Overview of Antimicrobial Stewardship

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Disclosures

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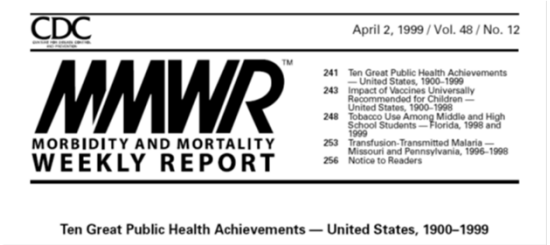
- **No other financial or other disclosures or conflicts of interest**

Objectives

- **Review the basics of antimicrobial resistance in the context of antimicrobial stewardship**
- **Outline an overview of antimicrobial stewardship principles and discuss measures to avoid development of antimicrobial resistance**
- **Discuss examples of antimicrobial stewardship interventions and tools for clinicians**


CDC

April 2, 1999 / Vol. 48 / No. 12

MMWR™

MORBIDITY AND MORTALITY WEEKLY REPORT

Ten Great Public Health Achievements — United States, 1900–1999

Ten Great Public Health Achievements — United States, 1900–1999

- Vaccination
- Motor-vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary heart disease and stroke
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard

- **Control of infectious diseases** has resulted from clean water and improved sanitation. Infections such as typhoid and cholera transmitted by contaminated water, a major cause of illness and death early in the 20th century, have been reduced dramatically by improved sanitation. In addition, the discovery of antimicrobial therapy has been critical to successful public health efforts to control infections such as tuberculosis and sexually transmitted diseases (STDs).

***MMWR* 1999;48:241-242**

Time Magazine—Feb 25, 1966

- **"Nearly all experts agree that (by the year 2000) bacterial and viral diseases will have been wiped out. Probably arteriosclerotic heart disease will also have been eliminated."**

Critical Impact of Antimicrobial Resistance

"If we do not act to address the problem of AR, we may lose quick and reliable treatment of infections that have been a manageable problem in the United States since the 1940s. Drug choices for the treatment of common infections will become increasingly limited and expensive - and, in some cases, nonexistent."

-A Public Health Action Plan to Combat Antimicrobial Resistance; Centers for Disease Control and Prevention

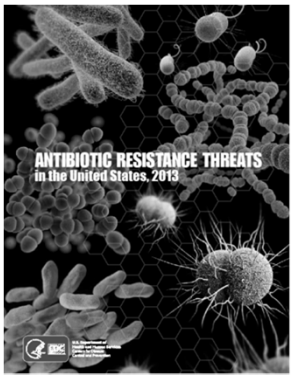
World Economic Forum

- **"…arguably the greatest risk…. to human health comes in the form of antibiotic resistant bacteria. We live in a bacterial world where we will never be able to stay ahead of the mutation curve. A test of our resilience is how far behind the curve we will allow ourselves to fall."**

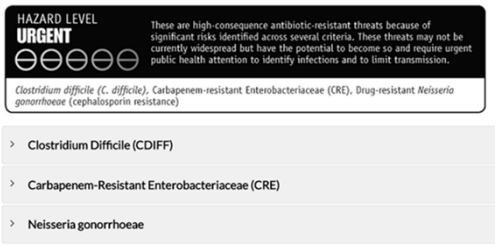
Howell L editor. Global Risks 2013, Eighth edition: an initiative of the Risk Response Network. World Economic Forum 2013

Perspective

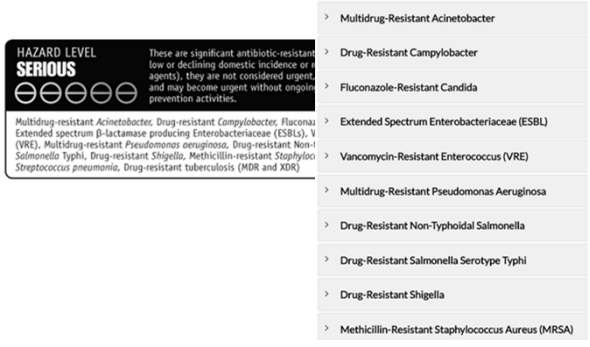
- **In order to appreciate the urgent need for antimicrobial stewardship it is critical to understand the climate of escalating drug resistance.**
- **The increasing degree of resistance has the potential to evolve into a highly critical public health issue.**



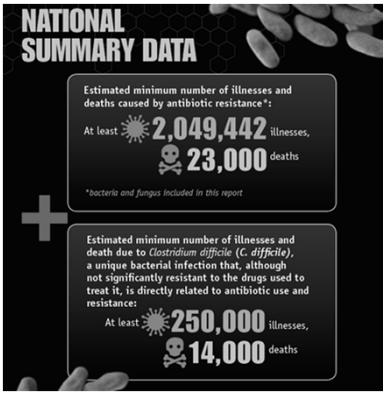
https://www.cdc.gov/drugresistance/threat-report-2013/index.html



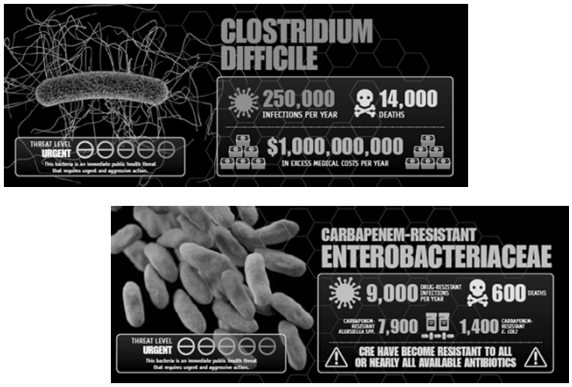
CDC Antibiotic Resistance Threats 2013



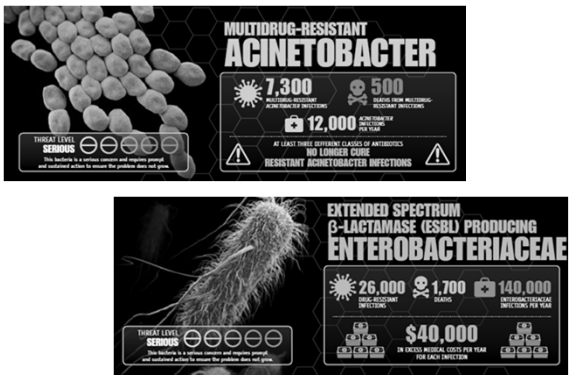
CDC Antibiotic Resistance Threats 2013



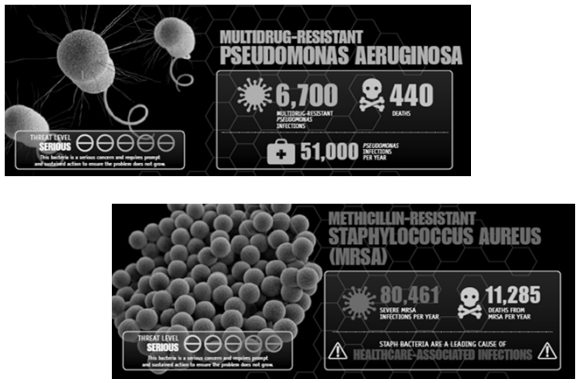
CDC Antibiotic Resistance Threats 2013



CDC Antibiotic Resistance Threats 2013

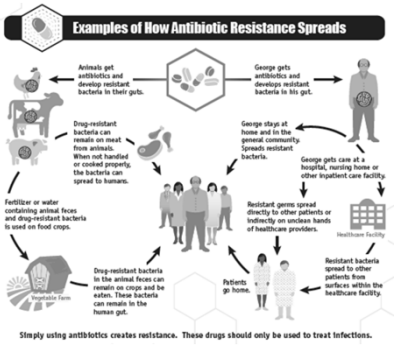


CDC Antibiotic Resistance Threats 2013



CDC Antibiotic Resistance Threats 2013

CDC Antibiotic Resistance Threats 2013



ONE HEALTH CONCEPT:
Humans
Animals
Environment

CDC Antibiotic Resistance Threats 2013

Antimicrobial Overuse

- **200-300 million antibiotic prescriptions annually**
  - **45% outpatient**
- **25-40% of hospitalized patients receive antibiotics**
  - **10-70% are unnecessary or sub-optimal**
  - **5% of hospitalized patients who receive antibiotics experience an adverse reaction**
- **Changes in antibiotic use are paralleled by changes in resistance patterns**
- **Antibiotics are unlike any other agent in that use in one patient can compromise efficacy in another**

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

WHO Strategies

- **Commit to a comprehensive, financed national plan with accountability and civil society engagement**
- **Strengthen surveillance and laboratory capacity**
- **Ensure uninterrupted access to essential medicines of assured quality**
- **Regulate and promote rational use of medicines, including in animal husbandry, and ensure proper patient care**
- **Enhance infection prevention and control**
- **Foster innovations and research and development for new tools**

http://www.who.int/mediacentre/news/releases/2011/whd_20110406/en/

Antimicrobial Stewardship (ASP)

"Antimicrobial stewardship includes not only limiting inappropriate use but also optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection while limiting the unintended consequences, such as the emergence of resistance, adverse drug events, and cost."

Clin Infect Dis 2007;44:159-177.

CDC Core Elements

- **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.

www.cdc.gov/antibiotic-use/community/pdfs/16_268900-A_CoreElementsOutpatient_check_2_508.pdf

Centers for Medicare & Medicaid Services

- **Moving towards ASP as a condition for participation by the end of 2019??**
- **Prior draft Infection Control Survey includes ASP requirements:**
  - **ASP policies & procedures**
  - **Designated leader for ASP**
  - **Indication in medical record for all antimicrobial use**
  - **Antibiotic time out**
  - **Monitor antibiotic use at the unit and/or hospital level**

Joint Commission

- **June 2, 2015, JC announced its commitment to increase efforts in promoting ASP**
- **Standard for Antimicrobial Stewardship effective January 1, 2017**
  - **Standard MM.09.01.01**
    - **Eight elements of performance**

Joint Commission

Element of Performance	Text
MM.09.01.01, EP 1	Leaders establish ASP as an organizational priority
MM.09.01.01, EP 2	Educate staff and providers upon hire & periodically thereafter
MM.09.01.01, EP 3	Educate patients and families on appropriate antibiotic use
MM.09.01.01, EP 4	Multidisciplinary ASP team of MDs, ICPs, PharmDs*
MM.09.01.01, EP 5	ASP core elements present**
MM.09.01.01, EP 6	ASP uses multidisciplinary protocols, guidelines, etc.
MM.09.01.01, EP 7	Collect & analyze data on antibiotic prescribing & resistance
MM.09.01.01, EP 8	Take action on improvement opportunities

***Consultant staff are acceptable as members of the ASP team**
****Core elements include drug expertise, tracking, reporting, etc.**

https://www.jointcommission.org/topics/hai_antimicrobial_stewardship.aspx

National ASP Guidelines

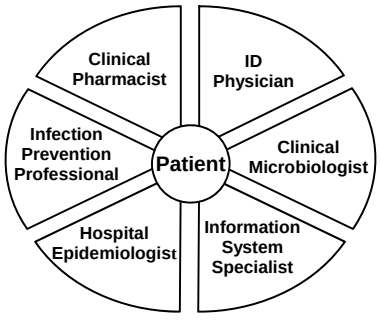
Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

[1]Harborview Medical Center and the University of Washington, Seattle; [2]Maine Medical Center, Portland; [3]Emory University, Atlanta, Georgia; [4]Hines Veterans Affairs Hospital and Loyola University Stritch School of Medicine, Hines, and [5]Stroger (Cook County) Hospital and Rush University Medical Center, Chicago, Illinois; [6]University of Utah, Salt Lake City; [7]Mayo Clinic College of Medicine, Rochester, Minnesota; [8]University of Pittsburgh Medical Center, Pittsburgh, and [9]University of Pennsylvania, Philadelphia, Pennsylvania; [10]William Beaumont Hospital, Royal Oak, Michigan; [11]Ochsner Health System, New Orleans, Louisiana; and [12]University of Miami, Miami, Florida

***Clin Infect Dis* 2007; 44:159–77.**

ASP Core Membership



Dellit TH et al. *Clin Infect Dis*. 2007;44:159-177.
Drew RH. *J Manag Care Pharm*. 2009;15:S18-23..

Components of Antimicrobial Management

- **"Front End"—provided at the point of prescribing**
  - **Formulary Restriction and Preauthorization**
  - **Interactive decision support**
  - **Guidelines, order sets**
  - **Requires additional IT support and 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)**

Diagnostic Stewardship

- **World Health Organization developed a sequence of steps in using the clinical microbiology laboratory and appropriate de-escalation of antibiotics.**
  - **Step One: patient presents at healthcare facility and is assessed by clinician with preliminary diagnosis**

Targeted ASP Interventions-Step 1

- **Develop standardized treatment protocols/clinical practice guidelines for empiric management of common infections**
  - **Community acquired pneumonia**
  - **Urinary tract infections/pyelonephritis**
  - **Skin and wound infections**
  - **Clinical sepsis**
  - **Intra-abdominal infections**
- **Develop guidance on appropriate cultures prior to starting antimicrobials based on clinical practice guidelines**
- **Train providers and lab personnel on the proper collection, timing, and processing of clinical specimens**

Diagnostic Stewardship

- **World Health Organization developed a sequence of steps in using the clinical microbiology laboratory and appropriate de-escalation of antibiotics.**
  - **Step Two: appropriate cultures are obtained and empiric antibiotics are started based on preliminary diagnosis**

Targeted ASP Interventions-Step 2

- **Assurance of appropriate cultures prior to starting antimicrobials**
- **Start broader spectrum empiric antimicrobials based on suspected clinical infection and associated organism**
- **Review of local antibiograms and antimicrobial susceptibility profiles based on institution cultures**
  - **Adjust empiric treatment recommendations**
  - **Assist with formulary selection**
- **Education of clinicians on empiric management**

Diagnostic Stewardship

- **World Health Organization developed a sequence of steps in using the clinical microbiology laboratory and appropriate de-escalation of antibiotics.**
  - **Step Three: clinical microbiology laboratory completes cultures of clinical specimens and forwards results to clinician who then modifies antibiotics accordingly**

Targeted ASP Interventions-Step 3

- **De-escalation of therapy based on culture results.**
- **Educate on the basic principles of antimicrobial stewardship—"culture-driven prescribing":**
  - **Assess patient**
  - **Preliminary diagnosis**
  - **Obtain appropriate cultures**
  - **Start empiric antibiotics**
  - **Modify antibiotics based on culture results**
- **Develop guidance on duration of therapy**

Summary of principles of antimicrobial use

- **Correct choice**
- **Correct dosage**
- **Source control (e.g., surgical drainage)**
- **Thought process**
  - **Thorough history and physical examination**
  - **Exposure history, travel history, animal or insect exposure**
  - **Community vs Healthcare associated**
  - **Obtain cultures**
  - **Empiric choice**
  - **Streamline therapy: culture results, clinical course**

Antimicrobial Stewardship (ASP)

- **Optimize clinical outcomes**
  - **Limit inappropriate antimicrobial utilization**
  - **Optimize antimicrobial selection, dosing, route and duration of therapy**
- **Limit unintended consequences**
  - **Antimicrobial resistance**
  - **Adverse drug events**
  - **Cost**

***Clin Infect Dis* 2007;44:159-177.**
Pharmacotherapy 2009;29:593-607.

Antimicrobial Data Mart

"What gets measured gets managed, and what gets managed gets done."

- Peter Drucker

- **Partnership with Ohio State University Wexner Medical Center Information Warehouse**
- **Collation of antimicrobial data since the launch of EPIC electronic medical record**
- **Allows for the calculation of antimicrobial days adjusted for the census**
- **Data can be stratified by unit or service**

CDC Antibiotic Resistance Threats 2013

Updated National ASP Guidelines

Clinical Infectious Diseases
IDSA GUIDELINE

IDSA Infectious Diseases Society of America | hivma

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 R. Seo,[21] and Kavita K. Trivedi[22]

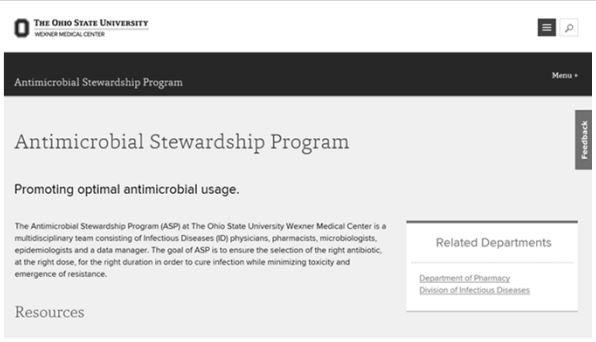
[1]Section of Infectious Diseases, Boston University School of Medicine, Boston, Massachusetts; [2]Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland; [3]Division of Infectious Diseases, University of Miami Miller School of Medicine, Miami, Florida; [4]Department of Clinical Pharmacy, School of Pharmacy, University of California, San Francisco; [5]Department of Medicine, Weill Cornell Medical Center/New York–Presbyterian Hospital, New York, New York; [6]Department of Internal Medicine, Texas A&M Health Science Center College of Medicine, Houston; [7]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; [8]Division of Allergy and Infectious Diseases, University of Washington School of Medicine, Seattle; [9]Department of Medicine, Case Western Reserve University and Veterans Affairs Medical Center, Cleveland, Ohio; [10]Department of Medicine, University of Pennsylvania Health System, Philadelphia; [11]Hamilton House, Virginia Beach, Virginia; [12]Division of Infectious Diseases, Denver Health, Denver, Colorado; [13]Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University Schools of Medicine and Nursing, Baltimore, Maryland; [14]Division of Infectious Diseases, University of Michigan Health System, Ann Arbor; [15]Department of Emergency Medicine, University of California, Davis; [16]Department of Emergency Medicine, David Geffen School of Medicine, University of California, Los Angeles Medical Center, Sylmar; [17]Department of Veterans Affairs, Hines, Illinois; [18]Department of Pediatrics, Washington University School of Medicine at St Louis, Missouri; [19]Section on Infectious Diseases, Wake Forest University School of Medicine, Winston-Salem, North Carolina; [20]Department of Veterans Affairs and University of Utah, Salt Lake City; [21]Infectious Diseases, Memorial Sloan Kettering Cancer Center, New York, New York; and [22]Trivedi Consults, LLC, Berkeley, California

Evidence-based guidelines for implementation and measurement of antibiotic stewardship interventions in inpatient populations including long-term care were prepared by a multidisciplinary expert panel of the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. The panel included clinicians and investigators representing internal medicine, emergency medicine, microbiology, critical care, surgery, epidemiology, pharmacy, and adult and pediatric infectious diseases specialties. These recommendations address the best approaches for antibiotic stewardship programs to influence the optimal use of antibiotics.

Keywords. antibiotic stewardship; antibiotic stewardship programs; antibiotics; implementation.

Clin Infect Dis **2016;62:e51-e77.**

Ohio State University Wexner Medical Center ASP Website



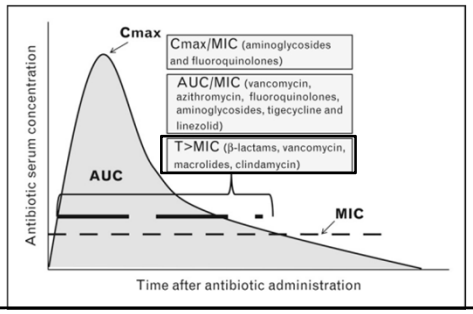
Electronic tool readily and always available to our clinicians

ASP Website Tools

- **Antibiograms**
  - **Guide for empiric therapy by organism**
  - **Multiple types at Ohio State University Wexner Medical Center**
    - **Hospital-wide**
    - **ICU-specific**
    - **Combination**
    - **Fungal**
- **Infection by Site Grid-empiric antibiotic selection**
- **Antimicrobial Guides**
  - **Detailed monographs on each antibiotics on our formulary**
  - **Dosing guidance—*Example of extended infusions of selected agents***

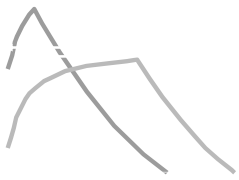
β-lactam Pharmacodynamics

- **Knowledge of pharmacodynamics killing activity of antibiotics can provide guidance for best dosing strategies**
- **Time-dependent killing**
  - **Duration of time drug level exceeds MIC relative to dosing interval**



Optimizing β-lactam Therapy-
Maximizing Percent T>MIC

- **Increased duration of infusion**
  - **Same dose and dosing interval, 100-250ml, however, change duration of infusion (0.5 hr → 3-4hr)**



Cefepime Extended Infusion
Ohio State University Wexner Medical Center Experience: PSA PNA and/or Bacteremia

	Intermittent infusion *n* = 54	Extended infusion *n* = 33	P-value
Mortality	11 (20)	1 (3)	0.03
LOS			
Hospital	14.5 (6–30)	11 (7–20)	0.36
Infection related	12 (6–21)	10 (6–16)	0.45
ICU	18.5 (5.5–32.5)	8 (4–20)	0.04
Duration (days) of mechanical ventilation	14.5 (5–30)	10.5 (8–18)	0.42
Cost (US$)			
Total hospital costs	51,231 (17,558–107,031)	28,048 (13,866–68,991)	0.13
Infection-related hospital costs	15,322 (8,343–27,337)	13,736 (10,800–23,312)	0.78

Bauer KA et al. *Antimicrob Agents Chemother* 2013;57(7):2907-12.
http://aac.asm.org/content/57/7/2907/T2.expansion.html

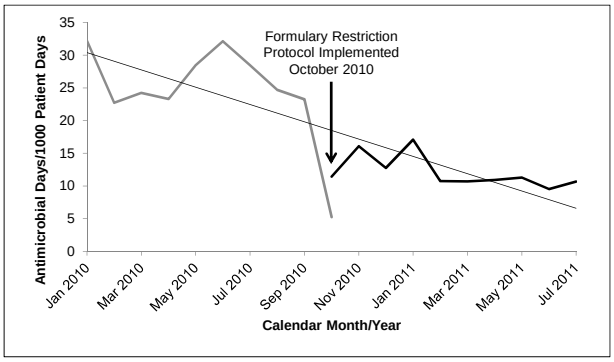
Other ASP Website Tools

- **Pre-operative Antibiotics order Grid**
- **Antimicrobial Formulary**
  - **List of formulary antibiotics, antifungals, antivirals, and HIV drugs**
- **Antimicrobial Duration of Therapy Guide**
  - **Recommendations for appropriate duration of therapy by indication**
- **Evidence Based Practice Guides**
  - **Candidemia**
  - ***C. difficile* Infection (CDI)**
  - **Febrile Neutropenia**
  - **Fecal Microbiota Transplant for CDI**
  - **Community Acquired Pneumonia**
  - ***S. aureus* Bacteremia**
  - **UTI Prevention, Diagnosis and Management**

Restricted Antimicrobials

- **To ensure appropriate utilization due to cost, toxicity or concern for resistance development with overutilization**
- **Require prior authorization 8am-5pm, 7 days/week**
  - **-OR- obtain Infectious Diseases consultation**
- **Approval code must be entered in the order question in electronic medical record**
- **After hours orders should be dispensed as written at an appropriate dose and interval**
  - **Reviewed the following business day**

Anti-Pseudomonal Carbapenem Restriction

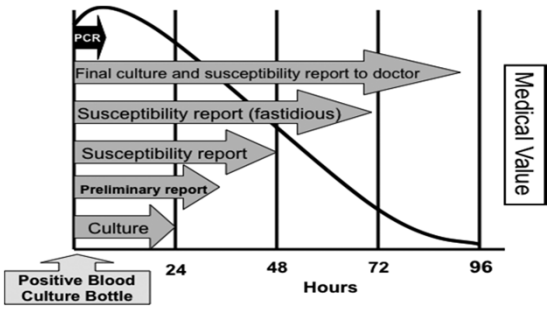


Reed EE, et al. *Virulence* 2013;4(2):1-5.

Antibiotic Time Out

- **The goal is to be performed on every patient, every day to ensure that agents no longer needed based on cultures, clinical condition or completion of therapy are discontinued**
- **Antibiotic Time Out Questions**
  - ***What is the indication for this drug?***
  - ***What is the appropriate dose for the patient?***
  - ***What is the planned duration of treatment?***
- **Noted in the daily progress note and the actions taken**
- **Templated notes in electronic medical record**

Microbiology Timeline



Goff DA, et al. *Pharmacotherapy* 2012;32(8):677-687.

ASP Rapid Diagnostic Interventions

- **Antimicrobial therapy**
  - **Initiate another agent**
  - **De-escalate therapy**
  - **IV to PO conversion**
  - **Duration of therapy**
- **Other interventions**
  - **Source control**
  - **Repeat blood cultures**
  - **Laboratory monitoring/imaging**
  - **ID consultation**
- ***C. difficile* management**

Rapid Diagnostics at Ohio State University Wexner Medical Center

- **New advances in rapid diagnostic testing (RDT) provide collaborative opportunities for ASP**
- **Enhance functions of clinical microbiology labs**
  - **Accurate & timely organism identification & antimicrobial susceptibilities**
- **Benefit patients and increase effectiveness of ASP**
- **RDT examples at Ohio State University Wexner Medical Center**
  - **Verigene® Gram-positive and Gram-negative blood culture test (BC-GP and BC-GN)**
  - **Xpert® *C. difficile***
  - **MALDI-TOF**

Impact of ASP Implementation of RDT

An Antimicrobial Stewardship Program's Impact with Rapid Polymerase Chain Reaction Methicillin-Resistant *Staphylococcus aureus*/*S. aureus* Blood Culture Test in Patients with *S. aureus* Bacteremia

Kerri A. Bauer,[1] Jessica E. West,[1] Joan-Miquel Balada-Llasat,[2] Preeti Pancholi,[2] Kurt B. Stevenson,[3] and Debra A. Goff[1]

Departments of [1]Pharmacy and [2]Pathology, The Ohio State University Medical Center, [3]Division of Infectious Diseases, College of Medicine, The Ohio State University, Columbus, Ohio

Figure 1. Time to antibiotic switch

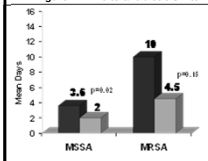


Figure 2. Length of stay

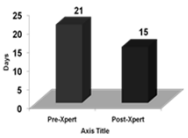


Figure 3. Mean hospital costs

Bauer K, et al. *Clin Infect Dis* 2010;51:1074-1080.

MALDI-TOF

- **Matrix Assisted Laser Desorption/Ionization - Time of Flight**
- **Rapid, precise, and cost-effective**
- **Allows identification of organisms directly from samples (blood & respiratory cultures)**
- **Sample converted into charged particles which are separated to produce a molecular "signature" for the organism**
- **Simultaneously screens a multitude of molecules to determine the identify of the organism by analyzing the mass-to-charge ratio**

MALDI-TOF at Ohio State University Wexner Medical Center

- **Performed on all positive blood & respiratory cultures**
  - **Issues with polymicrobial specimens**
- **Results available within a few hours of microbial growth 7 days/week**
  - **Reports emailed twice daily**
  - **Reviewed by ASP on weekdays**
  - **Initiate or de-escalate therapy faster**
- **Traditional methods (e.g., Microscan®, E test) still used for susceptibility testing**

Impact of MALDI-TOF at Ohio State University Wexner Medical Center

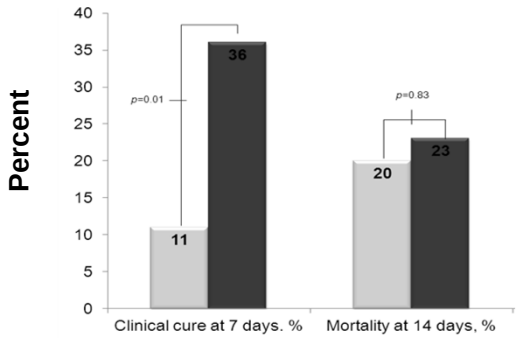
***A. baumannii* bacteremia and/or pneumonia**

Group	Time to effective therapy, hours	95% CI	*P*-value
Pre-Intervention	77.7	73.1 - 84.8	<0.001
Intervention	36.6	25.9 - 50.9	

Wenzler E et al. *Diagn Micr Infect Dis* 2016 Jan;84(1):63-8.

Impact of MALDI-TOF at Ohio State University Wexner Medical Center

***A. baumannii* bacteremia and/or pneumonia**



Wenzler E et al. *Diagn Micr Infect Dis* 2016 Jan;84(1):63-8.

Candidemia

- **Delay in time to effective therapy significantly increases risk of mortality**
  - **Mortality up to 50%**
  - **Caspofungin should be initiated when yeast seen on Gram stain or sooner if high clinical suspicion**
- **MALDI-TOF assists in rapid species identification**
  - **Susceptibilities determined by traditional methods**
- **Yeast in blood is NEVER a contaminant**

ASP Impact on Candidemia Management

Variable/Outcome	Pre-Intervention (n = 85)	Post-Intervention (n = 88)	P-value
Time to effective antifungal therapy, hours	13.5 [2-25.9]	1.3 [0-3.2]	0.04
Effective antifungal therapy	67 (88%)	80 (99%)	0.008
ID consult	50 (59%)	54 (61%)	0.76
Ophthalmology consult	32 (38%)	47 (53%)	0.05
Echocardiogram	56 (66%)	69 (78%)	0.09
Length of stay, days	15 [9-28]	19 [11.5-29.5]	0.37
Mortality	16 (19%)	26 (30%)	0.11

Reed EE et al. *Diagn Microbiol Infect Dis* 2014;78:157-61.