

# Antimicrobial Stewardship and the Role of the Infection Preventionist

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4/23/24



1

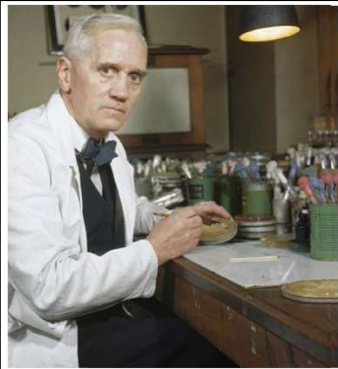
## Disclosures

I have the following financial relationships with the manufacturer(s) and/or provider(s) of commercial services discussed in this activity:

- Contracted research with:
  - Pfizer (pediatric nirmatrelvir-ritonavir)
  - Pfizer (maternal RSV vaccine)
  - Merck (monoclonal antibody for RSV prevention)

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

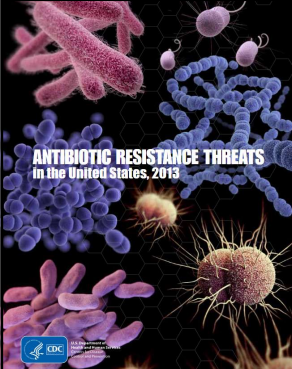
2



The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out.... In such cases the **thoughtless person playing with penicillin is morally responsible for the death** of the man who finally succumbs to infection with the penicillin-resistant organism.

Sir Alexander Fleming,  
6/14/1945, New York Times

3



Estimated minimum number of illnesses and deaths caused by antibiotic resistance\*:

At least **2,049,442** illnesses,  
**23,000** deaths

\*bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least **250,000** illnesses,  
**14,000** deaths

<https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf>

4

### CDC's 2019 AR Threats Report: PREVENTION WORKS.

↓18% fewer deaths from antibiotic resistance overall since 2013 report    ↓28% fewer deaths from antibiotic resistance in hospitals since 2013 report


AND DECREASES IN INFECTIONS CAUSED BY:

|  |   |
|--|---|
| ↓41% Vancomycin-resistant <i>Enterococcus</i>                  | ↓33% Carbapenem-resistant <i>Acinetobacter</i>  |
| ↓29% Multidrug-resistant <i>Pseudomonas aeruginosa</i>         | ↓25% Drug-resistant <i>Candida</i>  |
| ↓21% Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) | STABLE Carbapenem-resistant Enterobacteriaceae (CRE) & drug-resistant tuberculosis (TB disease cases) |

<https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf>

5

## What Was Working?



- Infection Prevention
  - Known MDRO infections:
    - Screening, isolation
    - Information sharing between facilities
    - Surveillance
  - Reduction in Hospital-Acquired Infections
    - CLABSI, VAP, CAUTI
- Antimicrobial Stewardship

6

**2022 SPECIAL REPORT**

**COVID-19**

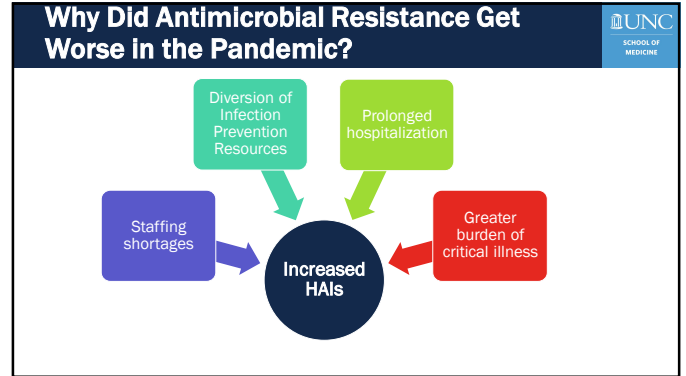
**U.S. IMPACT ON ANTIMICROBIAL RESISTANCE**

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

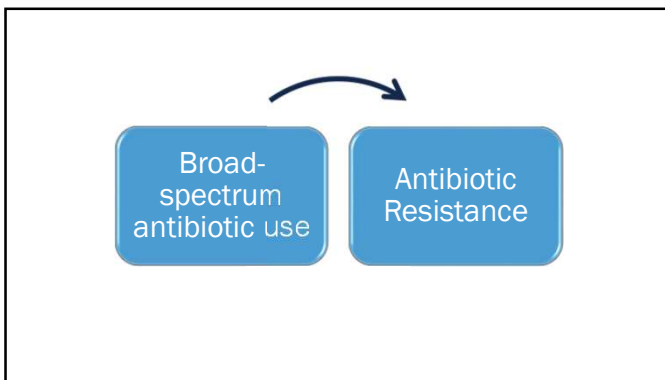
- Carbapenem-resistant *Acinetobacter* (+78%)
- Antifungal-resistant *Candida auris* (+60%)\*
- Carbapenem-resistant Enterobacterales (+35%)
- Antifungal-resistant *Candida* (+26%)
- ESBL-producing Enterobacterales (+32%)
- Vancomycin-resistant Enterococcus (+14%)
- Multidrug-resistant *P. aeruginosa* (+32%)
- Methicillin-resistant *Staphylococcus aureus* (+13%)

https://www.cdc.gov/drgresistance/pdf/covid19-impact-report-508.pdf

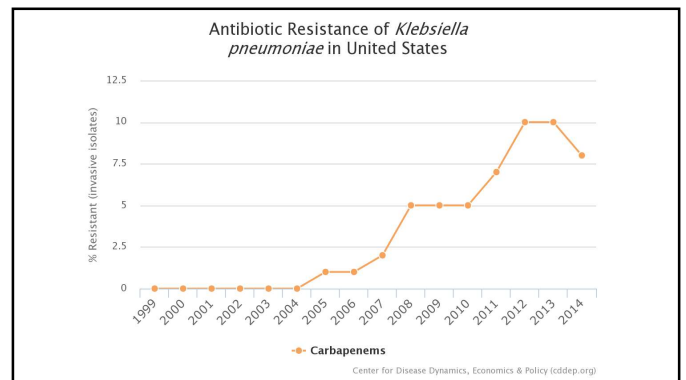
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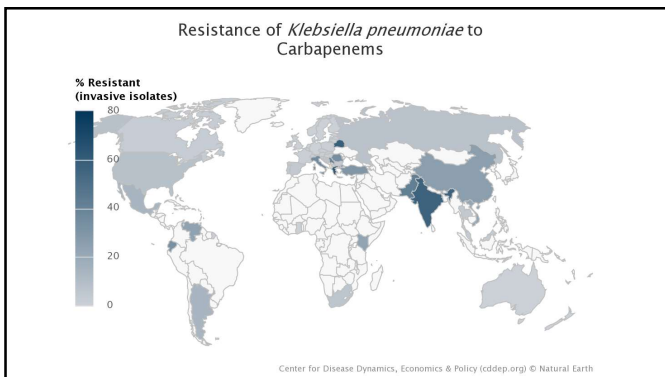
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9



10



11

**IP and AS Goal**

Prevent antimicrobial resistant infections and C-diff


**CDC strategies that work in healthcare:**

- Preventing device- and procedure-related infections, such as from urinary catheters or central lines
- Stopping the spread of resistant germs within and between healthcare facilities
- Containing emerging threats through early detection and aggressive response
- Tracking and improving appropriate antibiotic use
- Infection prevention and control in non-hospital settings, such as long-term care facilities

Antibiotic Resistance Threats in the United States, 2019 (cdc.gov)  
Slide courtesy of Emily Sickbert-Bennett, PhD

12

## AS: Core Elements



**Core Elements of Hospital Antibiotic Stewardship Programs**

- Hospital Leadership Commitment**  
Dedicate necessary human, financial, and information technology resources.
- Accountability**  
Assign a leader or co-leaders, such as a physician and pharmacist, responsible for program management and outcomes.
- Pharmacy Expertise (previously "Drug Expertise")**  
Assign a pharmacist, ideally as the co-leader of the stewardship program, to help lead implementation efforts to improve antibiotic use.
- Action**  
Implement interventions, such as prospective audit and feedback or preauthorization, to improve antibiotic use.
- Tracking**  
Monitor antibiotic prescribing, impact of interventions, and other important outcomes, like *C. difficile* infections and resistance patterns.
- Reporting**  
Regularly report information on antibiotic use and resistance to prescribers, pharmacists, nurses, and hospital leadership.
- Education**  
Educate prescribers, pharmacists, nurses, and patients about adverse reactions from antibiotics, antibiotic resistance, and optimal prescribing.

4 of 7 have direct link to IP

<https://www.cdc.gov/antibiotic-use/healthcare/pdfs/hospital-core-elements-H.pdf>  
Slide courtesy of Emily Sickbert-Bennett, PhD

13


## AS/IP Strategy Alignment



- MDRO epidemiology
- *C. difficile* prevention
- Diagnostic stewardship
  - CLABSI
  - HAP and VAP
  - CAUTI
  - *C. difficile*

14

## Key ASP Tactics



- Prospective Audit and Feedback
  - AKA "postprescription review"
- Prior authorization/Restriction
  - Preapproval required for certain antibiotics to be released
- Clinical Pathway/Guideline development
  - Incorporates diagnosis and management guidelines; good for standardization
- Provider education

15

## Additional ASP Tactics




- 48-hour antibiotic time-outs
- Handshake stewardship
  - ASP rounds
- Patient education
- Antimicrobial formulary management
- Medication use evaluations (MUE) and targeted education



16


## ASP: Tracking Data



- Antibiotic use in days of therapy/1000 patient-days (DOT/1000)
  - Can look at individual antibiotics, groups of antibiotics
  - Hospital-wide, specific units, groups of units...
- NHSN Antimicrobial Use (AU data)
  - Adds: reasonable(ish) antibiotic groupings
  - Benchmarks with similar(ish) units at other hospitals
  - SAAR ≈ SIR
- Major limitation:
  - Don't know if the patient *should* be on antibiotics
  - Don't know if the antibiotic choices were optimal

17

## IP vs AS



|             | Infection Prevention       | Antimicrobial Stewardship          |
|-------------|----------------------------|------------------------------------|
| #1 audience | Bedside staff esp. nursing | Ordering providers and pharmacists |

18

### Stewardship: A Multidisciplinary Endeavor

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Essential, "Core-Team" Personnel

- Lead Physician
- Lead Pharmacist
- Clinical Microbiologist
- Infection Preventionist
- Information Technologist

19

### Case

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A surgical ICU has noticed an increase in the incidence of HA-CDI over the past six months, from 5 cases in the prior 4 quarters to 7 in the past 2 quarters. They have had no significant changes in staffing or patient population. What should they look at first?

- Adherence to isolation precautions
- Post-operative antibiotic prophylaxis
- Post-discharge deep cleaning
- Empiric antibiotic selection
- Handwashing practices

20

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21

### C-diff Prevention

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| IP   | Both  | ASP  |
|--|---|--|
| <ul style="list-style-type: none"> <li>• Handwashing</li> <li>• Surveillance</li> <li>• Isolation</li> <li>• Unit layout</li> <li>• Deep cleaning</li> </ul> | <ul style="list-style-type: none"> <li>• Diagnostic Stewardship!</li> </ul> | <ul style="list-style-type: none"> <li>• Avoid highest-risk CDI antibiotics</li> <li>• Basically everything we do</li> </ul> |

22

### C-diff: Don't blame me!

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**Longitudinal genomic surveillance of carriage and transmission of *Clostridioides difficile* in an intensive care unit**

Articles: August 2022, August 2023

- Cultured almost 4,000 stools and rectal swabs from 1,289 ICU admissions
- Only 1% of eligible patients had acquisition of toxigenic *C. difficile* via cross-transmission
- Colonized with toxigenic *C. difficile* on admission: **24x greater risk of CDI**

23

### Impact of AS programs *C. difficile*

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| Study                             | Events/patient-days | Incidence ratio (95% CI) |                  |
|-----------------------------------|---------------------|--------------------------|------------------|
| Cruz-Rodriguez et al <sup>1</sup> | 8/2026              | 2/95507                  | 0.11 (0.02-0.58) |
| Leung et al <sup>2</sup>          | 8/1373              | 3/3207                   | 0.14 (0.02-1.14) |
| McCarthy et al <sup>3</sup>       | 32/2444             | 18/30487                 | 0.20 (0.23-0.67) |
| Pinto et al <sup>4</sup>          | 35/271538           | 25/373513                | 0.53 (0.45-0.62) |
| Maher et al <sup>5</sup>          | 46/2976             | 20/2408                  | 0.54 (0.32-0.91) |
| Burke et al <sup>6</sup>          | 71/127596           | 20/51256                 | 0.65 (0.40-1.07) |
| Lalor et al <sup>7</sup>          | 126/24952           | 122/324560               | 0.73 (0.58-0.93) |
| Dubrovskaya et al <sup>8</sup>    | 8/2553              | 2/2489                   | 0.90 (0.33-2.47) |
| Cook and Gough <sup>9</sup>       | 134/220474          | 143/276118               | 0.94 (0.74-1.18) |
| Schwin et al <sup>10</sup>        | 182/169886          | 193/270548               | 1.05 (0.95-1.28) |
| Frank et al <sup>11</sup>         | 50/103273           | 48/303965                | 1.08 (0.73-1.61) |
| Overall                           |                     |                          | 0.68 (0.53-0.88) |

*I<sup>2</sup>* = 27%, *p* = 0.000

Figure 4: Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of *Clostridium difficile* infections

Baur, Gladstone, Burkert, et al. Lancet Infectious Diseases; 17:9:990-1001, 2017

24

Journal of Antimicrobial Chemotherapy

J Antimicrob Chemother 2021; 76: 1676-1688  
doi:10.1093/jac/dkz091 Advance Access publication 31 March 2021

**Antibiotics and healthcare facility-associated *Clostridioides difficile* infection: systematic review and meta-analysis 2020 update**

Claudio Stimpings<sup>1\*</sup> and Thomas V. Riley<sup>2,3</sup>

- Which antibiotics are most likely to cause CDI?
- Highest-risk classes (highest to lowest):
  - Carbapenems
  - 4<sup>th</sup>-gen and 3<sup>rd</sup>-gen cephalosporins
  - Vancomycin
  - Fluoroquinolones
  - Clindamycin
  - Piperacillin-tazobactam
  - No association: narrow penicillins, 1<sup>st</sup>-gen cephalosporins, TMP-SMX, tetracyclines
- Allows ASP to prioritize high-risk

25

**Meropenem Use 2017-2023**

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Days of therapy/1000 days-present

26

**Antibiotics with high risk for CDI in SICU**

Quarterly SAAR values for antibacterial agents posing the highest risk for CDI used in adult ICUs

27

**Diagnostic Stewardship: Why?**

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- Most infectious diseases diagnostics have imperfect specificity and positive predictive value
  - Patients can have C-diff colonization, urinary tract colonization, ET tube or trach colonization, Group A Strep colonization, CVC colonization...
- False-positives:
  - Mask the patient's true problem
  - Cause unnecessary antibiotic exposure
  - Overcount HAIs
- Not the goal: missing HAIs, saving money

28

**Diagnostic Stewardship Principles**

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- Perform infectious diseases diagnostic testing *appropriately*
  - Examples:
    - Adequate blood culture volumes sent from fresh peripheral sticks
    - Reject formed stools sent for C-diff testing
- Only send testing when infection reasonably suspected
  - Avoid false-positives
  - Especially nonsterile sites

29

**Diagnostic Stewardship Stakeholders**

**Frontline staff**

Obtain most samples for testing  
Often suggest testing to providers

**Microbiology lab**

Assess sample adequacy (rejecting formed stools, rejecting "sputum" that's all spit)  
Reporting algorithms:  
• Urine culture with 3 organisms in low numbers vs "mixed urogenital flora"

**Ordering providers and pharmacists**

Order diagnostic tests and make treatment decisions

30

### C. difficile Diagnostic Stewardship

- C. difficile colonization is common
  - Nontoxicogenic strains
  - Toxicogenic strains not causing symptoms
- Diarrhea is common in the hospital
  - Laxatives, enteral feeds, withdrawal symptoms, most drugs, etc...
- Use high-specificity test algorithms
  - Avoid PCR-only CDI testing
- Avoid C. difficile testing if:
  - Not true diarrhea (<3 episodes/24 hours, formed stool)
  - Recent laxative exposure
  - Recent negative test

31

### QUALITY IMPROVEMENT C. difficile test ordering: "hard stop"

You cannot sign these orders because information is missing or requires your attention:

C. Diff testing is not currently indicated for this patient. If after review of the C Diff ordering guidelines, you still need to place the order, contact your designated approval point person and document the name and the date of contact in the C Diff order.

Slide courtesy of Emily Sickbert-Bennett, PhD

32

### HAP/VAP Diagnostic Stewardship

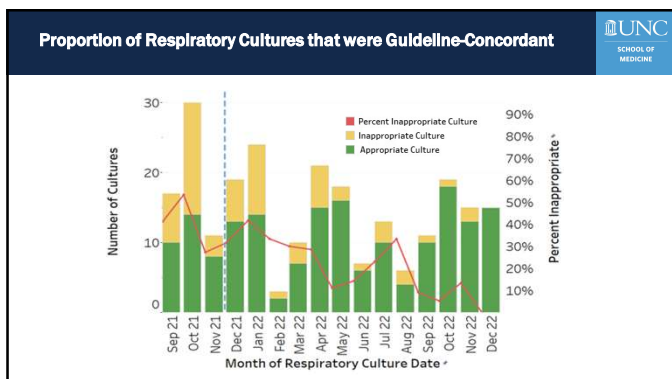
- Surveillance definition ≠ Clinical definition
- Respiratory cultures from airway devices have very poor specificity and PPV
- False-positive cultures → treatment courses
  - Often repetitively in one patient
  - Usually broad-spectrum

33

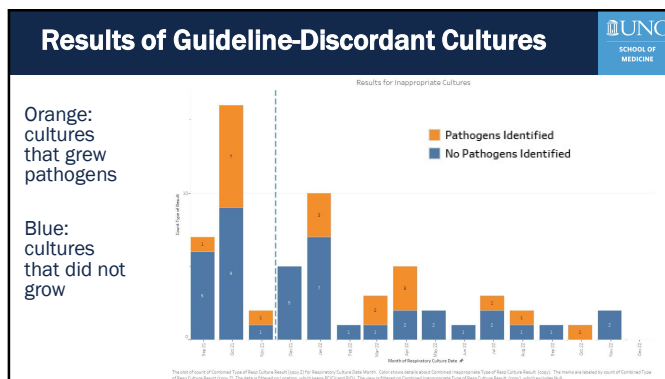
### Diagnostic Stewardship Project

- Education provided to PICU before launch
- Audited every respiratory culture sent from patients in PICU
  - 9/1/21-12/31/22 (15 months)
    - 3 months pre- and 12 months post-intervention.
  - Cultures assessed as guideline-concordant or -discordant
    - Systemic signs of illness (fever, leukocytosis, etc) PLUS respiratory symptoms (persistently increased PEEP/FiO2, CXR changes, purulent ETT output)
- Periodic feedback to PICU providers

34

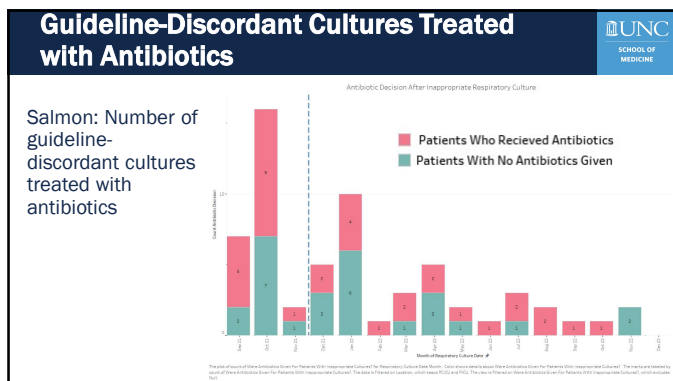


35



36





37

### Blood Culture Diagnostic Stewardship

JAMA Pediatrics | Original Investigation

#### Association of Diagnostic Stewardship for Blood Cultures in Critically Ill Children With Culture Rates, Antibiotic Use, and Patient Outcomes Results of the Bright STAR Collaborative

Charlotte Z. Woods-Hill, MD, MSPH, Elizabeth A. Colantuoni, PhD, Danielle W. Koontz, MA, MS, Annie Voskertchian, MPH, Anping Xie, PhD, Cary Thurm, PhD, Marlene R. Miller, MD, MSc, James C. Fackler, MD, Aaron M. Milstone, MD, MHS, and the Bright STAR Authorship Group

- Can we steward *blood cultures*? Should we?
- Logic: Fever → blood cultures → empiric antibiotics
- Would CLABSIs go down?? Would septic shock go up?

38

### Blood Culture Diagnostic Stewardship

- 14 PICUs independently developed blood culture best practices
  - Reduce variability in blood culture decision, source, frequency of repeats
  - Studied 24 months pre- and 18 months post-implementation
- Results:
  - Blood cultures fell 33% (49 blood cultures/1000 patient-days fewer)
  - Broad-spectrum antibiotics use fell 13%
  - Unchanged: PICU mortality, LOS, readmission, sepsis, severe sepsis
  - CLABSIs fell 36%** (1.79 → 1.14 CLABSIs/1000 line-days)

39

### UTI Diagnostic Stewardship

- 2 major scenarios:
  - Inpatient with indwelling catheter (at risk for CAUTI)
  - Outpatients
- Asymptomatic bacteriuria is common
  - Older adults
  - Patients with indwelling catheters
- Overdiagnosis leads to:
  - Missed diagnoses
  - Antibiotic exposure (often repeatedly)
  - False-positive CAUTIs

40

### CAUTI Diagnosis Pitfalls

- Pyuria and asymptomatic bacteriuria are very common with long-dwelling urinary catheters
  - You can have ASB with or without pyuria, and pyuria may be sterile
  - You can NOT have a UTI without pyuria
    - Exception: neutropenia
- BUT ICU patients often unable to report symptoms
- Always get a UA BEFORE or at least with the urine culture
  - Use fresh catheter for culture whenever possible
- "Pan-culture" for febrile patients with an ETT and a Foley is likely to turn up a positive culture
  - Avoid this approach

41

### Asymptomatic bacteriuria

DO I REALLY NEED TO TREAT MY PATIENT FOR A UTI?

TREATING ASYMPTOMATIC BACTERIURIA HAS NO BENEFITS AND CAUSES HARM. IN FACT, IT LEADS TO AN INCREASE IN...

Healthcare costs, Length of stay, CAUTI infections, Antibiotic resistance, Misdiagnosis of CAUTI

MY PATIENT IS SICK AND I SUSPECT A UTI. SHOULD I TEST?

UA only helpful for predicting UTI among patients with appropriate urinary symptoms

No UA Needed: Color, Odor, Striated normal sterile urine, Fever or leukocytosis, without urinary symptoms

Send UA: Frequency, Burning, Pain

WHAT IS THE BEST WAY TO TEST?

1. Obtain UA if symptomatic, 2. Obtain urine culture and UA, 3. Treat based on culture results, 4. Treat based on culture results

### Adult UTI Guideline Update

4 New Algorithms

Diagnosis, Altered Mental Status, Treatment, Urine Culture Interpretation

Reserve UTI diagnostic workup for those with UTI symptoms

- Painful urination
- New or increasing urinary frequency or urgency
- Unpleasant odor
- Flank pain or tenderness

Inappropriate urine cultures pose harm to patients

- Unnecessary antibiotics
- Misdiagnosis

Bladder Infection or Cystitis

UNC first-line options: Nitrofurantoin, Trimethoprim-Sulfamethoxazole (TMP-SMX)

Caution: does NOT cover E. coli strains at UNCSC

Pyelonephritis

UNC first-line options: Ceftriaxone, Gentamicin

Target therapy to culture & use initial effective therapy

42

**Case**

The neonatal ICU has had three CLABSIs in the past four months with a similar pattern. The infections have occurred during the time period of days of life 3-7. The infants have all had umbilical venous catheters; all had had negative blood cultures at birth and received 48 hours of empiric antibiotics.

A NICU clinician notes that at their previous employer, it was common to continue the birth antibiotics until day of life 7, regardless of birth culture results.

43

**AS/IP: Are we ever at odds?**

- Head in the sand approaches
  - No culture → No HAI!
- Antibiotic prophylaxis example:
  - Reduced incidence of VAP in neuro ICU patients who received a single dose of ceftriaxone

44

**Future Directions**

- Diagnostic stewardship
  - Only scratched the surface
  - Requires IP/ASP collaboration and *many* stakeholders
- NHSN AR data
  - Becomes mandatory by next year
  - May give us *much* more data about AR patterns, relationships between AU and AR

45

**Questions?**

46

**References**

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47