Internal Medicine

Lecture 7. CONGESTIVE HEART FAILURE

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DEFINITION

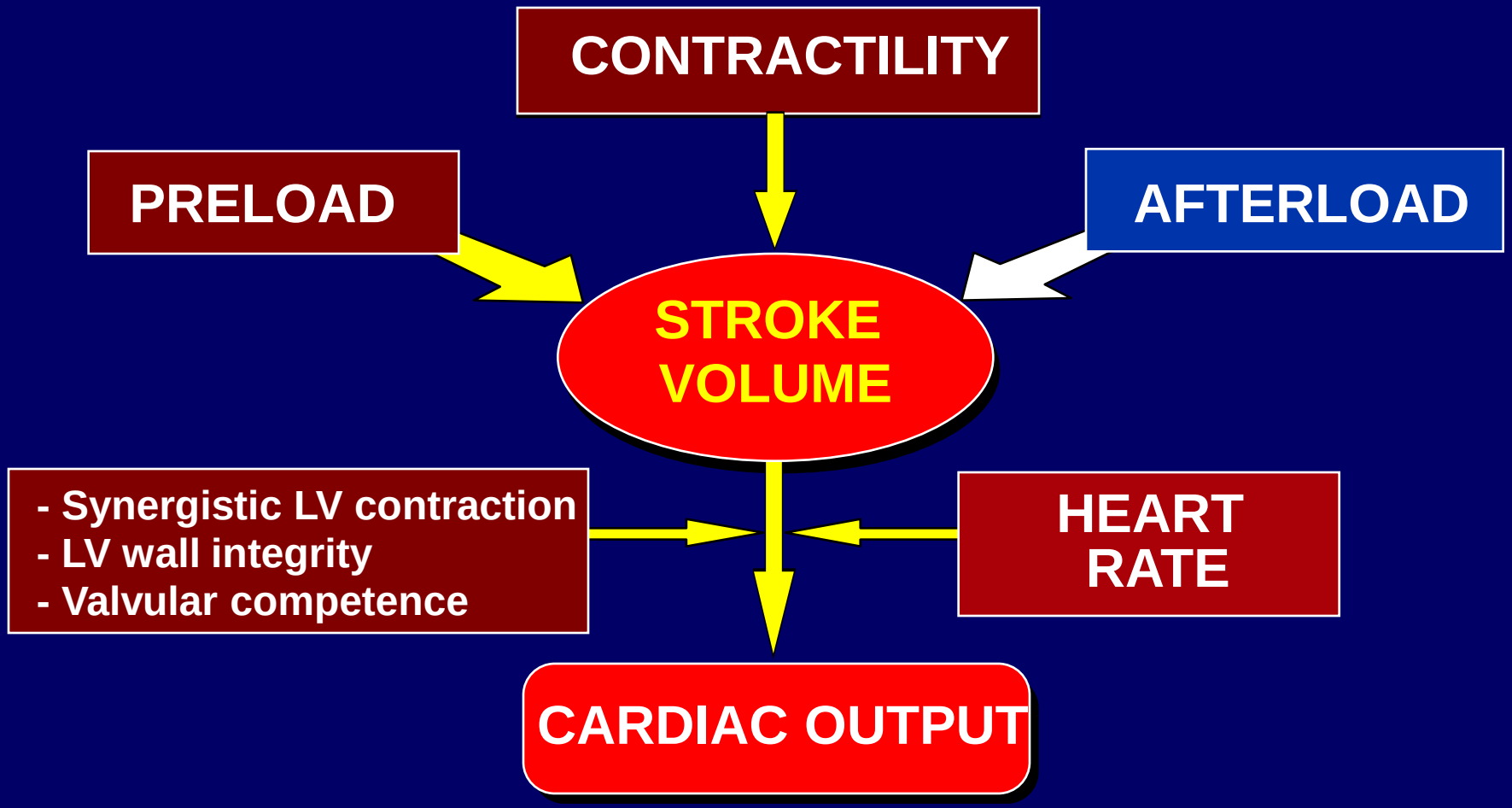
"The situation when the heart is incapable of maintaining a cardiac output adequate to accommodate metabolic requirements and the venous return."

E. Braunwald

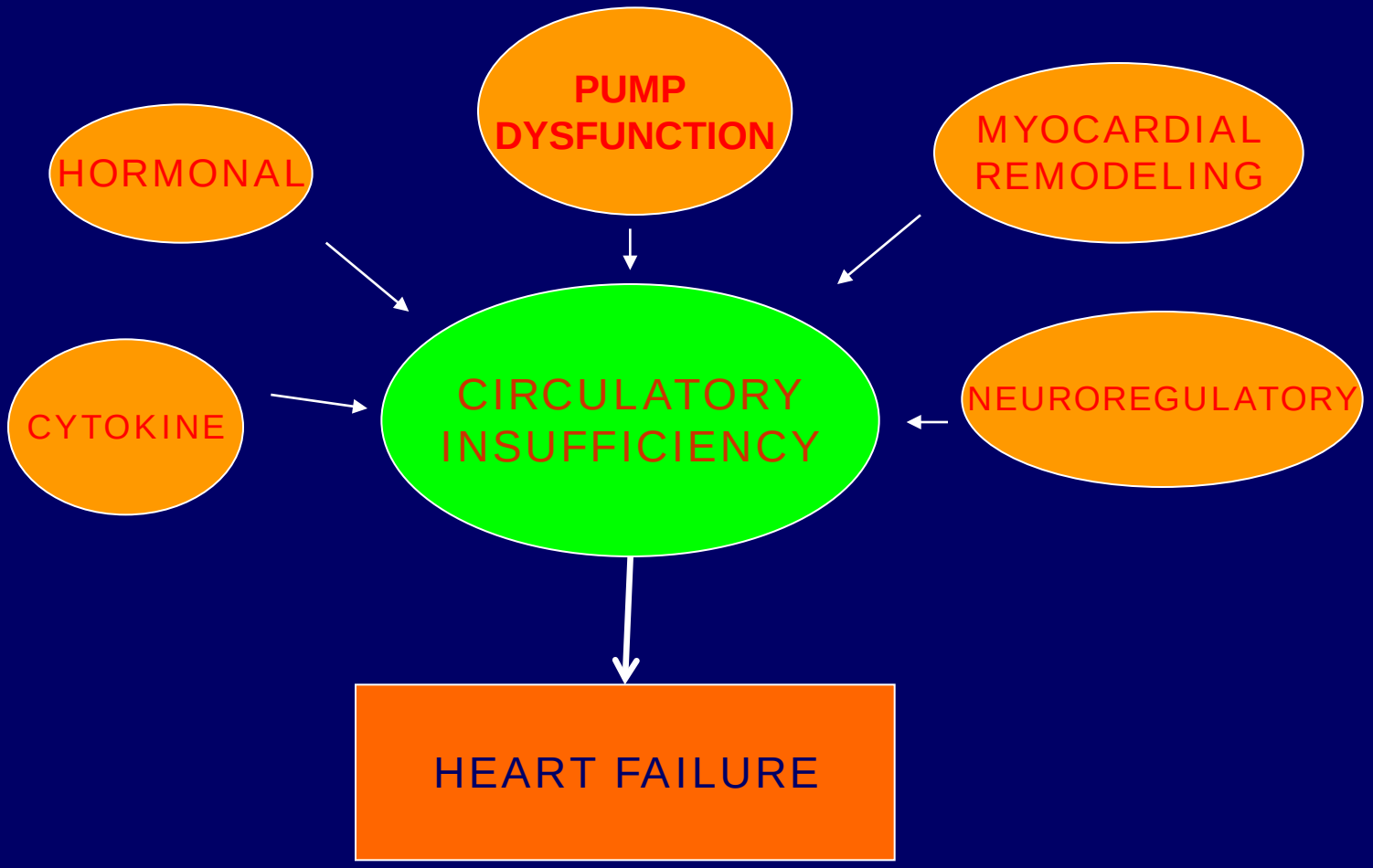
Incidence and prevalence

- Heart failure is an epidemic affecting 1-2 million Ukraineans and nearly 15 million people worldwide.
- Heart failure carries worse prognosis, as 50% of patients with heart failure will die within 5 year, and in patient with sever heart failure more than 50% will die within 2 year.

DETERMINANTS OF VENTRICULAR FUNCTION



Pathophysiology of heart failure



DIAGNOSIS

- HISTORY.
- PHYSICAL EXAMINATION.
- APPROPRIAT INVESTIGATION.

1. SYMPTOMS OF HEART FAILURE (AT REST OR DURING EXERCISE).
2. Objective evidence of cardiac dysfunction.
3. Response to treatment directed towards heart failure.

CRITERIA FOR CONGESTIVE HEART FAILURE

- MAJOR CRITERIA

1.Paroxysmal nocturnal dyspnea or orthopnea.

2.Rales.

3.Cardiomegaly.

4.Acute pulmonary edema.

5.S_3 Gallop.

6.Increased venous pressure>16 cm of water.

7.Circulation time>25 sec.

8.Hepatojugular reflux.

- MINOR CRITERIA

1.Ankle edema.

2.Night cough.

3.Dyspnea on exertion.

4.Pleural effusion.

5.Vital capacity decreased 1/3 from maximum.

6.Tachycardia (rate>120/min).

- MAJOR OR MINOR

Weight loss>4.5 Kg in 5 days in response to treatment.

Symptomatic classification of exercise tolerance New York Heart Association (NYHA)

- NYHA Class I: No complaints under heavy physical load.
- NYHA Class II: Complaints under heavy physical load.
- NYHA Class III: Complaints under light physical load.
- NYHA Class IV : Complaints at rest.

Descriptive terms in heart failure

Acute vs Chronic heart failure.

Systolic vs Diastolic.

Right vs Left heart failure.

Types of Heart Failure

- include left, right or both sides
- left ventricular heart failure
  - most common
  - systolic failure: unable to contract
  - diastolic failure: unable to relax
- right ventricular heart failure
  - usually occurs after left failure
  - less blood received causes right damage
  - less pumping by right side
  - venous pooling of blood in legs

Causes of Chronic Heart Failure

- *Systolic dysfunction:*
  - *Coronary artery disease.*
  - *Hypertension.*
  - *Dilated Cardiomyopathy.*
  - *Myocarditis.*

Causes of Chronic Heart Failure cont.

- *Diastolic Dysfunction:*
  - *Coronary artery disease.*
  - *Systemic Hypertension.*
  - *Diabetis Mellitus.*
  - *Aortic stenosis.*
  - *Hypertrophic cardiomypathy.*
  - *Infiltrative cardiomypathy*
  - *Endocardial fibrosis.*
  - *Normal aging process.*

Causes of worsening Heart Failure cont.

Cardiac:

- Atrial fibrillation.
- Other supraventricular or ventricular arrhythmias.
- Bradycardia.
- Appearance or worsening mitral or ticusped regurgitation.
- Myocardial ischaemia.
- Excessive preload reduction(diuretics,ACE inhibitors).

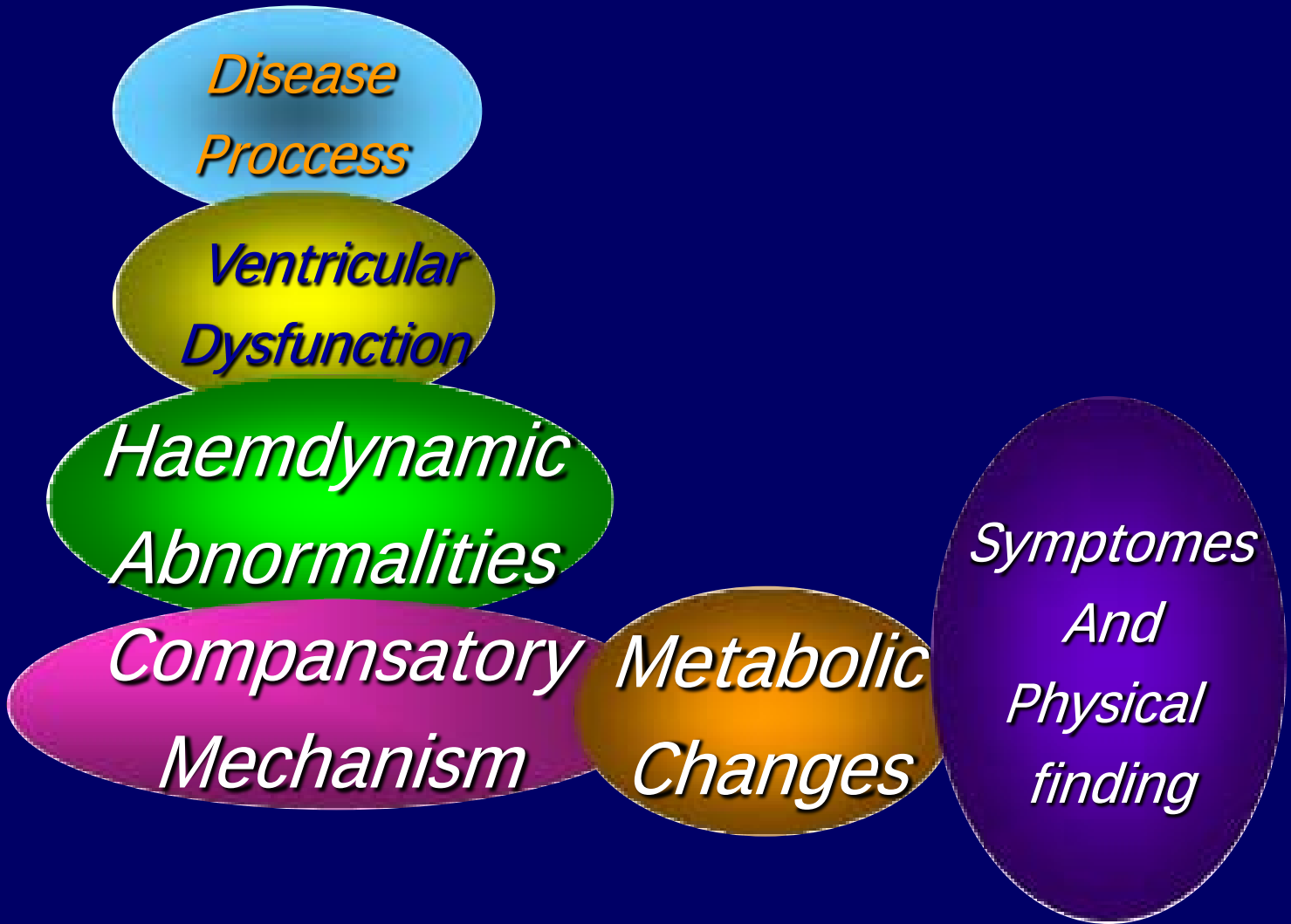
Causes of worsening Heart Failure

Non- cardiac:

- Non compliance to the prescribed regimen(salt,liquid,medication).
- Recently co-prescribed drugs (antiarrhythmic,beta-blockers,non steroidal anti-inflmatory drugs,verapamil,diltiazem).
- Renal dysfunction.
- Infection.
- Pulmonary embolism.
- Thyroid dysfunction.
- Anemia.
- Alcohol abuse.

The Heart Failure Milieu

Clinical Presentation



Metabolic Changes

- Azotemia.
- Hyponatraemia.
- Hypokalemia.
- Hypomagnesemia.
- Hyperuricemia.
- Acidosis/Alkalosis.
- Hypoxia/O2 desaturation.
- Decreased MVO2.

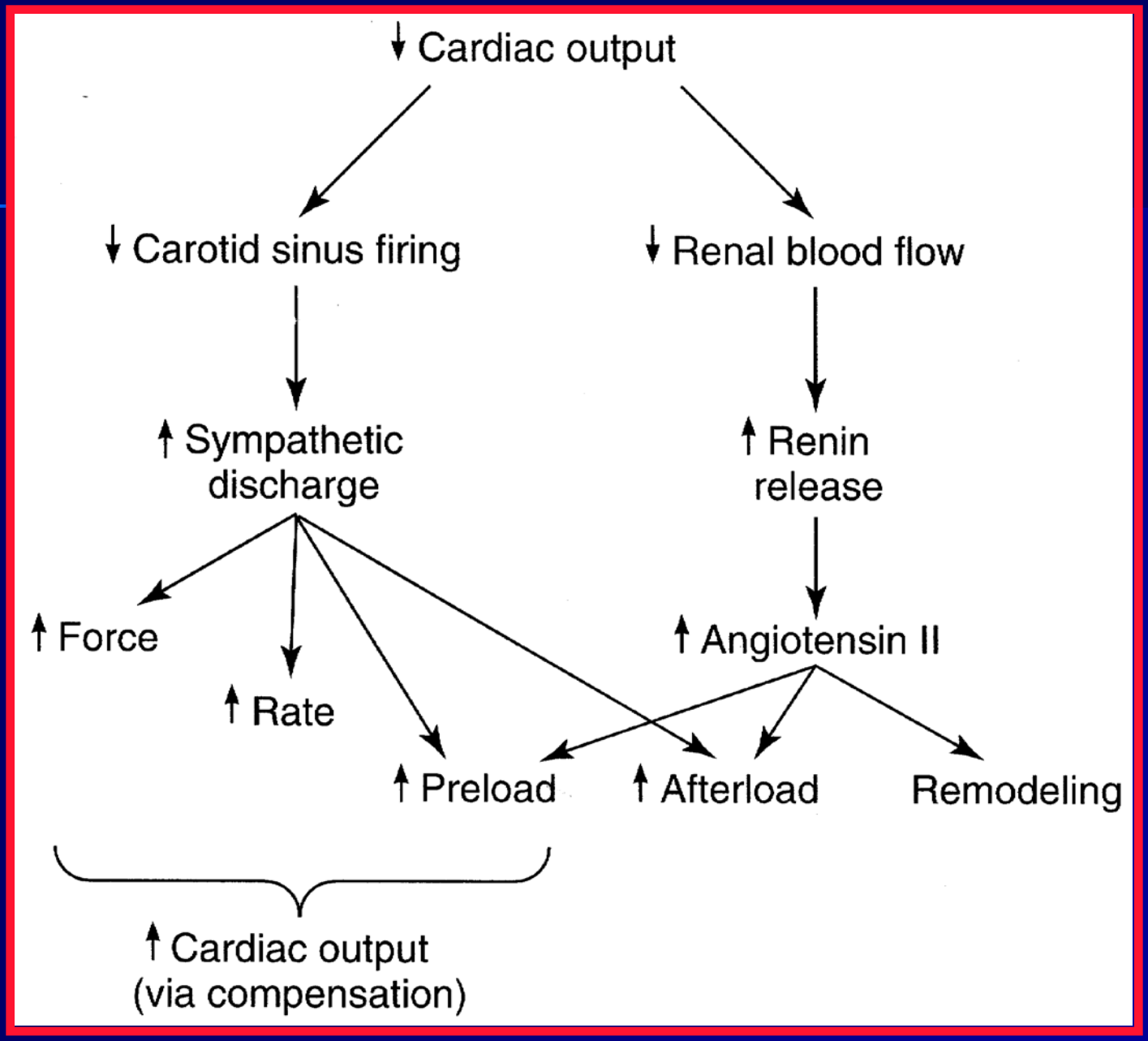
Symptomes

- ☹ Fatigue ,weakness and decreased exercice tolerance.
- ☹ Dyspnea and fluied retention symptomes.
- ☹ Nocturia.
- ☹ Gastrointestinal symptomes.
- ☹ Diminished mentation.

Physical Findings

- Peripheral edema.
- Ascites.
- Jugular venous distension.
- Rales.
- Tachycardia.
- Hypotention.
- Cachexia.
- Disease specific findings.

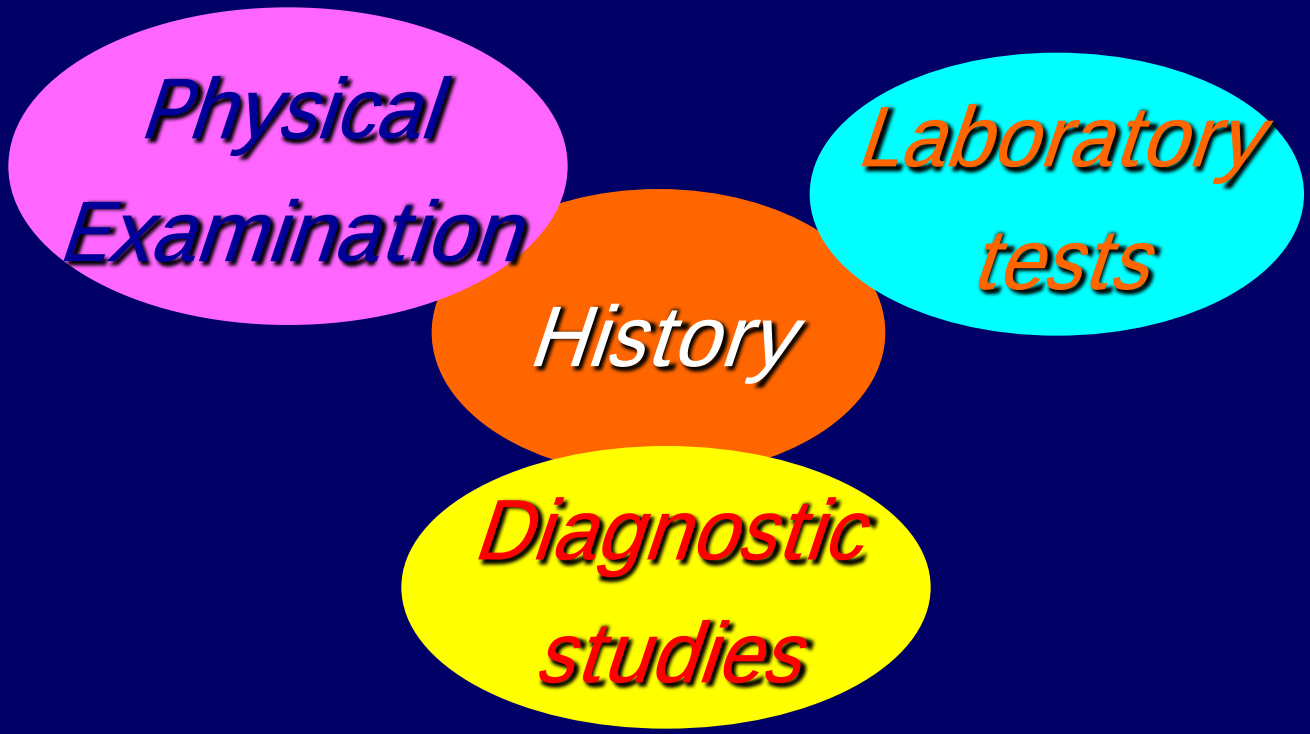
Compensatory Mechanisms



Systemic organ failure

- Renal failure.
- Hepatic failure.
- Respiratory failure.
- Multi-organ failure.
- Pulmonary embolism.
- Peripheral& cerebral embolism.

Evaluation of heart failure patient

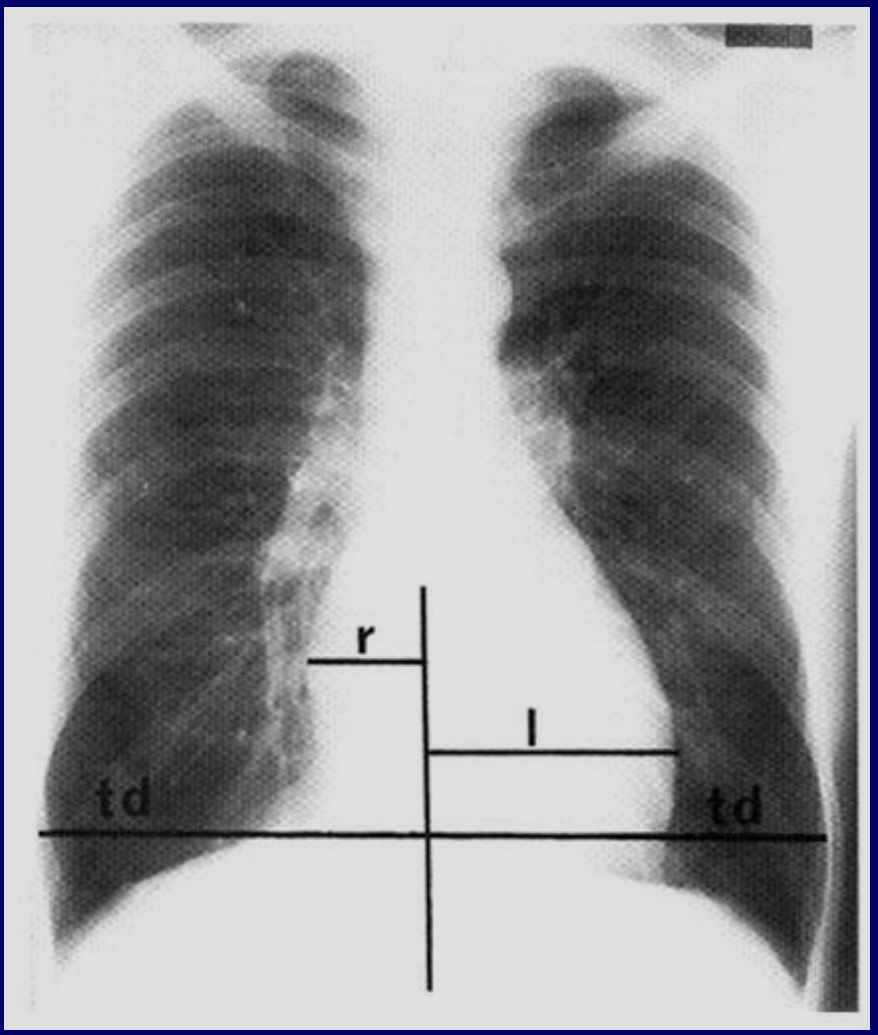


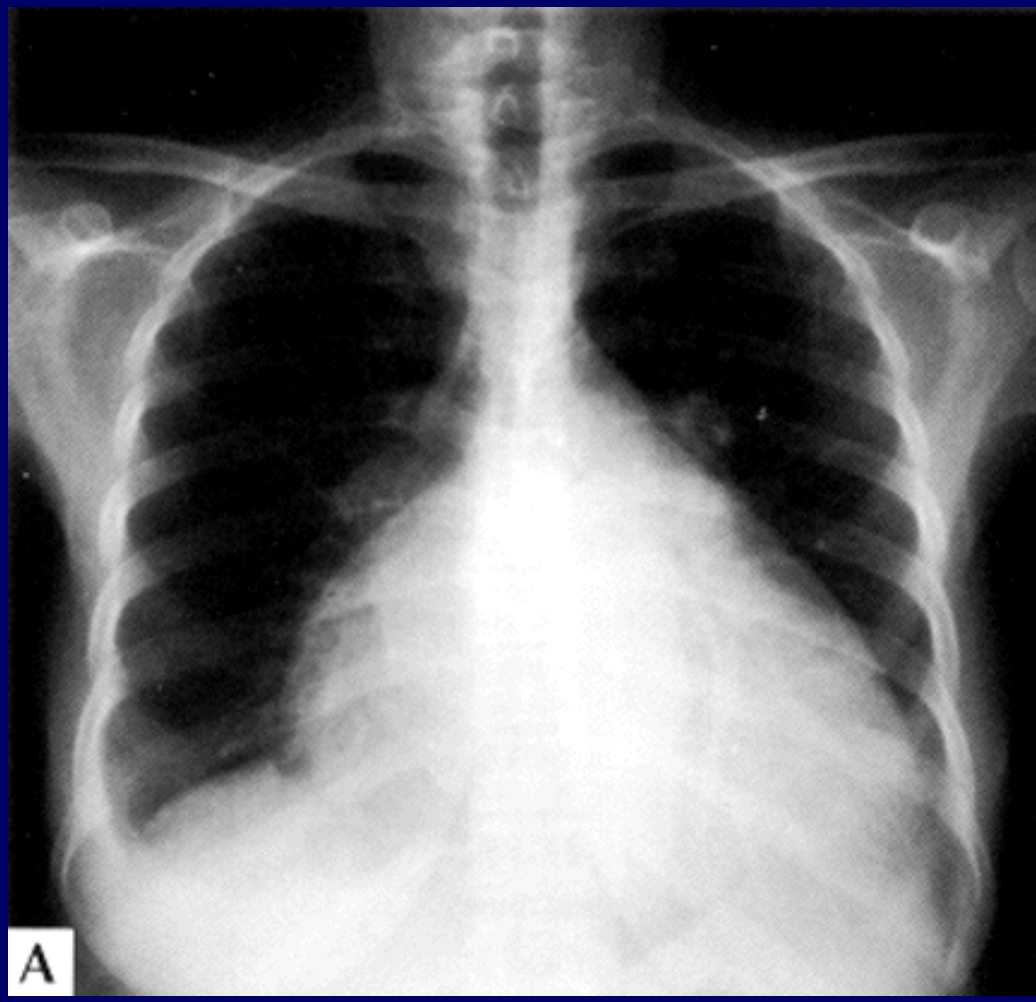
Investigation

Laboratory

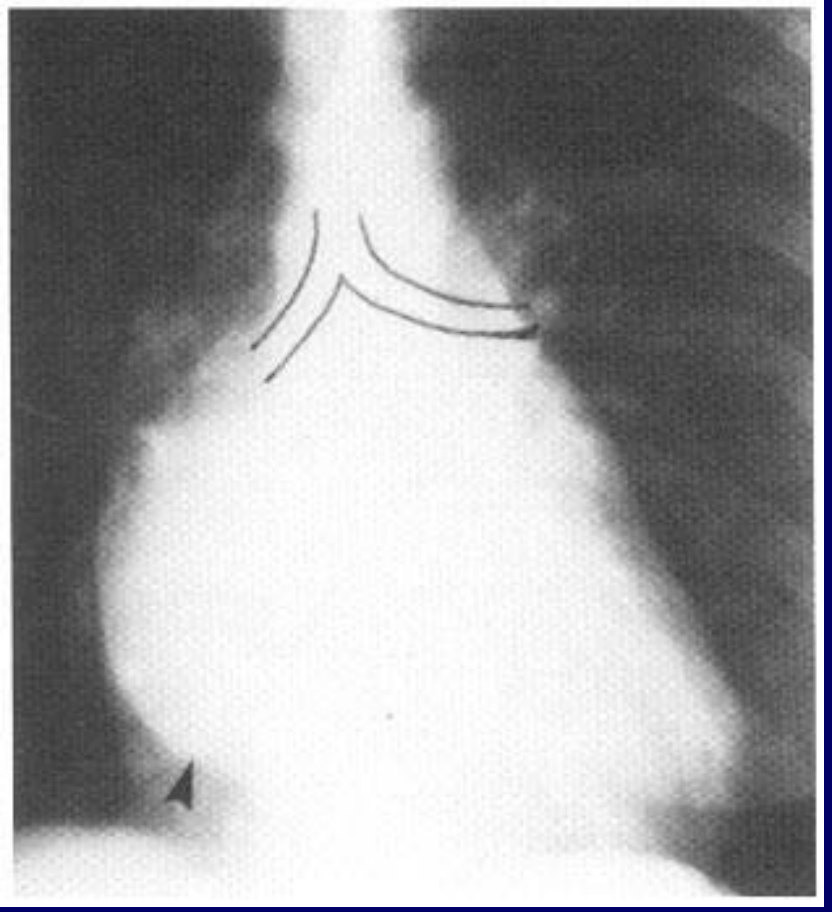
- Complete Blood Count.
- Serum electrolytes, blood urea nitrogen,serum creatinine.
- Liver function test.
- Prothrombin time.
- Lipid profile.
- Thyroid function test.
- Anaemia evaluation.
- Arterial blood gases.
- Serum drug levels(digoxin,phenytoin).
- Atrial natriuretic peptides.
- Urin analysis.

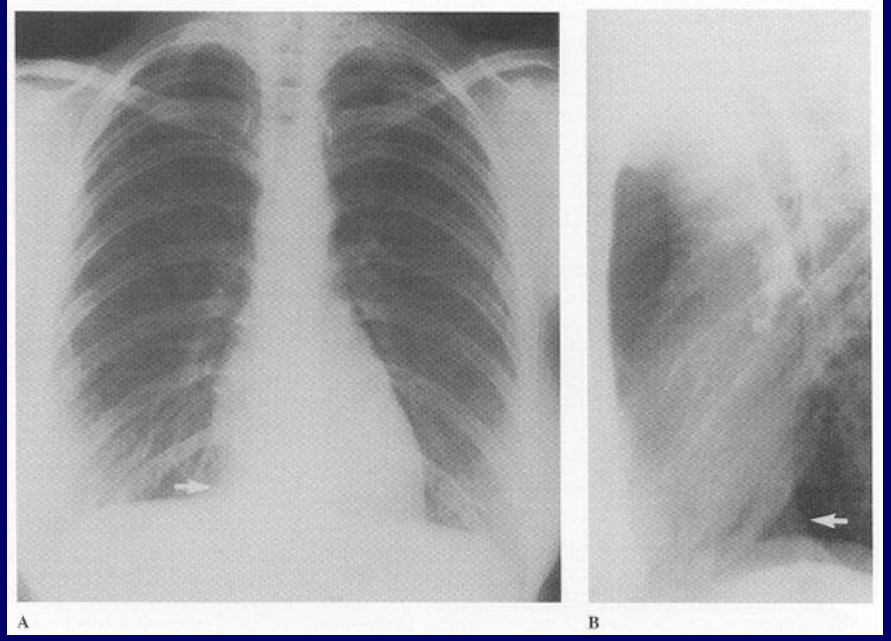
Chest X- ray





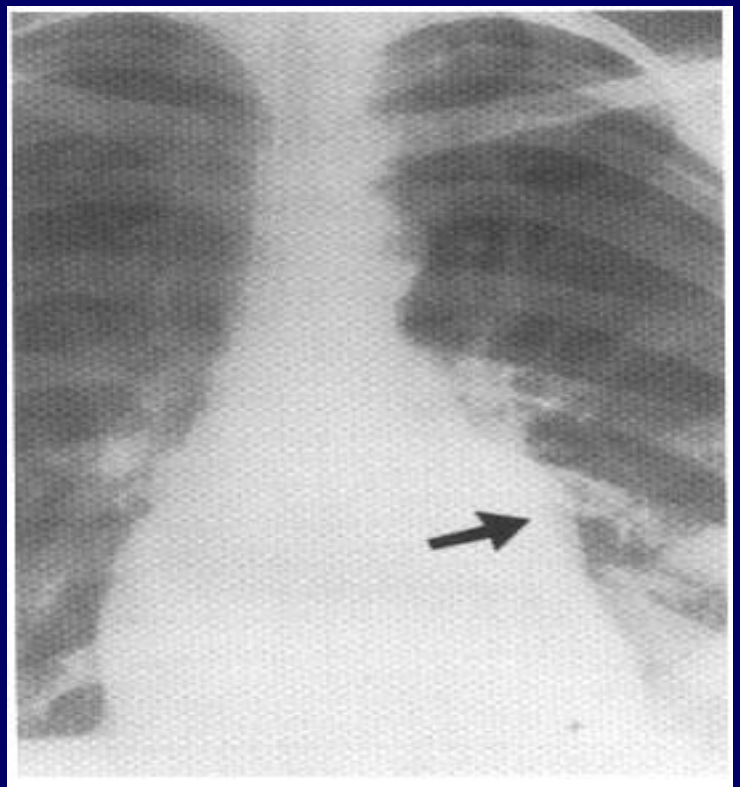
Chest roentgenogram of patient with heart failure. This roentgenogram demonstrates cardiomegaly (cardiothoracic ratio 0.77), pulmonary congestion, and bilateral pleural effusions (note blunted costophrenic angles).



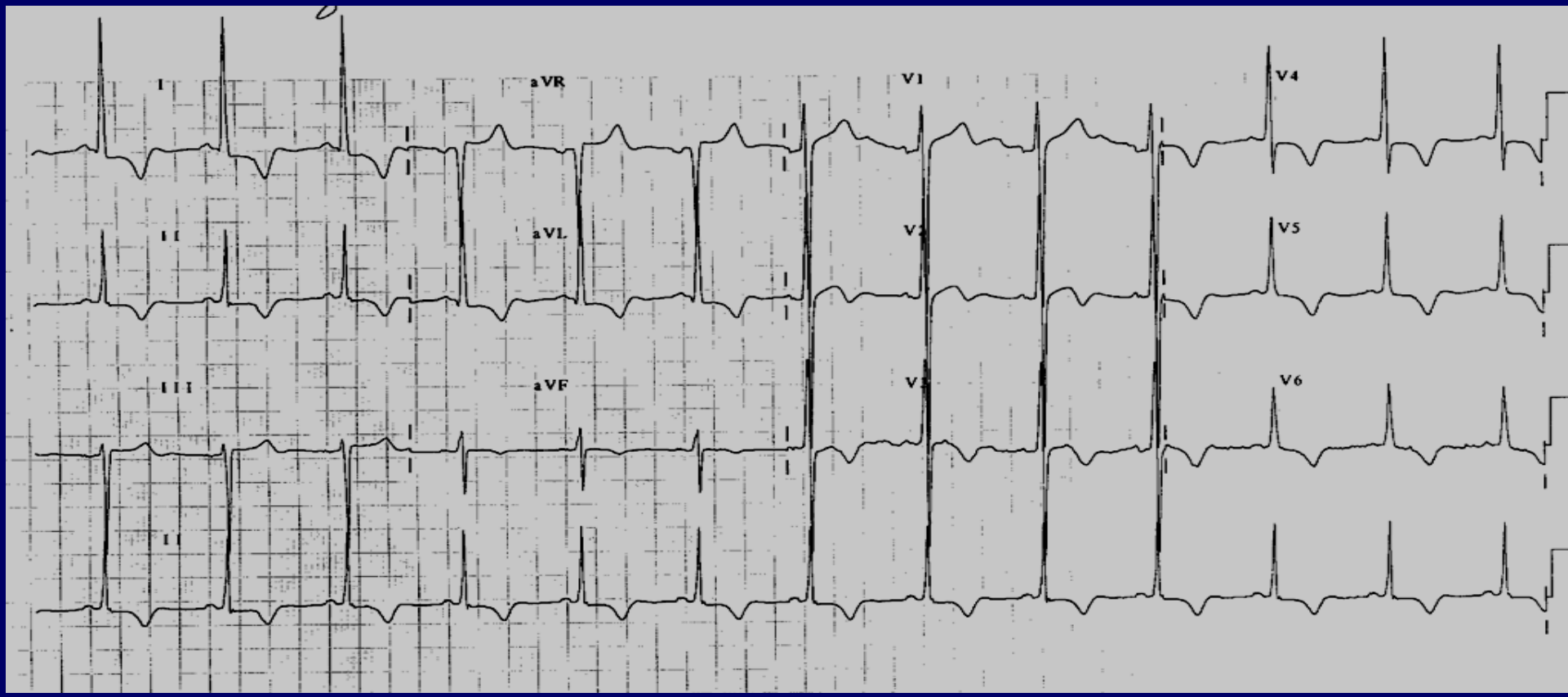


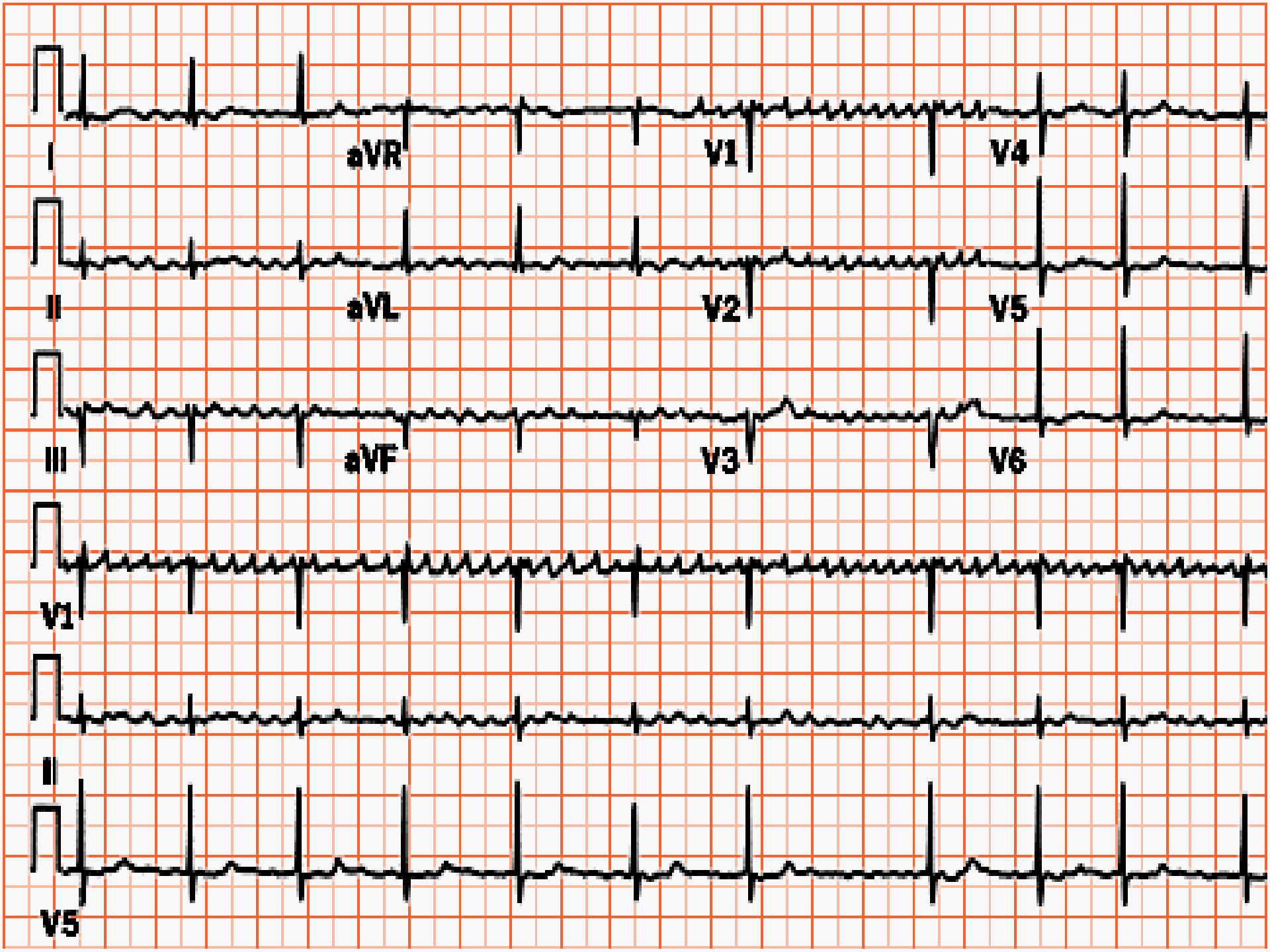
A

B



12-Leads ECG



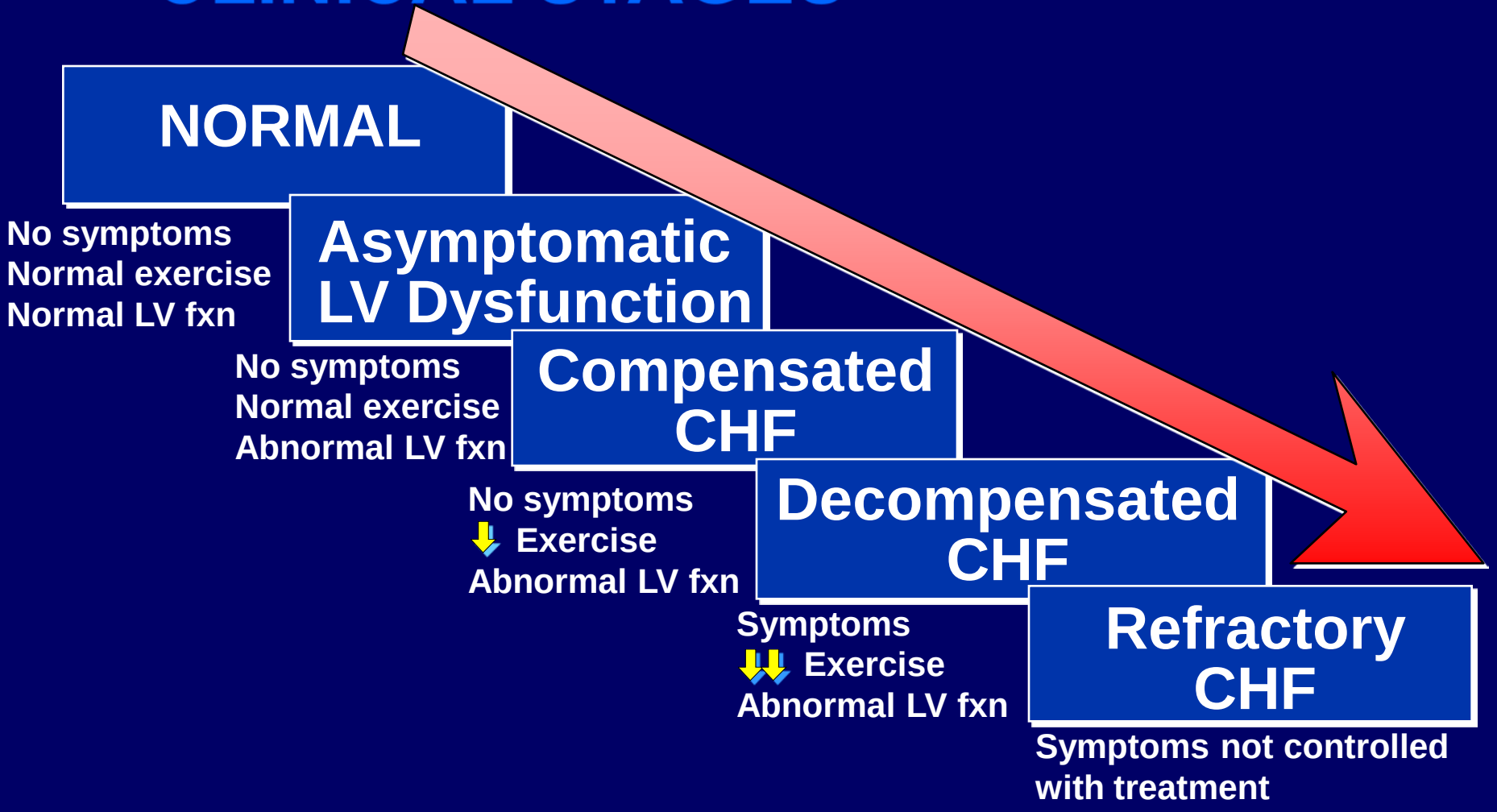

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5

Other investigation

- Transthoracic Echocardiography.
- Stress Echo.
- Exercise stress testing.
- 24- hour Holter monitoring.
- Nuclear imaging,thallium perfusion scan,cardiac MRI.
- Coronary angiography

Chronic Congestive Heart Failure

EVOLUTION OF CLINICAL STAGES



Treatment Options

- Non-pharmacological.

General advice and measures. Exercise and exercice training.Reduce cardiac work. Rest. Weight loss. Low Na diet.

Pharmacological therapy.

Angiotensin-converting enzyme inhibitors(ACI).

Beta-adrenoreceptor antagonists.

Cardiac glycosides.

Diuretics.

Vasodilators(nitrats,hydralazine).

Antiarrhythmic agent.

Anticoagulantion.

Oxyggen.

- Divices and surgery.

Revascularization.

Pacemaker.

Implantable cardioverter defibrillator(ICD).

Cadiac trnsplantation.

Ultrafiltration,haemodialysis.

TREATMENT
Correction of aggravating factors

- Pregnancy
- Arrhythmias (AF)
- Infections
- Hyperthyroidism
- Thromboembolism
- Endocarditis
- Obesity
- Hypertension
- Physical activity
- Dietary excess

- MEDICATIONS

TREATMENT
PHARMACOLOGIC THERAPY

- DIURETICS
- INOTROPES
- VASODILATORS
- NEUROHORMONAL ANTAGONISTS
- OTHERS (Anticoagulants, antiarrhythmics, etc)

TREATMENT

Normal

Asymptomatic
LV dysfunction
EF <40%

ACEI

Symptomatic CHF
NYHA II

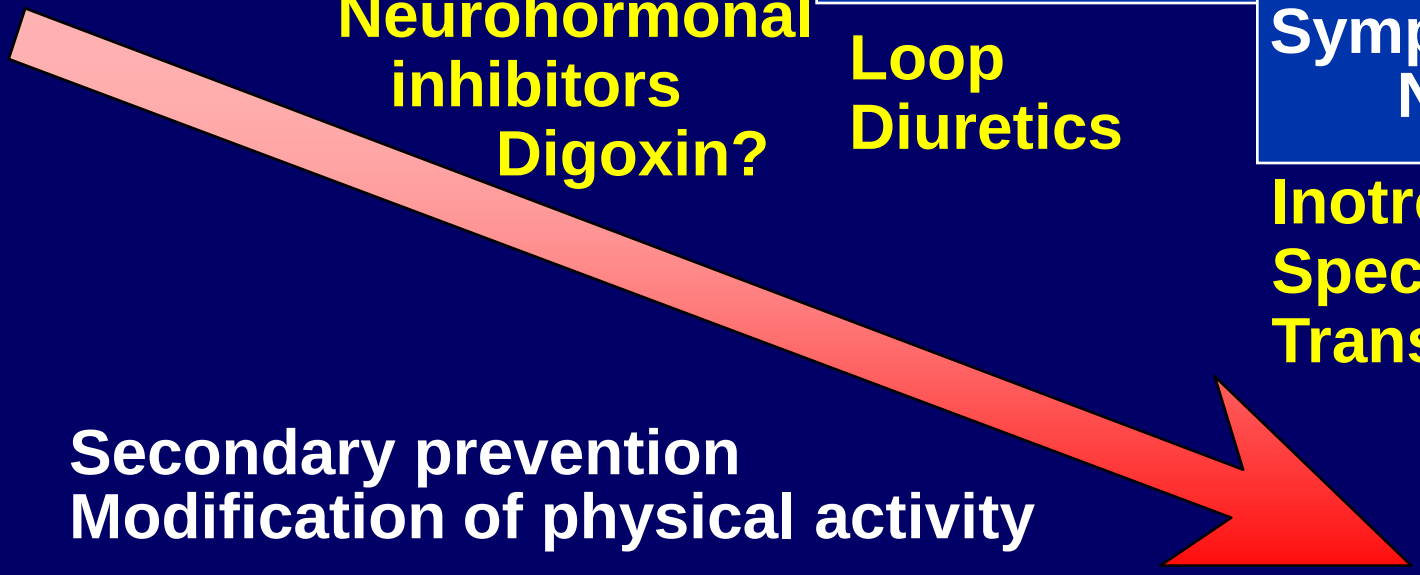
Diuretics mild
Neurohormonal
inhibitors
Digoxin?

Symptomatic CHF
NYHA - III

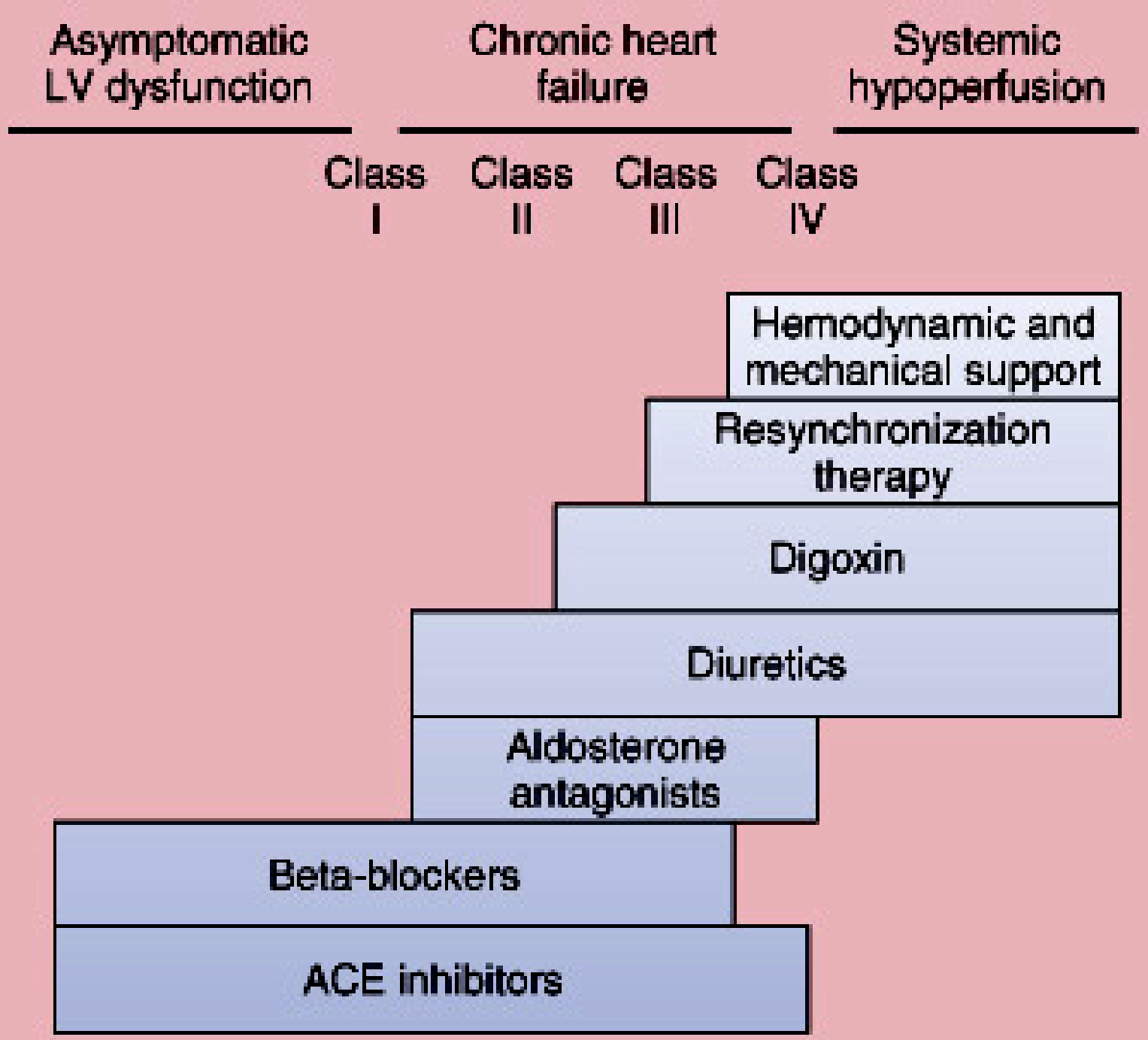
Loop
Diuretics

Symptomatic CHF
NYHA - IV

Inotropes
Specialized therapy
Transplant



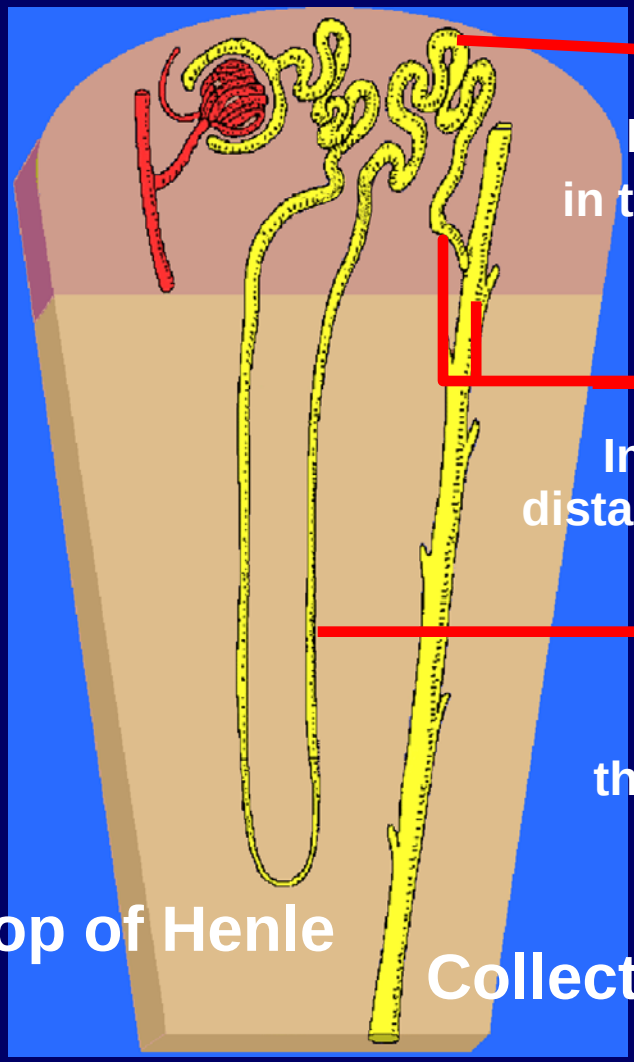
Secondary prevention
Modification of physical activity


Asymptomatic LV dysfunction
Chronic heart failure
Systemic hypoperfusion
Class I
Class II
Class III
Class IV
Hemodynamic and mechanical support
Resynchronization therapy
Digoxin
Diuretics
Aldosterone antagonists
Beta-blockers
ACE inhibitors

DIURETICS

Cortex

Medulla



Thiazides

Inhibit active exchange of Cl-Na in the cortical diluting segment of the ascending loop of Henle

K-sparing

Inhibit reabsorption of Na in the distal convoluted and collecting tubule

Loop diuretics

Inhibit exchange of Cl-Na-K in the thick segment of the ascending loop of Henle

CLINICAL AND PHARMACOLOGIC PROPERTIES OF DIURETICS

Drugs	*Rela-tive poten-cy*	*Site of Action*	*Onset of Action*	*Advantages*	*Adverse Effects*
Thiazide diuretics					
Hydrochlorothiazide Oral: 50-200 mg/day	Mode-rate	Excreted into proximal tu-bule, inhibiti-on of Na and Cl, absorption in distal segment	1-2 h	Mild, relati-vely nontoxic, oral admini-stration, antihyperten-sive	K loss. hyperglycemia, decreases platelets. ineffective when GFR < 20 mL/min. hyperuricemia
Loop diuretics					
Furosemide 40-200 mg 1, 2. or 3 times/day; IV: 40 mg initially; may increase to 200-400 mg, depending on response Torosimide 5-10 mg/d Ethacrynic acid IV: 50 mg initially; may increase, depending on response	High	Inhibition of Cl transport in ascending limb of loop of Henle	Oral: 1 h IV: 10-20 min	Rapid onset, potency, independent of acid-base balance, effective even when GFR is reduced	Excessive diuresis; hypovolemia; K loss and hypokalemia; hyperuricemia; transient or irreversible deafness with IV administration, especially when used with aminoglycoside antibiotic

DIURETICS
ADVERSE REACTIONS
Thiazide and Loop Diuretics

- Changes in electrolytes:
  - ↓ Volume
  - ↓ Na^+, K^+, Ca^{++}, Mg^{++}
  - metabolic alkalosis
- Metabolic changes:
  - ↑ glycemia, uremia, gout
  - ↑ LDL-C and TG
- Cutaneous allergic reactions

POSITIVE INOTROPES

- CARDIAC GLYCOSIDES
- SYMPATHOMIMETICS
  - Catecholamines
  - ß-adrenergic agonists
- PHOSPHODIESTERASE INHIBITORS
  - Amrinone
  - Enoximone
  - Milrinone
  - Piroximone
- Others

DOPAMINE AND DOBUTAMINE EFFECTS

	DA (µg / Kg / min)			Dobutamine
	< 2	2 - 5	> 5	
Receptors	DA_1 / DA_2	$ß_1$	$ß_1$ + α	$ß_1$
Contractility	±	++	++	++
Heart Rate	±	+	++	±
Arterial Press.	±	+	++	++
Renal perfusion	++	+	±	+
Arrhythmia	-	±	++	±

POSITIVE INOTROPES

Agent	Dose and Route	Comment
ADRENERGIC AGONISTS		
Epinephrine	300-500mug SC or IM (0.3-0.5 mL of 1/1000 solution of hydrochloride salt); 25-50 mug IV (slowly) every 5-15 min; titrate as needed	Nonselective alpha and beta agonist; increases BP, heart rate Bronchodilation
Norepinephrine	2-4 mug of NE base/min IV; titrate as needed	Alpha and $beta_1$ agonist Vasoconstriction predominates Extravasation causes tissue necrosis; infuse through IV cannula
Dobutamine	2.5-25 (mug/kg)/min IV	Selective betai agonist with greater effect on contractility than heart rate; a congener of dopamine but not a dopaminergic agonist
DOPAMINERGIC AG ONLSTS		
Dopamine	2-5 (mug/kg)/min IV (dopaminergic range) 5-10 (mug/kg)/min IV (dopaminergic and beta range) 10-20 (mug/kgVmin IV (beta range) 20-50 (mug/kg)/min IV (alpha range)	Pharmacologic effects are dose dependent: renal and mesenteric vasodilation predominate at lower doses; cardiac stimulation and vasoconstriction develop as the dose is increased

POSITIVE INOTROPES
CONCLUSIONS

- May increase mortality
- Safer in lower doses
- Use only in refractory CHF
- NOT for use as chronic therapy

VASODILATORS CLASSIFICATION

VENOUS

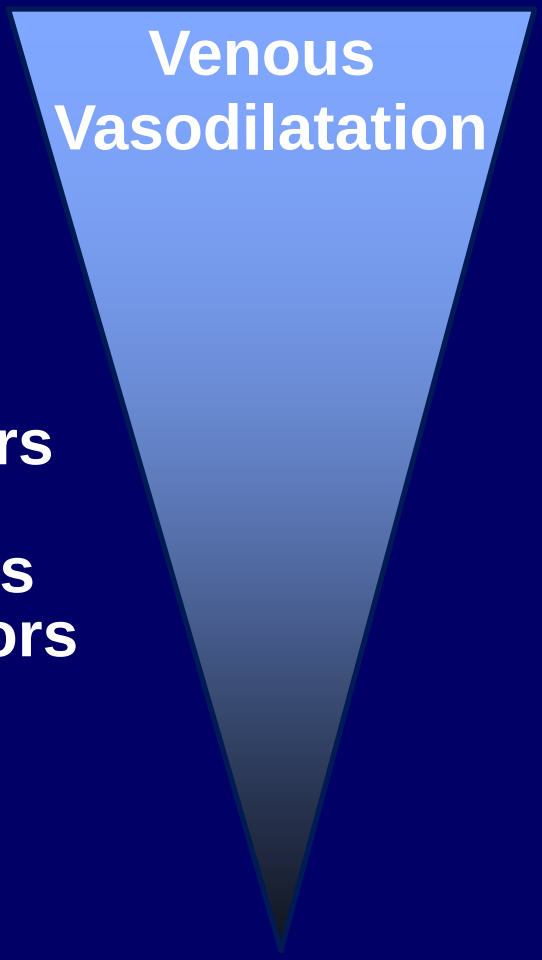
Nitrates
Molsidomine

MIXED

Calcium antagonists
α-adrenergic Blockers
ACEI
Angiotensin II inhibitors
K^+ channel activators
Nitroprusside

ARTERIAL

Minoxidil
Hydralazine



NITRATES
HEMODYNAMIC EFFECTS

1- VENOUS VASODILATATION

↓ Preload →

- ↓ Pulmonary congestion
- ↓ Ventricular size
- ↓ Vent. Wall stress
- ↓ MVO_2

2- Coronary vasodilatation

↑ Myocardial perfusion

3- Arterial vasodilatation

↓ Afterload →

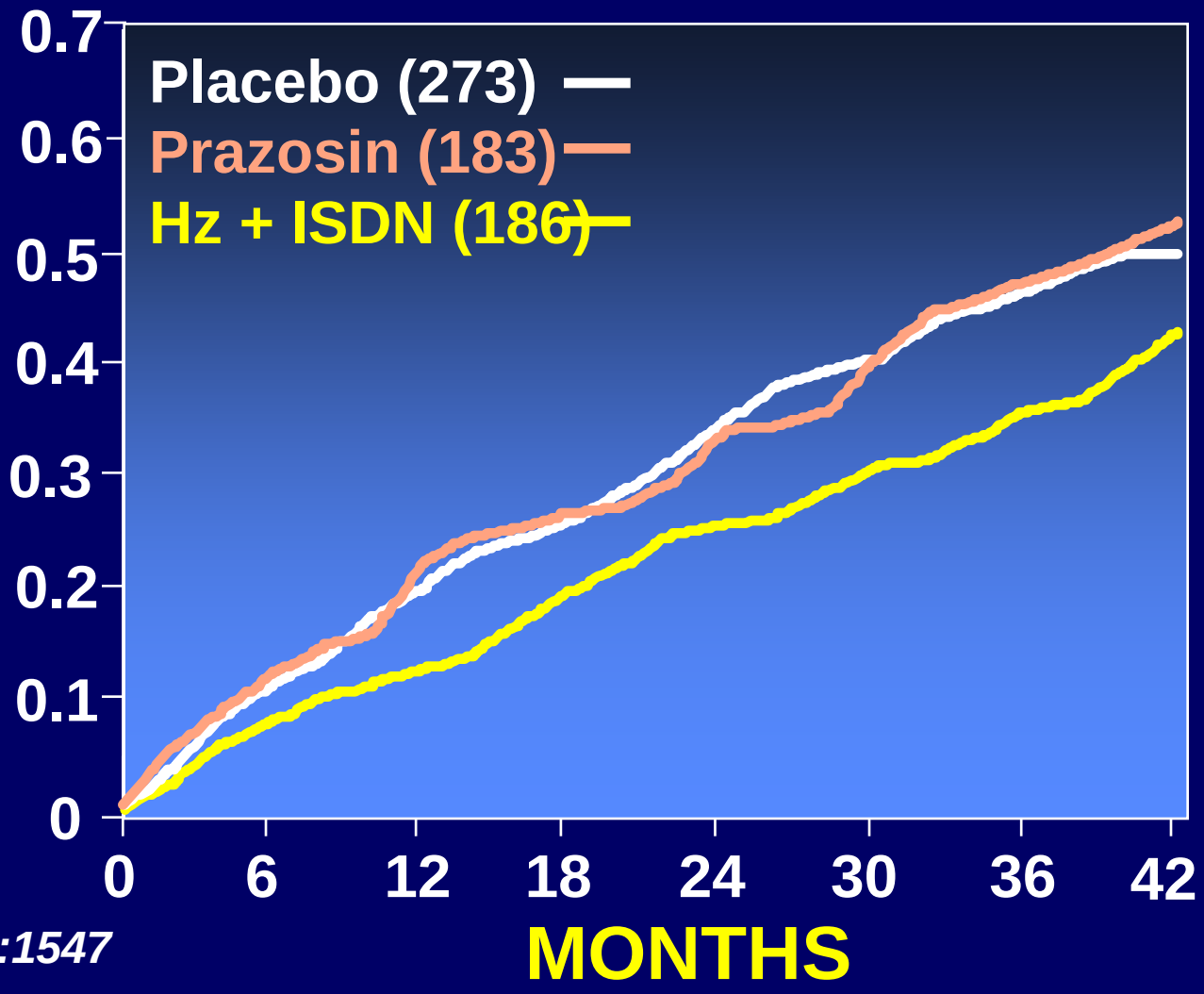
- ↓ Cardiac output
- ↓ Blood pressure

4- Others

CLINICAL AND PHARMACOLOGIC PROPERTIES OF VASODILATORS

Classi-fication	*Drugs*	*Site of Action*	*Onset of Action*	*Advantages*	*Adverse Effects*
Nitrates	Nitrogtycerin Sublingual: 0.4 mg pm Spray: 0.4 mg pm IV: 10-100 µg/min Isosorbide dinitrate Sublingual:2.5-10mg q 2-4 h Oral: 20-60 mg q 4-6 h	Nitrate receptor	Immediate Immediate Immediate 30-60 min 30-60 min 2-5 min 20-40 min	Rapid onset; various routes of admnistra-tion; good for emergencies	Headache; hypotension; methemoglobinemia; tolerance if not given intermittently
Arterial vasodi-lators	Hydralazine Oral: 25-100 mg q 6 h Minoxidil Oral: 25-40 mg twice daily Diazoxid IV: 1-3 mg/kg up to 150 mg rapidly Nitroprusside 10-500 (µg/min)	Smooth muscle	30-45 min Immediately	Specific arteriolar vasodilator Dilates arteries and veins	Tachycardia; lupus phenomenon; long-term benefit requires nitrates Hypotension; thiocyanate accumulation Tachycardia; aggravates angine; marked fluid retensiot; hair growth on face and body, coarsening of facial features Hyperglycemia, hyperuricemia, sodium retension Cianide toxicity

NITRATES SURVIVAL



PROBABILITY OF DEATH

VHefT-1

N Engl J Med 1986;314:1547

NITRATES
TOLERANCE

" Decrease in the effect of a drug when administered in a long-acting form"

- **Develops with all nitrates**
- **Is dose-dependent**
- **Disappears in 24 h. after stopping the drug**
- **Tolerance can be avoided**
  - **Using the least effective dose**
  - **Creating discontinuous plasma levels**

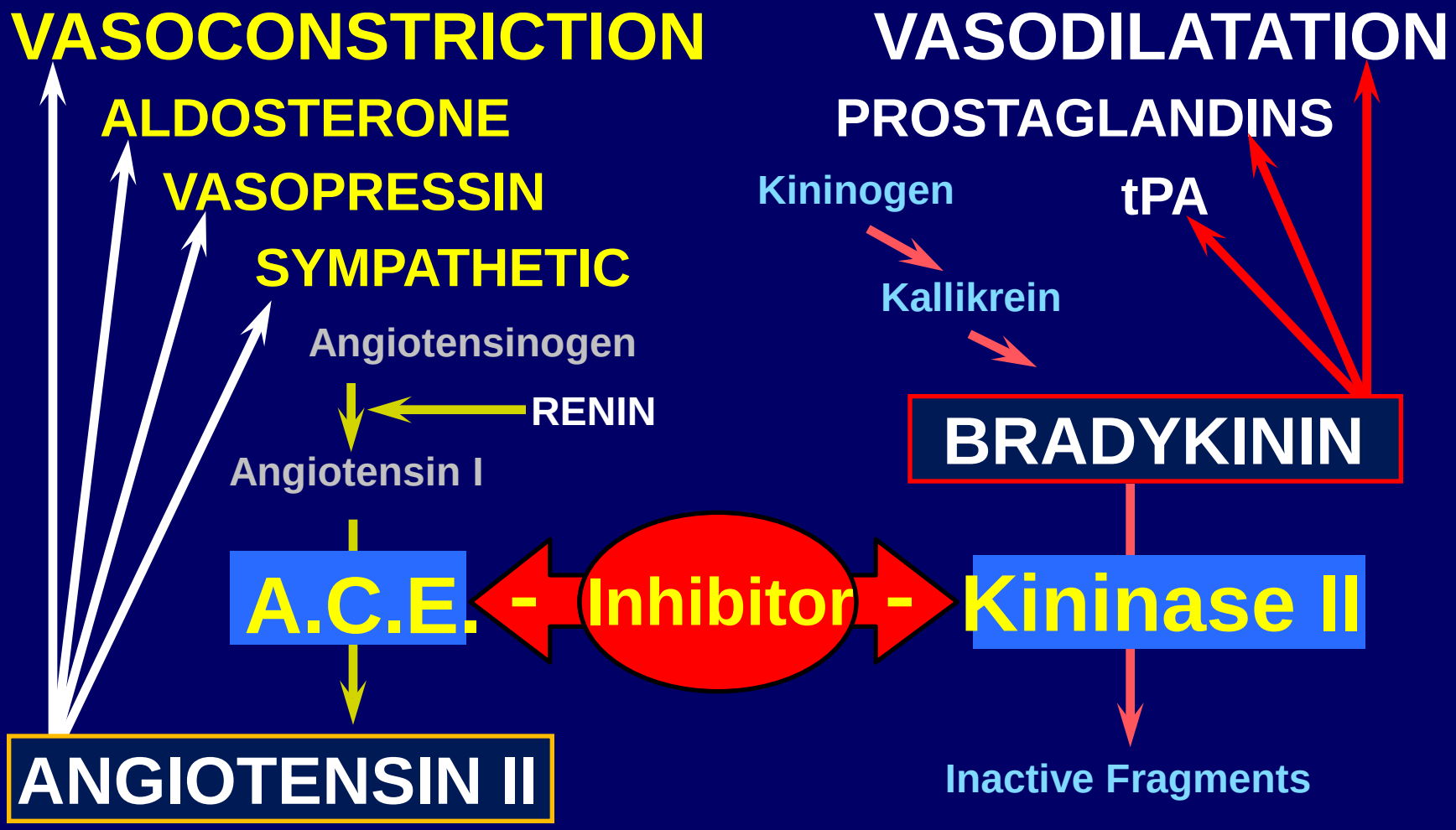
NITRATES
CONTRAINDICATIONS

- Previous hypersensitivity
- Hypotension (< 80 mmHg)
- AMI with low ventricular filling pressure
- 1st trimester of pregnancy

WITH CAUTION:

- Constrictive pericarditis
- Intracranial hypertension
- Hypertrophic cardiomyopathy

ACE-Inhibitors
MECHANISM OF ACTION

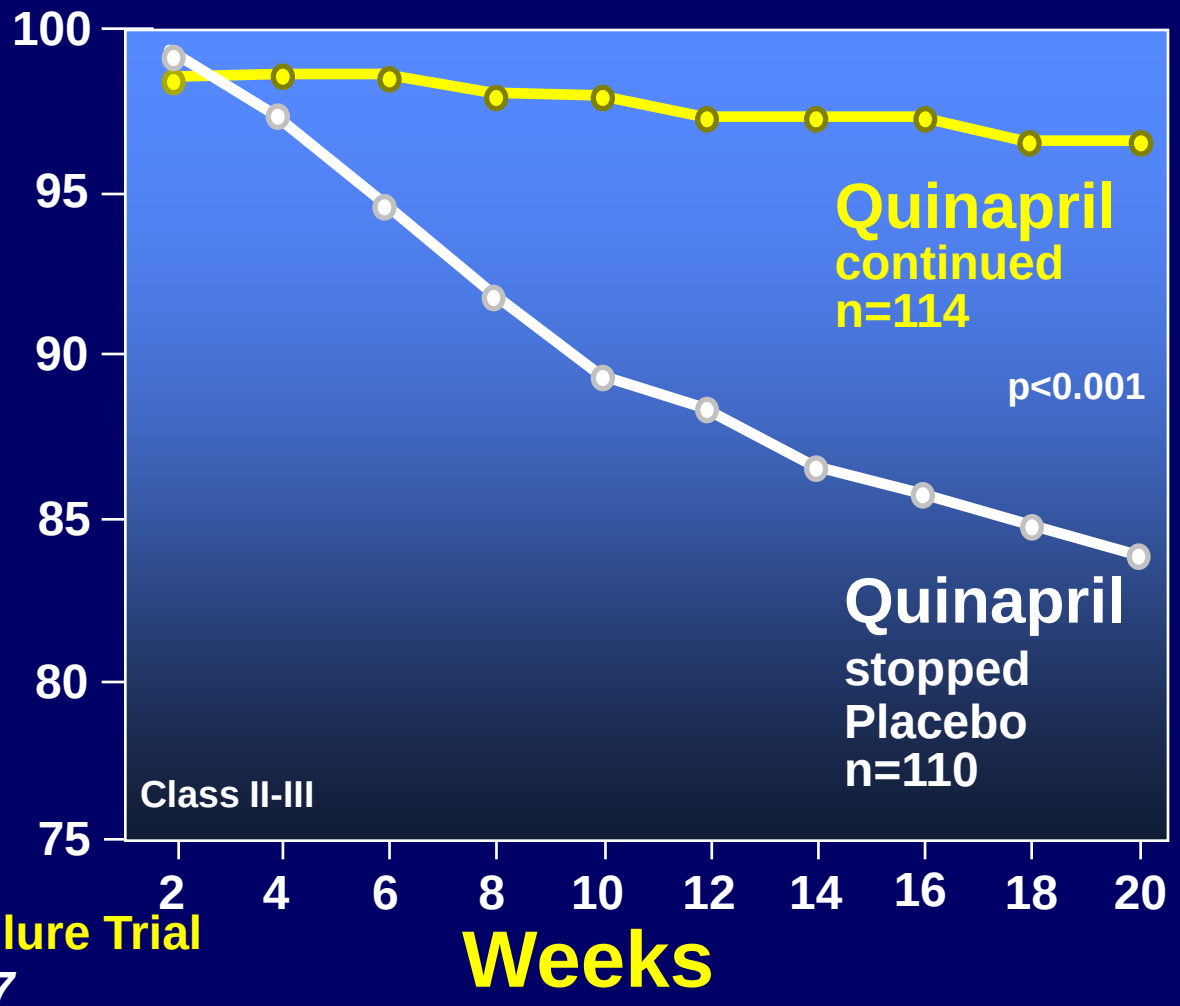


ACEI
HEMODYNAMIC EFFECTS

- Arteriovenous Vasodilatation
  - ↓ PAD, PCWP and LVEDP
  - ↓ SVR and BP
  - ↑ CO and exercise tolerance
- No change in HR / contractility
- ↓ MVO_2
- ↑ Renal, coronary and cerebral flow
- Diuresis and natriuresis

ACEI
FUNCTIONAL CAPACITY

No Additional Treatment Necessary (%)



Quinapril Heart Failure Trial
JACC 1993;22:1557

ACEI
INDICATIONS

- **Clinical cardiac insufficiency**
  - **All patients**
- **Asymptomatic ventricular dysfunction**
  - **LVEF < 35 %**

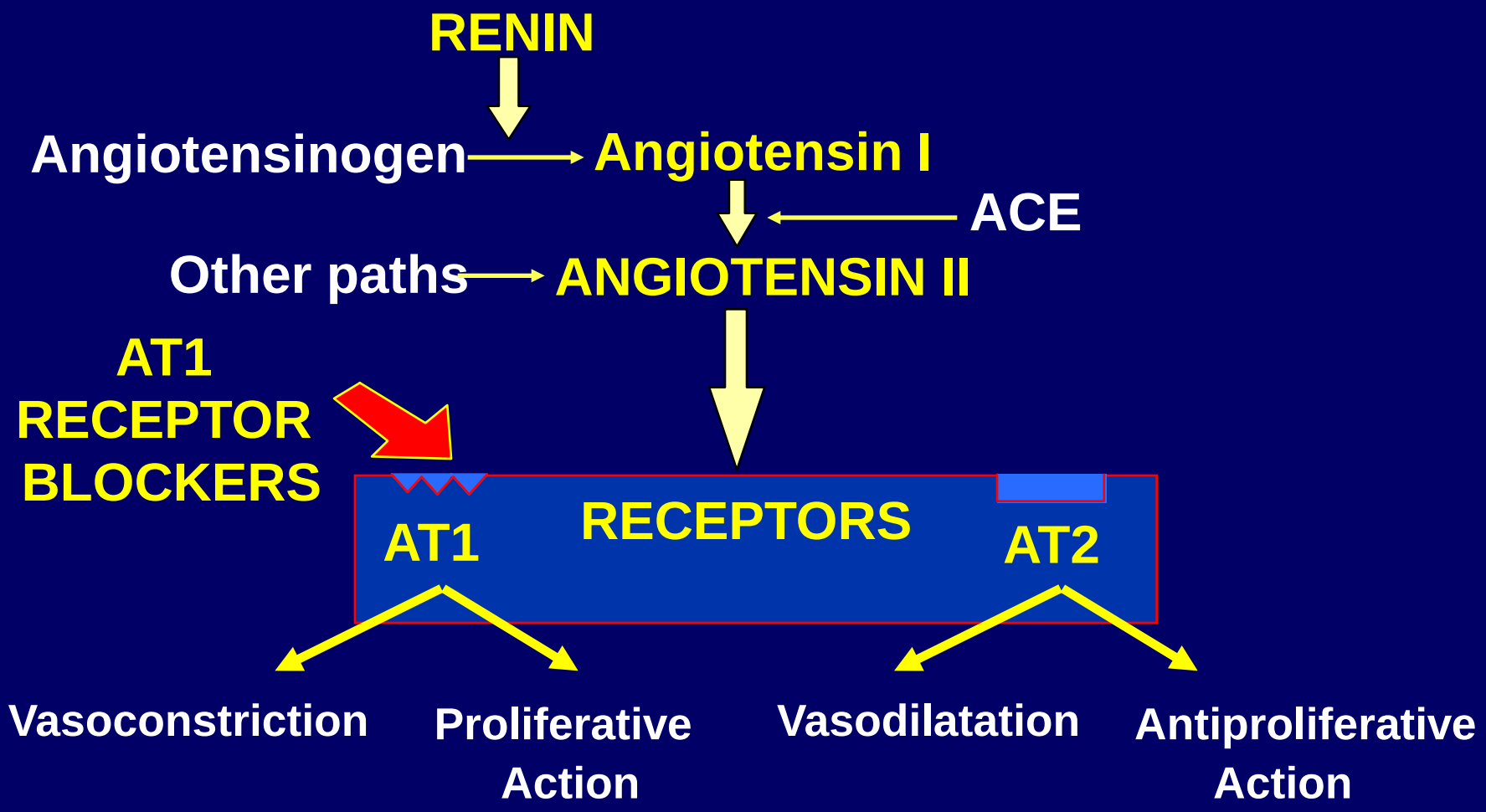
ACEI
UNDESIRABLE EFFECTS

- **Inherent in their mechanism of action**
  - Hypotension
  - Hyperkalemia
  - Angioneurotic edema
  - Dry cough
  - Renal Insuff.
- **Due to their chemical structure**
  - Cutaneous eruptions
  - Neutropenia, thrombocytopenia
  - Digestive upset
  - Dysgeusia
  - Proteinuria

ACEI
CONTRAINDICATIONS

- Renal artery stenosis
- Renal insufficiency
- Hyperkalemia
- Arterial hypotension
- Intolerance (due to side effects)

ANGIOTENSIN II INHIBITORS
MECHANISM OF ACTION



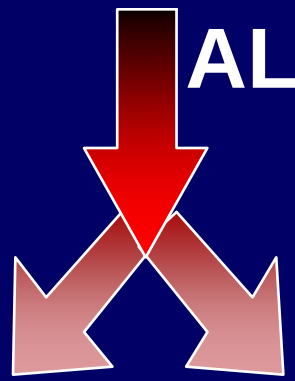
AT1 RECEPTOR BLOCKERS DRUGS

- Losartan
- Valsartan
- Irbersartan
- Candersartan

Competitive and selective blocking of AT1 receptors

ALDOSTERONE INHIBITORS

Spironolactone



Competitive antagonist of the aldosterone receptor (myocardium, arterial walls, kidney)

- Retention Na^+
- Retention H_2O

→ Edema

- Excretion K^+
- Excretion Mg^{2+}

→ Arrhythmias

- Collagen deposition

→ Fibrosis

- myocardium
- vessels

CLINICAL AND PHARMACOLOGIC PROPERTIES OF VASODILATORS

Classifi-cation	***Drugs***	***Site of Action***	***Onset of Action***	***Advantages***	***Adverse Effects***
Inhibitors of Angiotensin converting enzyme (ACE)	Captopril 6.25 mg bid. up to 200 mg/d Enalapril 2.5-40 mg/d Lisinopril 5-40 mg/d Quinapril 10-80 mg/d Ramipril 2.5-20 mg/d Quinapril 10-30 mg bid; Fosinopril 5-30 mg qd;	Angiotensin converting enzyme (ACE) [inhibition of]	60-90 min 60 min 60 min 60-90 min 60-90 min	Proven symptomatic relief and improved survival	Impaired renal function; proteinuria; dysgeusia; glomerulonephritis; leukopenia; cough Contraindications: pregnancy, bilateral renal artery stenosis
Angiotensine receptor antagonists	Losartan 25-50 mg once or twice daily Irbesartan 5-10 mg once or twice daily		2-4 h 60-90 min	Proven symptomatic relief and improved survival	Hypotension, ocute renal failure in bilateral renal artery stenosis, hyperkalemia Contraindications: pregnancy, bilateral renal artery stenosis

ALDOSTERONE INHIBITORS INDICATIONS

FOR DIURETIC EFFECT

- Pulmonary congestion (dyspnea)
- Systemic congestion (edema)

FOR ELECTROLYTE EFFECTS

- Hypo K^+, Hypo Mg^+
- Arrhythmias
- Better than K^+ supplements

FOR NEUROHORMONAL EFFECTS

- ? Pending the RALES results

CLINICAL AND PHARMACOLOGIC PROPERTIES OF DIURETICS

Drugs	*Relative Potency*	*Site of Action*	*Onset of Action*	*Advantages*	*Adverse Effects*
Potassium-sparing diuretics					
Spironolactone Oral: 25-50 mg bid to qid	Moderate to low	Aldosterone homolog, competitive inhibition for receptor site in distal tubule. Secondary: inhibition of aldosterone biosynthesis	2-3 days for maximum effect	Useful in combination with more proximal-acting diuretic to spare K	Hyperkalemia when K salts are given concomitantly or renal function is reduced markedly

ALDOSTERONE INHIBITORS CONTRAINDICATIONS

- Hyperkalemia
- Severe renal insufficiency
- Metabolic acidosis

ß-ADRENERGIC BLOCKERS
POSSIBLE BENEFICIAL EFFECTS

- ↑ Density of $ß_1$ receptors
- Inhibit cardiotoxicity of catecholamines
- ↓ Neurohormonal activation
- ↓ HR
- Antihypertensive and antianginal
- Antiarrhythmic
- Antioxidant
- Antiproliferative

BETA-ADRENERGIC RECEPTOR BLOCKERS

Drugs	Site of Action	Precautions and special considerations	Side effects
Carvedilol 3.125 mg bid; titrate to target dose 25 mg bid.	Noncardioselective β- and α1-adrenergic receptor block, without ISA	Should not be used in patients with asthma, chronic obstructive pulmonary disease (COPD) with bronchospasm, congestive heart.failufe, heart block (greater than first degree), sick sinus syndrome. Use with caution in insulin-dependent diabetics and patients with peripheral vascular disease. Should not be discontinued abruptly in patients with ischemic heart disease.	Bronchospasm, peripheral arterial insufficiency, fatigue, insomnia, sexual dysfunction, exacerbation of congestive heart failure, may mask symptoms of hypoglycemia; hyperglycemia; hypertriglyceridemia, decreased high-density lipoprotein (HDL) cholesterol (except for drugs with ISA and labetalol)
Bisoprolol 1.25 mg bid; titrate to target dose 10 mg bid.	Noncardioselective, without ISA		
Metoprolol tartrate 6.25 mg bid; titrate to target dose 50 mg bid.	Cardioselective, without ISA		
Metoprolol succinate (extended release) 12.5- 25 mg bid; titrate to target dose 200 mg bid.	Cardioselective, without ISA		

ISA = intrinsic sympathomimetic activity.

ß-ADRENERGIC BLOCKERS
IDEAL CANDIDATE?

- Suspected adrenergic activation
- Arrhythmias
- Hypertension
- Angina

ß-ADRENERGIC BLOCKERS CONTRAINDICATIONS

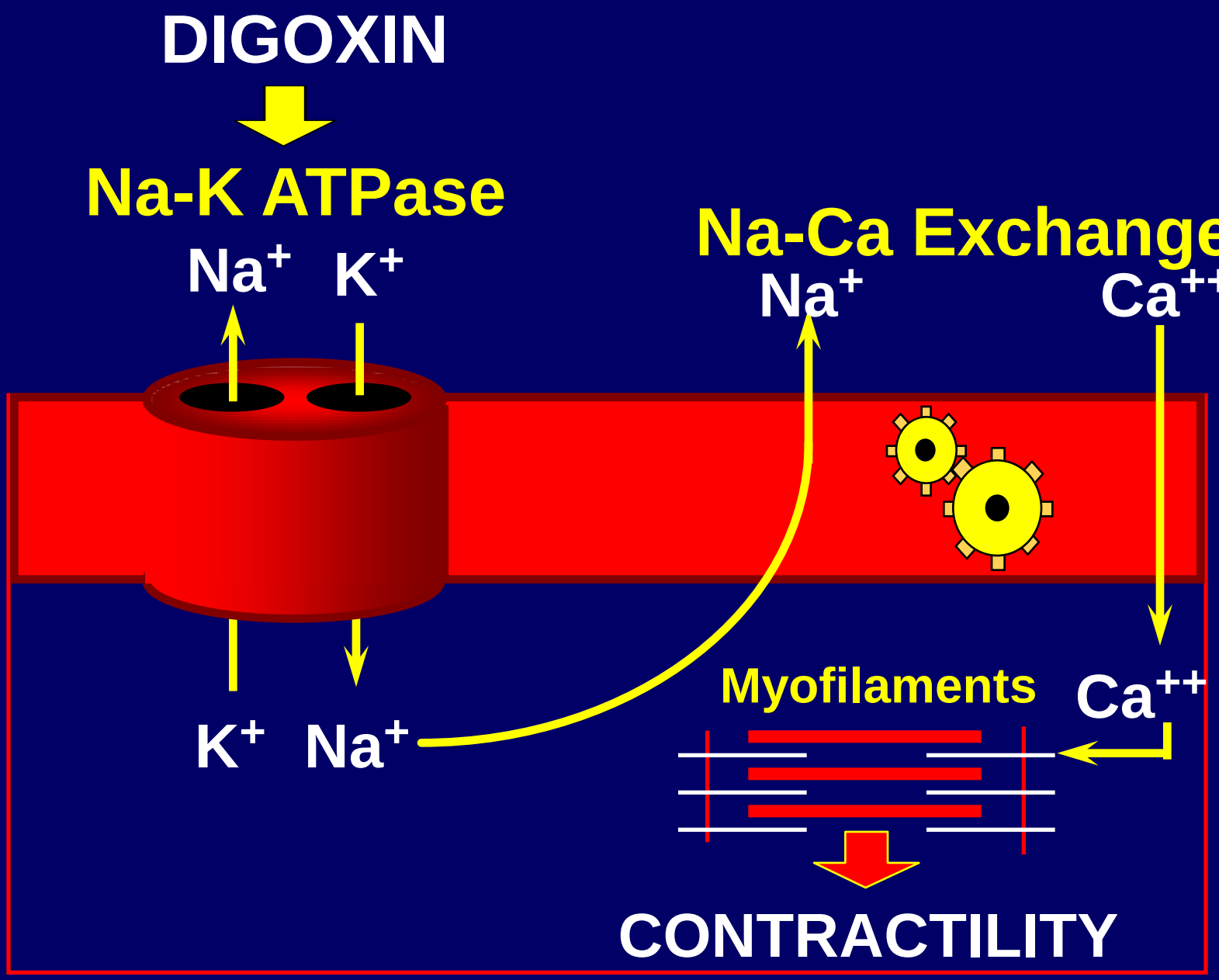
- Hypotension: BP < 100 mmHg
- Bradycardia: HR < 50 bpm
- Clinical instability
- Chronic bronchitis, ASTHMA
- Severe chronic renal insufficiency

CALCIUM ANTAGONISTS POTENTIAL EFFECTS

- Antiischemic
- Peripheral Vasodilatation
- ⬇ Inotropy

CALCIUM ANTAGONISTS
POSSIBLE UTILITY

- Diltiazem contraindicated
- Verapamil and Nifedipine not recommended
- Vasoselective (amlodipine, nisoldipine), may be useful in ischemia + CHF
- Amlodipine may be useful in nonischemic CHF


DIGOXIN
Na-K ATPase
Na+ K+
Na-Ca Exchange
Na+ Ca++
K+ Na+
Myofilaments
Ca++
CONTRACTILITY

DIGOXIN
PHARMACOKINETIC PROPERTIES

Oral absorption (%)	60 - 75
Protein binding (%)	25
Volume of distribution (l/Kg)	6 (3-9)
Half life	36 (26-46) h
Elimination	Renal
Onset (min)	
i.v.	5 - 30
oral	30 - 90
Maximal effect (h)	
i.v.	2 - 4
oral	3 - 6
Duration	2 - 6 days
Therapeutic level (ng/ml)	0.5 - 2

DIGOXIN
DIGITALIZATION STRATEGIES

Loading dose (mg)			Maintenance Dose
i.v	oral 12-24 h	oral 2-5 d	(mg)
0.5 + 0.25 / 4 h ILD: 0.75-1	0.75 + 0.25 / 6 h 1.25-1.5	0.25 / 6-12 h 1.5-1.75	0.125-0.5 / d 0.25 / d

ILD = average INITIAL dose required for digoxin loading

DIGITALIZATION SCHEDULE[+]

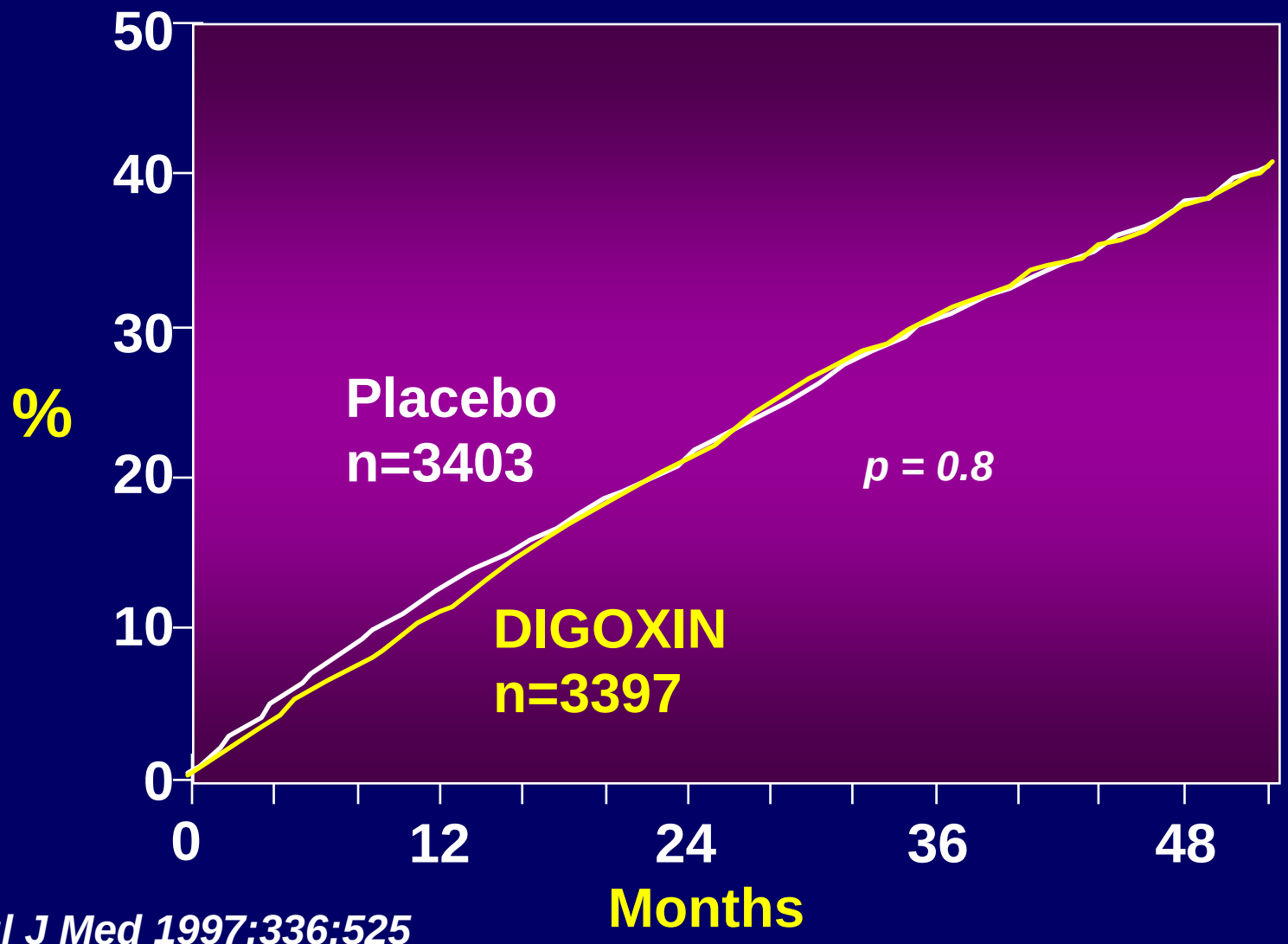
	Digoxin	*Digitoxin*	*Ouabain*
Oral. 24 h	0 h: 0.5 mg 8 h: 0.25 mg 16 h: 0.25 mg 24 h: 0.25 mg Thereafter, daily maintenance dose[++]	0 h: 0.6 mg 8 h: 0.3 mg 16 h: 0.2 mg 24 h: 0.1 mg Thereafter, daily maintenance dose	
Oral. 48 h	0.25 mg q 8 h x 6 Thereafter, daily maintenance dose[++]	0.2 mg q 8 h x 6 Thereafter, daily maintenance dose	
Oral, gradual	0.25 mg/day (digitalization achieved in 5-7 days)[++]	0.1 mg/day (digitalization achieved in 10-14 days)	
IV. 24 h	0 h: 0.5 mg 6 h: 0.25 mg 12 h: 0.125 mg 18 h: 0.125 mg Thereafter, daily maintenance dose[++]	0 h: 0.6 mg 8 h: 0.3 mg 16 h: 0.2 mg 24 h: 0.1 mg Thereafter, daily maintenance dose	0 h: 0.3 mg 4 h: 0.2 mg 8 h: 0.1 mg 12 h: 0.1 mg[++]
Daily maintenance dose, oral	0.25-0.375 mg/day	0.1 mg 5 times/wk to 1.5 mg/day	

[+] Doses are designed to produce effective but prudent plasma and tissue concentrations (see text for details).
[++] Abnormal renal function prolongs plasma half-life, necessitating *reduction* in suggested dosage.*Digoxin**Digitoxin**Ouabain*Preferred route*Oral. IV

DIGOXIN
HEMODYNAMIC EFFECTS

- ↑ Cardiac output
- ↑ LV ejection fraction
- ↓ LVEDP
- ↑ Exercise tolerance
- ↑ Natriuresis
- ↓ Neurohormonal activation

OVERALL MORTALITY



DIG

N Engl J Med 1997;336:525

DIGOXIN
LONG TERM EFFECTS

- Survival similar to placebo
- Fewer hospital admissions
- More serious arrhythmias
- More myocardial infarctions

DIGOXIN
CLINICAL USES

- **AF with rapid ventricular response**
- **CHF refractory to other drugs**
- **Other indications?**
- **Can be combined with other drugs**

DIGOXIN CONTRAINDICATIONS

- **ABSOLUTE:**
  - Digoxin toxicity
- **RELATIVE**
  - Advanced A-V block without pacemaker
  - Bradycardia or sick sinus without PM
  - PVC’s and TV
  - Marked hypokalemia
  - W-P-W with atrial fibrillation

DIGOXIN TOXICITY
CARDIAC MANIFESTATIONS

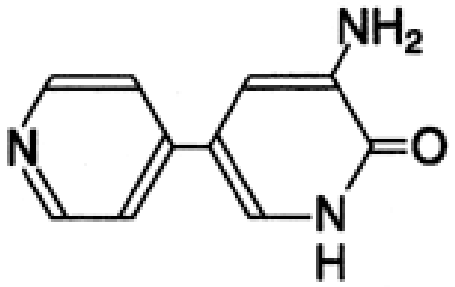
- **ARRHYTHMIAS :**
  - Ventricular (PVCs, TV, VF)
  - Supraventricular (PACs, SVT)
- **BLOCKS:**
  - S-A and A-V blocks
- **CHF EXACERBATION**

TREATMENT OF DIGITALIS INTOXICATION

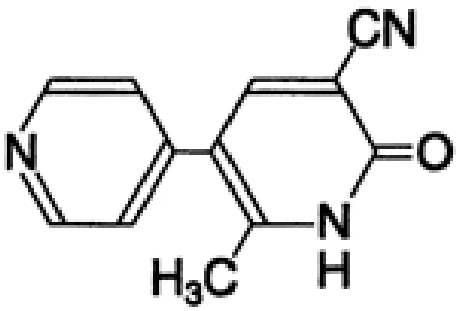
- Discontinue the drug
- ECG monitoring
- If serum K is low, 80 mEq of potassium chloride IV should be given in 1 L 5% D/W at a rate of 6 mL/min (0.5 mEq/min). *Potassium must not be employed in the presence of atrioventricular block or hyperkalemia*
- Administration of specific antibody fragments to digoxin (digoxin immune fab, Digibind®)
- Ventricular arrhythmias are treated with a 50- to 100-mg rapid IV injection of lidocaine, repeated in 3 to 5 min until a therapeutic effect is obtained, a total of 300 mg is given, or CNS toxicity occurs. When the arrhythmia is controlled, a continuous infusion of 2 to 4 mg/min should be started
- Alternatively, phenytoin 100 mg q 3 to 5 min can be given slowly up to a total of 1000 mg
- Heart block is best treated with a temporary perivenous pacemaker
- Electrical conversion may be lifesaving in digitalis-induced ventricular fibrillation
- Isoproterenol is *contraindicated* in digitalis intoxication because of the increased tendency to ventricular arrhythmia

Phosphodiesterase Inhibitors

- primarily used for management of acute heart failure
- positive inotropic effects
- increase rate of myocardial relaxation
- decrease total peripheral resistance and afterload



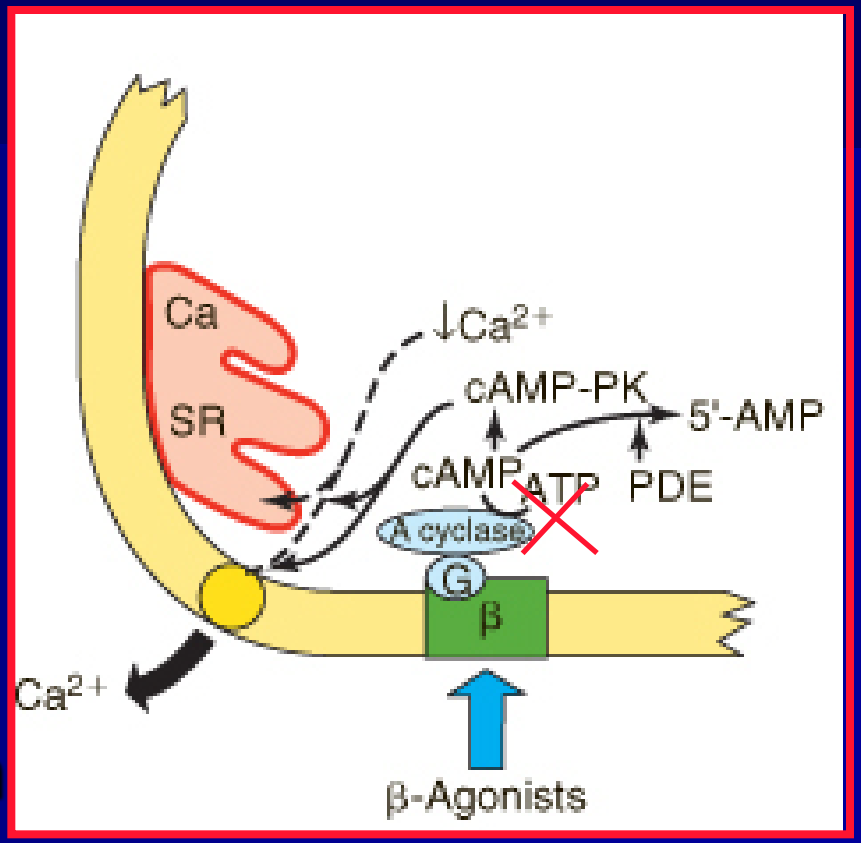
amrinone



milrinone

Mechanism of Action

- inhibitor of type III cAMP phosphodiesterase
- increased [cAMP]
- increased PKA phosphorylation of Ca2+ channels in cardiac muscle
- increased cardiac contraction
- relaxes vascular smooth muscle



Therapeutic Use

- Amrinone (Inocor) and Milrinone (Primacor)
- administered IV
- milrinone is ~1o fold more potent
- T 1/2 = 2.5 h for amrinone and 30-60 min for milrinone
- effective in patients taking Beta-blockers
- does not stop disease progression or prolong life in CHF patients
- prescribed to patients non-responsive to other therapies

Side Effects

- sudden death secondary to ventricular arrhythmia
- hypotension
- thrombocytopenia
- long term clinical trials associated with increased adverse effects and increased mortality
- now only prescribed for acute cardiac decompensation in patients non-responsive to diuretics or digoxin

ANTICOAGULANTS

- PREVIOUS EMBOLIC EPISODE
- ATRIAL FIBRILLATION
- Identified thrombus
- LV Aneurysm (3-6 mo post MI)
- Class III-IV in the presence of:
  - EF < 30
  - Aneurysm or very dilated LV
- Phlebitis
- Prolonged bed rest

ANTIARRHYTHMICS

- Sustained VT, with/without symptoms
  - ß Blockers
  - Amiodarone
- Sudden death from VF
  - Consider implantable defibrillator

Risk factors for increased mortality in heart failure include all of the following,except:

1. Anaemia (Hgb 8.0 g/dl).
2. Sleep apnea.
3. Chronic renal insufficiency.
4. Elevated BNP level.
5. Sustained VT.

Indications for anticoagulation with warfarin in heart failure patients include:

1. AF with controlled ventricular response.
2. LV thrombus.
3. Protein C or protein S deficiency.
4. Previous cardioembolic stroke.
5. All of the above.

EMERGENCY THERAPEUTIC MEASURES IN PATIENTS WITH PULMONARY EDEMA

- Morphine is administered intravenously repetitively, as needed, in doses from 2 to 5 mg
- 100% oxygen should be administered, preferably under positive pressure
- The patient should be maintained in the sitting position, with the legs dangling along the side of the bed
- Intravenous loop diuretics, such as furosemide or ethacrynic acid (40 to 100 mg), or bumetanide (1 mg)
- Intravenous sodium nitroprusside at 20 to 30 ug/min in patients whose systolic arterial pressures exceed 100 mmHg
- Inotropic support should be provided by dopamine or dobutamine
- Patients with systolic heart failure who are not receiving digitalis should receive 1.0 mg digoxin intravenously
- Aminophylline (theophylline ethylenediamine), 240 to 480 mg intravenously
- Rotating tourniquets should be applied to the extremities


THANK
YOU