Antibiotics for Treatment of Pneumonia

I. MICROORGANISMS THAT CAN CAUSE PNEUMONIA

A. Gram-Positive Bacteria

- ***Streptococcus pneumoniae***
- ***Staphylococcus aureus***

B. Gram-Negative Bacteria

- ***Haemophilus influenzae***
- ***Pseudomonas aeruginosa***
- **Enterobacteriaceae Family:**
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Enterobacter* species
  - *Proteus* species
  - *Serratia* species
  - *Acinetobacter* species

C. Atypical Bacteria

- ***Mycoplasma pneumoniae***
- ***Chlamydia pneumoniae***
- ***Legionella pneumophila***

Causative Agents of Pneumonia:

Community-acquired pneumonia (CAP):
- **Streptococcus pneumoniae + Atypical Bacteria**
- Haemophilus influenzae (mainly in smokers and COPD).

Hospital-acquired and ventilator-associated pneumonia (HAP/VAP) or Severe CAP / ICU / Immunocompromised patients:
- **Gram-negative bacteria**
- **Staphylococcus aureus**
- **Pseudomonas aeruginosa**

Aspiration pneumonia:
- **Anaerobic bacteria**

Resistant / multidrug-resistant pneumonia:
- MRSA, VRSA
- Resistant Gram-negative bacteria

II. ANTIBIOTIC CLASSES AND THEIR ACTIVITY

1. β-lactam Antibiotics:

*(**Penicillins, Cephalosporins, Carbapenems, Monobactams**)*

- **General Properties: Bactericidal**; **Inhibit bacterial cell wall synthesis**; **No activity against atypical bacteria.**

A. Penicillins (Amoxicillin, Ampicillin):

c. *Coverage:* **Gram-positive bacteria** and **some Gram-negative bacteria**.

B. Penicillins + β-lactamase inhibitor (Amoxicillin–clavulanate, Ampicillin–sulbactam):

- *Coverage:* **Gram-positive**, **Gram-negative**, and **anaerobic bacteria**.

Aspiration pneumonia: Caused by **anaerobic bacteria aspirated from the oral cavity or gastric contents into the lungs**. These organisms commonly **produce β-lactamases**, making **simple penicillins ineffective unless combined with β-lactamase coverage.**

C. Antipseudomonal penicillin (Piperacillin–tazobactam): -*Potent Penicillins*-

- *Coverage:* **Gram-positive, Gram-negative, *Pseudomonas aeruginosa*, and anaerobic bacteria**.

(Often combined with **aminoglycosides or fluoroquinolones in severe infections for a broader coverage**)

D. Anti-staphylococcal penicillins (Oxacillin, Nafcillin):

- *Coverage:* Highly effective against **Methicillin-sensitive *Staphylococcus aureus* (MSSA).**

(Clinical Point: **Drugs of choice in case MSSA is confirmed to be the infecting agent**; preferred over broader agents because they are highly effective, narrow-spectrum, and less likely to promote resistance)

E. Cephalosporins

- **Second generation (Cefuroxime):** Covers **Gram-positive** and **Gram-negative bacteria**.

(effective against **CAP caused by β-lactamase–producing H. influenzae and Klebsiella** because it is **resistant to β-lactamase degradation**, unlike ampicillin)

- **Third generation (Ceftazidime):** Covers **Gram-negative bacteria** and ***Pseudomonas aeruginosa*.**

- **Fourth generation -Potent- (Cefepime):** Covers **Gram-positive, Gram-negative, *Pseudomonas aeruginosa***, and **penicillin-resistant *Streptococcus pneumoniae***.

F. Carbapenems (Imipenem, Meropenem)

- **Coverage: Gram-positive**, **Gram-negative, *Pseudomonas aeruginosa***, **anaerobes, and multidrug-resistant organisms.**
- **Clinical Points:**
  - **last-line** reserve drugs for **severe infections** or **febrile neutropenia**
  - **Meropenem** has **less Gram-positive activity** than imipenem.

G. Monobactams (Aztreonam)

- **Coverage: Gram-negative bacteria only,** used **only as add-on therapy** to **widen Gram-Negative coverage.**

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2. Antibiotics for Atypical Pneumonia Bacteria:

A. Macrolides (Azithromycin, Clarithromycin, Erythromycin)

- **Mechanism: Inhibit protein synthesis**
- **Coverage: Atypical bacteria** and **Gram-positive bacteria**.
- **Clinical Uses:**
  - Mainly used to **cover Atypical strains that cause CAP** as an **add-on drug,**
  - Drug of choice for **Corynebacterial infections** (Diphtheria, sepsis, erythrasma) and **Legionnaires' disease.**

B. Fluoroquinolones (Levofloxacin, Ciprofloxacin, Moxifloxacin)

- **Mechanism: Inhibit DNA synthesis** (By **inhibiting bacterial topoisomerase (DNA gyrase))**
- **Coverage: Gram-positive**, **Gram-negative**, **atypical bacteria**, and **intracellular organisms**.
- **Use:** Has a **very wide spectrum**, thus could be used as a **CAP Monotherapy**, covering both **Strep. Pneumoniae** and **Atypical Bacteria.**

- **Distinctions:**
  - **Levofloxacin:** Superior activity against ***S. pneumoniae***.
  - **Ciprofloxacin:** Most active against ***Pseudomonas aeruginosa*.**
  - **Moxifloxacin:** Most active against **anaerobic bacteria.**

C. Tetracyclines (Doxycycline, Minocycline, Tigecycline)

- **Mechanism: Inhibit protein synthesis.**
- **Coverage:** Very potent against **atypical bacteria**, effective also against **Gram-positives**, **Gram-negatives** and **Anaerobs**.
- **Clinical Relevance: Alternatives to macrolides and fluoroquinolones** in case they fail to treat **Atypical pneumonia**.

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3. Aminoglycosides (Gentamicin, Amikacin, Tobramycin):

- **Mechanism: Bactericidal; inhibit protein synthesis**.
- **Coverage: Gram-negative bacteria only** (including *Pseudomonas*).
- **Note:** Just **like Monobactams**, used **only as add-on therapy** to **widen Gram-Negative coverage**.

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4. Antibiotics for Multidrug-Resistant Strains:

A. Resistant Gram-Positive Drugs:

- **Vancomycin:**
  - Mechanism: **Inhibits Cell Wall synthesis**
  - *Coverage:* **Resistant Gram-positives only**
  - *Uses:* **Penicillin-Resistant strains of Staph and Strep**, **Methicillin-Resistant strains** (**Ex: MRSA),** or in **patients allergic to penicillin**.
- **Linezolid:**
  - Mechanism: **Inhibit protein synthesis,** primarily **bacteriostatic**, but **bactericidal against streptococci.**
  - *Coverage:* **Resistant Gram-positives** (Including **Vancomycin-Resistant Staph. Aureus and Enterococcus)**

B. Resistant Gram-Negative Drugs:

- **Polymyxin B, Polymyxin E (Colistin):**
  - Mechanism: Act as **cationic detergents; disrupt cell membranes**.
  - Coverage: **Multidrug-Resistant Gram-negative bacteria**.

CLINICAL SCENARIOS, LIKELY BACTERIA, AND TREATMENT

Clinical Scenario	Likely Bacteria	Clinical Logic (Explanation)	Antibiotic Family/Class	Specific Examples
Community-Acquired (CAP)	*S. pneumoniae*, Atypical bacteria	Treatment must cover both *S. pneumoniae and* Atypical bacteria	**Beta-Lactam** + **Macrolide** (or Respiratory Quinolone)	**Ampicillin** + **Azithromycin** (or Levofloxacin)
Aspiration Pneumonia	Anaerobic bacteria	Occurs when stomach/mouth contents enter the lungs; requires drugs that work in low-oxygen environments.	**Beta-Lactam+ Beta-Lactamase Inhibitor**	**Ampicillin–Sulbactam** or **Amoxicillin–Clavulanate**
Hospital-Acquired (HAP / VAP) Or Severe Immunocompro-mised patient	Gram-negative, *P. aeruginosa*, *S. aureus*	Hospital bugs are often resistant. We need drugs specifically designed to kill *Pseudomonas*.	**Strong, Antipseudomona-l Beta-Lactam** (± Aminoglycoside)	**Piperacillin–Tazobactam** or **Cefepime**
MRSA Pneumonia	MRSA	Standard antibiotics cannot bind to MRSA. We need drugs that target its specific resistant wall.	**----**	**Vancomycin** or **Linezolid**

Adverse Effects of Pneumonia Antibiotics

Penicillins:

- **Hypersensitivity reactions** (**Penicillin Allergy**)→ rash, urticaria, anaphylaxis
- **Sodium overload** with **antipseudomonal penicillins → heart failure, hypokalemia**
- **Ampicillin rash in infectious mononucleosis patients (100%)**
- **Superinfection**: **pseudomembranous colitis** and **vaginal candidiasis**

Cephalosporins:

- **Bleeding disorders** (hypoprothrombinemia, platelet dysfunction)
- **Cross-reactivity with penicillin allergy (5–10%)**

Carbapenems (Imipenem, Meropenem):

- **Seizures** (especially imipenem)

Monobactam (Aztreonam):

- **Minimal allergy cross-reactivity with penicillins**
- **Elevation of serum aminotransferases**

Aminoglycosides (Gentamicin, Amikacin, Tobramycin):

Mnemonic (NO GAP):

- **N**ephrotoxicity
- **O**totoxicity
- **G**estational contraindication
- **A**pnea (**Neuromuscular junction block at high doses -> respiratory paralysis, Calcium gluconate** and **neostigmine are antidotes)**
- **P**ain at injection site

Fluoroquinolones:

- **Tendonitis and tendon rupture**
- **Cartilage damage → contraindicated in children <18 & pregnancy**
- **QT prolongation → arrhythmias**
- **Hyperglycemia** (especially gatifloxacin)
- **CNS effects** (dizziness, insomnia)
- **Photosensitivity**

Macrolides (Erythromycin mainly):

- **Cholestatic hepatitis -> Jaundice**
- **Increased gastrointestinal motility due to stimulation of motilin receptors -> Diarrhea**
- **CYP450 inhibition**

Tetracyclines (Doxycycline, Minocycline, Tigecycline):

- **Photosensitivity**
- **Teeth discoloration & bone growth inhibition (For fetal bone and teeth) -> contraindicated in pregnancy and children <8 years**

Vancomycin:

- **Red man (or Red Neck) syndrome** (infusion-related flushing), can be reduced by **prolonging infusion or increasing the dosing interval.**
- **Nephrotoxicity**
- **Ototoxicity**

Linezolid:

- **Thrombocytopenia**
- **MAO inhibition**

Polymyxins (Colistin, Polymyxin B):

- **Severe nephrotoxicity**
- **Neurotoxicity**
- **Electrolyte disturbances (Hypocalcemia, Hypomagnesemia, Hypokalemia ..)**
- **Rhabdomyolysis**
- **Clostridium difficile associated diarrhea**

General adverse effects of pneumonia antibiotics:

- Most of these pneumonia antibiotics share common adverse effects, including **gastrointestinal upset** (nausea, vomiting, diarrhea), **headache and dizziness**, **hypersensitivity reactions**, **nephrotoxicity**, and in some cases **bone marrow suppression**.

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