PRINCIPLES OF ANTIBIOTIC USE

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Duke University School of Medicine

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Duke Center for Antimicrobial Stewardship and Infection Prevention

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Objectives

Understand why antibiotics are “special” medications

The 4 Moments of Antibiotic Decision-Making

Antimicrobial Stewardship Programs

“Action” strategies in different clinical settings

We Love Antibiotics

Inpatient

At any given time, 65% of inpatients at DUMC are receiving at least one antibiotic

There are >31,000 antibiotic orders (new starts) placed at DUMC annually

DUMC spends >$10 million on antimicrobial agents each year

Long-term Care

Up to 70% of residents in a nursing home receive one or more courses of systemic antibiotics when followed over a year

40-75% of antibiotic prescriptions are inappropriate

Outpatient

423-553 antibiotic prescriptions per 1000 people in the US per year

30% are unnecessary, (representing 47 million prescriptions/year)

Why We Love Antibiotics

Wonder Drug

Active intervention

Experiences

Tangible

Insurance

Antibiotics are time-tested placebos

Antibiotic Rx is easy:

- Avoids doing a structured exam or long DDx
- Avoids time-consuming discussions
- i.e. Easier to treat than diagnose or educate

Identifying Infected vs. Not Infected is hard

“Just in case” perceived to be lower risk than “watchful waiting”

Why we HAVE TO improve Antibiotic Use

Antibiotics are unlike any other drug, in that the use of the agent in one patient can compromise its efficacy in another.

A lot of antibiotic prescriptions are unnecessary or sub-optimal.

We are running out of antibiotics.

Antibiotic misuse harms patients.

Improving antibiotic use has many benefits for patients and society.

Slide adapted from Arjun Srinivasan, MD (CDC)

Antimicrobial Use Impacts: Infection Prevention, HAIs, AND Patient Outcomes

Drug-resistance (MRSA, VRE, CRE, FQR-EC)

C. difficile infection

Infection treatment success/failure
- Complications
- Readmissions
- Mortality
- Length of Stay

Adverse Safety Events
- Allergic reactions
- Drug toxicity events
- Acute Kidney Injury

Healthcare Resources and Cost
- (all of the above)
- Pharmacy budget; ICU days

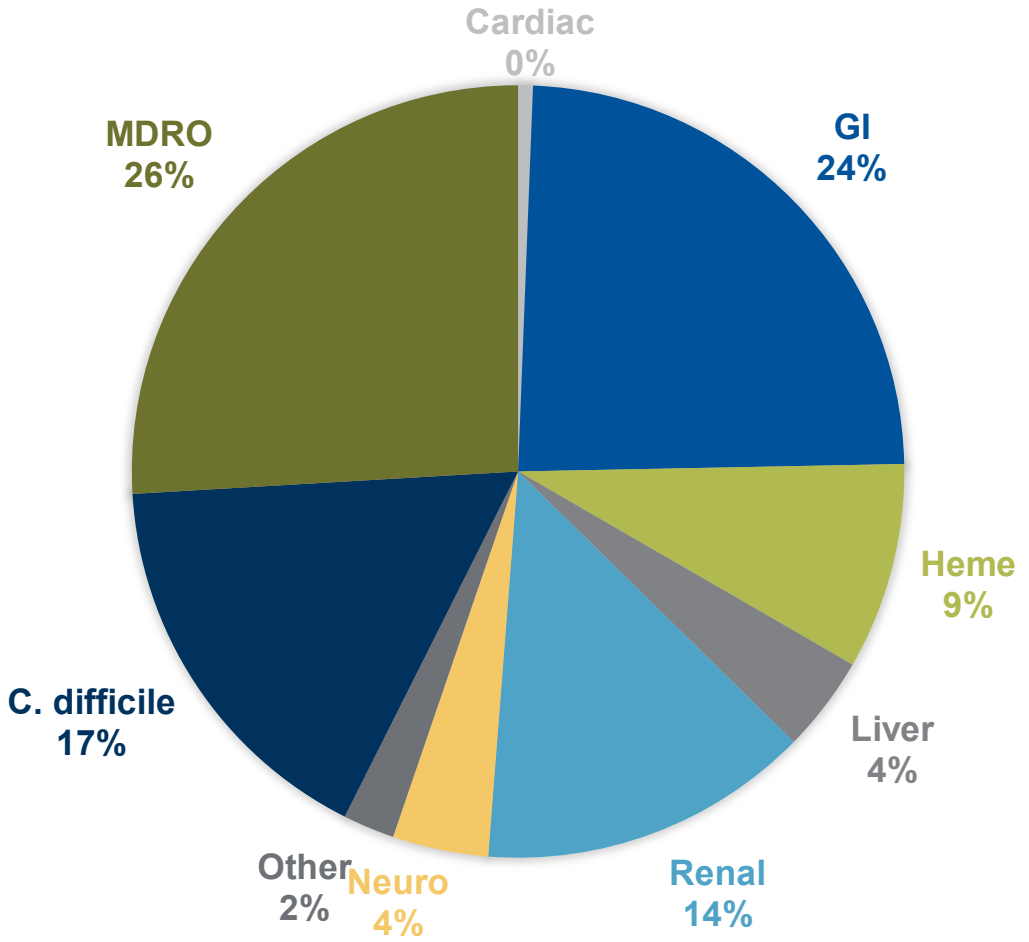
One in Five Inpatients get an Antibiotic Adverse Drug Event

1488 patients followed for 30 days after antibiotic initiation

Followed 90 days for CDI and MDRO acquisition

General medical inpatients who had at least 24h of antibiotics during admission

20% of patients experienced at least one antibiotic-associated ADE



Tamma et al. JAMA Int Med. 2017 177(9):1308-15.

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Making the Right Decision Is Important

Prospective study of febrile adult patients

30 day follow up

All cause mortality 20% vs 11.8% in febrile patients prescribed inappropriate vs. appropriate empiric abx (p=0.01; OR 1.88; 95% CI 1.29-2.72)

Length of stay >2 days longer if inappropriate empiric antibiotics prescribed (p = 0.002)

Fraser A, *et al.* Am J Med 2006;119:970-6

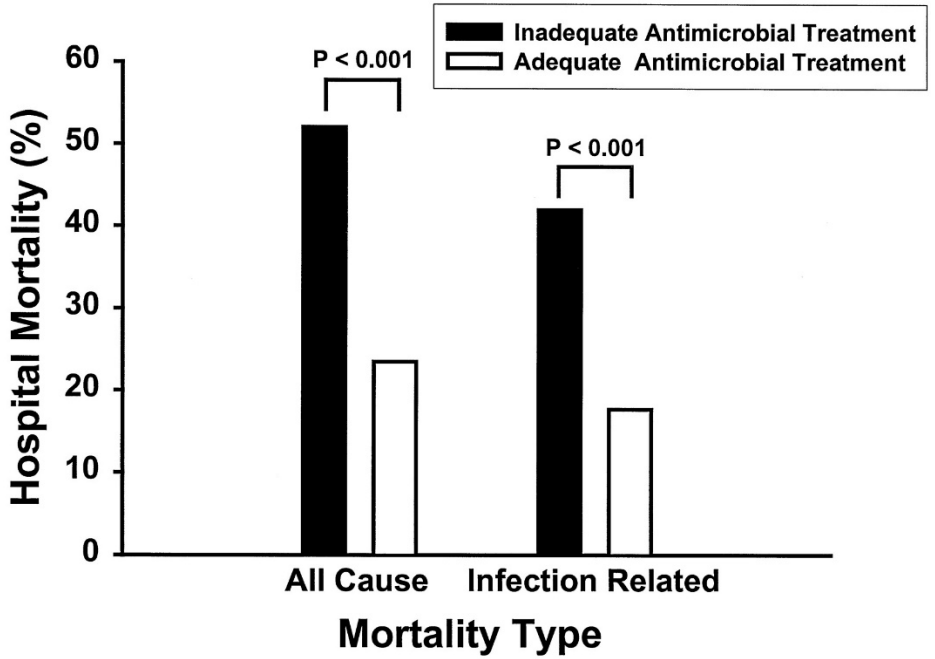
Wrong Antibiotic = Increased Mortality

655 ICU admissions with underlying infections

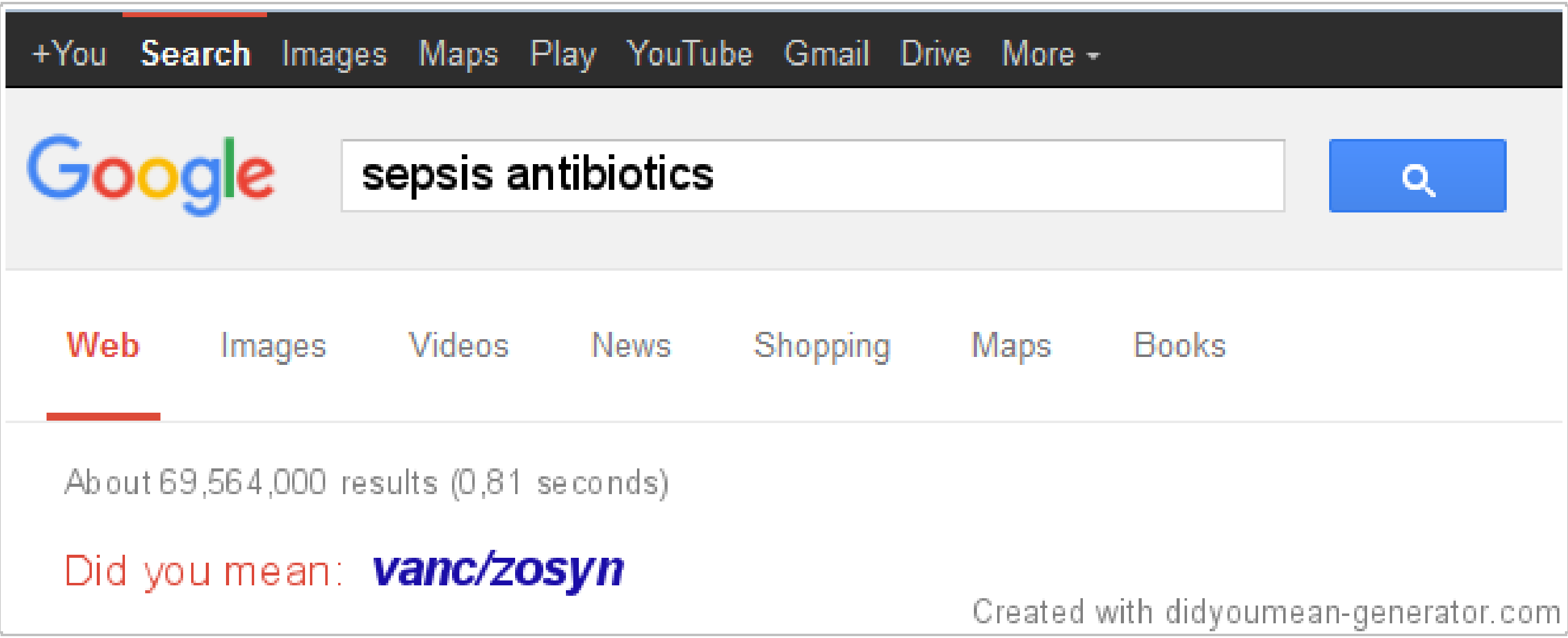
- 62% pneumonia
- 34% BSI

Inadequate antimicrobial therapy independently associated with increased mortality

- RR 4.26



Kollef, M. *et* al. Chest 1999. 115: 462-474.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Sometimes, You Don't Need An Antibiotic

Don't routinely prescribe antibiotics for acute mild-to-moderate sinusitis unless symptoms last for seven or more days, or symptoms worsen after initial clinical improvement

Don't order antibiotics for adenoviral conjunctivitis

Don't routinely provide antibiotics before or after intravitreal injections

Don't prescribe oral antibiotics for uncomplicated acute tympanostomy tube otorrhea

Antibiotics should not be used for apparent viral respiratory illnesses (sinusitis, pharyngitis, bronchitis)

Don't prescribe oral antibiotics for uncomplicated acute external otitis

Avoid antibiotics and wound cultures in emergency department patients with uncomplicated skin and soft tissue abscesses after successful incision and drainage and with adequate medical follow-up

Don't use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present

www.choosingwisely.org

AU represents a modifiable risk

AU in Nursing Homes is highly variable and correlated with AEs

Figure. Variability of Antibiotic Use (per 1000 Resident-days) Across Ontario Nursing Homes

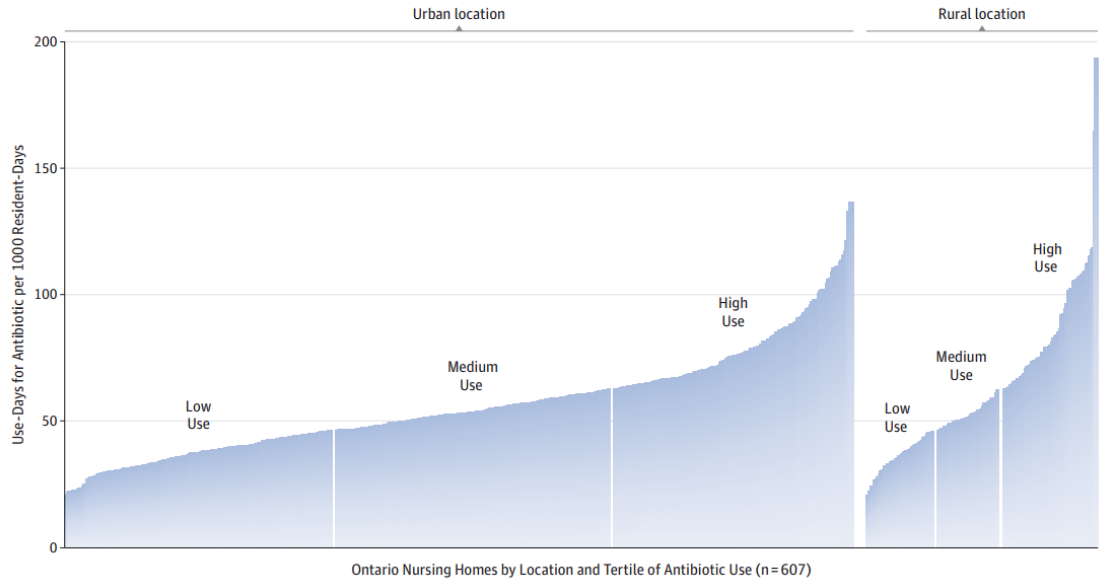
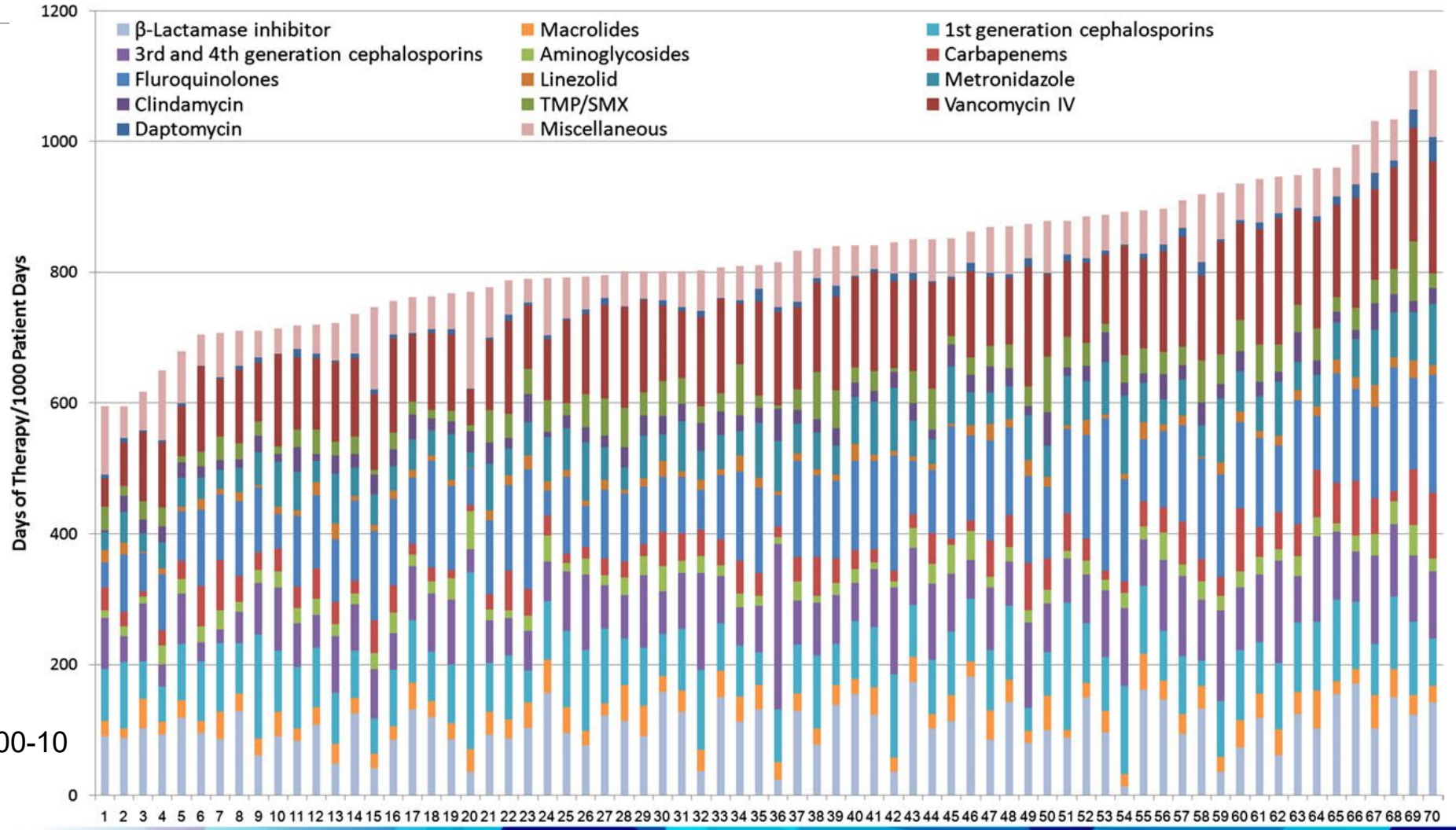


Table 3. Antibiotic-Related Adverse Outcomes Among Residents Living in Nursing Homes With Low, Medium, and High Antibiotic Use[a]

Characteristic	Antibiotic Use, No. (%)		
	Low (n = 33 822)	Medium (n = 31 425)	High (n = 24 943)
Clostridium difficile	274 (0.8)	268 (0.9)	221 (0.9)
Diarrhea or gastroenteritis	3347 (9.9)	3388 (10.8)	2889 (11.6)
Infection with antibiotic-resistant organism	412 (1.2)	431 (1.4)	319 (1.3)
Antibiotic allergy	13 (0.0)	25 (0.1)	22 (0.1)
General adverse event from medication	96 (0.3)	124 (0.4)	88 (0.4)
Any antibiotic complication with or without potential for indirect harms to nonrecipients (primary composite outcome[b])	3869 (11.4)	3890 (12.4)	3311 (13.3)
Only antibiotic complications with potential for indirect harms to nonrecipients (secondary composite outcome[c])	3797 (11.2)	3801 (12.1)	3237 (13.0)

Daneman et al. JAMA IM 2015;175 (8): 1331-1339

Acute Care Academic Hospitals



Polk et al. CID; 2011 Dec;53(11):1100-10

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What is optimal antibiotic therapy…?

Right Diagnosis

Right Drug

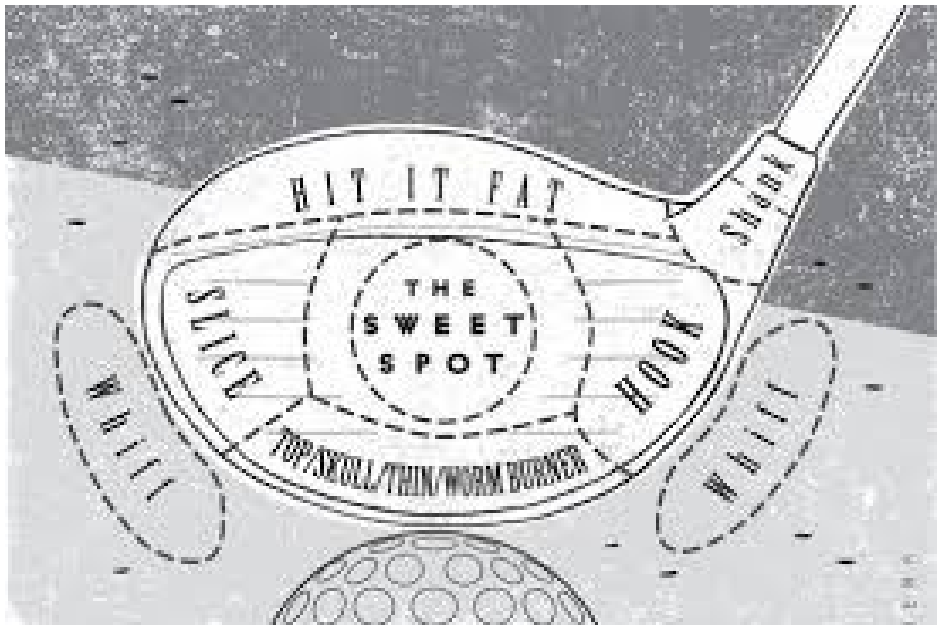
Right Dose

Right Timing

Right Duration

Improve therapeutic choices (underuse)

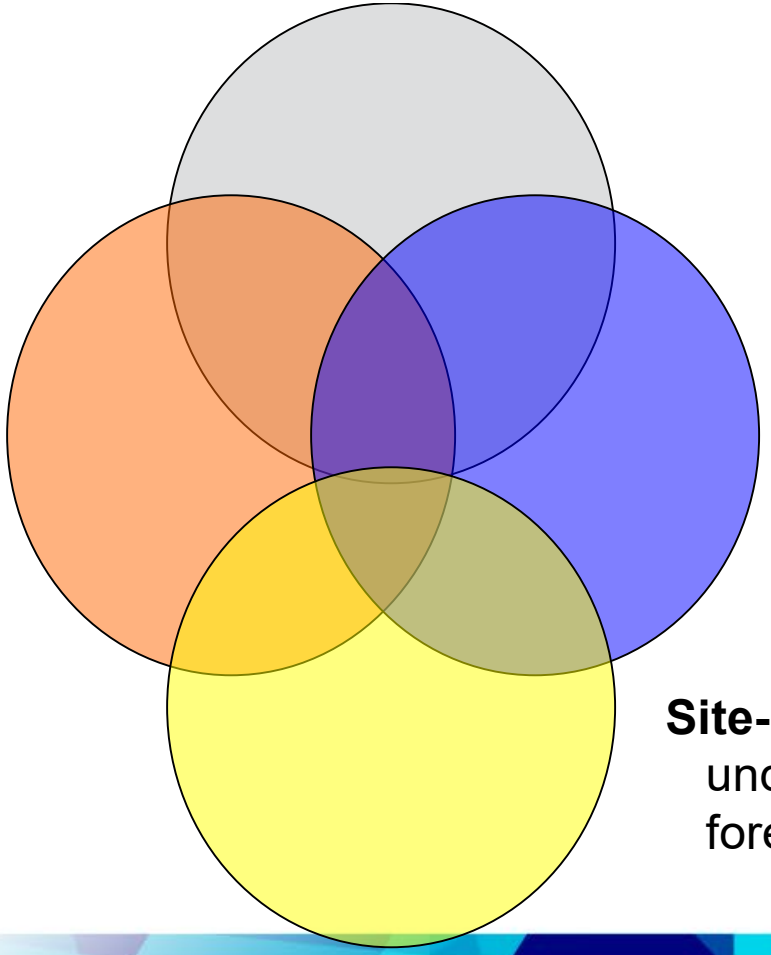
Reduce unnecessary use (overuse)



Why “Good” Antibiotics Fail

Patient-related
comorbidities
organ dysfunction
immunocompromised host

Pathogen-related
resistance
virulence
high inoculum
biofilms



Drug-related
suboptimal dosing
poor penetration

Site-related
undrained abscesses
foreign body

(modified) from Moise PA et al. Lancet Infect Dis. 2009;9:617-24.

The “4 Moments” of Antibiotic Decision-Making

1	2	3	4
Does the patient have an infection that requires antibiotics?	Have I ordered appropriate cultures before starting antibiotics? What empirical antibiotic therapy should I initiate?	A day or more has passed. Can I stop antibiotics? Can I narrow therapy? Can I change from IV to oral therapy?	What duration of antibiotic therapy is needed for this patient’s diagnosis?

Tamma PD et al. *JAMA*. 2019;321(2):139-140.

The “Six Ds” of Antimicrobial Stewardship

Diagnosis	Make and document the right diagnosis.
Debridement/Drainage	Drainage of abscesses and removal of necrotic tissue of foreign material when required.
Drug	Use the right drug empirically according to suspected or confirmed diagnosis, risk factors for resistant pathogens, allergy, or major side effects.
Dose	Use right dose according to diagnosis, site of infection, or renal/hepatic dysfunction.
Duration	Use drugs for an appropriate duration.
De-escalation	Re-evaluate diagnosis and therapy routinely and de-escalate therapy to narrow-spectrum and/or oral agents when appropriate.

Morency-Potvin, Schwartz, Weinstein. Clin Micro Rev 30: 381-407.

General Indications for Antibiotics

Prophylaxis: prevent infection

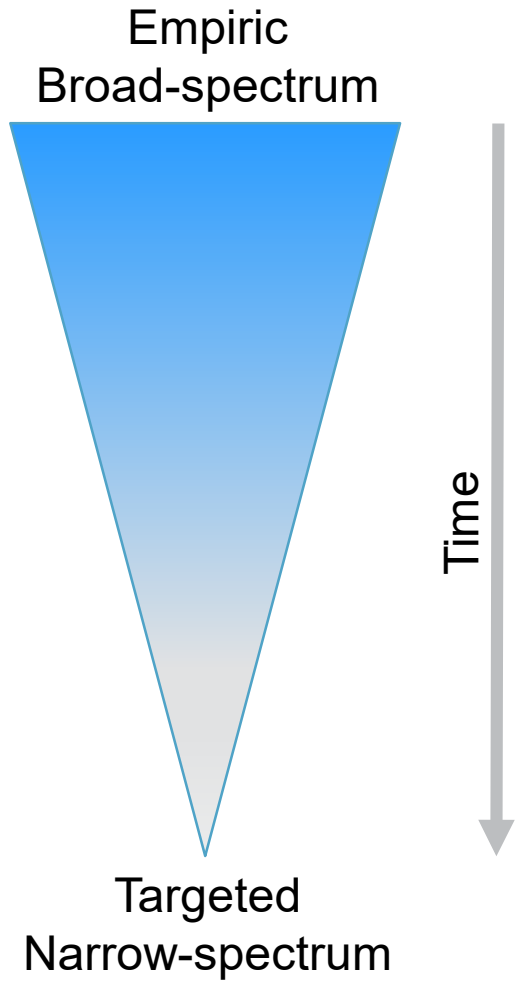
- EASY! Guidelines and ordersets

Empiric: when you suspect infection but don't exactly know with what pathogen

- Not easy. Local guidelines help (based on local micro data).

Directed: pathogen known

- Moderately easy. Follow and interpret patient-specific micro data.



Choice of Empiric Antimicrobials

What class of pathogen am I likely to be treating?

- (Bacterial? Viral? Fungal? Other?)

If bacterial, what organisms are most likely?

- (Gram positive? Gram negative? Anaerobe?)

What information can I get to guide treatment?

- Microbiology data?

Do I need to order any other diagnostic tests?

How sick is my patient? How risky would it be if I miss?

Is my patient “special”? – allergy, ADEs, immune status

Have I ordered appropriate cultures before starting antibiotics?

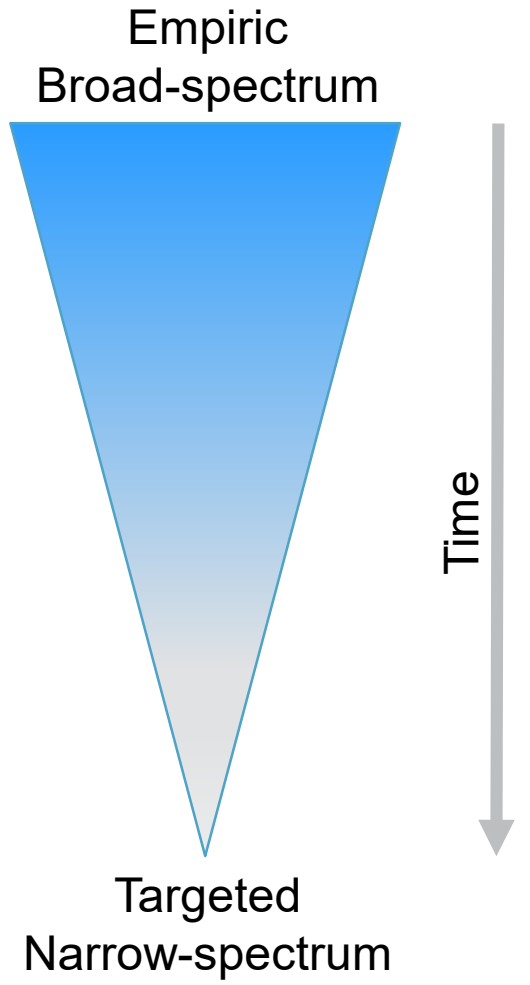
What empirical antibiotic therapy should I initiate?

De-escalation

De-escalation is a core principle of Antimicrobial Stewardship.

Target/narrow antibiotic therapies after more clinical data returns

Stop therapy when infection has been ruled out



3

A day or more has passed.

Can I stop antibiotics?
Can I narrow therapy?
Can I change from IV to oral therapy?

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Clinical information: Small pieces over time.

Clinical information trickles in over time.

This means clinicians have to reassess regularly.

This also means they get interrupted with ‘real-time’ notifications and need to respond.

This a complex process: unpredictable, unknowns, uncertainty.

Putting the puzzle together completely takes attention, follow up on details, ability to make decisions in the setting of unknowns, AND an eye on the long-term goals.

DIAGNOSIS

Microbiologic Culture

- "Gold standard"
- Requires sampling of site of infection *prior to* therapy
- Allows determination of antimicrobial susceptibility

Growth?

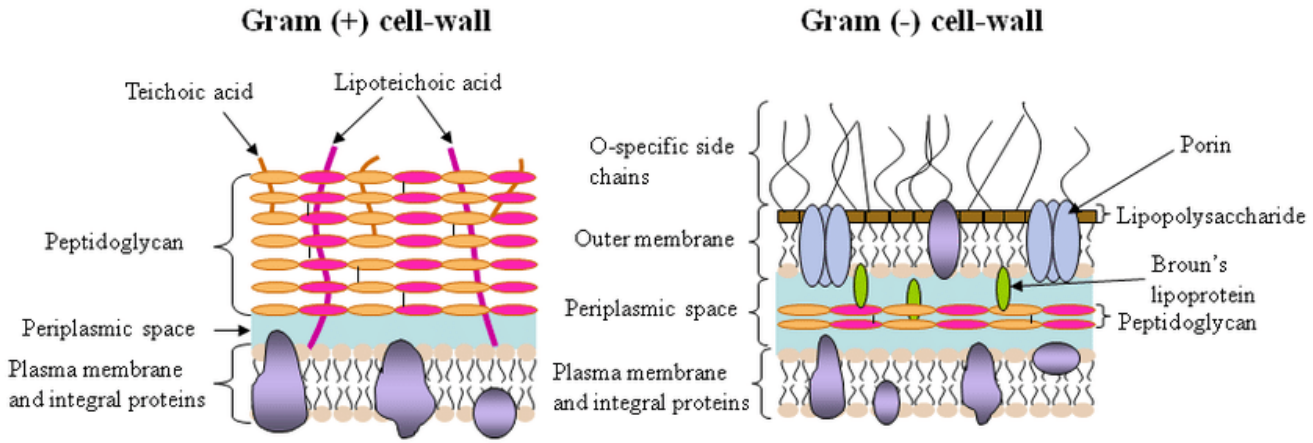
- Stain (Prelim ID)
- Definitive ID
- Susceptibility testing

DIAGNOSIS: Stain

Direct Visualization

Gram stain

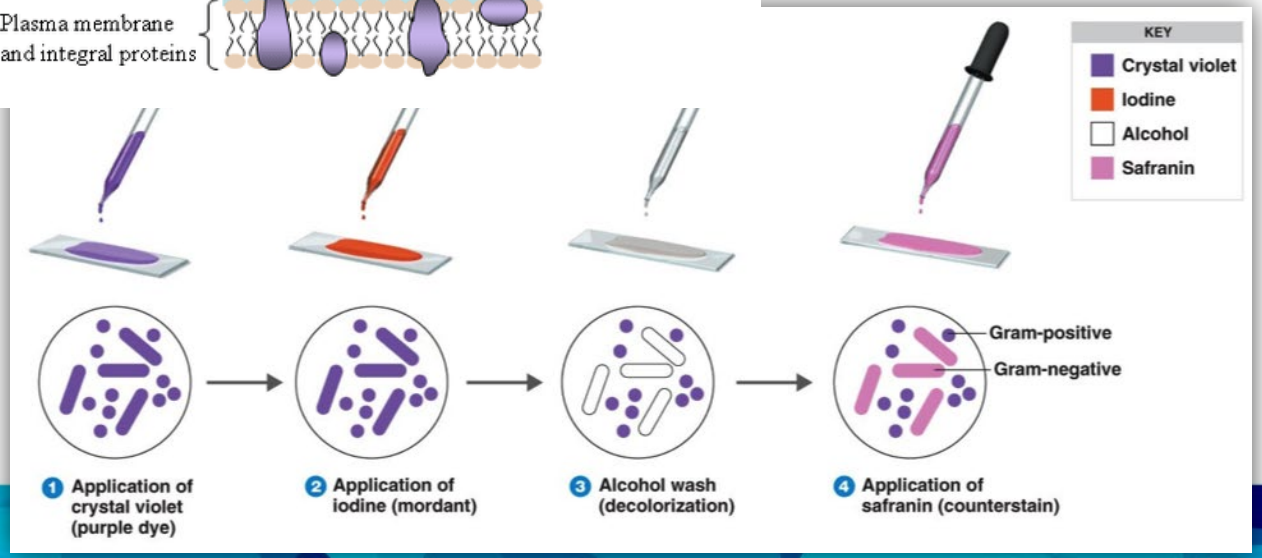
- Often provide clues to etiology (may allow presumptive diagnosis in some cases)
- Gram Positive
- Gram Negative
- Non-staining



Shape

- Cocci
- Rods

Aerobic/Anaerobic



Quick and Dirty Anti-bacterial Classification

Gram positive – skin, lung, guts, devices

Gram negative – guts, urine, some lung

Atypicals – lung, STIs

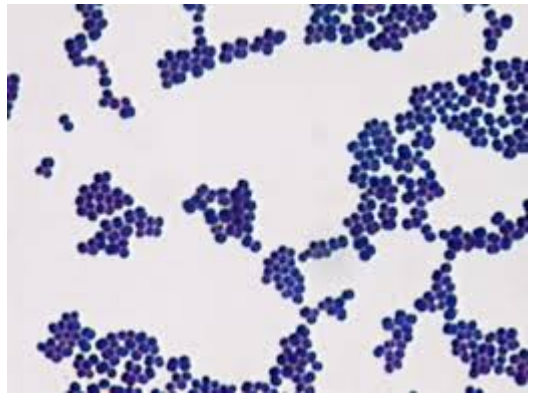
Anaerobes –gas- and abscess-forming, bad odors

Antifungals – guts, devices, immunosuppressed + abx-exposed hosts

GRAM POSITIVE ORGANISMS

Gram positive cocci

- *Staphylococcus aureus*
- Coagulase negative staphylococcus
- *Streptococcus pneumoniae*
- *Streptococcus* sp.
- *Enterococcus* sp.



Gram positive – skin, lung, guts, devices

Gram positive rods

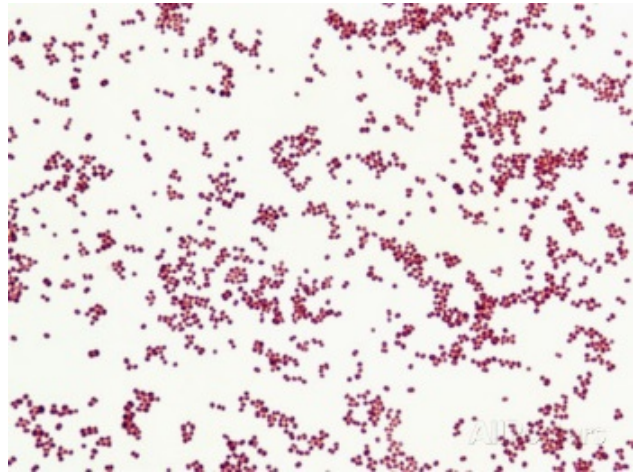
- *Bacillus* sp. (aerobes)
- *Clostridium* sp. (anaerobes)

Antibiotics with Gram Positive (+) Activity

S. aureus	MRSA	VRE	*E. faecalis*
Nafcillin/Oxacillin			Ampicillin
Ampicillin/Sulbactam, Piperacillin/Tazobactam			Ampicillin/Sulbactam, Piperacillin/Tazobactam
Cephalosporins	Ceftaroline (only)		
Carbapenems			
(Fluoroquinolones)			
Vancomycin	Vancomycin		Vancomycin
Clindamycin	Clindamycin +/-		
Linezolid	Linezolid	Linezolid	Linezolid
Daptomycin	Daptomycin	Daptomycin	Daptomycin
Telavancin	Telavancin		
TMP-SMX	TMP-SMX		
Dalvabancin, Oritavancin	Dalvabancin, Oritavancin		

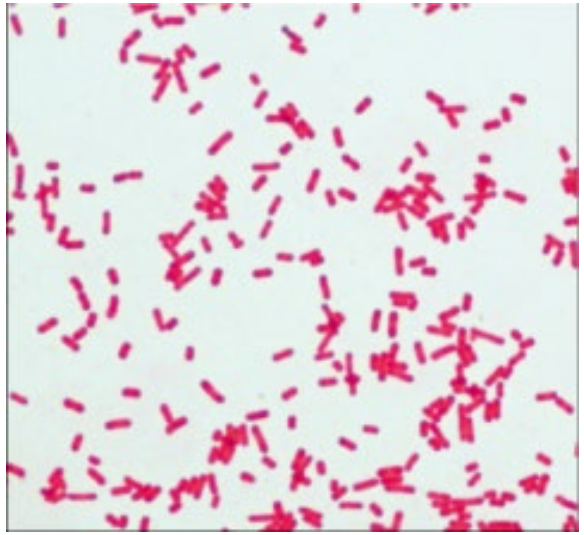
GRAM NEGATIVE ORGANISMS

Gram negative cocci
- *Neisseria meningitidis*
- *Neisseria gonorrhoeae*



Gram negative rods (enteric)
- *E. coli*
- *Klebsiella* sp.
- *Enterobacter* sp.
- *Proteus* sp.
- *Serratia* sp.

Gram- negative: guts, urine, some lung

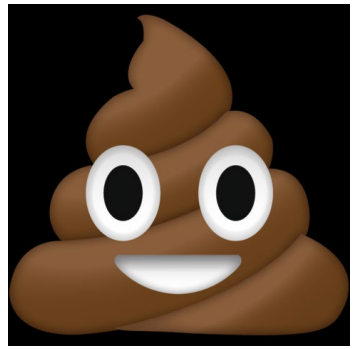


Gram negative rods (non-enteric, non-lactose fermenters)
- *Pseudomonas aeruginosa*
- *Stenotrophomonas maltophilia*
- *Acinetobacter* sp.

Antibiotics with Gram Negative (-) Activity

E. coli	*K. pneumoniae*	*Enterobacter*	*P. aeruginosa*
(Ampicillin)			
(Amp/sulb)	(Amp/sulb)		
Pip/Tazo	Pip/Tazo	Pip/Tazo	Pip/Tazo
Cephalosporins	Cephalosporins	3rd, 4th, 5th gen.	Ceftaz/Cefepime
Carbapenems	Carbapenems	Carbapenems	Imip, Mero, Dori
Aztreonam	Aztreonam	Aztreonam	Aztreonam
Aminoglycosides	Aminoglycosides	Aminoglycosides	Amino-glycosides
Fluoroquinolone	Fluoroquinolone	Fluoroquinolone	Cipro and Levo
Trimeth/Sulf	Trimeth/Sulf	Trimeth/Sulf	

Antibiotics with Anti-anaerobic Activity



Class	Agents (Route)	*B. fragilis* susceptibility[4-7]
Beta-lactam beta-lactamase inhibitor combinations	amoxicillin/clav (PO) ampicillin/sulb (IV) piperacillin/tazo (IV)	90-97% 97% > 99%
Cephalosporin	cefotetan (IV) cefoxitin (IV)	N/A 83-90%
Carbapenem	doripenem (IV) ertapenem (IV/IM) meropenem (IV) imipenem (IV)	> 99%
Fluoroquinolone	moxifloxacin (IV/PO)	66-70%
Other	clindamycin (IV/PO) metronidazole (IV/PO) tigecycline (IV)	66-70% > 99% 81-96%

B. fragilis is the most common group of gut anaerobes.
Then GPCs (*Clostridium* spp.)

Also consider: mouth, vaginal sources

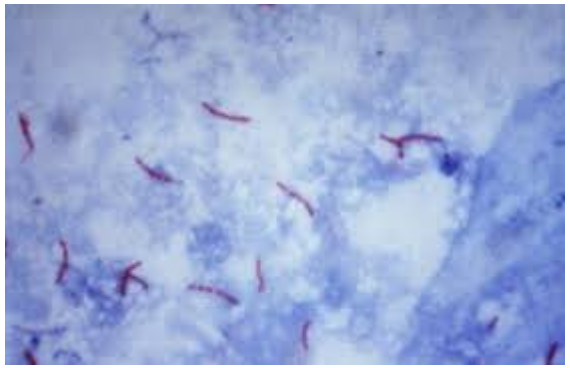
Gas- and abscess-forming, bad odors

C. difficile is a special case (oral vancomycin).

NON-STAINING PATHOGENS

- Not stained by Gram's method (Intracellular)
  - *Legionella* sp.
  - *Chlamydia*
  - *Rickettsia*

  - Mycobacteria
    - *M. tuberculosis*
    - Non-tuberculous mycobacteria



Ziehl-Neelsen Stain of TB

Atypicals

Macrolides:

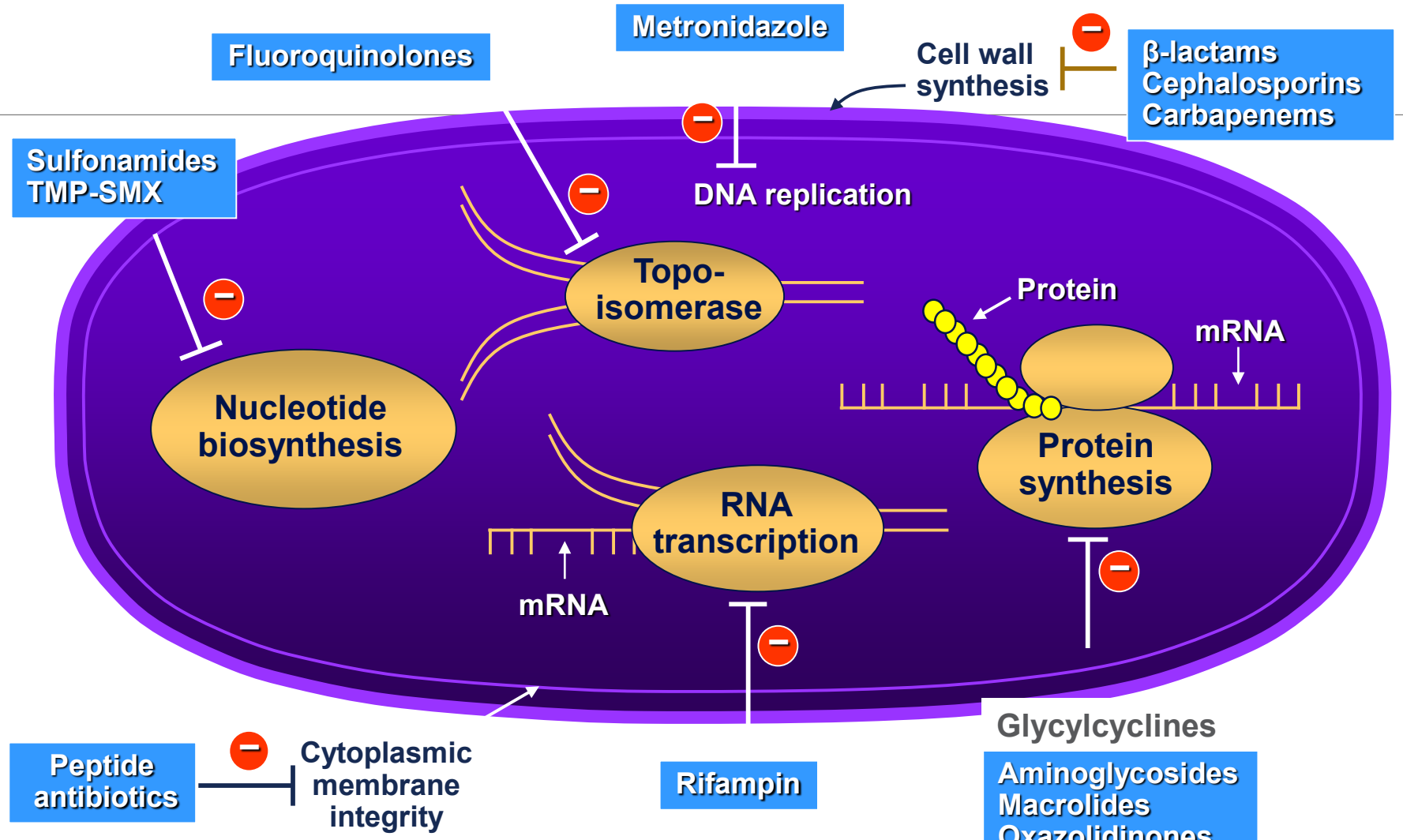
- Azithromycin
- Clarithromycin

Tetracyclines:

- Doxycycline
- Minocycline

Community-acquired pneumonia	Pathogens	CXR pattern
Typical pneumonia	Bacterial: *S. Pneumoniae* *H. Influenzae*	Lobar, dense
Atypical pneumonia	Viral: influenza, RSV Bacterial: *Legionella* *Mycoplasma* *Chlamydia*	Diffuse, patchy

Mechanisms of Action of Antibiotics



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Adapted from: Chopra I. *Curr Opin Pharmacol.* 2001;1:464-469.

Cell membrane and cell wall

Beta-lactams: Interfere with cell wall synthesis

- **Penicillins**:
  - Oxacillin, ampicillin, piperacillin
- **Cephalosporins**:
  - 1º, 2º, 3º, 4º, 5º cephalosporins
- **Carbapenems**:
  - Imipenem, meropenem, ertapenem, doripenem
- **Monobactams**:
  - Aztreonam

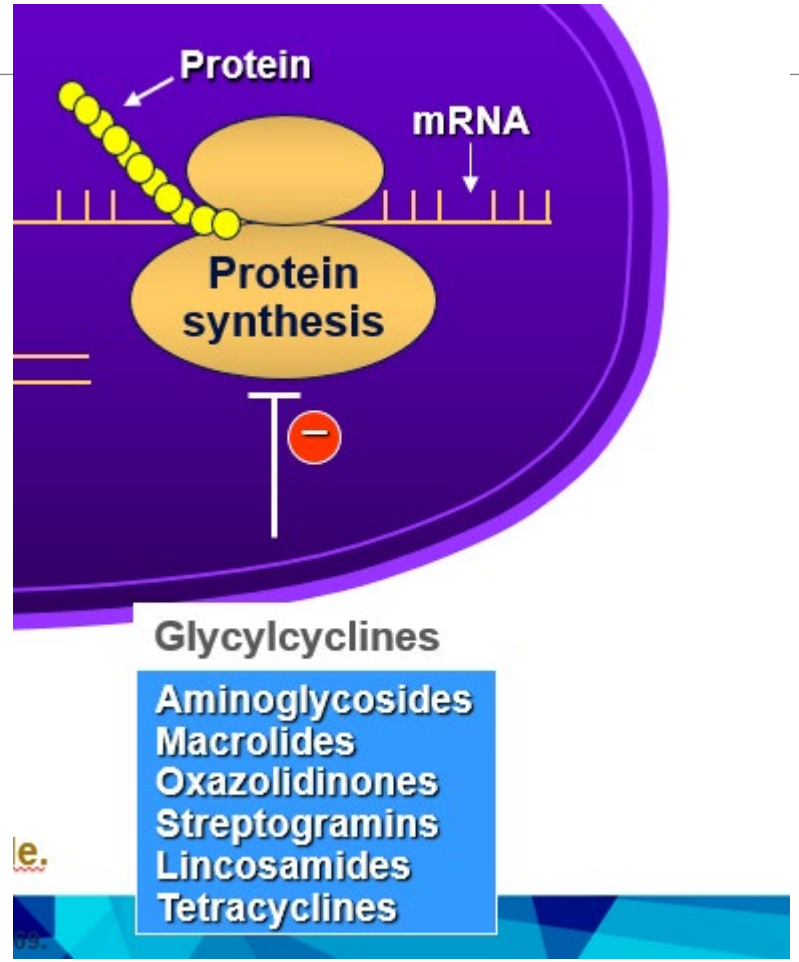
Peptide antibiotics disrupt cell membrane integrity

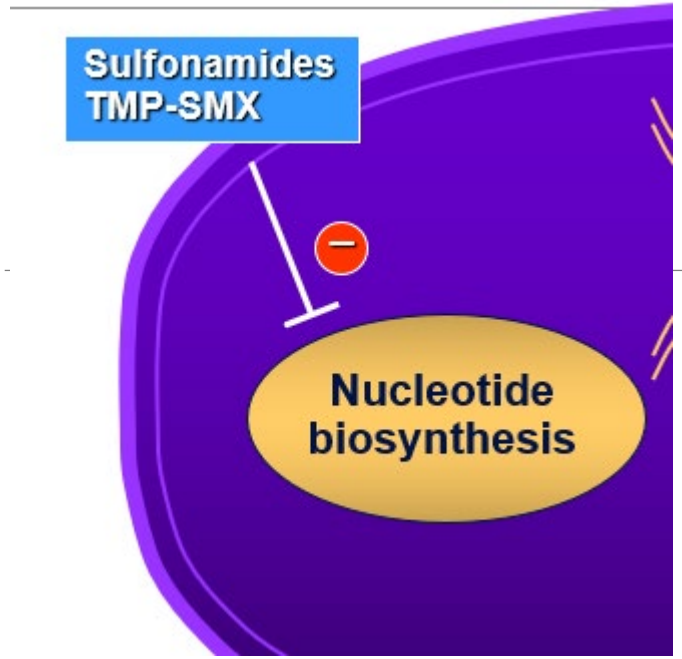
- **Glycopeptide:** Vancomycin, oritavancin, telavancin, dalbavancin
- **Cyclic Lipopeptide:** Daptomycin

ANTIBACTERIALS: MECHANISMS

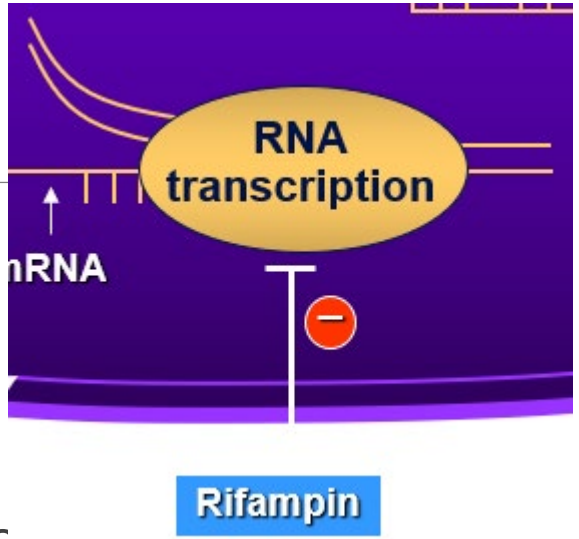
Interference with ribosomal function

- **Aminoglycosides:**
  - Gentamicin, tobramycin, amikacin
- **Tetracyclines**:
  - Tetracycline, minocycline, doxycycline
  - Omadacycline, eravacycline
- **Glycylcyclines**:
  - Tigecycline
- **Macrolides:**
  - Erythromycin, azithromycin, clarithromycin
- **Chloramphenicol**
- **Lincosamides**:
  - Clindamycin
- **Oxazolidinone**:
  - Linezolid, Tedizolid

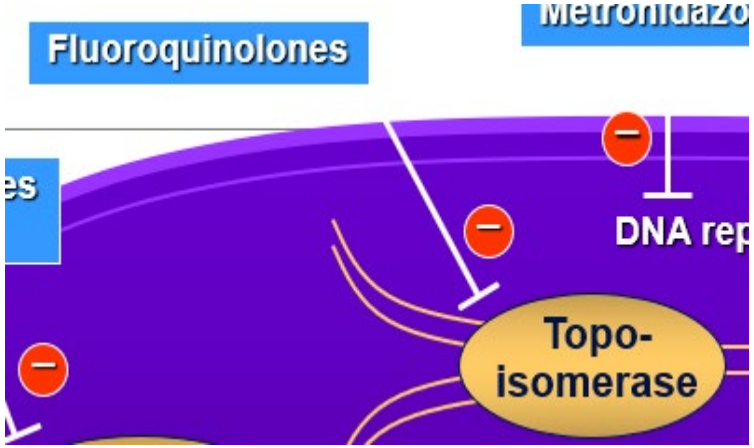




Antimetabolites
- Sulfonamides
- Trimethoprim-sulfamethoxazole



Inhibition of DNA-directed RNA polymeras
- Rifampin, rifapentine, rifabuten



Degradation of DNA
- Metronidazole

Inhibit of DNA gyrase (bactericidal)
- **Quinolones:**
  - Ciprofloxacin, levofloxacin, moxifloxacin

DIAGNOSIS

Antigen tests

- Very useful for following (and sometimes diagnosing) viral infections: HIV, HBV, HCV, EBV, CMV
- Occasionally useful for other pathogens (e.g., cryptococcus)

DIAGNOSIS

Serology

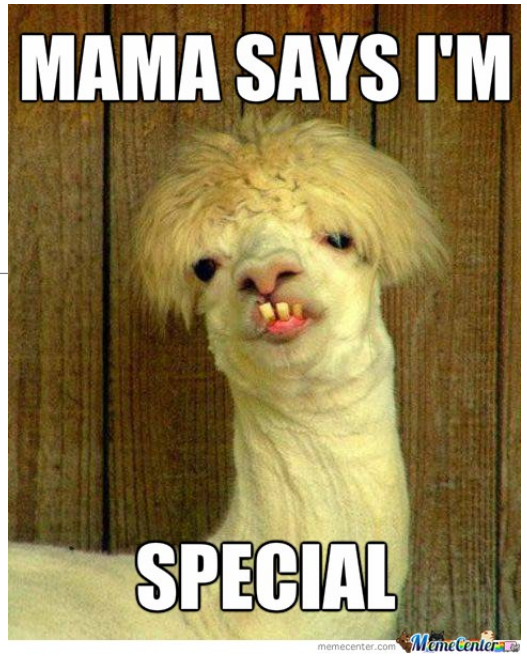
- For bacterial infections, generally not useful in early diagnosis (usually requires acute and convalescent tests)
- For viral infections, IgM may allow early diagnosis (e.g., HepA)

DIAGNOSIS

PCR and other “molecular” tests

- Increasingly used allows diagnosis of non-culturable pathogens (e.g., norovirus) and faster identification(e.g., pertussis, MRSA in blood);
- Subject to false positives due to sensitivity (e.g. *C. difficile*)

Patients are individuals.



Drug interactions

Age

Allergies

Pregnancy, breast feeding

Toxicity (idiosyncratic reactions)

Dose adjustment for renal and/or hepatic dysfunction

Ability to absorb an oral antibiotic

Immune status

Adherence:

- Cost
- Taste
- Frequency of administration
- Pill size
- Duration of therapy
- Multiple drug therapy
- Adverse effects
- Current symptoms

Pathogens are tricky.

Antibiotic = A drug that kills or inhibits the growth of bacterial pathogens

Resistant = Somewhat arbitrary designation that implies that an antimicrobial will not inhibit bacterial growth at clinically achievable concentrations

Susceptible = Somewhat arbitrary designation that implies that an antimicrobial will inhibit bacterial growth at clinically achievable concentrations

Key Terms

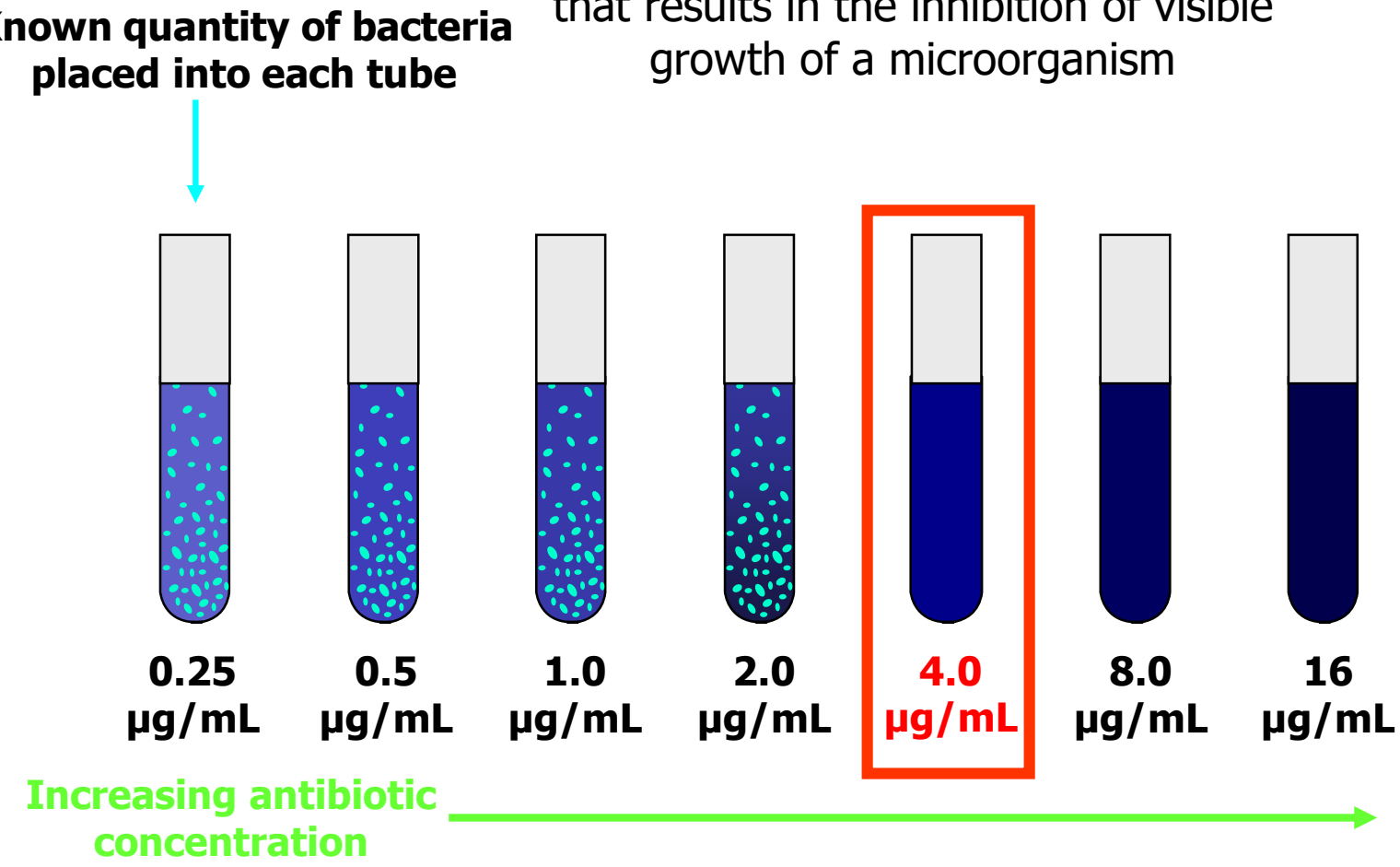
MIC = Minimal inhibitory concentration. Lowest concentration of antimicrobial that inhibits growth of bacteria. Commonly used in clinical lab

MBC = Minimal bactericidal concentration. Concentration of an antimicrobial that kills bacteria. Used clinically only in special circumstances

Breakpoint = The MIC that is used to designate between susceptible and resistant.

Methods for Testing Resistance: Minimal Inhibitory Concentration

Lowest concentration of an antimicrobial that results in the inhibition of visible growth of a microorganism



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Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg*. 2000;123(1 Pt 2):S1.

Durations

- Most guideline-recommended antibiotic durations are based on…
- Qualified with "it depends…"
- Duration questions are ~70% of ID consults.

The answer, Dr. Gilbert, is that this is highly-specialized knowledge, rarefied information that only 100% Board-Certified, USDA-inspected Infectious Diseases Doctors know. And since I'm concerned that your article might give readers the wrong impression about our scientific credibility, I'll now divulge what we've learned, and how to apply it.

To figure out how long antibiotics need to be given, use the following rules:

1. Choose a multiple of 5 (fingers of the hand) or 7 (days of the week).
2. Is it an outpatient problem that is relatively mild? If so, choose something less than 10 days. After application of our multiples rule, this should be 5 or 7 days.
3. Is it *really* mild, so much so that antibiotics probably aren't needed at all but clinician or patient are insistent? Break the 5/7 rule and go with 3 days. Ditto uncomplicated cystitis in young women.
4. Is it a serious problem that occurs in the hospital or could end up leading to hospitalization? With the exception of community-acquired pneumonia (5 or 7 days), 10 days is the minimum.
5. Patient not doing better at the end of some course of therapy? Extend treatment, again using a multiple of 5 or 7 days.
6. Does the infection involve a bone or a heart valve? Four weeks (28 days) at least, often 6 weeks (42 days). Note that 5 weeks (35 days) is not an option — here the 5's and 7's cancel each other out, and chaos ensues.
7. The following lengths of therapy are inherently weird, and should generally be avoided: 2, 4, 6, 8, 9, 11, 12, 13 days. Also, 3.14159265 days.

In this highly data-driven exercise, it is imporant also to note the *number* of rules — *seven*, as in days of the week.

https://blogs.jwatch.org/hiv-id-observations/index.php/how-to-figure-out-the-length-of-antibiotic-therapy/2010/10/22/

Paul E. Sax, MD

Contributing Editor

NEJM JOURNAL WATCH
INFECTIOUS DISEASES

Trials comparing short- vs. longer-course antibiotics have shown short-course is just as effective

	Antibiotic Duration	
Disease	**Short**	**Long**
Community-acquired pneumonia	3-5 days	7-10 days
Nosocomial pneumonia (HAP/VAP)	≤ 8 days	10-15 days
Pyelonephritis	5-7 days	10-14 days
Intraabdominal infection	4 days	10 days
Acute exacerbation of chronic bronchitis (AECB) and COPD	≤ 5 days	≥ 7 days
Acute bacterial sinusitis	5 days	10 days
Cellulitis	5-6 days	10 days
Chronic osteomyelitis	42 days	84 days

5 is the new 7

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Spellberg B. JAMA Intern Med 2016;176(9):1254-1255.

WHAT IS ANTIMICROBIAL STEWARDSHIP?

IDSA/SHEA/PIDS definition

"coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the

selection of the optimal [antibiotic] drug regimen including

dosing,

duration of therapy, and

route of administration."

-- Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS)

Barlam et al. *CID* 2016; 62(10): e51-77.
Fishman et al. *ICHE* 2012; 33:322-7.

Antimicrobial Stewardship Program

Decision support for prescribers of antimicrobials.

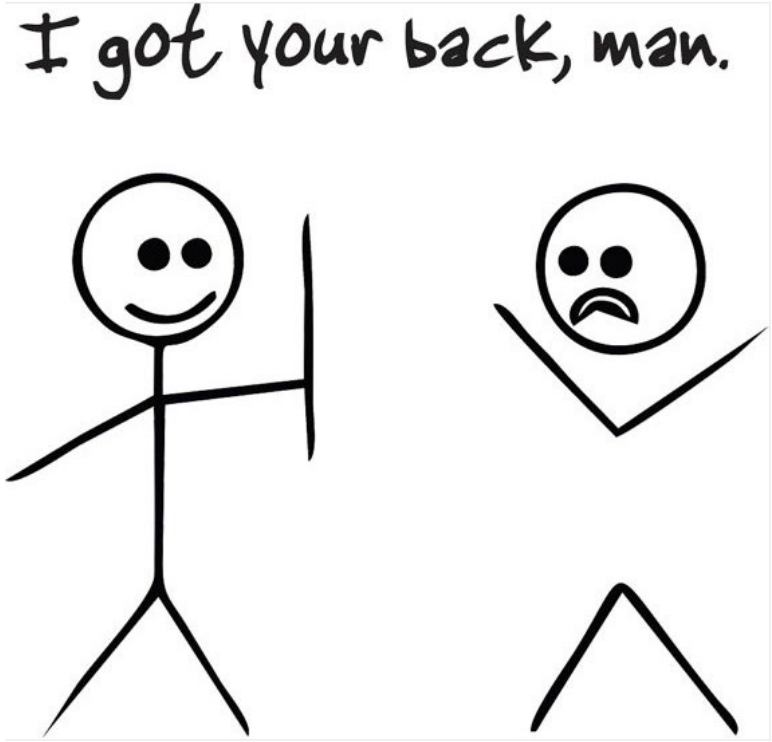
Coordinated program

Multidisciplinary teams

- MD, PharmD, RN, micro, IP, IT

Multi-level interventions:

- Educational
- Systems-based vs. 1:1
- Technology
- Active vs. Passive



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Dellit et al. Clin Inf Dis. 2007;44(2):159-177.

Goals of Antimicrobial Stewardship

Primary:

- Improve quality and increase safety through appropriate use of antimicrobials
  - Improve therapeutic choices (underuse)
  - Reduce unnecessary use (overuse)

Secondary:

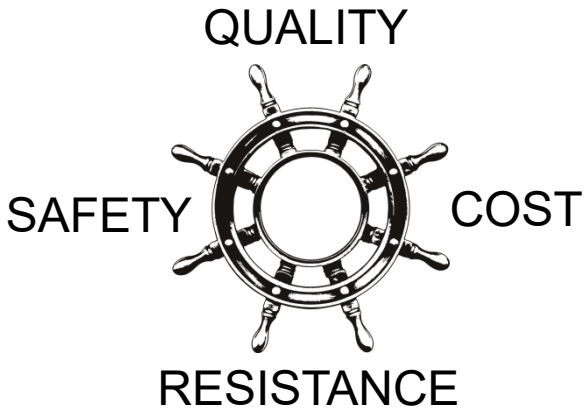
- Decrease emergence of resistance

Desirable "side effects" from an ASP:

- Decrease costs for health system
- Satisfy regulatory requirements

The goal is NOT to
decrease antibiotic use…

It's to IMPROVE antibiotic use!



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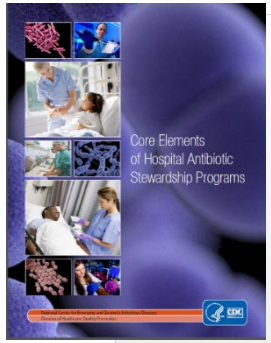
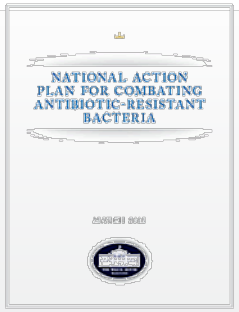
and Infection Prevention

Moehring and Anderson. Curr Infect Dis Rep 2012

Regulators are coming/here.





CDC Core Elements of ASP
Mar 2014

Presidential Executive Order/NQF Forum
Sept 2014

National Action Plan for Combating Antibiotic Resistant Bacteria Published
Mar 2015

IDSA AS Guidelines Updated
April 2016

CMS Proposal
Jun 2016

TJC Proposed Standards for AS
Jun 2016

TJC Standards for AS in ACH Implemented
Jan 2017

Mar | Aug | 2015 | Jun | Nov | 2016 | Nov

2017

AS, antimicrobial stewardship; ASP, antimicrobial stewardship programs

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Resources for Inpatient Stewardship

IDSA/SHEA guidelines on Implementing an ASP: *CID* 2016;62(10):e51–e77

CDC Core Elements Document(s):

https://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf

The Joint Commission Standard:

https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf

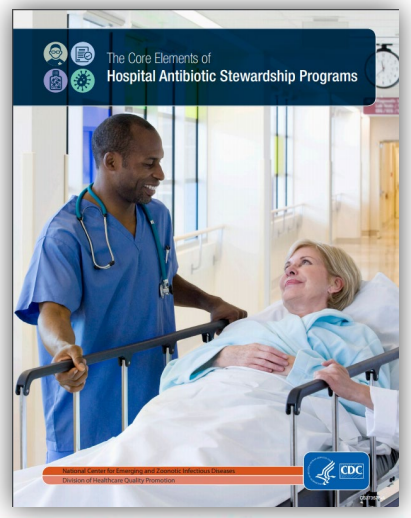

Clinical Infectious Diseases

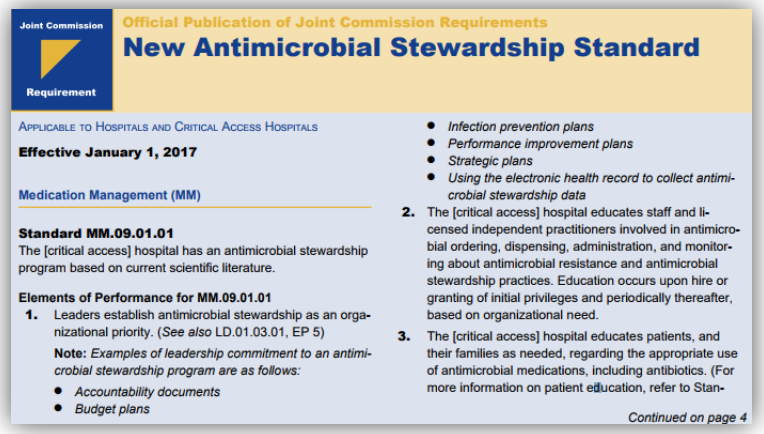
IDSA GUIDELINE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

Tamar F. Barlam,[1,a] Sara E. Cosgrove,[2,a] Lilian M. Abbo,[3] Conan MacDougall,[4] Audrey N. Schuetz,[5] Edward J. Septimus,[6] Arjun Srinivasan,[7] Timothy H. Dellit,[8] Yngve T. Falck-Ytter,[9] Neil O. Fishman,[10] Cindy W. Hamilton,[11] Timothy C. Jenkins,[12] Pamela A. Lipsett,[13] Preeti N. Malani,[14] Larissa S. May,[15] Gregory J. Moran,[16] Melinda M. Neuhauser,[17] Jason G. Newland,[18] Christopher A. Ohl,[19] Matthew H. Samore,[20] Susan K. Seo,[21] and Kavita K. Trivedi[22]




Joint Commission

Requirement

Official Publication of Joint Commission Requirements

New Antimicrobial Stewardship Standard

Applicable to Hospitals and Critical Access Hospitals

Effective January 1, 2017

Medication Management (MM)

Standard MM.09.01.01

The [critical access] hospital has an antimicrobial stewardship program based on current scientific literature.

Elements of Performance for MM.09.01.01

1. Leaders establish antimicrobial stewardship as an organizational priority. (*See also* LD.01.03.01, EP 5)

   Note: *Examples of leadership commitment to an antimicrobial stewardship program are as follows:*

   - *Accountability documents*
   - *Budget plans*
   - *Infection prevention plans*
   - *Performance improvement plans*
   - *Strategic plans*
   - *Using the electronic health record to collect antimicrobial stewardship data*

2. The [critical access] hospital educates staff and licensed independent practitioners involved in antimicrobial ordering, dispensing, administration, and monitoring about antimicrobial resistance and antimicrobial stewardship practices. Education occurs upon hire or granting of initial privileges and periodically thereafter, based on organizational need.

3. The [critical access] hospital educates patients, and their families as needed, regarding the appropriate use of antimicrobial medications, including antibiotics. (For more information on patient education, refer to Stan-

Continued on page 4

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Strength of Rec	Strategies
Strong	Preauthorization/restriction Prospective audit & feedback CDI-focused intervention PK monitoring (AG) IV/PO switch Duration-focused intervention
Weak	Facility-specific guidelines Syndrome-specific intervention Time-out/Auto Stop Computerized Decision Support PK monitoring (Vanco) Alternate dosing for Beta Lactams Penicillin allergy assessments Stratified antibiograms Cascaded reporting of susceptibilities Rapid diagnostics: virus, blood culture Serial procalcitonin in ICU sepsis Fungal markers in Hem malignancy Febrile Neutropenia guidelines Antifungals in immunocompromised DOT>DDD AU data
Good Clinical Practice	Cost > purchasing data Choose clinical outcome metrics wisely Promote AS in SNFs, NICUs, terminally ill
Rec Against	Antibiotic Cycling Didactic education alone

"Action" for inpatient ASPs

LOTS of potential AS strategies suggested in Guidelines

Must be tailored to institutional need and priorities

AVOID: overtaxed ASP personnel

CID 2016;62(10):e51–e77

“Actions” for Inpatient Stewardship

Preauthorization/restriction (before prescribing)

- Can be time/personnel intensive
- Must think through unintended consequences and process snafus
- Not for all hospitals – local culture plays a role
- Best if for targeted agents (not every antibiotic order…)

Post-prescription audit and feedback (after prescribing)

- Front-line stewardship “experts” actively review patients on antibiotics and give feedback to prescribers 1:1
- Time intensive, but effective
- Better for personal relationships
- Need ID “back up” for tough cases

CID 2016;62(10):e51–e77

https://www.cdc.gov/nhsn/PDFs/pscManual/11pscAURcurrent.pdf

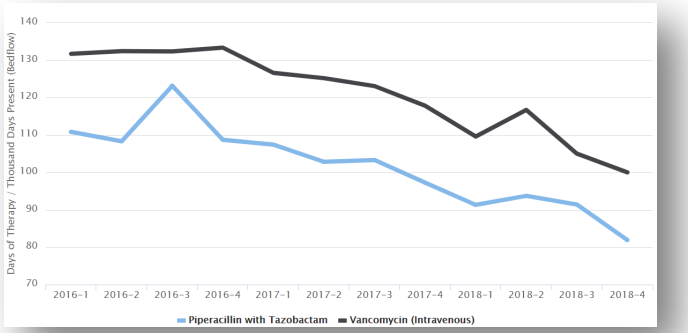
"Tracking" Antibiotic Use

NHSN AU Option is optional/voluntary for acute care hospitals

- ONLY uses electronic data from EHRs (no manual surveillance and no subjective components)

Rate: Days of therapy (DOT) per 1,000 days present

- DOT = calendar days of treatment regardless of number of doses
- Separate drugs counted separately
- Denominator is DIFFERENT than patient days



Data is stratified by Agent, Route, Unit location

Certain agent groups/locations have a benchmark – "SAAR"

- Standardized Antibiotic Administration Ratio: Observed/Expected based on NHSN baseline + limited risk adjustment with information from annual survey
- Example group: "Agents primarily used for resistant gram positive infections"
- Only med/surgical units and ICUs (no benchmarks for specialized areas)

Benchmarking AU between Hospitals

Ongoing area of research, more data emerging

What you want to measure:

- Prescribing practices and decision-making

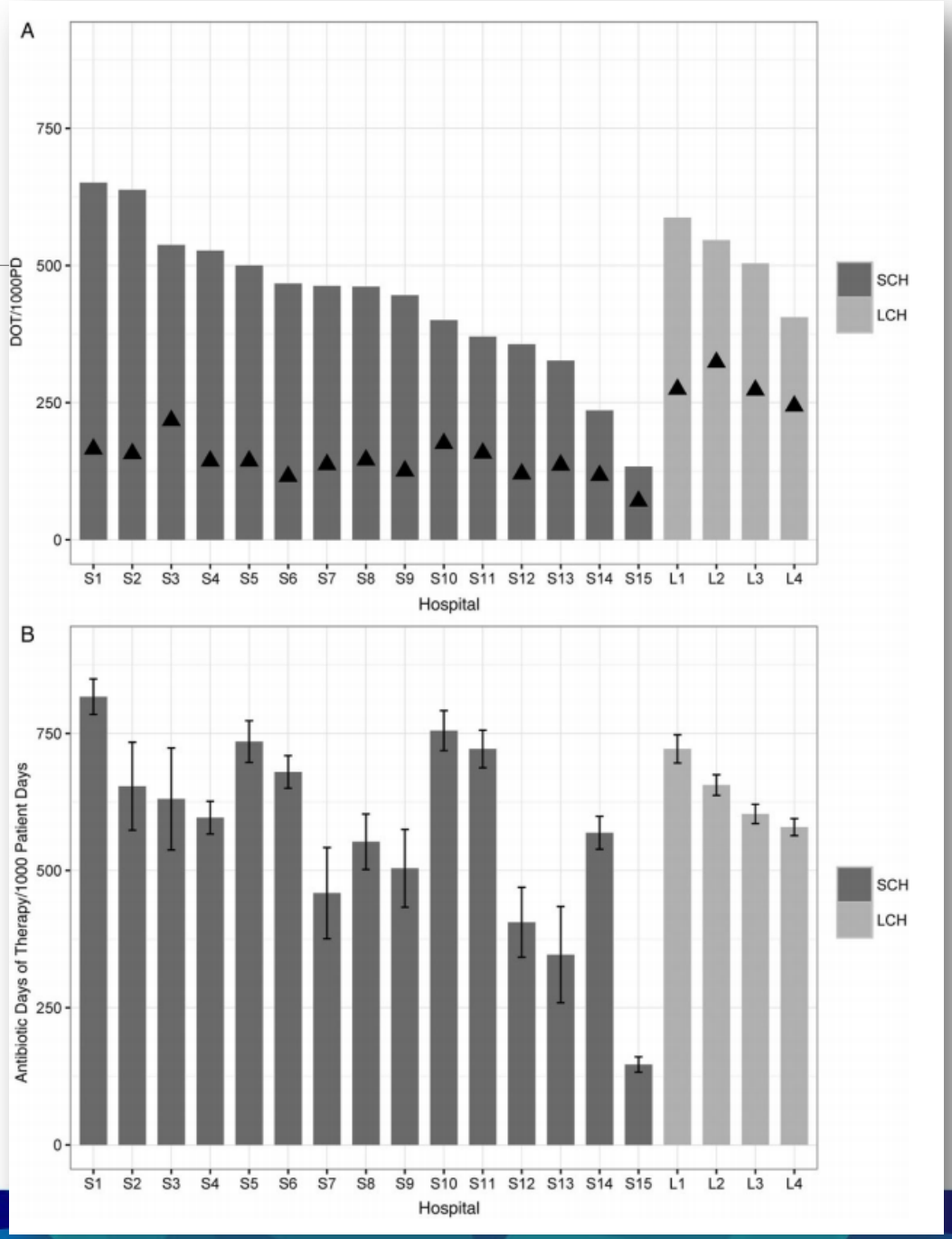
What you get:

- Tonnage or measure of abx exposure – not "appropriate" abx

Problems:

- Case mix
- Hospital size
- Clinical service lines (e.g. surgical specialties, types of ICUs, moms/babies)
- Assume more = bad (not always true clinically)

<u>Should be viewed as a starting point for further investigation and explanation.</u>



Ibrahim, Polk. Expert Rev Anti Infect Ther 10 (4):445-57.
Stenehjem. CID 2016;63(10):1273–80

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CMS: ASP required in Long-term Care

CMS Requirement for Long-term Care ASPs Nov 2017*

*deferred citations for 18 months

<u>Barriers to Implementation of AS in LTC</u>:

Knowledge/Evidence

Expertise

Different stakeholders + processes of care than acute care

Personnel and turnover

Resources for LTC Stewardship

JAMDA

journal homepage: www.jamda.com

Special Article

Template for an Antibiotic Stewardship Policy for Post-Acute and Long-Term Care Settings

Robin L.P. Jump MD, PhD [a,b,*], Swati Gaur MD, MBA, CMD [c], Morgan J. Katz MD [d], Christopher J. Crnich MD, PhD [e,f], Ghinwa Dumyati MD [g], Muhammad S. Ashraf MBBS [h], Elizabeth Frentzel MPH [i], Steven J. Schweon RN, MPH, MSN, CIC, HEM [j], Philip Sloane MD, MPH [k], David Nace MD, MPH, CMD [l] on behalf of the Infection Advisory Committee for AMDA—The Society of Post-Acute and Long-Term Care Medicine

CDC Core Elements

AHRQ Guide

CMS Standard Interpretive Guidance

Table 1
Resources for Antibiotic Stewardship in LTC

Category	Institution	Resource (type of link)
General Antibiotic Stewardship Principles	CDC[a]	The Core Elements of Antibiotic Stewardship for Nursing Homes (website)
		Core Elements of Antibiotic Stewardship for Nursing Homes (pdf)
		Checklist for the Core Elements of Antibiotic Stewardship for Nursing Homes (pdf)
	AHRQ	Nursing Home Antimicrobial Stewardship Guide (website)
	AHS and BC CDC	Do Bugs Need Drugs? (website)
	Rochester Patient Safety *C difficile* Prevention Collaborative	Rochester Nursing Home Collaborative (website)
	Minnesota Department of Health	Minnesota Antimicrobial Stewardship Program Toolkit for Long-term Care Facilities (website)
		Antimicrobial Stewardship in Long-Term Care (pdf)
	Massachusetts Coalition	Evaluation & Treatment –UTI in Elderly (website)
	University of North Carolina	Promoting Wise Antibiotic Use in Nursing Homes (pdf)
Policy and Implementation	CDC	Policy and Practice Actions to Improve Antibiotic Use (pdf)
		Leading Antibiotic Stewardship in Nursing Homes (pdf)
		Creating a Culture to Improve Antibiotic Use in Nursing Homes (pdf)
	AHRQ	Starting an Antimicrobial Stewardship Program (website)
		Monitor and Sustain Stewardship (website)
	Minnesota Department of Health	Action Steps and Strategies for Implementing Antimicrobial Stewardship in Long-term Care Facilities (pdf)
		Antimicrobial Stewardship Gap Analysis Tool (pdf)
	New York Department of Health	The Core Elements of Antibiotic Stewardship with CMS and QAPI Updates (pdf)
Antibiotic Use Protocols	AHRQ	Common Suspected Infections: Communication and Decision Making for Four Infections (website)
		Suspected UTI SBAR Toolkit (website)
		Minimum Criteria for Common Infections Toolkit (website)
		Protocol for Three Common Infections (word document; also included as Appendix 2)
	Rochester Patient Safety *C difficile* Prevention Collaborative	Managing Common Infections in Older Adults (pdf)
		Guidelines for Treatment of Urinary Tract Infections (pdf)
	Minnesota Department of Health	Minimum Criteria for Initiation of Antibiotics in Long-Term Care Residents (pdf)
	Massachusetts Coalition	ABCs for Diagnosing Urinary Tract Infection in Long Term Care (pdf)
Measuring and Monitoring Antibiotic Use	CDC	Measures of Antibiotic Prescribing, Use and Outcomes (pdf)
	AHRQ	Working With Your Lab to Improve Antibiotic Prescribing (website)
		Using Nursing Homes Antibiograms to Choose the Right Antibiotic (website)
	Rochester Patient Safety *C difficile* Prevention Collaborative	Antibiotic Tracking Worksheet (excel file)
		Antibiotic Tracking Sheet Instructions for Use (word document)
		Antibiotic Order Sheet Template (pdf)
	Minnesota Department of Health	Antimicrobial Use Assessment for Long-term Care Facilities (pdf)
		About Antibiograms (pdf)
	World Health Organization	WHONET Collaborating Centre for Surveillance of Antimicrobial Resistance (Website)
Family and Resident Education	CDC	What to Ask Your Healthcare Provider about Antibiotics (pdf)
		What You Need to Know About Antibiotics in a Nursing Home (pdf)
	AHRQ	Toolkit to Education and Engage Residents and Family Members (website)
		Be Smart About Antibiotics (pdf)
		Talking With Residents (pdf)
		Talking With Residents' Family Members (pdf)
		Resident Information Sheet: Antibiotic-Resistant Bacteria(pdf)
	ABIM	AMDA Choosing Wisely List (pdf)
		AGS Choosing Wisely List (website with pdfs)
		Tests & treatments for UTIs in older people – When you need them and when you don't (website with pdfs)
	AHS and BC CDC	FAQ for Families, Guardians and Health Care Aides-UTI in LTCF (pdf)
		FAQ for Families, Guardians and Health Care Aides-NHAP in LTCF (pdf)
	Rochester Patient Safety *C difficile* Prevention Collaborative	Antibiotics for Urinary Tract Infections in Older Adults (pdf)
		Asymptomatic Bacteriuria Family Letter Template (pdf)
	University of North Carolina	Why Not Antibiotics? (pdf)

ABIM, American Board of Internal Medicine; AGS, American Geriatrics Society; AHRQ, Agency for Healthcare Research and Quality; AHS, Alberta Health Services; BC CDC, British Columbia Center for Disease Control; CDC, Centers for Disease Control and Prevention; UTI, urinary tract infection.

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Examples of Stewardship "Action" in LTC

Antibiotic use protocols – "Minimum Criteria" for Abx starts

Test/diagnostic stewardship

- UA/culture
- *C. difficile*

Durations/length of therapy

- UTI
- Pneumonia
- Cellulitis

"Active monitoring" as an alternative to empiric antibiotics in patients who have a clinically undifferentiated problem (e.g. "not at baseline")

Example: Antibiotic Use Protocol

Target: nursing assessment

Identifies “red flag” symptoms

Includes “notes” that identify key areas for baseline knowledge

Provides next steps alternative (other than an antibiotic)

AHRQ Toolkit: “Minimum Criteria for Common Infections”

Minimum Criteria for Initiating Antibiotics for a Skin and Soft Tissue Infection

Initiate antibiotics if the following criteria are met:

○ New or increasing purulent drainage at a wound, skin, or soft-tissue site

OR

○ At least **two** of the following:

- Fever (temperature > 100°F [37.9°C] or two repeated temperatures of 99°F [37°C]), or
- Redness, or
- Tenderness, or
- Warmth, or
- Swelling that is new or increasing at the affected site

Notes:

1. For residents that regularly run a lower temperature, use a temperature of 2°F (1°C) above the baseline as a definition of a fever.
2. Herpes zoster is a virus and therefore does not require antibiotics but appropriate antivirals.
3. Odor is not a standalone criterion for treatment with antibiotics
4. Deeper infections such as bursitis may present with similar signs/symptoms.
5. Underlying osteomyelitis should be considered when managing a resident with an infected diabetic or decubitus ulcer.
6. Thromboembolic disease should be considered when a resident presents with an erythematous or swollen leg.
7. These criteria do not apply to residents with burns.
8. Gout can at times be mistaken for cellulitis or vice versa.

If none of the minimum criteria are met, consider initiating the following:

- Assess vital signs, including temp, every _____ hours for _____ hours; and/or
- Notify Physician/NP/PA if symptoms worsen or if unresolved in _____ hours.

Regardless of whether the minimum criteria are met or not, consider initiating the following:

- For discomfort or prior to cleaning/dressing changes, consider using acetaminophen or other pain relievers as needed.

Careful Observation
~~Watchful Waiting~~

- This is an active process
- More frequent vital signs
- Oral hydration
- Assess for pain, changes in medicine, other reasons like a bad night's sleep
- (or disagreement with a loved one)

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and Inf

Careful Observation Order Set

- ☐ Obtain vital signs (BP, Pulse, Resp Rate, Temp, Pulse Ox) every ____ hours for ____ days.
- ☐ Record fluid intake each shift for _____ days.
- ☐ Notify physician if fluid intake is less than _____ cc daily.
- ☐ Offer resident _____ ounces of water / juice every _____ hours.
- ☐ Notify physician, NP, or PA if condition worsens, or if no improvement in _____ hours.
- ☐ Obtain the following blood work _____ .
- ☐ Consult pharmacist to review medication regimen.
- ☐ Contact the physician, NP, PA with an update on the resident's condition on _____.

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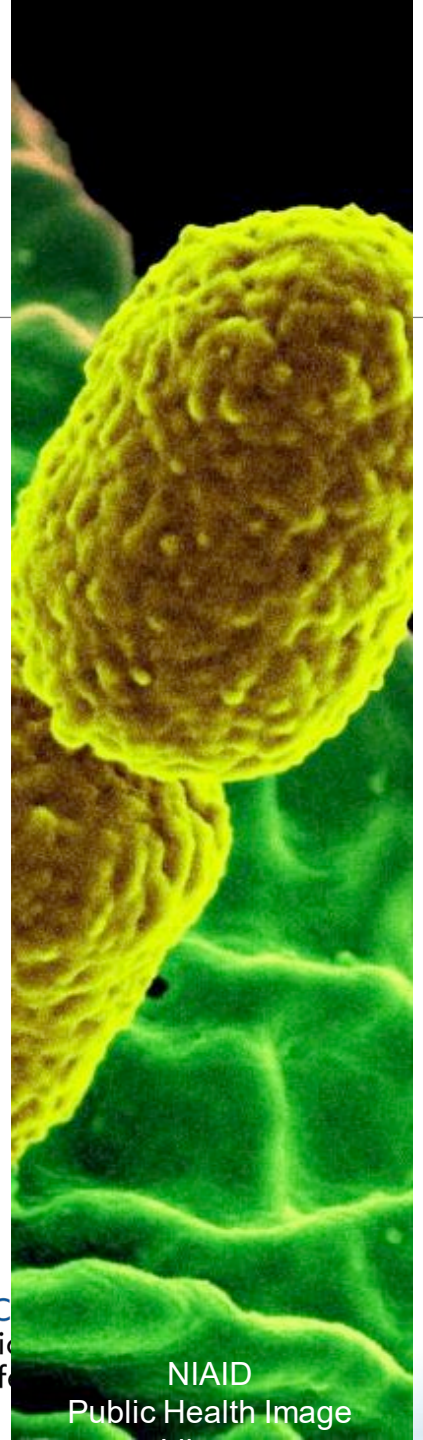
Nace *et al.*, JAMDA 2014;15:133-139



NIAID
Public Health Image

Potential Policies & Procedures

- Concerns about stinky or cloudy urine should lead to increased hydration and perhaps, watchful waiting/careful observation.
- Automatic review of all medication changes by outside providers.
- Send residents to the Emergency Room with a note clearly stating what you are (and are not) worried about.

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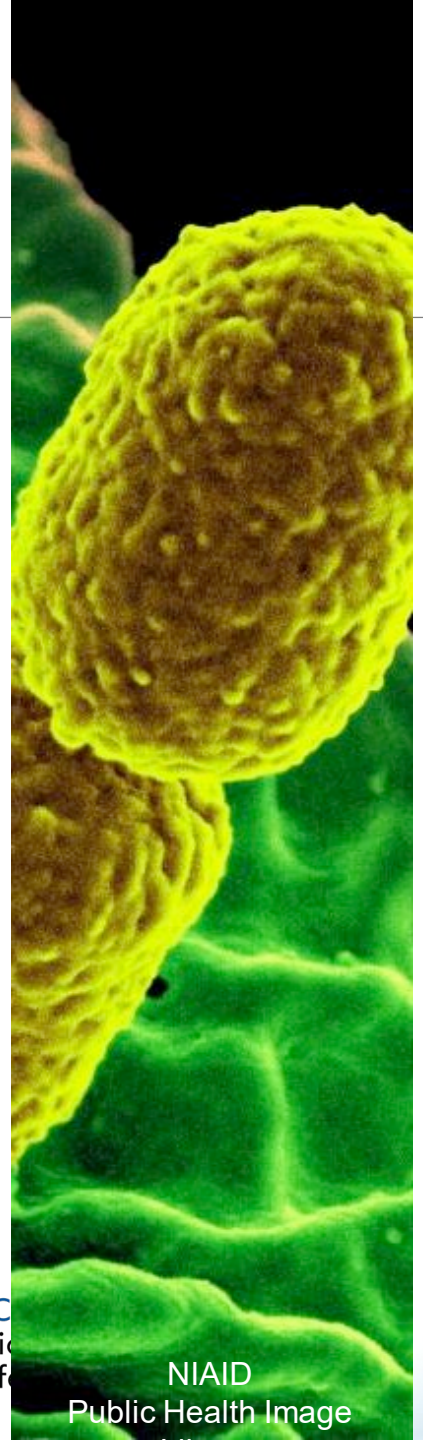


NIAID
Public Health Image

Potential Policies & Procedures

- Clear criteria for collecting a urine sample
- Documented protocol for proper sample collection and handling
- Communication tools when nurses call a covering provider
- Proactively talk to residents and their family members—on admission and during change of status

Resources for Outpatient Stewardship

No regulatory requirements (yet)

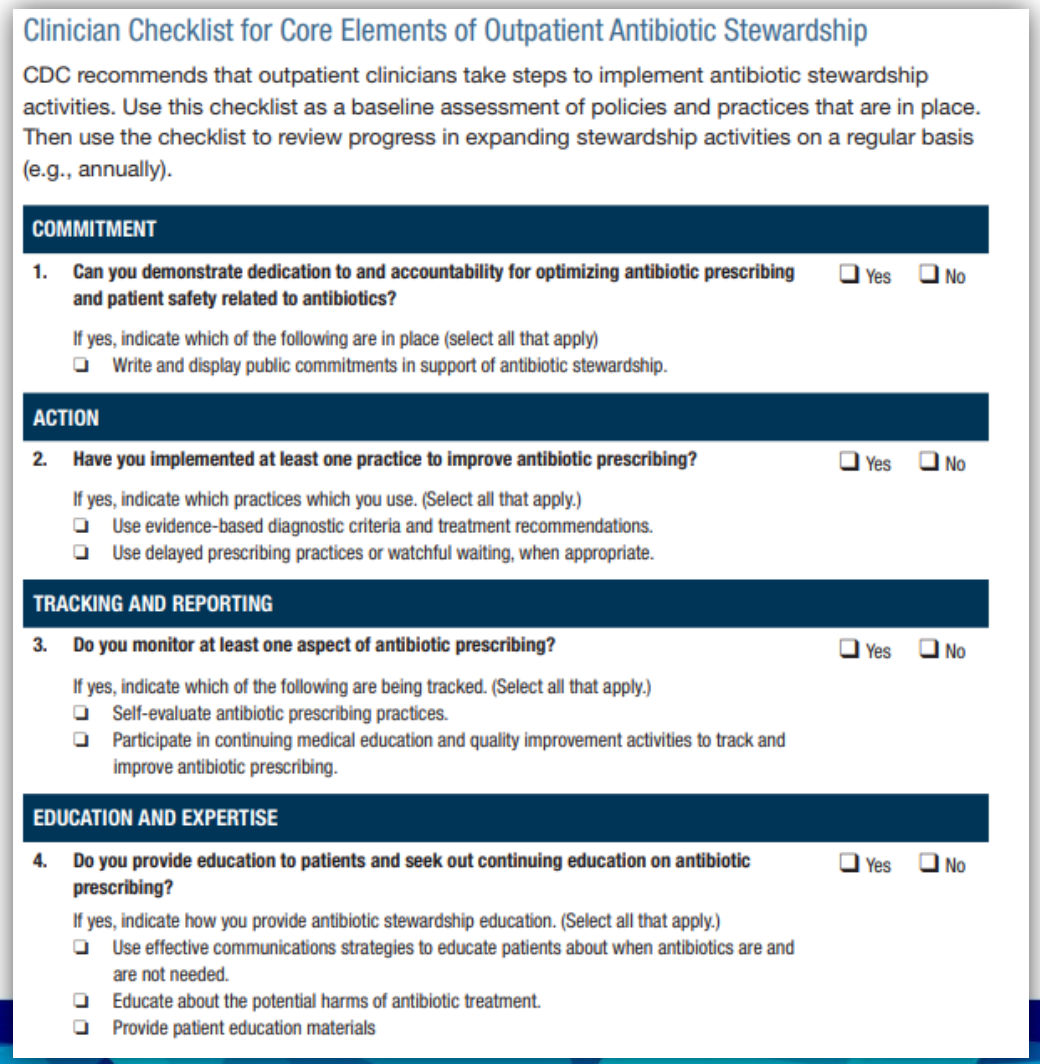
- Drafted for TJC, open for public comment

4 “Core Elements”

Type of outpatient practice setting is highly varied

- Adult/pediatric
- Specialty clinics
- Retail clinics
- Urgent Care

https://www.cdc.gov/antibiotic-use/community/pdfs/16_268900-A_CoreElementsOutpatient_508.pdf



Clinician Checklist for Core Elements of Outpatient Antibiotic Stewardship

CDC recommends that outpatient clinicians take steps to implement antibiotic stewardship activities. Use this checklist as a baseline assessment of policies and practices that are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually).

COMMITMENT

1. **Can you demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety related to antibiotics?** ❑ Yes ❑ No

   If yes, indicate which of the following are in place (select all that apply)
   - ❑ Write and display public commitments in support of antibiotic stewardship.

ACTION

2. **Have you implemented at least one practice to improve antibiotic prescribing?** ❑ Yes ❑ No

   If yes, indicate which practices which you use. (Select all that apply.)
   - ❑ Use evidence-based diagnostic criteria and treatment recommendations.
   - ❑ Use delayed prescribing practices or watchful waiting, when appropriate.

TRACKING AND REPORTING

3. **Do you monitor at least one aspect of antibiotic prescribing?** ❑ Yes ❑ No

   If yes, indicate which of the following are being tracked. (Select all that apply.)
   - ❑ Self-evaluate antibiotic prescribing practices.
   - ❑ Participate in continuing medical education and quality improvement activities to track and improve antibiotic prescribing.

EDUCATION AND EXPERTISE

4. **Do you provide education to patients and seek out continuing education on antibiotic prescribing?** ❑ Yes ❑ No

   If yes, indicate how you provide antibiotic stewardship education. (Select all that apply.)
   - ❑ Use effective communications strategies to educate patients about when antibiotics are and are not needed.
   - ❑ Educate about the potential harms of antibiotic treatment.
   - ❑ Provide patient education materials

“Action” in Outpatient Stewardship

Most literature in Primary or Urgent Care

Peer comparison + data feedback

- Most commonly done for upper respiratory infection
- Identify diagnoses (e.g. viral URI) for which antibiotics should not be given. Benchmark % given abx with peers
  - HEDIS measures (primary care and pediatrics)

Suggested alternatives

Accountable justification

“Nudge” letter/poster

Education combined with the above

We want to give you some important information about antibiotics.

Antibiotics, like penicillin, fight infections due to bacteria that can cause some serious illnesses. But these medicines can cause side effects like skin rashes, diarrhea, or yeast infections. If your symptoms are from a virus and not from bacteria, you won't get better with an antibiotic, and you could still get these bad side effects.

Antibiotics also make bacteria more resistant to them. This can make future infections harder to treat. This means that antibiotics might not work when you really need them. Because of this, it is important that you only use an antibiotic when it is necessary to treat your illness.

How can you help? Carefully follow your doctor's instructions. He or she will tell you if you should or should not take antibiotics.

When you have a cough, sore throat, or other illness, your doctor will help you select the best possible treatments. If an antibiotic would do more harm than good, your doctor will explain this to you, and may offer other treatments that are better for you.

Your health is very important to us. As your doctors, we promise to treat your illness in the best way possible. We are also dedicated to avoid prescribing antibiotics when they are likely to do more harm than good.

If you have any questions, please feel free to ask your doctor, nurse, or pharmacist.

Gerber. JAMA 2013;309(22):2345-2352
Meeker. JAMA 2016; 315(6)562-570
Meeker. JAMA Intern Med. 2014;174(3):425-431.

Summary

Antibiotics are life-saving medicines that are often misused.

Antimicrobial decision-making is complex.

Optimized antimicrobial use through antimicrobial stewardship protects patients from unintended consequences.

Antimicrobial use affects individuals AND populations. Healthcare exposed populations are the most at risk.

Antimicrobial Stewardship Programs should be supported in all US healthcare facilities and is a key component of infection prevention.

THANK YOU!

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Duke Center for
Antimicrobial Stewardship
and Infection Prevention