Treatment of Respiratory Tract Infections

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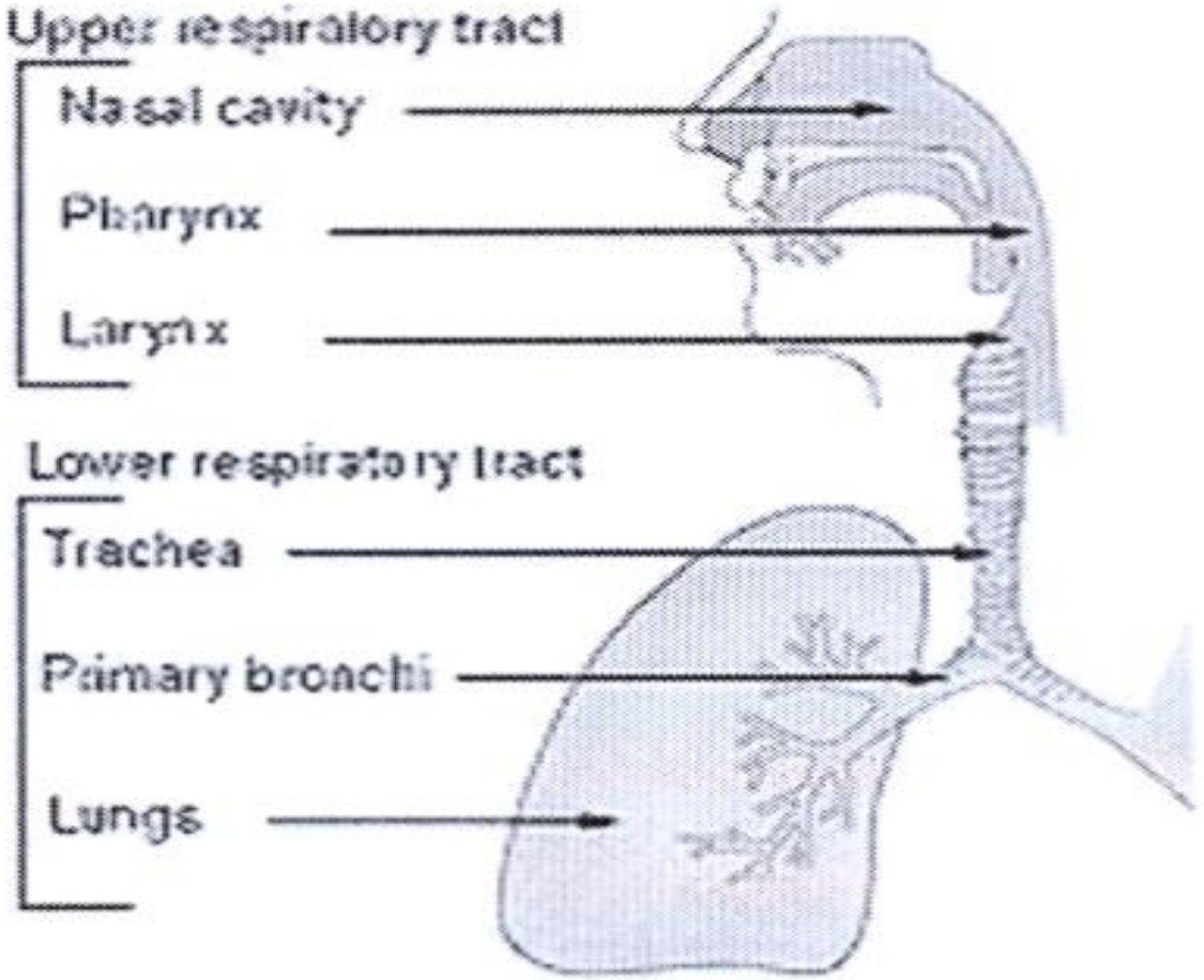
Objectives of the lecture

At the end of lecture, the students should be able to understand the following:

- The **types** of respiratory tract infections (RTI)
- The **antibiotics** that are commonly used to treat RTIs & their side effects
- Understand the **mechanism** of action & **pharmacokinetics** of individual drugs.

Classification of RTIs

- **Upper respiratory tract infections (URTI)**
- **Lower respiratory tract infections (LRTI)**


Upper respiratory tract
Nasal cavity
Pharynx
Larynx
Lower respiratory tract
Trachea
Primary bronchi
Lungs

Causes of URTIs

- **Viruses**; Most URTIs are of viral etiology

  (Should NOT be treated with antibiotics)

Treatment: rest & plenty of fluids, OTC cold & pain relievers

- **Bacteria (mainly Group A streptococcus, H. influenza)**

Treatment: Antibiotics. The type depends on:

Type of bacteria

Sensitivity test.

LRTIs (costly & more difficult to treat)

- **Bronchitis** (inflammation of major bronchi & trachea)

Acute, or Chronic, or Acute exacerbation of chronic bronchitis

Causes: viruses or bacteria (*H. influenza*, *Streptococcus pneumonia* & *Moraxella catarrhalis*).

- **Pneumonia** (Serious infection of bronchioles & alveoli)

Community –Acquired (CAP)

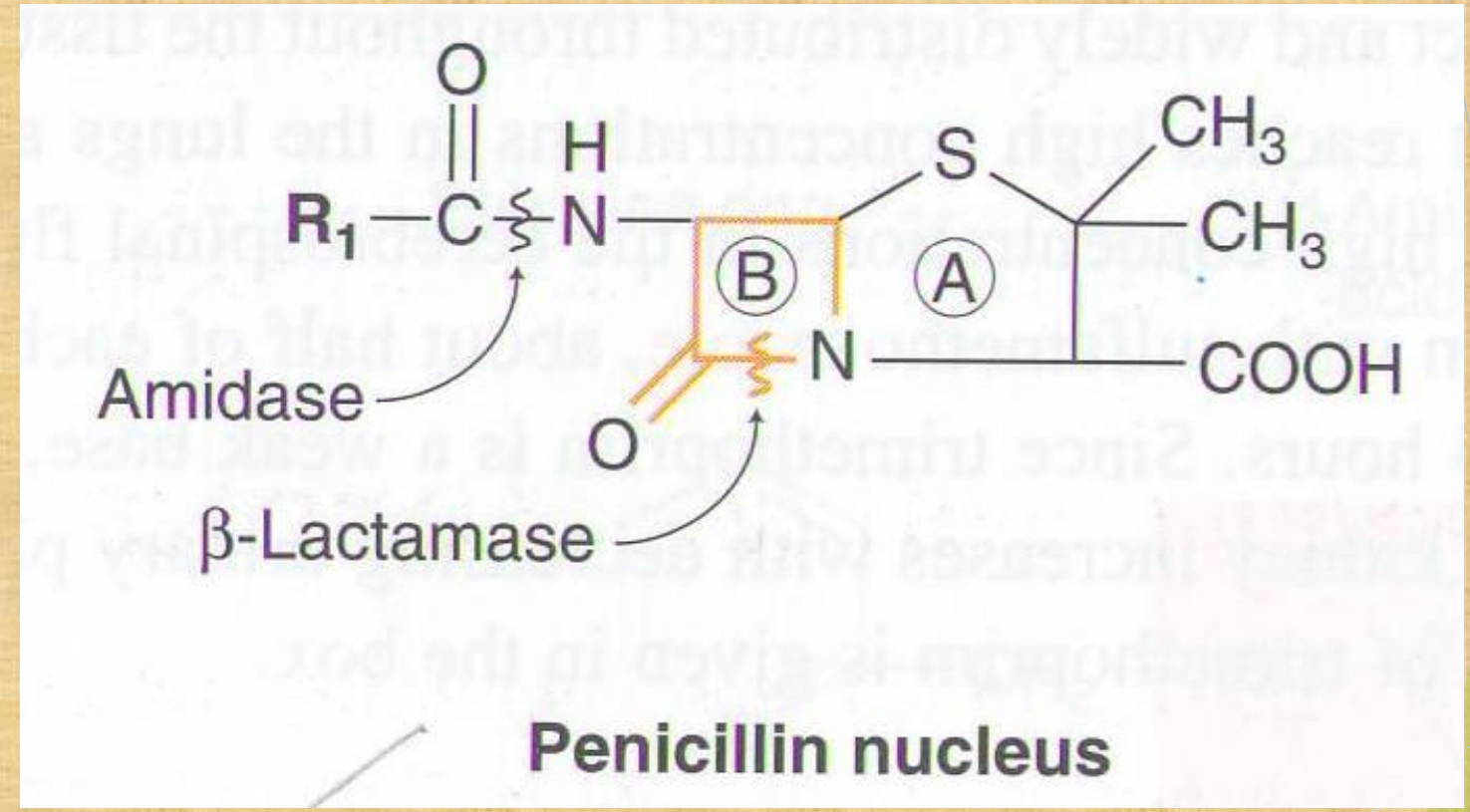
Hospital-acquired

Causes: Bacteria S. pneumonia(66%), H. influenza (20%), M. catarrhalis (20%).**

Antibiotics commonly used in the treatment of RTIs

- **Beta-lactam antibiotics (Penicillins / Cephalosporins)**
- **Macrolides**
- **Fluoroquinolones**
- **Aminoglycosides**
- **Doxycycline.**

Penicillins



Penicillin nucleus

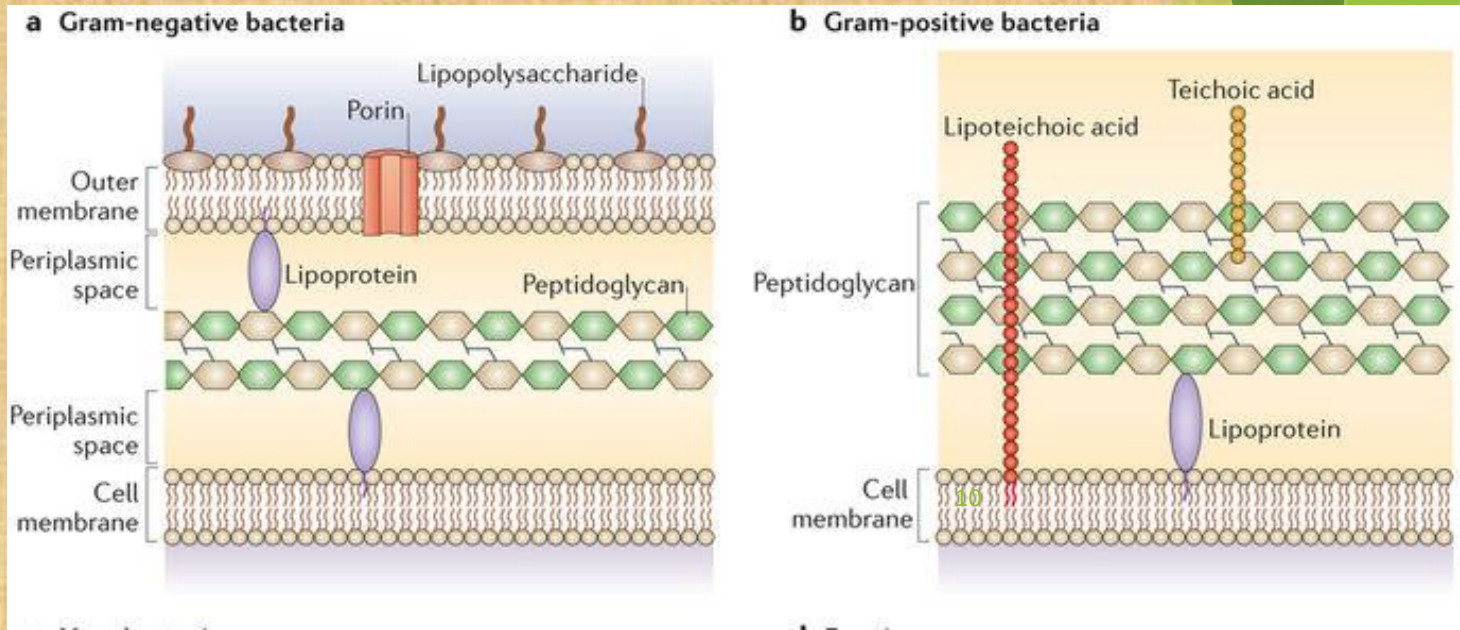
Broad-spectrum penicillins

- **Amoxicillin-Clavulanic acid**
- **Ampicillin-Sulbactam**
- **Piperacillin-tazobactam**

Act on both gram+ve & gram-ve microorganisms.

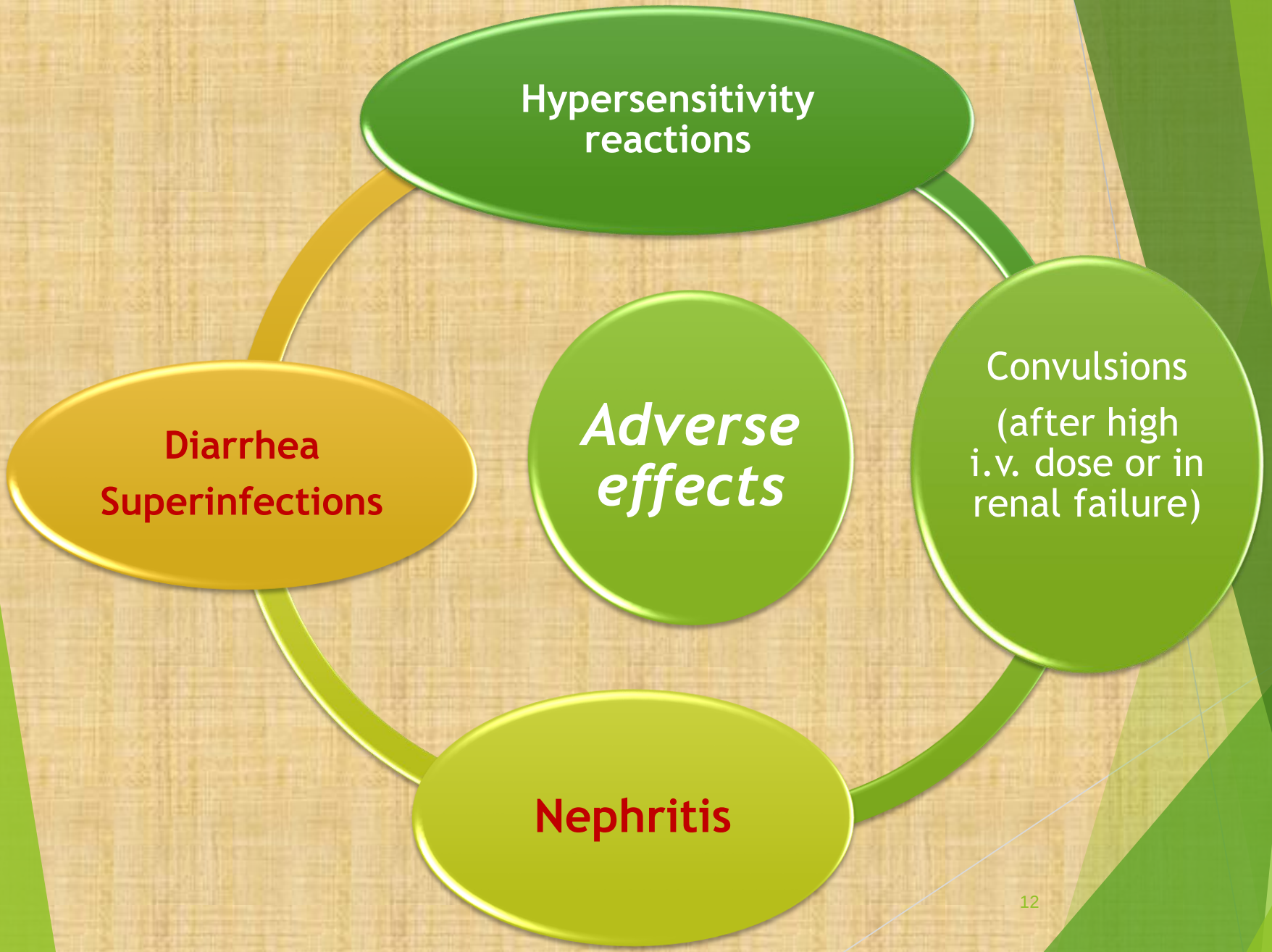
Mechanism of action of Penicillins

- **Inhibit bacterial cell wall synthesis through inhibition of peptidoglycan layer of the cell wall.**
- **Bactericidal.**



Pharmacokinetics of Penicillins

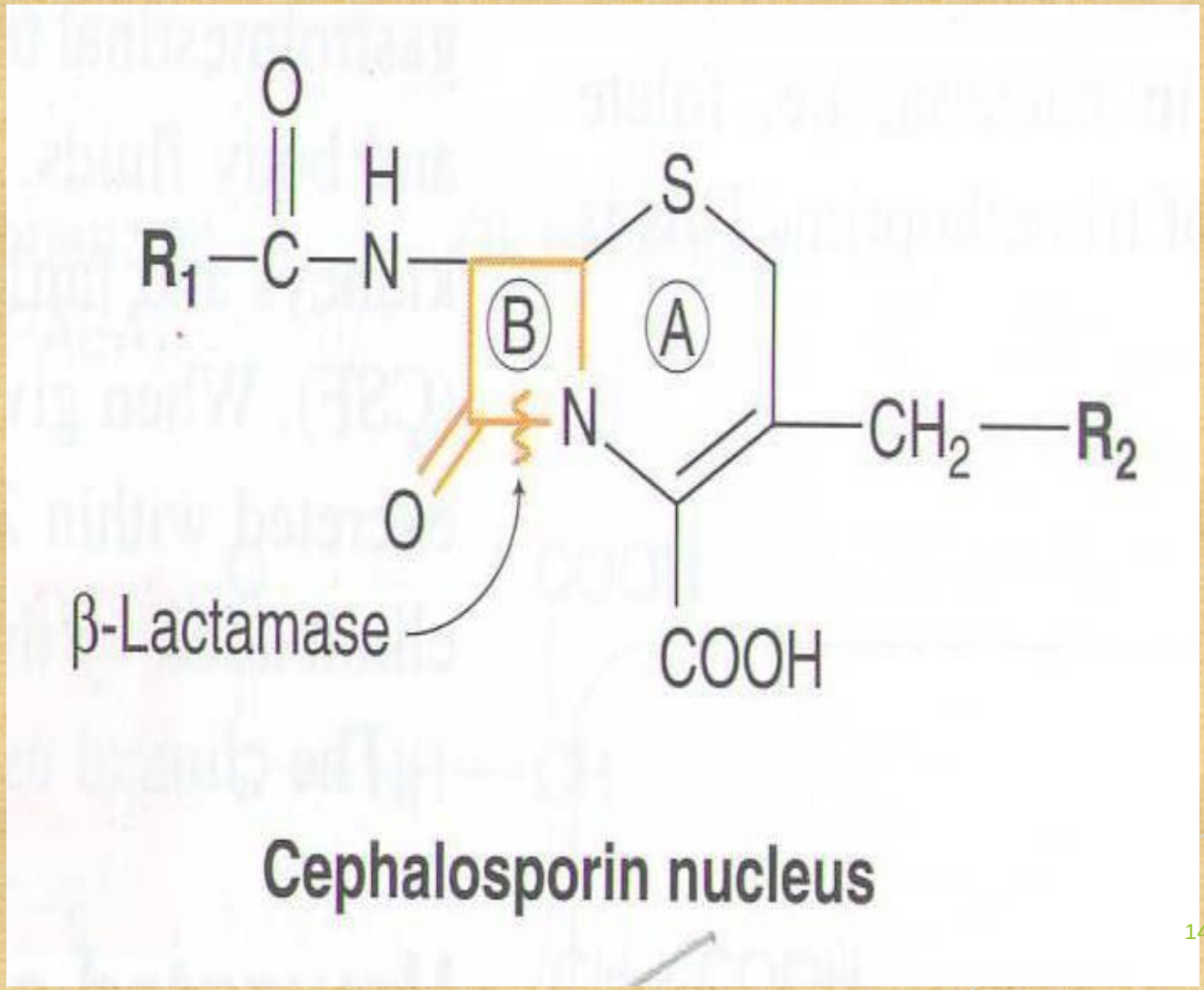
- Given po or parenterally
- Not metabolized in human
- Relatively lipid insoluble
- Excreted mostly unchanged in urine
- Probenecid slows their elimination & prolong their half live
- Half-life 30-60 min (increased in renal failure).


Hypersensitivity reactions
Convulsions (after high i.v. dose or in renal failure)
Nephritis
Diarrhea Superinfections
Adverse effects

Therapeutic uses of Penicillins

- **URTIs**
- **LRTIs.**

Cephalosporins



Cephalosporin nucleus

Mechanism of action of Cephalosporins

- **Inhibit bacterial cell wall synthesis**
- **Bactericidal**

(Similar to Penicillins)

Classified into 3 gps:

1st Generation Cephalosporins

- **e.g. Cephalexin**
  - **Given po**
  - **Effective against gram positive bacteria**
  - **Effective in URTIs.**

2nd Generation Cephalosporins

E.g. Cefuroxime, cefaclor

- **Given po**
- **Effective mainly against Gram-negative bacteria**
- **Well absorbed po**
- **Active against β-lactamase –producing bacteria**

Uses:

- **Upper & lower RTIs.**

3rd Generation Cephalosporins

Ceftriaxone / Cefotaxime / Cefixime

- Given by intravenous route
- More effective against gram-negative bacilli
- Effective in treatment of pneumonia.

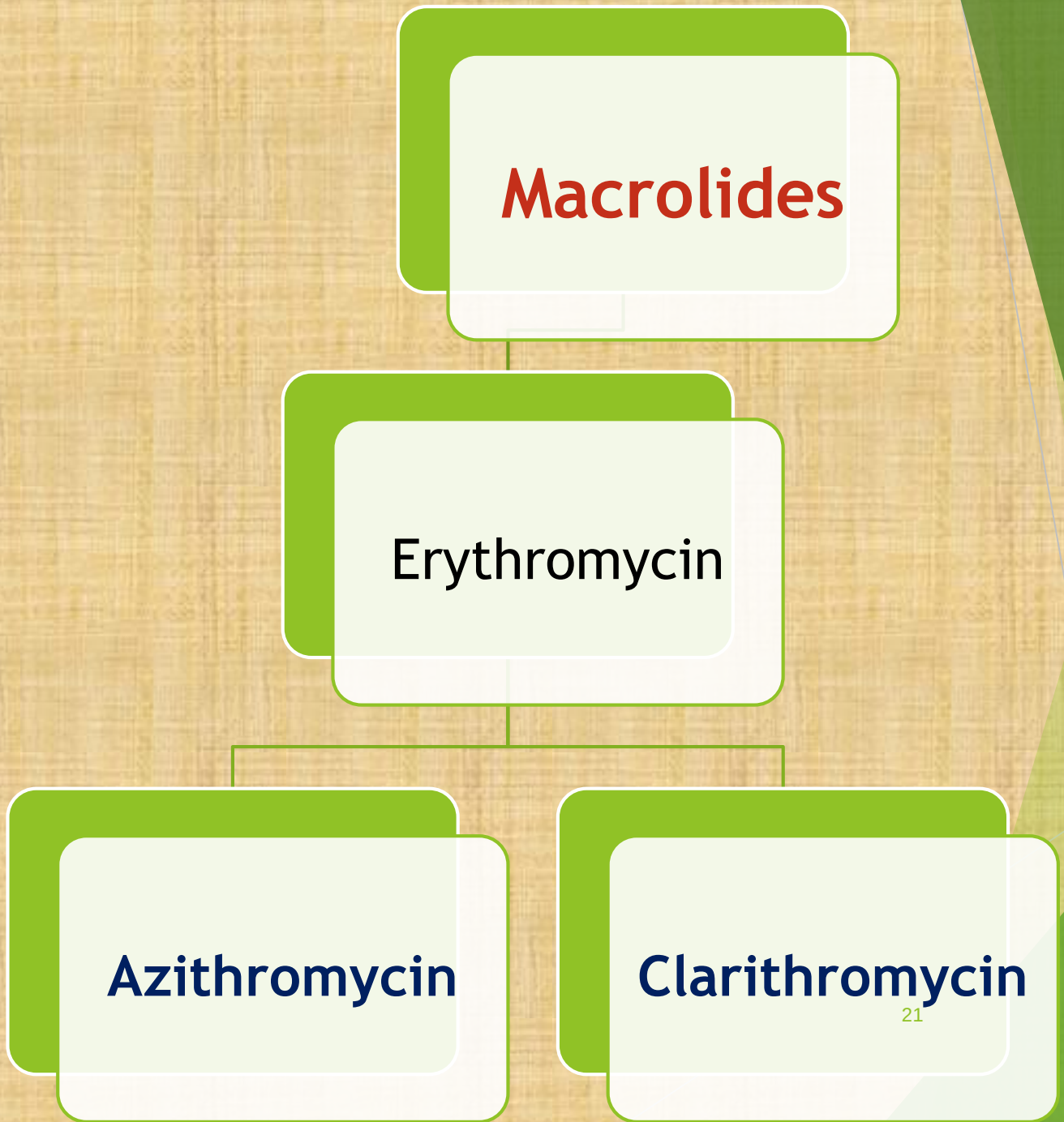
Pharmacokinetics of Cephalosporins

- Cephalosporins are given parenterally & po
- Relatively lipid insoluble (like penicillins)
- Hence, do not penetrate cells or the CNS, except for third generations
- Mostly excreted unchanged by the kidney (glomerular & tubular secretion)
- Probenecid slows their elimination & prolong their half lives

Half-life: 30-90 min; except ceftriaxone 4-7 hr.

Adverse effects of cephalosporins

1. Hypersensitivity reactions
2. Thrombophilibitis
3. Superinfections
4. Diarrhea


Macrolides
Erythromycin
Azithromycin
Clarithromycin

Mechanism of action

Inhibit bacterial **protein** synthesis by binding to 50S subunit of the bacterial ribosomal RNA

Bacteriostatic

Bactericidal at high concentrations.

Clarithromycin

- More effective on G+ve bacteria
- Stable at gastric acidity
- Inhibits cytochrome P450 system
- Metabolized in liver to active metabolite
- Biliary route is the major route of elimination
- Only 10-15% excreted unchanged in the urine
- Half-life 6-8 hours.

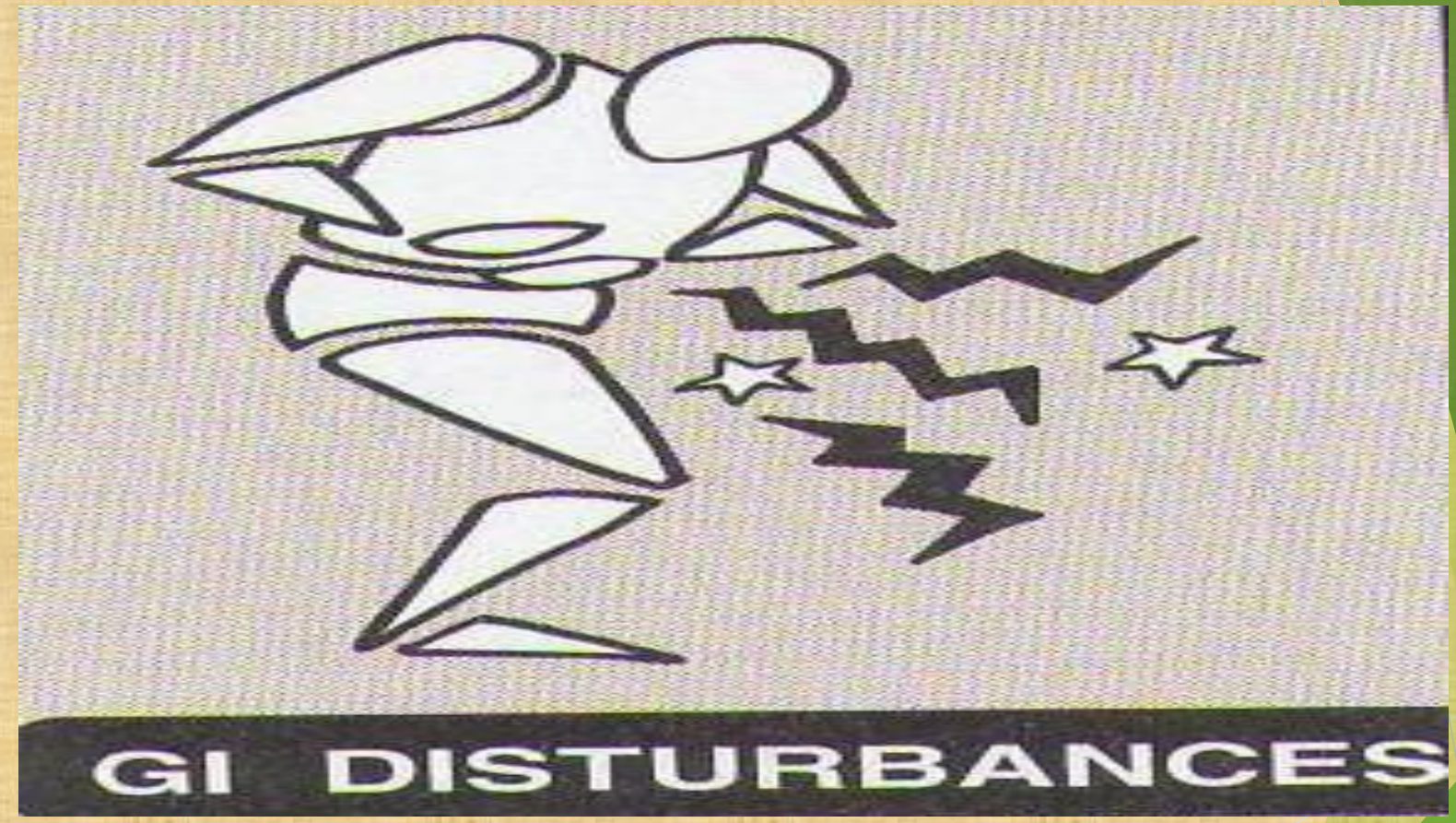
Azithromycin

- More effective on G-ve bacteria
- Stable at gastric acidity
- Undergo some hepatic metabolism (inactive metabolite)
- Biliary route is the major route of elimination
- Only 10-15% excreted unchanged in the urine
- Half-life (3 days)
- Once daily dosing
- No effect on cytochrome P- 450.

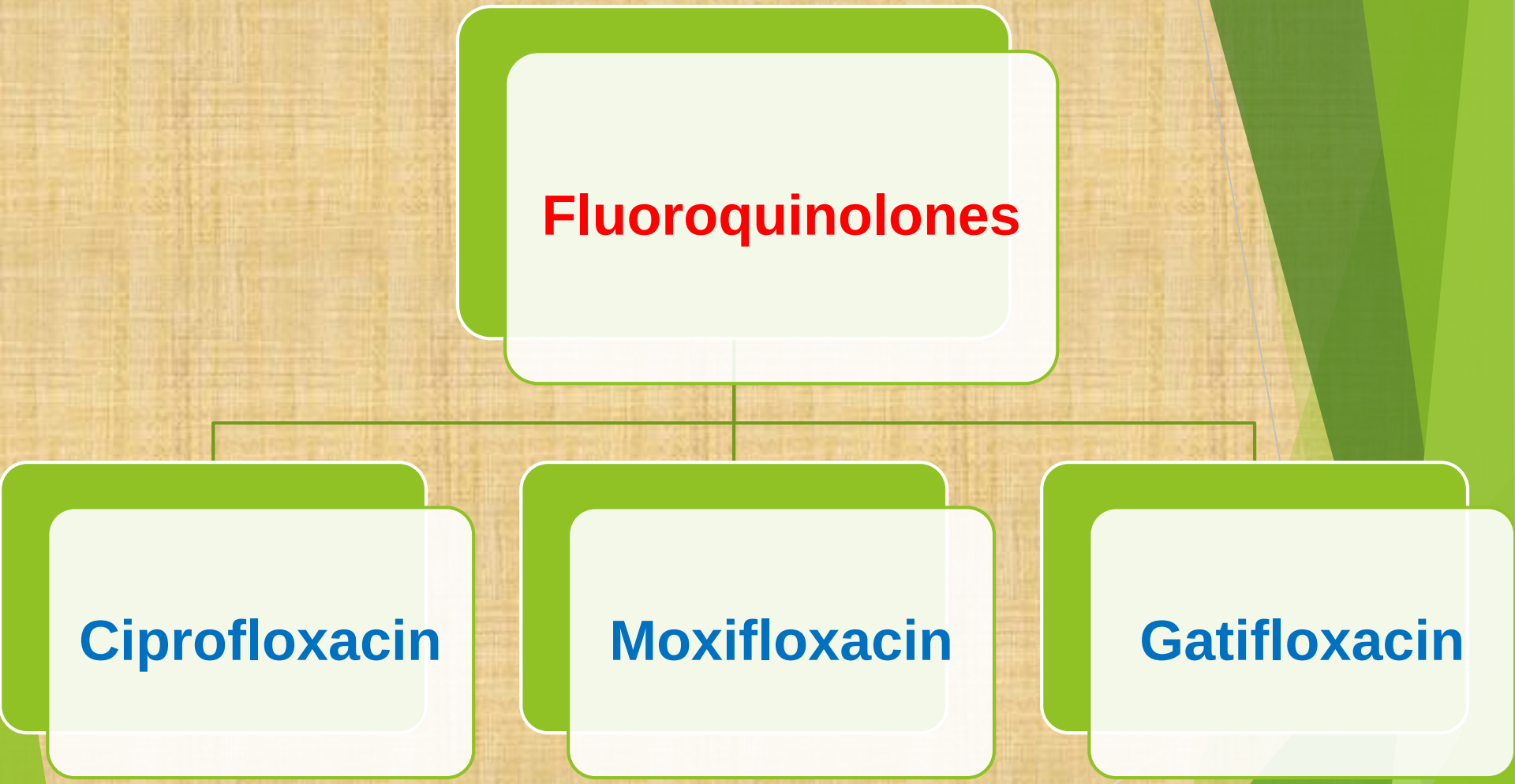
Clinical uses of Macrolides

- **Chlamydial pneumonia**
- **Legionella pneumonia.**

Adverse effects



- ✓
- ✓ **Hypersensitivity Reactions.**


Fluoroquinolones
Ciprofloxacin
Moxifloxacin
Gatifloxacin

Mechanism of action

Block bacterial DNA synthesis by inhibiting DNA Gyrase enzyme (an enzyme involved in DNA supercoiling).

Antibacterial spectrum

- **Ciprofloxacin mainly effective against G–ve bacteria**
- **Moxifloxacin & Gatifloxacin G –ve & G+ve & given once daily.**

(highly active against Pseudomonas species)

Pharmacokinetics

- Given po or parenterally
- Concentrates in many tissues (kidney, prostate, lung & bones/ joints)
- Excreted mainly through the kidney
- Their relatively long Half-life allow once daily (moxifloxacin & Gatifloxacin) & twice-daily (ciprofloxacin) dosing.

Clinical Uses

1. Acute exacerbation of chronic obstructive pulmonary disease
2. Community acquired pneumonia
3. Legionella pneumonia

Adverse effects

- Nausea, vomiting, diarrhea
- CNS effects (confusion, insomnia, headache, anxiety)
- Damage of growing cartilage (arthropathy)
- Phototoxicity (avoid excessive sunlight).

Contraindications

- Not recommended for patients younger than 18 years
- Pregnancy
- Breast feeding women.

THANK YOU