

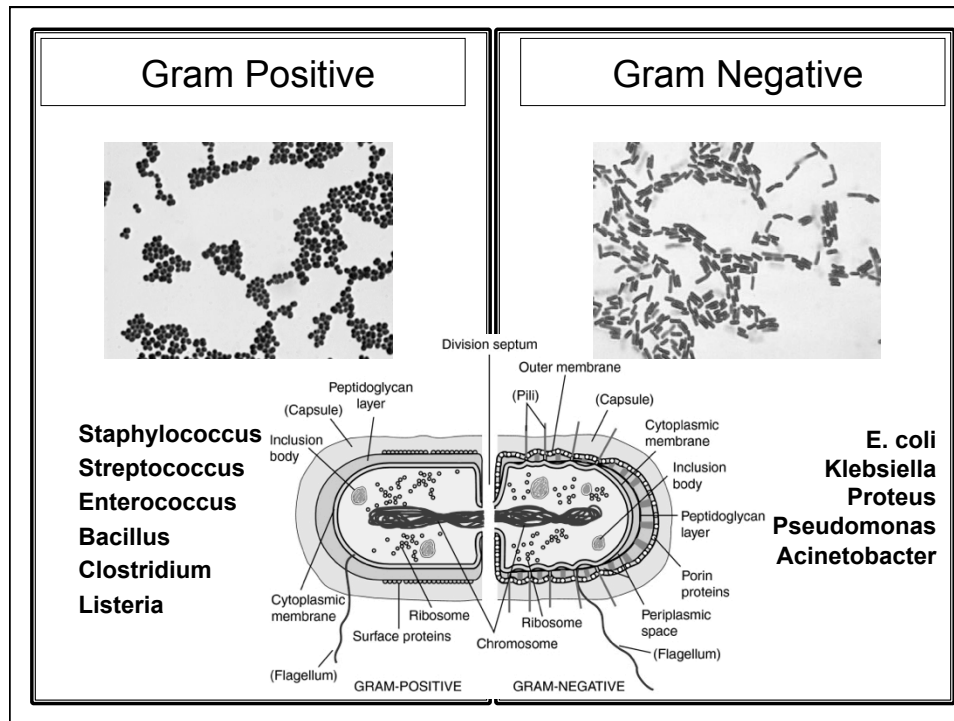
Antibiotic Review

Gram Stain and Spectrum of Activity

John Jantz, PharmD
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Objectives

- ▶ Understand and interpret gram stain results
- ▶ Identify spectrum of activity for each antibiotic

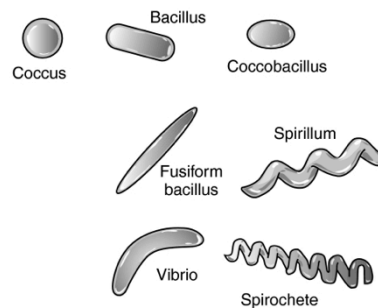


Importance of Gram Stain

- ▶ Mainstay of rapid diagnostic tests
 - Gram stain results usually reported a day prior to culture and sensitivity results
- ▶ Provides useful, presumptive information as to the etiology of many infections
- ▶ Potential to improve empiric regimen prior to culture results

Clinically useful results

- ▶ **GPC in clusters**
 - Staph aureus (including MRSA)
- ▶ **GPC in chains**
 - Enterococcus faecalis
 - Enterococcus faecium
 - Group A strep
 - Group B strep
 - Strep viridans
- ▶ **GPC in pairs (diplococci)**
 - Strep pneumo



Site of infection matters

- | | |
|---|---|
| <ul style="list-style-type: none"> ▶ Sterile site <ul style="list-style-type: none"> ◦ Blood ◦ CSF ◦ Pleural fluid ◦ Peritoneal fluid ◦ Bone ◦ Joint fluid | <ul style="list-style-type: none"> ▶ Non-sterile site <ul style="list-style-type: none"> ◦ Sputum ◦ Skin ◦ Wound |
|---|---|

Bugs and Drugs

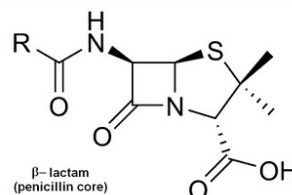
»» Spectrum of activity

Beta-Lactams

Penicillins	Cephalosporins	Carbapenems
<i>"Natural Penicillins"</i> Penicillin G & Penicillin V	1st- generation Cefazolin & Cephalexin	Imipenem & Meropenem & Doripenem
Anti-staph penicillins Nafcillin & Dicloxacillin	2nd-generation Cefuroxime	Ertapenem
Aminopenicillins Ampicillin & amoxicillin	Cefotetan & Cefoxitin	
Ampicillin/sulbactam & Amoxicillin/clavulanate	3rd-generation Ceftriaxone & Cefotaxime	Monobactams Aztreonam
Antipseudomonal penicillins Piperacillin/tazobactam	4th-generation Cefepime	
	5th-generation Ceftaroline	

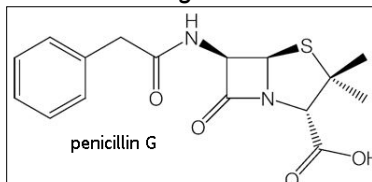
Beta-Lactams

- ▶ MOA:
 - Interfere with cell wall synthesis during multiplication leading to cell wall destruction and bacterial cell death
 - Targets peptidoglycan synthesis by inhibiting enzymes called penicillin binding proteins [PBP]
 - Clinical efficacy
 - Time above the MIC



Natural Penicillins

- ▶ Basics: penicillin G (IV), V (PO); *benzathine* (IM depot), *procaine* (IM depot)
- ▶ Spectrum Summary
 - **Excellent activity**
 - *Strep pyogenes*, *T. pallidum*, *Listeria*, *Neisseria meningitidis*
 - **Good activity**
 - *Strep pneumoniae*, viridans Strep, *Enterococcus faecalis*
 - Poor activity
 - MSSA
 - No activity
 - MRSA, Gram-negative rods, “atypicals”, *Bacteriodes fragilis*



Anti-staphylococcal Penicillins

- Basics: nafcillin, oxacillin, [*methicillin*] (IV); dicloxacillin (PO)
- Spectrum Summary: PCN + MSSA– *Enterococcus*

Organism	Activity		Organism	Activity	
	PCN	Naf		PCN	Naf
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	--	--
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	X	X
Staph aureus (MSSA)	--	++	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	X	X	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	++	--	<u>Anaerobes</u>	PCN	Naf
<i>Enterococcus faecium</i> (VRE)	--	--	<i>Bacteroides fragilis</i>	--	--

Aminopenicillins

- Basics: ampicillin (IV, PO); amoxicillin (PO); ampicillin/sulbactam (IV); amoxicillin/clavulanate (PO)
- Spectrum Summary: PCN + “HNpek” + *B. fragilis*

Organism	Activity		Organism	Activity	
	Amp	Amp/sul		Amp	Amp/sul
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	+	++
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	--	+
Staph aureus (MSSA)	--	++	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	X	X	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	++	++	<u>Anaerobes</u>	Amp	Amp/sul
<i>Enterococcus faecium</i> (VRE)	--	--	<i>Bacteroides fragilis</i>	--	++

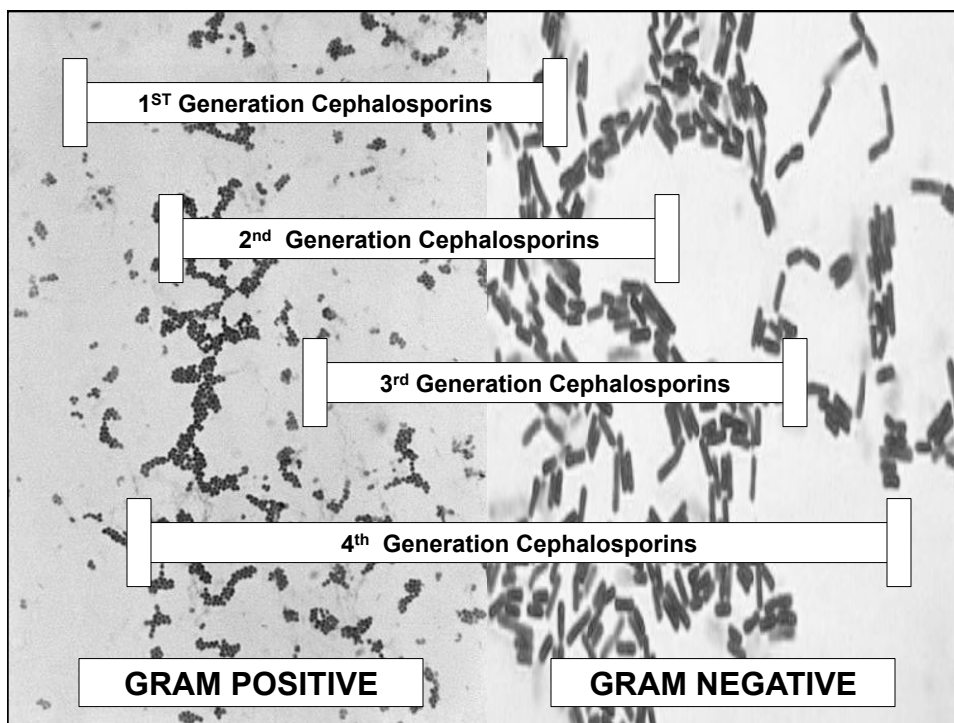
HNpek - Haemophilus, Neisseria, proteus, e.coli, klebsiella

Antipseudomonal Penicillins

- ▶ Basics: *Piperacillin*, piperacillin/tazobactam, *ticarcillin*, *ticarcillin/clavulanate*(IV)
- ▶ Spectrum Summary: Amp/sulb + (more) GNRs (“HNPEK/CaPES”)

Organism	Activity		Organism	Activity	
	Amp/sul	Pip/tazo		Amp/sul	Pip/tazo
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	++	++
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	+	++
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	X	++
<i>Staph aureus</i> (MRSA)	X	X	<i>Pseudomonas</i>	X	+
<i>Enterococcus faecalis</i>	++	++	<u>Anaerobes</u>	Amp/sul	Pip/tazo
<i>Enterococcus faecium</i> (VRE)	--	--	<i>Bacteroides fragilis</i>	++	++

CaPES – Citerobacter, acinetobacter, Pseudomonas, Enterobacter, Serratia



1st-Generation Cephalosporins

- ▶ Basics: Cefazolin(IV), cephalexin (PO)
- ▶ Spectrum Summary: Nafcillin + GNRs (“pek”)

Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	Naf	1GC	<u>Gram-negative</u>	Naf	1GC
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	--	--
<i>Streptococcus pneumoniae</i>	++	++	Proteus/E.coli/Klebsiella	X	+
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	X	X	<i>Pseudomonas</i>	X	X
Enterococcus faecalis	--	X	<u>Anaerobes</u>	Naf	1GC
Enterococcus faecium (VRE)	--	X	<i>Bacteroides fragilis</i>	--	--

- ▶ Cephalosporins are **LAME**
 - Do not cover Listeria, Atypicals, MRSA*, Enterococcus*

*Except Ceftaroline

2nd-Generation Cephalosporins

- ▶ Basics: Cefuroxime (IV, PO); *cefoxitin*, *cefotetan*(IV)
 - 2 “groups” differ by spectrum: cefuroxime group &cephamycin group (cefoxitin/cefotetan)
- ▶ Spectrum Summary: 1st-Gen + “HN” +/- *B. fragilis*

Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	1GC	2GC	<u>Gram-negative</u>	1GC	2GC
<i>Streptococcus pyogenes</i>	++	++	H. influenzae	--	++
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	+	+
Staph aureus (MSSA)	++	+	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	X	X	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	X	X	<u>Anaerobes</u>	1GC	2GC
Enterococcus faecium (VRE)	X	X	Bacteroides fragilis	--	+*

*cefoxitin/cefotetan only

3rd-Generation Cephalosporins

- ▶ Basics: ceftriaxone, cefotaxime, ceftazidime (IV); cefpodoxime, cefixime (PO)
- ▶ Spectrum Summary: cefurox + “Ca(P)ES”

Organism	Activity		Organism	Activity	
	CTX	CTZ		CTX	CTZ
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	++	++
<i>Streptococcus pneumoniae</i>	++	--	<i>Proteus/E.coli/Klebsiella</i>	++	++
<i>Staph aureus (MSSA)</i>	++	--	<i>Enterobacter/Serratia</i>	+	+
<i>Staph aureus(MRSA)</i>	X	X	<i>Pseudomonas</i>	X	+
<i>Enterococcus faecalis</i>	X	X	<u>Anaerobes</u>	CTX	CTZ
<i>Enterococcus faecium(VRE)</i>	X	X	<i>Bacteroides fragilis</i>	--	--

CTX – Ceftriaxone/Cefotaxime
CTZ - Ceftazidime

4th-Generation Cephalosporins

- ▶ Basics: cefepime (IV)
- ▶ Spectrum Summary: Ceftaz + Ceftriaxone

Organism	Activity		Organism	Activity	
	CTZ	CFP		CTZ	CFP
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	++	++
<i>Streptococcus pneumoniae</i>	--	++	<i>Proteus/E.coli/Klebsiella</i>	++	++
<i>Staph aureus (MSSA)</i>	--	++	<i>Enterobacter/Serratia</i>	+	++
<i>Staph aureus(MRSA)</i>	X	X	<i>Pseudomonas</i>	+	+
<i>Enterococcus faecalis</i>	X	X	<u>Anaerobes</u>	CTZ	CFP
<i>Enterococcus faecium(VRE)</i>	X	X	<i>Bacteroides fragilis</i>	--	--

“5th-Generation Cephalosporin?”

- ▶ Basics: ceftaroline (IV)
- ▶ Spectrum Summary: Ceftriaxone + MRSA + E. faecalis

Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	CTX	CTL	<u>Gram-negative</u>	CTX	CTL
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	++	++
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	++	++
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	+	+
<i>Staph aureus</i>(MRSA)	X	++	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	X	++	<u>Anaerobes</u>	CTX	CTL
<i>Enterococcus faecium</i> (VRE)	X	X	<i>Bacteroides fragilis</i>	--	--

Carbapenems

- ▶ Basics: Imipenem/cilastatin, meropenem, doripenem (IV); ertapenem (IV)
 - 2 groups differ by spectrum: imi/mero/dori group & erta group
- ▶ Spectrum Summary: Pip/tazo enhanced

Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	ETP	M/I/D	<u>Gram-negative</u>	ETP	M/I/D
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	++	++
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	++	++
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	++	++
<i>Staph aureus</i> (MRSA)	X	X	<i>Pseudomonas</i>*	X	+
<i>Enterococcus faecalis</i> *	X	±	<u>Anaerobes</u>	ETP	M/I/D
<i>Enterococcus faecium</i> (VRE)	X	X	<i>Bacteroides fragilis</i>	--	--

*ertapenem has no activity vs these organisms

Monobactams

- ▶ Basics: Aztreonam (IV)
- ▶ Spectrum Summary: Ceftaz – Gram Positive Cocci

Organism	Activity		Organism	Activity	
	CTZ	ATM		CTZ	ATM
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	X	<i>H. influenzae</i>	++	++
<i>Streptococcus pneumoniae</i>	--	X	<i>Proteus/E.coli/Klebsiella</i>	++	++
<i>Staph aureus (MSSA)</i>	--	X	<i>Enterobacter/Serratia</i>	+	+
<i>Staph aureus(MRSA)</i>	X	X	<i>Pseudomonas</i>	+	+
<i>Enterococcus faecalis</i>	X	X	<u>Anaerobes</u>	CTZ	ATM
<i>Enterococcus faecium(VRE)</i>	X	X	<i>Bacteroides fragilis</i>	--	--

Beta-Lactams: Other Key Pathogens

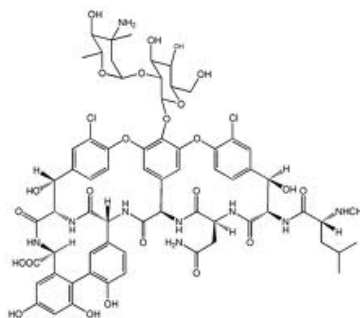
Organism	PCN	AMP	PIP/TZ	1GC	2GC	3GC	4GC	IMI
"Atypical" respiratory pathogens : CML*	X	X	X	X	X	X	X	X
<i>Neisseria meningitidis</i>	++	++	++	--	++	++	++	++
viridans group streptococci	++	++	++	++	++	++	++	++
<i>Listeria monocytogenes</i>	+	++	+	X	X	X	X	+
<i>Moraxella catarrhalis</i>	X	--	++	+	++	++	++	++
<i>Stenotrophomonas maltophilia</i>	X	X	X	X	X	--	X	X

**Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella pneumophila*

Glycopeptides

▶ Vancomycin

- MOA: Binds to D-Ala-D-Ala residue of peptidoglycan precursor at surface of cytoplasmic membrane (inhibits cell wall synthesis)
- Bacteriocidal



Glycopeptides: Basics/Spectrum

- ▶ Basics: Vancomycin (IV,PO*)
- ▶ Spectrum Summary: only Gram-positives

Organism	Activity	Organism	Activity
<u>Gram-positive</u>	VAN	<u>Gram-negative</u>	VAN
<i>Streptococcus pyogenes</i>	++	<i>H. influenzae</i>	X
<i>Streptococcus pneumoniae</i>	++	<i>Proteus/E.coli/Klebsiella</i>	X
Staph aureus (MSSA)	++	<i>Enterobacter/Serratia</i>	X
Staph aureus(MRSA)	++	<i>Pseudomonas</i>	X
Enterococcus faecalis	++	<u>Anaerobes**</u>	VAN
<i>Enterococcus faecium</i> (VRE)	--	<i>Bacteroides fragilis</i>	X

Spectrum does include some anaerobes including **Clostridium difficile

*PO vancomycin not systemically absorbed

Lipopeptides

- ▶ Daptomycin
 - MOA: Binds to bacterial membrane causing rapid depolarization of membrane potential
 - Inhibits protein, DNA and RNA synthesis
 - No lung penetration!
 - Inactivated by lung surfactants
 - Bacteriocidal

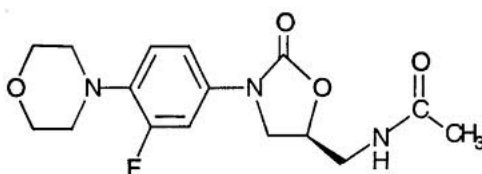
Lipopeptides: Basics/Spectrum

- ▶ Basics: Daptomycin (IV)
- ▶ Spectrum Summary: Vanco + VRE/VISA/VRSA

Organism	Activity		Organism	Activity	
	VAN	DAP		VAN	DAP
<u>Gram-positive</u>			<u>Gram-negative</u>		
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	X	X
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	X	X
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	++	++	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	++	++	<u>Anaerobes</u>	VAN	DAP
<i>Enterococcus faecium</i> (VRE)	--	+	<i>Bacteroides fragilis</i>	X	X

Oxazolidinone

- ▶ Linezolid
 - MOA: Inhibits protein synthesis by binding to a site on the ribosomal RNA 50S subunit
 - Bacteriostatic



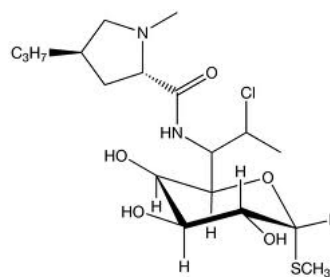
Oxazolidinones: Basics/Spectrum

- ▶ Basics: Linezolid (IV, PO)
- ▶ Spectrum Summary: Vanco + VRE/VISA/VRSA

Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	VAN	LZD	<u>Gram-negative</u>	VAN	LZD
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	X	--
<i>Streptococcus pneumoniae</i>	++	++	<i>Proteus/E.coli/Klebsiella</i>	X	X
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	++	++	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	++	++	<u>Anaerobes</u>	VAN	LZD
<i>Enterococcus faecium</i> (VRE)	--	++	<i>Bacteroides fragilis</i>	X	X

Lincosamides

- ▶ Clindamycin
 - MOA: binds to the 50S subunit preventing peptide-bond formation and inhibiting protein synthesis
 - Also inhibits bacterial toxin production
 - Bacteriostatic



Lincosamides: Basics/Spectrum

- ▶ Basics: Clindamycin (IV, PO)
- ▶ Spectrum Summary: Linezolid – *Enterococcus* + anaerobes

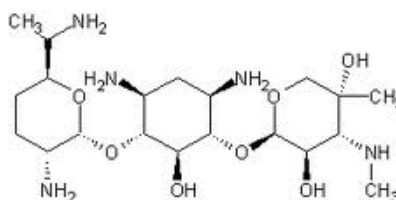
Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	LZD	CLI	<u>Gram-negative</u>	LZD	CLI
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	X	X
<i>Streptococcus pneumoniae</i>	++	+	<i>Proteus/E.coli/Klebsiella</i>	X	X
<i>Staph aureus</i> (MSSA)	++	++	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	++	+	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	++	X	<u>Anaerobes</u>	LZD	CLI
<i>Enterococcus faecium</i> (VRE)	++	X	<i>Bacteroides fragilis</i>	X	+

- ▶ Also active against: *Pneumocystis jiroveci*

Aminoglycosides

- ▶ MOA:
 - Inhibition of protein synthesis (30S ribosome) → cell death
 - Bacteriocidal vs. Bacteriostatic
 - Dependant of organism and concentration

Gentamicin



Aminoglycosides: Basics/Spectrum

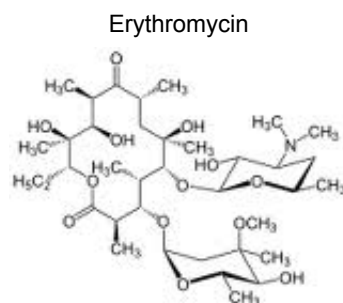
- ▶ Basics: Gentamicin, tobramycin, *amikacin*,
- ▶ Spectrum Summary: used as monotherapy only for Gram-negatives

Organism	Activity	Organism	Activity
<u>Gram-positive</u>	GEN	<u>Gram-negative</u>	GEN
<i>Streptococcus pyogenes</i>	--	<i>H. influenzae</i>	--
<i>Streptococcus pneumoniae</i>	--	<i>Proteus/E.coli/Klebsiella</i>	++
Staph aureus (MSSA)	syn	<i>Enterobacter/Serratia</i>	++*
<i>Staph aureus</i> (MRSA)	syn	<i>Pseudomonas</i>	+*
Enterococcus faecalis	syn	<u>Anaerobes</u>	GEN
<i>Enterococcus faecium</i> (VRE)	syn	<i>Bacteroides fragilis</i>	--

*gent more active than tobra vs *Serratia*,
tobra more active vs *Pseudomonas*

Macrolides

- ▶ MOA: binds to 50S ribosomal subunit, prevents protein synthesis
- ▶ Bacteriostatic



Macrolides: Basics/Spectrum

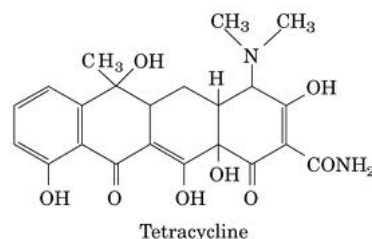
- ▶ Basics: *Erythromycin*, azithromycin (IV, PO); clarithromycin (PO)
- ▶ Spectrum Summary: *Strep* & *H. influenzae* + **Atypicals**

Organism	Activity		Organism	Activity	
<u>Gram-positive</u>	<i>ERY</i>	<i>AZM</i>	<u>Gram-negative</u>	<i>ERY</i>	<i>AZM</i>
<i>Streptococcus pyogenes</i>	++	++	<i>H. influenzae</i>	--	+
<i>Streptococcus pneumoniae</i>	+	+	<i>Proteus/E.coli/Klebsiella</i>	--	--
<i>Staph aureus</i> (MSSA)	--	--	<i>Enterobacter/Serratia</i>	X	X
<i>Staph aureus</i> (MRSA)	--	--	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	X	X	<u>Anaerobes</u>	<i>ERY</i>	<i>AZM</i>
<i>Enterococcus faecium</i> (VRE)	X	X	<i>Bacteroides fragilis</i>	--	--

- Also active against: atypical respiratory pathogens, *Moraxella catarrhalis*, *Chlamydia trachomatis*, *Pneumocystis jiroveci*, *Helicobacter pylori*, non-tuberculous mycobacteria

Tetracyclines

- ▶ MOA: inhibition of protein synthesis by binding to 30s ribosome subunit
- ▶ Bacteriostatic



Tetracyclines: Basics/Spectrum

- ▶ **Basics:** *Tetracycline*, doxycycline, *minocycline* (IV, PO); tigecycline (IV)
- ▶ **Spectrum Summary:**

Organism	Activity		Organism	Activity	
	DOX	TGC		DOX	TGC
<i>Gram-positive</i>			<i>Gram-negative</i>		
<i>Streptococcus pyogenes</i>	--	--	<i>H. influenzae</i>	+	++
<i>Streptococcus pneumoniae</i>	+	++	<i>Proteus*/E.coli/Klebsiella</i>	--	++
<i>Staph aureus (MSSA)</i>	++	++	<i>Enterobacter/Serratia</i>	--	+
<i>Staph aureus(MRSA)</i>	++	++	<i>Pseudomonas</i>	X	X
<i>Enterococcus faecalis</i>	--	++	<i>Anaerobes</i>	DOX	TGC
<i>Enterococcus faecium(VRE)</i>	--	++	<i>Bacteroides fragilis</i>	--	++

- **Also active against:** atypical respiratory pathogens, *Moraxella catarrhalis*, *Chlamydia trachomatis*, *Helicobacter pylori*, *Borrelia*, *Rickettsiae*, *Plasmodium spp*

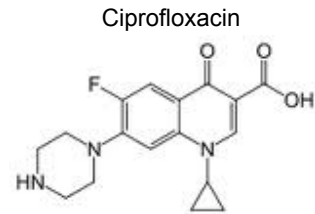
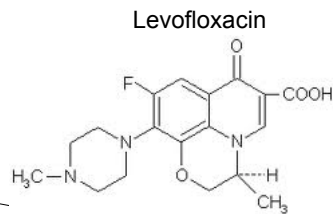
*TGC not active vs *Proteus*

Tigecycline

- ▶ “Cadillac of tetracyclines”
- ▶ Great for ESBL organisms
- ▶ Tigecycline does not cover **MP3**
 - **Morganella, Proteus, Pseudomonas, Providencia**
- ▶ Poor blood and urine concentration
 - Not a great option for bacteremias and UTIs

Quinolones

- ▶ MOA: Inhibit DNA-gyrase in bacteria, promote breakage of double-stranded DNA
- ▶ Bacteriocidal



Fluoroquinolones: Basics/Spectrum

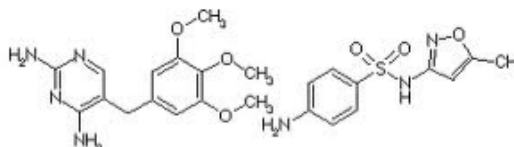
- ▶ Basics: Ciprofloxacin, levofloxacin, moxifloxacin (IV, PO)
- ▶ Spectrum Summary:

Organism	Activity			Organism	Activity		
	CIP	LVX	MOX		CIP	LVX	MOX
<u>Gram-positive</u>				<u>Gram-negative</u>			
<i>Streptococcus pyogenes</i>	++	++	++	<i>H. influenzae</i>	++	++	++
<i>Streptococcus pneumoniae</i>	--	++	++	<i>Proteus/E.coli/Klebsiella</i>	+	+	+
Staph aureus (MSSA)	--	+	+	<i>Enterobacter/Serratia</i>	++	++	++
<i>Staph aureus</i> (MRSA)	--	--	--	Pseudomonas	+	+	X
Enterococcus faecalis	--	--	--	<u>Anaerobes</u>	CIP	LVX	MOX
<i>Enterococcus faecium</i> (VRE)	--	--	--	<i>Bacteroides fragilis</i>	--	--	+

- Also active against: atypical respiratory pathogens, *Moraxella catarrhalis*, *Chlamydia trachomatis*, *Mycobacterium tuberculosis*

Sulfamethoxazole-Trimethoprim

- ▶ MOA:
 - Sulfamethoxazole: interferes with bacterial folic acid synthesis and growth via inhibition of dihydrofolate formation from PABA
 - Trimethoprim: inhibits dihydrofolate reduction to tetrahydrofolate, resulting in sequential inhibition of the folic acid pathway.
- ▶ Bacteriostatic – separately
- ▶ Bacteriocidal – in combination



Antifolates: Basics/Spectrum

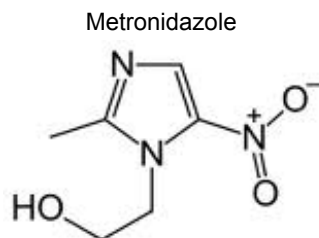
- ▶ Basics: Trimethoprim/sulfamethoxazole [TMP/SMX] (IV, PO); *trimethoprim (PO)*, *sulfadiazine (PO)*
- ▶ Spectrum Summary:

Organism	Activity	Organism	Activity
<u>Gram-positive</u>	T/S	<u>Gram-negative</u>	T/S
<i>Streptococcus pyogenes</i>	--	<i>H. influenzae</i>	+
<i>Streptococcus pneumoniae</i>	--	<i>Proteus/E.coli/Klebsiella</i>	+
<i>Staph aureus</i> (MSSA)	++	<i>Enterobacter/Serratia</i>	+
<i>Staph aureus</i>(MRSA)	++	<i>Pseudomonas</i>	X
<i>Enterococcus faecalis</i>	X	<u>Anaerobes</u>	T/S
<i>Enterococcus faecium</i> (VRE)	X	<i>Bacteroides fragilis</i>	--

- Also active against: *Pneumocystis jiroveci*, *Nocardia spp*, *Stenotrophomonas maltophilia*, *Listeria monocytogenes*

Metronidazole

- ▶ Metronidazole
 - MOA: interacts with DNA causing a loss of helical DNA structure and strand breakage, resulting in inhibition of protein synthesis
- ▶ Bacteriocidal



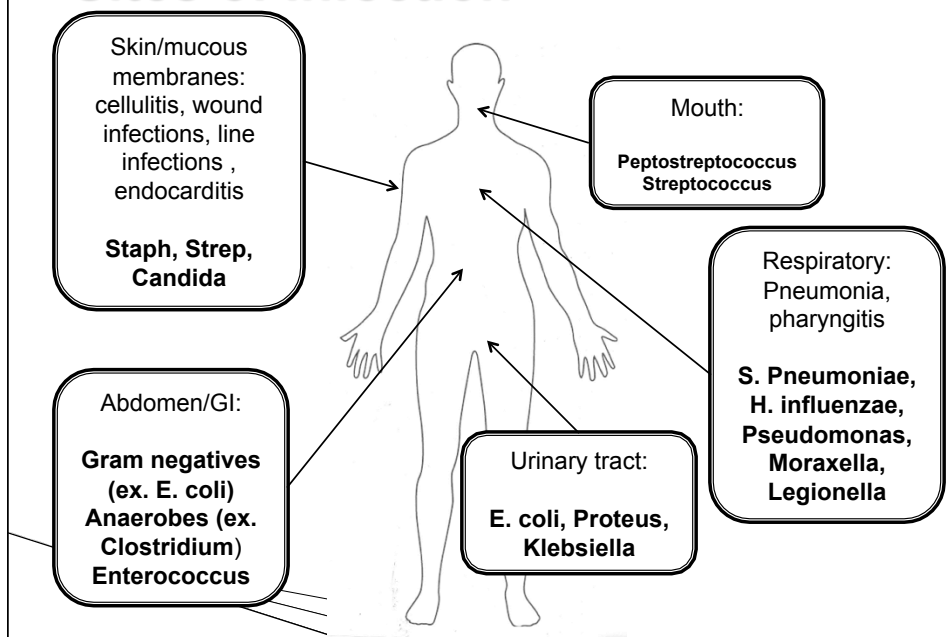
Nitroimidazoles: Basics/Spectrum

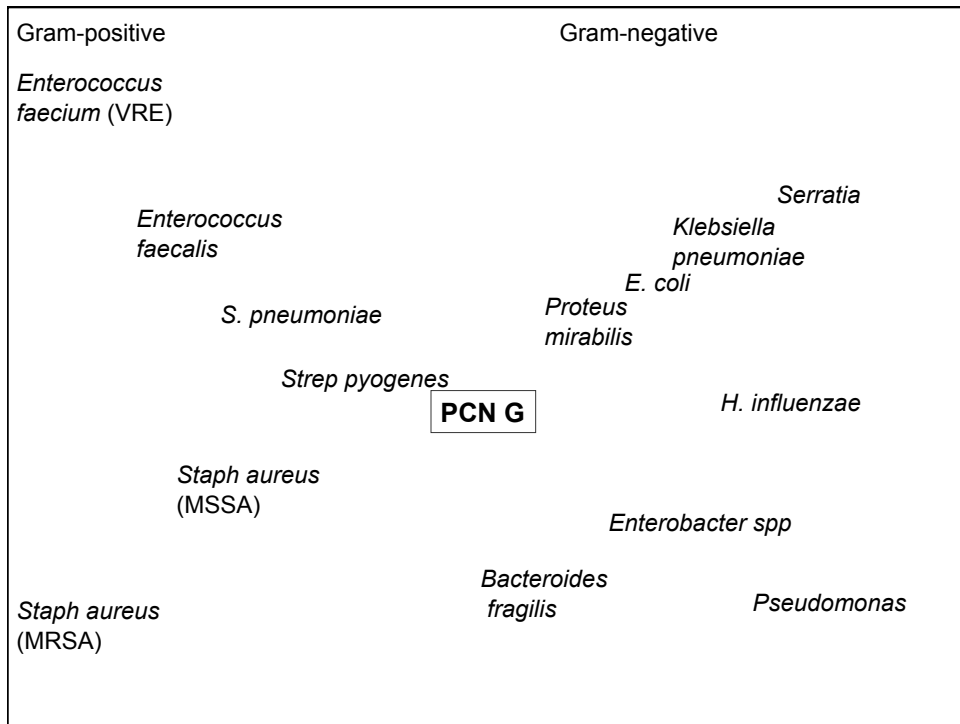
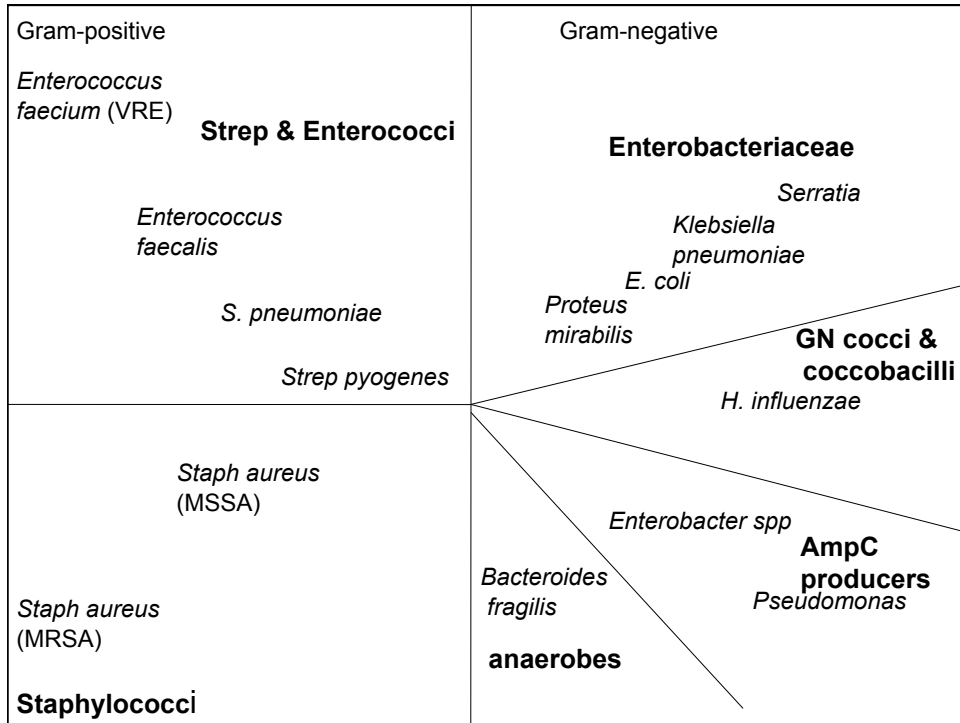
- ▶ Basics: Metronidazole (IV, PO)
- ▶ Spectrum Summary: anaerobes only (Gram-negative > Gram-positive)

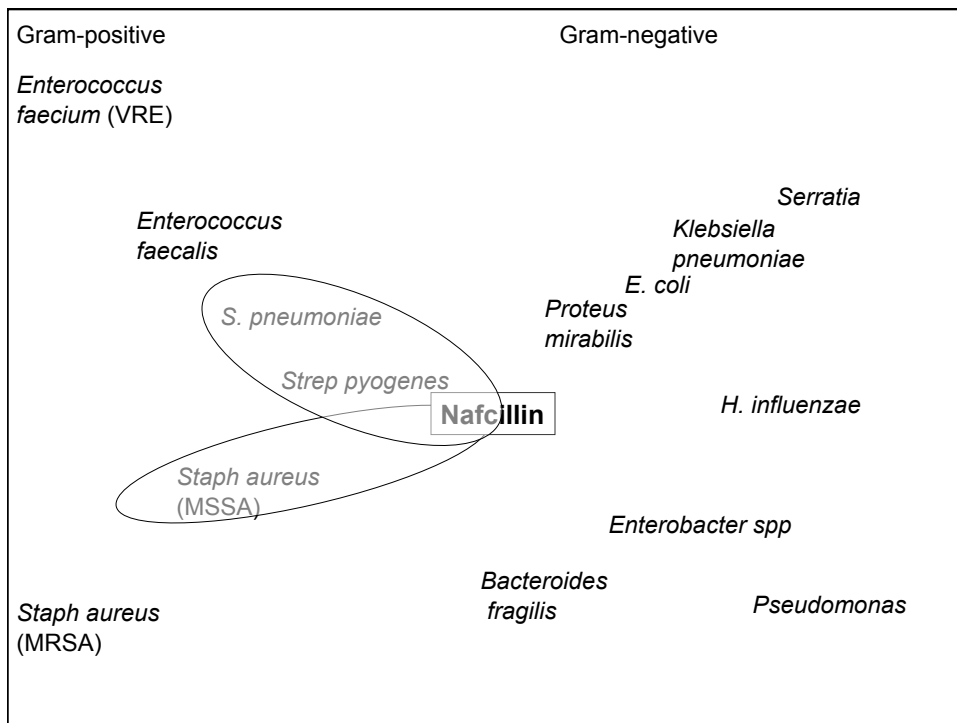
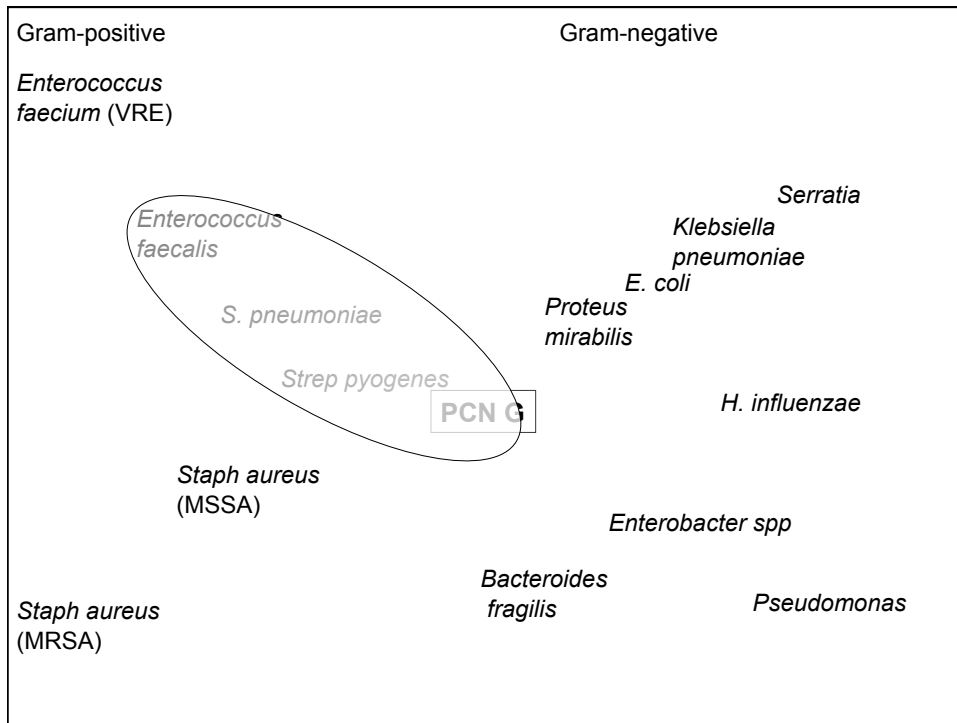
Organism	Activity	Organism	Activity
<u>Gram-positive</u>	MTZ	<u>Gram-negative</u>	MTZ
<i>Streptococcus pyogenes</i>	X	<i>H. influenzae</i>	X
<i>Streptococcus pneumoniae</i>	X	<i>Proteus/E. coli/Klebsiella</i>	X
Staph aureus (MSSA)	X	<i>Enterobacter/Serratia</i>	X
<i>Staph aureus</i> (MRSA)	X	<i>Pseudomonas</i>	X
Enterococcus faecalis	X	<u>Anaerobes</u>	MTZ
<i>Enterococcus faecium</i> (VRE)	X	<i>Bacteroides fragilis</i>	++

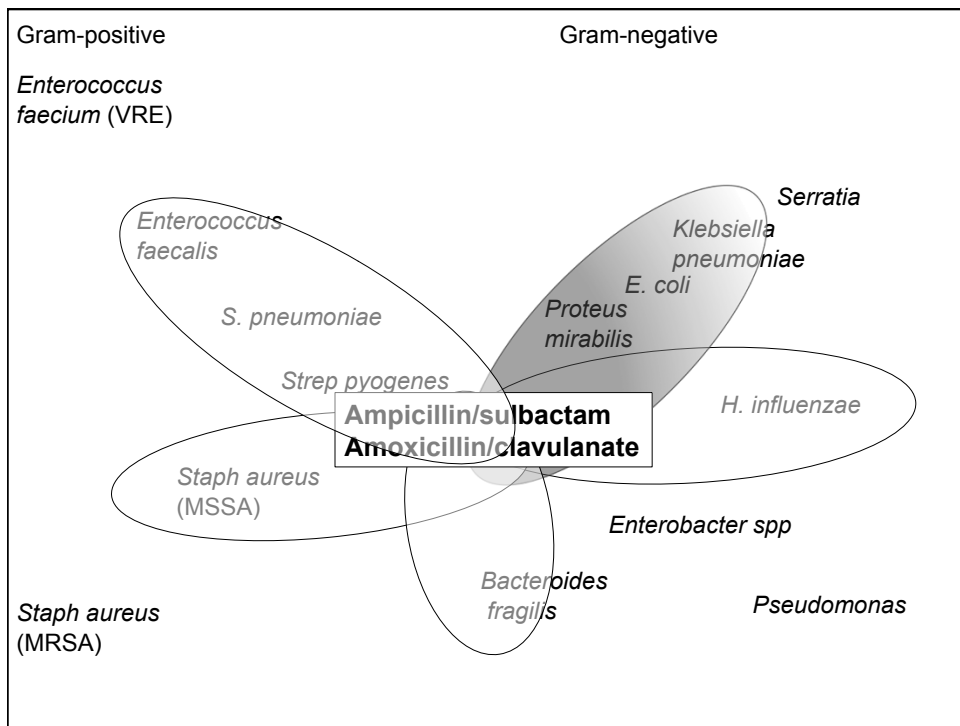
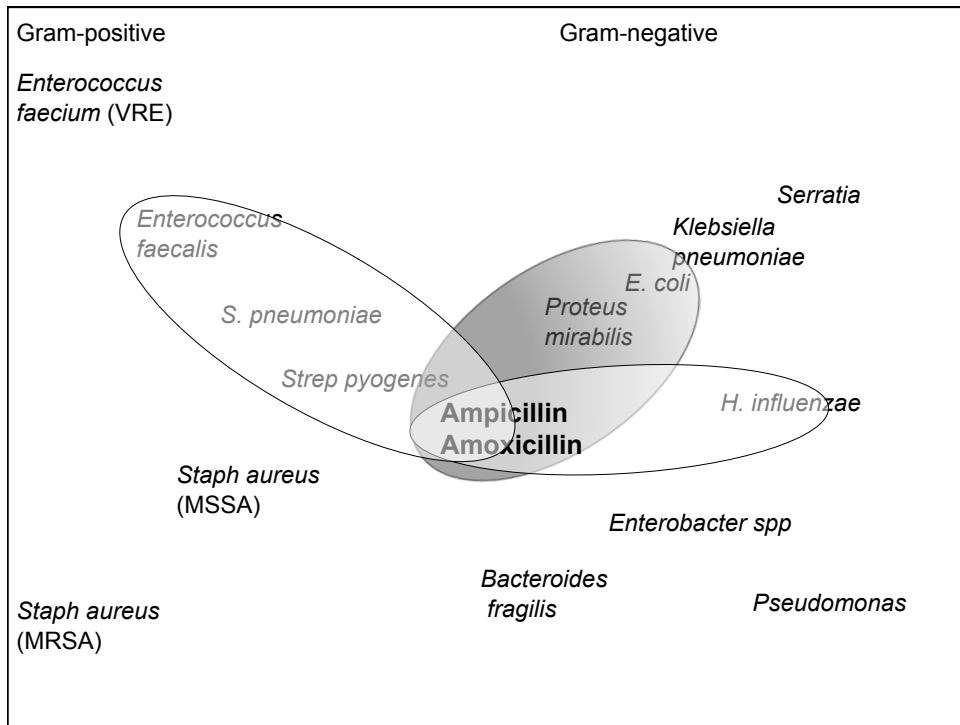
- Also active against: *Trichomonas vaginalis*, *Gardnerella vaginalis*, *Giardia lamblia*, *Clostridium difficile*, *Helicobacter pylori*

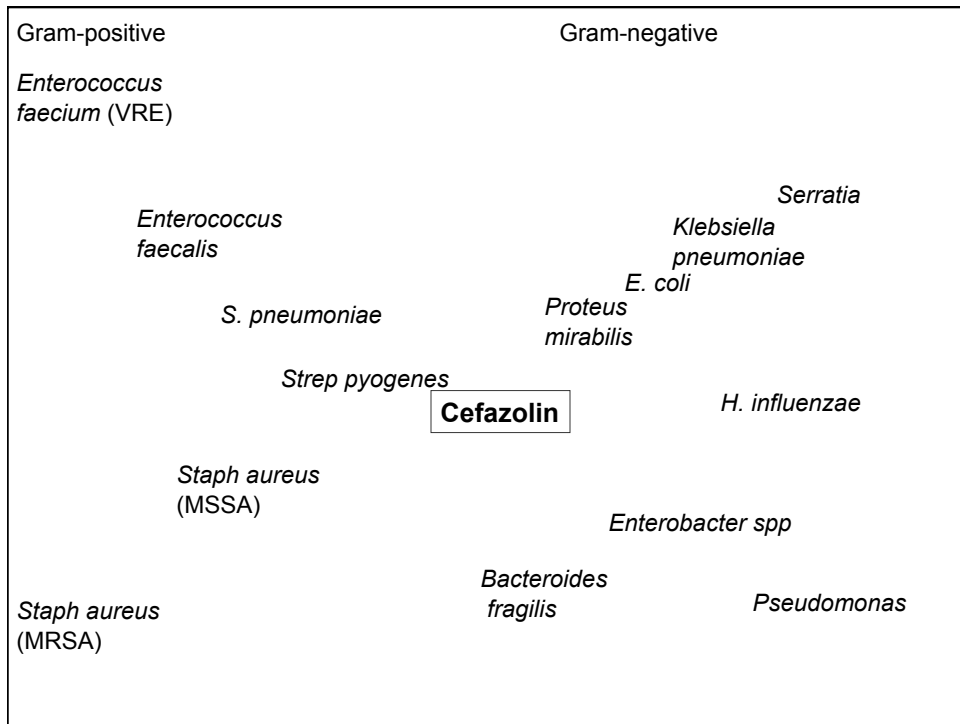
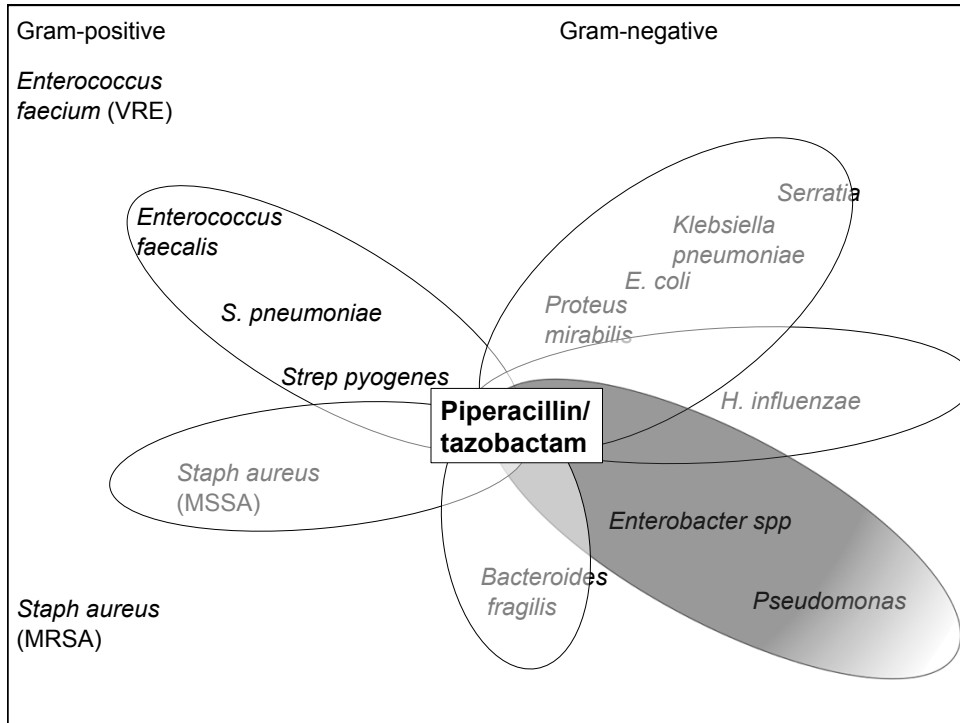
Sites of Infection

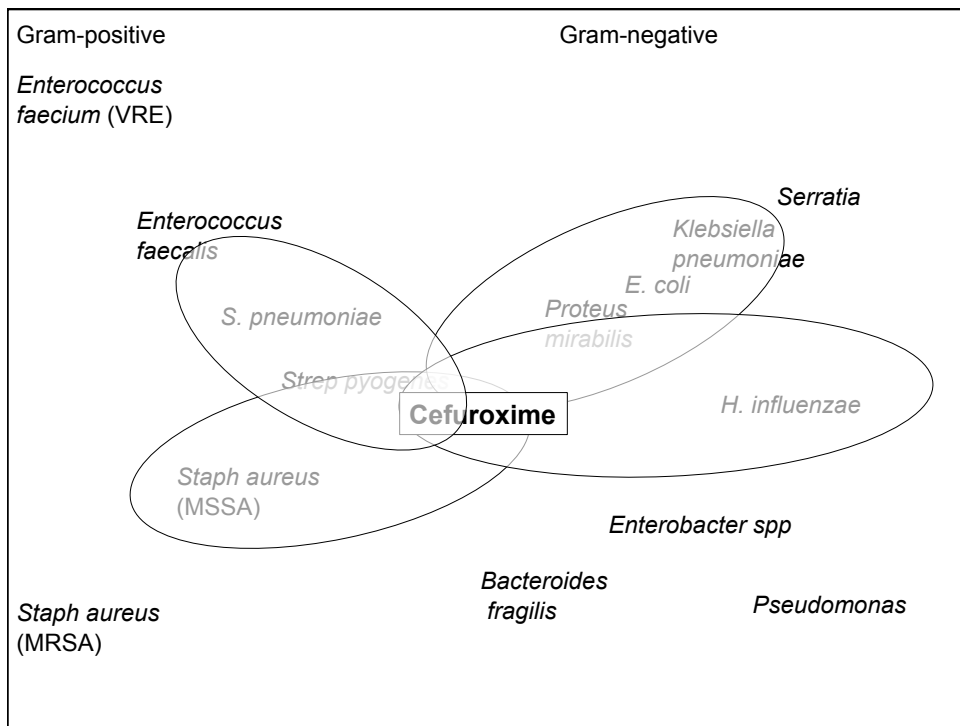
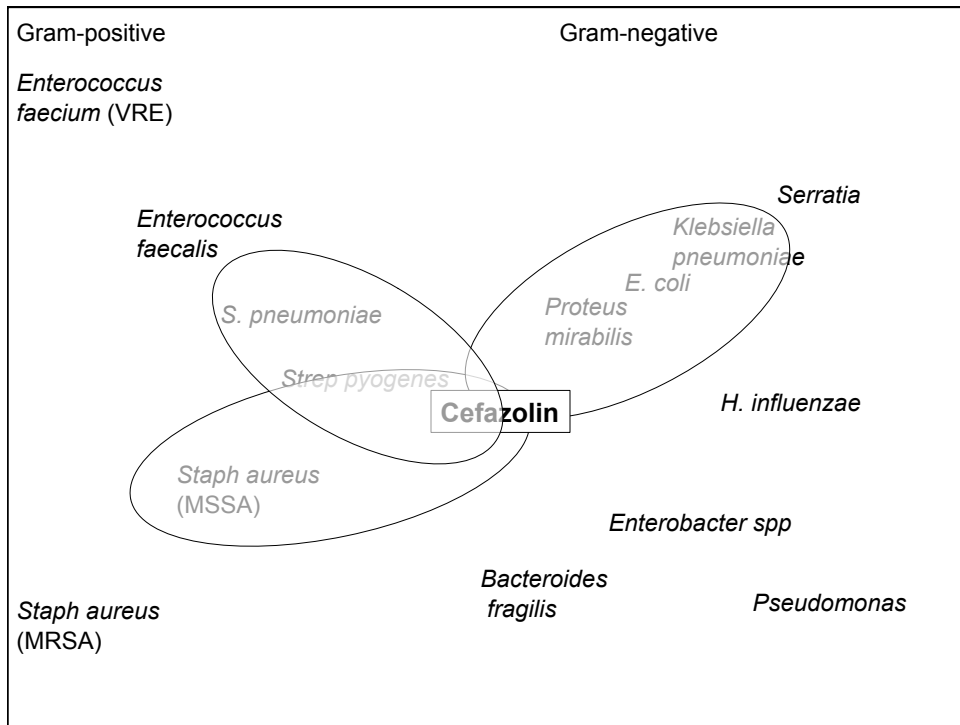


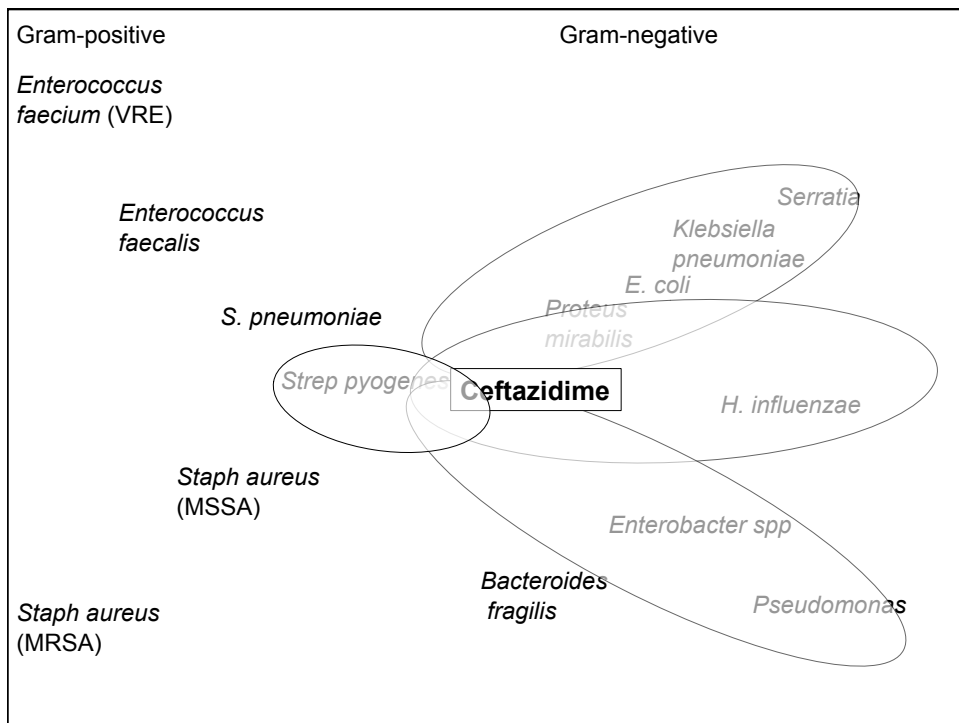
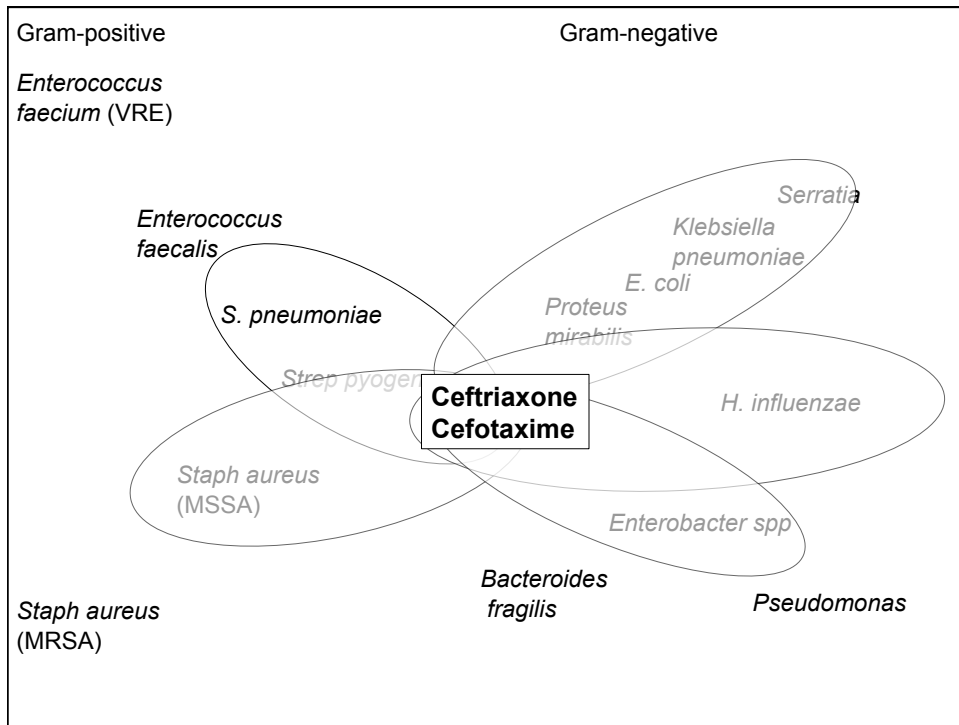


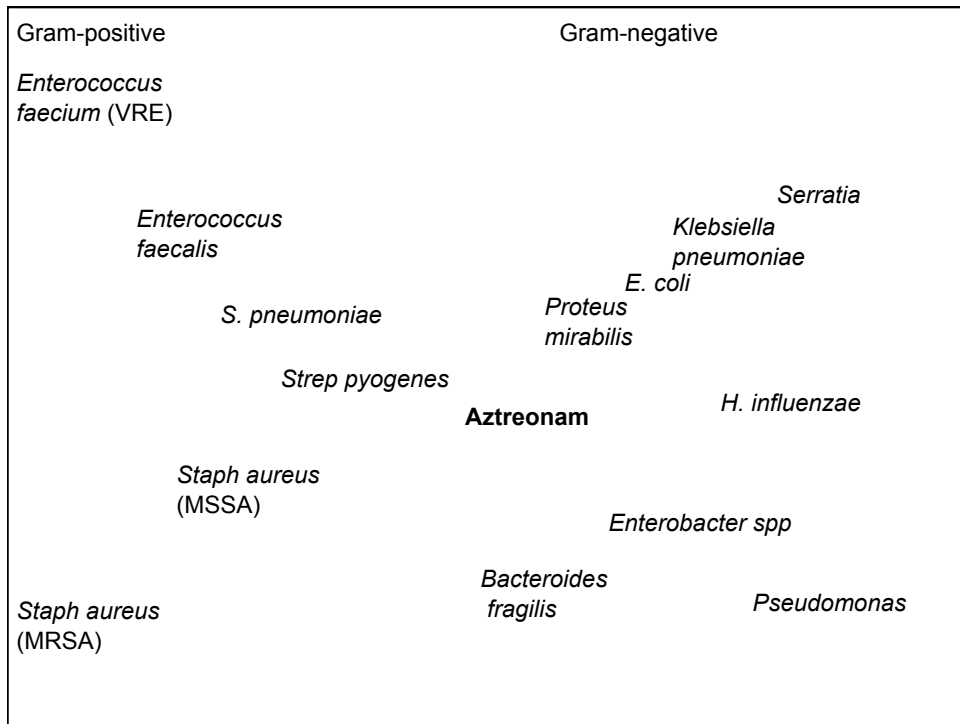
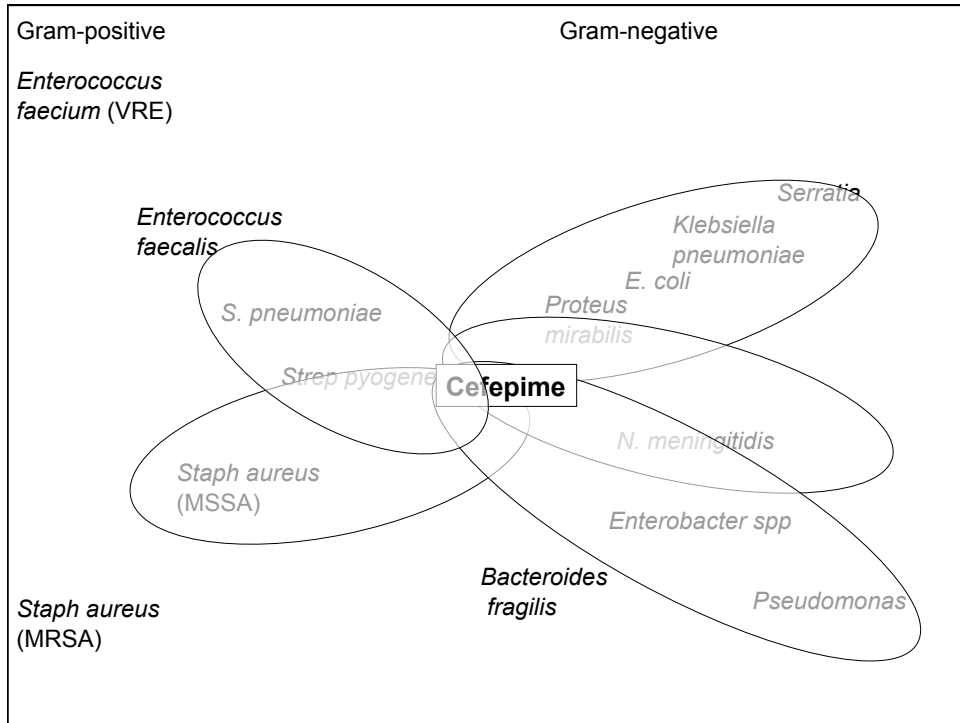


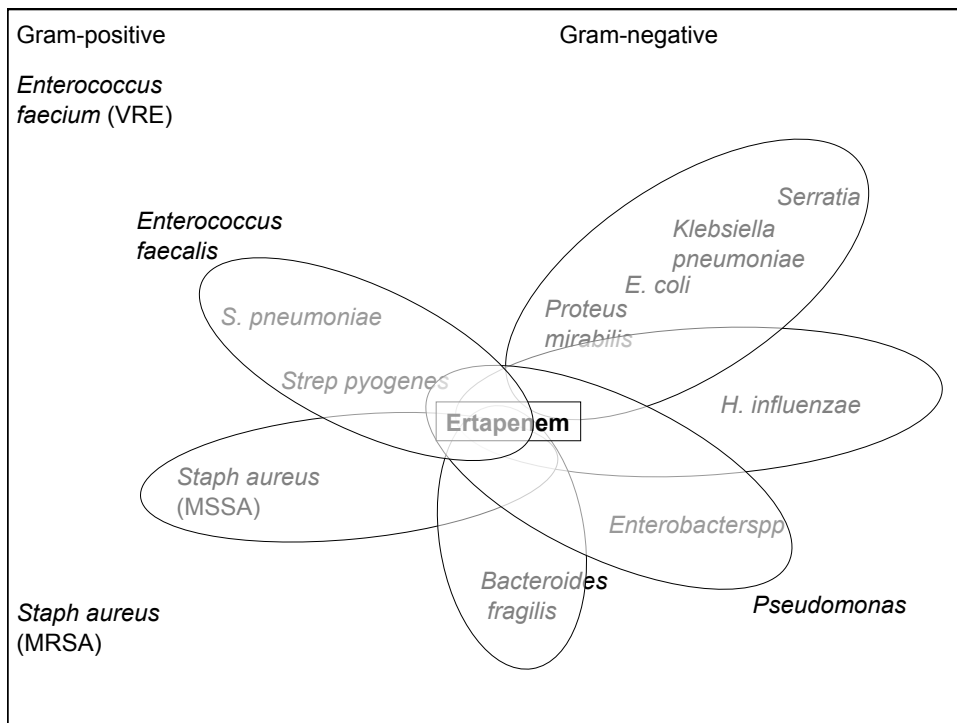
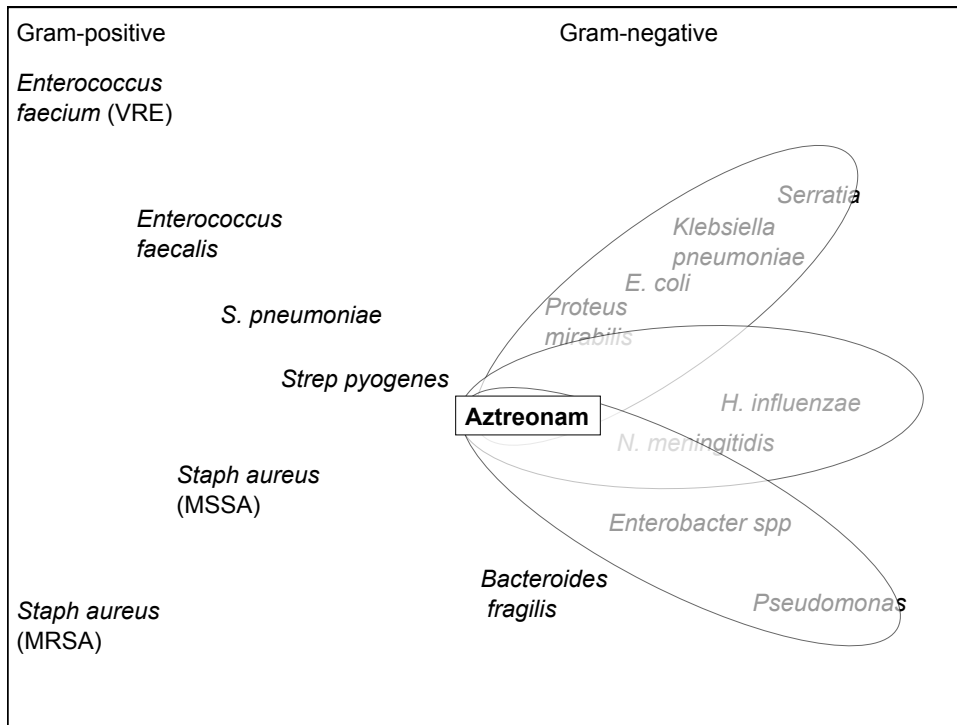


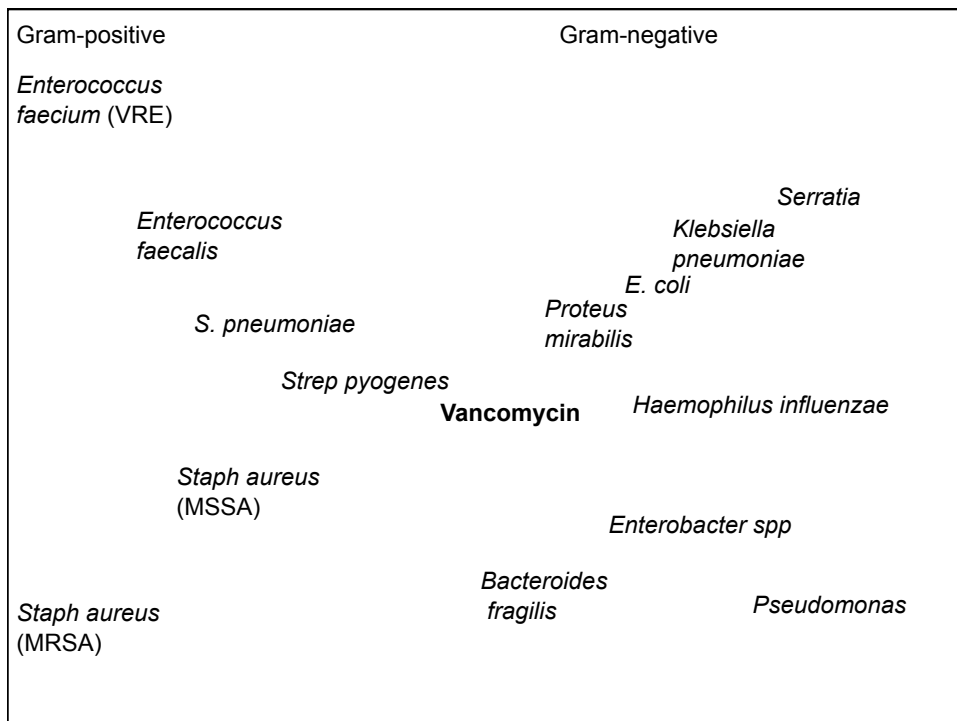
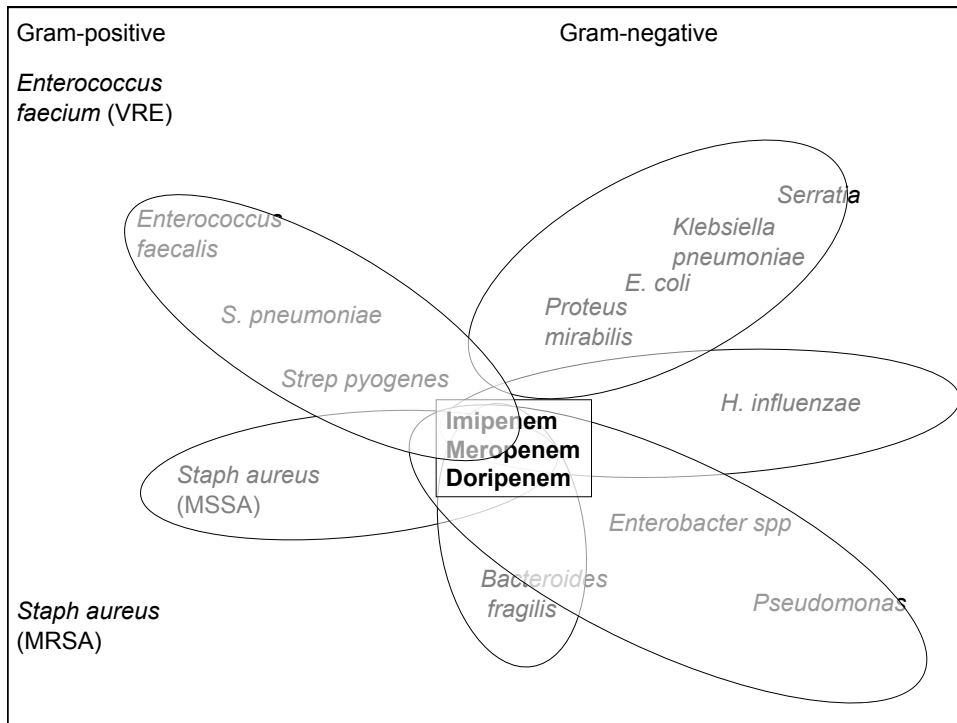


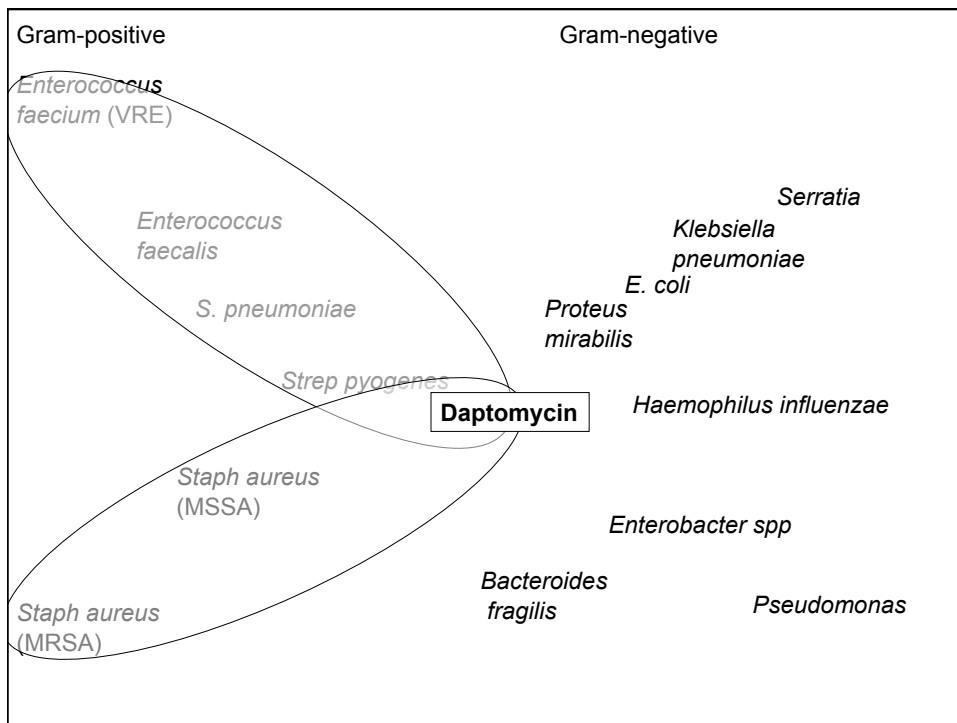
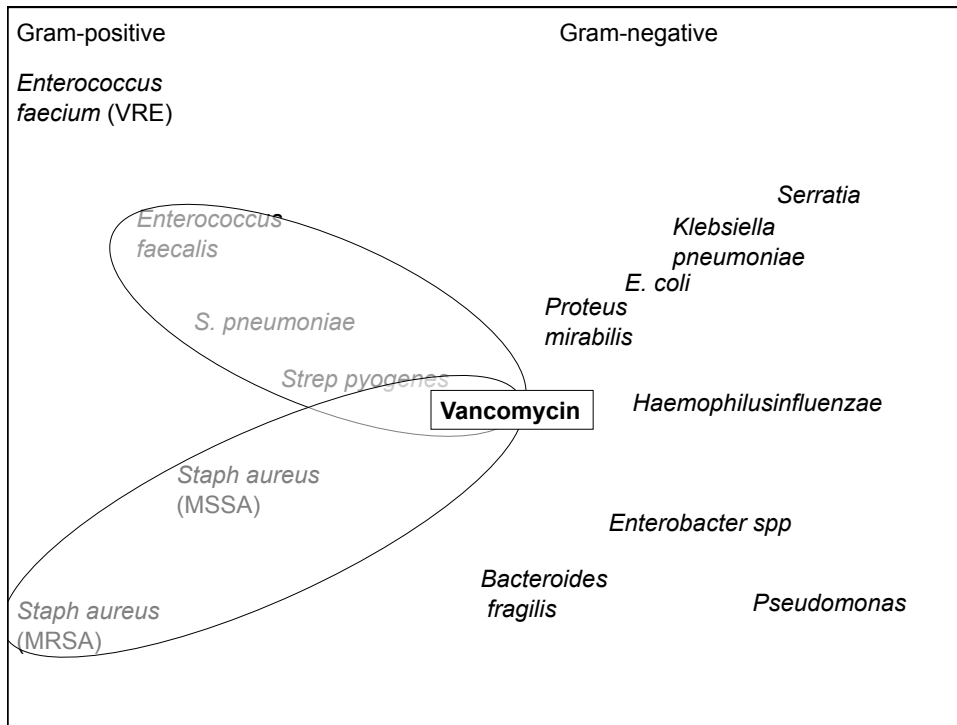


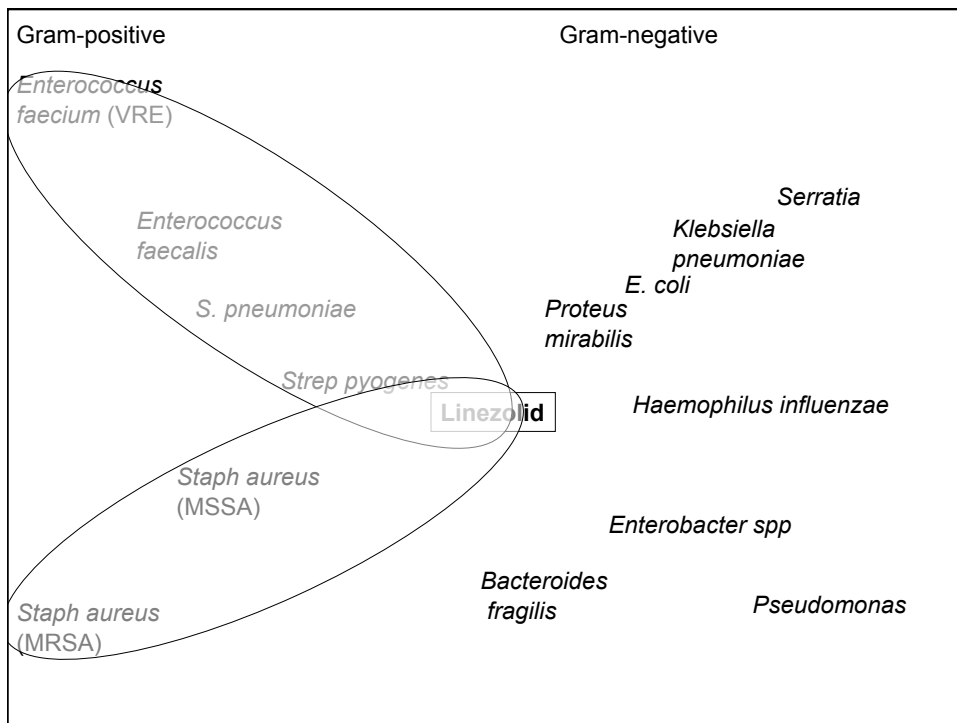
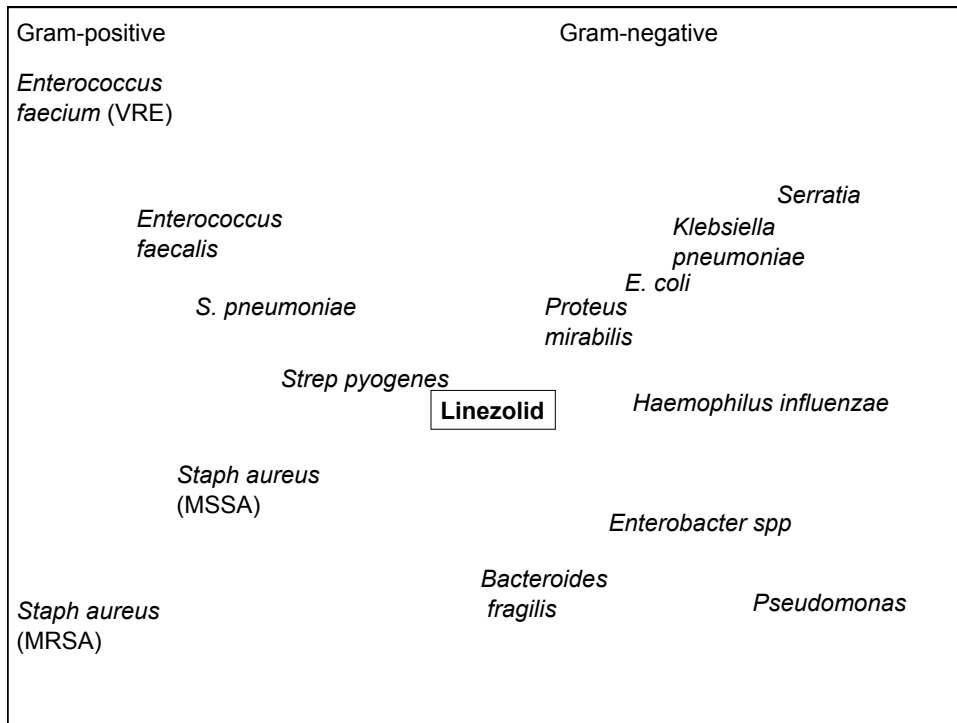


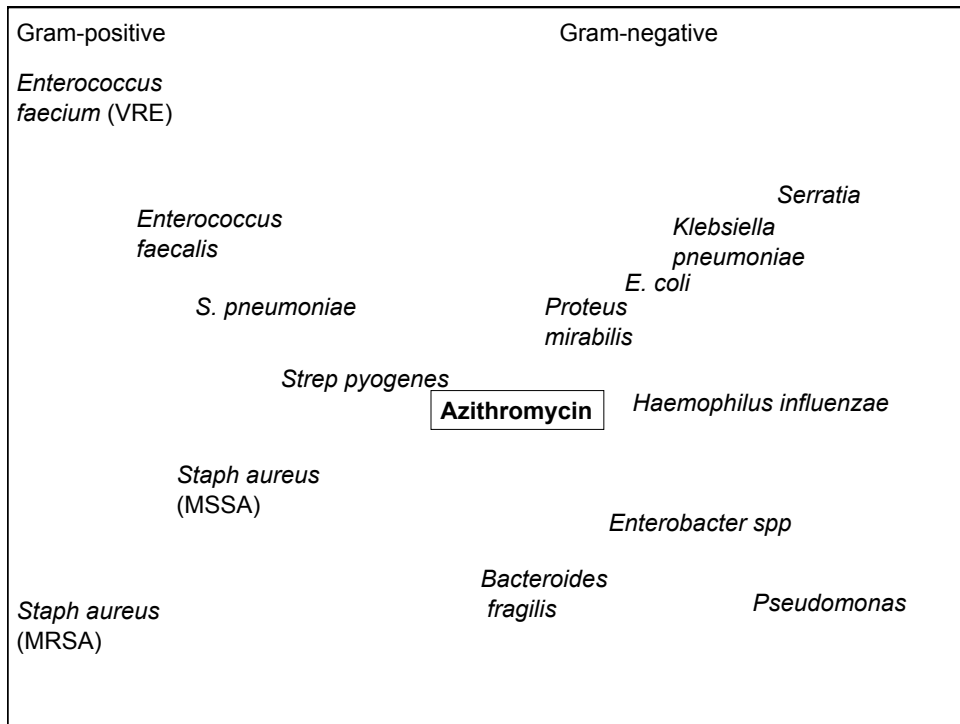
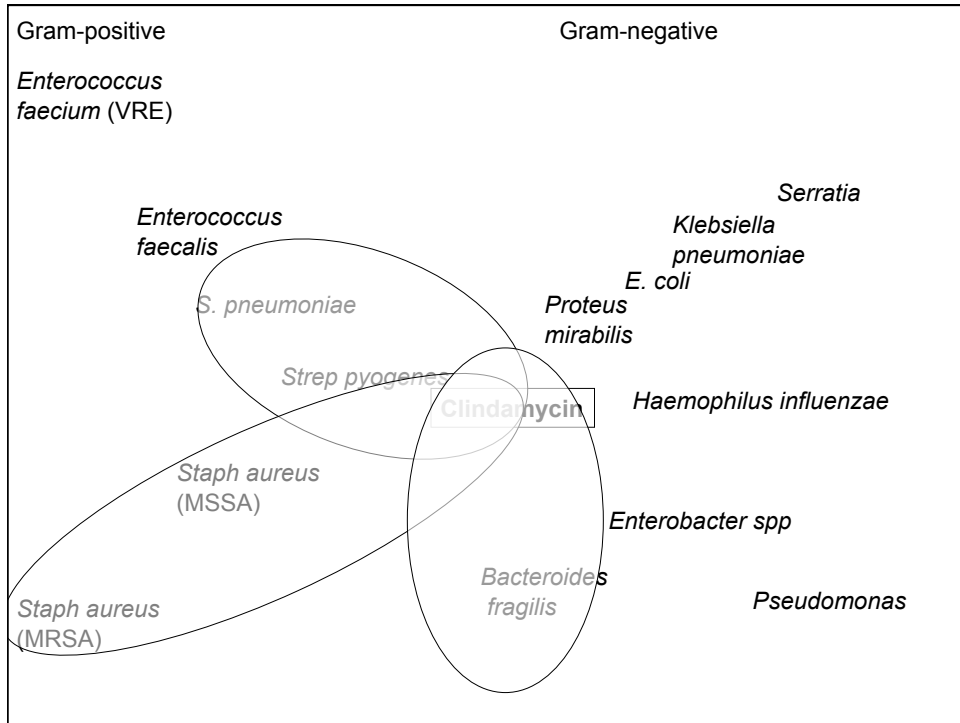


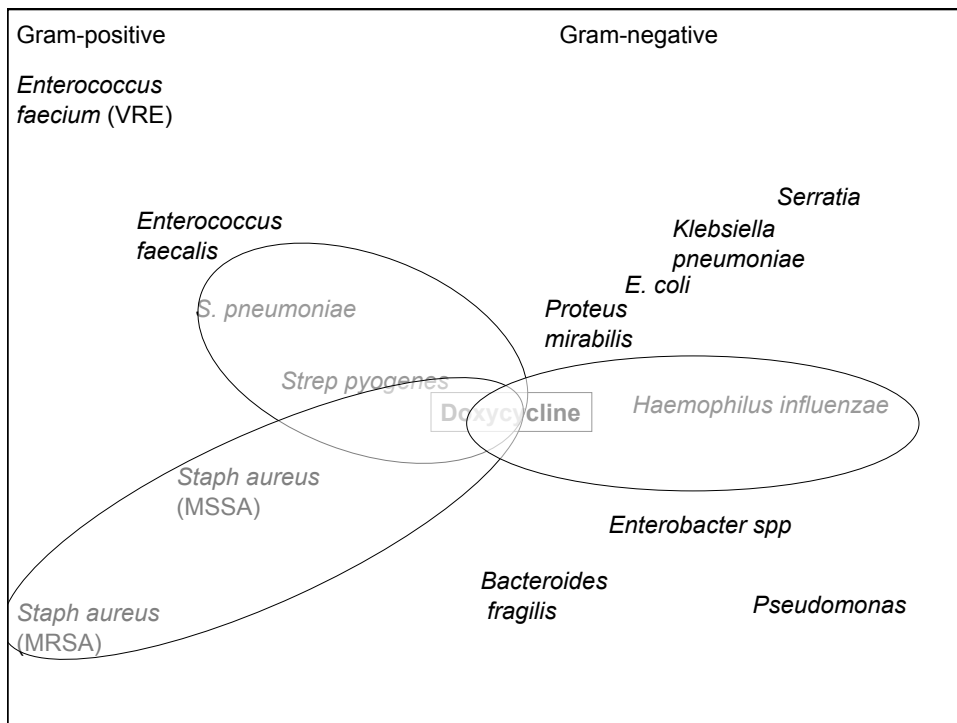
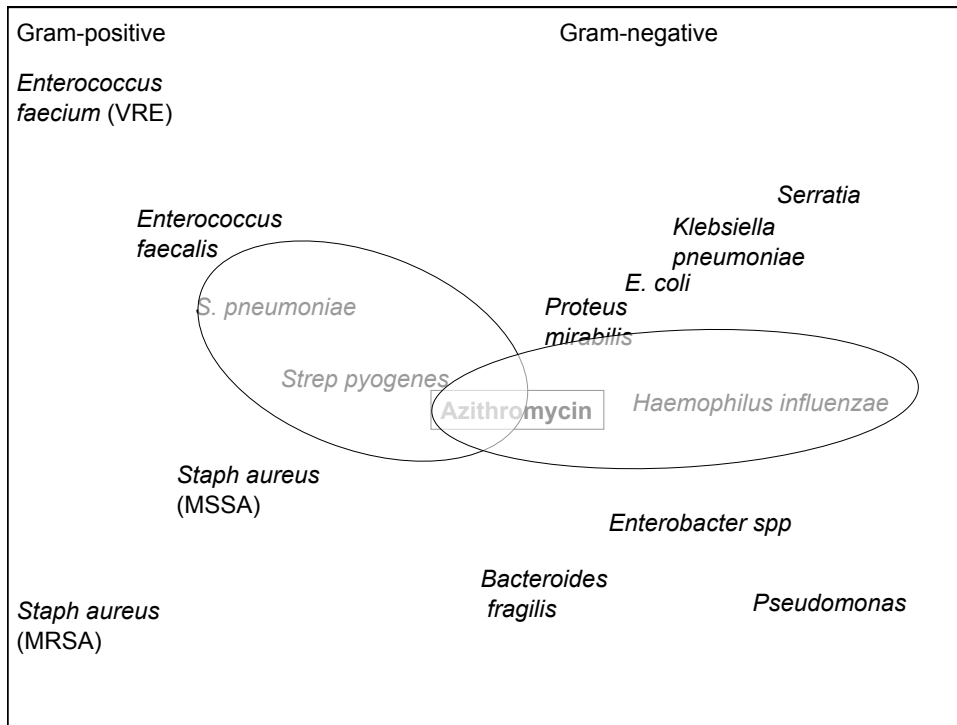


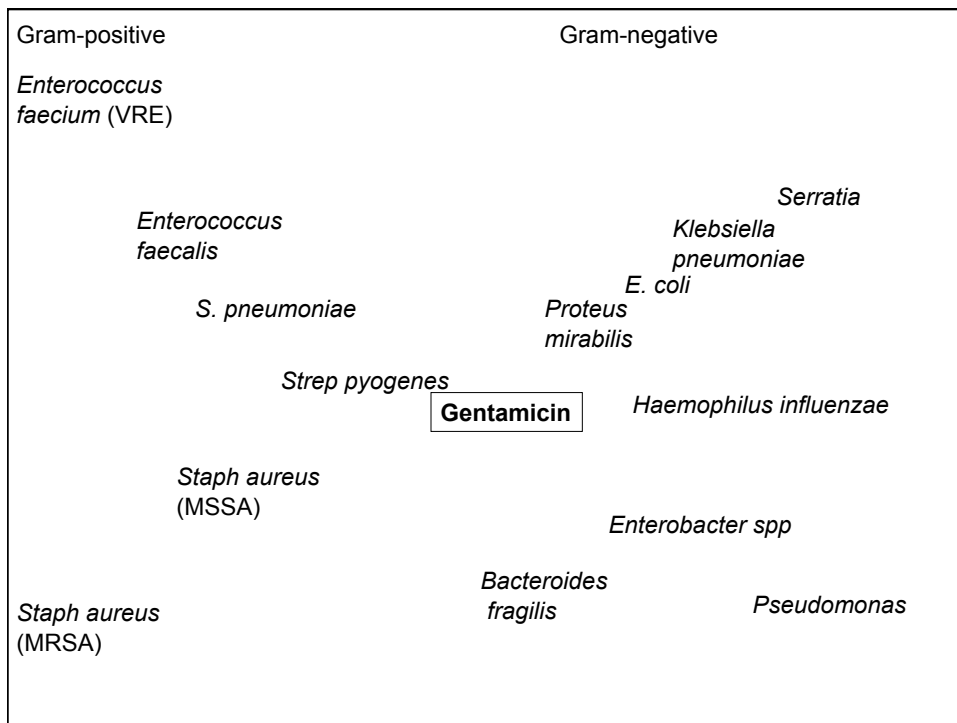
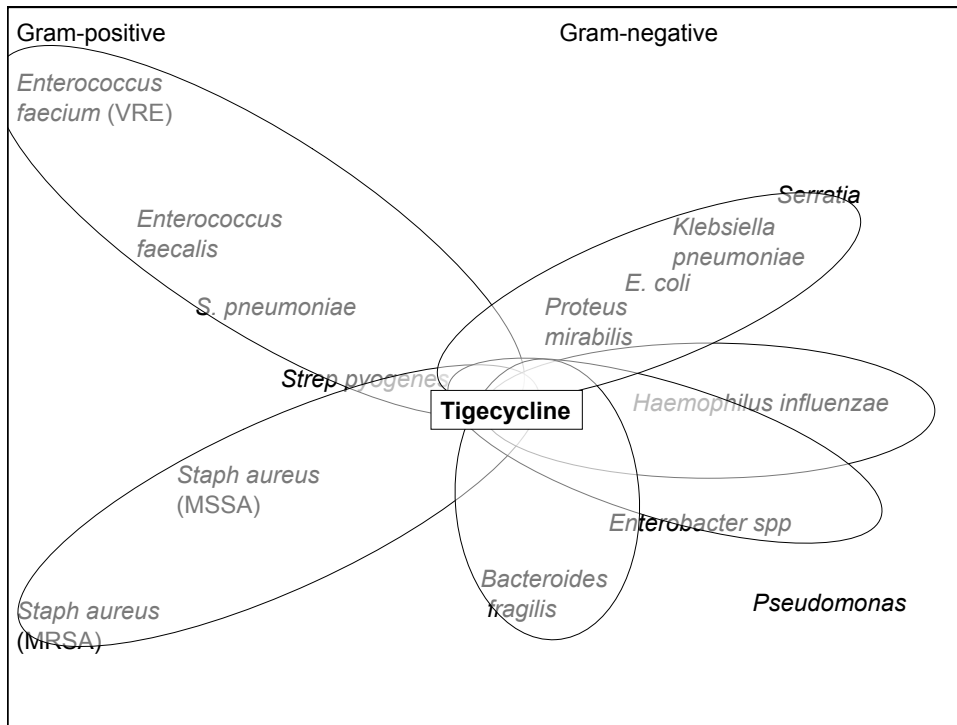


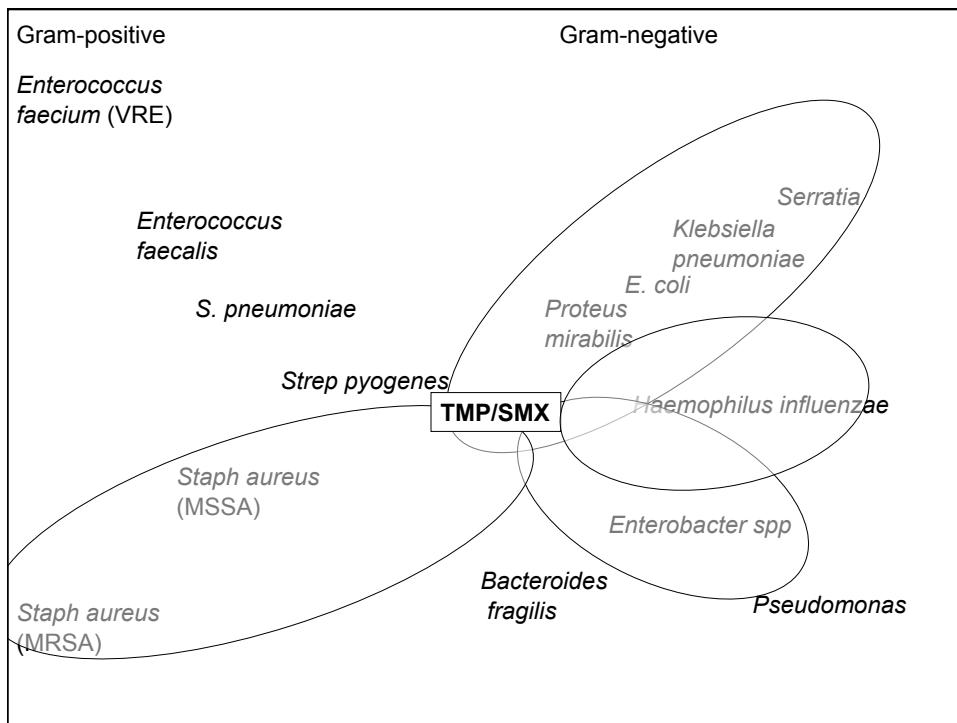
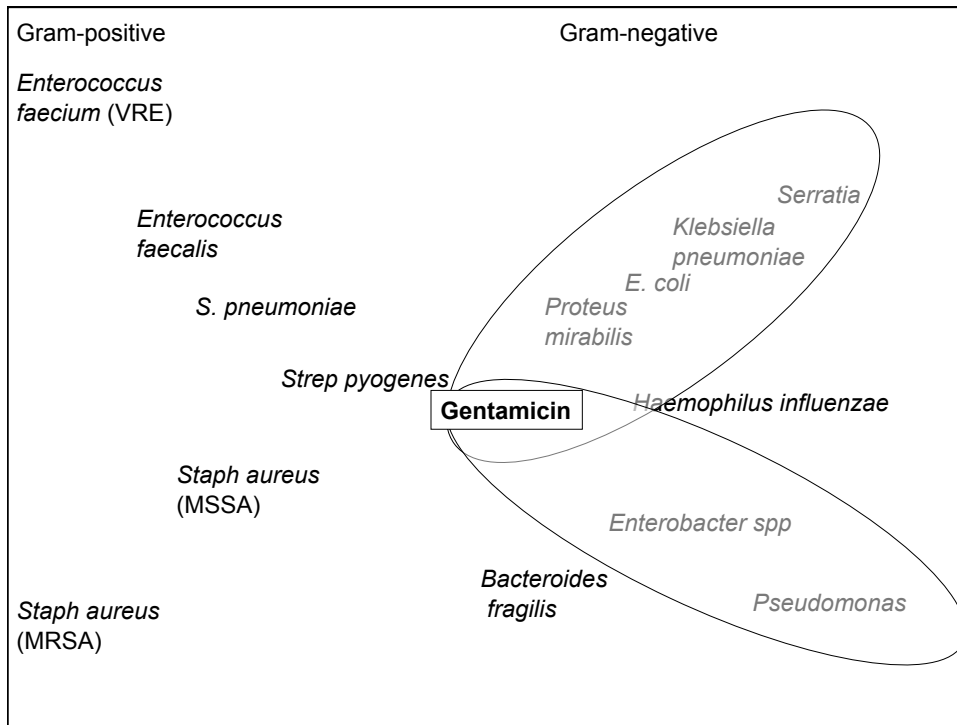


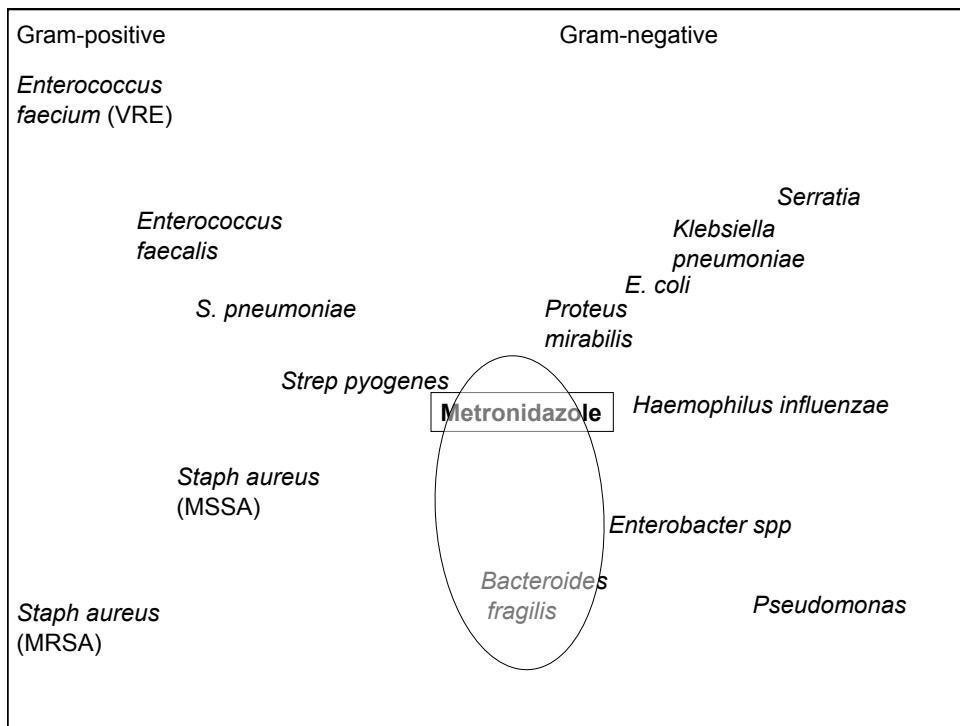
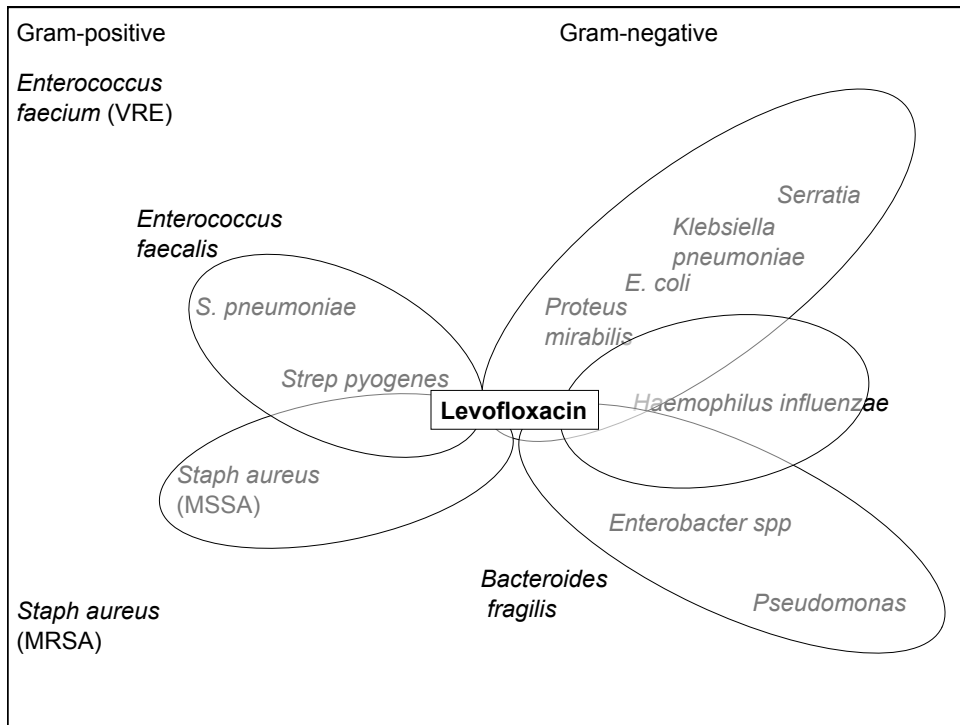












MRSA Drugs

- ▶ Tigecycline
- ▶ Vancomycin
- ▶ SMZ/TMP
- ▶ Rifampin (in combo only)
- ▶ Quinupristin-dalfopristin (Synercid)
- ▶ Linezolid
- ▶ Daptomycin
- ▶ Televancin
- ▶ Clindamycin, Tetracyclines (CA-MRSA)

Pseudomonal Drugs

- ▶ Antipseudomonal Penicillins (Zosyn)
- ▶ Carbapenems except Ertapenem
- ▶ 3rd and 4th gen. Cephalosporins (Fortaz, Cefepime)
- ▶ Some FQ – Cipro > Levaquin
- ▶ Aminoglycosides (Gentamicin, Tobramycin, Amikacin)
- ▶ Aztreonam

Enterococcus Drugs

- ▶ Penicillin G/V, Ampicillin, Amoxicillin
- ▶ PCN with Beta Lactamase Inhibitors
- ▶ Carbapenems (E. faecalis except Etrapanem)
- ▶ FQ (E. faecalis)
- ▶ Tigecycline
- ▶ Vancomycin
- ▶ Quinupristin/Dalfopristin
- ▶ Linezolid
- ▶ Daptomycin
- ▶ Rifampin (E. faecalis)
- ▶ Aminoglycoside (synergy with β -lactams for E. faecalis)
- ▶ Televancin (VSE)
- ▶ Nitrofurantoin

References

- ▶ Micromedex
- ▶ According to Dr. Conan MacDougall (Antimicrobial presentation, UCSF College of Pharmacy)