HENRY FORD HEALTH



HENRY FORD HEALTH + MICHIGAN STATE UNIVERSITY Health Sciences



Integrated Activity and Tools for Antimicrobial Stewardship, Infection Prevention & Diagnostic Stewardship

## Introduction to Antibiotics









## Overview

- 1. Principles of pharmacology
- 2. Principles of basic microbiology
- 3. Antibiotic classes
- 4. Practical utility of antibiotics



Four Moments of Antibiotic Decision Making. Content last reviewed November 2019. Agency for Healthcare Research and Quality, Rockville, MD.

### **Pharmacokinetic Concepts** *What the body does to the drug*

Absorption	<ul> <li>IV administration is rapid and complete</li> <li>IV/PO conversion recommended for high bioavailable drugs</li> </ul>
Distribution	<ul> <li>Highly dependent on drug class</li> <li>Tissue penetration is important for specific infections</li> </ul>
Metabolism	<ul> <li>Some antimicrobials are eliminated through hepatic system</li> <li>Source of some drug interactions</li> </ul>
Excretion	<ul> <li>Most antimicrobials require dose adjustment in renal dysfunction</li> </ul>

### Pharmacodynamic Concepts What the drug does to the organism

### **Concentration Dependent Killing**

- As concentration increases, extent of bacterial killing increases
- Goal of therapy: maximize <u>concentration</u> of drug exposure

### **Time Dependent Killing**

- The longer the duration of exposure, the greater the antibacterial activity
- Goal of therapy: optimize <u>duration</u> of drug exposure

# Antibiotic Mechanism of Action

# **General Mechanisms of Action (& Resistance)**



# **Basics of microbiology**







# Antibiotic Spectrum of Activity: General Considerations

### Caveat

- "Coverage" trends here are based on general, empirical data.
  - -You should always be aware of local microbiology, patient risk factors, and known culture/susceptibility results when available
- This portion of the presentation is a <u>basic guide</u> and is not intended as a replacement for actual references

## Various classes of antibiotics

- Beta lactams
  - Penicillins, cephalosporins, carbapenems, aztreonam
- Aminoglycosides
- Macrolides
- Quinolones
- Tetracyclines
- Misc gram positive antibiotics
- Polymyxins





### Access. Watch. Reserve.

## ACCESS GROUP

- first or second choice antibiotics
- offer the best therapeutic value, while minimizing the potential for resistance

WATCH GROUP

- first or second choice antibiotics
- only indicated for specific, limited number of infective syndromes
- more prone to be a target of antibiotic resistance and thus prioritized as targets of stewardship programs and monitoring

RESERVE GROUP

- "last resort"
- highly selected patients (lifethreatening infections due to multi-drug resistant bacteria)
- closely monitored and prioritized as targets of stewardship programs to ensure their continued effectiveness

## Are there differences in how antibiotics from the different groups are administered?





Generally, antibiotics in ACCESS group are more often available as oral formulations (nearly 60% of them), while this percentage is lower in the two other groups. 40% of WATCH antibiotics have oral formulations; the number is only 10% in the RESERVE group.

### EML updates 2017 / 2019 / 2021



## **Review of infections**

# Frequent infections Mostly community-acquired infections Mostly empiric use

- Certain infections by specific pathogens
   ✓ syphilis, cholera, gonorrhea, shigellosis,...
- Review of systematic reviews and guidelines



Drug Class	
Drugs	
Gram-positive highlights	
Gram-negative highlights	
Other highlights	

### ACCESS antibiotics

### WATCH antibiotics

#### **RESERVE** antibiotics

## PENICILINS









Other PCN + BLI Combos	
Drugs to Remember	Piperacillin/tazobactam (IV)
Gram-positive highlights	Similar to aminopenicillin/BLI combos
Gram-negative highlights	Broad Gram-negative coverage Adds PsA coverage Does NOT cover ACBI
Other highlights	Broad anaerobic coverage

# CEPHALOSPORINS



	1 <sup>st</sup> Gen Cephalosporins
Drugs to Remember	Cefazolin (IV) Cephalexin (PO) Cefadroxil (PO)
Gram-positive highlights	Good MSSA, strep No enterococcus, no MRSA CoNS frequently resistant
Gram-negative highlights	Covers basic enterics, Proteus spp.
Other highlights	Minimal









4th Gen Cephalosporins	
Drugs to Remember	Cefepime
Gram-positive highlights	Good strep, MSSA NO Enterococcus
Gram-negative highlights	Broad, including PsA and "fancy" enterics NO ESBLS
Other highlights	Adequate mouth anaerobe

# CARBAPENEMS



# Which carbapenem is more associated with seizures?

- Ertapenem
- Meropenem
- Imipenem
- Doripenem

## Meropenem has additional coverage of what organisms compared to ertapenem?

- Acinetobacter
- Enterococcus
- Pseudomonas
- Streptococcus
- Neisseria

# AMINOGLYCOSIDES



# What are common side effects of aminoglycosides

- Tendon rupture
- Ototoxicity
- Neurotoxicity
- Nephrotoxicity
- Ocular toxicity

# MACROLIDES





# What are common side effects of macrolides?

- Hearing loss
- GI upset
- QT prolongation

QUINOLONES



# **GLYCOPEPTIDES**



Glycopeptides	
Drugs to Remember	Vancomycin
Gram-positive highlights	BROAD, including MRSA VRE- others MAY be active
Gram-negative highlights	None
Other highlights	Gram-positives "mouth" anaerobes Oral vancomycin – <i>C. difficile</i>



## **Notes on Vancomycin**

- Side effects:
  - -Red Man Syndrome
- Oral is *only* for C difficile infections
- What should you do in this case if this happens to your patient?



## MISCELLANEOUS



# What side effects are associated with linezolid?

- Thrombocytopenia
- Skeletal muscle toxicity and rhabdomyolysis
- Elevated CK
- Serotonin syndrome
- Peripheral neuropathy
- Eosinophilic pneumonia



## **Notes on Tetracyclines**

- Side effects:
  - -Phototoxicity
  - -Pill-esophagitis
- Cannot be used in pregnancy
- Should not be used in children < 8 years old
- Should be taken on empty stomach to enhance absorption, avoid taking with multivitamins





Polymyxins		
Drugs to Remember	Colistin (polymyxin E)	
Gram-positive highlights	None	
Gram-negative highlights	VERY BROAD, including MDRO POOR vs. Proteus, Providencia, Serratia	
Other highlights	None	

## **Notes on Polymyxins**

- Side effects:
  - -Nephrotoxic
  - -Neurotoxic
- Adjunctive therapy, monotherapy associated with increased resistance



## **Notes on Trimethoprim/Sulfamethoxazole**

- Side effects:
  - -Bone marrow suppression (dose dependent)
  - -Aseptic meningitis
  - -Hyperkalemia
  - -Crystalluria
- Do not use in patients with sulfa allergies and G6PD deficiency





Metronidazole	
am-positive ghlights	No aerobes
am-negative ghlights	No aerobes
her Jhlights	Great vs. wide range of anaerobes Not great vs. "mouth anaerobes" Also: Protozoa, trichomonas, entamoeba, Giardia

## **Notes on Metronidazole**

- Side effects:
  - -Metallic taste
  - -Peripheral neuropathy



# Using AWaRe in a practical setting

## MRSA Bacteremia

# WATCH GROUP

# RESERVE GROUP

### VANCOMYCIN

LINEZOLID DAPTOMYCIN

## **In summary**

- Prior to prescribing antibiotics, remember which bacteria/syndrome you are treating
- Think about pharmacology of each antibiotic, special circumstances (ex/ renal dosing)
- Use AWaRe classification when thinking about which antibiotics to prescribe

# Thank you