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Fluoroquinolones: Their Niches & Negatives

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Outline

- Clinical niches
- Important side effects and adverse events
- Case review

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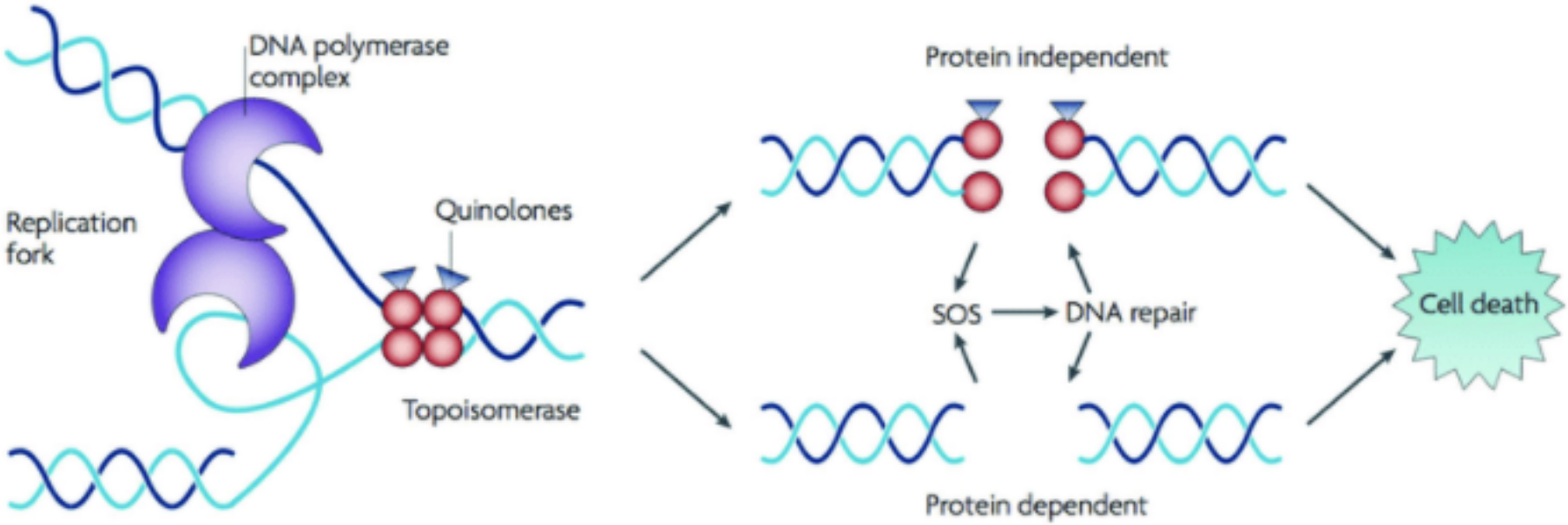
Fluoroquinolones: What are they?



- Ciprofloxacin
- Levofloxacin
- Moxifloxacin

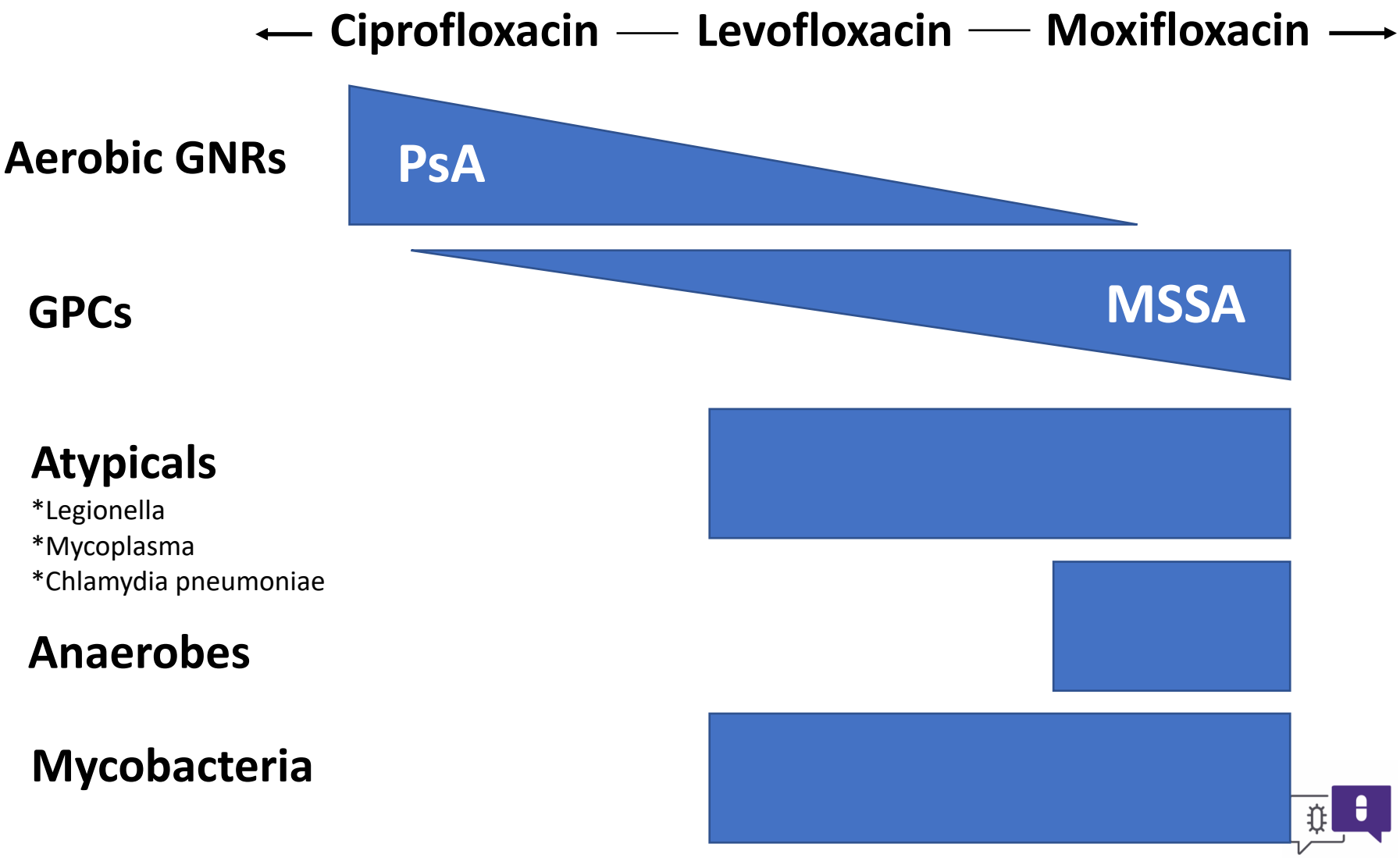
- D[illegible]in
- No[illegible]cin
- C[illegible]

Figure adapted from: Kohanski et al 2010 Nature Review Microbiology

Fluoroquinolones: Why are they so good?

- Bactericidal
- Highly bioavailable
  - Ciprofloxacin: 70%
  - Moxifloxacin: 86%
  - Levofloxacin: >95%
- Large volume of distribution!
  - Accumulates in prostate, bile, lung parenchyma
  - Excellent kidney penetration for all but moxifloxacin
- Easy IV → PO conversion
- Easy to take: QD or BID!

Fluoroquinolones: Not all the same!



Fluoroquinolones: Resistance on the rise

- Chromosomal gene mutations
  - Altered structure of DNA gyrase and topoisomerase
  - Cytoplasmic efflux pumps
- Plasmid-mediated resistance
  - Enzymes that alter fluoroquinolones

Fluoroquinolones: Gram positive resistance

Organism (% susceptible)	Levofloxacin [c]			Moxifloxacin		
	H	ML	NW	H	ML	NW
MSSA [a]	92	90	85	92	90	85
MRSA (HMC 47%, ML 37%, NW 49%	15	16	16	16	17	16
Enterococcus faecalis	84	84	83			
Enterococcus faecium		19				

Use for staph aureus:
- Only with confirmed susceptibility
- Beware low barrier to resistance in undrained infection!

Unreliable for enterococcus – avoid use!

Figure excerpts from: 2021 UW Medicine Antibiogram

Fluoroquinolones: Gram negative resistance

Organism (% susceptible)	Ciprofloxacin [e]			Levofloxacin [e]		
	H	ML	NW	H	ML	NW
Enterobacter cloacae complex [f]	93	92	92	96	95	94
Escherichia coli	73	66	79	75	68	80
Pseudomonas aeruginosa (non-CF)	83	79	71	82	79	72
Pseudomonas aeruginosa (CF) [i]		53			48	

Rising rates of resistance for Pseudomonas and E coli

Figure excerpts from: 2021 UW Medicine Antibiogram

Fluoroquinolones: Why are they so bad?

- Lots of side effects
- Some very bad side effects
- 2016 FDA Black Box Warning:
  - Use FQ's only when there are no other options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis (COPD exacerbation) and uncomplicated UTI
  - "...the risk of these serious side effects generally outweighs the benefits in these patients."

Fluoroquinolones: The bad

Most common side effects:

- Nausea
- Diarrhea
- Headache
- Dizziness
- Lightheadedness
- Trouble sleeping

Fluoroquinolones: The bad

CNS effects:

- Anxiety
- Depression
- Insomnia
- Hallucinations
- Confusion
- Delirium
- Memory impairment
- Psychosis
- Suicidal thoughts

Fluoroquinolones: The bad

MSK toxicity:

- Muscle pain/weakness
- Joint pain/swelling
- Tendinitis
- Tendon rupture

Risk factors:

- Age >60
- Nonobese
- Glucocorticoids

Fluoroquinolones: The bad

- C. Diff colitis
- Photosensitivity
- Neuropathy

Fluoroquinolones: The ugly

- MG crisis
- Aorta
- QT
- Hypoglycemic coma
- ? Retinal detachment

Fluoroquinolones: The ugly

- Pregnancy/breastfeeding
- Pediatrics

- What to do if they develop?
- Med interactions

Case #1

An otherwise healthy 28 F presents to Urgent Care with suprapubic pain, dysuria, and urinary frequency. She has no fever or CVA tenderness.

How often would she receive a FQ at your facility?

- Never
- 1 - 50%
- > 50%

FQ Alternatives: Uncomplicated UTI

- **Nitrofurantoin 100mg PO BID x5d**
  - Beware: Cannot use in pyelonephritis!
- **Fosfomycin 3gm PO x1 dose**
  - Beware: Cannot use in pyelonephritis!
- **TMP-SMX 1 DS PO BID x3d**

- If TMP-SMX resistance >20% …
  - Consider cefpodoxime 100mg PO BID x7d
  - Consider ciprofloxacin

Slide credit: Paul Pottinger, MD

Case #2

A 65M presents with nasal congestion, purulent nasal discharge, maxillary tooth pain, and severe sinus pressure. His symptoms began 2 weeks ago. Despite initial improvement, his symptoms are now worsening.

How often would he receive a FQ at your facility?

- Never
- 1 – 50%
- > 51%

FQ Alternatives: Bacterial rhinosinusitis

- **Amoxicillin-clavulanate 875-2000mg PO BID**

Second line:

- Doxycycline 100mg BID
- Cefpodoxime 200mg BID +/- Clindamycin 300mg Q6H
- Levofloxacin 500mg QD
- Moxifloxacin 400mg QD x 5-7d

Not recommended: Azithromycin, TMP-SMX

Slide credit: Paul Pottinger, MD

Case #3

A 45 M presents to his PCP with a cough x12 days. His cough is productive of purulent sputum, and he also has nasal congestion, sore throat, and fatigue. He is afebrile with normal O2 saturations, and he has no focal infiltrate on CXR.

How likely is he to receive a FQ at your facility?

- Never
- 1 – 50%
- > 51%

FQ Alternatives: Acute bronchitis

- **No antibiotics!**

- Remember:
  - Acute bronchitis is a self-limited illness
  - Only ~6% of cases are caused by bacterial pathogens (vast majority are viral!)
  - Presence of purulent sputum does not distinguish viral from bacterial causes

FQs for these patients are all risk, no benefit!

Take-Away Points

- Fluoroquinolones are a diverse class, and each drug has its niche!
- Like all drugs, resistance is on the rise
- Beware the broad side effect profile
  - Counsel your patients!
  - Treat like “informed consent”
- Consider non-fluoroquinolone alternatives whenever possible – especially for UTI, URI, and sinusitis

Questions?

We’re happy to chat!

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Thank you!