Protecting Antibiotics to Protect the Commonwealth

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Disclosures

- Ashley Wilde
  - Co-principle investigator on respiratory syncytial virus research grant supported by Pfizer
- Matthew Song
  - Nothing to disclose
- All relevant financial relationships have been mitigated

Objectives

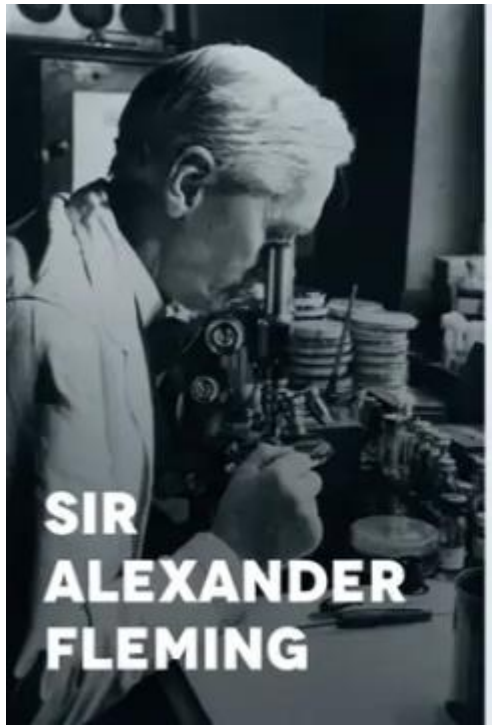
- Identify basic antimicrobial stewardship principles relevant to routine healthcare provided by APRNs in a variety of healthcare settings
- Identify basic pharmacologic and clinical microbiologic principles relevant to antimicrobial stewardship strategies
- Apply antimicrobial stewardship best practices across healthcare settings and patient presentations
  - Asymptomatic bacteriuria & urinary tract infections
  - Upper respiratory tract infections & pneumonia
  - Skin and soft tissue infections

Dawn of a New Age: The Antibiotic Era

- Alexander Fleming discovers penicillin in 1928
- Anne Miller hospitalized with sepsis in 1942
  - Successfully treated with penicillin
  - Died at age 90 in 1992

Rothman, L. (March 14, 2016). This Is What Happened to the First American Treated With Penicillin. TIME.
CDC. Antibiotic Resistance Threats in the United States, 2019.

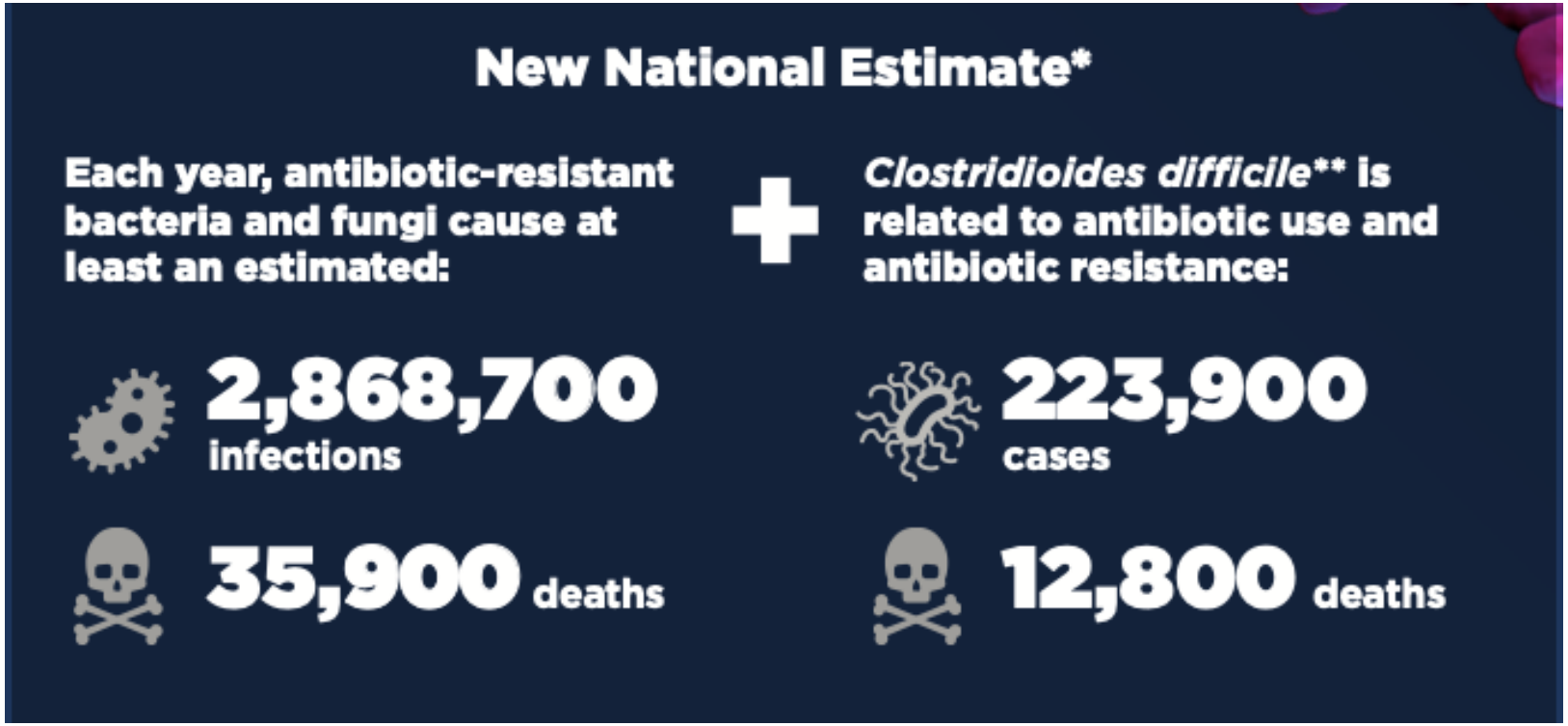
Knew It From The Start



The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism.

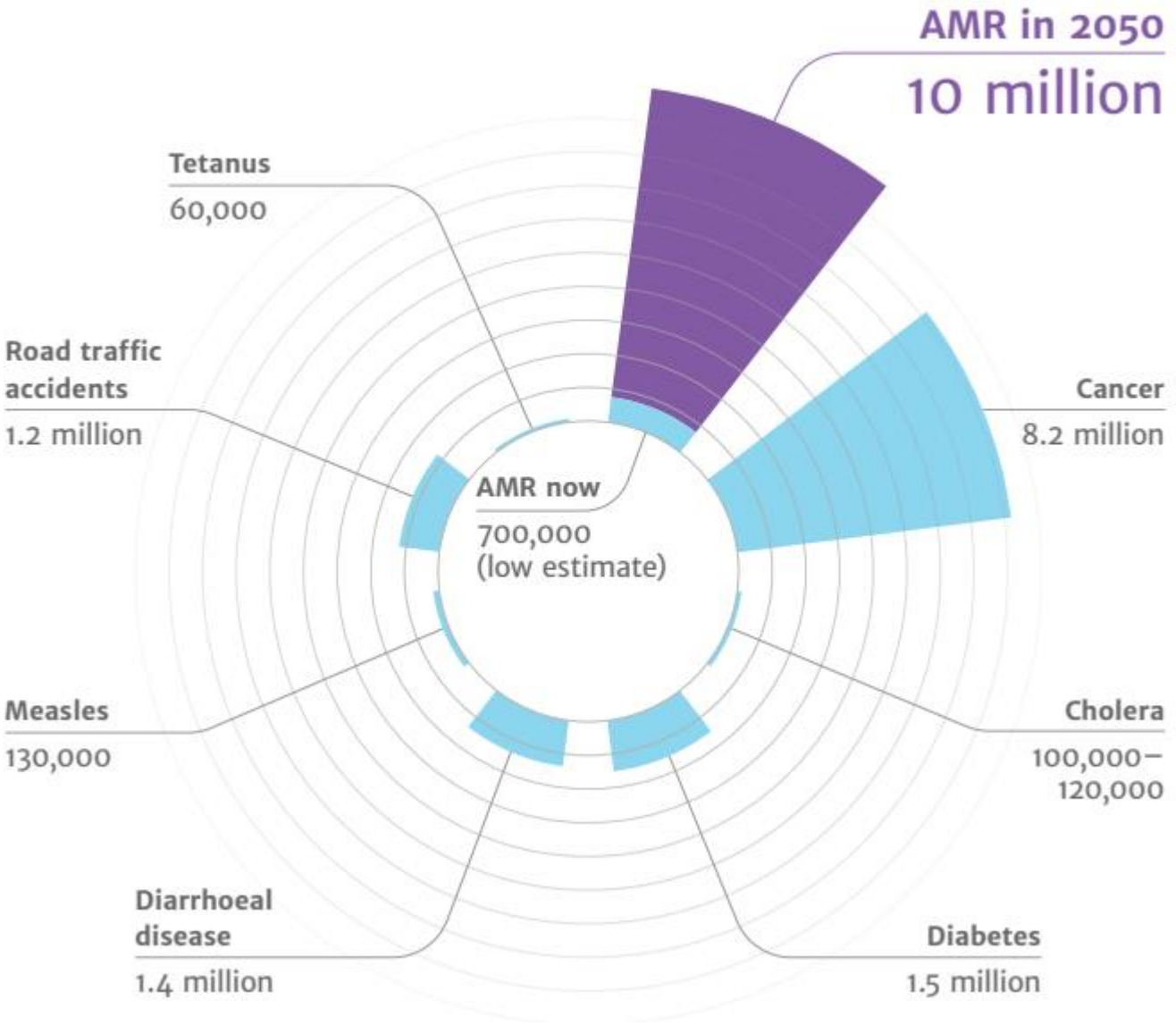
Penicillin's discoverer predicted our coming post-antibiotic era 70 years ago. (2015, August 7). Business Insider. https://www.businessinsider.com/alexander-fleming-predicted-post-antibiotic-era-70-years-ago-2015-7?international=true&r=US&IR=T

Post-Antibiotic Era?



CDC. Antibiotic Resistance Threats in the United States, 2019.

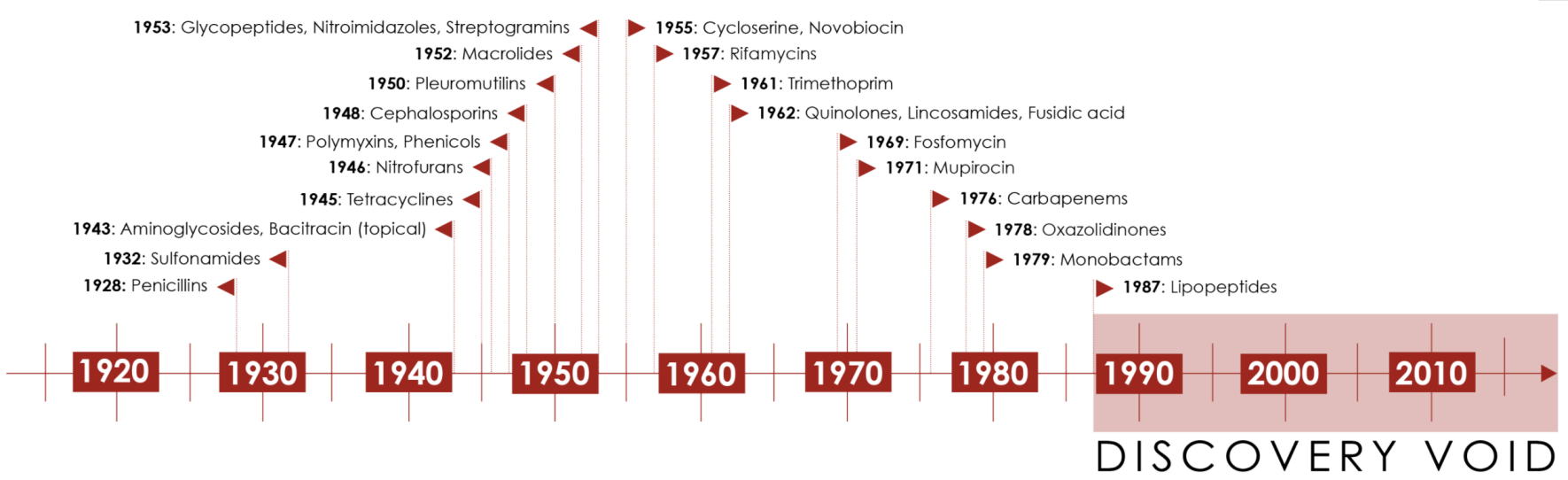
It doesn’t look good



Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. 2016.

Nothing Gold Can Stay

- Last novel class of antibiotic discovered in 1984



- November 14th, 2022
- No antibiotic approval in 3 years!

Hyun D. Pew Charitable Trusts. 18 Feb, 2021

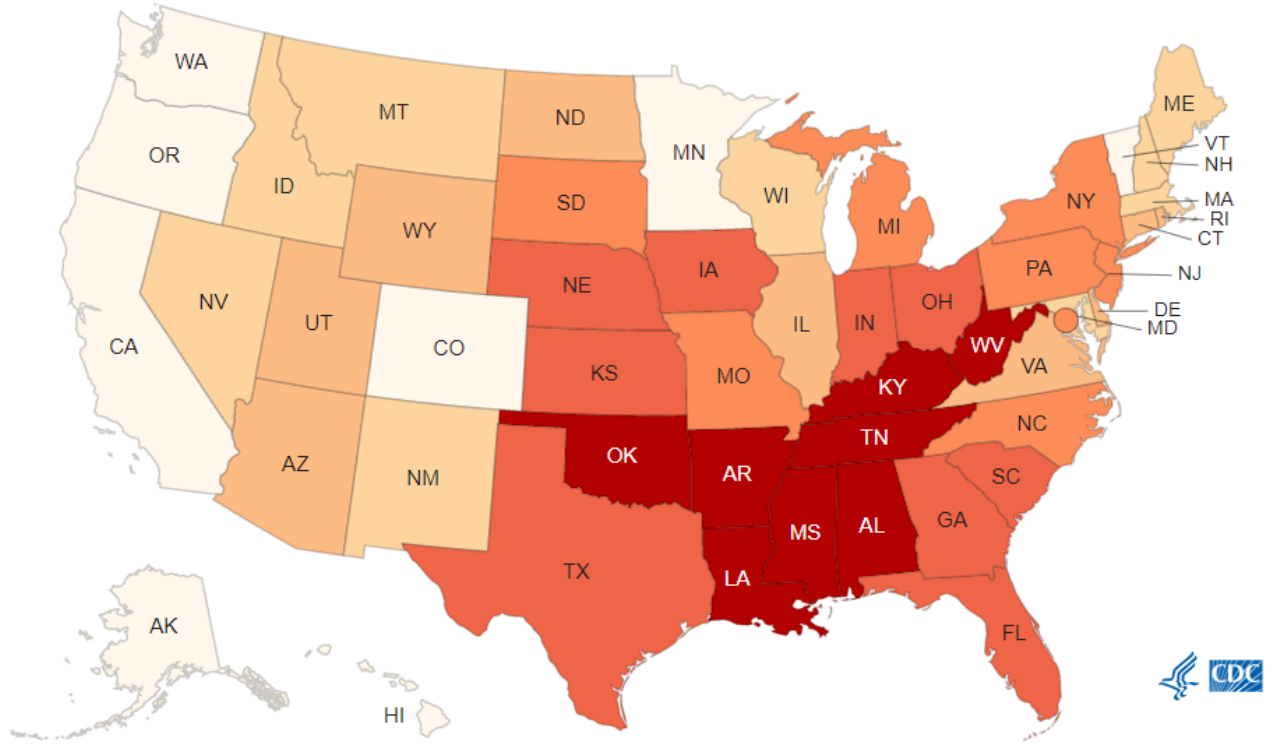
Figure - ReAct Group. www.reactgroup.org/toolbox/understand/how-did-we-end-up-here/few-antibiotics-under-development

Outpatient Antibiotic Prescription Rate

- 211.1 million courses of antibiotics were dispensed in 2021 in US
- At least 28% of outpatient antibiotics are unnecessary
  - No antibiotic was needed at all
- Up to 50% of antibiotics prescriptions are inappropriate
  - Unnecessary use
  - Inappropriate selection
  - Dosing
  - Duration
- What if we changed the word antibiotic to *chemotherapy*

Centers for Disease Control and Prevention. Outpatient antibiotic prescriptions — United States, 2021.
Hersh AL, et al. *Clin Infect Dis.* 2021;72(1):133-137.
Centers for Disease Control and Prevention (CDC). *MMWR*. 2011;60(34):1153-6.
Pichichero ME. *JAMA*. June 19, 2002;287(23):3133-5.
Shapiro DJ, et al. J *Antimicrob Chemother*. 2014;69(1):234-40.

Community Antibiotic Prescriptions per 1,000 Population by State - 2021



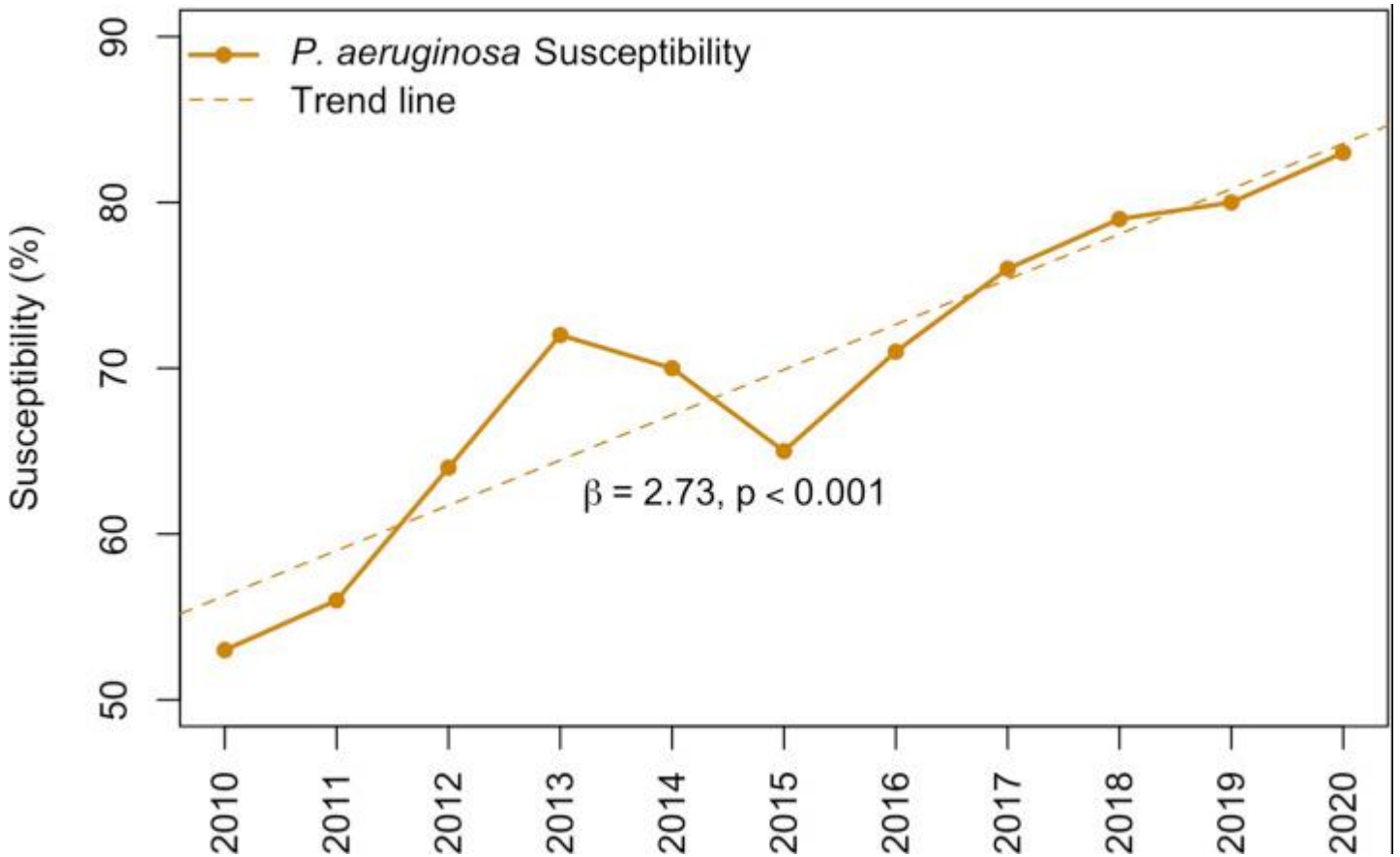
Prescriptions Per 1,000 Population

- 354-466
- 555-619
- 677-765

- KY is 5th highest state
- Kentucky: 938
- National average: 636
- ≈50% higher than average

What can we do?

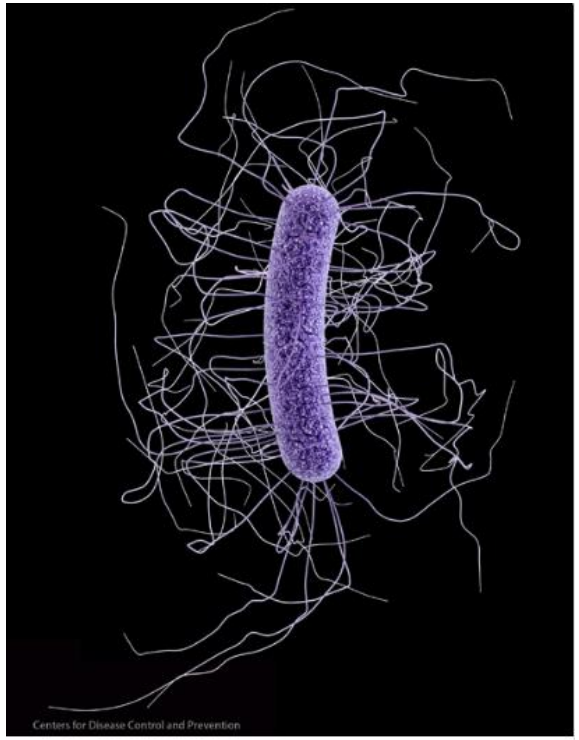
- **Antimicrobial Stewardship**
  - Optimize infectious diseases clinical outcomes while minimizing unintended consequences of antimicrobial use



Swingler EA, et al. *Antimicrob Steward Healthc Epidemiol*. 2022 Nov 16;2(1):e186.

Consequences of Antimicrobial Use

- Toxicity
  - #1 cause of emergency department visit for adverse event in children
  - 1 out of 5 ED visits for adverse drug events
- *C. difficile* infections
  - 500,000 cases in US annually
    - Incidence in the community is increasing
  - 29,000 die within 30 days annually
  - 15,000 deaths directly attributable annually
  - $4.8 billion - excess health costs



Clostridium difficile (*C. difficile*)

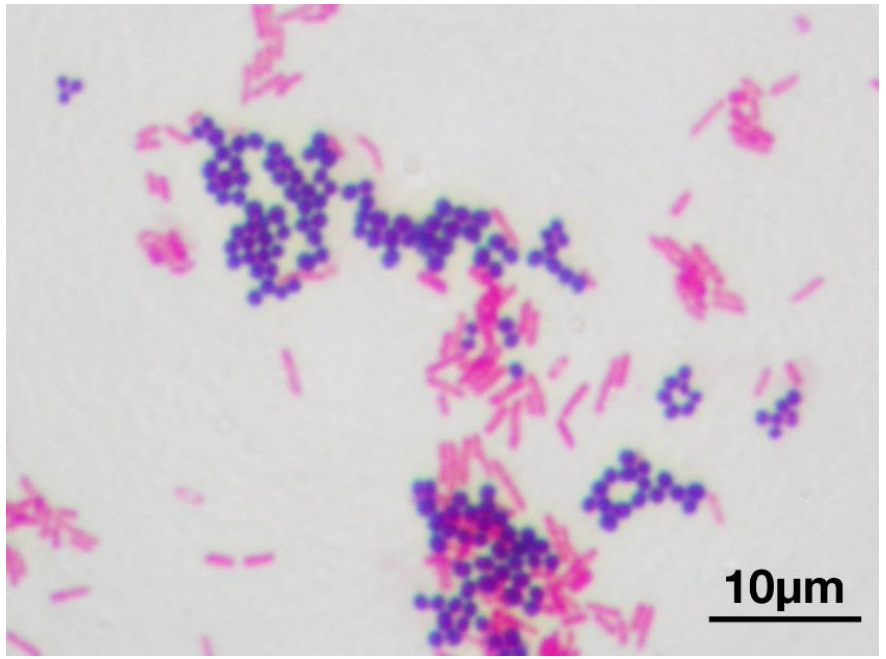
Shehab N, et al. JAMA. 2016 Nov;316(20):2115–25
Guh AY, et al. N Engl J Med 2020;382:1320–30
Centers for Disease Control and Prevention, 2019

Be an Antimicrobial Steward

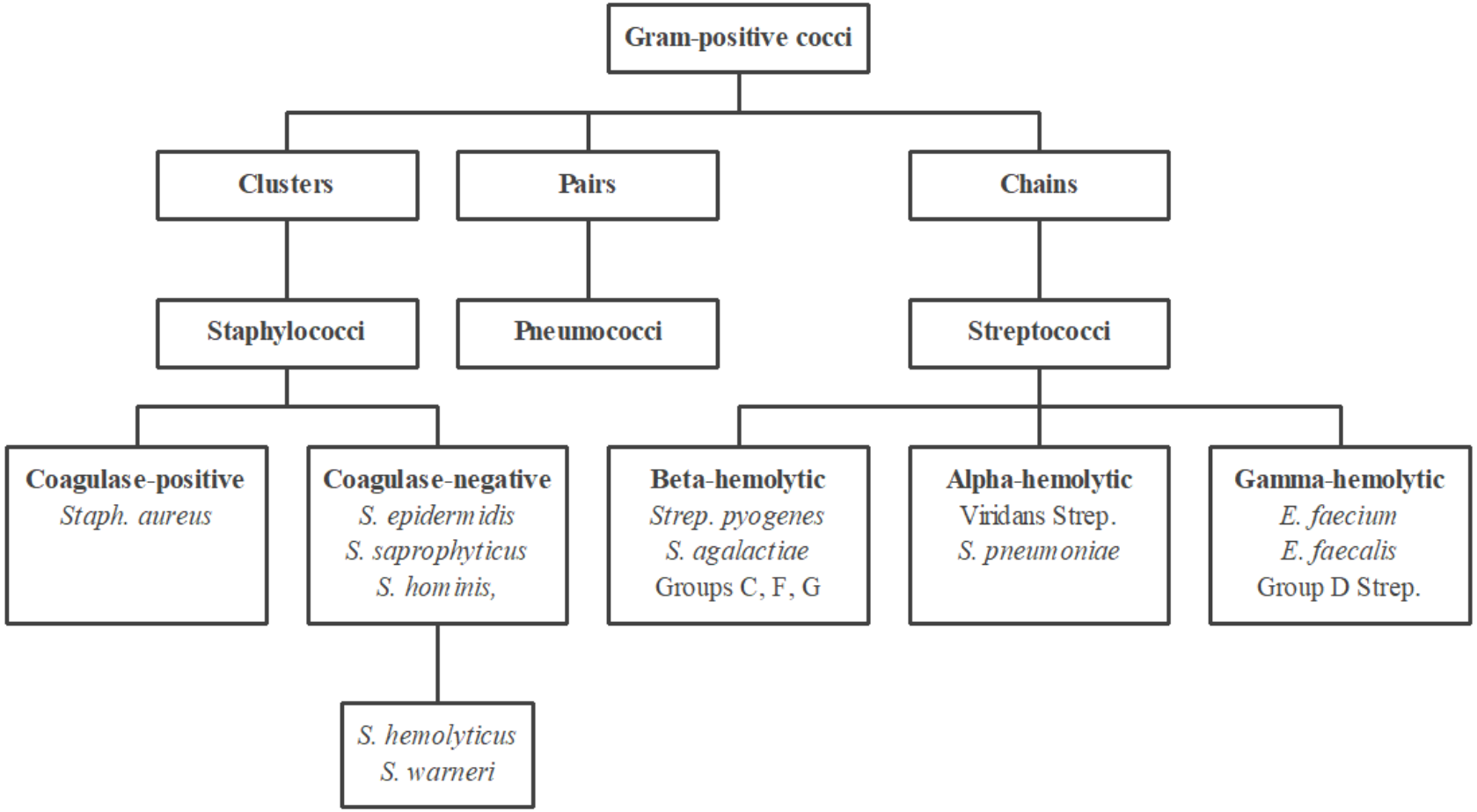
- Clinical microbiology principles
  - Bacterial nomenclature
  - Antimicrobial susceptibility testing
- Basic pharmacologic principles
  - Antimicrobial spectrums
  - Common antimicrobial adverse events
  - Antimicrobial dosing
- Apply to common infectious diseases
  - Asymptomatic bacteriuria & urinary tract infections
  - Upper respiratory tract infections & pneumonia
  - Skin and soft tissue infections

Bacterial Nomenclature

- Gram stain
  - Gram positive (purple)
  - Gram negative (pink)
- Morphology – “shape”
  - Cocci → spheres
  - Bacilli → rods
  - Coccobacilli → in between
- Arrangement
  - Pairs
  - Chains
  - Clusters
- Example: Gram positive cocci in clusters → suspect *Staphylococcus* spp.



Identification of Bacteria

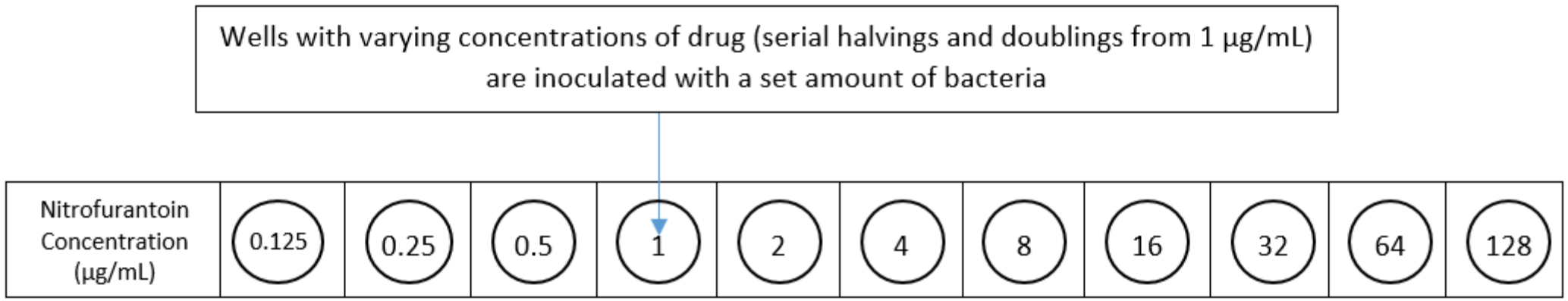


Antimicrobial Susceptibility Testing

- Minimum Inhibitory Concentration (MIC)
  - Lowest concentration that prevents visible growth of bacteria
  - Lowest does NOT mean the best
    - Different antibiotics have different pharmacokinetics
- Breakpoints
  - Concentrations used to define antimicrobial susceptibility

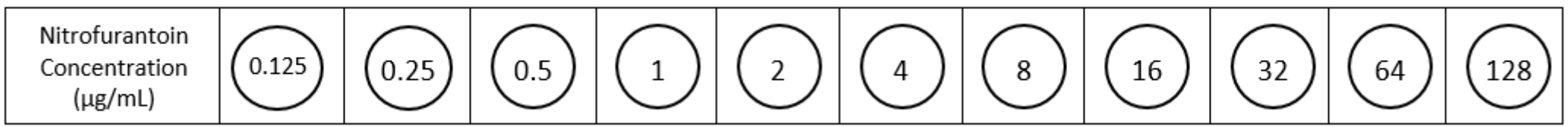
Interpretive Categories for MICs	
Susceptible	High likelihood of treatment success. Standard doses of antibiotic are likely to be effective
Intermediate	Moderate likelihood of treatment success. Likelihood of success can be increased if drug dose is increased and/or infection is at a site where the drug concentrates.
Resistant	Low likelihood of treatment success. Safe doses of antimicrobial are unlikely to be effective.

1. Set up


Wells with varying concentrations of drug (serial halvings and doublings from 1 µg/mL) are inoculated with a set amount of bacteria
Nitrofurantoin Concentration (µg/mL)
0.125
0.25
0.5
1
2
4
8
16
32
64
128

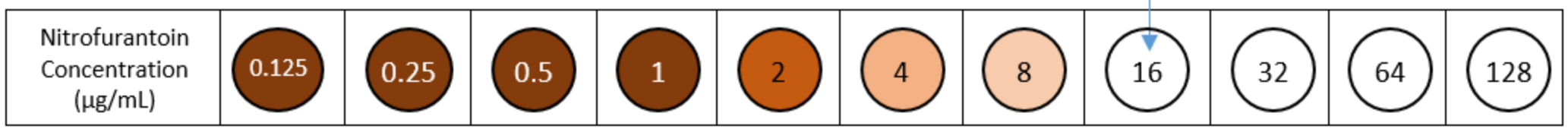
2. Incubate

Wells are incubated for ~24 hours



3. Read

With increasing antibiotic concentrations, bacterial growth decreases. Lowest concentration with **no** visible growth = MIC. The MIC here is 16 µg/mL



Example: Clinical and Laboratory Standards Institute Breakpoints for Enterobacterales (e.g. *E. coli*) for nitrofurantoin

Drug	Susceptible	Intermediate	Resistant
Nitrofurantoin	≤ 32 µg/mL	64 µg/mL	≥ 128 µg/mL

4a. Interpret with breakpoints – Susceptible *E. coli*

Nitrofurantoin Concentration (µg/mL)	0.125	0.25	0.5	1	2	4	8	16	32	64	128
Interpretation								S			

MIC of ≤ 32 µg/mL is considered **susceptible** per Clinical and Laboratory Standards Institute breakpoints for nitrofurantoin

= Bacterial growth

S = Susceptible
I = Intermediate
R = Resistant

Example: Clinical and Laboratory Standards Institute Breakpoints for Enterobacterales (e.g. *E. coli*) for nitrofurantoin

Drug	Susceptible	Intermediate	Resistant
Nitrofurantoin	≤ 32 µg/mL	64 µg/mL	≥ 128 µg/mL

4b. Interpret with breakpoints – Intermediate *E. coli* (different *E. coli* from 4a)

Nitrofurantoin Concentration (µg/mL)	0.125	0.25	0.5	1	2	4	8	16	32	64	128
Interpretation										I	

MIC of = 64 µg/mL is considered **intermediate** per Clinical and Laboratory Standards Institute breakpoints for nitrofurantoin

= Bacterial growth

S = Susceptible
I = Intermediate
R = Resistant

Example: Clinical and Laboratory Standards Institute Breakpoints for Enterobacterales (e.g. *E. coli*) for nitrofurantoin

Drug	Susceptible	Intermediate	Resistant
Nitrofurantoin	≤ 32 µg/mL	64 µg/mL	≥ 128 µg/mL

4c. Interpret with breakpoints – Resistant *E. coli* (different *E. coli* from 4a and 4b)

Nitrofurantoin Concentration (µg/mL)	0.125	0.25	0.5	1	2	4	8	16	32	64	128
Interpretation											R

MIC of **≥** 128 µg/mL is considered **resistant** per Clinical and Laboratory Standards Institute breakpoints for nitrofurantoin

= Bacterial growth

S = Susceptible
I = Intermediate
R = Resistant

Antimicrobial Stewardship

- Confident selection of antibiotic based on susceptibility results
- Selection should then take into consideration
  - Safety and efficacy
  - Patient specific factors
    - Allergies
    - Drug interactions
  - Antibiotic spectrums to minimize broad spectrum exposure

Clinically Significant Hospital Bugs

Pseudomonas aeruginosa

~18 anti-pseudomonals

MRSA

~19 anti-MRSA

Pseudomonas aeruginosa

- Piperacillin/tazobactam
- Cefepime
- Ceftazidime
  - (+/- avibactam)
- Ceftolozane/tazobactam
- Cefiderocol
- Imipenem
  - (+/- relebactam)
- Meropenem
  - (+/- vaborbactam)
- Doripenem
  - Not ertapenem
- Aztreonam

- Amikacin
- Tobramycin
- Gentamicin
- Plazomicin
- Levofloxacin
- Ciprofloxacin
  - Not moxifloxacin
- Delafloxacin
- Polymyxin B
- Colistin (aka polymyxin E)

MRSA

- Vancomycin
- Linezolid
- Tedizolid
- Daptomycin
- Ceftaroline
- Quinupristin/dalfopristin
- Telavancin
- Dalbavancin
- Oritavancin

- TMP/SMX
- Clindamycin
  - (most but not all)
- Doxycycline
- Minocycline
- Tetracycline
- Tigecycline
- Omadacycline
- Eravacycline
- Delafloxacin
- Lefamulin

Antibiotic Spectrum

Narrow

- Penicillin
- Vancomycin
- Doxycycline
- Nitrofurantoin
- Amoxicillin/ ampicillin
- Azithromycin
- Cefazolin/ cephalexin

Medium

- Amoxicillin-clavulanate
- Ampicillin-sulbactam
- Cefuroxime
- Ceftriaxone
- Cefdinir/ cefpodoxime
- TMP/SMX

Broad

- Ciprofloxacin
- Levofloxacin
- Cefepime
- Piperacillin-tazobactam
- Meropenem

Antimicrobial Resistance

- Resistance rates vary among different isolates
  - Geography
  - Patient populations
- Review locale susceptibility rates on antibiogram

		Penicillins						Cephalosporins					Monobactam	Carbapenems		Aminoglycosides				Gram + Coverage					Others				
Norton Hospital 2021	Number Tested	Amoxicillin/Clavulanate	Ampicillin	Ampicillin/Sulbactam	Oxacillin	Penicillin	Piperacillin/Tazobactam	Oral cephalosporins for uncomplicated UTI	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Aztreonam	Ertapenem	Meropenem	Amikacin	Gentamicin	Gentamicin Synergy	Tobramycin	Clindamycin [1, 2]	Erythromycin [2]	Vancomycin	Linezolid	Daptomycin	Ciprofloxacin	Levofloxacin	Nitrofurantoin [2]	Tetracycline	Trimeth/Sulfa
Acinetobacter baumannii complex [3]	20	0	0	75	0	0			0	65	80		0	0	75	85	75		85	0	0	0	0	0	85	75			75
Citrobacter freundii complex [4]	29	0	0	0	0	0	93		0	97	83	79	83	97	97	100	90		93	0	0	0	0	0	90	93	89		83
Citrobacter koseri	19	89	0	84	0	0	95		89	100	100	89	95	100	100	100	100		100	0	0	0	0	0	89	100	62		95
Enterobacter cloacae complex [5]	89	0	0	0	0	0	79		0	88	71	56	65	82	97	100	99		98	0	0	0	0	0	97	100	21		94
Escherichia coli	965	85	47	55	0	0	97	86	66	92	91	87	88	99	99	99	91		91	0	0	0	0	0	74	75	97		72
Klebsiella aerogenes	41	0	0	0	0	0	88		0	98	85	80	83	95	100	100	100		100	0	0	0	0	0	95	95	18		98
Klebsiella oxytoca	53	98	0	81	0	0	100		15	98	94	96	94	100	100	100	100		96	0	0	0	0	0	98	98	80		96
Klebsiella pneumoniae	224	88	0	77	0	0	94	88	79	94	90	89	90	98	99	100	96		95	0	0	0	0	0	92	95	37		89
Morganella morganii	17	0	0	0	0	0	100		0	94	53	53	71	100	100	100	94		94	0	0	0	0	0	88	94	0		94
Proteus mirabilis	125	92	79	90	0	0	99	87	66	94	95	92	89	99	100	100	90		90	0	0	0	0	0	75	78	0	0	79
Proteus vulgaris	12	92	0	92	0	0	100		0	100	92	50	33	100	100	100	100		100	0	0	0	0	0	100	100	0	0	100
Pseudomonas aeruginosa	166	0	0	0	0	0	84		0	83	80	0	70	0	89	96	81		94	0	0	0	0	0	81	83	0	0	0
Serratia marcescens	47	0	0	0	0	0	57		0	98	43	53	38	100	100	98	96		91	0	0	0	0	0	100	100	0		98
Stenotrophomonas maltophilia	33	0	0	0	0	0	0		0		45	0	0	0	0	0	0		0	0	0	0	0	0		88		0	94

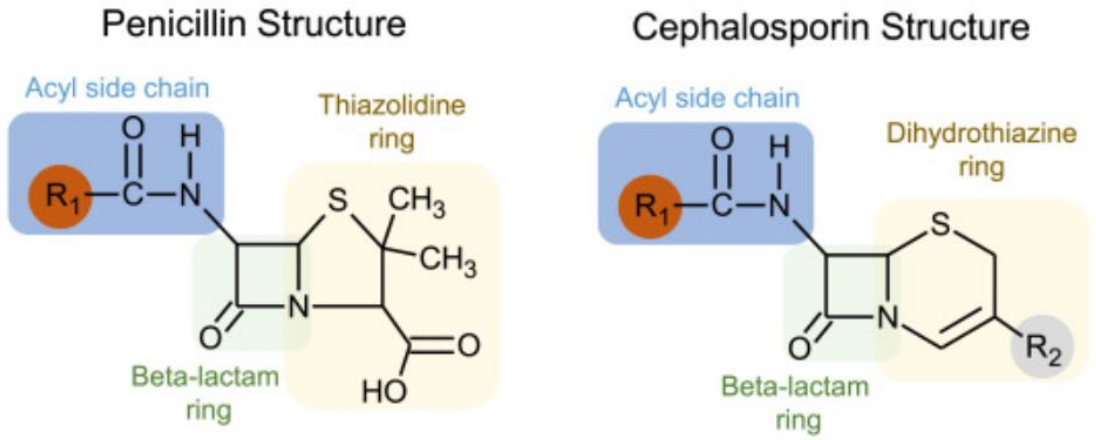
Microbiology Meets Antimicrobial Stewardship

- Empiric therapy → Don't know the pathogen yet
  - What are the likely pathogens? What are the local resistance rates?
    - *Be broad enough*
  - Broader antibiotic use leads to broader antibiotic resistance
    - *Don't be too broad*
- Definitive therapy → Pathogen has been identified
  - Culture results: Use the most narrow spectrum effective to preserve broader spectrum
- Selection should then take into consideration
  - Adverse events
  - Appropriate dosing

Common Antibiotics

Beta-lactams
Quinolones
Macrolides
Tetracyclines
Miscellaneous

Beta-lactams



- Penicillins, Cephalosporins, Aztreonam, Carbapenems
- Adverse events
  - Allergic reactions
  - Drug fever
  - Thrombocytopenia/ pancytopenia
  - Elevated liver enzymes
  - Increased seizure risk
- *C. difficile* infection
  - Penicillins & 1st generation cephalosporins: moderate
  - 2nd – 4th generation cephalosporins, aztreonam, carbapenems: high
- Overall severe adverse events are rare and beta-lactams are often preferred therapies when available

Khan DA, et al. J Allergy Clin Immunol. 2022;150(6):1333-93

Beta-lactams

- Dosing varies according to indication
- Dose adjusted in renal insufficiency
- Commonly used antibiotic doses

Beta-lactam	Dose	Frequency	Route
Amoxicillin	500 mg – 1 g	BID – TID	PO
Amoxicillin-clavulanate	500 mg – 2 g	BID – TID	PO
Ampicillin-sulbactam	1.5 – 3 g	Q6H	IV
Piperacillin-tazobactam	3.375 – 4.5 g	Q6H	IV
Cephalexin	500 mg – 1 g	BID – QID	PO
Cefazolin	1 – 3 g	Q8H	IV
Ceftriaxone*	1 – 2 g	Q24H – Q12H	IV
Cefepime	1 – 2 g	Q8H – Q12H	IV
Aztreonam	1 – 2 g	Q6H – Q8H	IV
Ertapenem	1 g	Q24H	IV
Meropenem	500 mg – 2 g	Q6H – Q8H	IV

*no dose adjustment needed in renal dysfunction

Fluoroquinolones

- Ciprofloxacin, levofloxacin, moxifloxacin, delafloxacin
- Black box warnings
  - Tendonitis/Tendon rupture
  - Peripheral neuropathy
  - Seizures
  - Altered mental status
  - Myasthenia gravis exacerbation
- Adverse events
  - QT prolongation
  - Dysglycemias
  - Aortic aneurysms/aortic dissection
- *C. difficile* infection risk: high
- Generally avoid if there are alternatives available

Fluoroquinolones

- Dosing varies according to indication
- Dose adjusted in renal insufficiency
- Ciprofloxacin
  - IV: 400 mg Q8H – Q12H
  - PO: 250 – 750 mg BID
- Levofloxacin
  - IV & PO: 250 – 750 mg Q24H
- Moxifloxacin
  - IV & PO: 400 mg Q24H
- Delafloxacin
  - IV: 300 mg Q12H
  - PO: 450 mg BID

Macrolides

- Azithromycin, clarithromycin, erythromycin
- Adverse events
  - Nausea/vomiting/diarrhea
    - Erythro>>>>clarithro>>azithro
  - QTc prolongation
- *C. difficile* infection risk: moderate

Macrolides

- Dosing varies according to indication
- **Azithromycin:** 250 – 500 mg Q24H IV & PO, 1 - 2 g x 1 dose
- Clarithromycin: 250 – 500 mg PO Q12H
  - Dose requires renal adjustments
- Erythromycin: 250 – 500 mg PO Q6-12H

Tetracyclines

- Tetracycline, doxycycline, minocycline
- Adverse events
  - Photosensitivity
  - Esophagitis
  - Nausea/vomiting/diarrhea
  - Vestibular toxicity (minocycline)
    - Dizziness, vertigo, tinnitus
- *C. difficile* infection risk: low

Tetracyclines

- Dose adjustments NOT needed in renal insufficiency
- Tetracycline: 250 – 500 mg PO QID
- Doxycycline: 100 mg IV & PO BID
- Minocycline: 200 mg x 1 followed by 100 mg IV and PO BID

Nitrofurantoin

- Nitrofurantoin: 100 mg PO BID
- Okay to use if CrCl >30 mL/min
- Do NOT use in pyelonephritis
  - High urine concentrations but low kidney tissue concentrations
- Rare adverse events
  - Pneumonitis
  - Peripheral neuropathy
- Generally well tolerated
- *C. difficile* infection risk: low

TMP-SMX

- Trimethoprim-Sulfamethoxazole (Bactrim)
- Adverse events
  - Rash
  - Hyperkalemia, hyponatremia
  - Liver toxicity
  - Crystalluria
  - Hematologic toxicities
- *C. difficile* infection risk: moderate
- Dose varies widely by indication
  - 5 – 10 mg TMP/kg – 15 – 20 mg TMP/kg
  - Commonly 1 -2 DS Tablet PO BID
- Renal adjustments required

Antimicrobial Stewardship Summary

- Selection of antibiotics should take into consideration
  - Antibiotic spectrum
    - Be broad enough in empiric therapy
    - Narrow once able in definitive therapy
  - Antibiotic adverse events
    - Know what to look for and have a monitoring plan to address
    - Use alternatives if appropriate
    - Use lowest *C. difficile* risk when possible
  - Appropriate dosing
    - Efficacy to treat infection
    - Safety to minimize toxicities

Asymptomatic bacteriuria

- Guideline
  - “presence of 1 or more species of bacteria growing in the urine at specified quantitative counts (≥ 10^5 colon-forming units [CFU]/mL or ≥ 10^8 CFU/L), irrespective of the presence of pyuria, in the absence of signs or symptoms attributable to urinary tract infection (UTI)”
- Practical definition
  - UA with nitrites or bacteria or positive urine culture + **no symptoms** +/- pyuria
- Do NOT look for or treat EXCEPT in
  - Pregnant patients
  - Urological procedures with expected mucosal bleeding (e.g., TURBT)
- Altered mental status
  - In patients with no systemic signs (e.g. fever or hypotension), monitor off antibiotics and look for/treat alternative causes

Nicolle LE, Gupta K, Bradley SF, et al. *Clin Infect Dis*. 2019;68(10):e83-e110.

Asymptomatic bacteriuria

An 85 year old female with a PMH of COPD, dementia, and hypertension presents to the ER from a nursing home with altered mental status. No review of systems was obtained due to the patient's mental status. The patient's family states that "she always gets like this when she has a UTI."

Vitals: heart rate 86 bpm, blood pressure 124/82 mmHg, respiratory rate 14 bpm, temp 98.4° F.

Pertinent Labs: WBC 7,340 cells/mm3, Na+ 126 mEq/L, BUN 54 mg/dL, and SCr 2.01 mg/dL.

Urinalysis: 100 WBC and +bacteria.

What do you do?

Asymptomatic bacteriuria

- Monitor off antibiotics
  - ASB present in up to 50% of elderly adults from long-term care facilities
  - No systemic signs of infection (e.g. Afebrile, hemodynamically stable, no SIRS)
  - Alternative explanation for AMS
    - Dehydration
    - Dementia
  - ↓ *C. difficile* risk
  - ↓ risk for drug toxicity
  - ↓ risk for emergence of drug resistant bacteria
- If does not improve consider treatment with most narrow spectrum agent from susceptibility report

Cystitis

- Infection of the bladder
- Urinary symptoms
  - Increased frequency
  - Urgency
  - Dysuria
  - Suprapubic pain
- Systemic signs of infection very rare
- Pyuria
  - Poor positive predictive value
  - Good negative predictive value
- Urine culture positive
- Most common pathogens: *E. coli*, other gram negatives

Gupta K et al., *Clin Infect Dis*. 2011;52(5):e103-e120.
Cheng B et al., Am J Med. 2022;135(9):e353-e358

Cystitis

A 55 year old female with a PMH of hypertension presents to her family doctor with a chief complaint of burning with urination.

Vitals: heart rate 80 bpm, blood pressure 144/92 mmHg, respiratory rate 22 bpm, temp 98.4° F.

Urinalysis: 118 WBC and +bacteria.

Cystitis – Antibiogram

Drug	Likelihood of activity against *E. coli*
Nitrofurantoin	98%
Ceftriaxone	95%
Oral cephalosporins for uncomplicated UTI (e.g., cephalexin)	92%
Ciprofloxacin	85%
TMP-SMX	79%
Ampicillin	57%

What do you do?

Cystitis

- Nitrofurantoin 100 mg PO BID to complete 5 days of therapy
  - No systemic signs of infection (e.g. afebrile, hemodynamically stable, SIRS but not sepsis)
  - High local likelihood of activity against *E. coli* (98%)
  - Low risk for C. difficile risk
  - Narrow spectrum
- Cephalexin 500 mg PO BID
  - High local likelihood of activity against *E. coli* (92%)
  - Low risk C. difficile risk
  - Narrow spectrum
- Avoid fluoroquinolones (e.g., ciprofloxacin, levofloxacin)
  - Moderate likelihood of activity against *E. coli* (85%)
  - Toxicities can be catastrophic (e.g., tendon rupture, aortic dissection)
  - High risk for C. difficile infection
  - Broad spectrum to preserve (e.g. *Pseudomonas aeruginosa*)

Upper Respiratory Tract Infection

- Rhinosinusitis
- Nasal congestion, discharge, facial pain, fever, fatigue, cough, anosmia, ear pressure
- Most commonly due to viruses
- Antibiotic therapy NOT recommended **unless**
  - Persistent symptoms ≥ 10 days
  - ≥ 102°F + purulent nasal discharge or facial pain for 3 - 4 days
  - Initial improvement and then worsening after 5 – 6 days
- Common pathogens: *S. pneumoniae, H. influenza, M. catarrhalis*

Chow AW, et al. *Clin Infect Dis*. 2012;54(8):e72-e112.

Upper Respiratory Tract Infection

A 35 year old female with a no past medical history presents to an immediate care center with a chief complaint of facial pressure and nasal congestion for the past five days. She asks for an antibiotic to help with her symptoms.

Vitals: heart rate 80 bpm, blood pressure 104/72 mmHg, respiratory rate 12 bpm, temp 98.4° F.

What do you do?

Upper Respiratory Tract Infection

Counsel patient

- Likely viral and symptoms typically go away on their own after 10 days
- Antibiotics don’t treat viruses
- Threat of antibiotic resistance
- Antibiotic risk for toxicities including *C. difficile* infection
- Can utilize delayed prescribing
  - Do not fill before date
  - Call back if still with symptoms after period of time

Communicating Antibiotic Decision Making

Patients want to feel HEARD	"What I am hearing you say is [repeat the main concerns]." • Sit at eye level with the patient. • Nod your head when you agree instead of interjecting with words. • When examining the patient, verbally state the pertinent negatives based on the review of symptoms. "The good news is your lungs sound clear and you are not wheezing."
Patients want their feelings VALIDATED	"I am glad you came in today." "I am sorry you are not feeling well." "It sounds like you are not feeling well, let me see how I can help."
POSITIVE discussion about antibiotic nonuse	"The good news is that you do not need an antibiotic." "Fortunately, you do not need an antibiotic, so here are a few other things I can offer you." "We now know that sometimes antibiotics can actually cause more problems, like diarrhea. The good news is that I can offer you a couple of good options today."
Patients want to know when they will GET BETTER and when to RETURN to medical attention	• Provide details about when the patient is expected to feel better. • Provide specific guidance on when and where to return to medical attention. • Request patients repeat the plan and when to return to medical care to avoid misunderstandings.

Adapted from Agency for Healthcare Research and Quality. Communicating with your patients clinician one-pager

Upper Respiratory Tract Infection

5 days pass and the patient calls back saying her symptoms are still there.

What do you recommend?

Upper Respiratory Tract Infection

- Amoxicillin-clavulanate 875 mg PO BID x 5 days
  - Recommended first line by guidelines
- Doxycycline 100 mg PO BID x 5 days
  - Alternative per guidelines
- Levofloxacin 500 mg PO QD x 5 days
  - Alternative per guidelines
  - Only use if beta-lactam not available
    - Broad spectrum, toxicities, high *C. difficile* infection risk
- Azithromycin
  - Not recommended per guidelines due to high resistance
- TMP-SMX
  - Not recommended per guidelines due to high resistance

Chow AW, et al. *Clin Infect Dis*. 2012;54(8):e72-e112.

Community-acquired Pneumonia

- Clinical diagnosis
  - Signs and symptoms + radiographic imaging
- Symptoms
  - Cough, sputum production, shortness of air, chest pain, chills
- Signs
  - Tachypnea, rales, crackles, rhonchi, leukocytosis, fever
- Likely pathogens
  - Respiratory viruses, *S. pneumoniae, H. influenzae, M. catarrhalis, M. pneumoniae, Legionella* spp., *C. pneumoniae, S. aureus*

Metlay JP et al., *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Community-acquired Pneumonia

- 58 year old male with past medical history of hypertension presents to the ED with 4 day history of shortness of air, chest pain, and fever.
- Chest x-ray obtained shows a right lower lobe infiltrate.
- **Vitals:** heart rate 92 bpm, blood pressure 144/82 mmHg, respiratory rate 22 bpm, temp 101.4° F.
- The patient will be admitted. What antibiotics do you initiate?

Community-acquired Pneumonia

- Inpatient management
  - Beta-lactam (ampicillin-sulbactam, ceftriaxone, cefotaxime, ceftaroline) + macrolide (azithromycin, clarithromycin)
  - Respiratory fluoroquinolone (levofloxacin, moxifloxacin)
- Amp-sulbactam 3 g IV Q6H + azithromycin 500 mg PO daily x 3 doses
  - Amp-sulbactam lower risk for *C. difficile* infection than ceftriaxone
  - Azithromycin lower risk for toxicities than clarithromycin
  - Quinolones have catastrophic toxicities, high risk for *C. difficile* infection, and broader spectrum to preserve

Metlay JP et al., *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Cellulitis

- Purulent vs. non-purulent
- Purulent
  - Furuncles, carbuncles, abscesses
  - Most common cause *S. aureus* (MSSA & MRSA)
- Non-purulent
  - Cellulitis, erysipelas
  - *Streptococcus* spp.

Stevens DL et al., *Clin Infect Dis*. 2014;59(2):e10-e52.

Cellulitis

- 29 year old presents to an immediate care center with pain and redness in his left lower extremity for the past 5 days.
- Physical exam: inflammation in the left shin without fluctuation
- What antibiotics do you initiate?

Cellulitis

- Non-purulent cellulitis → Streptococcus spp.
  - Penicillin VK 500 mg PO QID
  - Cephalexin 500 mg PO QID
  - Dicloxacillin 500 mg PO QID
  - Clindamycin 300-450 mg PO TID-QID
    - Resistance rates can be high
    - High risk for *C. difficile* infection
- MRSA coverage not needed
  - Doxycycline
    - Does NOT have reliable *Streptococcus* spp coverage for cellulitis
  - TMP-SMX (Bactrim)
    - Gram negative coverage not needed

Stevens DL et al., *Clin Infect Dis*. 2014;59(2):e10-e52.

Disease State Summary

- Do NOT use antibiotics when not indicated
- Monitor off antibiotics when recommended
- Multiple options often available. Consider:
  - Local resistance rates
  - Overall spectrum
  - Adverse effect profile
  - *C. difficile* infection risk
- That’s a lot to remember! Where can I get help?

KASIC

Kentucky Antimicrobial Stewardship Innovation Consortium

- www.kymdro.org/kasic
- Educational videos on antimicrobial stewardship and clinical microbiology
  - One page educational pearls

  @KASIC_MDRO
- All assistance is free of charge
- Help us protect antibiotics to protect the Commonwealth!