Revision
Practical Pharmacology

DR/ Amany Atia Ali

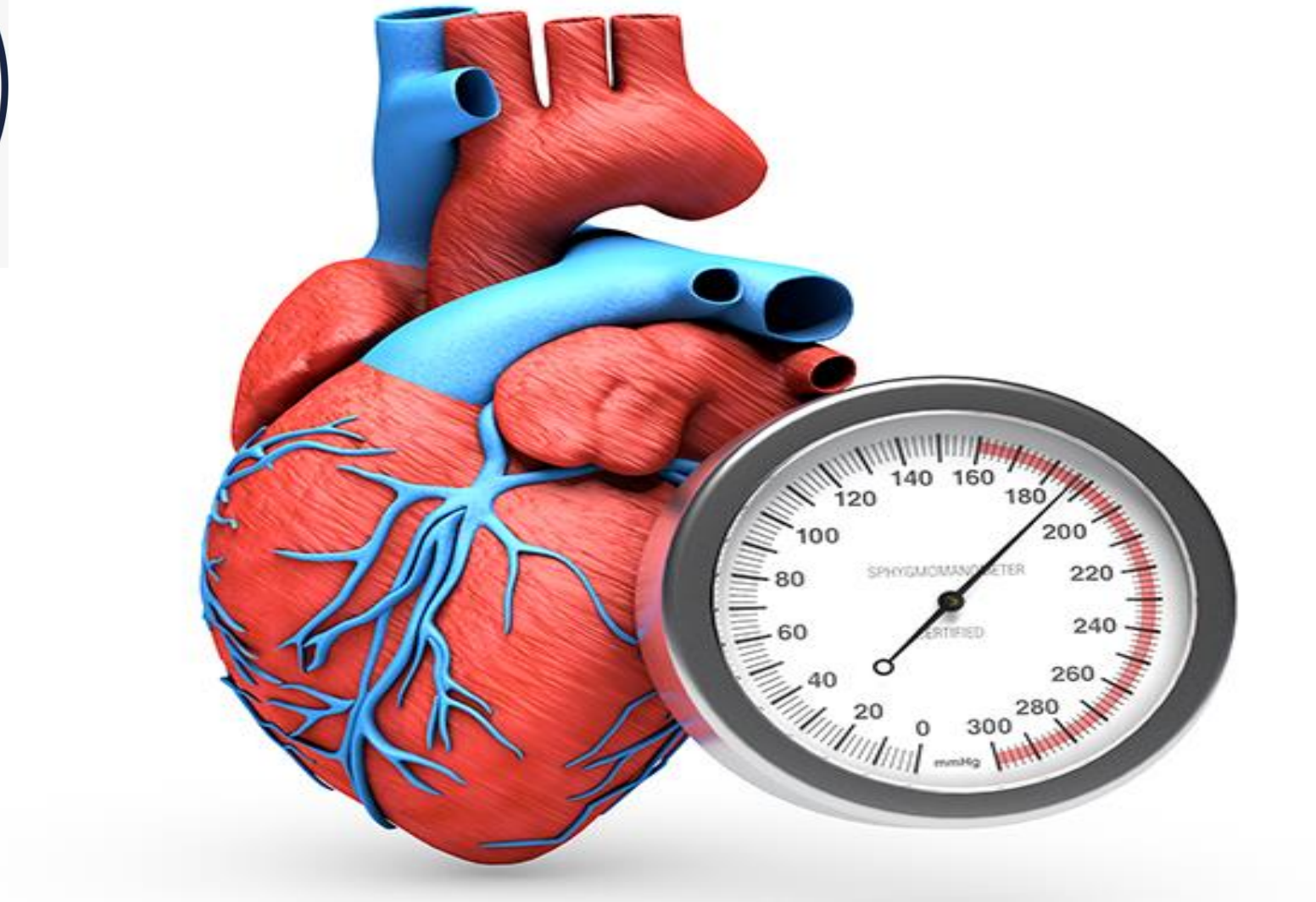
Amany Atia Ali Atia
M.D.

Contact : Amany Atia

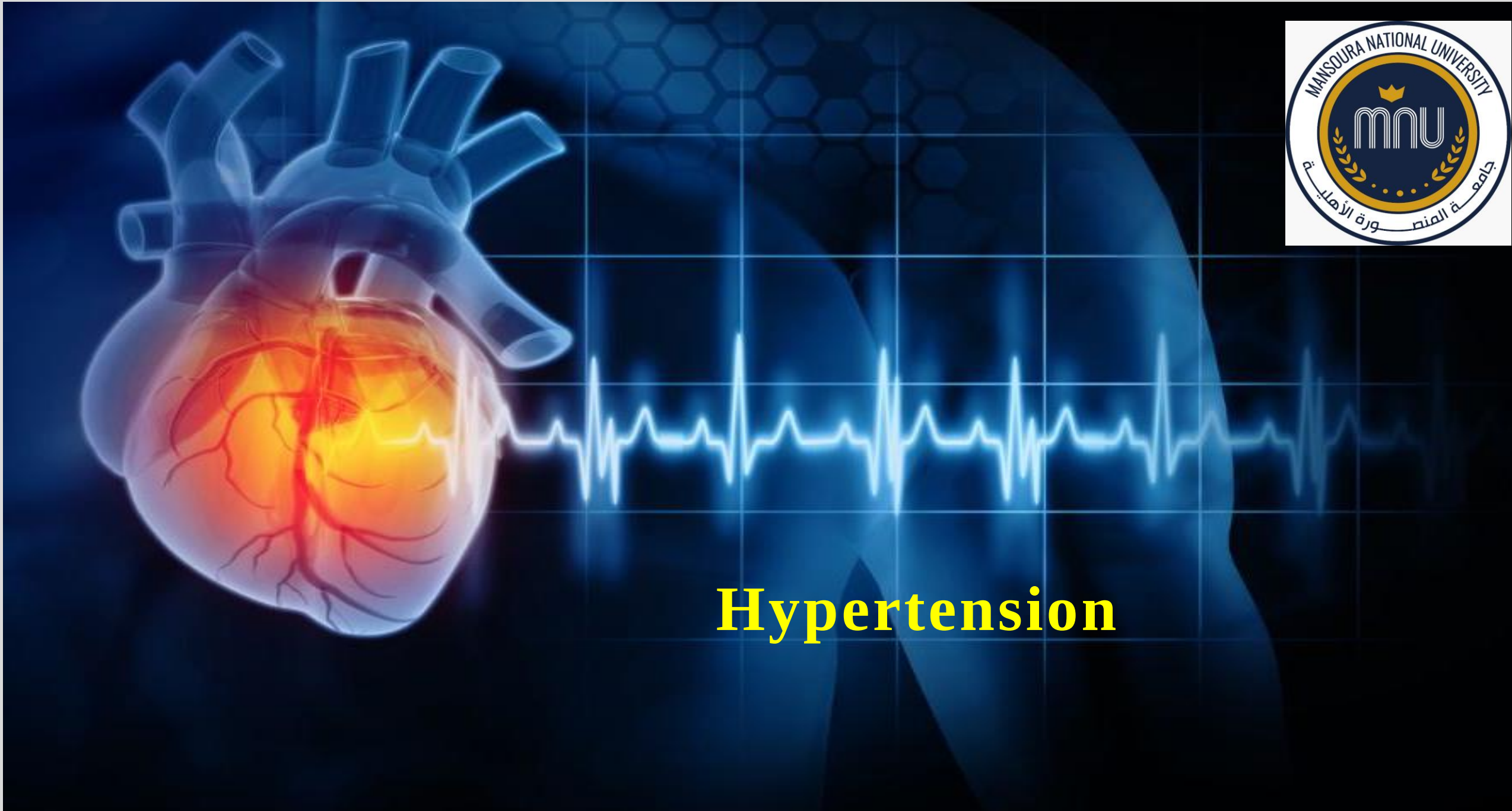
Email: amany_atteia@mans.edu.eg

Tel: 01094714077

Semester 3



CVS



Hypertension

Hypertension

Blood Pressure Categories

American Heart Association | American Stroke Association

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

❖ Pharmacotherapy of Hypertension

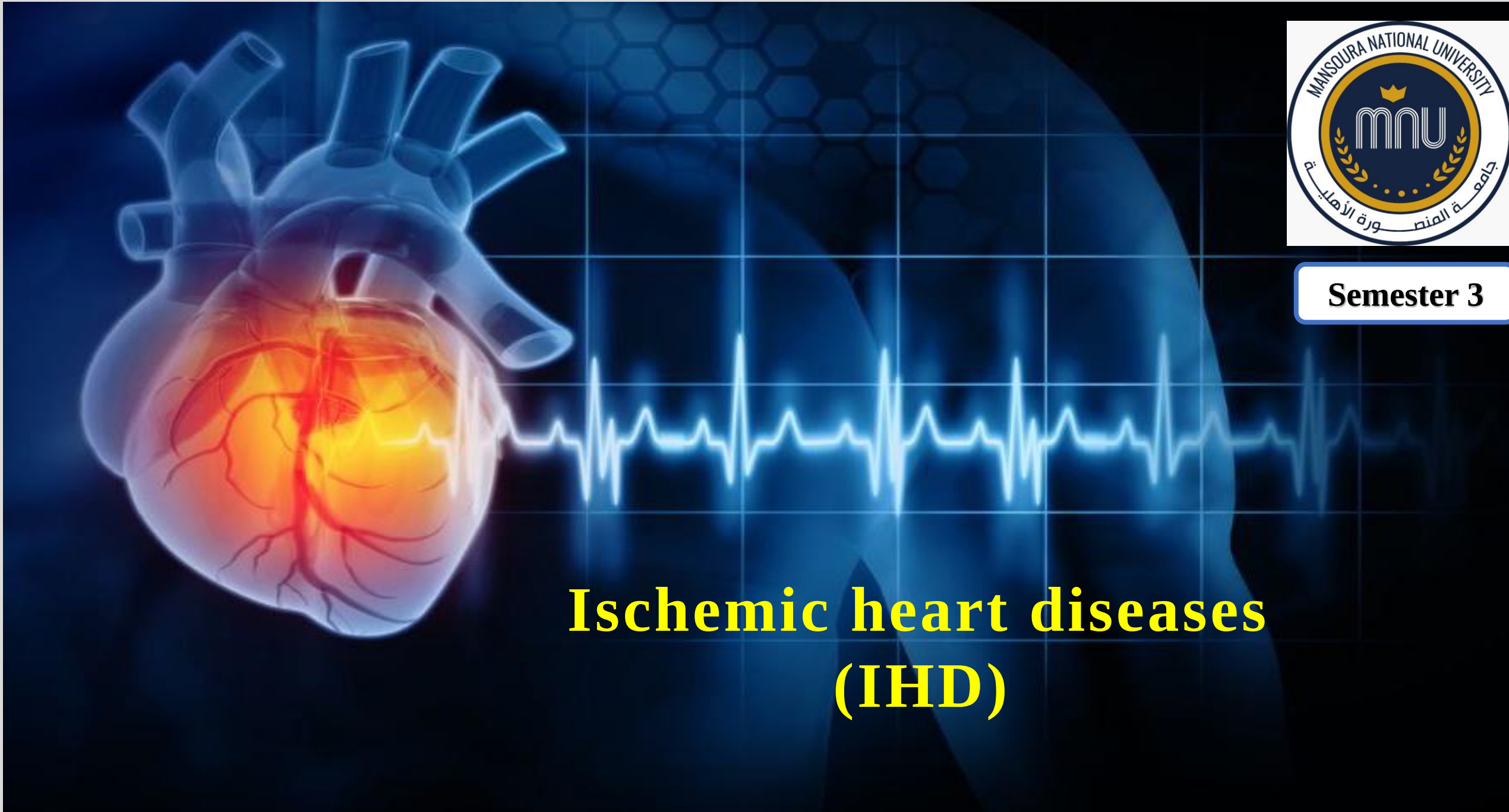
1st line drugs (commonly used)	2nd line drugs
✓ Renin-angiotensin-aldosterone system blockers • Angiotensin converting enzyme inhibitors (ACEIs) • Angiotensin receptor lockers (ARBs)	. α_1- blockers: prazosin and doxasosin. . Combined α and β-blockers: labetalol. . Adrenergic neuron blockers: α-methyldopa and reserpine. . Vasodilators: e.g. hydralazine. . Central α_2 stimulants: clonidine. . Endothelin blockers: Bosentan. . Dopamine agonists: fenoldopam.
✓ Calcium channel blockers (CCBs)	
✓ Thiazide diuretics	
β-blockers	

Choice of the antihypertensive drugs:

Clinical condition	Best choice
Starting therapy for non-complicated essential hypertension	Patient <55 years old not black African: ACE inhibitors Patient >55 years old or black African : CCBs. If not adequate, add thiazide or beta blockers.
Hypertension of pregnancy	α-methyldopa- Labetalol – Nifedipine - Hydralazine
Hypertension in a diabetic patient with diabetic nephropathy	ACE inhibitors
Hypertension with chronic kidney disease	S. creatinine <3 mg/dl: ACEIs S. creatinine >3 mg/dl: CCBs
Hypertension with CHF	ACE inhibitors - diuretics
Hypertension with bronchial asthma	CCBs
Hypertension with angina	CCBs - beta-blockers
Hypertension with thyrotoxicosis, sympathetic overactivity	Beta-blockers
Hypertension with BPH	α1 blockers
Primary pulmonary hypertension	Endothelin receptor antagonists

Side effects of ACEIs

ACEIs	ARBs
First-dose **hypotension**	**Same** as ACEIs
Dry cough May be due to accumulation of bradykinin	↓
Angioedema (rare) May be due to accumulation of bradykinin	↓
• **Hyperkalemia** Due to ↓ aldosterone K+ levels should be monitored	**Same**
• **Teratogenic** (2nd & 3rd trimesters) • **↓ renal function** in susceptible patients	**Same**



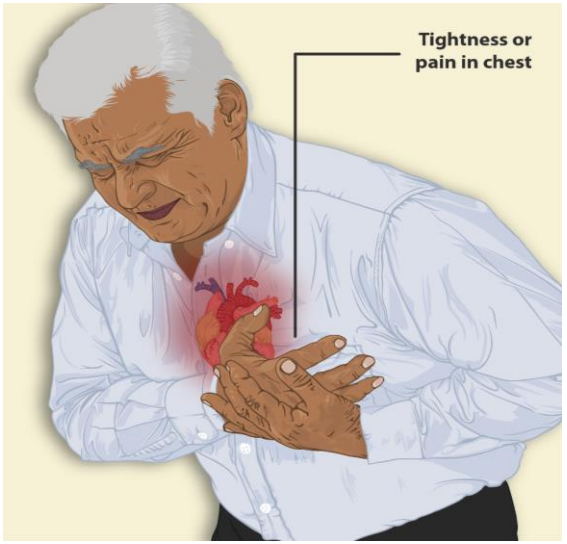
Semester 3

Ischemic heart diseases (IHD)

Ischemic heart diseases (IHD)

➢ Definition:

Retrosternal pain due to ischemia of the myocardium as a result of imbalance between heart work (**O2 demand**) and coronary blood flow (**O2 supply**).



Management of ischemic heart diseases:

I- Lifestyle modifications

II- Drugs decreasing atherosclerosis & reduce risk of myocardial infarction:

a. Antiplatelet (aspirin, clopidogrel)
b. Hypolipidemic drug (statin)
c. Angiotensin converting enzyme inhibitors (ACEI)

III- Antianginal drugs

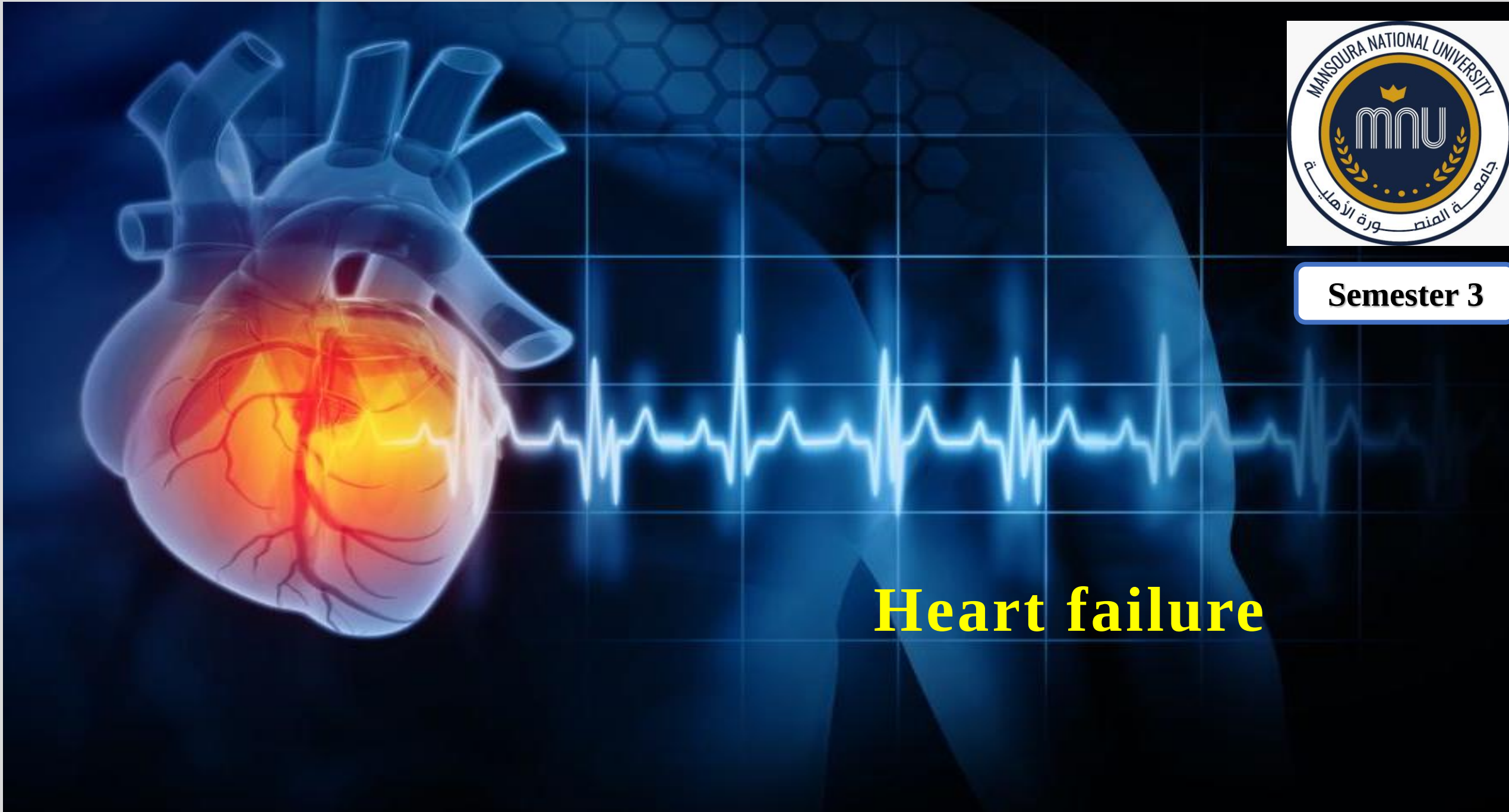
A . Acute anginal attack: Nitroglycerin or Isosorbide dinitrate (sublingual)

B . Maintenance therapy for chronic stable angina:

- Beta blocker (1st choice)
- CCBs: alternative if beta blocker are contraindicated.
- Long-acting nitrate if needed (isosorbide mononitrate)
- others: ranolazine, trimetazidine, ivabradine

Vasospastic angina (VSA)

1. Calcium channel blocker
2. Long-acting nitrate
3. Nicorandil

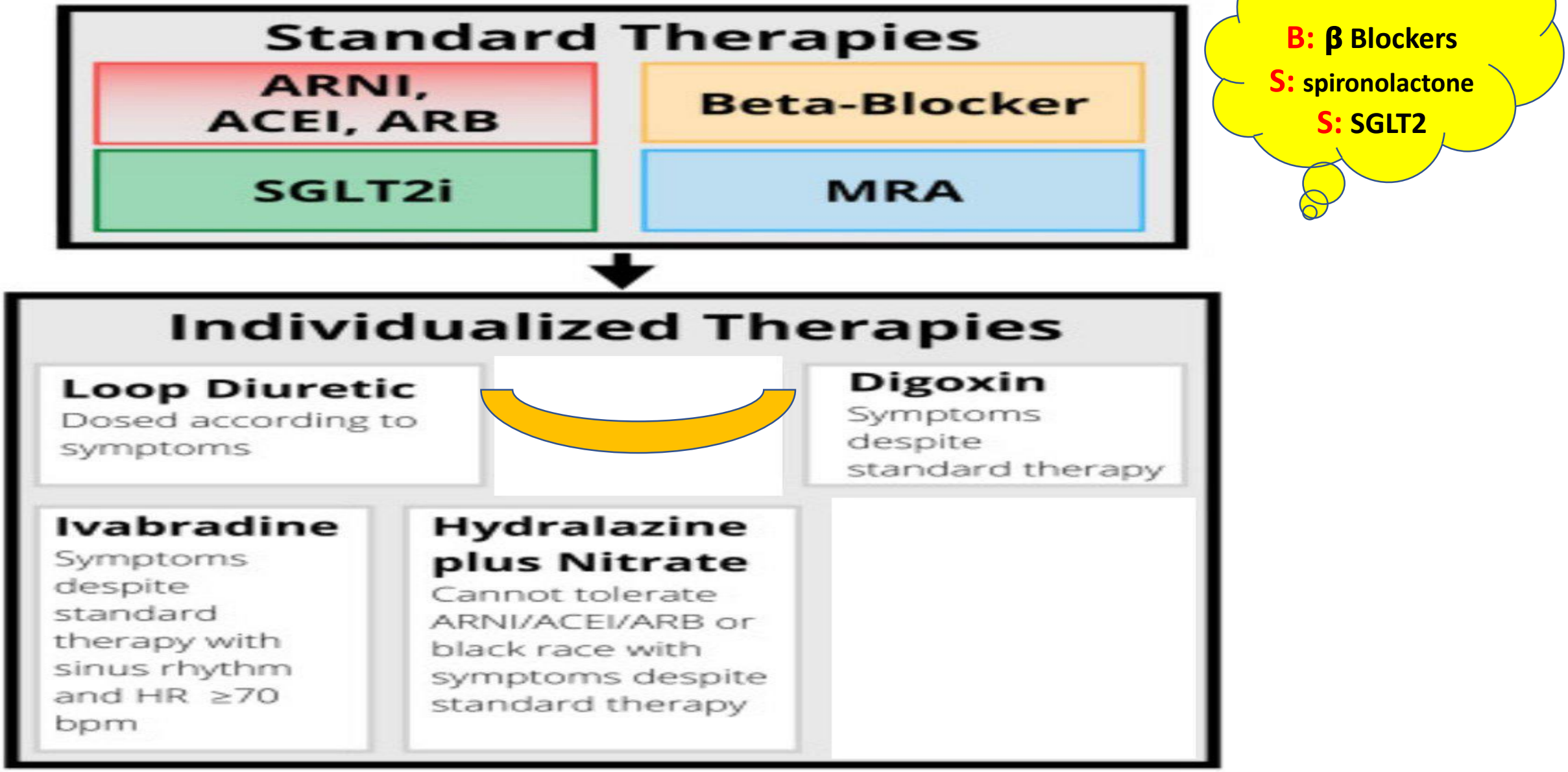


Semester 3

Heart failure

Management of Heart failure

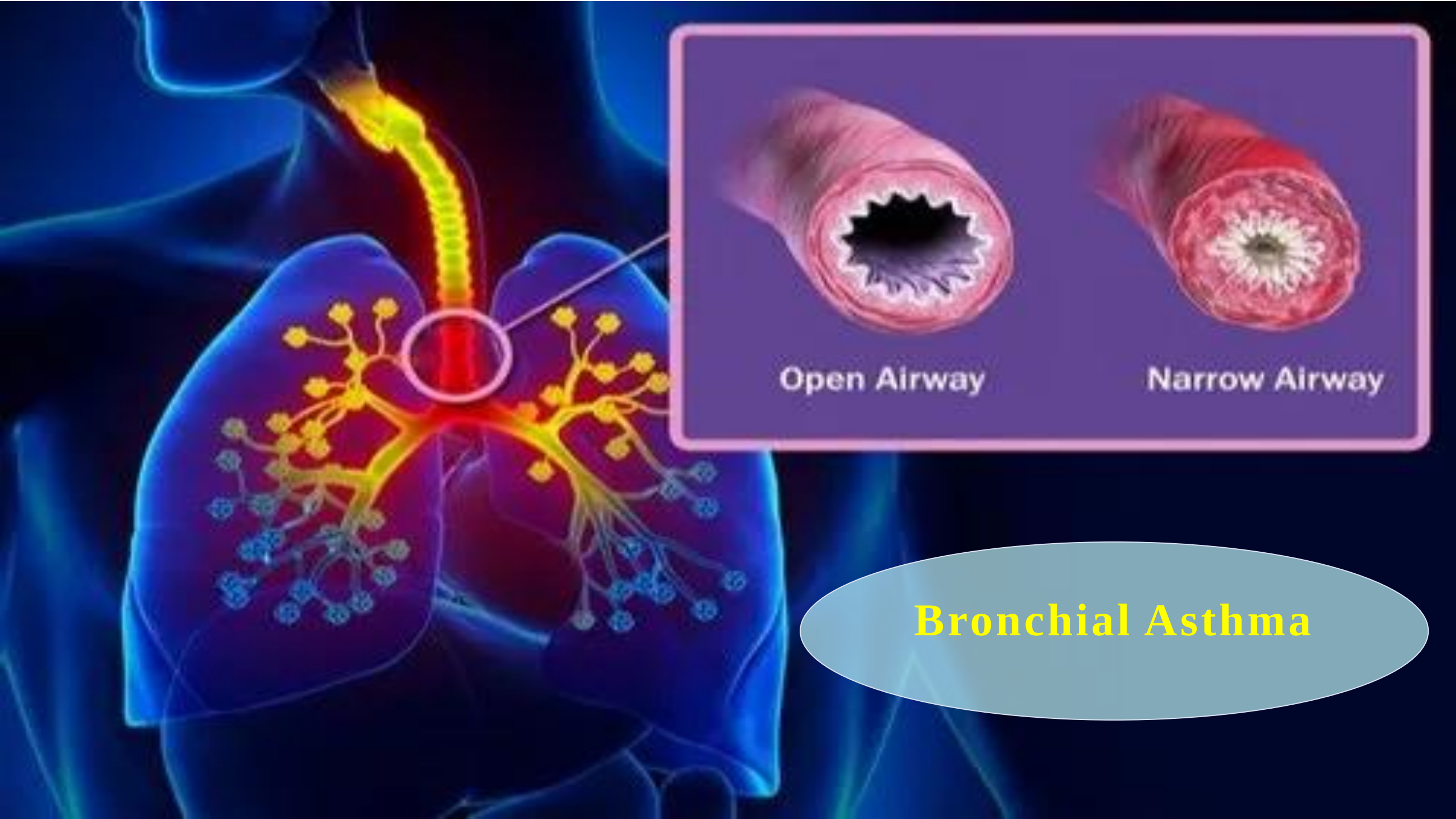
A: ARNI
B: β Blockers
S: spironolactone
S: SGLT2



A 64-year-old man has hypertension (160/100 mmHg). He has a history of asthma. He was treated with antihypertensive drug. His blood pressure fell to 130/84 mmHg, but he developed ankle edema as a side effect of the prescribed drug.

What is the antihypertensive most likely responsible for this side effect?

Respiratory

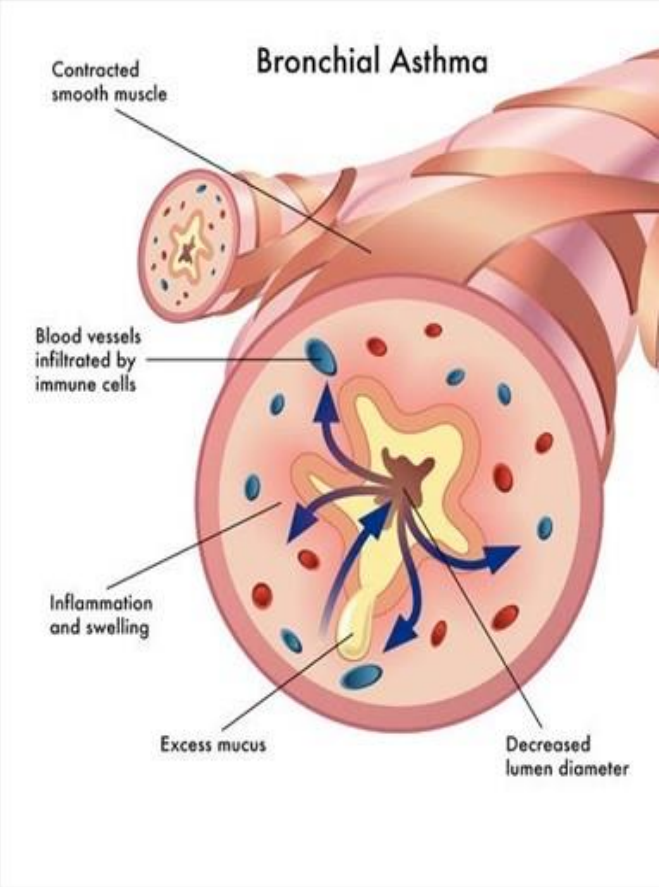


Bronchial Asthma

Bronchial asthma

➢ Definition:

- Chronic inflammatory disease of the airways (most commonly allergic), characterized by reversible bronchial obstruction with bronchial hyper-responsiveness



Treatment of bronchial asthma

1- Bronchodilators → relieve of bronchial spasm

* B2 agonists
* Anti-muscarinic drugs.
* Methylxanthines.

2- Anti-inflammatory drugs → Reduction of edema and congestion

* Corticosteroid

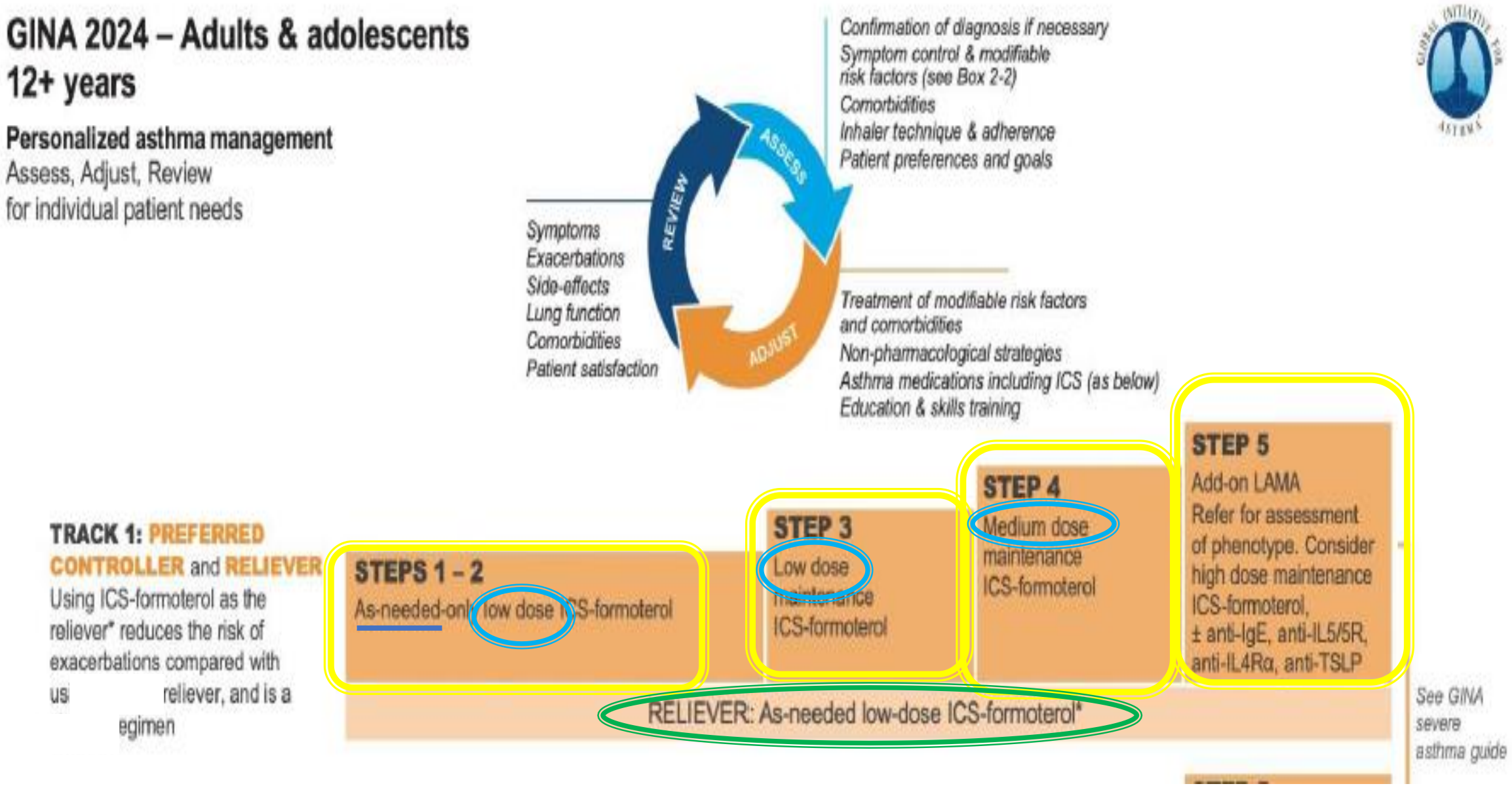
3-Adjuvant therapy: **Leukotriene receptor antagonist**

4-Biological therapy: **According to the results of phenotyping**

5-Others:

a-Avoid drugs precipitating the attack.
b-Desensitization or avoidance of antigen if it is known.
c-Treatment of respiratory infection.
d-O2 therapy
e-Expectorants and mucolytic.
f-Psychic support

Stepwise approach to asthma management



- Mechanism of action of formoterol : Long acting B2 agonist(LABA)

- Stimulate bronchial β2 receptors → ↑CAMP →
- 1-Bronchodilator
- 2-Decrease histamine release from mast cell
- 3-Improve mucociliary clearance

- **Adverse effects of beta2 agonists**

- 1-Tachycardia and arrhythmia due to:
- ▪ Direct activation of cardiac β1 (due to loss of selectivity in high doses).
- ▪ Reflex from hypotension (caused by VD of skeletal ms BV).
- 2-Tolerance with prolonged use (requiring temporary cessation of the drug).
- 3-Tremors of skeletal ms.
- 4-Hypokalemia (due to shift of K+ from blood to cells).

• Mechanism of action of corticosteroids

❖ **Corticosteroids can effectively ↓ bronchial inflammation and hyperreactivity**

- **Inhibit phospholipase A2 enzyme** →↓ synthesis of PGs, LTs & PAF.
- **Inhibit B cell function** → ↓ antigen-antibody reaction.
- **Inhibit T cell functions** → ↓ decrease the production of inflammatory cytokines e.g. IL 1 , 2 , 3 4 and TNFα leading to inhibition of early phase response to allergen
- Inhibit **macrophage** activity.
- Inhibit **mast cells** → ↓ histamine release and capillary permeability.
- Upregulation of **B 2 receptors**
- Increase airway diameter, reverse the shedding of epithelial cells, goblet-cell hyperplasia and basement-membrane thickening characteristic of the airway mucosa of patients with asthma.

- **Adverse effects of inhaled corticosteroids:**

- **1- Oropharyngeal candidiasis**: avoided by using spacing device or nystatin.
- 2- **Dysphonia**: leading to change of voice.

- **Mechanism and pharmacological effects of methylxanthines**

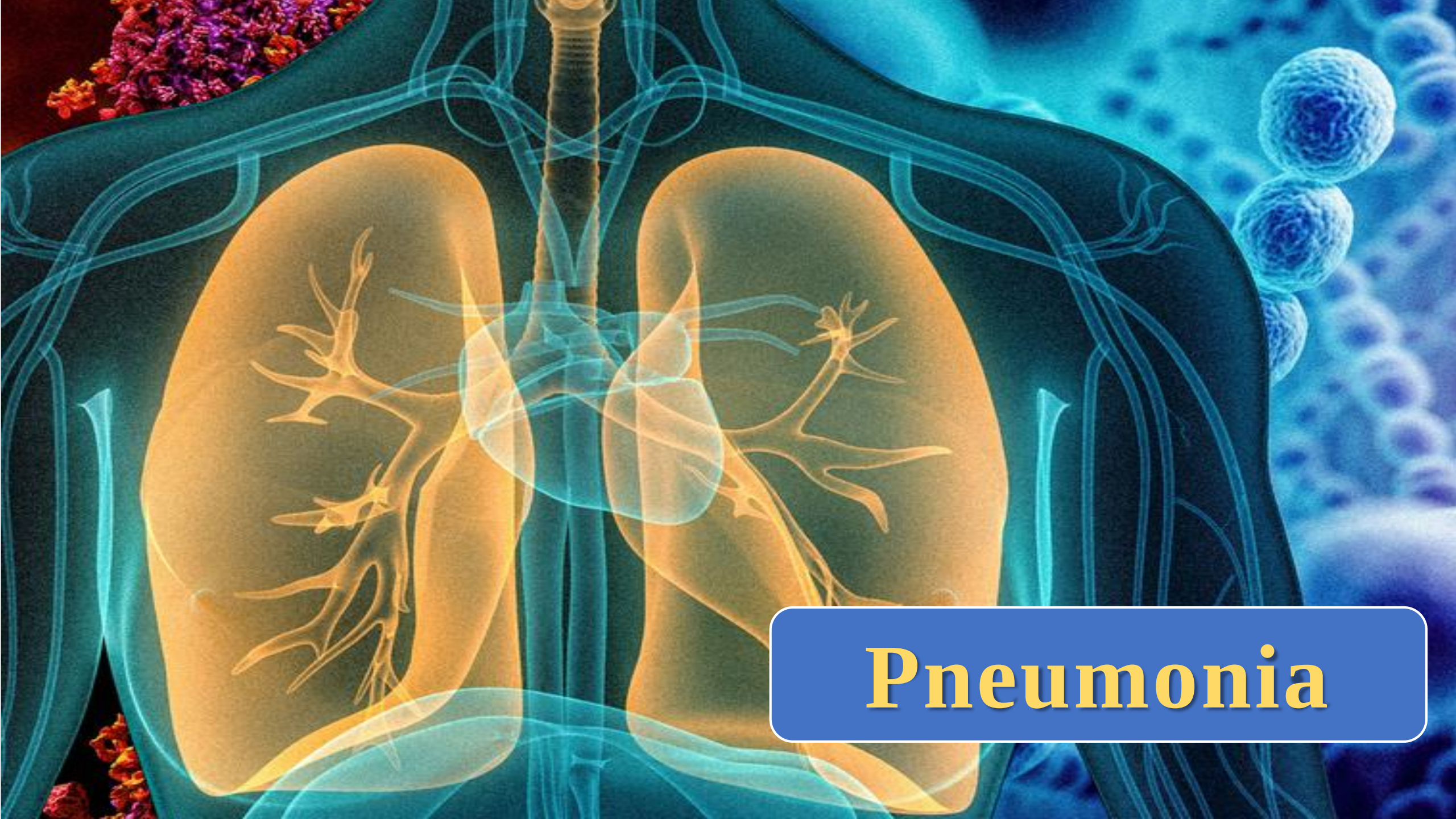
1-Inhibition of phosphodiesterase enzyme (PDE3 and PDE4) →↑cAMP lead to:

- Bronchodilator
- Decrease histamine release from mast cell
- Improve mucociliary clearance

2-Block of adenosine receptors (mech in ttt of BA) leading to:

- Bronchodilatation (block bronchoconstrictor effect of adenosine)
- ↓ Mediator release from mast cells

- **Adverse effects of methylxanthines:**
- **1-Narrow safety margin** so be caution in renal and hepatic
- **2-Irritant**: if given orally it causes gastritis, it is given after meals.
- **3-Rapid IV injection**: tachycardia, arrhythmia, hypotension & syncope.
- 4-Tachycardia, palpitation, angina, arrhythmia.
- 5-Insomnia, anxiety, tremors & may be seizures (**CNS stimulation**)

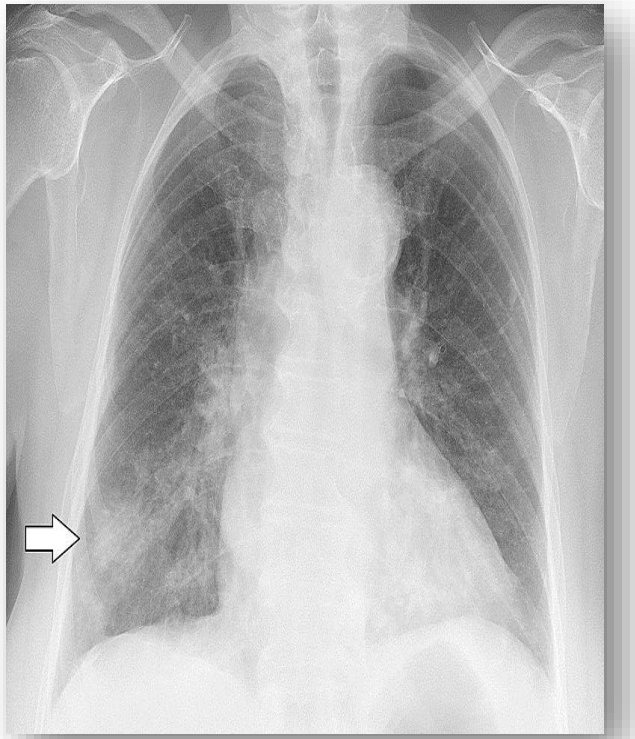


Pneumonia

Pneumonia

➢ Definition:

- Pneumonia is an infection in one or both lungs.
- It can be caused by bacteria, viruses, or fungi.
- **Bacterial pneumonia** is the most common type in adults.



Bacterial Pneumonia

I. Community-acquired pneumonia (CAP)

- Usually associated with **Strept pneumoni**
- Atypical bacteria is also common

II. Nosocomial pneumonia (Hospital acquired)(HAP)

- Occurs approximately **48 hours** after admission to hospital
- Mostly caused by **Gram-negative** bacteria
- But may be associated with resistant Staph "**MRSA**"
- Particularly difficult to deal with if pathogen is ***resistant to antibiotics***

Community-acquired pneumonia (CAP)

- Pneumococcus (30-60%)
- H.influenzae (10%)
- Moraxella catarrhalis
- Staphylococcus aureus
- Mycoplasma (10-30%)
- Legionella (2-10%)
- Chlamydophila (5-10%)
- Gram negative bacteria

Atypical organisms

- ✓ Macrolide
- ✓ Doxycycline
- ✓ Quinolones

Hospital-acquired pneumonia (HAP) (Nosocomial)

Occurs 48 hours after admission to hospital

- Gram -ve bacteria
- Klebsiella (4%)
- Escherichia coli
- Pseudomonas(5%)
- MRSA
- Polymicrobial (13%)
- Unknown(33%)

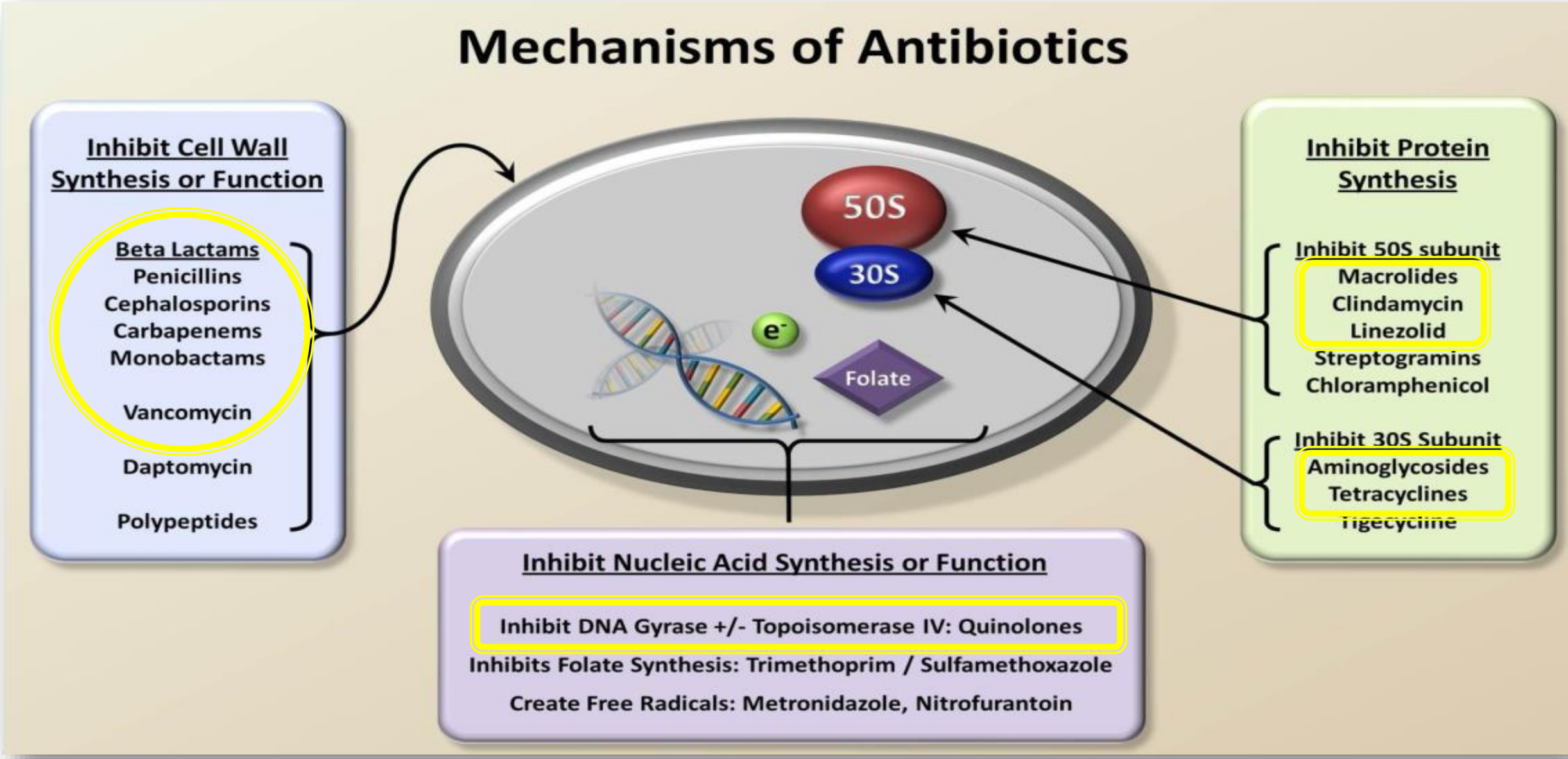
Treatment of CAP

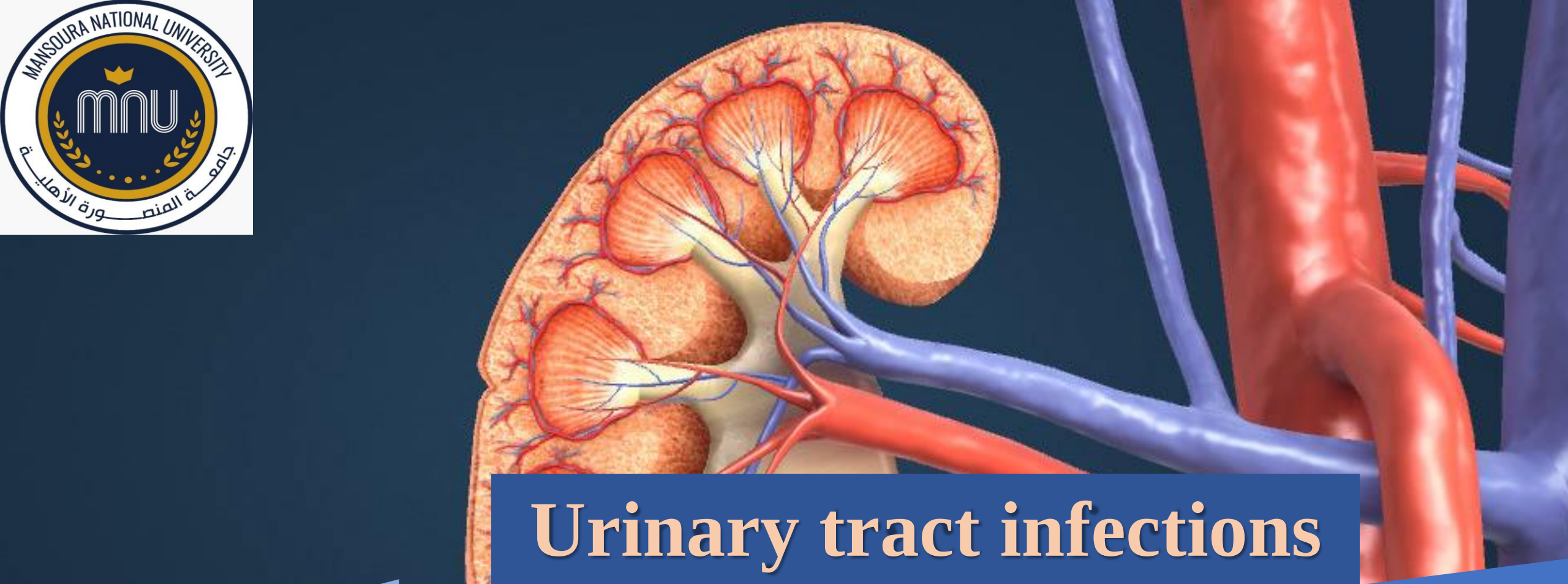
CAP	First choice	Alternative/Penicillin allergy
Out-patient (**Oral** for 5-7 days)	**Amoxicillin/Clavulanate** + **Azithromycin** (or Doxycycline)	**Resp. fluoroquinolone**
In-patient (**IV** until patient improvement **then** switch to **Oral**)	**Ampicillin/Sulbactam** (or Ceftriaxone) + **Azithromycin** (or Doxycycline) **(or Resp. fluoroquinolones)** ***in severe cases***	**Resp. fluoroquinolone** + **Aztreonam**

Treatment of HAP

HAP (Surely in-patient, IV firstly)	First choice	Alternative/Penicillin allergy
▪ No high risk of Mortality ▪ No high risk of Resistance	Piperacillin/tazobactam (or Ceftazidime) (or Cefepime)	Levofloxacin
▪ High risk of Mortality OR ▪ High risk of Resistance	Piperacillin/tazobactam (or Ceftazidime) (or Cefepime) + Levofloxacin + Vancomycin or linezolid (MRSA coverage)	Aztreonam + Levofloxacin + Vancomycin or linezolid (MRSA coverage)

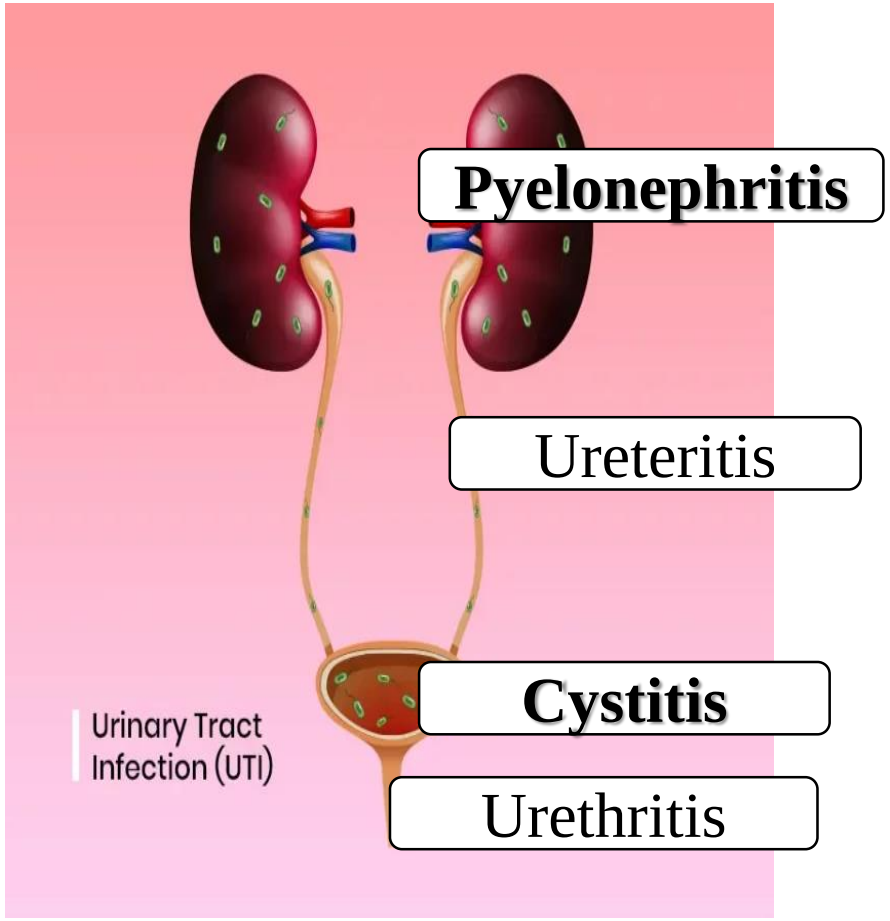
Mechanisms of Antibiotics





Urinary tract infections (UTIs) Pharmacotherapy

Symptoms and signs



Upper UTI:

- ✓ General : Fever, chills , nausea, vomiting, malaise.
- ✓ Flank pain, costovertebral angle tenderness
- ✓ with or without the typical symptoms of cystitis

Lower UTI:

- ✓ Frequency, urgency, dysuria
- ✓ Suprapubic pain

Empiric antimicrobial drugs

	Lower UTI	Upper UTI
	Outpatient (oral)	**Outpatient** (oral) **or Inpatient** (intravenous then oral)
Duration	**3-5 days** (except **Fosfomycin**, only **single** dose)	**7-14 days**
Options	• **First-line:** ✓ **Nitrofurantoin** ✓ **Fosfomycin** ✓ Trimethoprim **or** **Co-trimoxazole** • **Second-line**: ✓ Oral β-lactams (as **amoxicillin-clavulanate**, **cefadroxil**)	• **First-line:** ✓ **Fluoroquinolones** (**Levo**floxacin and **Cipro**floxacin) ✓ **Cephalosporins** as Cefotaxime and **Ceftriaxone** • **Second-line:** ✓ **Penicillin** as piperacillin/tazobactam ✓ **Aminoglycosides** as gentamycin

Nitrofurantoin

- **Mechanism of action:**
  causes bacterial **DNA** damage
- It is used **only** as a **urinary antiseptic** in **lower simple UTI.**
- against **E. coli**. , Other urinary tract Gram-negative bacteria are often resistant.
- It is **contraindicated** in renal failure.
- **Adverse effects:**
  - dark brown urine.
  - hemolytic anemia in patients with G-6-PD deficiency >>> Pregnancy ???
  - peripheral neuritis

Fosfomycin

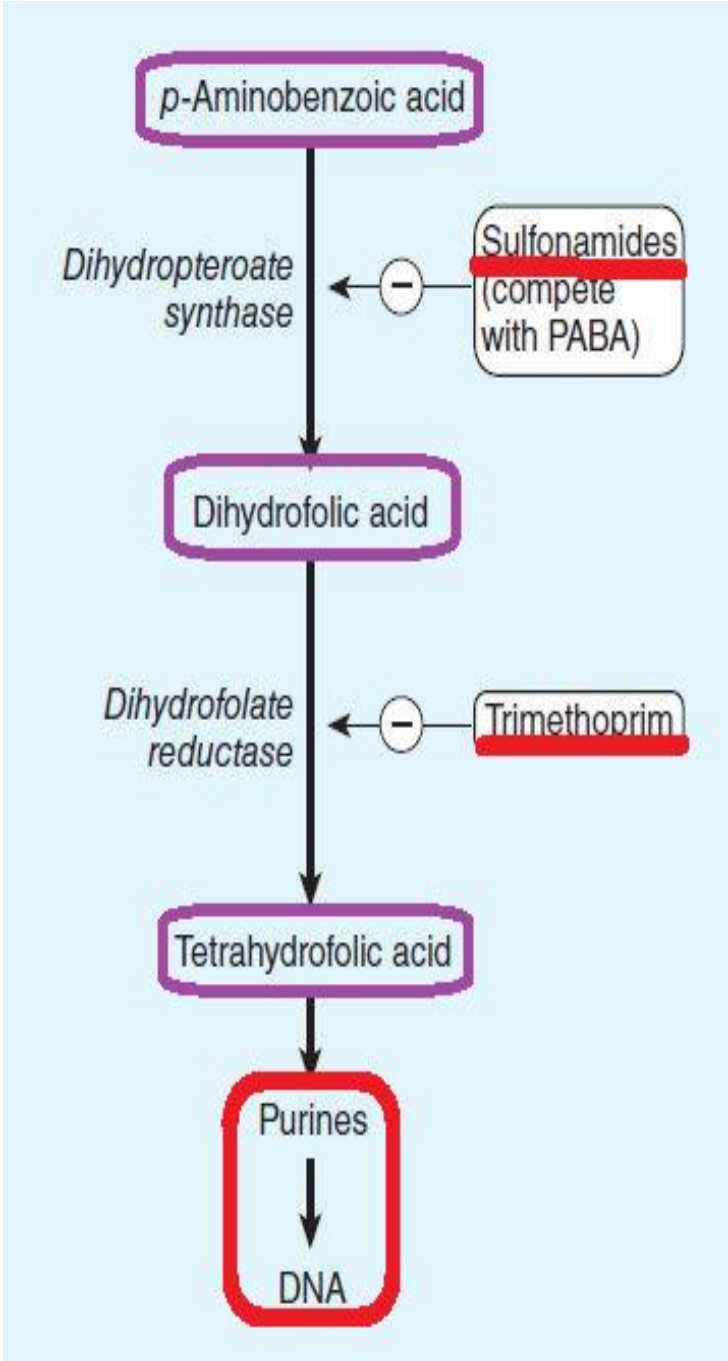
- **Mechanism of action:**
  inhibits bacterial **cell wall** synthesis
- It is used **only** as a **urinary antiseptic** in **lower simple UTI.**
- It is a **broad-spectrum** antibiotic against many Gram positive and negative bacteria.

- **Mechanism of action:**

✓ **Sulfonamides (Sulfamethoxazole)** are structural analogs of **PABA** (Para-aminobenzoic acid). They compete with PABA at the enzyme **dihydropteroate synthase** resulting in inhibition of **dihydrofolic acid synthesis**.

✓ **Trimethoprim** acts by inhibition of **dihydrofolate reductase** enzyme resulting in inhibition of formation of the active form **tetrahydrofolic acid**.

✓ **Co-trimoxazole** is a combination of **sulfamethoxazole** and **trimethoprim** to produce **sequential block** of folic acid synthesis.



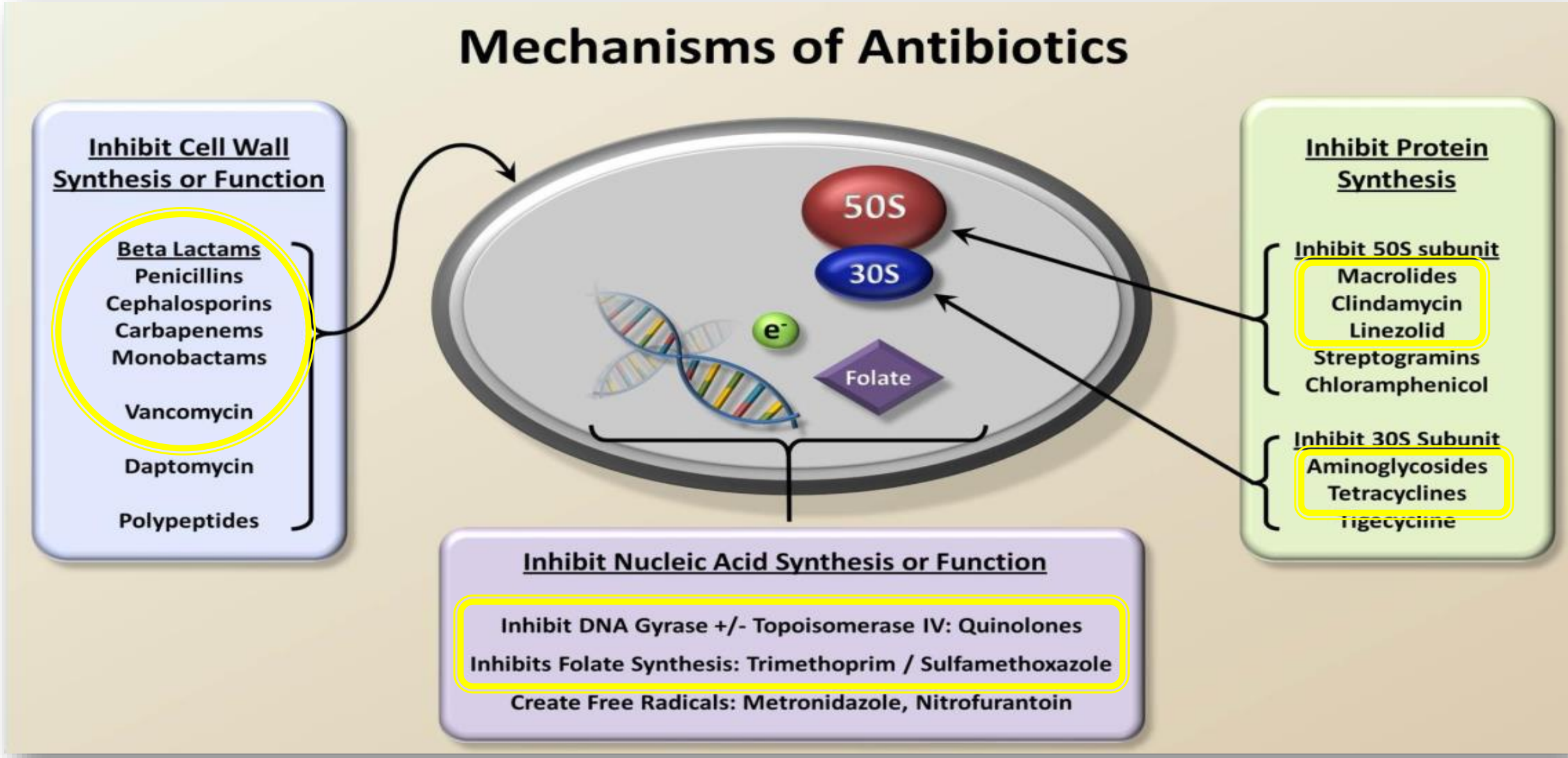
- **Adverse effects of Co-trimoxazole:**
  - ✓ **Hypersensitivity reactions:** Fever and rash

  - ✓ **Crystalluria:** due to precipitation of sulfonamide metabolites in urine.

  - ✓ **Kernicterus:** sulfonamides cause displacement of bilirubin from plasma protein binding sites. When they are given to neonates (or in the last 2 weeks of pregnancy), high free bilirubin levels in the blood can cross BBB and cause *permanent brain damage*.

  - ✓ **Megaloblastic anemia:** due to folic acid deficiency

Mechanisms of Antibiotics



UTI in pregnancy:

➢ **Recommended drugs:**

- ✓ **Nitrofurantoin** (*not after 37 weeks of pregnancy)*
- ✓ **Fosfomycin**
- ✓ **Cephalosporin** as cephalexin
- ✓ **Penicillin** as amoxicillin-clavulanate

(in Pregnancy > treatment course is prolonged up to **7 days** in lower UTI and **14 days** in Upper UTI)

➢ **Contraindicated drugs:**

- ✓ **Sulfonamides** (in the **last** trimester) → *kernicterus.*
- ✓ **Fluoroquinolones** → *arthropathy.*
- ✓ **Aminoglycosides** → *congenital deafness.*
- ✓ Tetracyclines → *teratogenic and cause yellow staining of teeth.*
- ✓ Chloramphenicol → *grey baby syndrome.*


Thank You
Wishing you
Success
in your
exams.