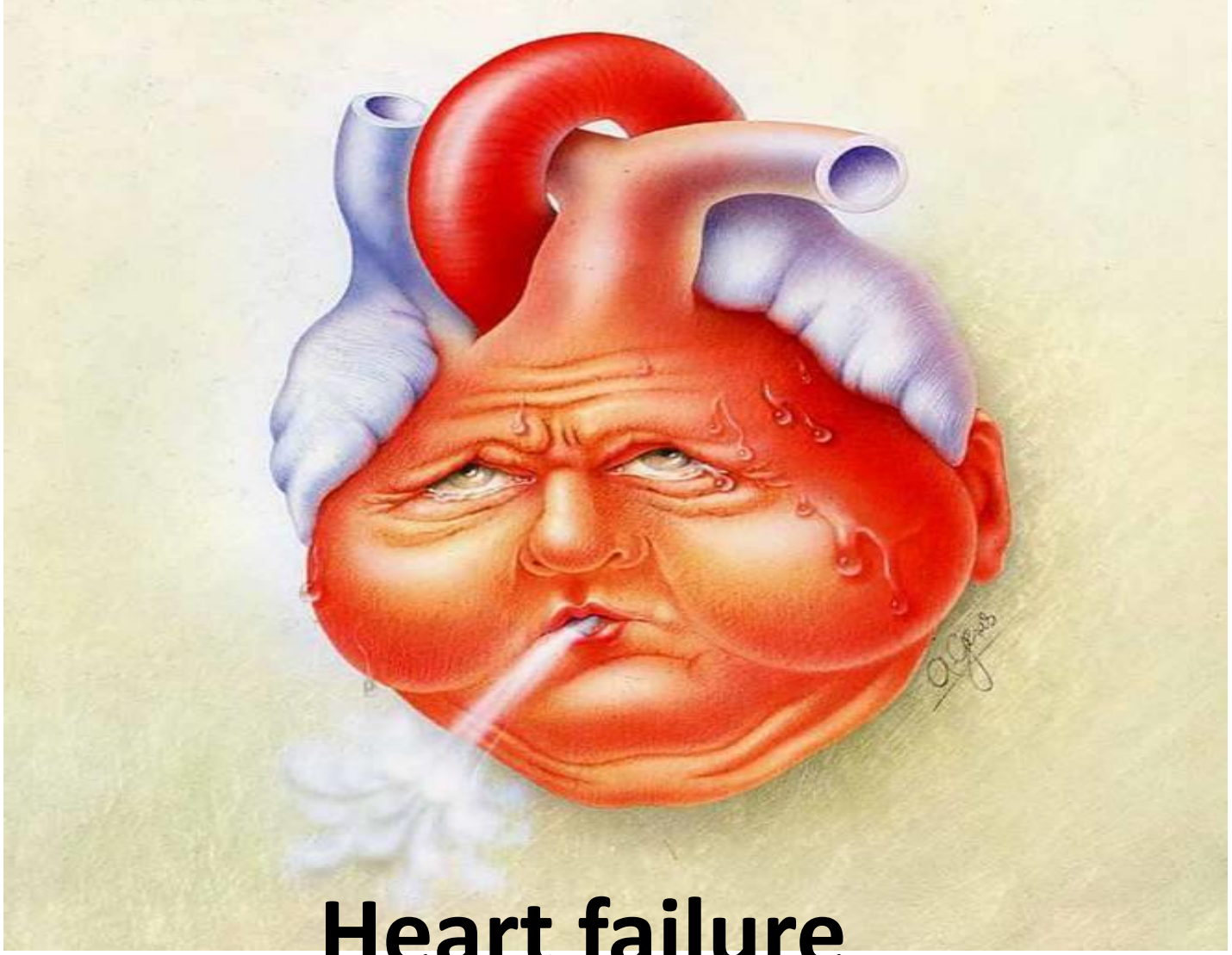
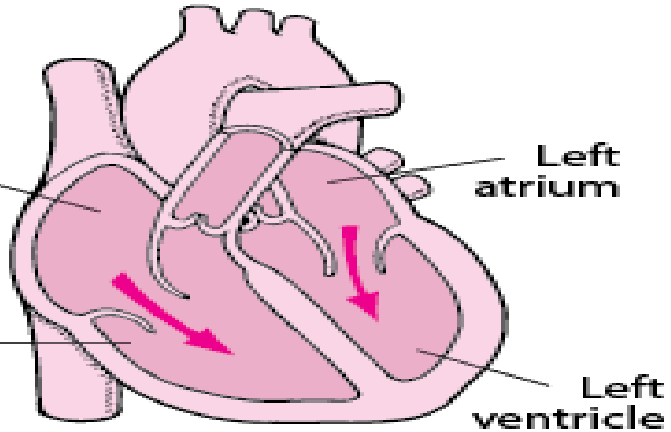
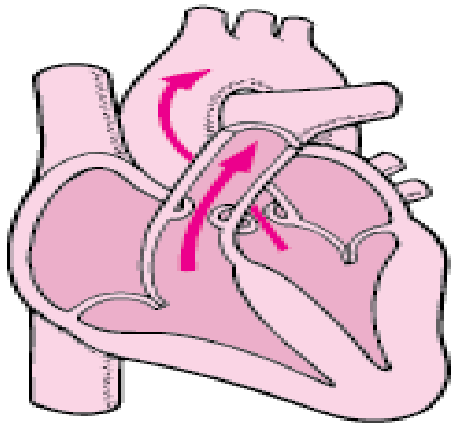


Heart failure

Normal

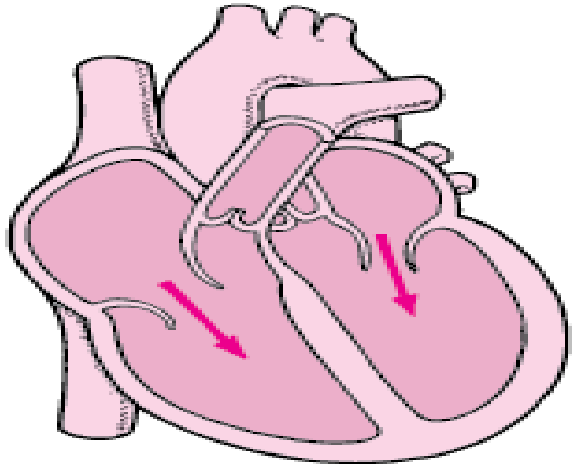


The ventricles fill normally with blood.

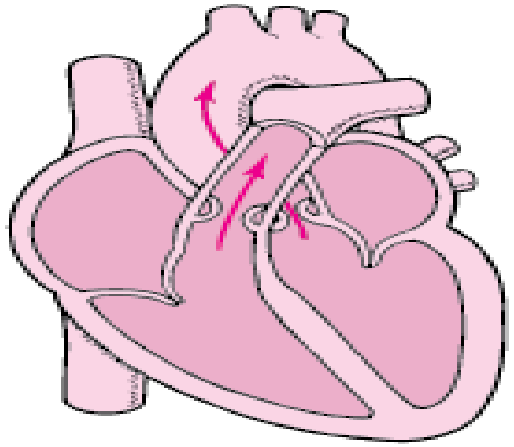


The ventricles pump out about 60% of the blood.

Systolic Dysfunction

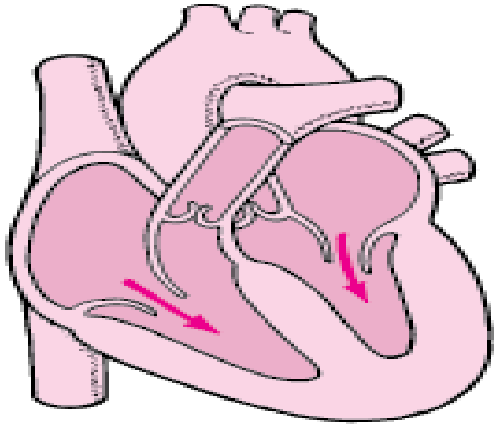


The enlarged ventricles fill with blood.

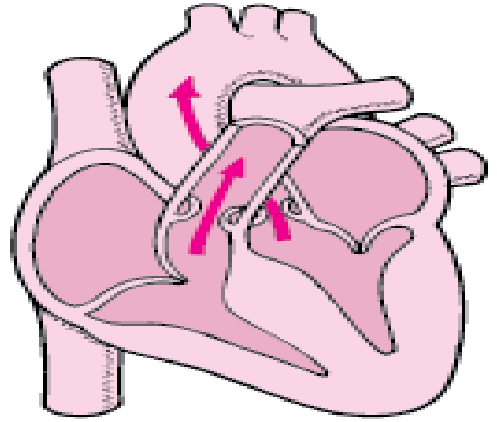


The ventricles pump out less than 40 to 50% of the blood.

Diastolic Dysfunction



The stiff ventricles fill with less blood than normal.

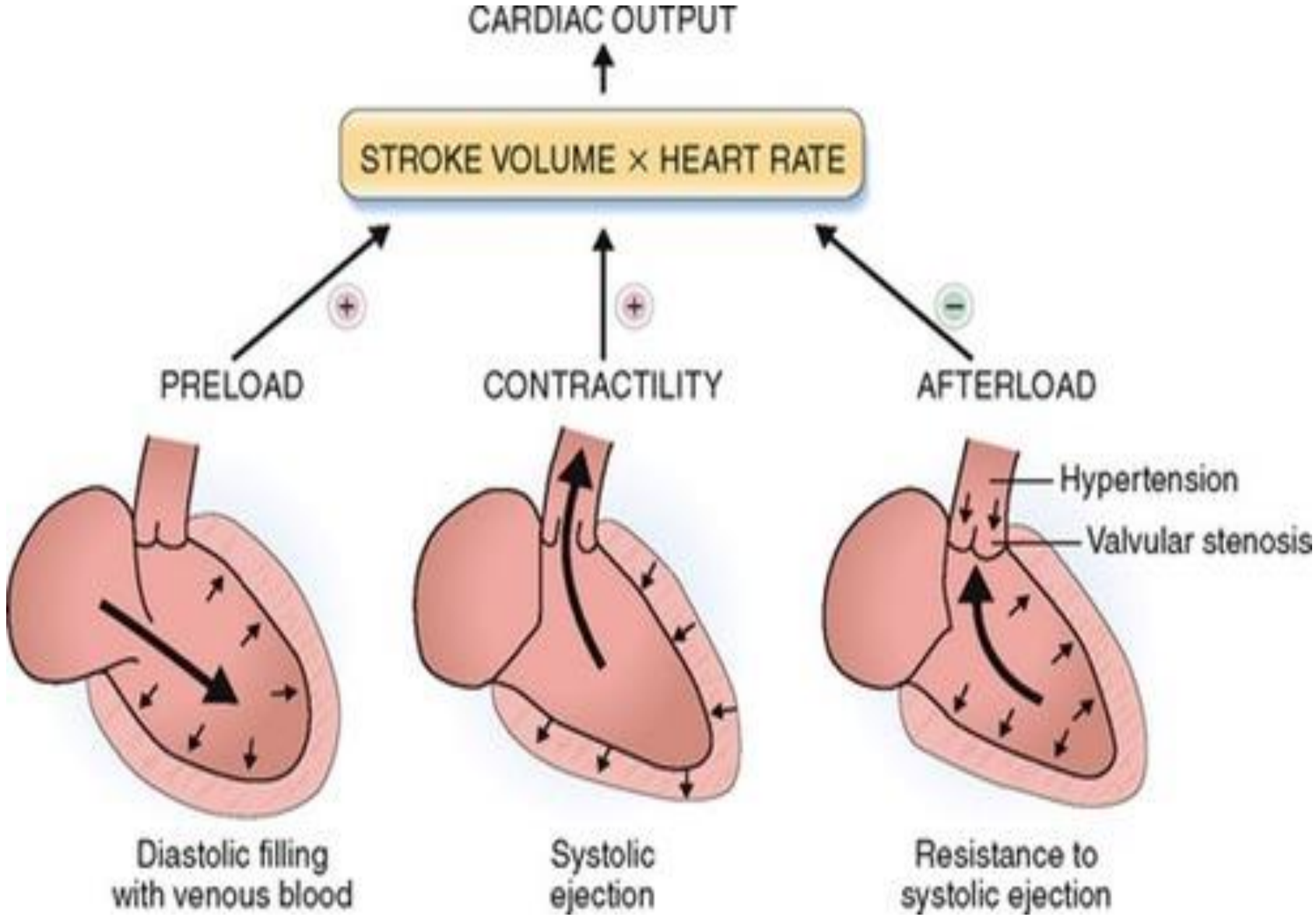


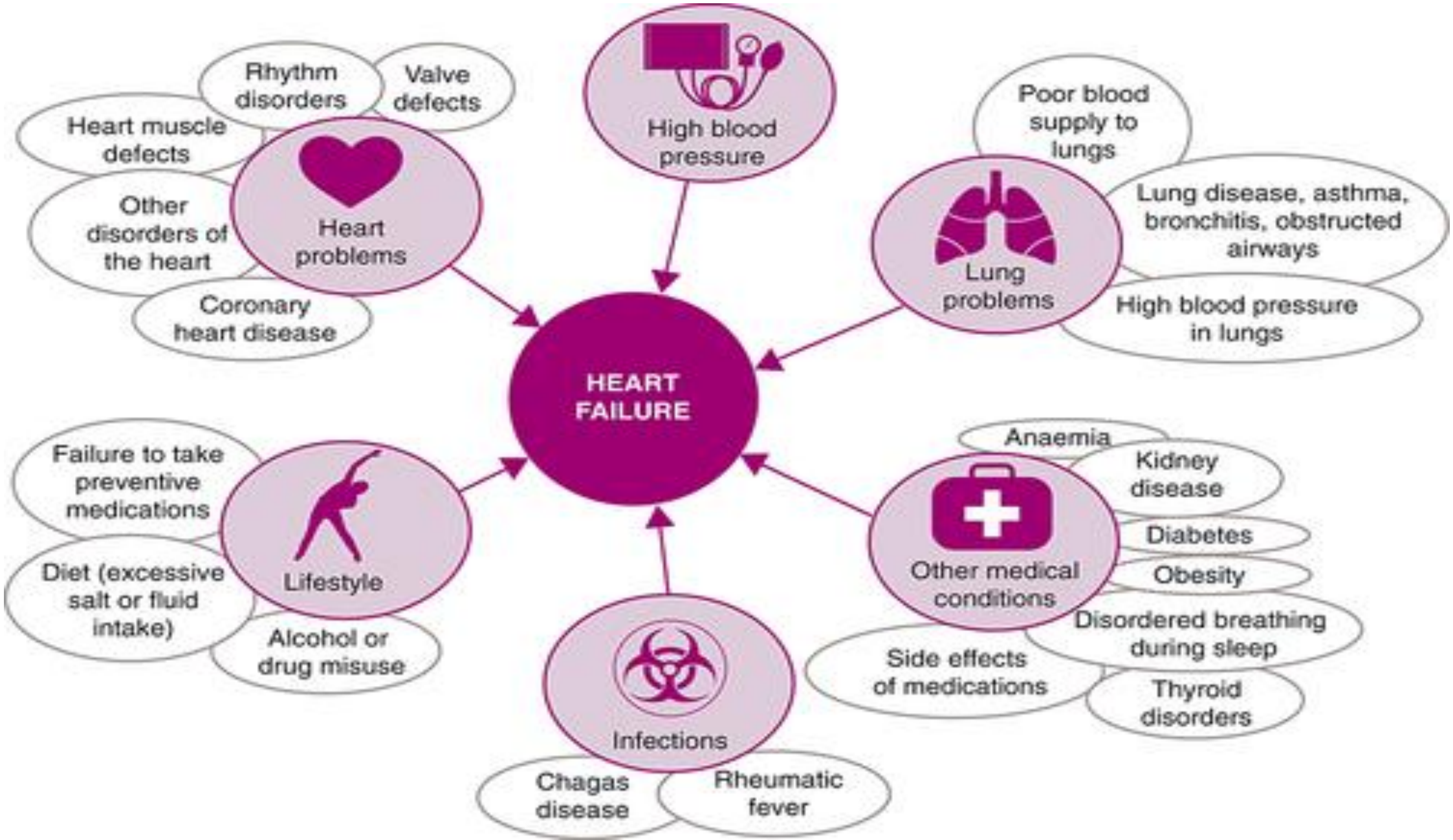
The ventricles pump out about 60% of the blood, but the amount may be lower than normal.

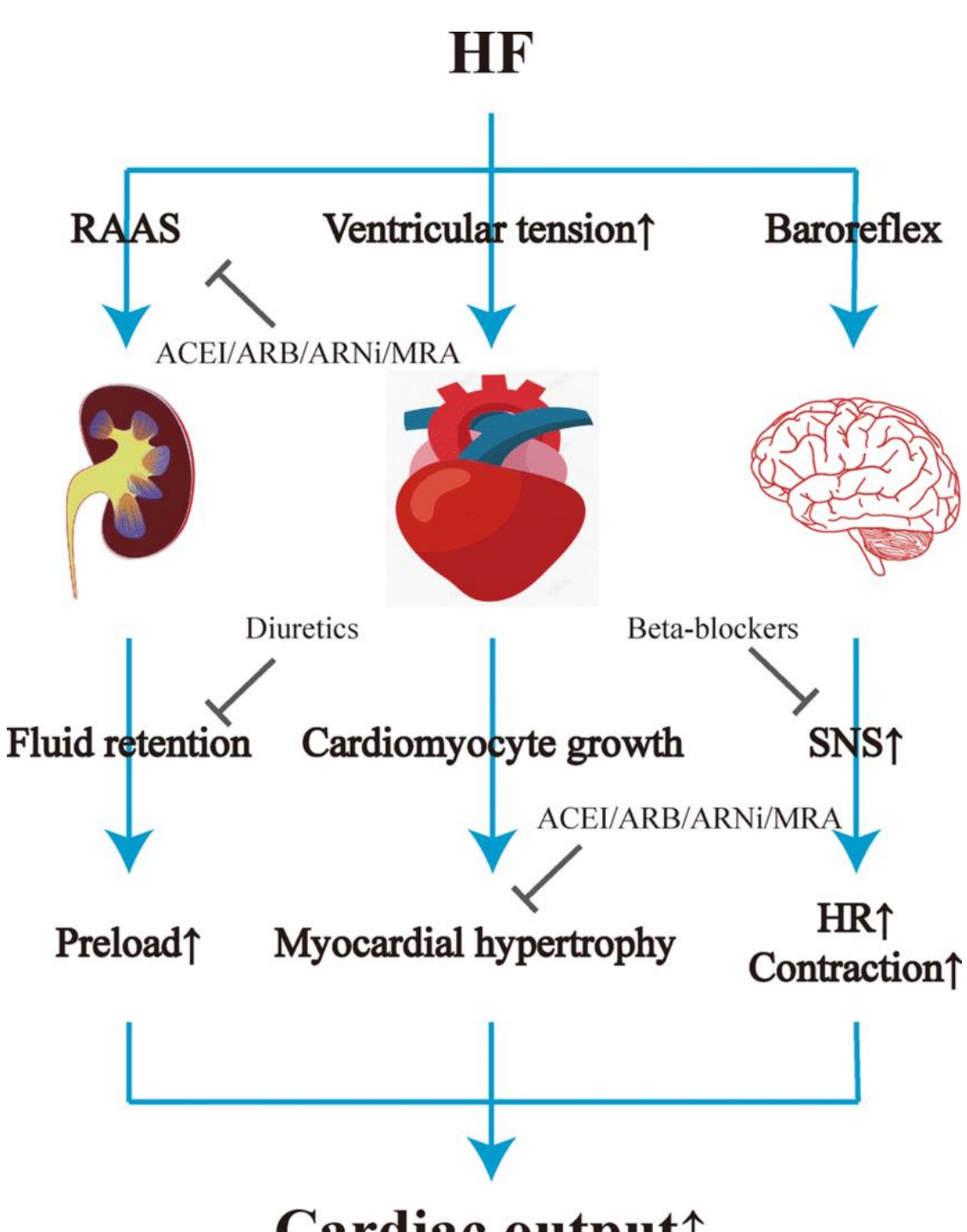
HFpEF vs HFrEF

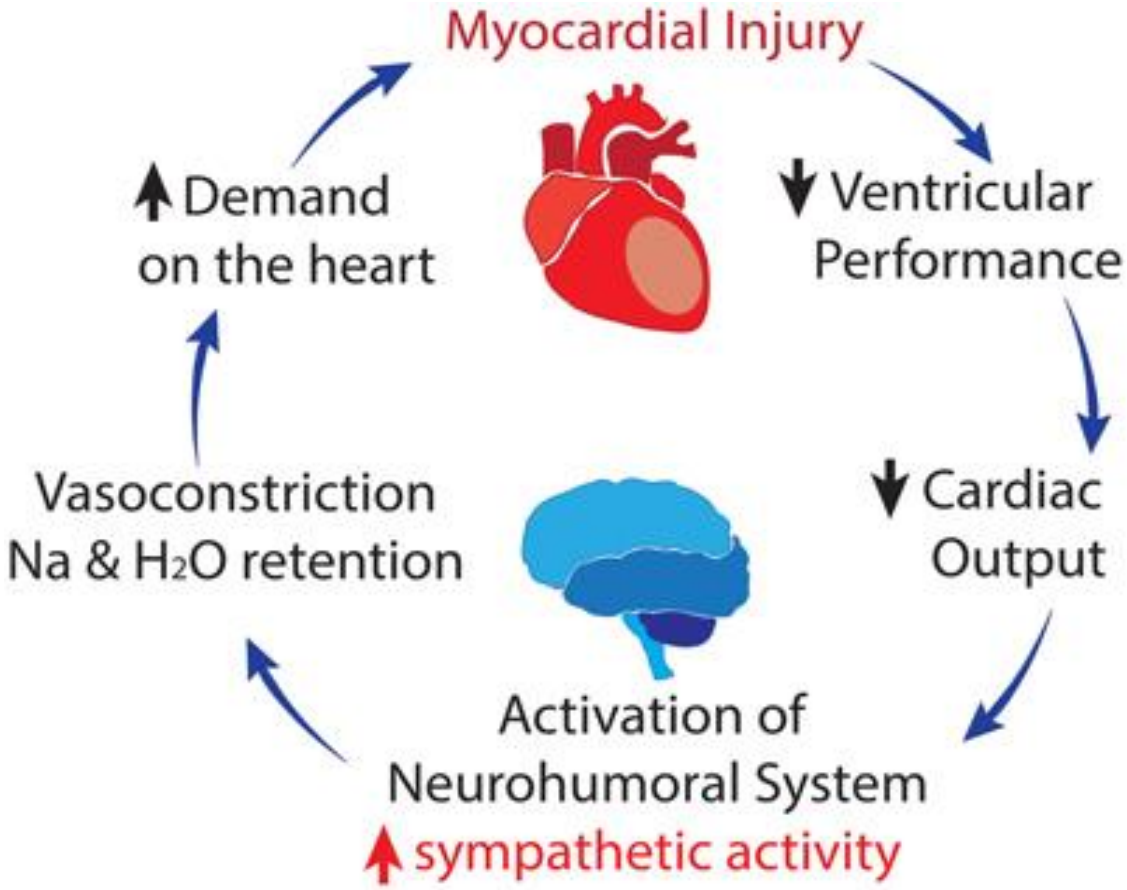
More Information Online WWW.DIFFERENCEBETWEEN.COM

	HFpEF	HFrEF
DEFINITION	HFpEF is a complex cardiovascular syndrome caused by left ventricular diastolic dysfunction	HFrEF is a complex cardiovascular syndrome caused by left ventricular systolic dysfunction
PHASE	Diastolic phase	Systolic phase
EJECTION FRACTION	Greater than 50%	Lower than 40%
CAUSE	Left ventricle's muscles are too stiff or thickened	Muscles of left side of the heart do not squeeze properly
RESULT	Left ventricle fails to fill with blood properly	Left ventricle fails to pump the amount of blood that body needs
DYSFUNCTION	Left ventricular diastolic dysfunction	Left ventricular systolic dysfunction

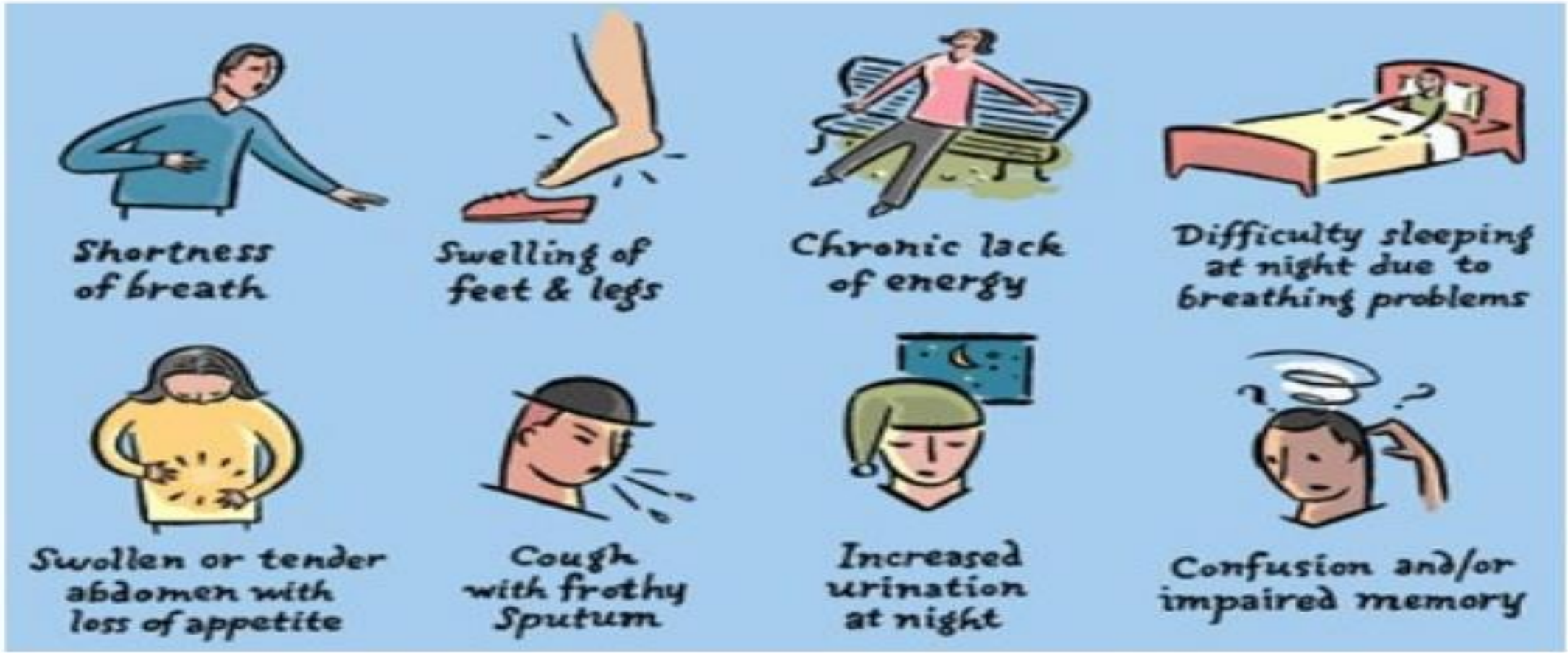

CARDIAC OUTPUT
STROKE VOLUME × HEART RATE
+
+
−
PRELOAD
CONTRACTILITY
AFTERLOAD
Hypertension
Valvular stenosis
Diastolic filling
with venous blood
Systolic
ejection
Resistance to
systolic ejection

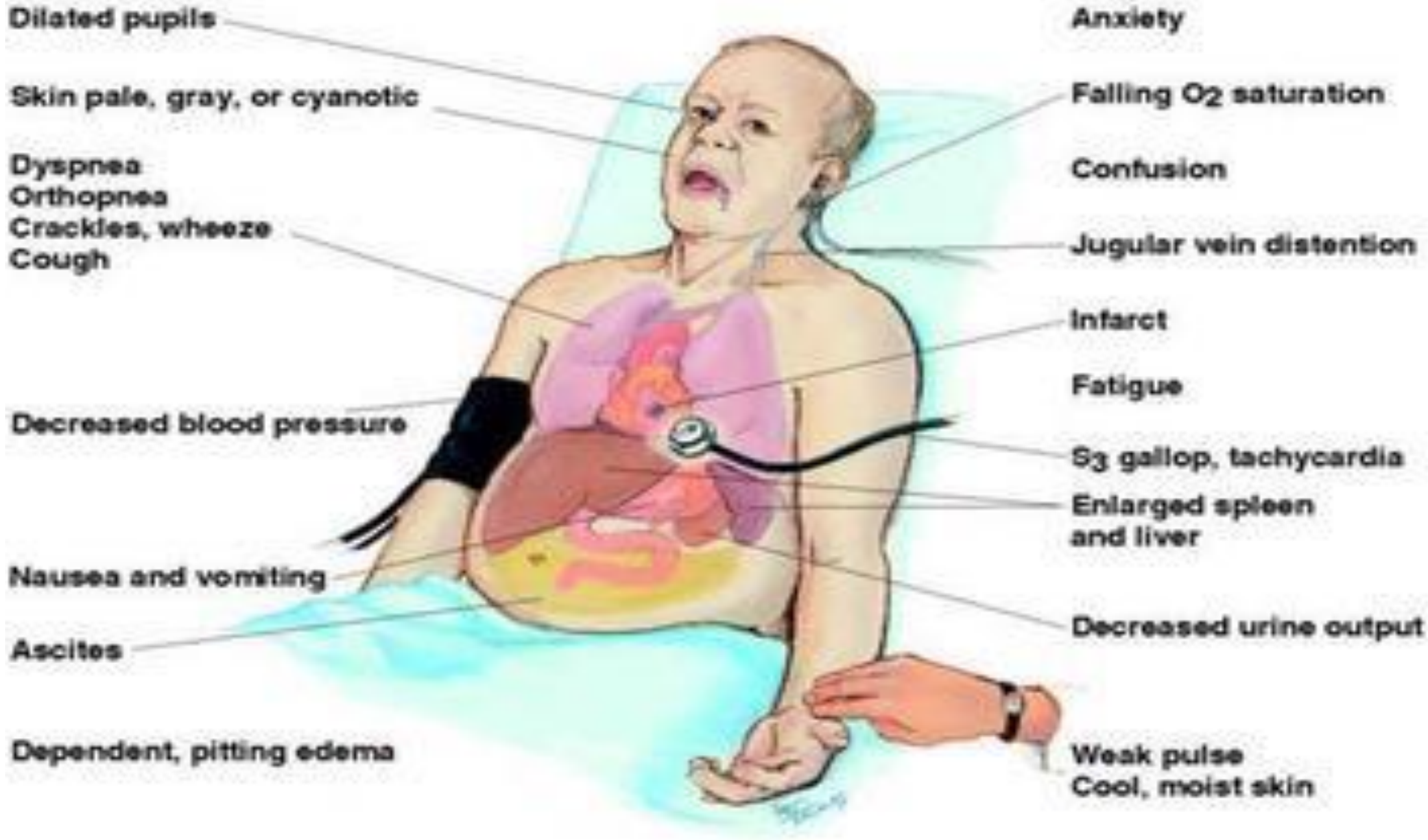

HEART FAILURE
High blood pressure
Heart problems
Rhythm disorders
Valve defects
Heart muscle defects
Other disorders of the heart
Coronary heart disease
Lung problems
Poor blood supply to lungs
Lung disease, asthma, bronchitis, obstructed airways
High blood pressure in lungs
Lifestyle
Failure to take preventive medications
Diet (excessive salt or fluid intake)
Alcohol or drug misuse
Infections
Chagas disease
Rheumatic fever
Other medical conditions
Anaemia
Kidney disease
Diabetes
Obesity
Disordered breathing during sleep
Thyroid disorders
Side effects of medications

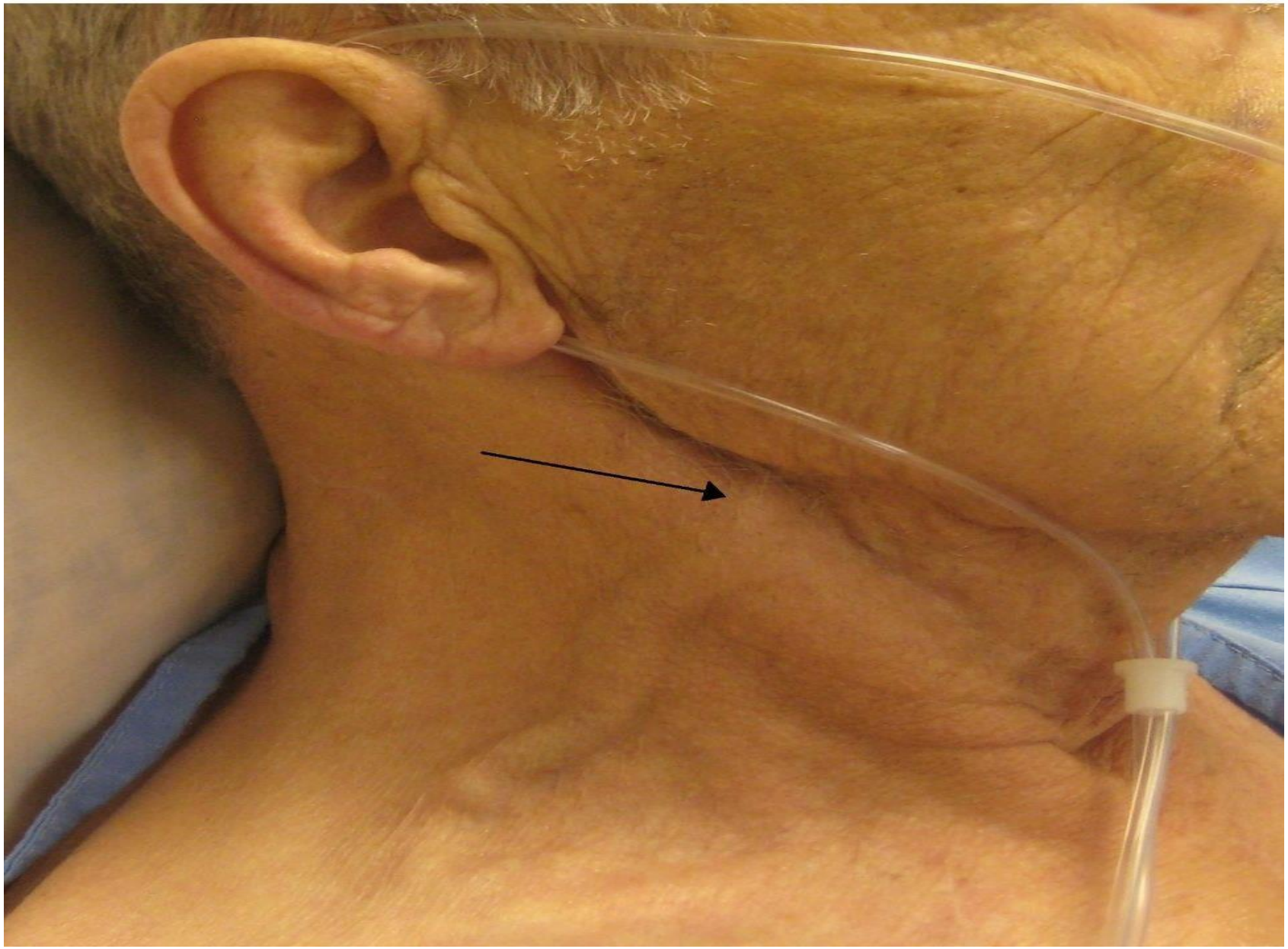

HF
RAAS
Ventricular tension↑
Baroreflex
ACEI/ARB/ARNi/MRA
Diuretics
Beta-blockers
Fluid retention
Cardiomyocyte growth
SNS↑
ACEI/ARB/ARNi/MRA
Preload↑
Myocardial hypertrophy
HR↑
Contraction↑
Cardiac output↑


Myocardial Injury
Demand on the heart
Ventricular Performance
Vasoconstriction
Na & H₂O retention
Cardiac Output
Activation of Neurohumoral System
sympathetic activity

Symptoms


Shortness of breath
Swelling of feet & legs
Chronic lack of energy
Difficulty sleeping at night due to breathing problems
Swollen or tender abdomen with loss of appetite
Cough with frothy Sputum
Increased urination at night
Confusion and/or impaired memory


Dilated pupils
Skin pale, gray, or cyanotic
Dyspnea
Orthopnea
Crackles, wheeze
Cough
Decreased blood pressure
Nausea and vomiting
Ascites
Dependent, pitting edema
Anxiety
Falling O_2 saturation
Confusion
Jugular vein distention
Infarct
Fatigue
S_3 gallop, tachycardia
Enlarged spleen and liver
Decreased urine output
Weak pulse
Cool, moist skin

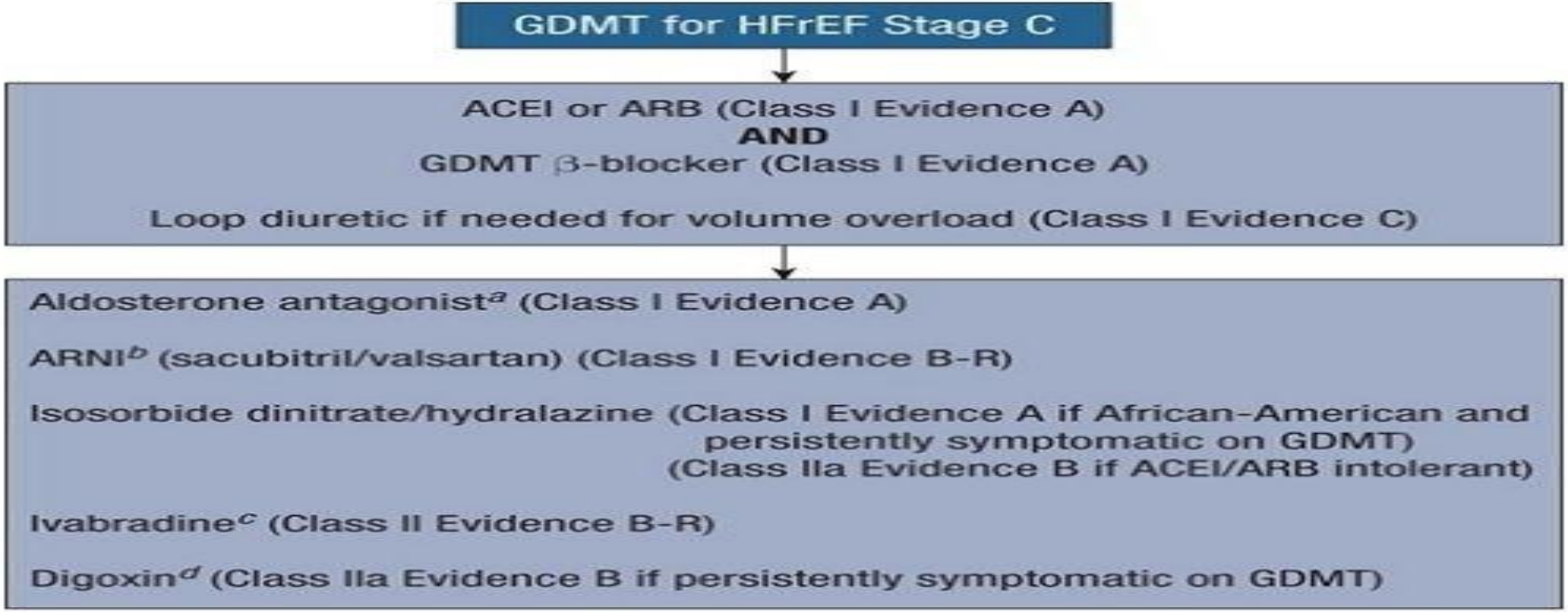


Classification of Heart Failure: ACC/AHA Stage vs NYHA Class

ACC/AHA Heart Failure Stage	NYHA Functional Class
A. At risk for heart failure but without structural heart disease or symptoms	None
B. Structural heart disease but without heart failure	I. Asymptomatic
C. Structural heart disease with prior or current heart failure symptoms	II. Symptomatic with moderate exertion III. Symptomatic with minimal exertion
D. Refractory heart failure requiring specialized interventions	IV. Symptomatic at rest

Hunt SA et al. *Circulation*. 2001;104:2996-3007.
Farrell MH et al. *JAMA*. 2002;287:890-897.

- The therapeutic goals for chronic HF are
- 1.relieve or reduce symptoms.
- 2.slow disease progression.
- 3. prolong survival.



[a]NYHA class II-IV symptoms, estimated creatinine clearance >30 mL/min and K^+ <5.0 mEq/L
[b]NYHA class II-III symptoms tolerating an ACEI or ARB — switching to ARNI can further reduce morbidity/mortality
[c]NYHA class II-III symptoms in normal sinus rhythm and HR ≥70 bpm on maximally tolerated β-blocker dose
[d]Indication is to reduce hospitalizations

Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

Stage A -------- smoking cessation and control of hypertension, diabetes mellitus, and dyslipidemia. Although treatment must be individualized, angiotensin-converting enzyme (ACEI) inhibitors or angiotensin receptor blockers (ARBs) are recommended for HF prevention in patients with multiple vascular risk factors.

STAGE B ---- stage A managements + patients with reduced LVEF should receive an ACEI (or ARB) and a β-blocker to prevent development of HF.

STAGE C ------ patients with HFrEF treated with ACEI or ARB and β-blocker. Loop diuretics, aldosterone antagonists.

Hydralazine–isosorbide dinitrate (ISDN) **for both acute or chronic HF**

ARB/NEPRILYSIN INHIBITOR (ARNI)

IVABRADINE

DIGOXIN

- STAGE D ------These are patients with persistent HF symptoms even at rest despite maximally tolerated GDMT. They should be considered for specialized interventions, including mechanical circulatory support, continuous IV positive inotropic therapy, cardiac transplantation, or hospice care (when no additional treatments are appropriate). Restriction of sodium and fluid intake may be

beneficial. High doses of diuretics, combination therapy with a loop and thiazide diuretic, or mechanical fluid removal methods such as ultrafiltration may be required.

ACEI

FIRST LINE------ START WITH LOW DOSE

All patients with HFrEF should receive ACE inhibitors unless contraindications are present. Post-MI patients without HF symptoms or reduced LVEF (Stage B) should also receive ACE inhibitors to prevent development of HF and to reduce mortality.

Side-effects of ACE inhibitors: *CAPTOPRIL*

Cough
Angioedema
Potassium excess
Taste changes
Orthostatic hypotension
Pregnancy contraindication/Pressure drop (hypotension)
Renal failure/Rash
Indomethacin inhibition
Leukopenia (rare)

Contraindications to ACE inhibitors: *PARK*

Pregnancy
Allergy/**A**ngioedema
Renal artery stenosis/**R**enal failure
K - hyperkalemia (potassium > 5.5)

ARB

- CANDESARTAN- LOSARTAN- VALSARTAN ONLY
- Alone in patients unable to tolerate (usually due to cough) ACE inhibitors.
- In combination in patients with HFrEF who remain symptomatic despite treatment with an ACE inhibitor and a β-blocker if an **aldosterone antagonist cannot be used**.

BB

- Carvedilol, metoprolol succinate (CR/XL), nebivilol and bisoprolol are the only β-blockers shown to reduce mortality in large HF trials. Because bisoprolol is not available in the necessary starting dose of 1.25 mg, the choice is typically limited to either carvedilol or metoprolol succinate.
- NEVER GIVE BB IN PT. WITH ACUTE HF.
- START WITH VERY LOW DOSE AND UP VERY SLOWLY
- in all stable patients with HF and a reduced LVEF in the absence of contraindications or a clear history of β-blocker intolerance. Patients should
- receive a β-blocker even if symptoms are mild or well controlled with ACE inhibitor and diuretic therapy.
- ALSO given IN ASYMPTOMATIC PT. TO PREVENT PROGRESION.

Propranolol
Timolol
Nadolol
Penbutolol

Atenolol
Metoprolol
Carteolol
Betaxolol
Esmolol
Bisoprolol

Acebutolol
Pindolol

Vasodilatory

Nebivolol

α & β blockers

Carvedilol
Labetalol

How they act ?

Beta blockers act on beta receptors thereby inhibit increase in cAMP and decrease both rate and force of contraction of the heart.

Side effects

- **Bronchospasm**
  - *Difficulty in breathing, wheezing, coughing*
  - *May be due to action on β_2 receptors*
  - *Less observed with selective β_1 blockers*
- **Bradycardia**
  - *Decrease in heart rate*
  - *It is due to action on heart through β_1 block*
- **Hypoglycemia**
  - *Fall in glucose levels*
  - *It is due to decreased insulin release through β_2 receptors*
- **Fatigue**
  - *Weakness, drowsiness and even dizziness*
  - *It is due to decreased blood supply as well as fall of glucose levels*
- **Cold sensation**
  - *Cold sensation in hands and feet*
  - *It is due to decreased cutaneous vasodilation by β_2 receptors*

DIURETICS

- is recommended for all patients with clinical evidence of fluid retention (symptomatic).

LOOP DIURETICS---**furosemide**, **bumetanide**, and **torsemide**)

- In addition to acting in the loop of Henle, they induce a **prostaglandin-mediated** increase in renal blood flow that contributes to their natriuretic effect.
- POTENT diuretics bc. They maintain their effectiveness in the presence of impaired renal function.

Thiazide diuretics

- Thiazide diuretics (eg, **hydrochlorothiazide**), or the thiazide-like diuretic **metolazone**
- **1.** can be used in combination with a loop diuretic to promote very effective diuresis--- but mostly in hospital bc. It need monitoring.
- 2. Thiazides may used alone only in patient with mild fluid retention and elevated BP because of their more persistent antihypertensive effects.

MRA

Spironolactone and eplerenone*****diuretic effects are minimal, suggesting that their therapeutic benefits result from other actions.

------attenuate cardiac fibrosis and ventricular remodeling+ antioxidant activity

(1) patients with mild to moderately severe HFrEF (NYHA class II–IV)

who are receiving standard therapy of ACEI and BB,

(2) Patient with LV dysfunction and either acute HF or diabetes early after MI.

Hydralazine plus nitrates

Venodilators and vasodilators

1. Used in pt. with HFrEF and NYHA class III–IV symptoms treated with ACE inhibitors and β-blockers.

2. The combination can also be useful in patients unable to tolerate either an ACE inhibitor or ARB because of renal insufficiency, hyperkalemia, or possibly hypotension.

ARB/NEPRILYSIN INHIBITOR (ARNI)

- Valsartan/sacubitril ------200 mg (sacubitril 97 mg/valsartan 103 mg)
- twice daily in patients with **symptomatic** HF(stage C & D, NYHA II,III,IV) and reduced LVEF.
- reduce the risk of cardiovascular death and hospitalization

IVABRADINE

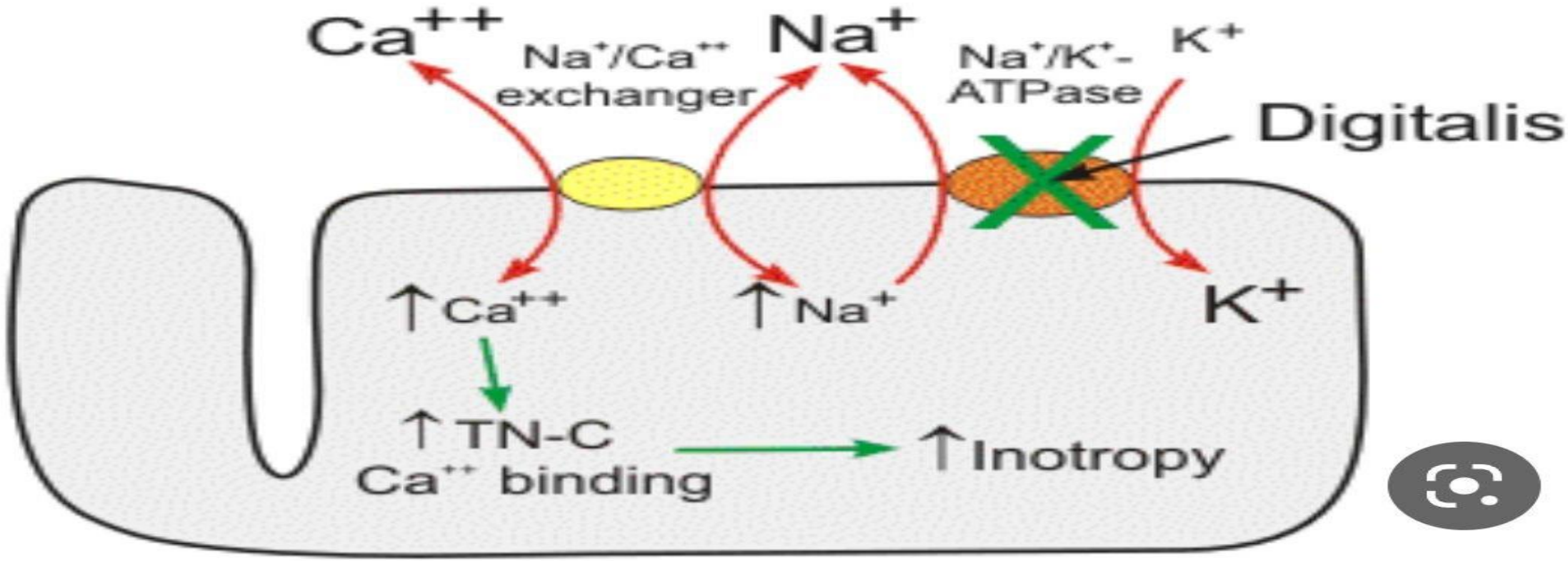
Ivabradine ----slowing of the heart rate.

- It is indicated to reduce the risk of hospitalization for worsening HF in patients with LVEF ≤ 35% who are resting heart rate ≥ 70 bpm and either are on maximally tolerated doses of β-blockers or have a contraindication to β-blocker use.
- The most common adverse effects are bradycardia, atrial fibrillation, and visual disturbances.

DIGOXIN

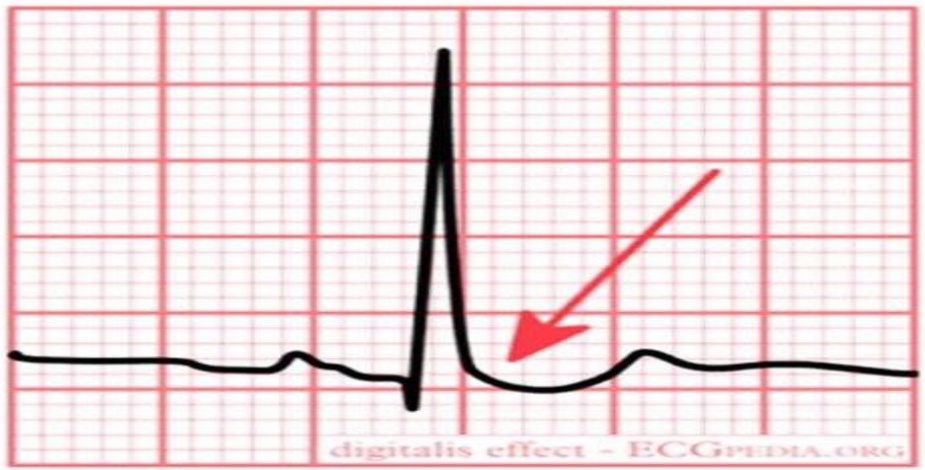
positive inotropic .

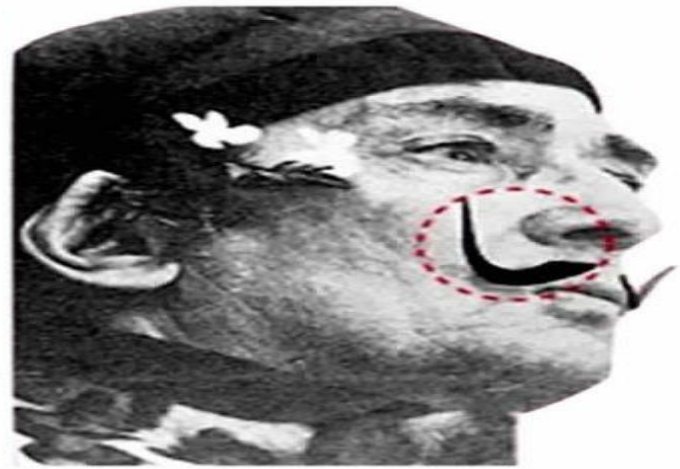
- Digoxin improves cardiac function, quality of life, exercise tolerance, and HF symptoms in patients with HFrEF but **does not** improve survival.
- digoxin is not considered a first-line agent in HF, but a trial may be considered in conjunction with GDMT including ACE inhibitors, β-blockers, and diuretics in patients with symptomatic HFrEF to improve symptoms and reduce hospitalizations.
- Digoxin may **DOC in pt. with HF+AF**
- Digoxin withdrawal may be considered for asymptomatic patients who have significant improvement in systolic function with optimal ACE inhibitor and β-blocker treatment.
- The target serum digoxin concentration for most patients is 0.5 to 0.9 ng/mL (0.6–1.2 nmol/L). Most patients with normal renal function can achieve this level with a dose of 0.125 mg/day.

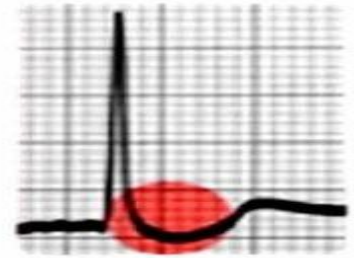

Ca++
Na+/Ca++
exchanger
Na+
Na+/K+-
ATPase
K+
Digitalis
↑Ca++
↑Na+
K+
↑TN-C
Ca++ binding
↑Inotropy

Digoxin Effect on ECG

- **Digoxin effect** on ECG is not a marker of digoxin toxicity
- It merely indicates that the patient is taking digoxin
- The QRS-ST morphology is described as:
  "slurred" , "sagging" , "scooped" , "reverse tick" , "hockey stick" or "**Salvador Dali's moustache**"







Digitalis Effect

Indication

- Heart Failure
- Tachyarrhythmias
- Atrial Fibrillation
- Atrial Flutter
- Paroximal atrial tachycardia

Contraindication and Precaution

- Hypersensitivity
- Uncontrolled Ventricular Arrhythmias
- AV block
- Constrictive Pericarditis
- Idiopathic Hypertrophic Subaortic Stenosis

changes make the situation even more complicated.

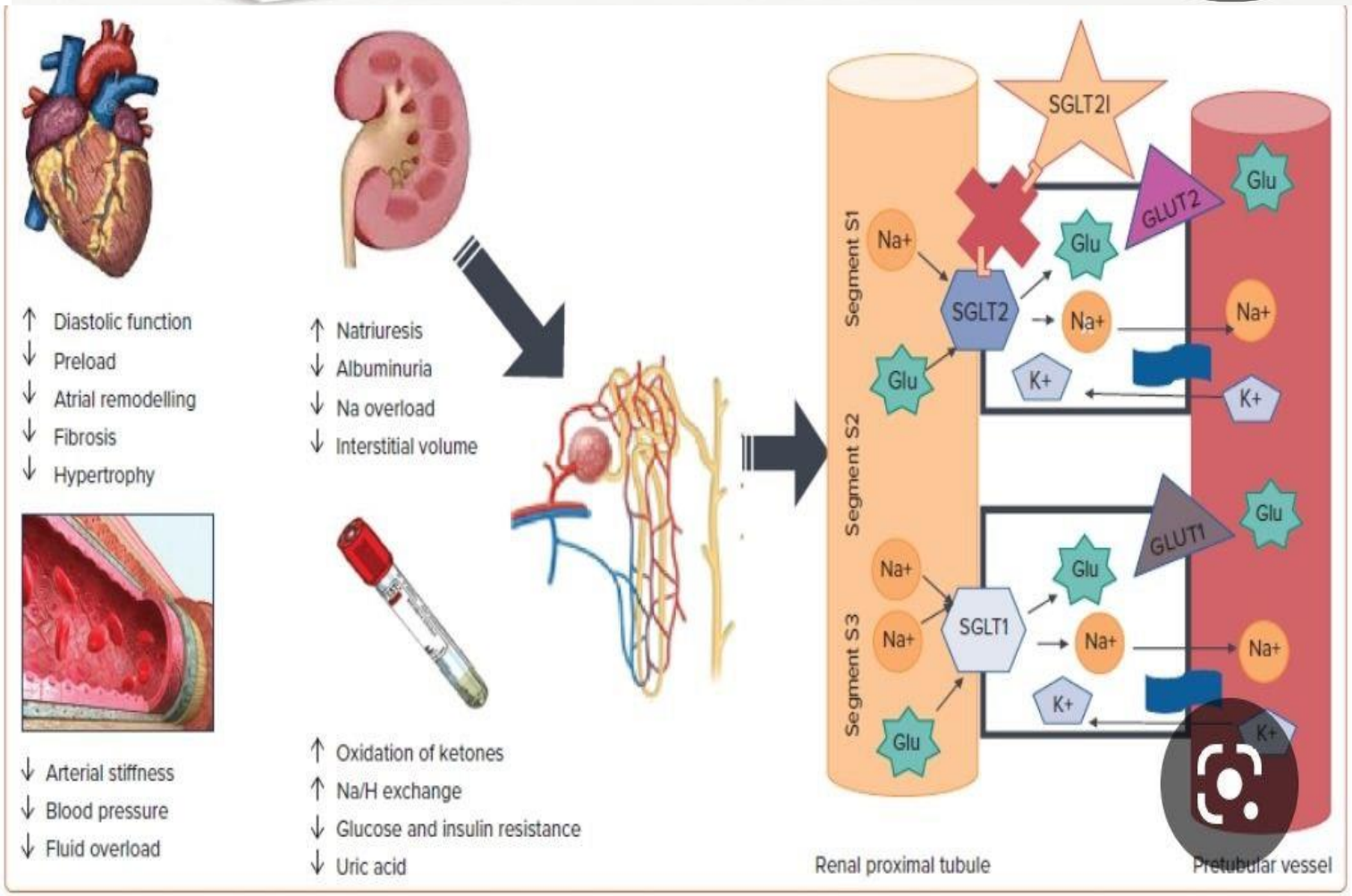
Digoxin toxicity
Acute versus Chronic

Acute

- Asymptomatic for several hours
- GI symptoms often occur first
- Bradydysrhythmias or supraventricular with AV block
- Severity correlates with K^+ not with digoxin level
- High digoxin level

Chronic

- Elderly on digoxin and diuretics
- May mimic influenza or gastroenteritis
- Mental status change
- Many dysrhythmias, but ventricular more common than in acute
- K^+ often low and digoxin is a poor predictor



2019

DAPA-HF TRIAL

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

AMERICAN COLLEGE of CARDIOLOGY

Randomized, parallel group, placebo-controlled trial

Objective: To evaluate dapagliflozin (a sodium-glucose cotransporter 2 [SGLT2] inhibitor) compared with placebo among patients with heart failure and a reduced ejection fraction (HFrEF).

4,744 patients

Inclusion criteria: patients with symptomatic HF; LVEF ≤40% NT-proBNP ≥600 pg/ml (if hospitalized for HF within last 12 months ≥400 pg/ml; if atrial fibrillation/flutter ≥900 pg/ml)

Dapagliflozin 10 mg daily (n = 2,373)		Placebo (n = 2,371)
PRIMARY OUTCOME		
16.3	Cardiovascular death, hospitalization for HF, or urgent HF visit% HR 0.74; 95% CI 0.65-0.85, P< 0.001	21.2
SECONDARY OUTCOME		
9.6	Cardiovascular death % HR 0.82; 95% CI 0.69 to 0.98	11.5
1.2	Worsening of renal function % HR 0.71; 95% CI 0.44 to 1.16	1.6

Conclusion: Dapagliflozin vs. placebo was associated with a reduction in cardiovascular deaths and HF events

McMurray JJV, Solomon SD, Inzucchi SE, et al., for the DAPA-HF Trial Committees and Investigators. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med*, 2019; [EPub Ahead of Print].

Farxiga™ - Dapagliflozin

Clinical Application

- Contraindications:
  - History of serous hypersensitivity reaction
  - Severe renal impairment, ESRD, dialysis
- Warnings and Precautions
  - May cause symptomatic hypotension
  - Impairment in renal function may occur
  - Risk of hypoglycemia when used with insulin or insulin secretagogues
  - Increased risk of genital mycotic infections
  - May cause increased LDL-C elevation

Pharmacologic Therapy for HFpEF

Treatment includes controlling HR and BP, alleviating causes of myocardial ischemia, reducing volume, and restoring and maintaining sinus

- rhythm in patients with atrial fibrillation. Many of the drugs are the same as those used to treat HFrEF (eg, diuretics, β-blockers), but the rationale
- and dosing may be different.
- A loop or a thiazide diuretic should be considered for patients with volume overload. Use a loop diuretic for more severe volume overload or
- inadequate response to a thiazide. Avoid lowering preload excessively, which may reduce stroke volume and CO. Start diuretics at low doses to
- avoid hypotension and fatigue.
- ACE inhibitors may be considered in all patients, especially patients with symptomatic atherosclerotic cardiovascular disease or diabetes and one
- additional risk factor.
- ARBs may be considered in all patients, especially those who are intolerant of ACE inhibitors.
- Aldosterone antagonists can reduce the risk of hospitalization in patients who do not have contraindications and are not at risk for hyperkalemia.
- They may be beneficial for patients with elevated BNP or NT-proBNP.
- β-Blockers should be considered in patients with one or more of the following conditions: (1) MI, (2) hypertension, and (3) atrial fibrillation
- requiring ventricular rate control.
- Nondihydropyridine calcium channel blockers (CCB; diltiazem or verapamil) should be considered for patients with atrial fibrillation warranting
- ventricular rate control who either are intolerant to or have not responded to a β-blocker. A nondihydropyridine or dihydropyridine (eg,
- amlodipine) CCB can be considered for symptom-limiting angina or hypertension.

TREATMENTS FOR ACUTE HF

- **1. Diuretics** ---- high iv bolus or continuous iv infusion dose loop ± thiazide.
- **2. Vd** -----Mixed vasodilators act on both arterial resistance and venous capacitance vessels, reducing congestive symptoms while increasing cardiac output.
- **nitroglycerin-hydralazine- nesiritide-nitroprusside**
- **3. Vasopressin Antagonists----Tolvaptan, Conivaptan**

V_{1A} or V_2. Stimulation of V_{1A} receptors (located in vascular smooth • muscle cells and myocardium) results in vasoconstriction, myocyte hypertrophy, coronary vasoconstriction, and positive inotropic effects. V_2 receptors are located in renal tubules, where they regulate water reabsorption.

Inotropes

- **Dobutamine, milrenone and dopamine**

MECHANICAL CIRCULATORY SUPPORT

intraaortic balloon pump (IABP) •

Ventricular assist devices •

Extracorporeal membrane oxygenation (ECMO) •

SURGICAL THERAPY•

- Orthotopic cardiac transplantation is the best therapeutic option for patients with irreversible
- advanced HF, as 10-year survival rates approach 60% in patients transplanted after 2001