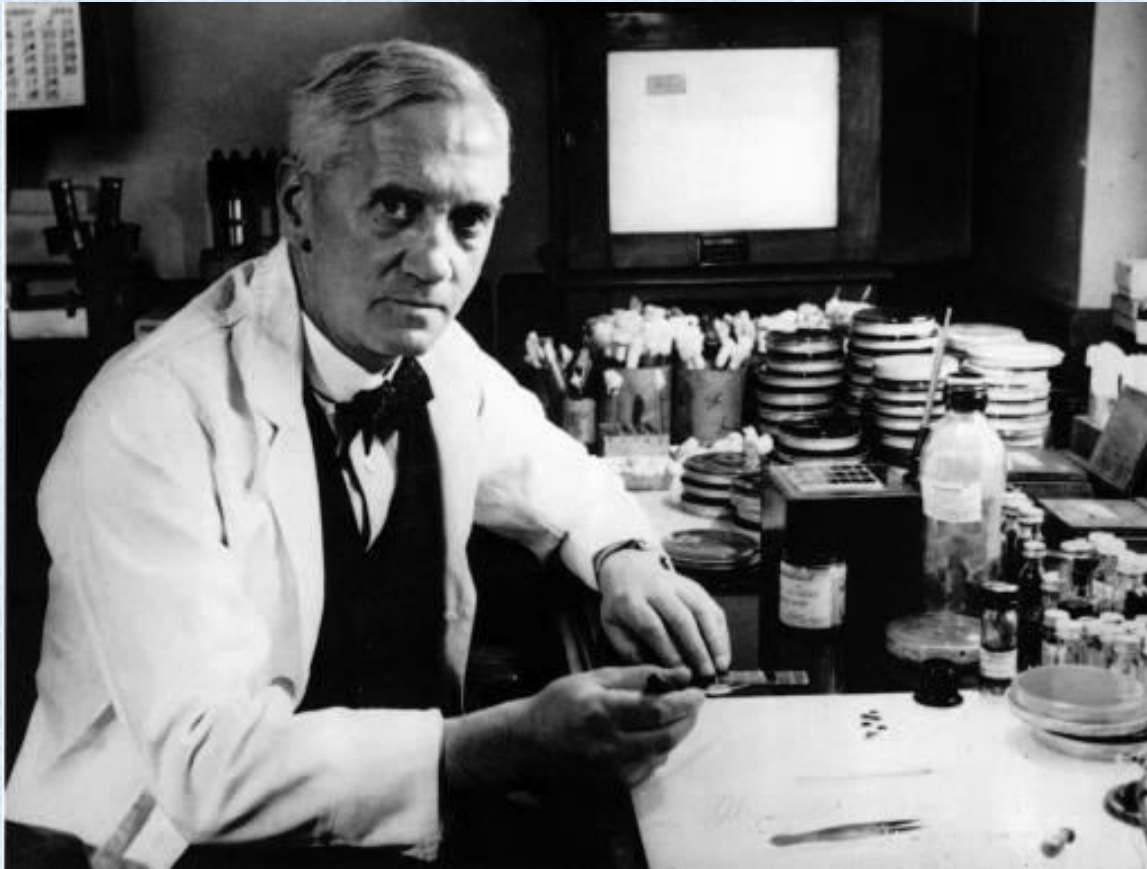


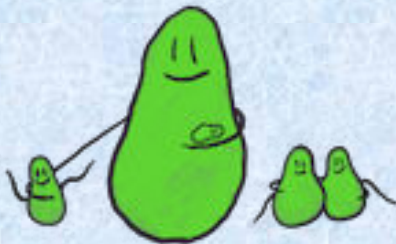
Antibiotics: An Overview

1928



Antibiotic effect

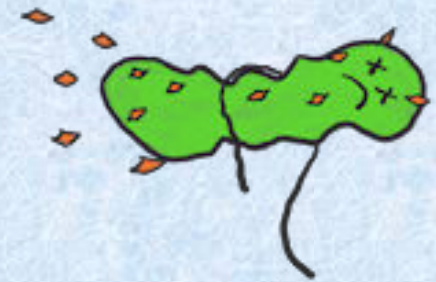
No antibiotics

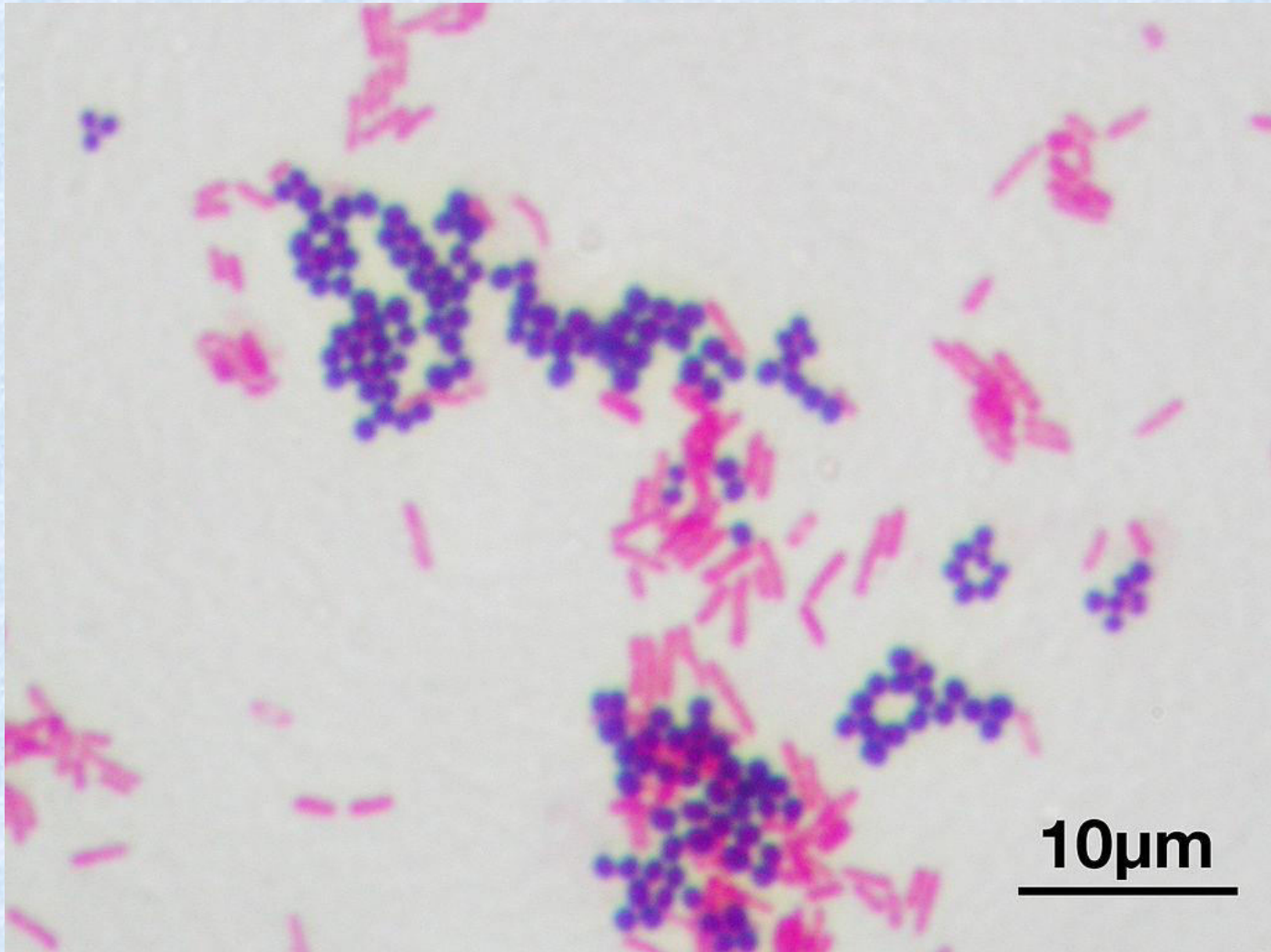


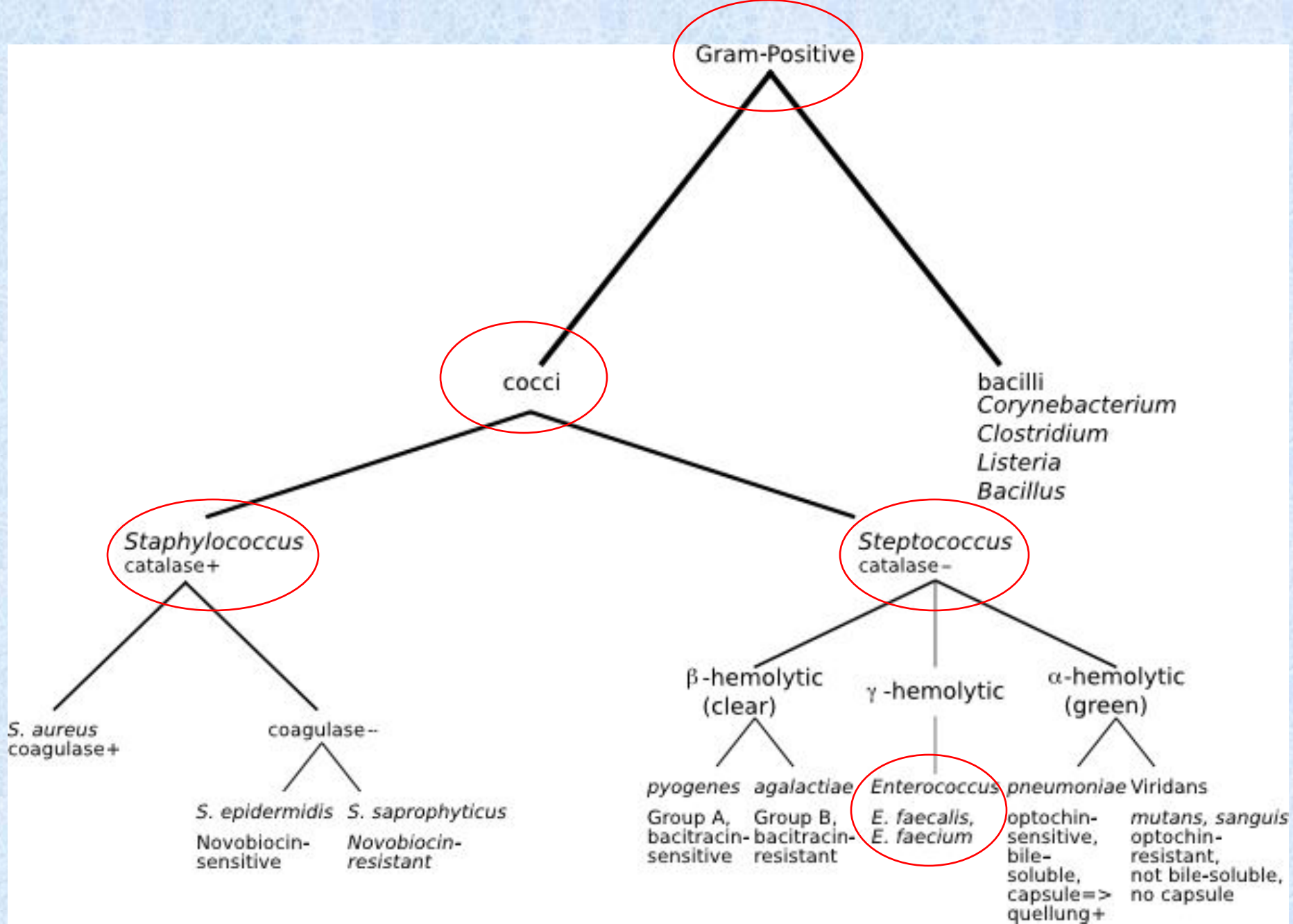
Bacterio-static



Bacteri-cidal







Organisms and associated infections

- **Staphylococcus Aureus:**
- **MSSA** (methicillin Sensitive S. aureus) and **MRSA**
- Skin/Soft tissue/bone/joint infections
- Central line infections
- Hospital acquired infections (MRSA)

Organisms and associated infections

- Streptococcus:
 - **S. Pneumonia**: Pneumonia, meningitis, otitis media, sinusitis, bacteremia
 - **S. Pyogenes (Group A strep)**: Tonsillitis, Skin/soft tissue infections
 - **S. Agalactiae (Group B strep)**: Neonatal sepsis
 - **Enterococcus**: UTI and Infective endocarditis

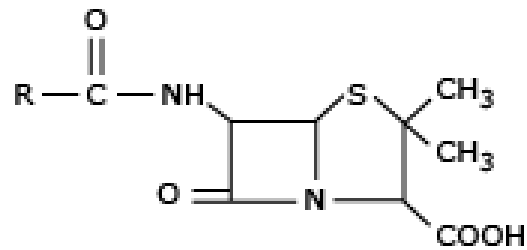
Organisms and associated infections

- **E. Coli:**
 - UTI and Intra-abdominal infections
- **Pseudomonas:**
 - Fever and neutropenia, immunocompromised
 - Hospital acquired infections
- **Anaerobes:** Intra-abdominal infections, aspiration pneumonia
- **Atypical bacteria:** Pneumonia (>5 y of age)

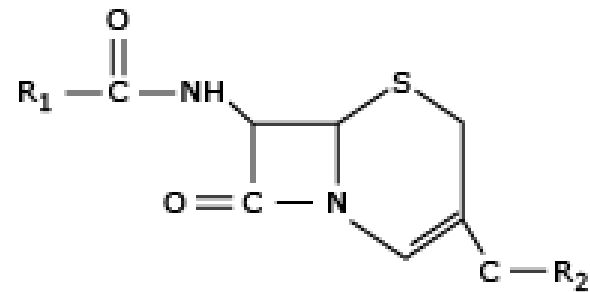
Classifications

- Penicillins
- Cephalosporins
- Glycopeptides
- Carbapenems
- Lincosamide
- Macrolides
- Metronidazole
- Trimethoprim-sulfamethoxazole
- Aminoglycosides
- Fluroquinolones
- Tetracyclines

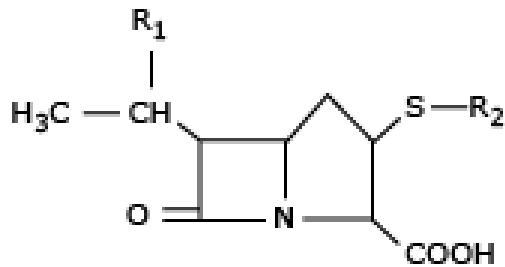
Beta-lactam antibiotics



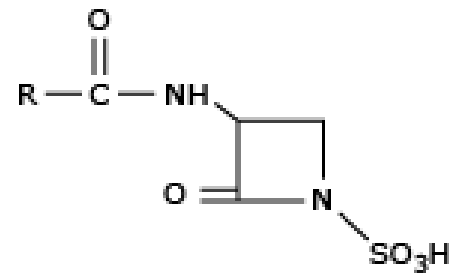
Penicillins



Cephalosporins



Carbapenems



Monobactams

Penicillins (PCN): Classification

- Inhibit cell-wall synthesis
- Natural PCN: PCN G (IV) and PCN V (Oral, Gi)
- Synthetic PCN:
 - Antistaphylococcal penicillins (penicillinase resistant) (nafcillin, oxacillin, cloxacillin and dicloxacillin): Against MSSA
 - Broad spectrum penicillins:
 - Amino-PCN (ampicillin IV, amoxicillin PO): more gram negative like E. coli
 - Ureidopenicillin: against pseudomonas(piperacillin IV, carbenicillin and ticarcillin)

Penicillins (PCN): Coverage and use

- Gram-positive cocci: Group A strep, Group B strep, some strep pneumonia and some enterococcus
- Mouth anaerobes (Not Bacteroides, the intestinal anaerobes)
- Some gram negative (Broad spectrum penicillins)
- When you add beta-lactamase inhibitor: (ampicillin and sulbactam, amoxicillin and clavulonic acid, piperacillin and tazobactam), that will extend to more gram negative, anaerobes and MSSA
- **Alteration in penicillin-binding protein (PBPs) (MRSA)**

Cephalosporins: Classification

- Inhibit cell-wall synthesis
- First generation (cefazolin IV and cefalexin PO)
- 2nd gen: (cefuroxime IV and PO)
- 3rd gen: (cefotaxime IV, ceftriaxone IV, and cefixime PO) and a subgroup against *Pseudomonas aeruginosa* (ceftazidime IV)
- 4th gen: (cefepime IV)
- 5th gen: (ceftaroline IV)

Cephalosporins: Coverage and use

- **First generation:** Most gram-positive cocci (Exceptions are MRSA, enterococcus). Some gram negatives like *E. coli*.
 - Skin/soft tissue infections, Group A strep
- **Second generation:** Haemophilus influenzae and *Moraxella catarrhalis*
 - Pneumonia and other URTI
- **Third generation:**
 - Meningitis, Sepsis, Pneumonia, UTI and many others
 - Ceftriaxone: formation of "sludge" in the biliary tract and displacement of bilirubin from albumin (not used < 1 mo of age)

Cephalosporins: Coverage and use

- **Fourth generation:**
- Cefepime is as active for *Pseudomonas aeruginosa*

- **Fifth generation** : Ceftaroline has a spectrum of activity similar to ceftriaxone but with improved gram-positive activity (MRSA)

Glycopeptides

- **Vancomycin IV and PO**, teicoplanin IV
- Inhibits bacterial cell wall synthesis
- Gram positive including MRSA and enterococcus

- **Meningitis**
- **Catheter-related infections**
- **Hospital-acquired infections**
- **Foreign body associated infections**
- ***C. difficile*** (PO only)



8/3/2023

Glycopeptides: Vancomycin

- Red man syndrome: slow the infusion rate to over 2 hours and increase the dilution volume
- Extravasation will cause serious injury with possible necrosis and tissue sloughing.

Carbapenems

- Very broad spectrum of activity.
- Inhibit bacterial cell wall synthesis
- **Imipenem, meropenem**, ertapenem, doripenem
- Stable to beta-lactamase including extended-spectrum beta-lactamases (ESBL)

- Carbapenems lack activity against *Enterococcus faecium*, MRSA
- Ertapenem lacks activity against *Pseudomonas aeruginosa*

- **intra-abdominal infections,**
- **nosocomial pneumonia,**
- **febrile neutropenia**

Lincosamide

- **Clindamycin**
- Anaerobic, streptococcal, and staphylococcal infections
- Antitoxin effect against toxin-elaborating strep and staph
- Disrupts protein synthesis

- **Bone/Joint and skin/soft tissue infection including MRSA**
- **Toxic shock syndrome**
- **Aspiration pneumonia**

Macrolides

- Azithromycin, Erythromycin, Clarithromycin
- Disrupts protein synthesis
- Gram-positive (strep, staph) and atypical bacteria, *Bordetella pertussis*
- *Common substitute for patients with a penicillin allergy*

Metronidazole

- Inhibits DNA Synthesis
- Anaerobic bacteria and protozoa
- *Clostridium difficile* infection
- Aspiration pneumonia
- Intra-abdominal infections
- lung abscess
- Amebiasis

Bactrim (Trimethoprim-sulfa)

- Inhibits folate biosynthesis and metabolism
- Gram negative and most gram positive (MRSA), no coverage for group A strep
- Not in G6PD or neonates (displaces Bilirubin)

- **Urinary tract infections**
- **Skin/soft tissue and bone/joint infections**
- **Treatment/prophylaxis of *Pneumocystis jirovecii* pneumonia (PCP)**

Aminoglycosides

- Gram-negative aerobic bacteria, including pseudomonas
- Gram positive usually as synergistic effect
- Inhibit protein synthesis
- **Gentamicin**, tobramycin, amikacin, neomycin
- Usually used for synergy or double coverage, or for UTI

Anti-specifics

- Anti-pseudomonas

Aminoglycosides, quinolones , cephalosporins (ceftazidime, cefepime), antipseudomonal penicillins, carbapenems

- Anti-Anaerobic

metronidazole, clindamycin, penicillin (i.e. ampicillin, piperacillin) and a beta-lactamase inhibitor (i.e. clavulanic acid, sulbactam, tazobactam), carbapenem

- Anti-Atypical

Macrolides and Tetracyclines

- Anti-MRSA

Vancomycin, Bactrim, Clindamycin, Doxycycline, Linezolid, ceftaroline

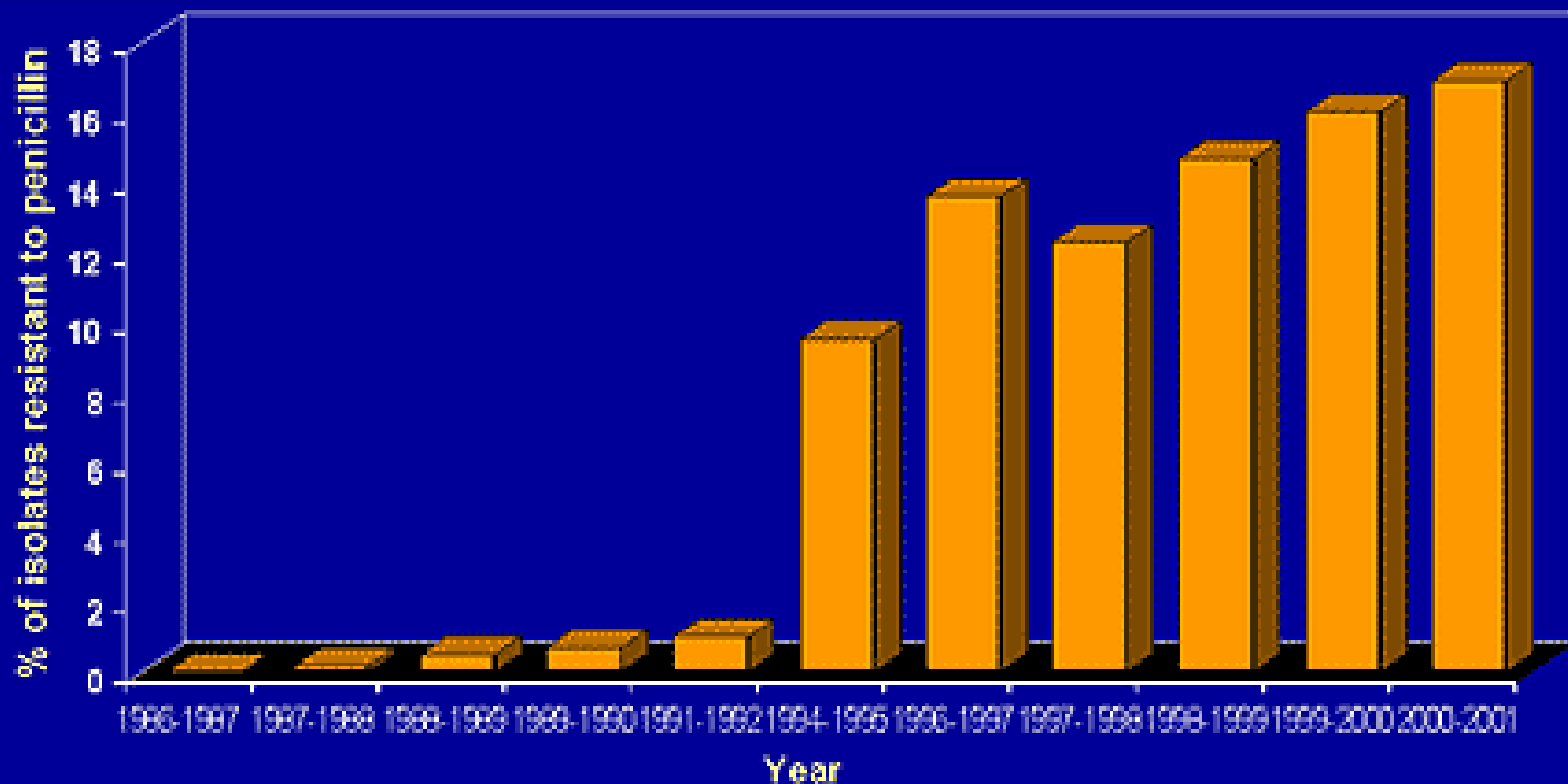
- Anti-C.diff

Metronidazole, Oral vancomycin

ANTIMICROBIAL INTRODUCED	YEAR	RESISTANCE REPORTED
	1940	Penicillin-resistant <i>Staphylococcus aureus</i>
Penicillin	1943	
Tetracycline	1950	
Erythromycin	1953	
	1959	Tetracycline-resistant <i>Shigella</i>
Methicillin	1960	
	1962	Methicillin-resistant <i>Staphylococcus aureus</i> MRSA
	1965	Penicillin-resistant pneumococci
Gentamicin	1967	
	1968	Erythromycin-resistant Streptococci
Vancomycin	1972	
	1979	Gentamicin-resistant enterococci
Ceftazidime and Imipenem	1985	
	1987	Ceftazidime-resistant Enterobacteriaceae
	1988	Vancomycin-resistant enterococci (VRE)
Levofloxacin	1996	Levofloxacin-resistant pneumococci
	1998	Imipenem-resistant Enterobacteriaceae
Linezolid	2000	XDR-TB
	2001	Linezolid-resistant <i>Staphylococcus aureus</i>
	2002	Vancomycin-resistant <i>Staphylococcus aureus</i>
Daptomycin	2003	
	2004	MDR Acinetobacter/ <i>Pseudomonas aeruginosa</i>
	2009	Carbapenem-resistant Enterobacteriaceae
Ceftaroline	2010	
	2011	Ceftaroline-resistant <i>Staphylococcus aureus</i>

- Thank you

High-Level Penicillin-Resistant (MIC ≥ 2 mcg/mL) *S pneumoniae* in the US



Breiman RF, et al. *JAMA*. 1994;271:1831-1835. Doern GV, et al. *AAC*. 1996;40:1208-1213. Thomsberry C, et al. *DMDD*. 1997;29:249-257. Thomsberry C, et al. *JAC*. 1999;44:749-759. Thomsberry C, et al. 39th ICAAC, 1999, abstract 820. Selman LJ, et al. 40th ICAAC, 2000, abstract 1789. Kelly LJ, et al. 41st ICAAC, 2001, abstract 2109. Data on file, Ortho-McNeil Pharmaceutical, Inc.

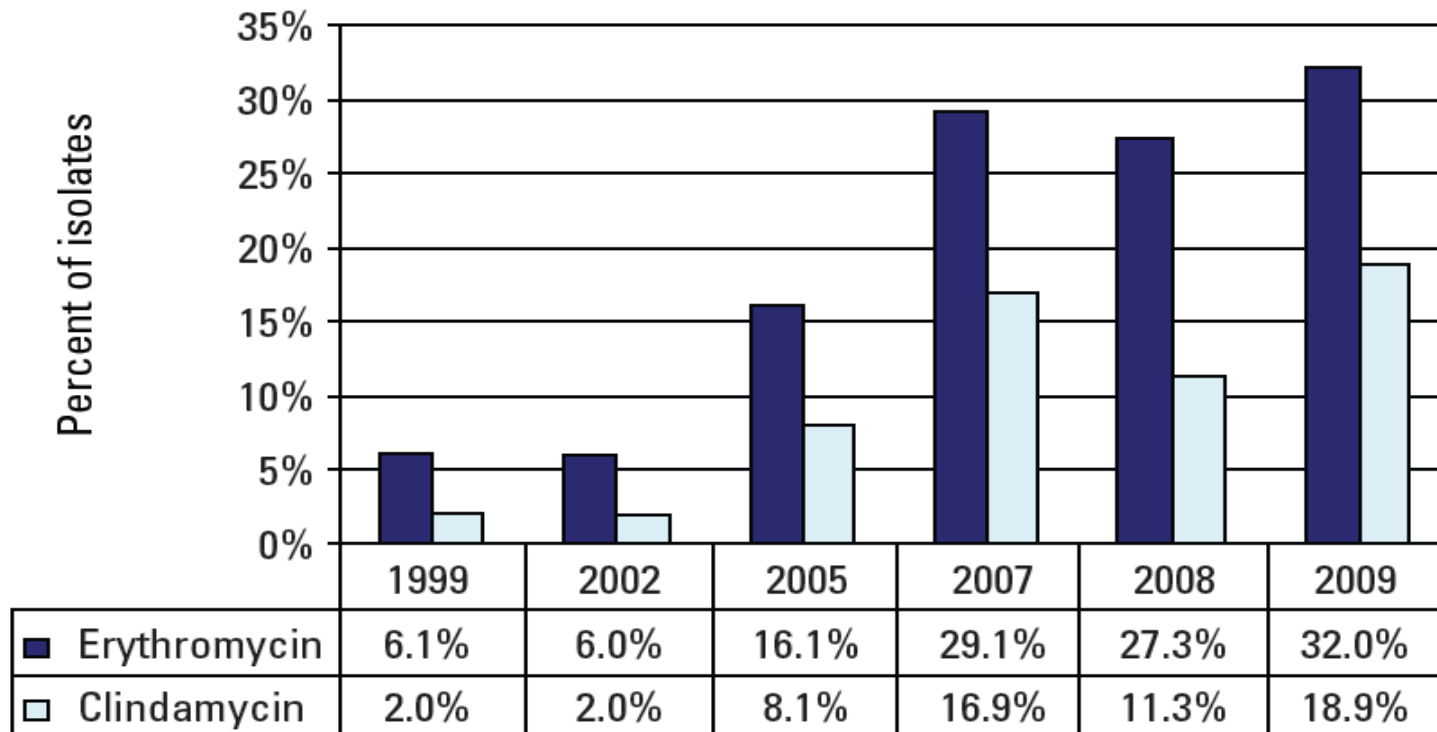


Figure 2. Percent of *S. pneumoniae* isolates resistant to erythromycin and clindamycin.

