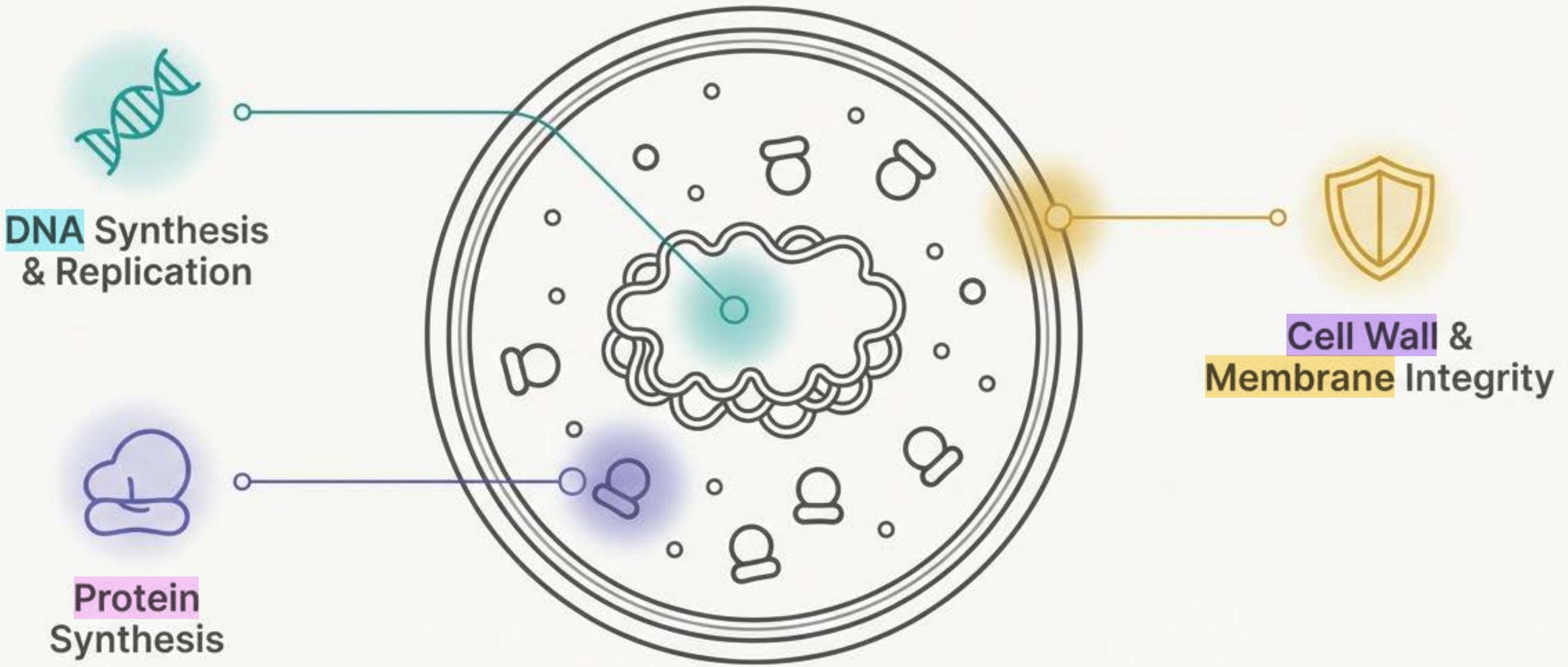
DOPAMINE
SCIENTIFIC TEAM

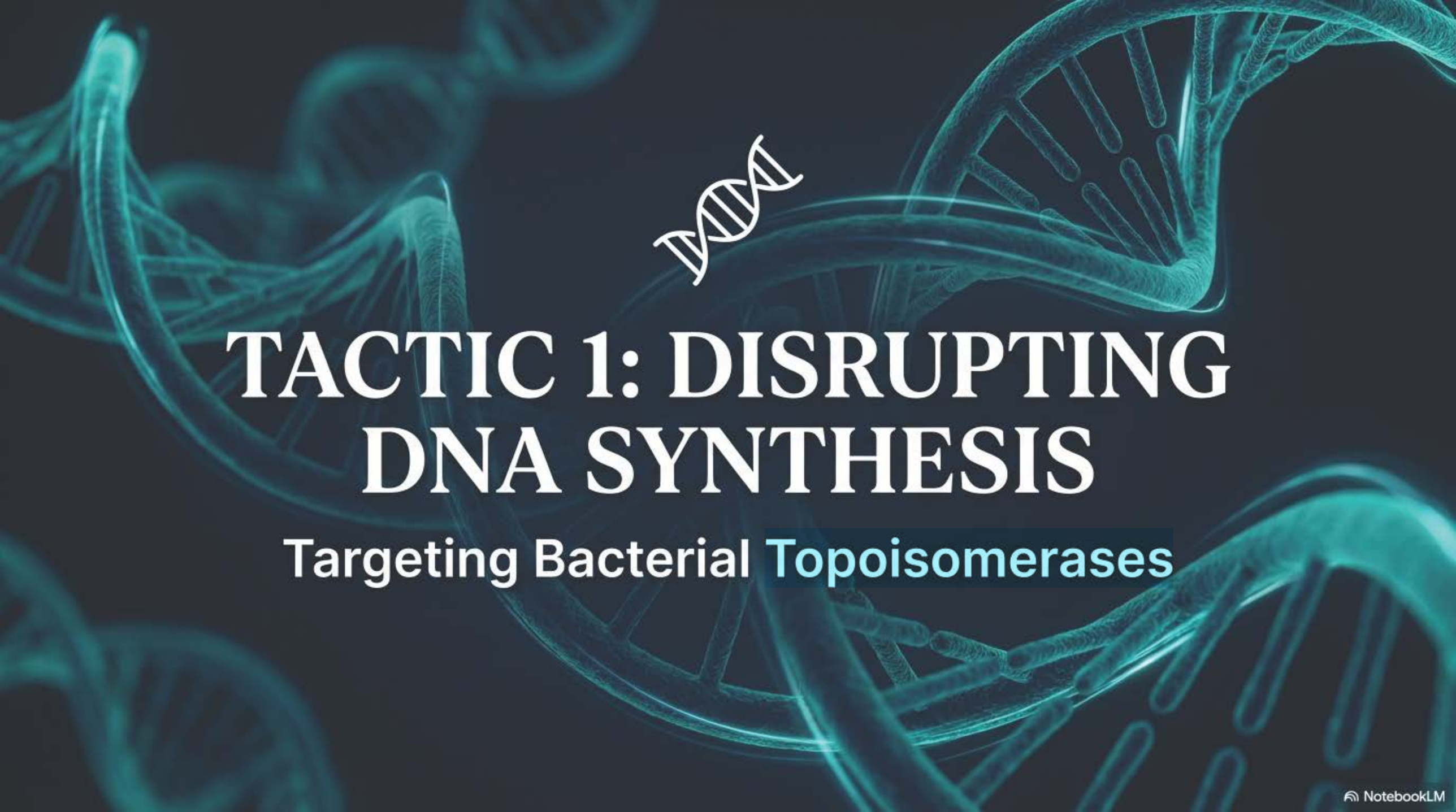
Drugs for Bacterial Pneumonia: A Tactical Guide

A Review of Key Antibiotic Classes | Pharmacology Lecture 7

The Bacterial Battlefield: Our Strategic Targets

To defeat bacterial pathogens, we must exploit their vulnerabilities. This guide is organized by three primary tactical approaches based on the bacterial targets they disrupt.





TACTIC 1: DISRUPTING DNA SYNTHESIS

Targeting Bacterial Topoisomerases

The Fluoroquinolones: Precision DNA Strikes

Mechanism of Action

Inhibit bacterial topoisomerase II (DNA gyrase) & topoisomerase IV, blocking bacterial DNA synthesis.

Spectrum of Activity

- Excellent Gram-negative activity (Enterobacteriaceae, Pseudomonas, Neisseria).& H.Infleunzae & Campylobacter
- Moderate-to-good activity against Gram-positive bacteria.
- Active against agents of atypical pneumonia (Mycoplasma, Chlamydia) and intracellular pathogens (Legionella).

& Mycobacterium

Key Agents & Strategic Use

Respiratory Fluoroquinolones

Levofloxacin, Gemifloxacin, Gatifloxacin, and Moxifloxacin (used for upper/lower respiratory tract infections).

Agent-Specific Superiority

Levofloxacin: Superior activity against *S. pneumoniae*.

Ciprofloxacin (Prototypical): Most active against *Pseudomonas aeruginosa*.

Moxifloxacin: Good activity against anaerobic bacteria.

Fluoroquinolones: Collateral Damage & Warnings

Common Adverse Reactions

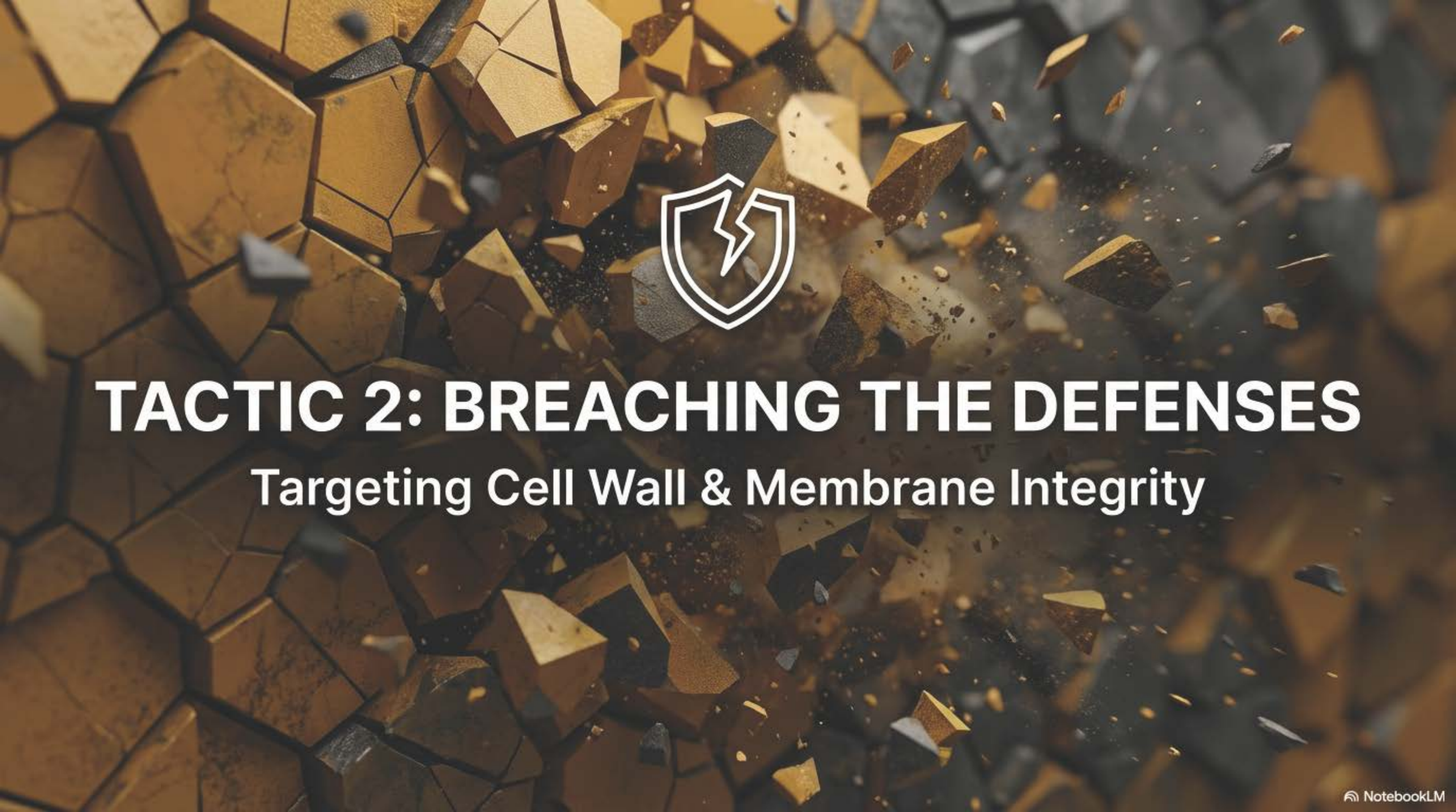
- GI: Nausea, vomiting, diarrhea.
- CNS: Headache, dizziness.
- Abnormal liver function tests.

Serious & Specific Reactions

- **QTc Prolongation:** Occurs with Gatifloxacin, Levofloxacin, Gemifloxacin, and Moxifloxacin (arrhythmogenic risk).
- **Cartilage Damage & Arthropathy:** Should not be used in patients under 18 years of age.
- **Tendonitis & Tendon Rupture:** Especially the Achilles tendon in adults.
- **Photosensitivity:** Reported with Lomefloxacin and Perfloxacin.

⚠ Special Alerts

- **Contraindicated in Pregnancy:** Damages fetal cartilage and impairs skeletal development.
- **Gatifloxacin-Associated Dysglycemia:** Damages pancreatic β-cells, causing initial hypoglycemia followed by hyperglycemia.
- **Hepatotoxicity Monitoring:** Elevation of liver enzymes ≥3 times the upper limit of normal warrants monitoring.



TACTIC 2: BREACHING THE DEFENSES

Targeting Cell Wall & Membrane Integrity

Vancomycin: The Wall Breaker

Mechanism: Inhibits cell wall synthesis.

Therapeutic Uses

- **IV:** Sepsis and endocarditis caused by Methicillin-resistant *Staphylococcus aureus* (MRSA). This is its main indication.
- **IV:** Staphylococcal/streptococcal endocarditis in patients with penicillin allergy.
- **Oral:** *Clostridium difficile* colitis (though Metronidazole is preferred).

Combination Therapy

- With Gentamicin for enterococcal endocarditis.
- With Cefotaxime/Ceftriaxone for highly penicillin-resistant pneumococcal meningitis.

Adverse Effects

⚠ 'Red Man Syndrome': Infusion-related flushing from histamine release. Mitigated by slowing the infusion rate.

- **Oto/Nephrotoxicity**: Risk increased with other toxic drugs.
- Neutropenia, Phlebitis. & Hypersensitivity fever

Monitoring

- **Peak:** 20-40 mg/L
- **Trough:** 5-10 mg/L

Polymyxins (~~Colistin~~): The Last Resort

Very Rarely Used

Mechanism, Spectrum & Role

- **Mechanism:** Act as cationic detergents, attaching to and disrupting bacterial cell membranes.

- **Spectrum & Role:** Active against Gram-negative bacteria.

- **Resistant organisms:** Gram-positives, Proteus, Neisseria.

- **Clinical Use:** Salvage therapy for multi-drug resistant Gram-negative infections (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*).

- **Administration:** Largely restricted to topical/inhalation use. ~~Parenteral use is reserved for dire situations due to toxicity.~~

High Toxicity Profile

- **Severe Nephrotoxicity:** "The most nephrotoxic drugs ever used."
- Neurotoxicity.
- Severe Electrolyte Disturbances: Hypocalcemia, hypomagnesemia, and hypokalemia.
- Rhabdomyolysis.

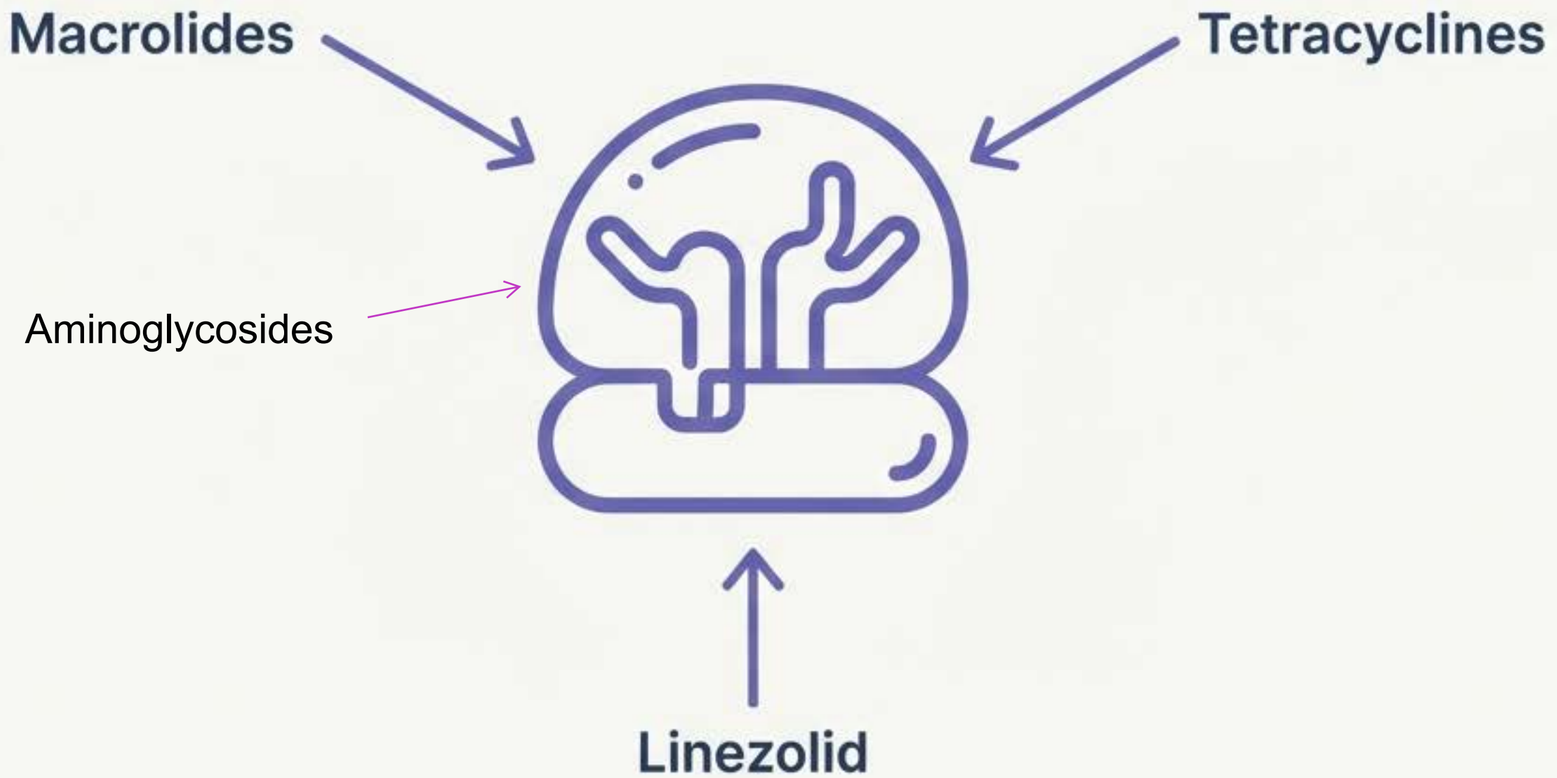
Can Cause (Cl.difficle) diarrhea if given oraly or IV (Rarerly)

TACTIC 3: HALTING PRODUCTION

Targeting Bacterial Protein Synthesis

Three Classes Targeting the Ribosome

This tactical group includes three distinct classes that interfere with the bacterial ribosome to halt protein production. While their target is the same, their specific mechanisms, uses, and risk profiles differ significantly.



Bacteriostatic Inhibitors for Protein Synthesis .

Macrolides & Tetracyclines: The Workhorses

Important notes

Macrolides (Erythromycin, Azithromycin, etc.)

Role

Drug of choice for Atypical Pneumonia (*Mycoplasma, Legionella*). Also used for Diphtheria and Chlamydia infections.

Key Adverse Effects

Major epigastric distress, Acute cholestatic hepatitis (Erythromycin), increased GI motility (Erythromycin via motilin receptors). & Eosinphilia , Rash , Fever due to allergy

Critical Interaction

Erythromycin is a potent inhibitor of CYP3A4 enzymes, increasing concentrations of many other drugs. This is not seen with Azithromycin.

Tetracyclines (Doxycycline, Tigecycline, etc.)

Role

Alternative for atypical pneumonia. Broad-spectrum but not a firstline therapy for typical infections.

Key Adverse Effects

Photosensitivity, GI distress, Superinfections (Pseudomonas, Candida, etc.), Vestibular reactions (dizziness, vertigo). & Liver,Kidney & Local Toxicity

CRITICAL WARNING

Contraindicated in pregnancy & children <8 years. Causes deposition in bone & teeth, leading to fluorescence, discoloration, enamel dysplasia, and growth inhibition.

Linezolid: The Specialist

Mechanism & Spectrum

- Unique inhibitor of protein synthesis *initiation*.
- Primarily bacteriostatic (bactericidal for streptococci).
- Active against Gram-positive organisms (Staphylococci, Streptococci, Enterococci).

Clinical Role

Reserved for multi-drug resistant Gram-positive infections.

Used for Vancomycin-resistant *S. aureus* (VRSA) and *E. faecium* (VRE), nosocomial pneumonia, and skin infections.

Adverse Effects

- Thrombocytopenia, neutropenia.
- Gastrointestinal upset, headache.

Significant Drug Interaction

Weak MAO Inhibition: Risk of hypertensive crisis or serotonin syndrome when combined with interacting agents.

The Arsenal at a Glance

Class	Primary Tactic (Mechanism)	Key Clinical Use	Signature Adverse Effect / Warning
Fluoroquinolones 	Inhibit DNA Synthesis	G- incl. Pseudomonas/Atypicals	Tendon Rupture / QTc Prolongation
Vancomycin 	Inhibit Cell Wall Synthesis	MRSA	Red Man Syndrome
Polymyxins 	Disrupt Cell Membrane	Multi-drug resistant G-	Severe Nephrotoxicity
Macrolides 	Inhibit Protein Synthesis	Atypical Pneumonia	CYP3A4 Inhibition (Erythro)
Tetracyclines 	Inhibit Protein Synthesis	Alt. for Atypicals	Contraindicated in Children <8
Linezolid 	Inhibit Protein Synthesis	MRSA/VRE	Weak MAO Inhibition

Strategic Imperatives

Know Your Target

Match the drug's spectrum to the pathogen. (e.g., Vancomycin for MRSA, Macrolides as the drug of choice for Atypicals).

Know Your Patient

Always consider contraindications like age and pregnancy (Tetracyclines, Fluoroquinolones) and the patient's immune status.

Know The Risks

Be vigilant for class-defining toxicities (Polymyxin nephrotoxicity, Vancomycin's Red Man Syndrome) and critical drug interactions (Erythromycin's CYP inhibition, Linezolid's MAO inhibition).

Resources & Feedback

Feedback

Scan for feedback.

Corrections from Previous Versions

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1		Source Serif Pro Regular	
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Acknowledgements

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