Treatment of Respiratory Tract Infections

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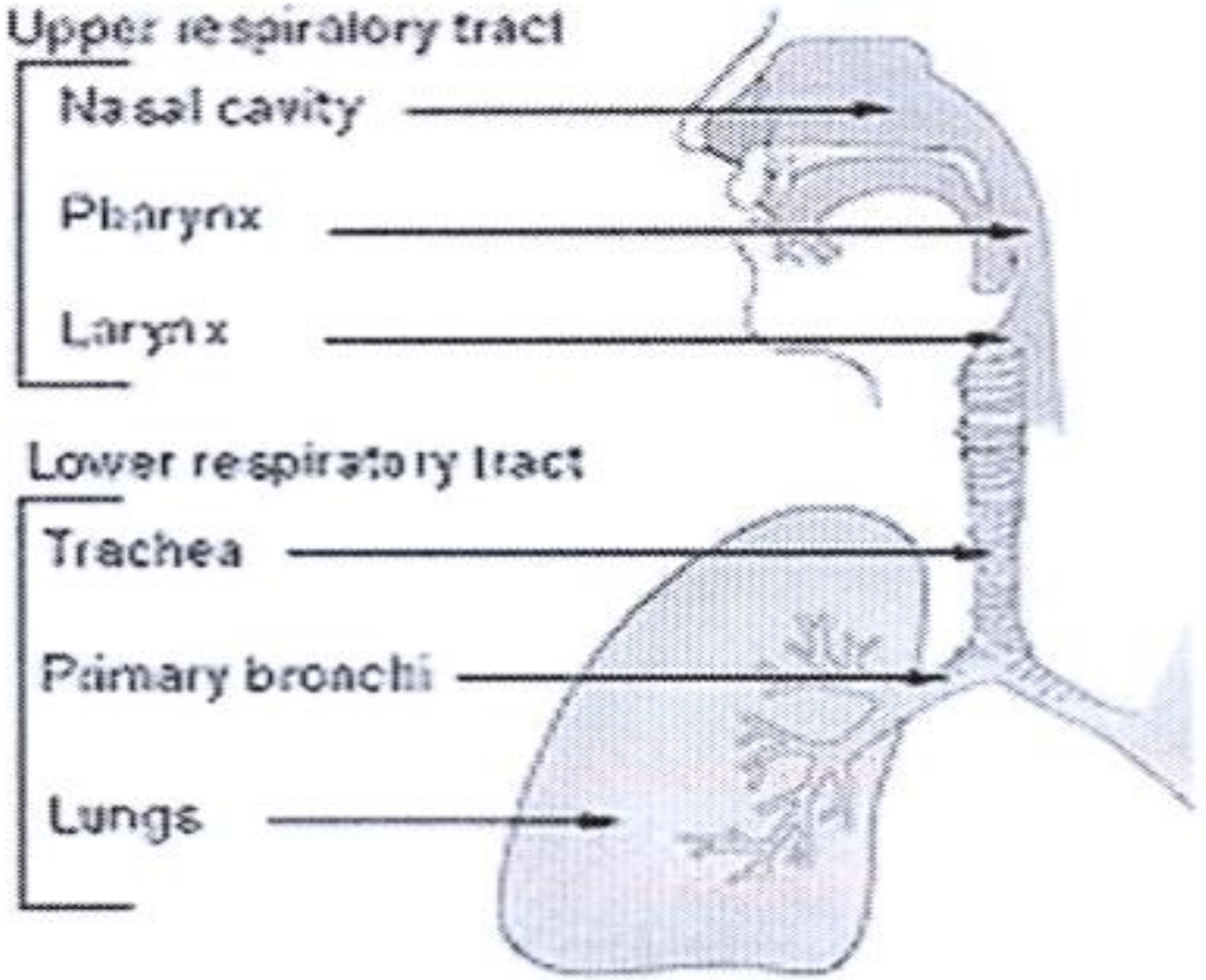
Objectives of the lecture

- At the end of lecture , the students should be able to understand the following:
- The types of respiratory tract infections
- The antibiotics that are commonly used to treat respiratory tract infections and their side effects.
- Understand the mechanism of action, pharmacokinetics of individual drugs.

Classification of respiratory tract infections

- 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 URTI›s

- **Viruses**

  (Should not be treated with antibiotics)

Treatment: rest and plenty of fluids, OTC cold, pain relievers.

- **Bacteria** (mainly Group A streptococcus
  H. influenzae

Treatment: Antibiotics. The type depends on:

Type of bacteria

Sensitivity test

LRTI's(costly & more difficult to treat)

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

  Acute

  Chronic

  Acute exacerbation of chronic bronchitis

  Causes: viruses or bacteria(H. influenza, S. pneumonia& M. catarralis).

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

  Community –acquired(CAP)

  Hospital-acquired

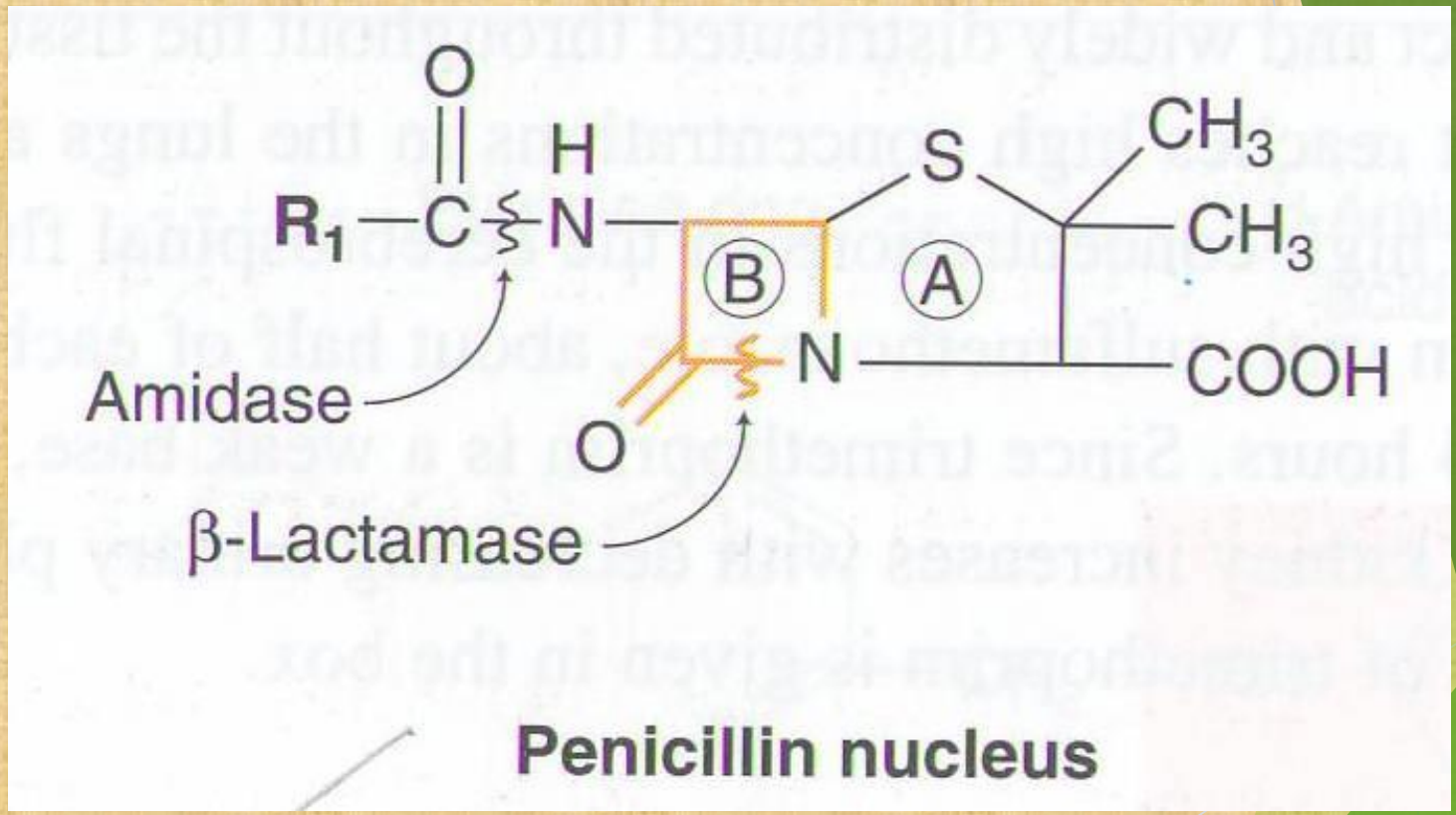
Causes:Bacteria

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

Antibiotics commonly used in the treatment of RTI's

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

Penicillins



Penicillin nucleus

Broad- spectrum penicillins

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

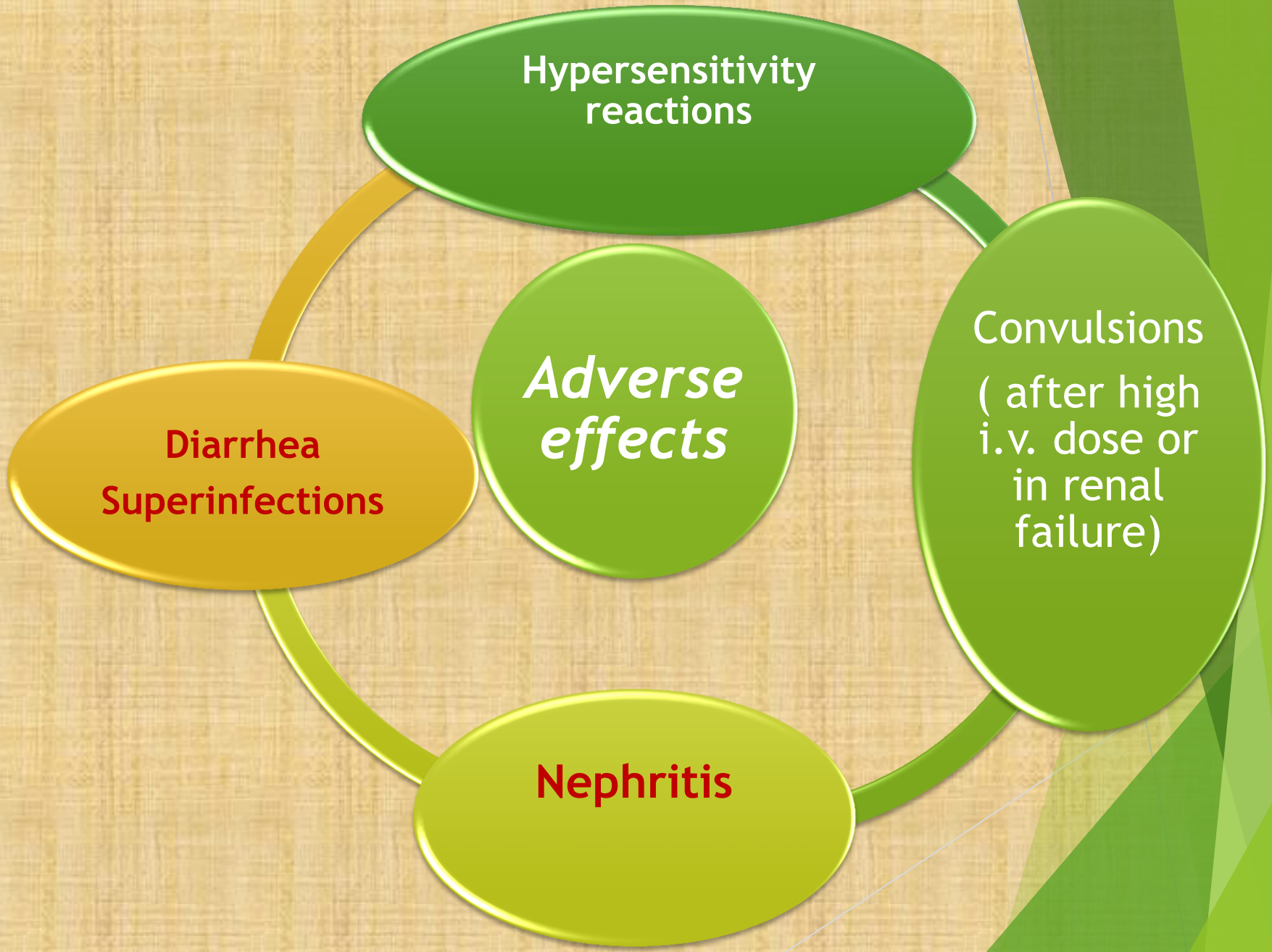
Act on both gram+ve & gram-ve microorganisms

Mechanism of action of Penicillins

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

Pharmacokinetics of Penicillins

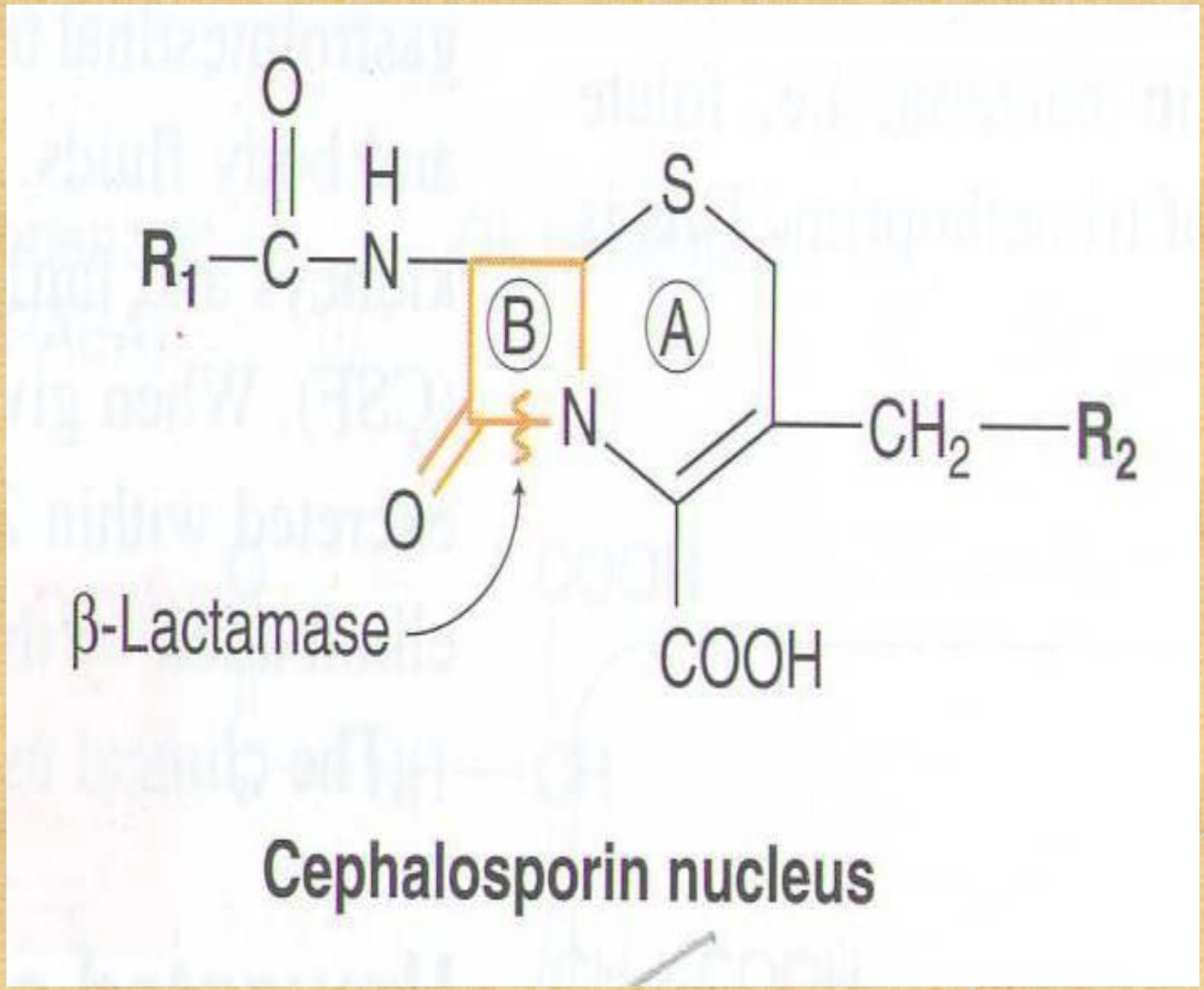
- Given orally or parenterally
- Not metabolized in human.
- Relatively lipid insoluble.
- Excreted mostly unchanged in urine.
- Probenecid slows their elimination and prolong their half live.
- Half-life 30-60 min(increased in renal failure renal failure).


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

Therapeutic uses of Penicillins

- Upper respiratory tract infections
- Lower respiratory tract infections

Cephalosporins



Cephalosporin nucleus

Mechanism of action of Cephalosporins

- Inhibit bacterial cell wall synthesis
- Bactericidal

(Similar to Penicillins)

1st Generation Cephalosporins

- Cephalexin
  - Given orally
  - Effective against gram positive bacteria.
  - Effective in URTI's

2nd Generation Cephalosporins

Cefuroxime axetil , cefaclor

- Given orally
- Effective mainly against Gram-negative bacteria.
- Well absorbed orally
- Active against ß-lactamase -producing bacteria

Uses:

- Upper and lower respiratory tract infections

3rd Generation Cephalosporins

Ceftriaxone / Cefotaxime / Cefixime

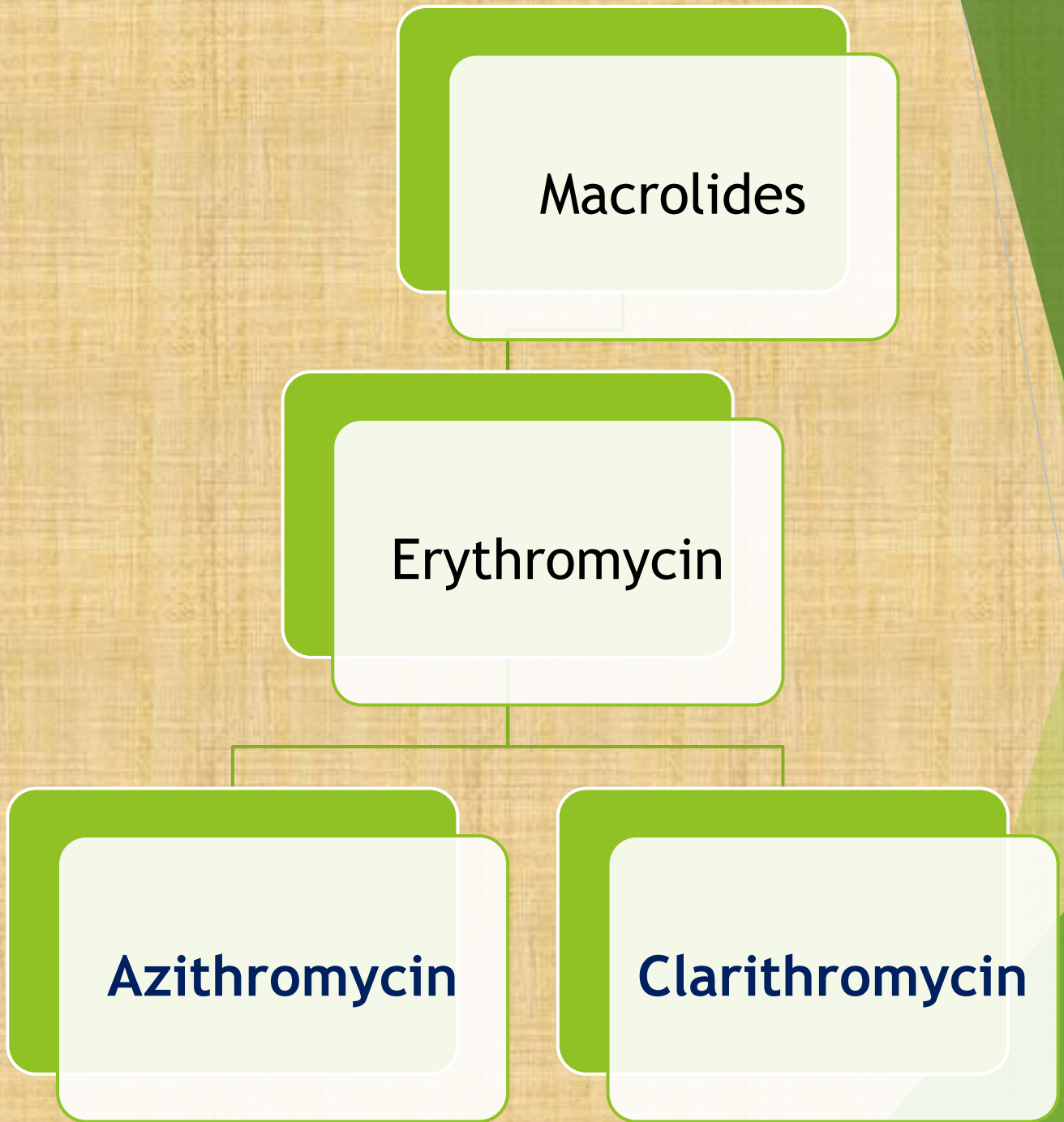
- Given by intravenous route
- More effective against gram-negative bacilli
- Effective treatment in pneumonia

Pharmacokinetics of Cephalosporins

Cephalosporins are given parenterally and orally.
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 and prolong their half live.
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 protein synthesis by binding to 50 S subunit of the bacterial ribosomes

Bacteriostatic

Bactericidal at high concentrations

Clarithromycin

- More effective on G+ve bacteria.
- Stable at gastric acidity
- Inhibits cytochrome P450 system
- Metabolized 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)

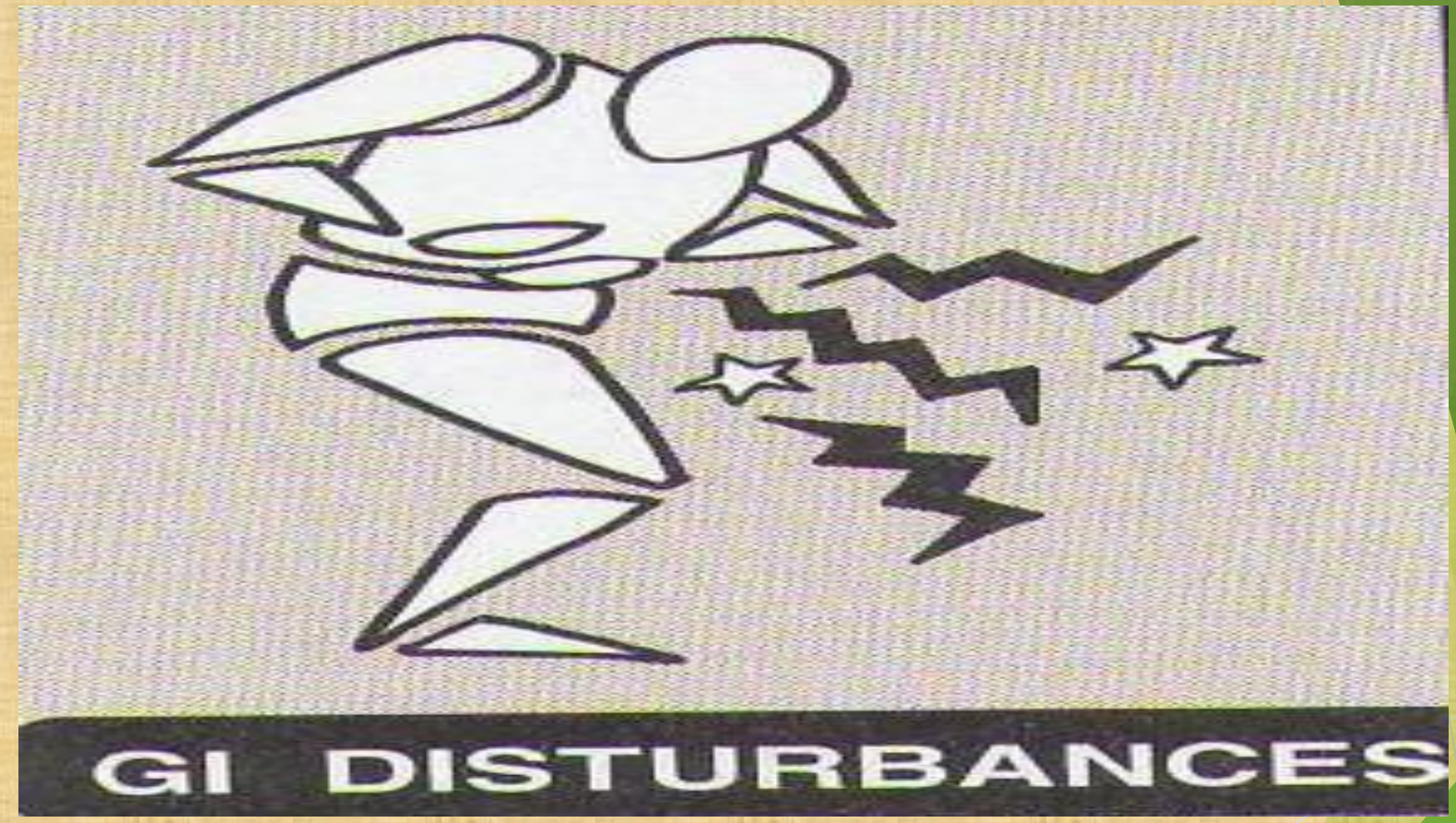
Once daily dosing

No effect on cytochrome P- 450

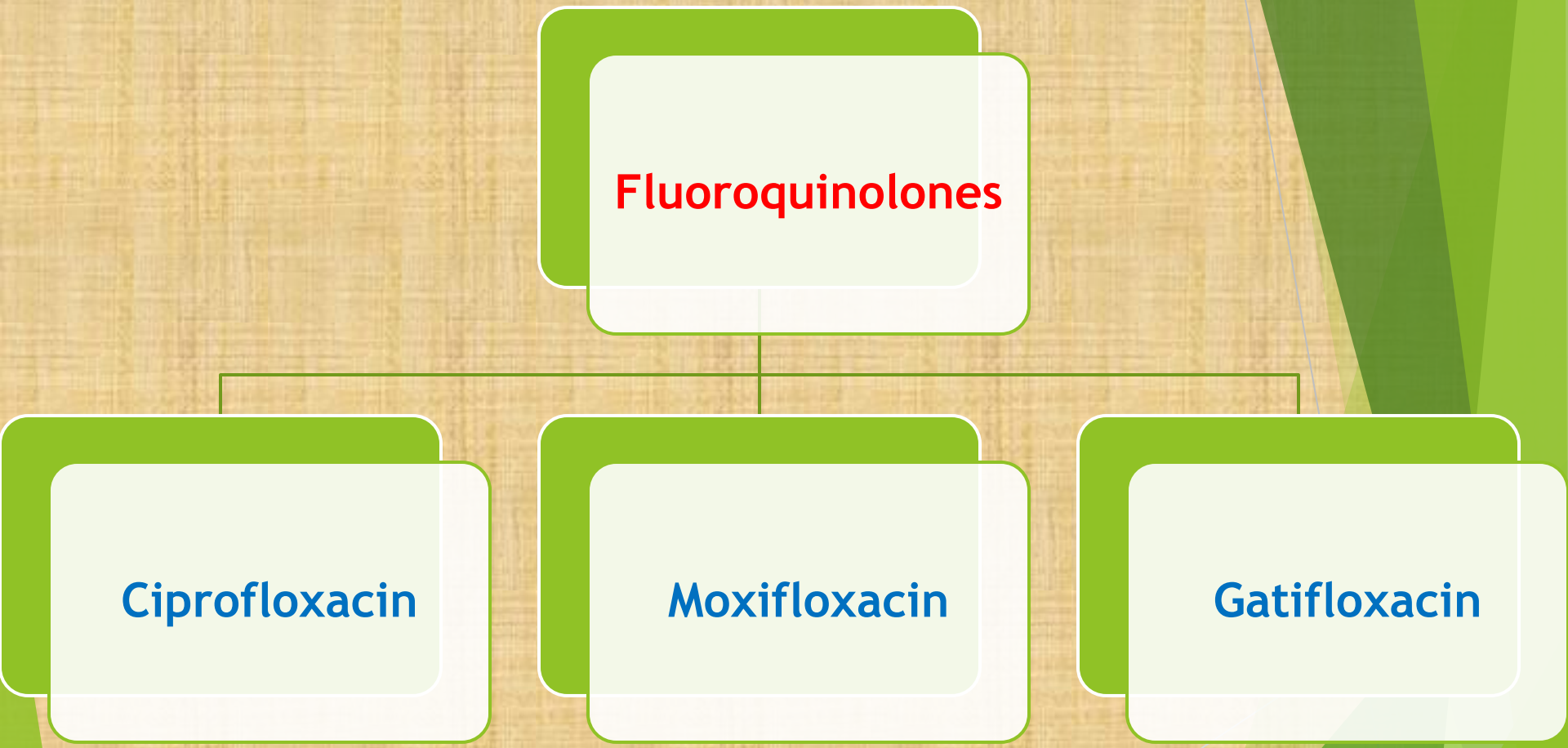
Clinical uses of Macrolides

- Chlamydial pneumonia
- Legionella pneumonia

Adverse effects



Hypersensitivity Reactions


Fluoroquinolones
Ciprofloxacin
Moxifloxacin
Gatifloxacin

Mechanism of action

Inhibit DNA Gyrase enzyme

(an enzyme involved in DNA supercoiling)

Antibacterial spectrum

Ciprofloxacin mainly effective against G – bacteria

Moxifloxacin & Gatifloxacin G – & G + & given once daily.

(highly active against Pseudomonas species)

Pharmacokinetics

- **Given orally 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

- Acute exacerbation of chronic obstructive pulmonary disease
- Community acquired pneumonia
- 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