Antibiotic Stewardship

Presenter

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Objectives

- **Objectives:**
- To understand the purpose of implementing an antimicrobial stewardship program (ASP)
- To recall the core elements of hospital and outpatient antibiotic stewardship programs as defined by the CDC
- To recognize key interventions that an antimicrobial stewardship program can implement in both the hospital and community settings

Part 1:
The Problem

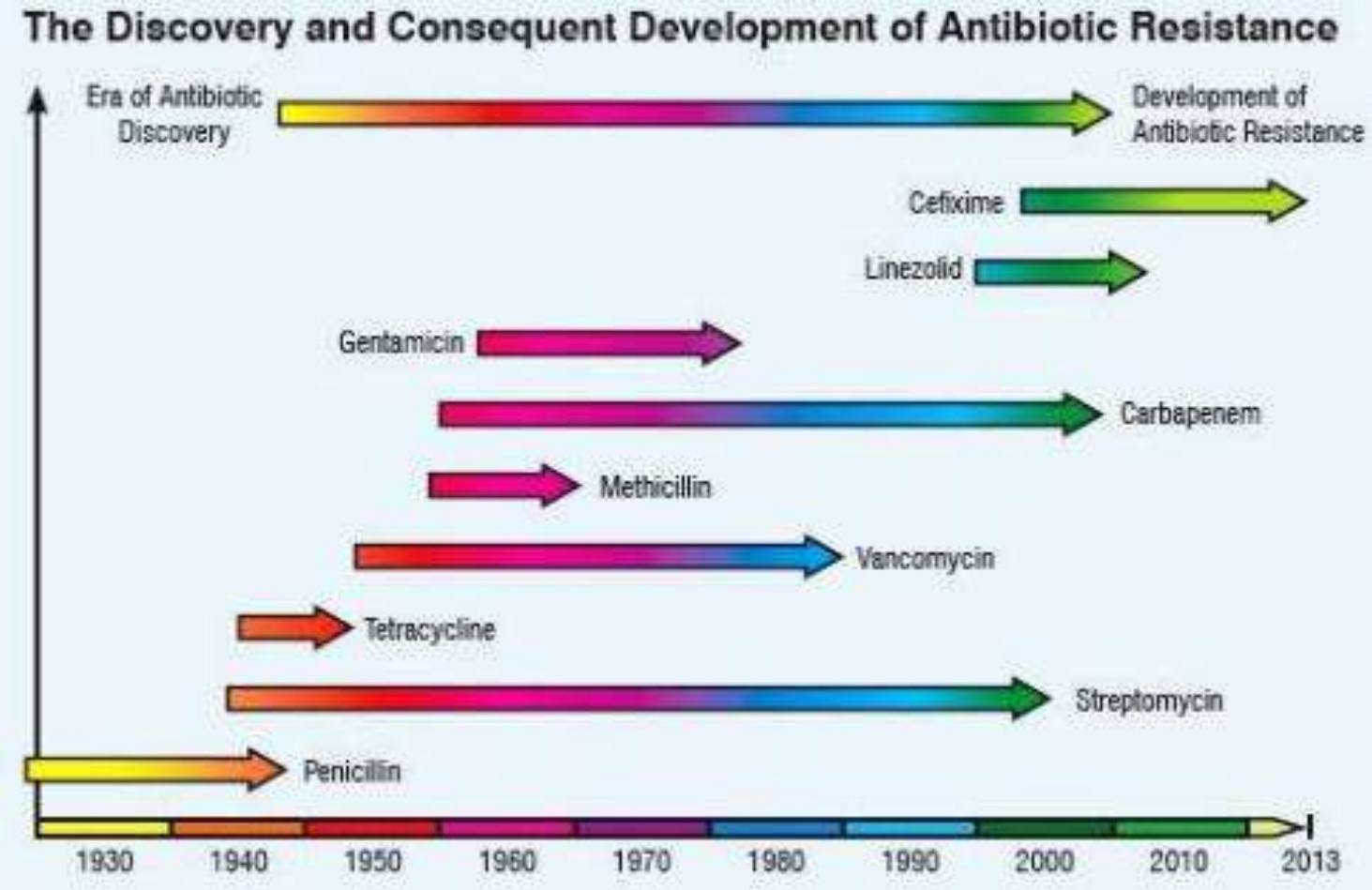
What is Antimicrobial Resistance?

- **The ability of a microorganism to stop an antimicrobial from working against it.**

- Standard treatments become ineffective, infections persist and may spread to others.
- New resistance mechanisms are emerging and spreading globally.
- Resistance increases the cost of health care with lengthier stays in hospitals and more intensive care required.

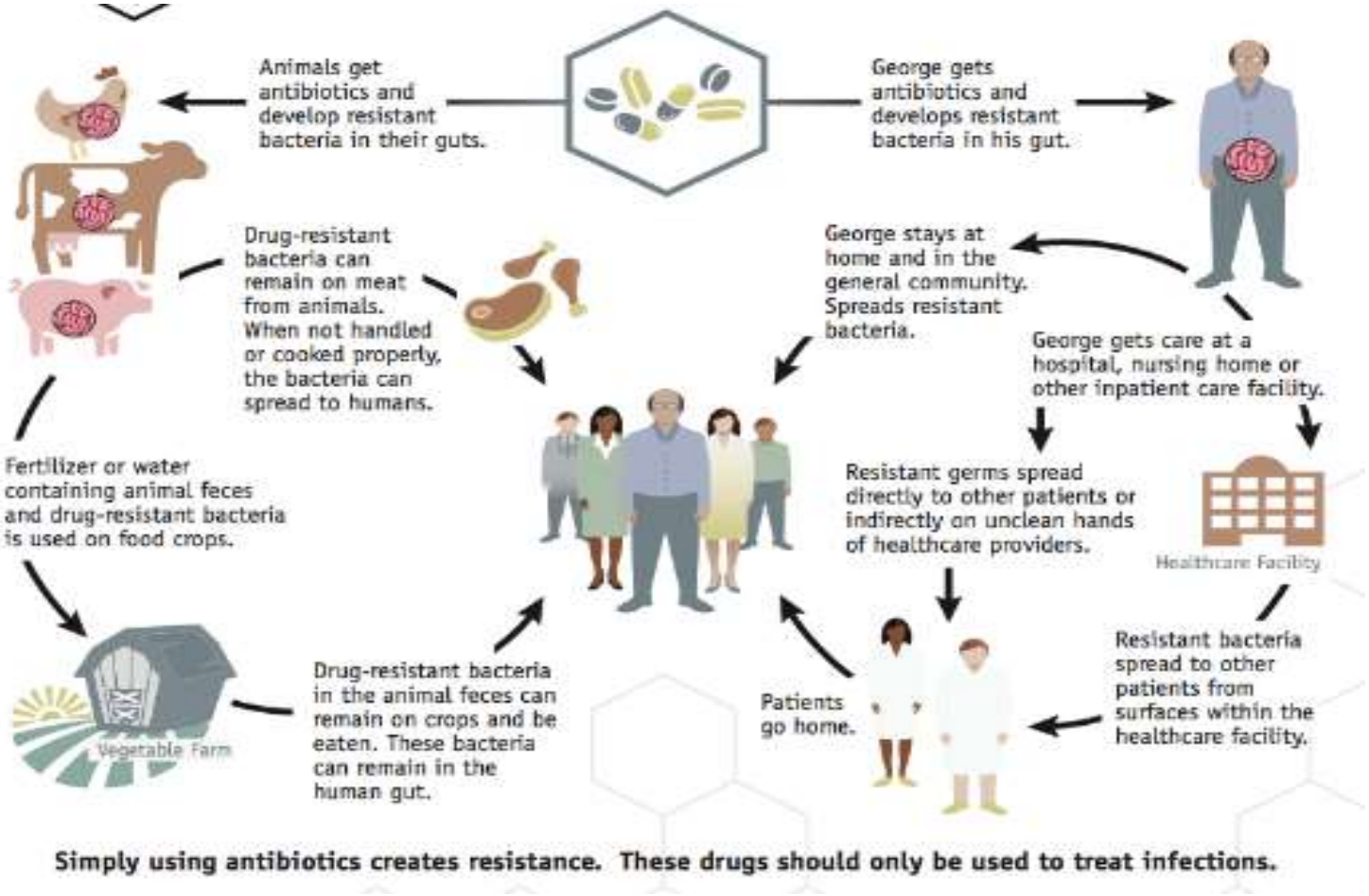
who.int/antimicrobial-resistance

Microbes are Smart



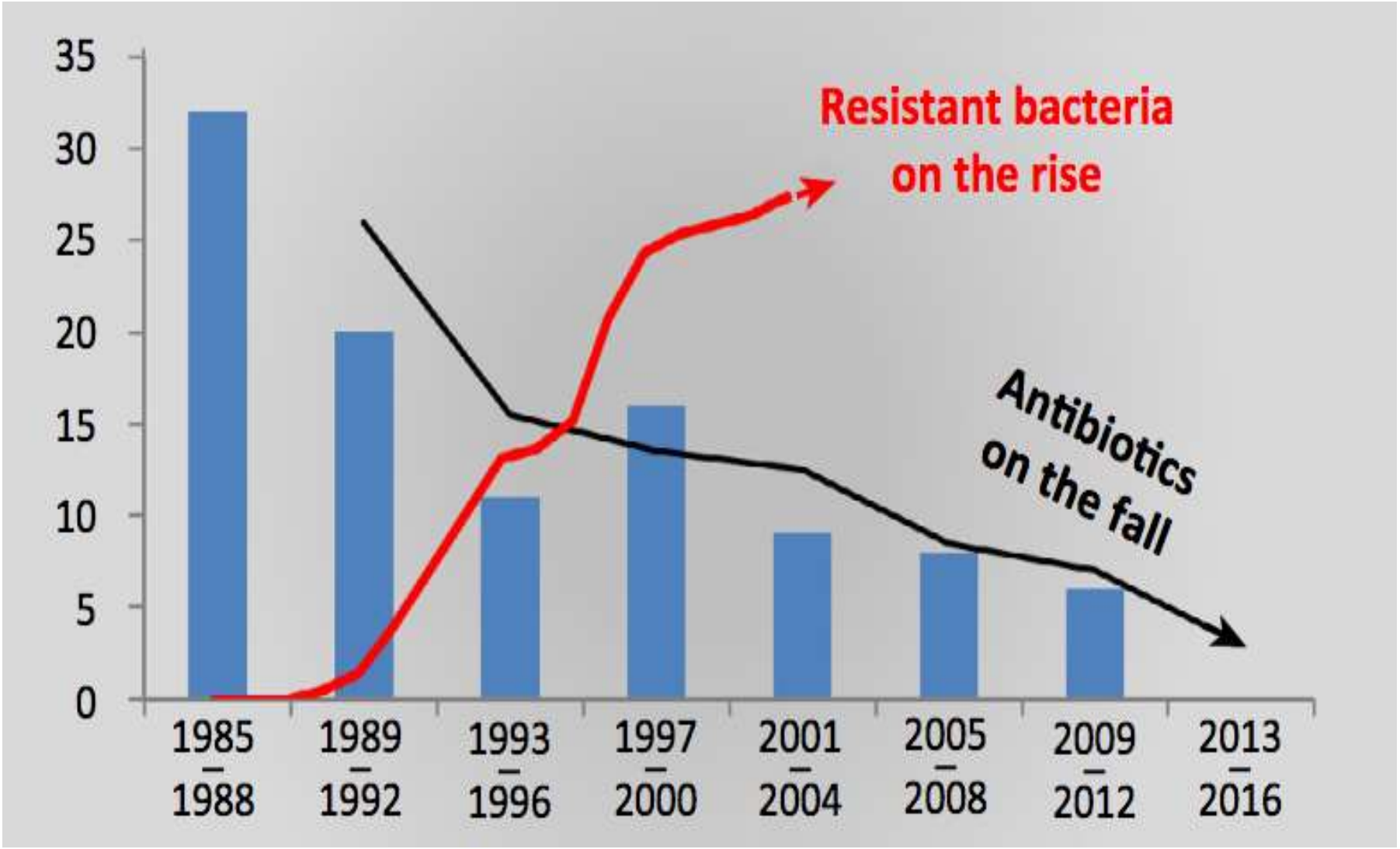
cdc.gov/drugresistance

Spreading Antimicrobial Resistance



Antibiotic Resistance Threats in the United States. CDC. 2013.

Antimicrobial Development



Trends In Microbiology. 2014;22(4):165-167.

PART 2:
A Piece of the puzzle

Fighting Back!

- The CDC has recommended four necessary actions to prevent antimicrobial resistance
  - Prevent infections, prevent the spread of resistance
  - Tracking
  - Developing new drugs and diagnostic tests
  - IMPROVING ANTIBIOTIC PRESCRIBING / STEWARDSHIP

Antibiotic Resistance Threats in the United States. CDC. 2013.

What is Antimicrobial Stewardship?

- The commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.
- Objectives:
  - Maximum antimicrobial benefit
  - Avoid harm from adverse reactions and drug allergies
  - Improve patient outcomes
  - Decrease antimicrobial resistance
  - Decrease healthcare costs

Antibiotic Resistance Threats in the United States. CDC. 2013.

Summary of Core Elements of Hospital Antibiotic Stewardship Programs

- **Leadership Commitment:** Dedicating necessary human, financial and information technology resources.
- **Accountability:** Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective.
- **Drug Expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- **Action:** Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. "antibiotic time out" after 48 hours).
- **Tracking:** Monitoring antibiotic prescribing and resistance patterns.
- **Reporting:** Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff.
- **Education:** Educating clinicians about resistance and optimal prescribing.

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Leadership Commitment

- Formal statements that the facility supports efforts to improve and monitor antibiotic use
- Including stewardship-related duties in job descriptions and annual performance reviews
- Ensuring staff from relevant departments are given sufficient time to contribute to stewardship activities
- Supporting training and education
- Ensuring participation from the many groups that can support stewardship activities

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Accountability and Drug Expertise

- **Stewardship program leader:**
  - Identify a single leader who will be responsible for program outcomes
  - Physicians have been highly effective in this role
- **Pharmacy leader:**
  - Identify a single pharmacy leader who will co-lead the program
- **Key support:**
  - The work of stewardship program leaders is greatly enhanced by the support of other key groups in hospitals where they are available
  - Clinicians and department heads, infection preventionists, hospital epidemiologists, quality improvement staff, laboratory staff, information technology staff, nursing

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Action

- **Implement policies that support optimal antibiotic use**
  - Document dose, duration, and indication
  - Develop and implement facility-specific treatment recommendations
- **Utilize specific interventions, divided into three categories:**
  - Broad
  - Pharmacy driven
  - Infection and syndrome specific
- **Avoid implementing too many policies and interventions simultaneously**
  - Prioritize based on the needs of the hospital as defined by measures of overall use and other tracking and reporting metrics

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Interventions: Broad

- **Antibiotic "time-outs"**
  - Prompts a reassessment of the continuing need and choice of antibiotics
  - Review after 48 hours
- **Prior authorization**
  - Restrict the use of certain antibiotics
  - Based on the spectrum of activity, cost, or associated toxicities
  - Ensure that timely expert review is conceivable to avoid delay in therapy
- **Prospective audit and feedback**
  - External reviews of antibiotic therapy by an expert in antibiotic use
  - Major function of the ASP pharmacist

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Interventions: Pharmacy Driven

- Automatic changes from intravenous to oral antimicrobial therapy
- Dose adjustments
- Dose optimization
- Automatic alerts in situations where therapy might be unnecessarily duplicative
- Time-sensitive automatic stop orders
- Detection and prevention of antimicrobial-related drug-drug interactions

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Interventions: Infection/Syndrome Specific

- Intended to improve prescribing for specific syndromes
  - Community-acquired pneumonia
  - Urinary tract infections
  - Skin and soft tissue infections
  - Empiric coverage of MRSA infections
  - *Clostridium difficile* infections
  - Treatment of culture-proven invasive infections
- Should NOT interfere with prompt and effective treatment for severe infection or sepsis

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Tracking

- Monitor antibiotic use prescribing
  - Identify opportunities for improvement
  - Assess impact of efforts
- Process measures
- Antibiotic use
  - Controversy regarding best methods for monitoring use
  - DDD = defined daily dose
  - DOT = days of therapy
- Outcomes measures

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Reporting

- **Center for Medicare & Medicaid Services**
  - Required
  - e.g. CLABSI, CAUTI, MRSA, *Clostridium difficile* infections
- **National Healthcare Safety Network (NHSN)**
  - Not yet required, but encouraged
  - Provides a mechanism for facilities to report and analyze antimicrobial use and/or resistance over time at the facility and national levels
  - Somewhat complex → requirements and setup outlined by CDC

CDC. Antimicrobial Use and Resistance (AUR) Module. 2017.

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Education

- Provide regular updates on antimicrobial prescribing, antibiotic resistance, and infectious disease management
- Address both national and local issues
- Choose format based on receptiveness at your institution:
  - Didactic presentations
  - Posters, flyers, newsletters, emails
- ASP website
- Review de-identified cases where changes in antimicrobial therapy could have been made

Urinary isolate antibiogram

Includes isolates from urine cultures. Note the differential sampling periods for Gram negative isolates below.
The **#strains** column indicates an annualised number. Actual tested strain numbers against specific antibiotics are indicated under each cell.

			Unrestricted antibiotics						Restricted antibiotics		
Organism group	# strains (annualised)	% total	Ampicillin	Amoxycillin+clavulanate	Cefazolin / cephalexin	Gentamicin (aminoglycoside)	Nitrofurantoin	Trimethoprim	Ceftriaxone	Piperacillin+tazobactam	Norfloxacin
All isolates	3,281	100%									
Escherichia coli	1,664	51%	46%	78%	57%	96%	98%	79%	97%	S	94%
			n=415	414	414	415	415	416	416		416
Klebsiella species	224	7%	R	89%	68%	96%	45%	84%	98%	S	95%
				55	56	56	55	56	56		56
Proteus mirabilis	132	4%	91%	94%	76%	100%	R	76%	100%	S	100%
			33	33	33	33		33	33		33
Enterobacter -like species**	304	9%	0%	11%	7%	93%	22%	74%	86%**	S	100%
			76	76	76	76	76	76	76		76
Pseudomonas aeruginosa	172	5%	R	R	R	93%	R	R	R	97%	84%
						43				38	43
Staphylococcus saprophyticus	38	1%	100%	S	S	n/a	100%	92%		S	n/a
			38				38	38			
Enterococcus faecalis	145	4%	98%	S	R	R	99%	R		S	R
			145				145				
Other species	785	24%									

Gram negative organism	2,712
Gram positive organism	569

NB. Gram negative tested are for the quarter April -June 2014

n/a	not available - not routinely tested in this laboratory
93%	>90% of isolates susceptible
S	Susceptible by extrapolation
75%	70-89% of isolates susceptible
45%	<70% of isolates susceptible
R	Intrinsically resistant
**	*Enterobacter, Serratia, Citrobacter, Providencia, Morganella* species. Though ceftriaxone frequently tests susceptible, this agent is NOT recommended for treatment as resistance will commonly emerge during therapy.

95% percent susceptible

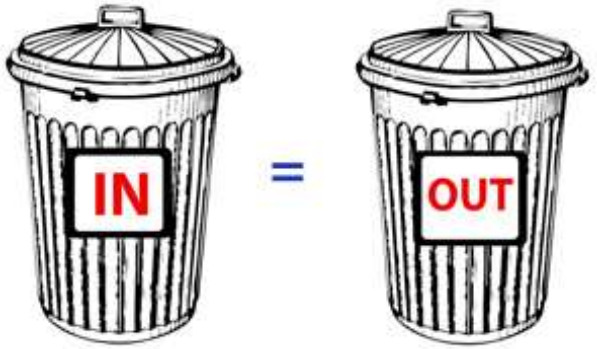
56 number of strains tested

Restricted - see http://www.hnequm.com for indications.

aimed.net.au

Antibiograms

- Requirements
  - Compile annually
  - Include only the first isolate per patient
  - Collaborative effort
- Limitations
  - MICs
  - Patient-specific factors (e.g. infection history, past antimicrobial use, comorbidities, age)
  - Single organism-antimicrobial combinations
    - Cross-resistance and synergy are not generally considered
    - Combination antibiograms
  - Generalizability



Pharmacotherapy. 2007;27(9):1306-1312.

health.state.mn.us

Cultures Before Antimicrobials (if possible)

- Improves the chances of identifying the offending microorganism
- Administration of antimicrobials before culture collection may decrease culture yields
- More difficult to deescalate therapy without cultures
- DO NOT DELAY THERAPY!

Does That Drug Cover That Bug?

- All parameters can be correct, but if the antimicrobial does not cover the causative pathogen, the patient is not likely to clear the infection
- Select empiric therapy based on patient, disease, and institution-specific characteristics
- Follow up on cultures and other diagnostic tests
- Caution with polymicrobial infections

Infection vs. Contamination vs. Colonization

- Infection – true positive from causative organisms
- Contamination – false positive due to contaminate
  - Time to culture positivity
  - Number of positive blood bottles
  - Consider what sites should normally be sterile
  - Consider common causes of culture contamination
  - Question polymicrobial culture results
  - Promote correct antiseptic technique when obtaining cultures
- Colonization – false positive due to pathogens that naturally occur at a specific site (e.g. anaerobes in the mouth)
  - Review other labs – WBC with differential, procalcitonin, fever curve, etc.
  - Consider the patient's presentation

Microorganism (No. of Isolates)	No. (%) of Isolates per Indicated Category		
	True Pathogen	Contaminent	Unknown
Staphylococcus aureus (204)	178 (87.2)	13 (6.4)	13 (6.4)
Coagulase-negative staphylococcus (703)	87 (12.4)	575 (81.9)	41 (5.8)
Streptococcus pneumoniae (34)	34 (100)	0	0
Viridans streptococci (71)	27 (38.0)	35 (49.3)	9 (12.7)
Other streptococci (31)	21 (67.7)	6 (19.4)	4 (12.9)
Enterococcus spp. (93)	65 (69.9)	15 (16.1)	13 (14.0)
Corynebacterium spp. (53)	1 (1.9)	51 (96.2)	1 (1.9)
Bacillus spp. (12)	1 (8.3)	11 (91.7)	0
Escherichia coli (143)	142 (99.3)	0	1 (0.7)
Klebsiella pneumoniae (65)	65 (100)	0	0
Other enteric gram-negative bacteria (108)	104 (96.3)	1 (0.9)	3 (2.8)
Pseudomonas aeruginosa (55)	53 (96.4)	1 (1.8)	1 (1.8)
Propionibacterium acnes (48)	0	48 (100)	0
Other Gram-positive anaerobes including *Clostridium* spp. (35)	19 (54.3)	15 (42.8)	1 (2.9)
Bacteroides fragilis group (18)	16 (88.9)	0	2 (11.1)
Other Gram-negative anaerobes (5)	2 (40)	2 (40)	1 (20)
Candida spp. (60)	56 (93.3)	0	4 (6.7)
Cryptococcus neoformans (8)	8 (100)	0	0

Clin Infect Dis. 1997;24:584-602.

Duration, Duration, Duration!

- Undertreating does not tend to be an issue
- Overtreating with unnecessary extensions of antimicrobial regimens are not uncommon
- Recommend durations based on published guidelines
  - e.g. – HAP duration is now 7 days
- Encourage use of stop dates

Get to Know the Micro Lab

- Provide timely, reliable, and reproducible identification and antimicrobial susceptibility results
- Promptly report unusual patterns of resistance
- Optimize communication of critical test result values and alert systems
- Provide guidance for adequate collection of microbiology specimens
- Provide, revise, and publicize annual antibiogram
- Use cascade or selective reporting
- Perform testing for susceptibility to new drugs
- Broaden use of validated rapid diagnostic and rapid antimicrobial susceptibility testing

Clin Microbiol Rev. 2017;30:381-407.

Rapid Diagnostics

- Ability to identify organisms quickly
- Decrease diagnostic uncertainty
- To be effective, rapid diagnostics should be tied to an ASP
- Multiple rapid diagnostics available:
  - Multiplex PCR (bacterial and viral)
  - MALDI-TOF
  - Urinary antigens (*Legionella, S. pneumoniae*)

Selective Reporting

- Antibiotic sensitivity results are restricted
- Predefined antimicrobial susceptibilities are released based on the identified pathogen
- Usually broad-spectrum antimicrobials would be hidden
  - Results available, but must be requested
- Influences prescribing patterns
  - Encourages prescribers to utilize preferred, narrow-spectrum agents

Eur J Clin Microbiol Infect Dis. 2013;32(5):627-36.

Post ASP Implementation

- Initially, resistance, prescribing patterns, and cost savings will likely improve dramatically
- Improvements eventually stabilize
- Continued decreases in antibiotic use and cost should not be expected
- But, if programs are terminated, previous gains will begin to decline

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2014.

Infect Cont Hosp Epi. 2012;33(4):338-45.

Outpatient Antimicrobial Stewardship

- ~60% of U.S. antibiotic expenditures for humans are related to care received in outpatient settings
- ~20% of pediatric visits and ~10% of adult visits in outpatient settings result in an antibiotic prescription
- In 2011, approximately one third of *C. difficile* infections in the U.S.were community-associated infections

CDC. Core Elements of Outpatient Antibiotic Stewardship. 2016.

CDC. Core Elements of Outpatient Antibiotic Stewardship. 2016.

Outpatient Stewardship Interventions

Patient care segment	Opportunity for action	Rationale
Need to seek care	• Immunization programs • Patient education • Preventive medicine and wellness initiatives • Postdischarge bridge calls	• If a physician visit for an infection is avoided, then there is not a risk for an antibiotic to be prescribed.
Decision to prescribe antibiotics and agent selection	• Use of POC diagnostics ◦ Clinic use ◦ Pharmacy use • Prescriber audit and feedback ◦ Peer comparison • Prescriber education, behavioral intervention ◦ Practice updates ◦ Development of practice guidelines ◦ Prescribing tools ▪ Suggested alternatives ▪ Accountable justification • Development of regional and local antibiograms of outpatient isolates • Development of outpatient or practice formularies • Development of allergy assessment and penicillin skin testing program or referral	• Improve the selection of antibiotics
Dispensing of an antibiotic	• Pharmacist education ◦ Encourage prescriber inclusion of ICD-10 code or diagnosis and duration on the prescription to allow pharmacist verification of the appropriateness of the agent, dose, and duration	• Improve the appropriateness of antibiotic use
Post-encounter care	• Telephone follow-up 24–48 hours after the initial encounter ◦ Allow for better use of delayed prescribing ◦ Safety net regarding the decision not to use antibiotics or on the appropriateness and safety of the agent prescribed	• Decrease rates of antibiotic overuse • Improve patient safety

JAPhA. 2017. Article in Press.

Common Mishaps

- Rhinosinusitis
  - 98% are viral and antibiotics often do not help even when due to bacteria
- Common cold
  - Over 200 viruses can cause the common cold
- Pharyngitis
  - Only 5-10% are GAS (“strep throat”)
- Uncomplicated UTI
  - Should not treat in absence of symptoms
- Acute otitis media
  - Most common infection for pediatric antibiotic prescribing
  - Watchful waiting appropriate in many cases

cdc.gov/getsmart/community

The Role of the Outpatient Pharmacist

- Educate patients and parents about properly taking antibiotics and the potential harms of antibiotic use, including antibiotic resistance and adverse drug events
- Serve as the final healthcare provider to see a patient before an antibiotic is dispensed
- Provide guidance for symptom relief for common infections which do not require an antibiotic
- Promote available vaccines

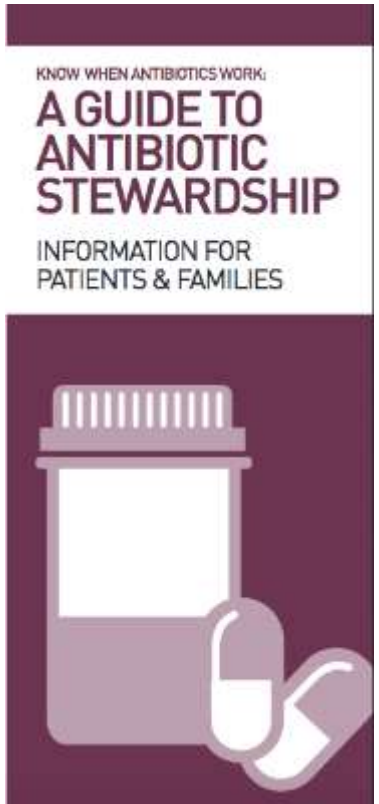
cdc.gov/getsmart/community

The Role of the Pharmacy Technician

- Identify recurring antimicrobial prescriptions for the same patient and inform the pharmacist
- Screen patient's for appropriate vaccinations
- Inquire about allergies to antimicrobials
- Assist with data collection and entry
- Update educational materials/website

Spread the Word – Educate the Masses

- Social media
  - Twitter, Facebook, etc.
- CDC Get Smart
- Patient and provider materials
- Engage, educate, and empower!



cdc.gov/getsmart/community

Antimicrobial Stewardship Resources

- CDC - Core Elements of Hospital ASPs
- CDC - Core Elements of Outpatient Antibiotic Stewardship
- IDSA guidelines – Implementing an ASP
- ASP training programs
  - SIDP
  - MAD-ID
- Institution specific ASPs or guidelines
  - Cleveland Clinic Foundation
  - John Hopkins Hospital
  - Nebraska Medical Center
  - University of California, San Francisco
- ECHO – Antimicrobial Stewardship (launched on 6/16/17)
  - http://echo.unm.edu/nm-teleecho-clinics/antimicrob/

Conclusions

- Antimicrobial resistance is a major problem and ASPs are a major part of the solution
- Learn the CDC core elements and understand how to employ them in your practice
- Question as many aspects of antimicrobial prescriptions as possible
- Utilize your resources, including other pharmacists and technicians
- Educate others – the more people are aware of the problem, the more people available to fix it

Thanks for your attention!

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