Preserving bacterial susceptibility Implementing Antimicrobial Stewardship Programs

Debra A. Goff, Pharm.D., FCCP

Clinical Associate Professor
Infectious Diseases Specialist
The Ohio State University Medical Center
Columbus, Ohio, USA

The Ohio State University Medical Center

Impact of Antibacterial Resistance

- Each year an estimated 1.7 million patients in U.S. hospitals acquire an infection resulting in **100,000** deaths[1]
- This results in an additional $6.5 billion in health care expenditures [2]

1. Klevens et al. *Public Health Rep.* 2007;122(2):160-166. 2. Stone et al. *Am J Inf Control*. 2005;33(9);542-547.

ESCAPE Pathogens

- ESCAPE: Describes the most critical drug resistant pathogens:
  - E = *Enterococcus faecium*
  - S = *Staphylococcus aureus*
  - C = *Clostridium difficile*
    A = *Acinetobacter baumannii*
  - P = *Pseudomonas aeruginosa*
  - E = *Enterobacteriaceae* (*E. coli* infection more numerous than *Klebsiella* and *Enterobacter* combined)

Peterson, LR. *Clin Inf Dis*. 2009;49;992.

Hospital and Societal Costs of Antimicrobial-Resistant Infections

organism	Mean cost (USD) per patients Health-care acquired
E VRE	$73,481
S MRSA	$60,984
A Acinetobacter resistant to amikacin or imipenem	$111,062
E Klebsiella or Ecoli resistant to quinolones or 3GC	$39,403

Roberts et al Clin Inf Dis 2009;49:1175-84.

Why have Antimicrobial Stewardship?

Antibiotics are unlike any other drugs in that use of the antibiotic in one patient can compromise its efficacy in another.

Anyone can prescribe antibiotics despite a lack of specialized training.

Unlike an antihypertensive agent, which benefits only the patient for whom it is prescribed, antimicrobials can impact countless others.

Resistant microorganisms can be spread to patients who have never received an antibiotic.

You can't "catch cancer" from the patient next to you.

You CAN catch drug-resistant microorganisms!

The Goal of Antimicrobial Stewardship Programs

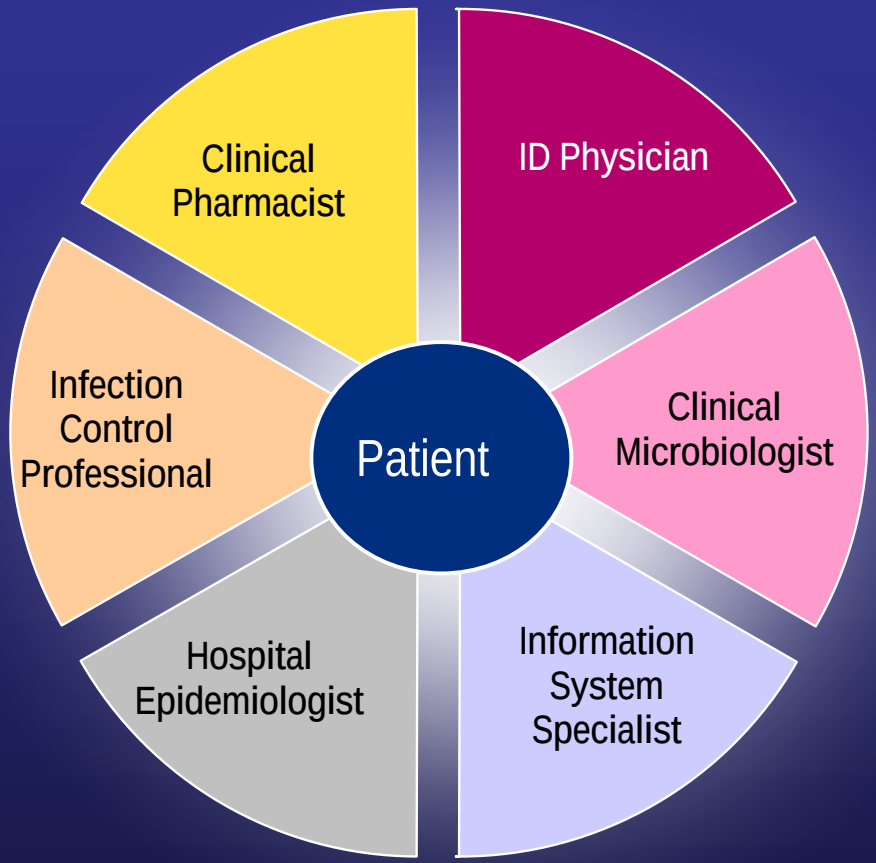
- To promote the appropriate use of antimicrobials[2,3]
  - The right selection, duration, dose, timing and route of administration
- To improve clinical outcomes[2]
  - By reducing the emergence of resistance
  - By limiting drug-related adverse events
  - By minimizing the risk of unintentional consequences
    - eg, *Clostridium difficile* infection

The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria.[1]

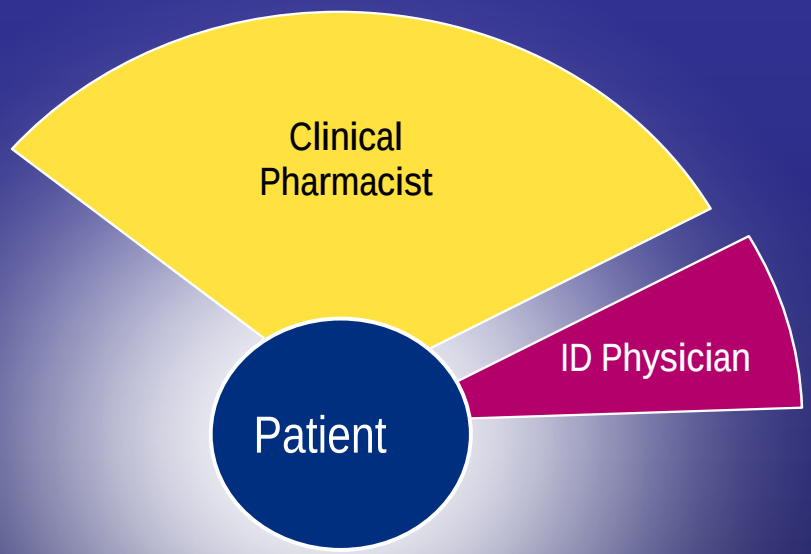
1. Dellit TH et al. *Clin Infect Dis*. 2007;44(2):159–77; 2. Drew RH. *J Manag Care Pharm*. 2009;15(2 Suppl):S18–23; 3. Drew RH et al. *Pharmacotherapy*. 2009;29(5):593–607

Antimicrobial Stewardship Team

Ideal versus Reality



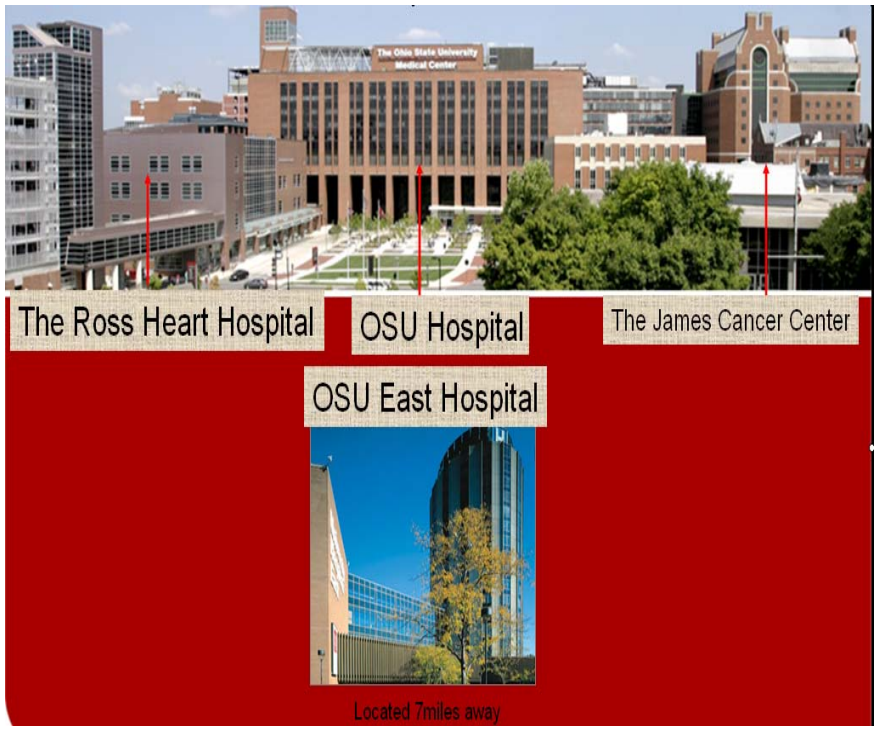
Optimal Team Members (A-III)[1]



Core Team Members (A-III)[1]

1. Dellit TH et al. *Clin Infect Dis* 2007;44(2):159-77.

OSU Antimicrobial Stewardship Program



ASP is a corporate commitment!

Tools to Get Started

- Practice Guidelines
  IDSA & Society for Healthcare Epidemiology of America publication
  Dellit TH et al. *Clin Infect Dis.* 2007; 44:159-77.
  Owens RC Jr. *Diagn Microbiol Infect Dis.* 2008; 61:110-28.
  Pagani L. *Clin Infect Dis* 2009:48;626-32

- Meet the other "team members" in your hospital
  Learn what they do and how they do it

Step 1: Develop an interdisciplinary team and define the roles and responsibilities of team members

Step 2: Select strategies by which to execute an antimicrobial stewardship program (ASP)

Step 3: Present results of ASP projects to the medical staff

Insights from ID Pharmacists on ASP guidelines

Patient safety in both medical literature and newspapers

antibiotics are the 2nd most common class of drugs to cause reactions

Reducing antibiotic purchases alone encourages the perception it's purely "cost-savings" rather than **quality improvement**

Size of ASP should meet hospital requirements

Before intervention, the **scope of authority** should be approved by administration

Drew et al. Pharmacotherapy 2009;29(5):593-607

Components of Antimicrobial Stewardship

- "Front End"—provided at the point of prescribing
  - Formulary Restriction and Preauthorization
  - Interactive decision support
  - Guidelines, order sets
  - Requires additional personnel (e.g. pharmacists)
- "Back End"—after the antimicrobial has been prescribed
  - Prospective Feedback Audit
  - Streamlining or de-escalation
  - Dose optimization
  - Parenteral to oral conversion
  - Requires additional personnel support (e.g. pharmacists)

How does an antimicrobial stewardship team actually work together?

The Epidemiologist and Infection Control

- Implement infection control measures[3]
- Gather data and monitor:[1]
  - -Process measures (eg, compliance with hand hygiene guidelines or timing of perioperative antibiotics)
  - -Patient outcomes (eg, rates of specific health care-associated infections)
- Use process and outcome measures to determine the impact of stewardship on antimicrobial use and resistance patterns[2]

- Investigate of local outbreaks of infection[2]

1. Coffin SE and Zaoutis TE. *Infect Dis Clin North Am*. 2005;19(3):647–65; 2. Dellit TH et al. *Clin Infect Dis*. 2007;44(2):159–77;
3. Paterson DL. *Clin Infect Dis*. 2006;42 Suppl 2:S90–5.

Soap-sniffing Technology Encourages Hand Washing To Reduce Hospital-acquired Infections, Save Money

ScienceDaily (June 5, 2009) — Call it a Breathalyzer for the hands. Using sensors capable of detecting drugs in breath, new technology developed at University of Florida monitors health-care workers' hand hygiene by detecting sanitizer or soap fumes given off from their hands.

Here's how it works.

1. The hospital workers squirt sanitizer gel before passing their hands under a wall-mounted sensor.
2. A wireless signal from a badge the worker is wearing activates a green light on the handwashing sensor.
3. When the worker approaches the patient's bedside, a monitor detects the status of the badge. Clean hands get a green light.
4. If the person has not washed, the badge will vibrate as a reminder to wash their hands again.

The Role of the Microbiologist

- Provides surveillance data on antimicrobial resistance[1] gathered through antibiograms[4]
  - -Assesses regional susceptibility
  - -Monitors trends over time
  - -Can be unit-specific or hospital-wide[2]

- Develops combination antibiograms[3]
  - -Used when there is a risk of resistant bacteria (eg, *P. aeruginosa*)
  - -Combination therapy against primary pathogen and resistant bacteria

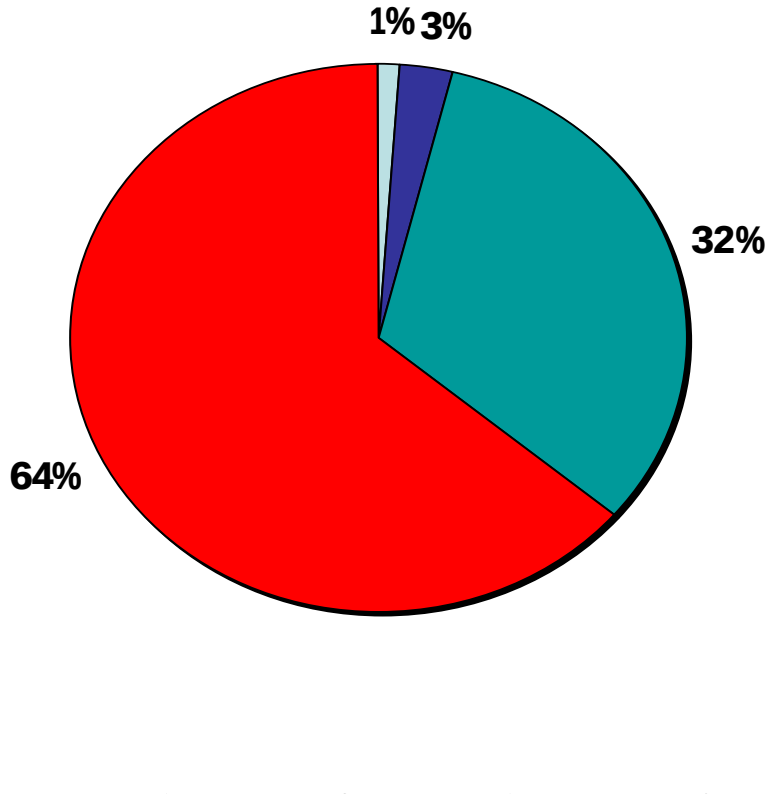
- Provides diagnostic testing to help make better antimicrobial choices[1]
  - -Rapid MRSA/SA testing (1hours)
  - -Hodge test to detect carbapenemases

1. Dellit TH et al. Clin Infect Dis. 2007; 44:159–77; 2. Kaufman D et al. *Arch Surg*. 1998;133(10):1041–5; 3. Mizuta M et al. *Infect Control Hosp Epidemiol*. 2006;27(4):413–5;
4. Stein CR et al. *Emerg Infect Dis*. 2003;9(2):211–6.

Local antibiograms should help ASP direct the empiric use of antibimicrobials

Do MD's Use Hospital Antibiograms?

Online survey of 545 residents at a University Teaching Hospital



- How data is communicated to the medical staff is critical

Mermel et al. *Clin Inf Dis.* 2008:46;1789.

Hospital-wide Antibiogram

% susceptiblity to antimicrobials

	Pip/tazo	Cefepime	Imipenem	Cipro	Tobramycin
K. pneumoniae **(954)**	**91**	**95**	**99**	**88**	**92**
E. cloacae **(287)**	**79**	**95**	**95**	**92**	**91**
E. coli **(1971)**	**96**	**99**	**99**	**98**	**98**
P. aeruginosa **(1039)**	**87**	**70**	**81**	**70**	**89**
A. baumannii **(121)**	**91**	**80**	**100**	**70**	**85**

ICU Antibiogram
First isolates only 1999

	Pip/tazo	Cefepime	Imipenem	Cipro	Tobramycin
K. pneumoniae (32)	66	71	100	63	63
E. cloacae (13)	77	77	92	77	69
E. coli (16)	94	94	94	100	94
P. aeruginosa (37)	81	59	70	78	95
A. baumannii (21)	86	14	86	52	19

ASP Management of complicated intra-abdominal infections

- *E. coli* is the most frequently cultured organism in cIAI
- Reviewed the antibiogram

  Ertapenem was selected for surgical patients with community-acquired cIAI

GRAM NEGATIVE RODS: ENTERICS						
	# isolates	Ampicillin/ Sulbactam	Piperacillin/ Tazobactam	Cefazolin	Cefepime	Imipenem (a)
MIC breakpoints (µg/ml)		≤8/4	≤16/4	≤8	≤8	≤4
Escherichia coli	1600	45	95	86	100	100
Escherichia coli-ESBL	36 (a)					100

Evidence-Based

Surgical Use of Ertapenem

- Ertapenem is FDA-approved for:
  - Complicated intra-abdominal infections (cIAI)

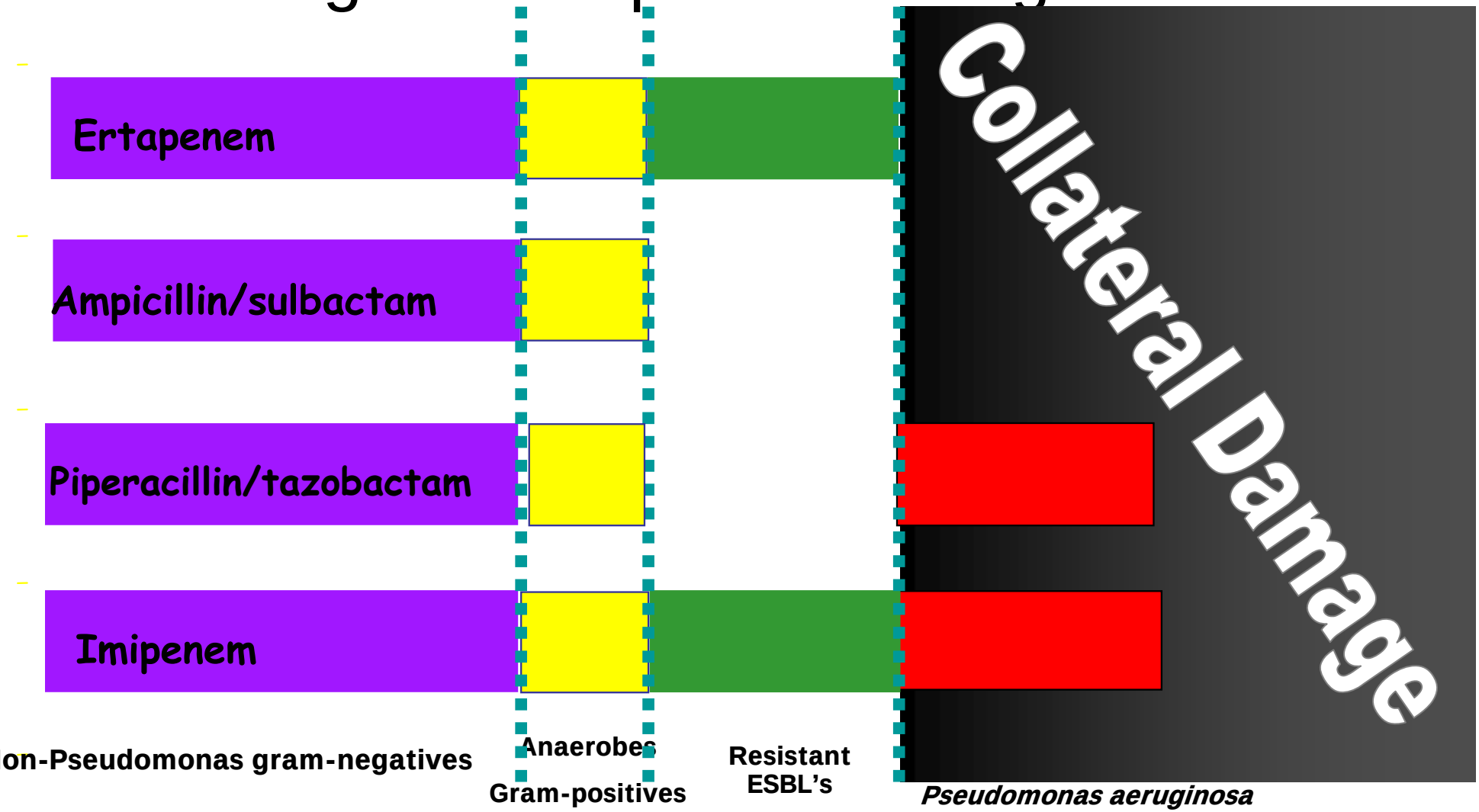
    Ertapenem 1 g daily vs. piperacillin/tazobactam 3.375 g every 6 hr

    665 patients with perforated/abscessed appendicitis, colonic, small intestine, or biliary infections, and generalized peritonitis

    Success rates: ertapenem 83.6% vs. 80.4% pip/tazo

    Solomkin JS et al. *Ann Surg.* 2003; 237:235-45.

Targeted Empiric Coverage



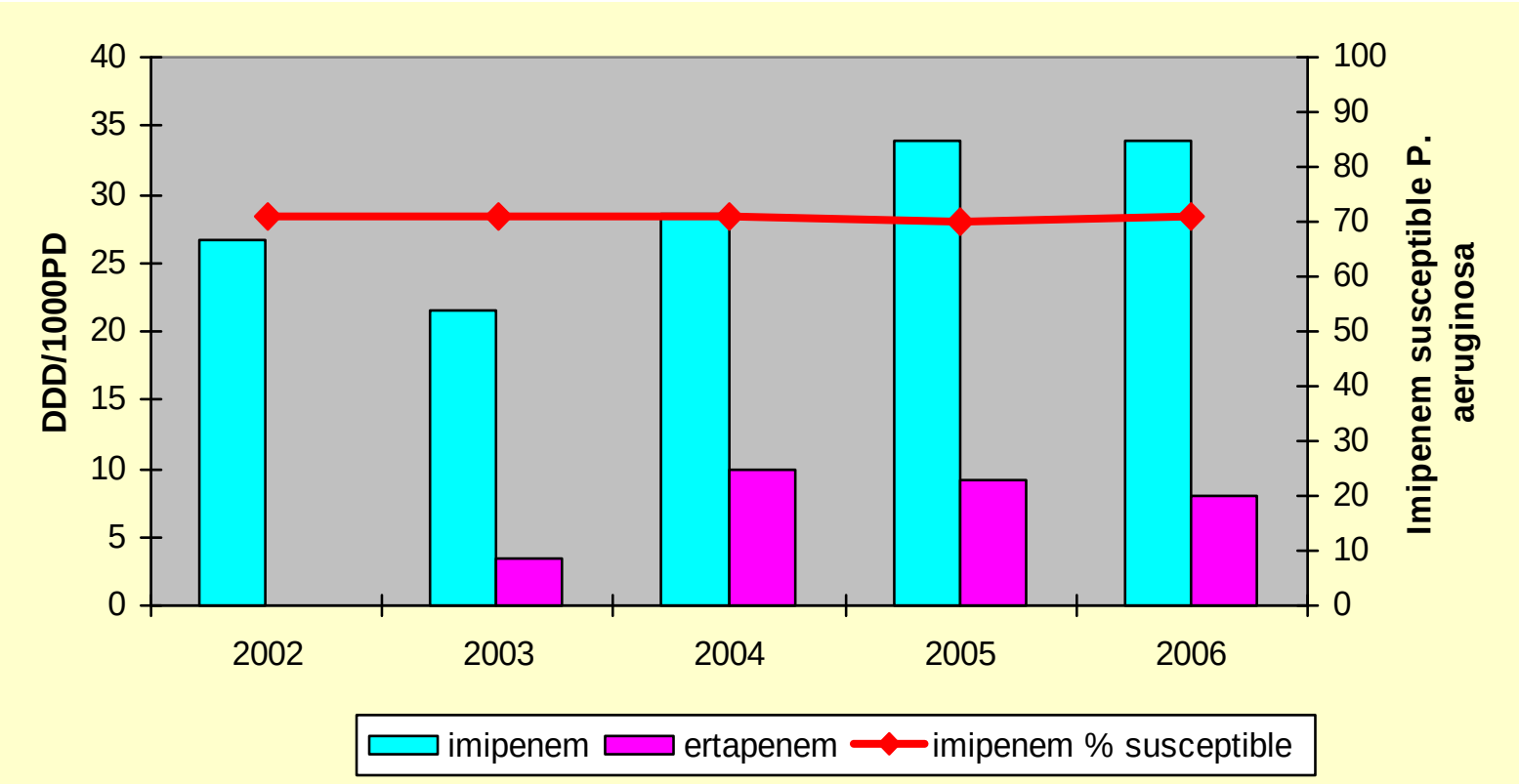
Empiric coverage

Study of Susceptibility of Gram-negative Pathogens After 4 Years with Ertapenem on Formulary

- Design
  - In vitro surveillance study
- Setting
  - Ohio State University Medical Center, Columbus, Ohio
- Methods
  - In vitro susceptibilities of gram-negative aerobes determined by Etest (ertapenem), or microdilution MICs for imipenem, piperacillin/tazobactam, cefepime, and tobramycin
- Primary endpoint
  - Effect of ertapenem on imipenem susceptibility to *P. aeruginosa*

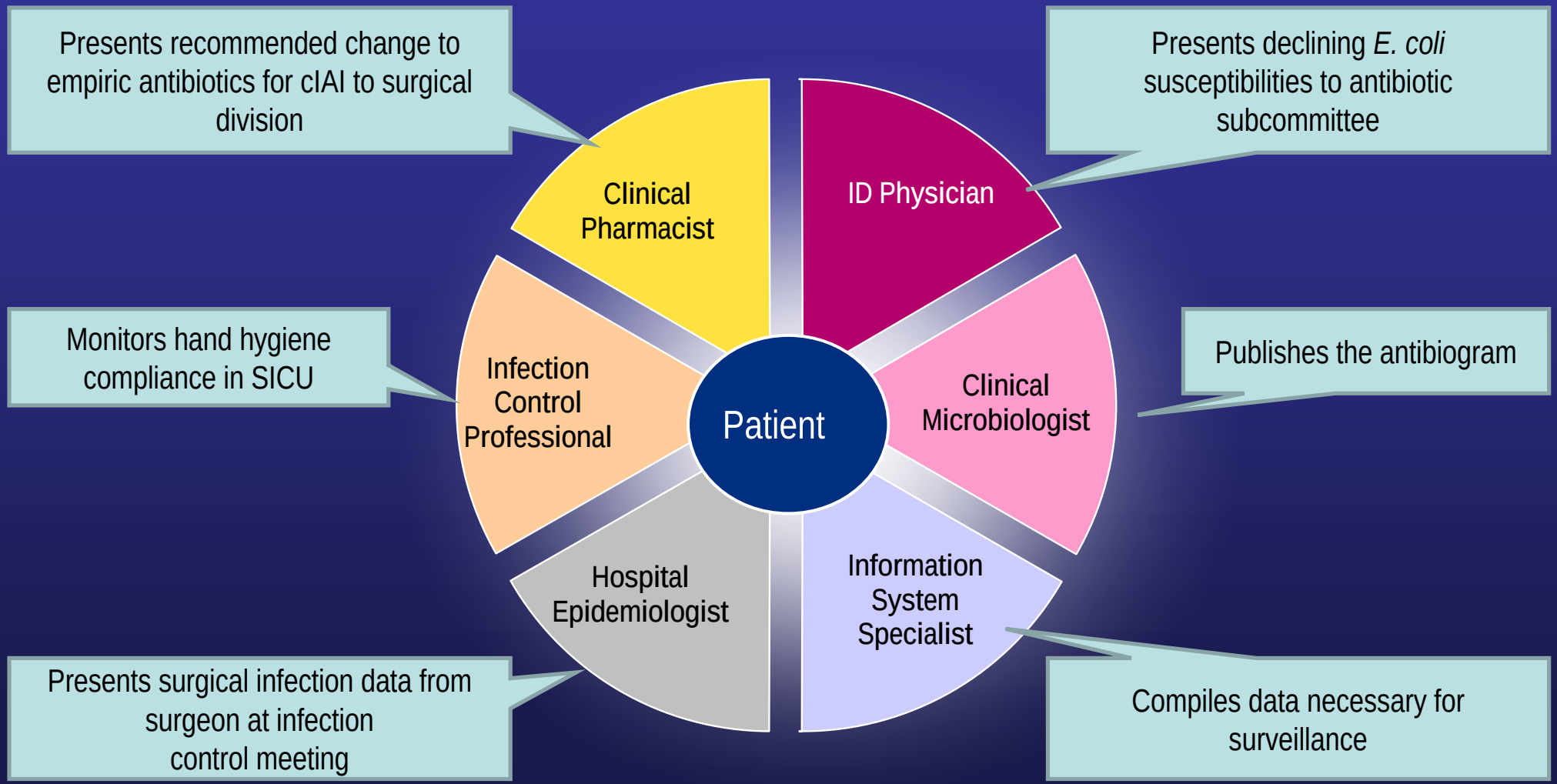
Goff DA, Mangino JE. *J Infection.* 2008;57:123-127.

Ertapenem: No Effect on aerobic Gram-Negative susceptibilities to imipenem



Ref: Goff D, Mangino J Inf 2008 57:123-7.

Example: ASP Team Approach to Complicated Intra-abdominal Infections



Study of Susceptibility of Aerobic Gram-negative Rods After 3 Years on Formulary

Design	Retrospective analysis of hospital susceptibility data from June 2002 to December
Setting	344-bed community teaching hospital in Santa Monica, California, US
Methods	In vitro susceptibilities of gram-negative rods to formulary antibiotics determined
Primary endpoint	Susceptibility of gram-negative rods to imipenem, ertapenem, levofloxacin, cefepime, gentamicin, and piperacillin/tazobactam

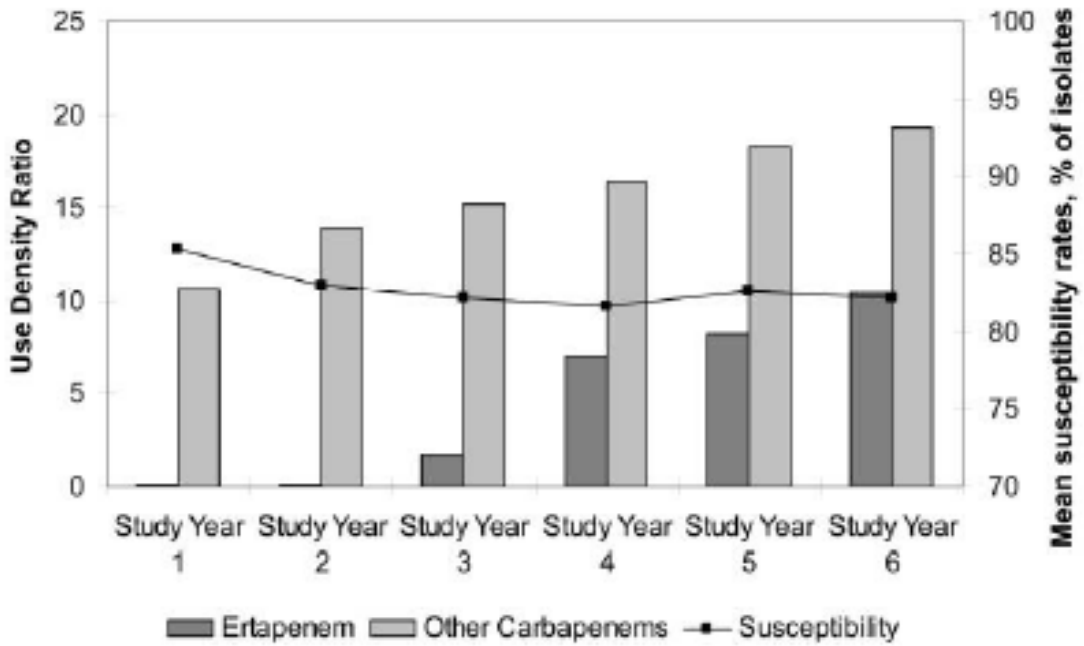
Goldstein EJ, et al. *Antimicrob Agents Chemother*. 2009;53:5122-5126.

Results

	Month	Susceptibility *P. aeruginosa* Imipenem (%)				
		Min	**Max**	**Mean**	**Median**	**Standard Error**
Before Ertapenem added	0-9	60.00	81.00	70.00	**69.0**	2.69
After Ertapenem was added, Before the substitution	10-20	63.00	91.00	77.00	77.00	2.90
After the substitution	21-48	67.00	100.00	87.86	**89.0**	1.62

Goldstein EJ, et al. *Antimicrob Agents Chemother.* 2009;53:5122-5126.

Absence of Association between use of Ertapenem and Change in Antipseudomonal Carbapenem Susceptibility rates in 25 Hospitals



Ref Eagye K., Nicolau D. Infect Control Hosp Epidemiol 2010;31(5);485-90

New diagnostic tests should be incorporated in ASP planning

Clinical and Economic Impact of rapid PCR blood culture test for detection of SA/MRSA in patients with SAB

- **Objective**: Evaluate the clinical & economic impact of the rapid PCR MRSA/SA blood culture test with interventions by ID pharmacists

- **Method**: A comparative study of hospitalized patients with SAB before and after PCR blood culture test implementation.

  Evaluate
  the difference in time from blood culture draw to optimal anti-staphylococcal therapy (OAT) for SAB,
  hospital length of stay (LOS),
  mortality,
  cost of care pre and post introduction of rapid PCR MRSA/SA BC

Ref: Bauer K, Goff DA Clin Inf Dis 2010; 51(9):1074–1080

Findings

The rapid PCR MRSA/SA BC test decreased the time to OAT after time of blood culture draw in MSSA bacteremia (p=0.002) by **1.6 days.**

The rapid differentiation of MSSA and MRSA in blood cultures enables faster switch to OAT

- Mean hospital costs were reduced by $21,287 in the post-PCR test group (p=0.02)
- ICU cost were $9,930 less in the post-PCR test group (p=0.03)

Communication by the microbiology tech of the PCR MRSA/SA BC test result to the ID PharmD resulted in earlier OAT that was associated with a decreased LOS and costs.

Measuring Success[1]

- Reduced:
  - Antimicrobial resistance
  - Hospital cost
  - Use of nontargeted antimicrobials
- Improved clinical outcomes
  - Decreased length of hospital stay
  - Reduced adverse events
  - Decreased length of antibiotic treatment

1. Dellit TH et al. *Clin Infect Dis*. 2007;44(2):159–77

Conclusion

- ASP can make a difference in patient care
- Each team member provides unique talents
- Escalating rates of antimicrobial resistance and lack of new antimicrobials, creates an urgent need for ASP in hospitals