

Other Antibiotics

Jason Ryan, MD, MPH

Other Antibiotics

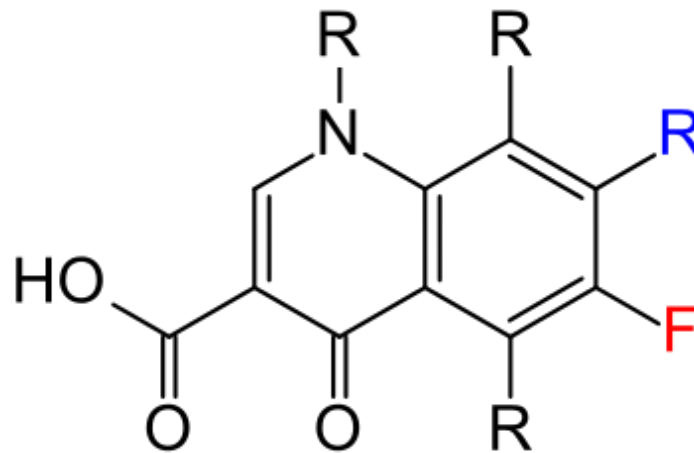
- Quinolones
- Vancomycin
- Metronidazole
- Nitrofurantoin

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Quinolones

Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin

- Inhibit enzymes for bacterial **DNA synthesis**
- **DNA gyrase**
- **Topoisomerase IV**



Quinolones

Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin

- Bacterial topoisomerase enzymes
- DNA Gyrase
 - Introduces double-stranded break
 - Repairs break
- Topoisomerase IV AfraTafreeh.com
 - Separates daughter chromosomes
 - “Decantation”
- Inhibition → DNA damage → **cell death**

Quinolones

Resistance Mechanisms

- Alterations of **DNA gyrase** and **topoisomerase IV**
- Alteration in cell permeability
- Efflux of drug

Quinolones

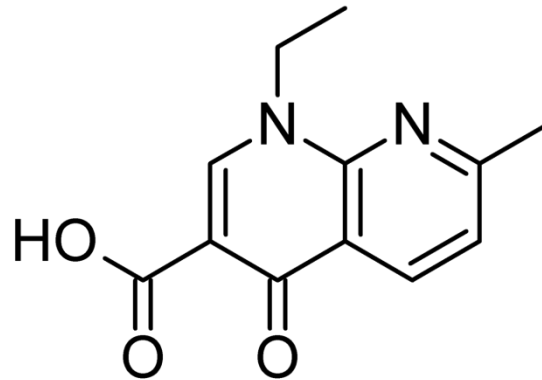
Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin

- Many gram (+), gram (-), atypicals
- Common clinical uses (adults only)
 - UTIs (E. Coli, other enteric gram negatives)
 - Pneumonia (S. pneumo, H. flu, atypicals)
 - Abdominal infections (enteric gram negatives)

Quinolones

Early Drugs

- Nalidixic acid (not a fluoroquinolone), Norfloxacin
- Mostly gram negative coverage
- Limited/no gram positive coverage

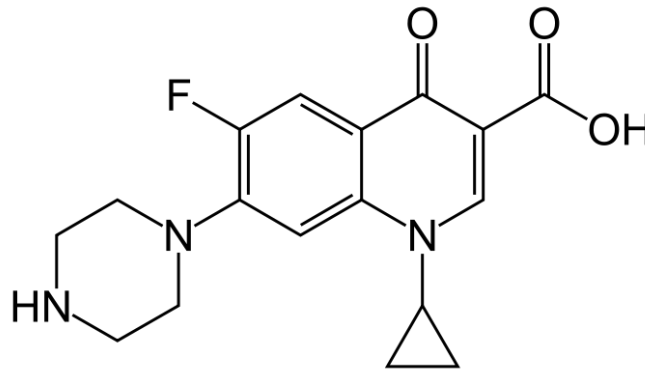


Nalidixic Acid

Quinolones

Ciprofloxacin

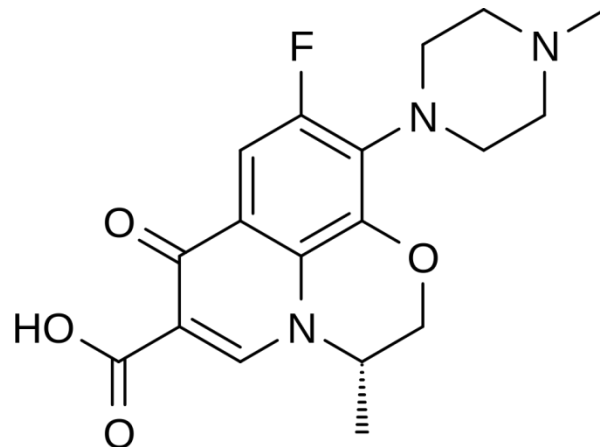
- Some gram positive coverage
 - Rarely used alone for gram positive coverage (resistance)
- Very good **gram negative coverage**
- Most reliable **pseudomonas** coverage
- Used in UTIs, GI infections
- Cipro ear drops for otitis externa



Quinolones

Levofloxacin

- More gram positive/atypical coverage than Cipro
 - Better strep pneumo coverage than Cipro
 - Covers most methicillin-susceptible Staph aureus
- Less effective against pseudomonas than Cipro
- Commonly used in pneumonia (strep, atypicals)



Quinolones

Gatifloxacin, Sparfloxacin, Moxifloxacin

- Better gram (+)/atypical coverage than Levofloxacin
- Less effective for pseudomonas than Levofloxacin
- Also used in pneumonia

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Quinolones

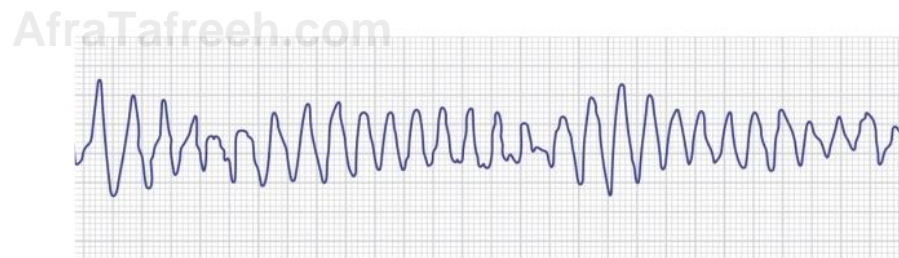
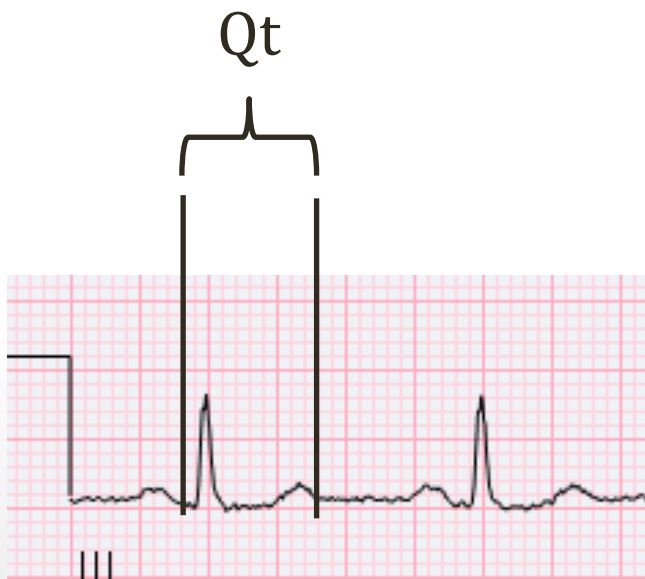
Adverse Reactions

- **Gastrointestinal** upset
 - Anorexia, nausea, vomiting, and abdominal discomfort
 - Up to 17% of patients
- **Neurologic** side effects
 - Headache, dizziness
 - 2 to 6% of patients

Quinolones

Adverse Reactions

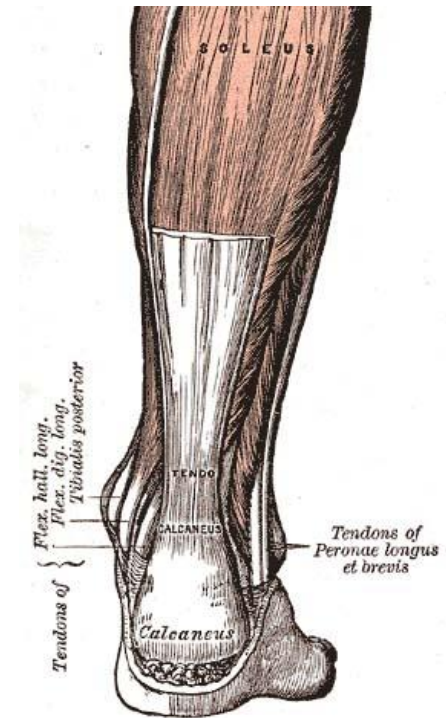
- QT prolongation on EKG
- Caused by blockade of K⁺ channels
- Can lead to torsade de pointes



Quinolones

Adverse Reactions

- **Tendon rupture/tendonitis**
 - Most commonly Achilles
 - More common older patients (>60), people on steroids
- Cannot use in pregnancy/children
 - Toxic to developing cartilage in animal studies



Wikipedia/Public Domain

Antacids

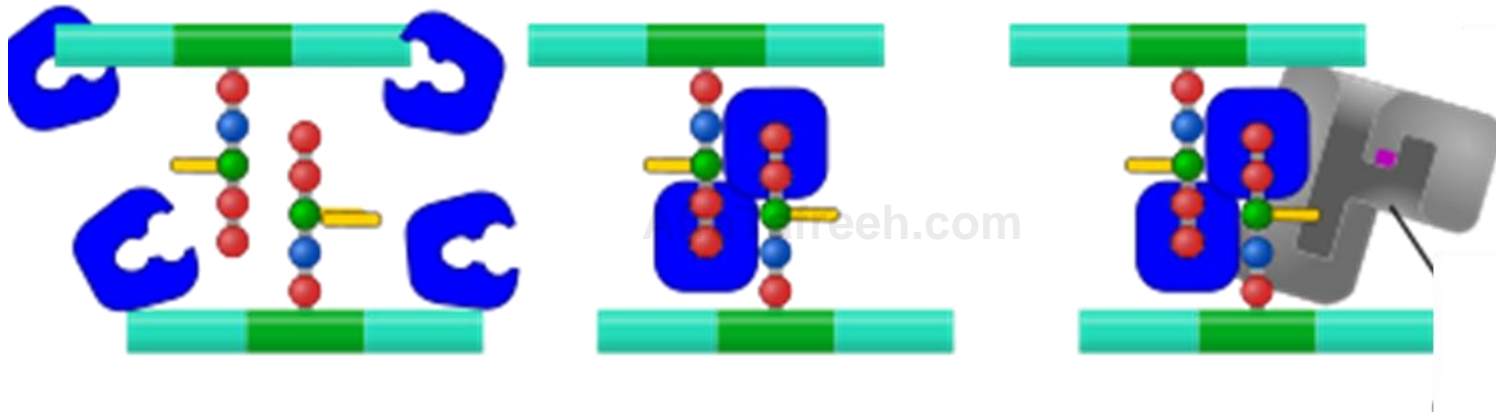
- Disrupt absorption of many drugs
- Aluminum and magnesium hydroxide
- Sucralfate (contains aluminum)
- Key drugs
 - Tetracycline
 - **Fluoroquinolones**
 - Isoniazid
 - Iron supplements

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Vancomycin

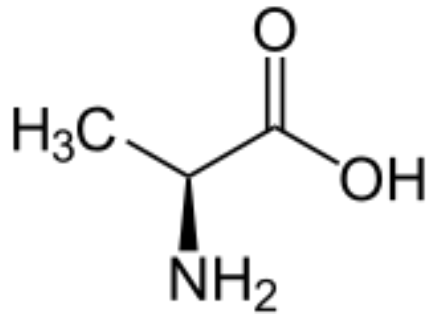
- Inhibits peptidoglycan formation (cell wall)
- Binds **D-alanyl-D-alanine peptides**
- Prevents crosslinking
- Cell wall breakdown > formation → **cell death**
- Same effect as beta lactams via different mechanism
 - Beta lactams: inhibit transpeptidases
 - Vancomycin: block transpeptidase binding

Vancomycin

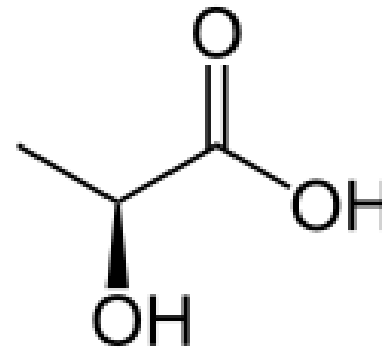


Vancomycin

- Resistance: terminal amino acids change
 - D-alanyl-D-alanine changed to **D-alanyl-D-lactate**
 - VRSA emerges



Alanine



Lactate

Vancomycin

- Two common uses:
 - #1: Methicillin resistant Staph Aureus (MRSA)
 - #2: Oral therapy for C. difficile pseudomembranous colitis
- Often given empirically when MRSA is a concern
 - Endocarditis
 - Severe pneumonia/sepsis

Vancomycin

Adverse Effects

- Generally well tolerated
- Nephrotoxicity
 - Less common with modern preparations
 - Increased risk if **concomitant aminoglycoside therapy**
- Ototoxicity AfraTafreeh.com
 - Tinnitus, vertigo, and hearing loss reported (rare)

Vancomycin

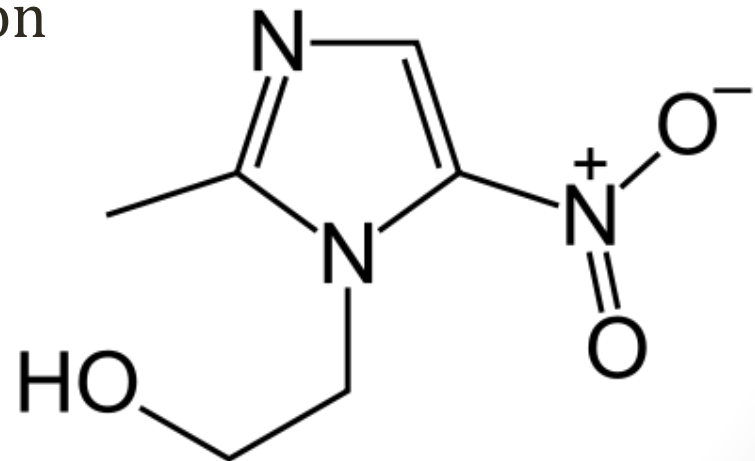
Adverse Effects

- **Vancomycin infusion reaction**
 - Flushing, erythema, itching
 - Usually affects upper body, neck, face more than lower body
 - Occurs 10-20 minutes after start of infusion
- Direct activation of mast cells → **histamine** release
 - “Pseudoallergic drug reaction”
- May develop with first administration
- Infusion related → slow infusion = no symptoms

Metronidazole

- Prodrug: Must be **reduced** to activate
- Only **anaerobic bacteria** capable of reduction
- Reduced metronidazole → more drug uptake
- Activated form generates free radicals
- Interact with DNA
- DNA breakage/destabilization
- Cell death

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Metronidazole

Uses

- Good coverage of anaerobes “below the diaphragm”
 - **Bacteroides fragilis**
 - **Clostridium difficile**
- Peritonitis, abdominal abscesses, diverticulitis
- Often given with quinolone for anaerobic/GI gram(-)
- Cipro/Flagyl often used for diverticulitis

Metronidazole

Uses

- **H. pylori** and **Gardnerella vaginalis**
 - Facultative anaerobic bacteria
 - Susceptible to metronidazole
- Triple therapy for H. Pylori
- Treatment of bacterial vaginitis.com

Metronidazole

Uses

- Anaerobic protozoa (lack mitochondria)
 - **Trichomonas vaginalis**
 - **Entamoeba histolytica**
 - **Giardia lamblia**
- Covered by metronidazole

Metronidazole

Adverse Reactions

- Unpleasant metallic taste
- **GI:** Abdominal discomfort, nausea
- **Neuro:** Neuropathy, headache

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Metronidazole

Adverse Reactions

- **Disulfiram-like reaction**
- Alcohol consumption with metronidazole
- Warmth, flushing, sweating
- Unclear mechanism
- Metronidazole may not inhibit alcohol metabolism
- Patients should **avoid alcohol**



Visapää JP. Lack of disulfiram-like reaction with metronidazole and ethanol.
Ann Pharmacother. 2002. Jun;36(6):971-4.

Nitrofurantoin

- Rarely used antibiotic
- Exact mechanism incompletely understood
- Bactericidal drug
- Only use is **UTIs** (concentrates in urine)
- Two things to know about this drug:
 - Used for UTIs in **pregnancy** (avoid TMP-SMX, quinolones)
 - Can trigger **hemolysis in G6PD patients**

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