Implementing and Sustaining Antimicrobial Stewardship Programs in Hospitals

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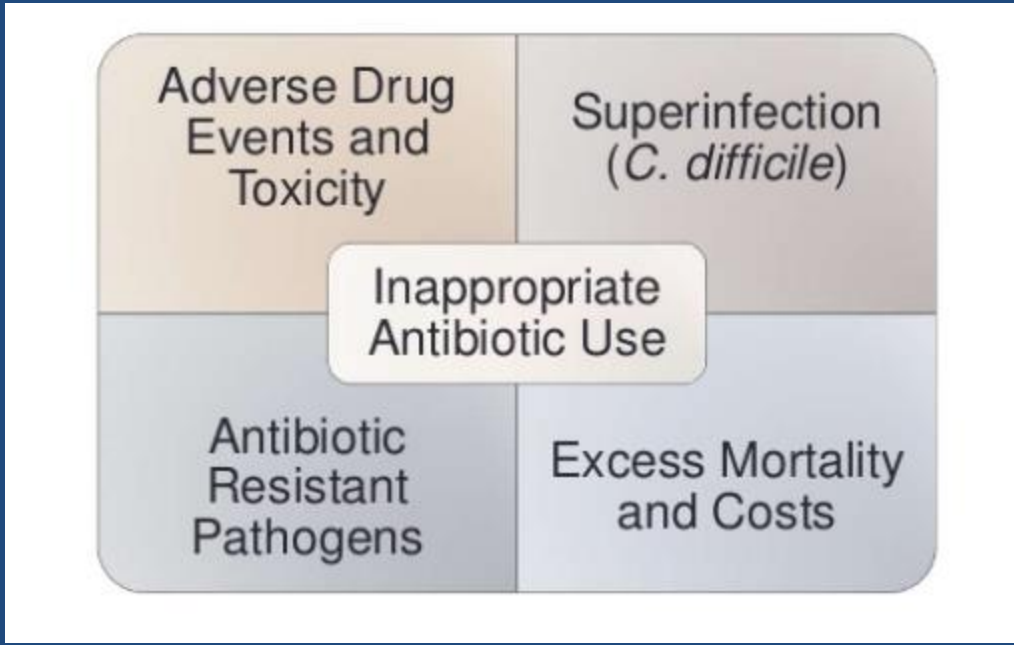
Objectives

- Understand the purpose of an antimicrobial stewardship program
- Define core elements of a hospital's antimicrobial stewardship program
- Review policies and interventions that support judicious antibiotic usage
- Review emerging developments in antimicrobial stewardship

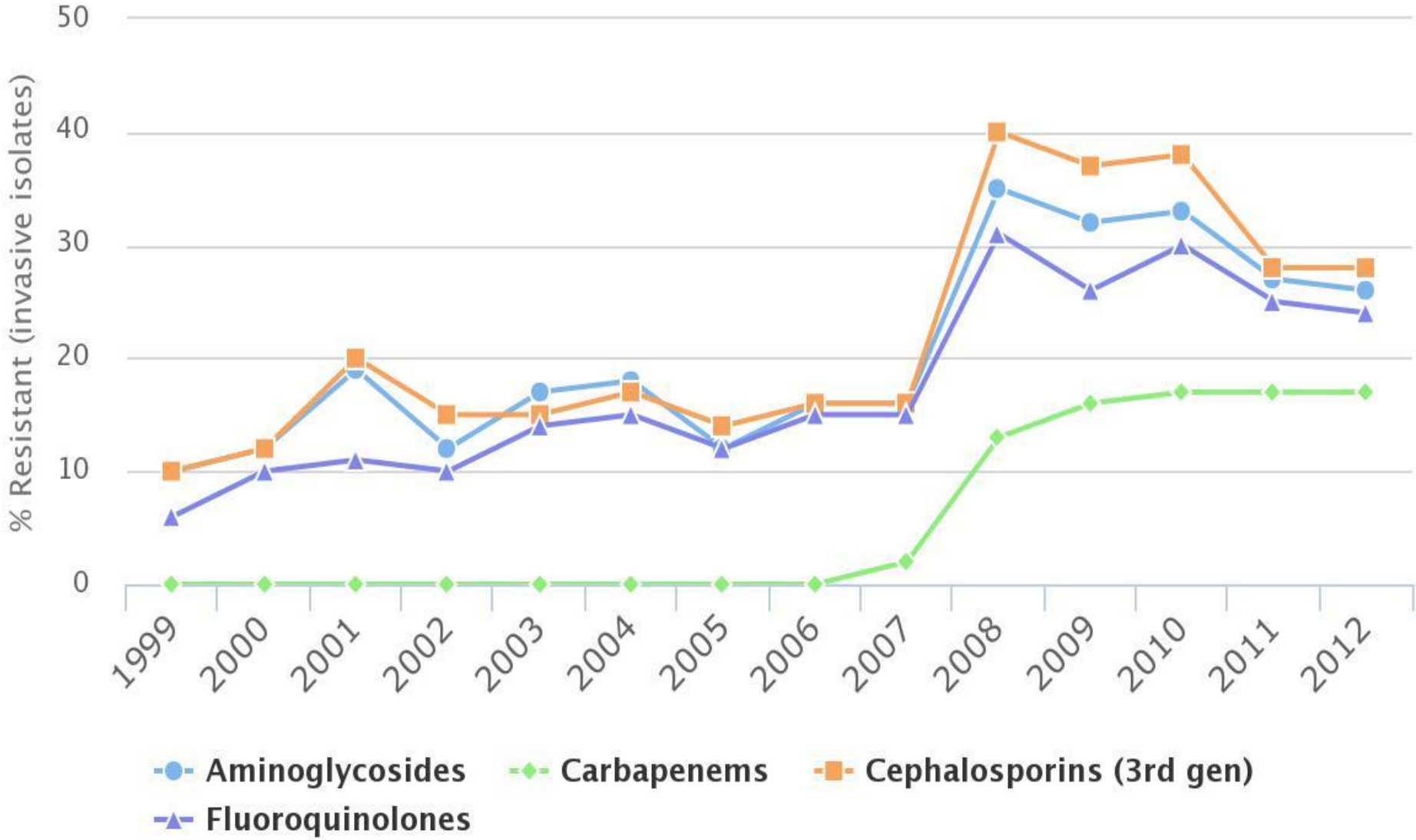
Alexander Fleming c. 1945

- “The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under dose himself and, by exposing his microbes to nonlethal quantities of the drug, educate them to resist penicillin…In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted.”



Dellit TH, et al. Clinical Infect Diseases. 2007 44: 159-77.

Antibiotic Resistance of *Klebsiella pneumoniae* in East North Central



Center for Disease Dynamics, Economics & Policy (cddep.org)

World Health Organization

Priority 1: CRITICAL[#]

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

World Health Organization

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

World Health Organization

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

Background

- The Centers for Disease Control and Prevention (CDC)
  - 20-50% of all antibiotics prescribed in U.S. acute care hospitals
    - Unnecessary or inappropriate
  - More than two million people are infected with antibiotic-resistant organisms
  - 23,000 deaths annually
  - Antibiotic exposure is the single most important risk factor for the development of Clostridium difficile associated disease (CDAD).
  - “Get Smart for Healthcare Campaign” in 2009
    - Promote improved use of antibiotics in acute care hospitals
  - Recommended that all acute care hospitals implement Antibiotic Stewardship Programs in 2014

Evidence to support stewardship

- CDC website
  - *C. difficile*, antimicrobial resistance, costs, other end points
- IDSA/SHEA guidelines (2007)
  - "Effective antimicrobial stewardship programs can be financially self-supporting and improve patient care (A-II)."
  - "Comprehensive programs have consistently demonstrated a decrease in antimicrobial use (22%–36%), with annual savings of $200,000–$900,000 in both larger academic hospitals and smaller community hospitals."

- Leadership support
- Accountability
- Drug Expertise
- Actions to Support Optimal Antibiotic Use
- Tracking: Monitoring Antibiotic Prescribing, Use and Resistance
- Reporting Information to Staff on Improving Antibiotic Use and Resistance
- Education

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Leadership support, Accountability, Drug Expertise

Who's involved?

- Infection control professionals
- Pharmacy (usually infectious disease trained)
- Microbiologists
- Physician
- Administration
- Staff

Actions to Support Optimal Antibiotic Use

Components of programs

- Physician surveys
  - Direct actions, priorities
- Pre-authorization programs for antimicrobials
  - Restricted, different “tiers”
- Standardized definition and identification of infection based on NHSN criteria, etc.
- Identification of colonization, contamination and active infection
  - “Stewardship of Culturing”
- Adoption of locally customized guidelines based on published guidelines (CAP, UTI, CDI, CR-BSI, sepsis, SSTI)

Mullin K, et al. A Multifaceted Approach to Reduction of Catheter-Associated Urinary Tract Infections in the Intensive Care Unit with an Emphasis on "Stewardship of Culturing." Infect Control Hosp Epidemiol. 2017 Feb;38(2):186-188.

CONFERENCE REPORTS AND EXPERT PANEL

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

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Surviving Sepsis Campaign

Diagnosis

We recommend that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis and septic shock if doing so results in no substantial delay in the start of antimicrobials. (BPS)

- Remarks: Appropriate routine microbiologic cultures always include at least two sets of blood cultures (aerobic and anaerobic).

Surviving Sepsis Campaign

Source Control

- **We recommend that a specific anatomic diagnosis of infection requiring emergent source control be identified or excluded as rapidly as possible in patients with sepsis or septic shock, and that any required source control intervention be implemented as soon as medically and logistically practical after the diagnosis is made. (BPS)**
- We recommend prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established (BPS).

Surviving Sepsis Campaign

Antimicrobial Therapy

Antibiotic Stewardship

- We recommend that empiric antimicrobial therapy be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted. (BPS)

- We suggest that an antimicrobial treatment duration of 7-10 days is adequate for most serious infections associated with sepsis and septic shock. (Weak recommendation; low quality of evidence)

- We recommend daily assessment for de-escalation of antimicrobial therapy in patients with sepsis and septic shock. (BPS)

Components of programs

- Lectures to staff on MRSA, *C. difficile*, UTI
- Hospital specific surgical prophylaxis guidelines
- Extended infusion of carbapenems, zosyn
- Create antibiograms specifically for MRSA, pseudomonas, enterococcus in ICU
- Renal adjustments to medications (at start and during therapy)

STVHCS ANTIBIOGRAM -January 1-December 31 2007

	Acinetobacter baumanii	*Citrobacter freundii*	*Citrobacter koseri*	*Enterobacter aerogenes*	*Enterobacter cloacae*	*E.faecalis*	*E.faecium*	*E.coli*	*Klebsiella pneumoniae*	*Morganella morganii*	*Proteus mirabilis*	*Providencia stuartii*	*Pseudomonas aeruginosa*	*Serratia marcescens*	*S.aureus*
# isolates	37	52	44	68	99	529	68	1073	394	63	301	21	446	75	806
Antibiotics															
Amikacin	97	100	100	100	100			100	99	100	100	100	92	99	
Ampicillin	0	0	0	0	3	100	16	43	0	0	62	0		0	
Amp/sulbactam	69	0	84	0	6			51	85	0	82	0		0	
Cefazolin	0	0	86	0	1			87	94	0	86	0		0	41
Cefepime	57	100	100	99	97			98	97	98	98	100	92	100	
Ceftriaxone	0	79	89	82	81			97	96	95	96	100		99	
Ceftazidime	46	79	86	79	80			97	95	95	94	95	92	97	
Ciprofloxacin**	59	81	86	94	87			68	95	84	57	33	78	95	
Clindamycin*															81*
Gentamicin	73	87	100	100	95			88	97	81	83	0	85	99	
Imipenem	84	100	100	100	100			100	100		100	95	90	100	
Oxacillin															41
Penicillin G						99	15								6
Pip/tazobactam	62	90	93	85	86			98	98	92	99	100	93	99	
Tetracycline															95
Tobramycin	81	96	100	100	96			90	97	92	84	0	94	93	
TMP/sulfa	54	73	86	100	85			71	90	68	65	71		99	99
Vancomycin						99	28								100

*may not reflect inducible MLS resistance

**can be used to predict susceptibility to moxifloxacin except for Pseudomonas

Components of programs

- IV-PO conversion
- Sepsis protocol “surviving sepsis”
- De-escalation therapy at 48-72 hours
- Review of “outliers”
- Vaccine preventable infections
- “dose, duration and indication”
  - Antimicrobial order forms (BII)
- “antibiotic time-out”
  - Few studies and intervention successes vary
  - Target some vs all antibiotics?
    - Lee et al. Ann Int Med, 2014. Montreal. Usage declined with some though not all antibiotics
    - Reduction in annual costs but no change in overall antibiotic usage

Components of programs

- Computer surveillance and decision support
- Pharmacist rounds with physicians (active)
- Antimicrobial cycling
  - van Duijn et al studied 8 ICUs in Europe from 2011-2014
    - 745 patients cycling period (6 wks) vs 853 mixing period
    - Cycling does not reduce prevalence of carriage of antibiotic-resistant gram neg
- Selective susceptibility reporting
  - Suppression of ciprofloxacin susceptibility to *Enterobacteriaceae* if lack of resistance to other antibiotics noted
    - Mean monthly Ciprofloxacin utilization decreased from 87 to 39 DDD (defined daily dose) per 1000 patient days
      - Increase in amoxicillin-clavulanate usage
      - Increase in *E. coli* but not *pseudomonas* susceptibility
- Automatic stop orders
- Review of key "never" combinations (ex—anaerobic coverage)

Langford, B., et al. Antimicrobial Stewardship in the Microbiology Laboratory: Impact of Selective Susceptibility Reporting on Ciprofloxacin Utilization and Susceptibility of Gram-Negative Isolates to Ciprofloxacin in a Hospital Setting. J Clin Microbiol 2016:54-9 S4:2343-2347

Joppe van Duijin et al. The effects of antibiotic cycling and mixing on antibiotic resistance in intensive care units: a cluster-randomized crossover trial. Lancet, Infectious Diseases 2018:18, 4:401-409

Procalcitonin

- “We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients” (weak recommendation, low quality of evidence).
- “We suggest that procalcitonin levels can be used to support the discontinuation of empiric antibiotics in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection” (weak recommendation, low quality of evidence).

Procalcitonin

- Schuetz P et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. Lancet Infect Dis 2018; 18:95-107
  - Cochrane review – meta-analysis of data from 26 randomized controlled trials
  - 6708 participants with acute respiratory illness
  - Mortality at 30 days was significantly lower in procalcitonin-guided patients than in control patients
- Some conflicting data
- Strongest data in favor of procalcitonin in meningitis, pneumonia, upper respiratory tract infection and sepsis.
  - Sager R et al, BMC Medicine 2017:15.

Rapid diagnostic testing

- Develop implementation protocol for education and adoption of testing
  - Reporting of results
  - Periodic feedback
    - Is testing leading to actionable plan and results?
    - How is the testing contributing to stewardship?
      - Not just antibacterial stewardship…consider antiviral and antifungal stewardship
- Role in maintaining a stewardship program

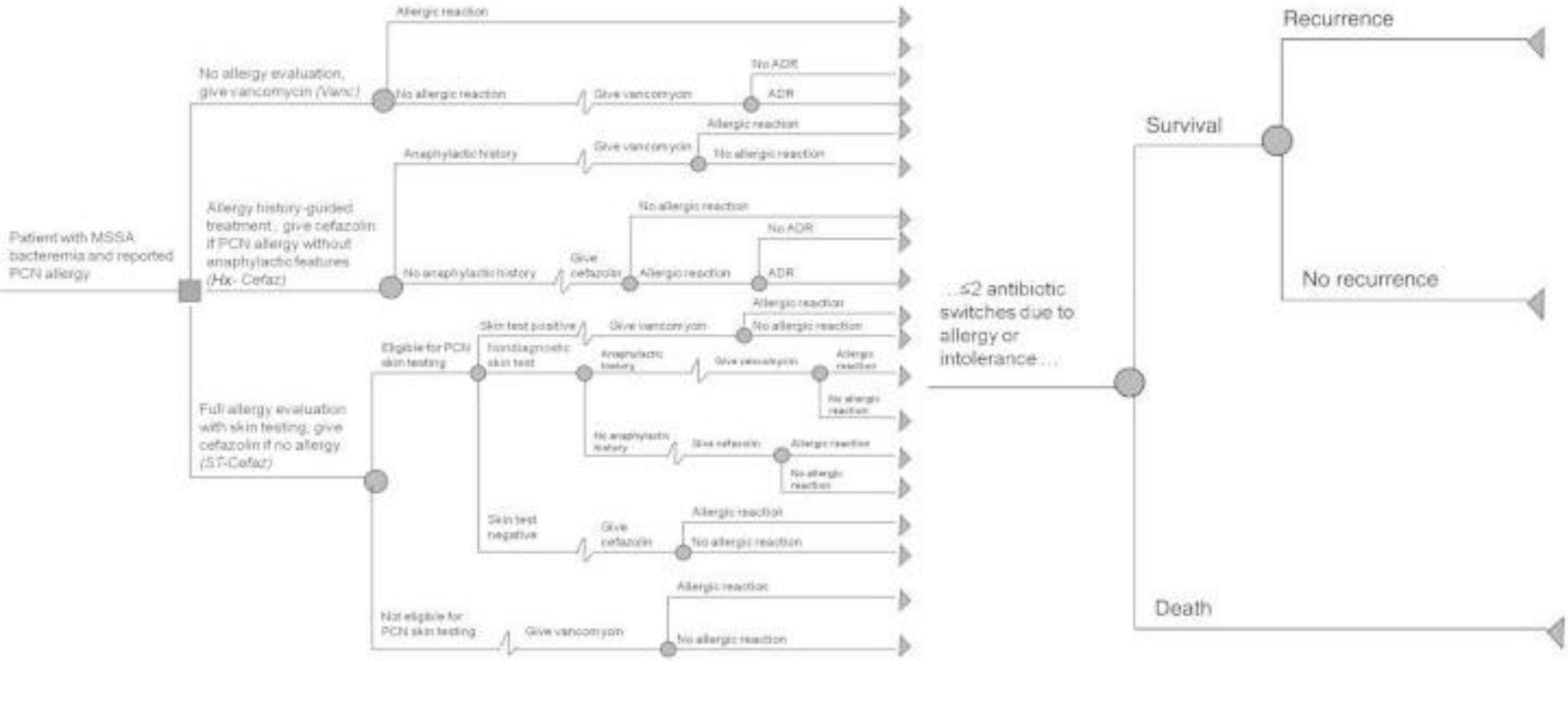
Allergy testing

- 2-15% of patients with reported penicillin allergy actually have an allergy to penicillin (multiple references)
- Differences in availability of testing in US versus Europe
- Huang K-H G et al noted a statistically significant trend towards increased 3 month mortality in hematologic malignancy in patients with B-lactam allergy (16% versus 12% p = 0.01). AAAI 2017.

Staphylococcus aureus bacteremia and penicillin allergy

- Blumenthal et al evaluated a decision tree to determine optimal evaluation and treatment for patients with MSSA bacteremia and reported PCN allergy
  - Vancomycin found to result in fewer cures (vs Cefazolin)
  - Vancomycin resulted in highest rate of recurrence (vs Cefazolin)
  - Vancomycin had greatest frequency of allergic reactions and adverse drug reactions (vs Cefazolin)
  - CONCLUSION: PCN allergy should be addressed in patient with MSSA bacteremia for optimal treatment.

Blumenthal K, et al. Improving Clinical Outcomes in Patients with Methicillin-Sensitive Staphylococcus aureus Bacteremia and Reported Penicillin Allergy. Clin Infect Dis 2015 Sept 1; 61(5):741-749.



(1) no allergy evaluation, give vancomycin (*Vanc*); (2) allergy history–guided treatment: if history excludes anaphylactic features, give cefazolin (*Hx-Cefaz*); and (3) complete allergy evaluation with history-appropriate PCN skin testing; if skin test negative, give cefazolin (*ST-Cefaz*). Blumenthal K, et al. Improving Clinical Outcomes in Patients with Methicillin-Sensitive Staphylococcus aureus Bacteremia and Reported Penicillin Allergy. Clin Infect Dis 2015 Sept 1; 61(5):741-749.

Tracking and Reporting

- Identification of goals
  - Important to measure impact on patient safety, cost, resistance patterns, antimicrobial use
    - Reduction of *C. difficile* rates (ex—focus of fluoroquinolone use)
    - Reduction of carbapenemase resistant *enterobacteriaceae*
    - Reduction of mupirocin-resistance rates (ex—stop date for mupirocin use)
- Process measures
- Outcome measures
- How to provide feedback
  - Clinical impact, economic impact

Addressing clusters of nosocomial infections

- Working through a “pain point”
  - Mediastinitis, device related infections, Ca-UTI, etc
- Apply core elements of CDC’s Hospital Antibiotic Stewardship Programs
  - Leadership support
  - Accountability
  - Drug Expertise
  - Actions to Support Optimal Antibiotic Use

Actions to Support Optimal Antibiotic Use

Components of programs

- Physician surveys
  - Direct actions, priorities
- Pre-authorization programs for antimicrobials
  - Restricted, different “tiers”

- Standardized definition and identification of infection based on NHSN criteria, etc.
- Identification of colonization, contamination and active infection
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Actions to Support Optimal Antibiotic Use

Components of programs

- Tracking: Monitoring Antibiotic Prescribing, Use and Resistance
- Reporting Information to Staff on Improving Antibiotic Use and Resistance
- Education

ASP in small hospitals

- In-house expertise
- Telemedicine
- Quality improvement projects
  - Evaluate impact of an intervention
  - Gain visibility and “buy-in”

ASP in special populations

- Orthopedic surgeries
- Cardio-thoracic surgeries
- Immunocompromised
- ER
- Various ICU settings
- Transitions of care

U.S. Antibiotic Awareness Week is November 12-18, 2018.

U.S. Antibiotic Awareness Week (formerly "Get Smart About Antibiotics Week") is an annual one-week observance to raise awareness of the threat of antibiotic resistance and the importance of appropriate antibiotic prescribing and use. Join CDC and partners as we celebrate the effort to combat the spread of antibiotic resistance and improve patient safety.

Choose the Appropriate Antibiotic

Think before prescribing, Are we using Right drug for the Right bug ?

Our Vision

IDSA developed the Antimicrobial Stewardship Centers of Excellence Program to promote excellence in optimizing antimicrobial use and combating antimicrobial resistance (AMR) by identifying institutions that effectively demonstrate these activities. The IDSA AS Centers of Excellence program aligns with evidence-based national guidelines such as the IDSA-SHEA guidelines and CDC's Core Elements.

References

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