Treatment of Respiratory Tract Infections

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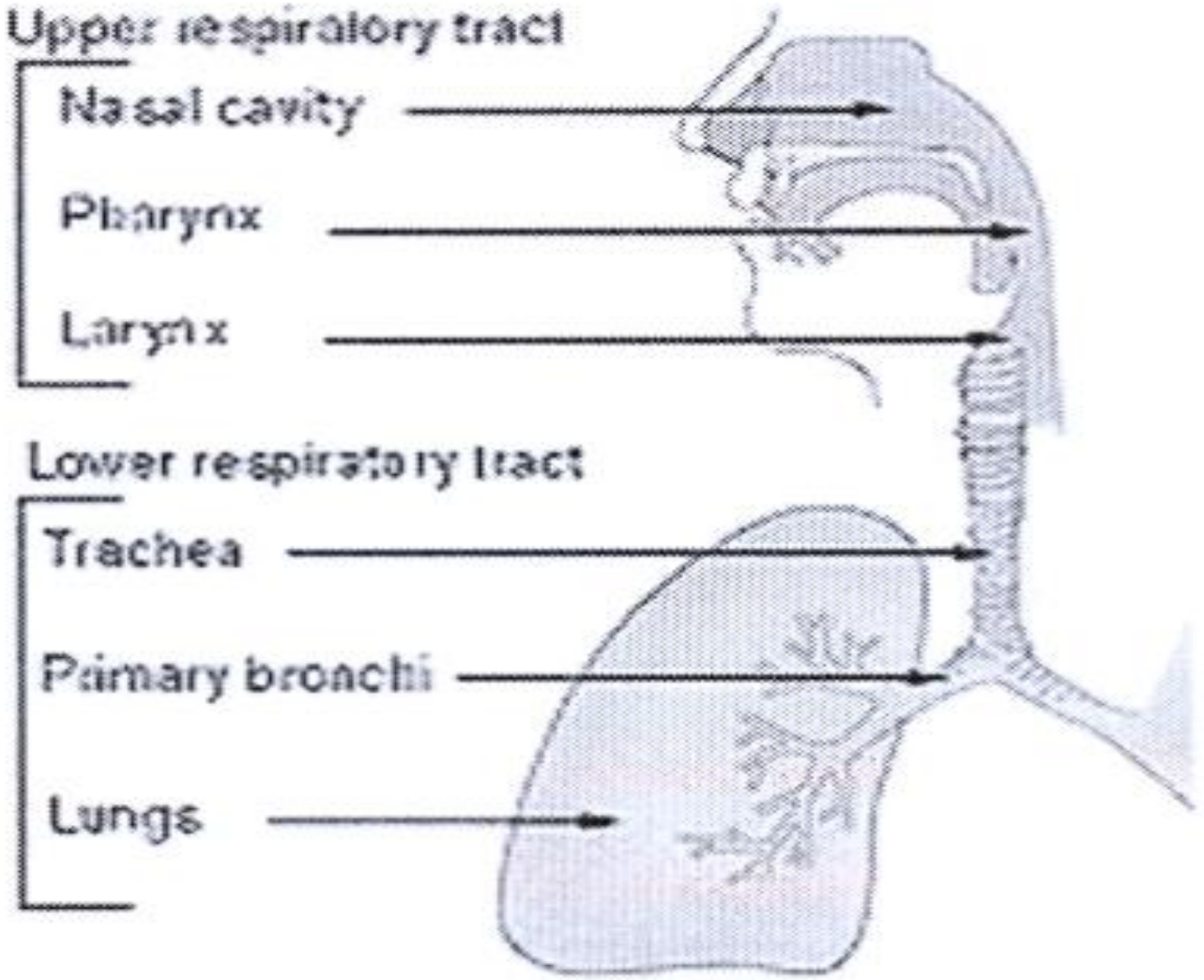
Objectives of the lecture

- 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

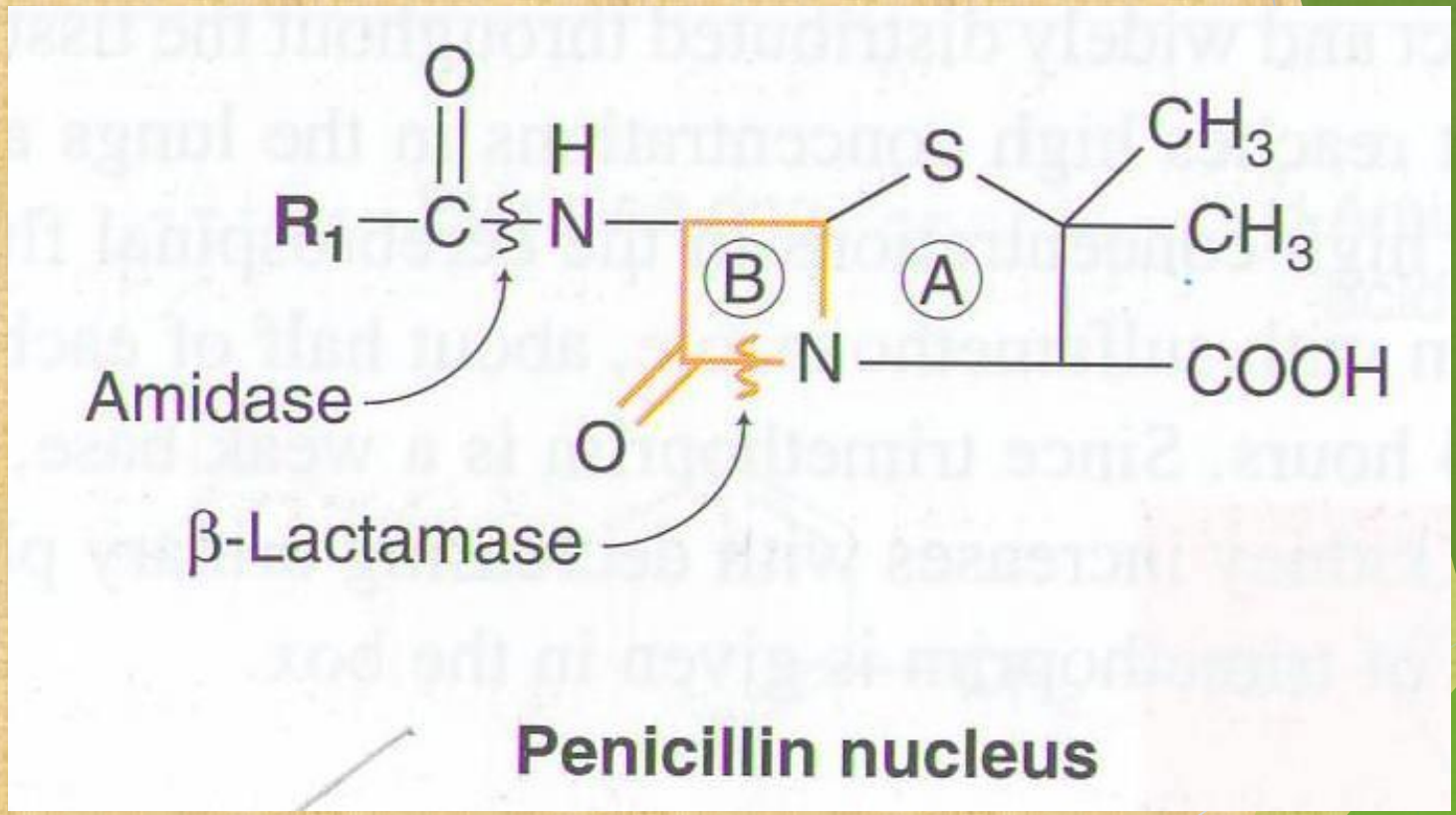
Causes:Bacteria

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

Antibiotics 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

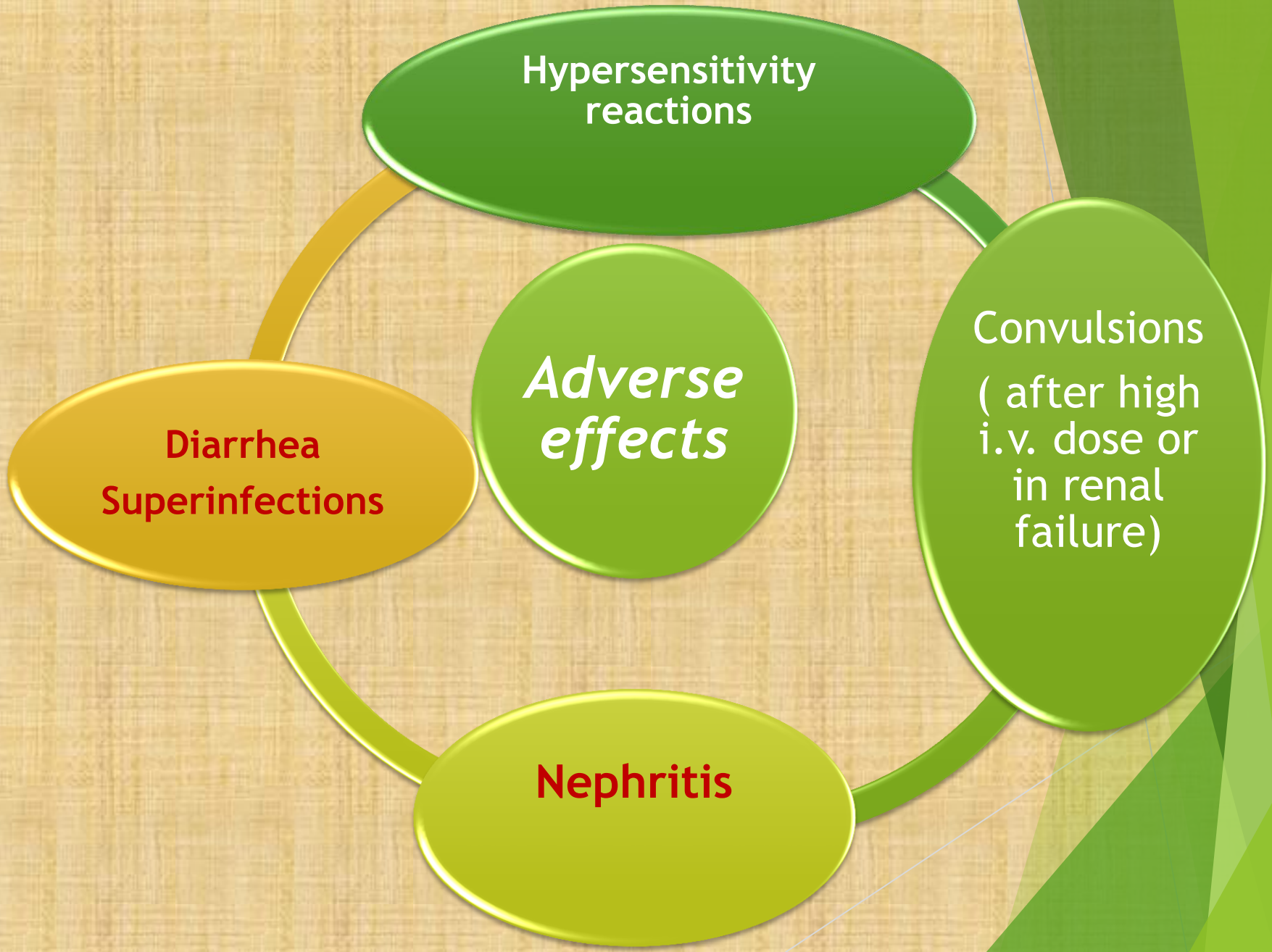
Acts on both gram+ve & gram-ve microorganisms

Mechanism of action

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

Pharmacokinetics

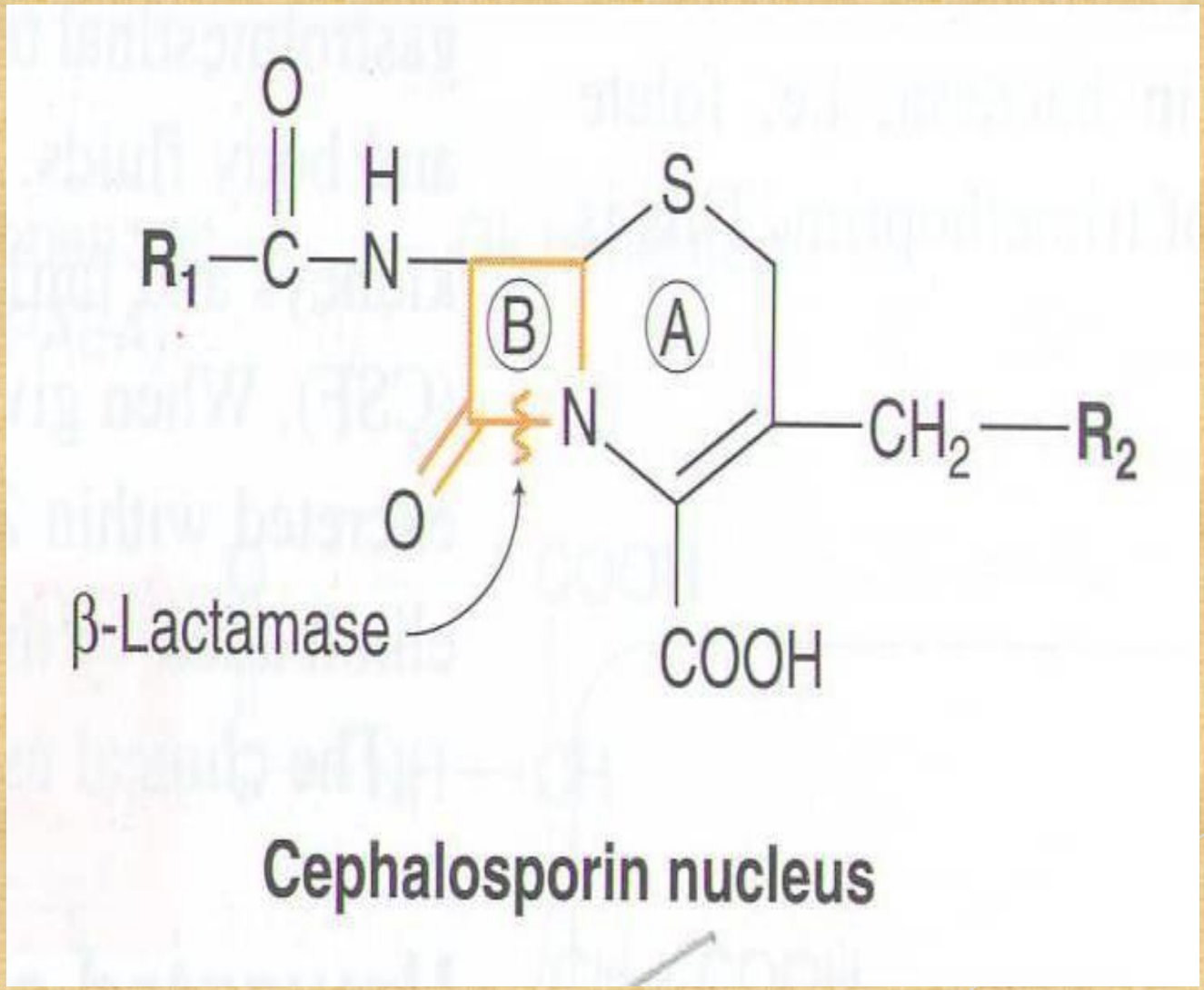
- Given orally or parenterally
- Not metabolized in human.
- Relatively lipid insoluble.
- Excreted mostly unchanged in urine.
- Half-life 30-60 min (increased in renal failure).


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

Therapeutic uses

- Upper respiratory tract infections, Acute otitis media especially those produced by Group A gram positive beta-hemolytic streptococci.
- Lower respiratory tract infections

Cephalosporin



Cephalosporin nucleus

Mechanism of action

- Inhibit bacterial cell wall synthesis
- Bactericidal

1st Generation Cephalosporins

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

2nd Generation Cephalosporins

Cefuroxime axetil , cefaclor

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

Uses:

- Upper and lower respiratory tract infections
- Sinusitis, otitis media

3rd Generation Cephalosporins

Ceftriaxone / Cefotaxime / Cefixime

- More effective against gram-negative bacilli
- Given by intravenous route
- Effective treatment in pneumonia produced by ß-lactamase bacteria

Pharmacokinetics

Given mainly parenterally

Oral preparation : Cefixime

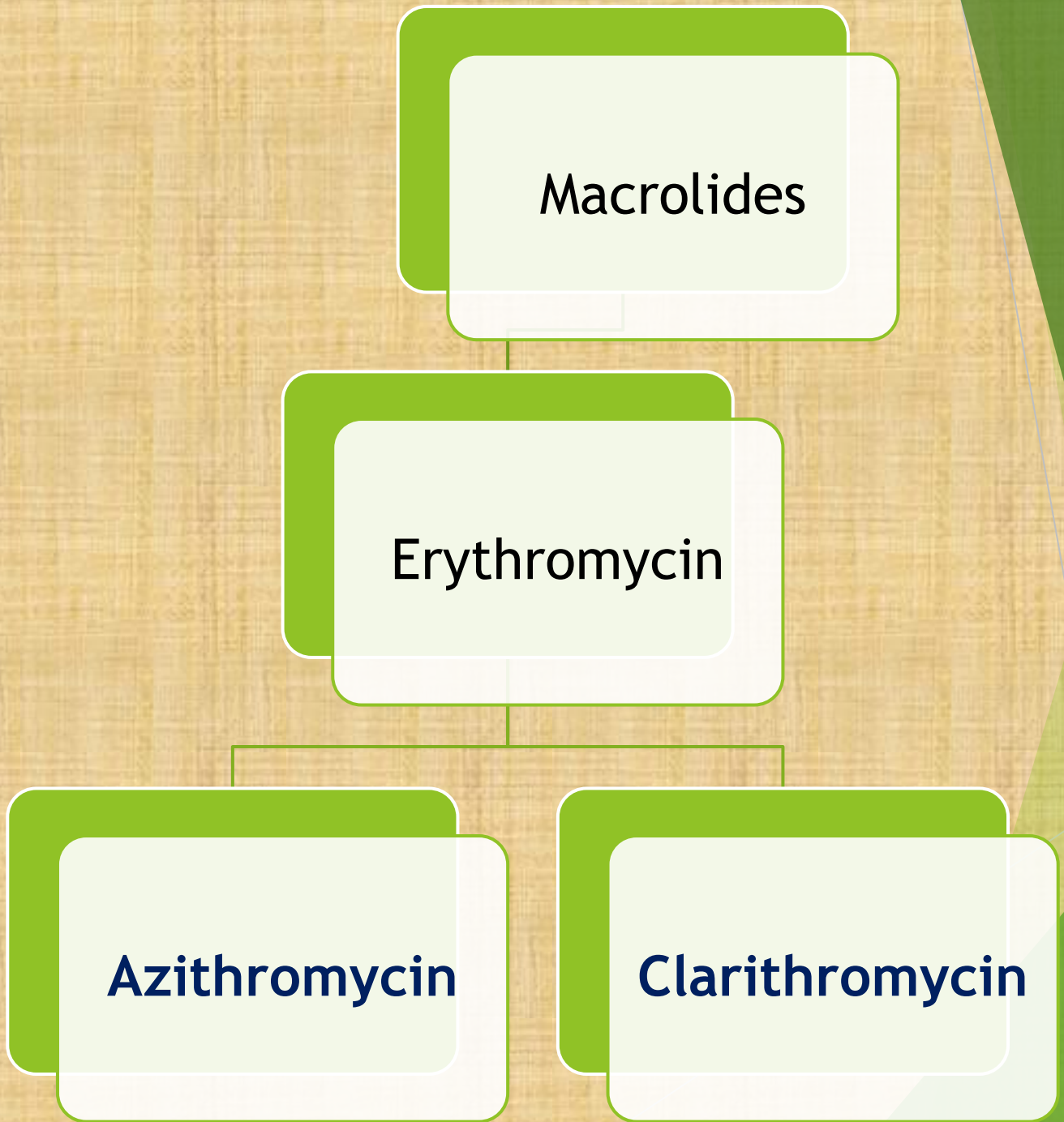
Penetration into CSF

Excreted Mostly unchanged in the urine.

Long Half-life(4-7h) (ceftriaxone)

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
- Excreted in urine 20-40%unchanged or metabolite & 60% in bile
- Half-life 6-8 hours

Azithromycin

More effective on Gram negative 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)

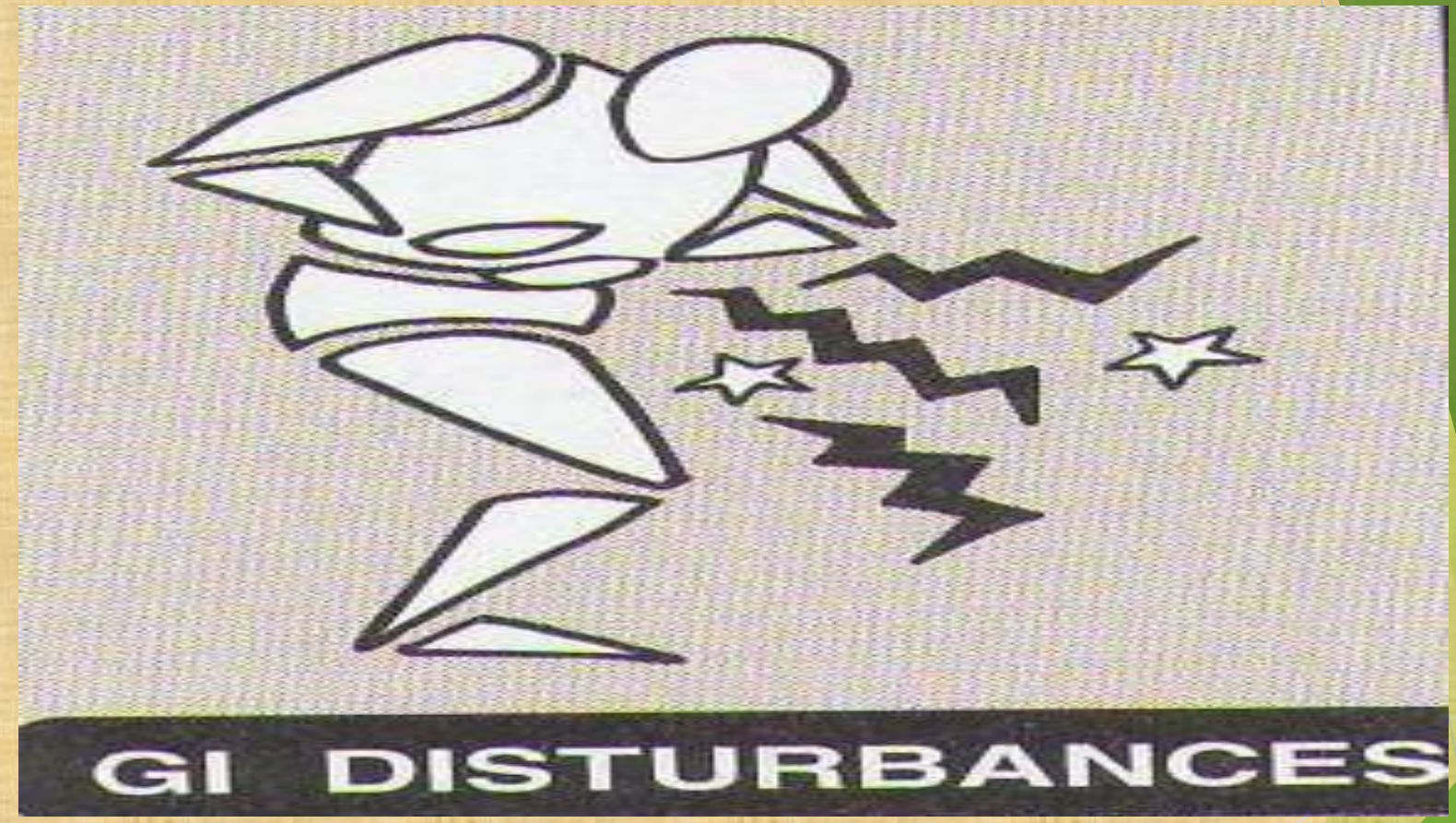
Once daily dosing

No effect on cytochrome P- 450

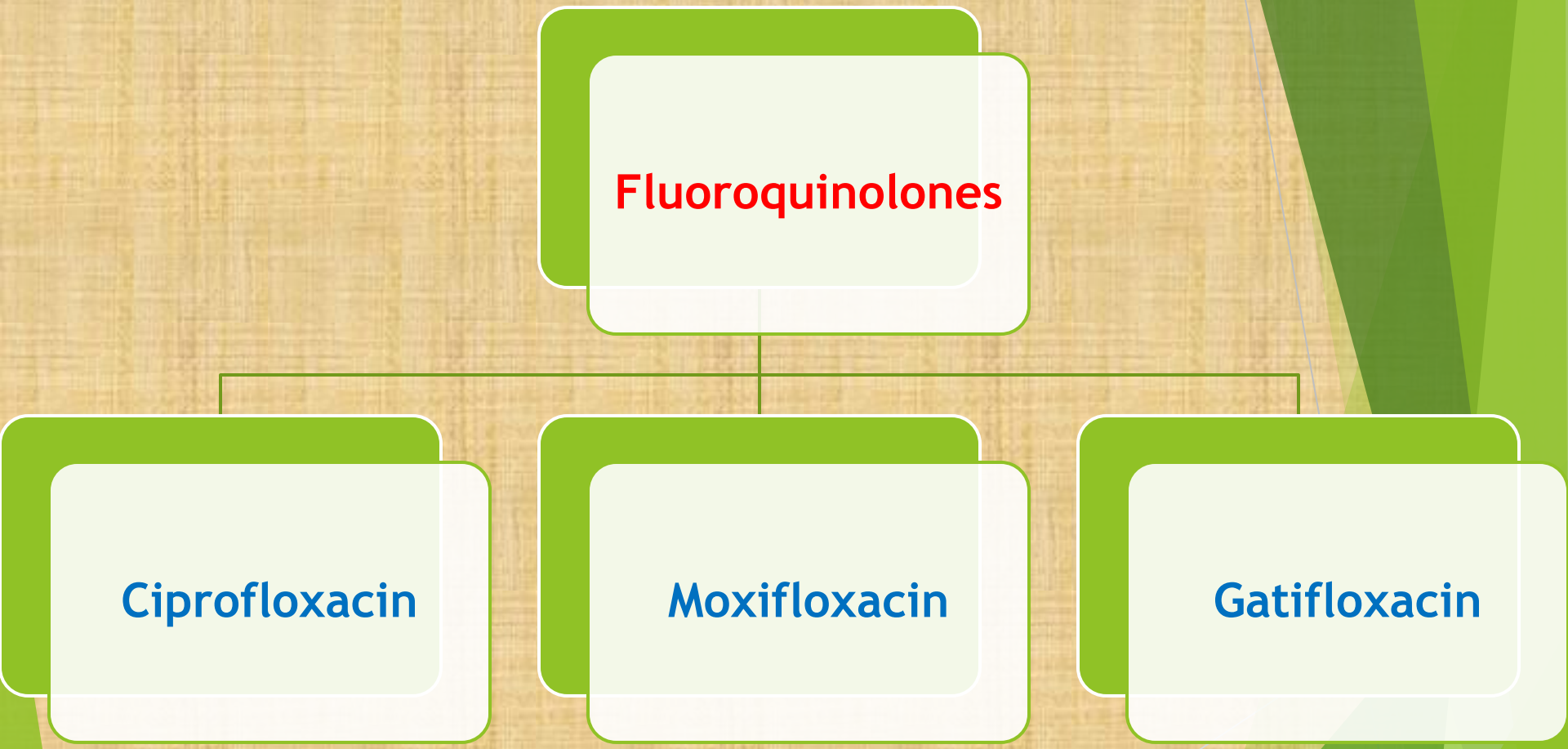
Clinical uses of Macrolides

- 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 allows 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