Antimicrobial Stewardship and the Role of the Infection Preventionist

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4/23/24

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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.

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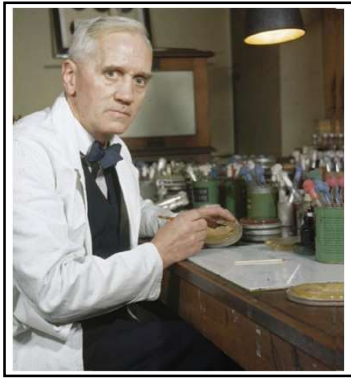

The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out.... In such cases the **thoughtless person playing with penicillin is morally responsible for the death** of the man who finally succumbs to infection with the penicillin-resistant organism.

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

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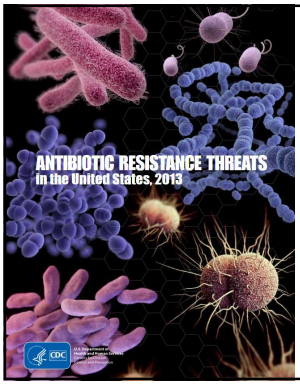

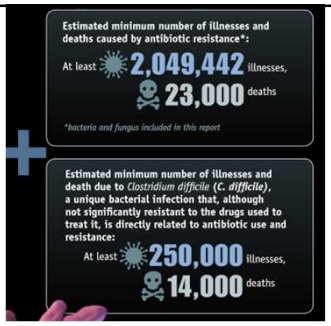

https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf

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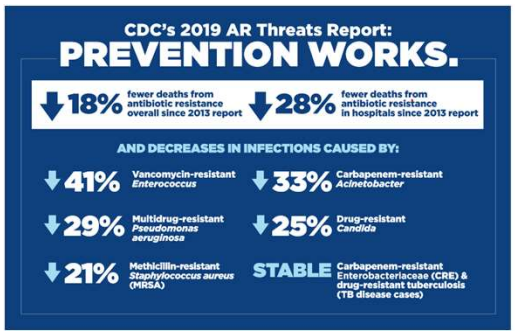

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

5

What Was Working?

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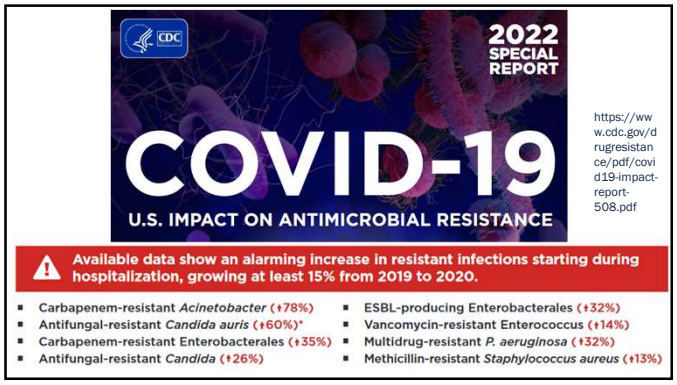
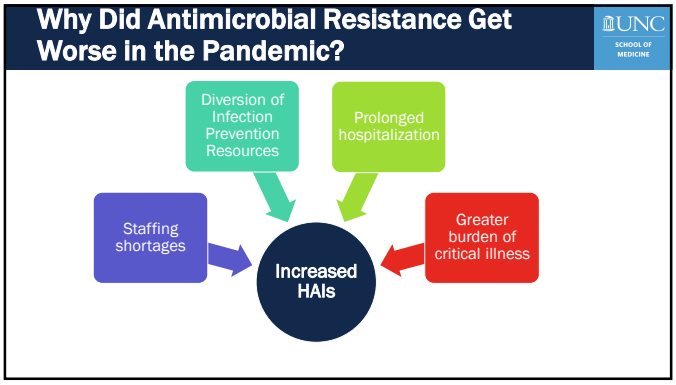
- Infection Prevention
  - Known MDRO infections:
    - Screening, isolation
    - Information sharing between facilities
    - Surveillance
  - Reduction in Hospital-Acquired Infections
    - CLABSI, VAP, CAUTI
- Antimicrobial Stewardship

6


2022 SPECIAL REPORT
COVID-19
U.S. IMPACT ON ANTIMICROBIAL RESISTANCE
https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf
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%)

7


Why Did Antimicrobial Resistance Get Worse in the Pandemic?
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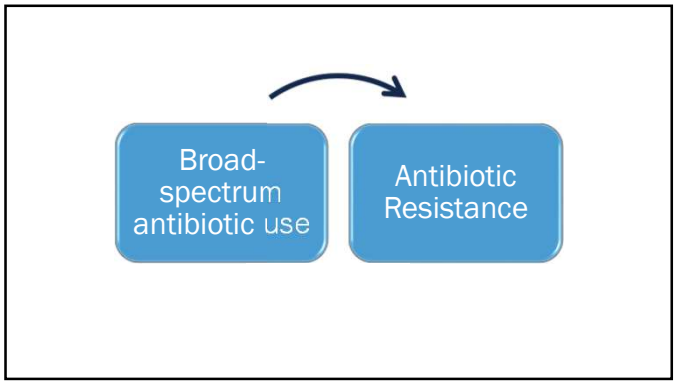
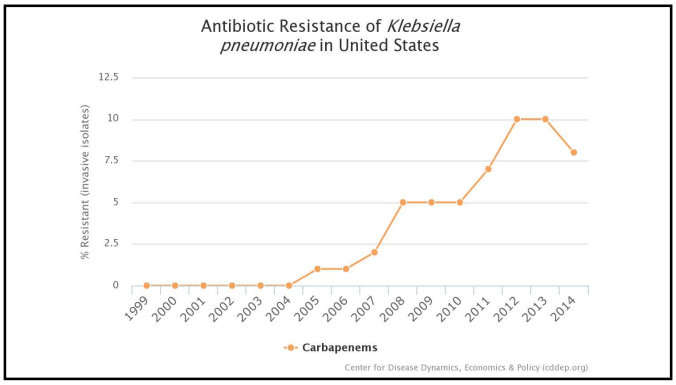
Diversion of Infection Prevention Resources
Prolonged hospitalization
Staffing shortages
Increased HAIs
Greater burden of critical illness

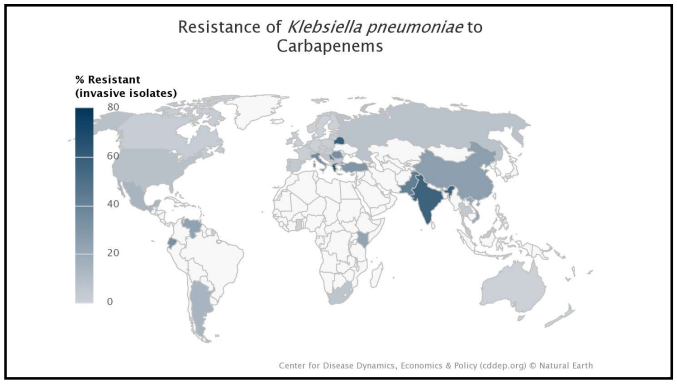
8


Broad-spectrum antibiotic use
Antibiotic Resistance

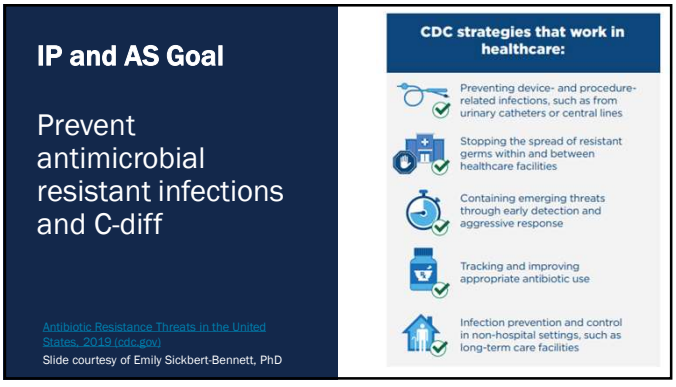
9


Antibiotic Resistance of Klebsiella pneumoniae in United States
% Resistant (invasive isolates)
12.5
10
7.5
5
2.5
0
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
Carbapenems
Center for Disease Dynamics, Economics & Policy (cddep.org)

10

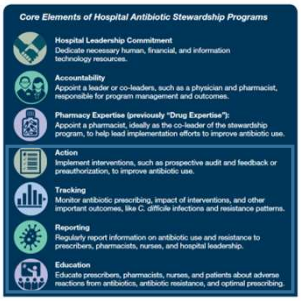

Resistance of Klebsiella pneumoniae to Carbapenems
% Resistant (invasive isolates)
80
60
40
20
0
Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

11


IP and AS Goal
Prevent antimicrobial resistant infections and C-diff
Antibiotic Resistance Threats in the United States, 2019 (cdc.gov)
Slide courtesy of Emily Sickbert-Bennett, PhD
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

12

AS: Core Elements



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

Essential, "Core-Team" Personnel

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

19

Case

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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- **Empiric antibiotic selection**
- **Handwashing practices**

21

C-diff Prevention

IP

- Handwashing
- Surveillance
- Isolation
- Unit layout
- Deep cleaning

Both

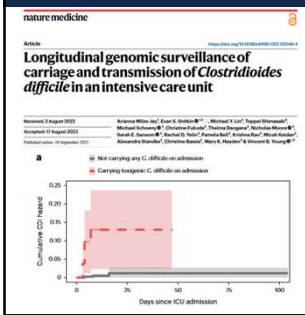
- Diagnostic Stewardship!

ASP

- Avoid highest-risk CDI antibiotics
- Basically everything we do

22

C-diff: Don't blame me!


nature medicine

Article

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

- 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*

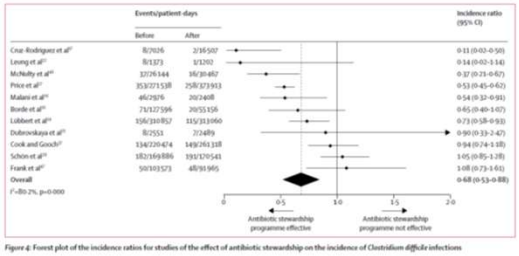


Figure 4: Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of Clostridium difficile infections

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

24

J Antimicrob Chemother 2021; 76: 1676–1688
doi:10.1093/jac/dkab091 Advance Access publication 31 March 2021

Journal of Antimicrobial Chemotherapy

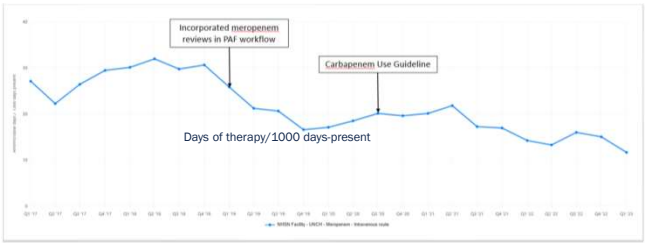
Antibiotics and healthcare facility-associated *Clostridioides difficile* infection: systematic review and meta-analysis 2020 update

Claudia Slimings [1]* and Thomas V. Riley[2,3]

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

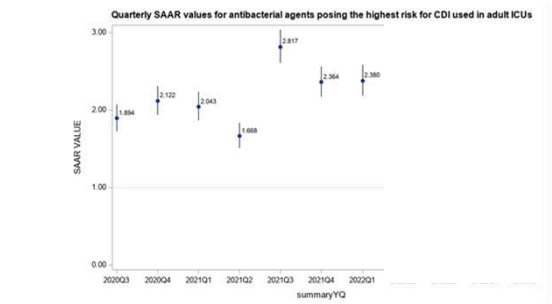
25

Meropenem Use 2017-2023



26

Antibiotics with high risk for CDI in SICU



27

Diagnostic Stewardship: Why?

- 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

- 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

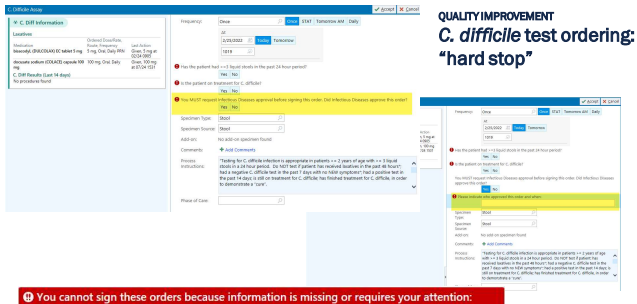
Order diagnostic tests and make treatment decisions

30

C. difficile Diagnostic Stewardship

- *C. difficile* colonization is common
  - Nontoxigenic strains
  - Toxigenic 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



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

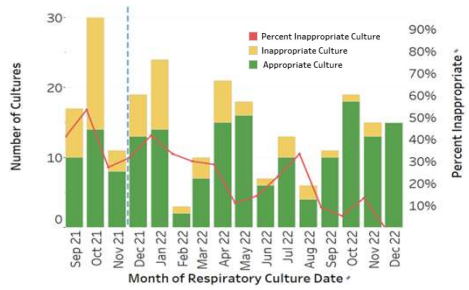
33

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

Proportion of Respiratory Cultures that were Guideline-Concordant

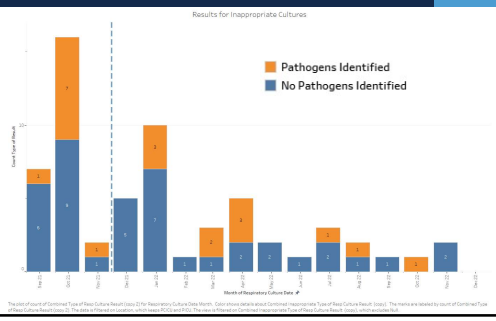


35

Results of Guideline-Discordant Cultures

Orange: cultures that grew pathogens

Blue: cultures that did not grow



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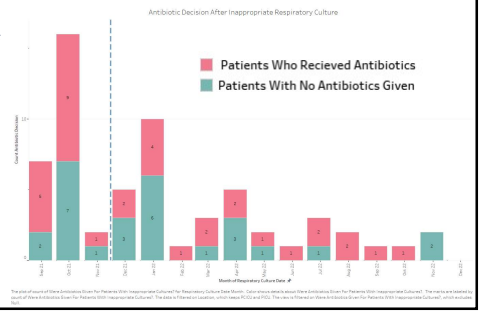
Guideline-Discordant Cultures Treated with Antibiotics

Salmon: Number of guideline-discordant cultures treated with antibiotics



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, MSHP; 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 CLABSI/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

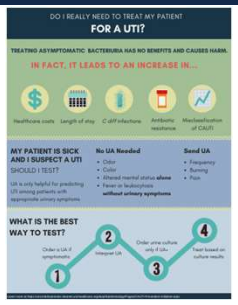
40

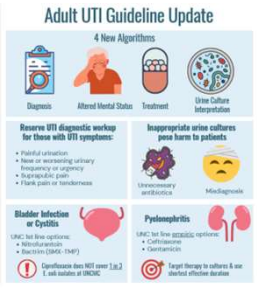
CAUTI Diagnosis Pitfalls

- 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





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