Sepsis Wave II
Balancing Antibiotics Stewardship with Sepsis
Presenters

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Antibiotics. Easy.
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I have no financial relationships of any kind with any of the manufacturers of the drugs or the software discussed in this presentation and the opinions expressed are mine alone.
Things we all need

Working knowledge (How to get smart)
overview today

Pearls and Pitfalls (How to practice smart)
high risk and common mistakes

Resources (How to stay smart)
antibiograms and pocket brain resources

Updated Information (How to look smart)
new antibiotics in the news
Meningitis:
vancomycin
cefdinir (Rocephin)
+/- ampicillin

Pearl:
acyclovir
steroids prior to antibiotics

Pitfall:
delay
ey early bacterial meningitis can look viral

Ears/ Sinuses/ Pharynx:

- amoxicillin/ clavulanate (Augmentin)
- cephalosporins
- trimethoprim/sulfamethoxazole (Bactrim)
- doxycycline
- macrolides (*) / azithromycin/ clarithromycin

**Pearl:**
Steroids make people feel better

**Pitfall:**
Growing resistance against azithromycin
MRSA
Mouth:

amoxicillin/ clavulanate (Augmentin)
clindamycin
pen Vee K
cefdinir (Rocephin)

Pearl:
Source control

Pitfall:
MRSA
**Lungs:**

**Bronchitis:**
- doxycycline
- azithromycin, clarithromycin

**Pneumonia:** (above +)
- amoxicillin/ clavulanate (Augmentin)
- cephalosporins
- trimethoprim/sulfamethoxazole (Bactrim)

*Or*
- levofloxacin (Levaquin) / moxifloxacin

**Hospital Acquired:** (*Pseudomonas*, MRSA)
- Zosyn/ Levaquin/ Meropenem/ cefepime

**Pearl:**
- remember atypicals (Mycoplasma)

**Pitfall:**
- PE
Abdomen:

- pipercillin + tazobactam (Zosyn)
- levofloxacin (Levaquin) / cipro
  + metronidazole (Flagyl)
- amoxicillin/ clavulanate (Augmentin)
  + metronidazole (Flagyl)
- metronidazole (Flagyl) / oral vancomycin for C. Diff

**Pearl:**
probiotics

**Pitfall:**
appendicitis is an infection; may be sepsis
Bladder:

trimethoprim/sulfamethoxazole (Bactrim)
macrobid
cephalosporins
amoxicillin/ clavulanate (Augmentin)

Pearl:
Consider doxycycline or azithromycin

Pitfall:
fluoroquinolones NOT recommended 1st line

"Guidelines for Antimicrobial Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women”
Clin Inf Dis; 2011; 52: e103 - e120
When you have no idea what’s going on....

... then use vancomycin and pipercillin + tazobactam (Zosyn)

OR

Carbapenem +/- MRSA coverage
Don’t forget fungal infections, viral infections, autoimmunity

trimethoprim/sulfamethoxazole (Bactrim) – renal failure, SJS
azithromycin – long QT
fluoroquinolones – tendinopathies, long QT, seizures
clindamycin – C. Diff
metronidazole (Flagyl) – disulfiram-like reaction
Antibiogram

Usually obtained through pharmacy

| Organism                          | # Isolates Tested | % Interpretation | Penicillin | Ampicillin | Amp/Sub | Pip/Tazo | Ceftazolin | Ceftazidime | Ceftriaxone | Ceftoxitin | Ceprotoxin | Aeronem | Metronem | Gentamicin | Tobramycin | Pefloxacin | Levofloxacin | Trimeth/Sulfa | Tetracycline | Nitrofurantoin |
|----------------------------------|-------------------|------------------|------------|------------|---------|----------|------------|------------|------------|------------|-----------|----------|---------|---------|-----------|-----------|------------|-------------|-------------|---------------|---------------|
| MSSA                             | 411               | S                | 21         | --         | --      | --       | --         | --         | --         | --         | --        | --       | --      | --       | --        | --        | --         | --           | --           | --            |
| MRSA                             | 535               | S                | --         | --         | --      | --       | --         | --         | --         | --         | --        | --       | --      | --       | --        | --        | --         | --           | --           | --            |
| Total Staph (coag. neg.)         | 946               | S                | 9          | 43         | 44      | 43       | 61         | 61         | 97         | 73         | 99        | 60       | 60      | 90       | 100       | 100       | 100         | 100          | 100          | 100           |
| Staph (coag. neg.)               | 239               | S                | 15         | --         | --      | --       | --         | --         | --         | --         | --        | --       | --      | --       | --        | --        | --         | --           | --           | --            |
| Strep pneumoniae                 | 88                | S                | 59         | --         | --      | --       | --         | --         | 69         | 88         | --        | --       | --      | --       | --        | --        | --         | --           | --           | --            |
| E. faecalis                      | 283               | S                | 98         | 98         | --      | --       | --         | --         | --         | --         | --        | 98       | 99      | 99       | 99        | 95        | 98         | 99          | 74           | --            |
| E. faecium                       | 27                | S                | 30         | 30         | --      | --       | --         | --         | 19         | 22         | --        | 67       | 50      | 100     | 33        | 15        | --          | --           | --           | --            |

| Organism                          | # Isolates Tested | % Interpretation | Penicillin | Ampicillin | Amp/Sub | Pipl/Tazo | Ceftazolin | Ceftazidime | Ceftriaxone | Cefpigine | Aeronem | Metronem | Gentamicin | Tobramycin | Pefloxacin | Levofloxacin | Trimeth/Sulfa | Tetracycline | Nitrofurantoin |
|----------------------------------|-------------------|------------------|------------|------------|---------|----------|------------|------------|------------|-----------|---------|---------|---------|-----------|-----------|------------|-------------|-------------|---------------|---------------|
| Escherichia coli                 | 968               | S                | 44         | 50         | 96      | 84       | 80         | 85         | 85         | 87        | 95       | 85      | 100     | 98        | 88        | 86        | 62          | 63          | 68            |
| Klebsiella pneumoniae            | 270               | S                | 3          | 84         | 97      | 100      | 90         | 98         | 99         | 100       | 97       | 100     | 99      | 99        | 99        | 98        | 94          | 94          | 48            |
| Klebsiella oxytoca               | 67                | S                | 6          | 75         | 95      | --       | 81         | 98         | 97         | 100       | --       | 90       | 100     | 97        | 94        | 98        | 94          | 92          | 90            |
| Proteus mirabilis                | 136               | S                | 69         | 78         | 98      | --       | 79         | 85         | 85         | 84        | 100      | 83      | 99       | 90        | 90        | 59        | 63          | --          | --            |
| E. aerogenes                     | 52                | S                | 12         | 66         | 92      | --       | 62         | 72         | 84         | 100       | --       | 84       | 100     | 96        | 96        | 96        | 96          | 98          | 17            |
| E. cloacae                       | 140               | S                | 13         | 28         | 83      | 100      | 38         | 78         | 77         | 93        | --       | 81       | 100     | 98        | 98        | 92        | 95          | 92          | 25            |
| Serratia marcescens              | 57                | S                | 5          | 3          | 83      | --       | --         | 72         | 91         | 100       | --       | 78       | 97      | 97        | 95        | 91        | 95          | 95          | 95            |
| P. aeruginosa                    | 239               | S                | --         | --         | --      | 95       | --         | --         | 87         | --        | 84       | 70       | 91      | 98        | 78        | 89        | 70          | --          | --            |
| A. baumannii                     | 48                | S                | 60         | --         | --      | --       | --         | 48         | 27         | 42        | --       | 50       | 52      | 50        | 46        | 46        | 48          | 42          | 46            |
| Stenotrophomonas                 | 41                | S                | --         | --         | --      | --       | --         | 45         | --         | --        | --       | --       | --      | --        | --        | --        | --           | --           | --            |
Favorite Resources
(Tools for staying smart)

Why I love it:

Clear and concise
evaluate by organism, body part or drug
not overwhelming
accurate

$17 app
Favorite Resources
(Tools for staying smart)

Why I love it:
comprehensive
accurate

Why I don’t love it:
overwhelming
difficult to navigate

$30 app subscription 1 yr
Favorite Resources

(Tools for staying smart)

Medscape App

Now optimized for point-of-care decision making

Why I love it:
- comprehensive
- evaluate by disease or drug
- read more about disease

Why I don’t love it:
- sometimes buggy/
- updates

free
LOOKING SMART – NEW STUFF
Dalbavancin (Dalvance)

Glycopeptide (same class as vancomycin)

Approved for treatment of uncomplicated soft tissue infections by Gram + bacteria

Effective against MRSA

Dilute in sterile water or D5W; can dialyze
New Stuff
(Tools for looking smart)

Oritavancin (Orbactiv)

- Glycopeptide (same class as vancomycin)
- Approved for treatment of uncomplicated soft tissue infections by Gram + bacteria
- Effective against MRSA

1200mg single dose in 3 hour infusion

- No adjustment for mild/ mod renal impairment
- Never studied in severe renal or hepatic impairment
- Must be in D5W
- Falsely elevated pTT for 5 days
New Stuff
(Tools for looking smart)

ESBL

Extended Spectrum Beta-Lactamase Producing
  *E. coli*
  *Enterobacteriaceae*

Resistant to penicillins, cephalosporins, aztreonam, and Fluoroquinolones

Usually susceptible to Carbapenems, fosfomycin
Sepsis, Antibiotic Stewardship and the Emergency Department

Lauren Epstein, MD, MSc

Sepsis Lead

Epidemiology Research and Innovations Branch
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention
Objectives

- Review the importance of antibiotic stewardship
- Discuss how antibiotic stewardship and sepsis treatment align
- Discuss public health and sepsis prevention and identification activities
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- Review the importance of antibiotic stewardship

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- Discuss public health and sepsis prevention and identification activities
Antibiotics

- More than half of all hospitalized patients receive an antibiotic during their hospitalization

- However, 20-50% of all antibiotics prescribed in U.S. acute care hospitals are either unnecessary or inappropriate

- ED has a role to play in improving antibiotic prescribing

https://www.cdc.gov/getsmart/healthcare/implementation/clinicianguide.html
Inpatient Antibiotics

- 4 antibiotics made up approximately 45% of all antibiotic treatment
  - Vancomycin
  - Piperacillin-tazobactam
  - Ceftriaxone
  - Levofloxacin

Magill et al. 2014 JAMA
What is Antibiotic Stewardship?

- Measure antibiotic prescribing
- Improve antibiotic prescribing so that antibiotics are only prescribed and used when needed
- Minimize misdiagnoses or delayed diagnoses leading to underuse of antibiotics
- Ensure that the **right drug, dose, and duration** are selected when an antibiotic is needed

It’s about patient safety and delivering high-quality healthcare.
Antibiotic Stewardship – why?

- In the context of other medications, antibiotics are generally well-tolerated medications
  - Difficult to stop antibiotics if a patient is doing well or if a patient is doing poorly
  - Antibiotics are life-saving medicines that have risks and benefits
Antibiotic Resistance

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

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

*bacteria and fungus included in this report

$20 billion in excess direct healthcare costs annually

Antibiotics and Patient Safety

1. Antibiotic adverse events can be severe, examples:
   - Antibiotic-associated diarrhea (e.g., *C. difficile* infection)
   - Life-threatening allergic reactions (e.g., anaphylaxis)

2. Antibiotic adverse events can lead to ER visits
   - 1 in 1000 antibiotic prescriptions leads to an ER visit for an adverse event
     - ~200,000 estimated ER visits/year in U.S.

3. Antibiotic may have long-term consequences through disruption of microbiome

Antibiotic Stewardship Infrastructure

- Infrastructure within a facility should help providers choose appropriate antibiotic therapy and facilitate rapid administration of antibiotics:
  - There are hospitals that have pharmacy protocols that position antibiotics within units to facilitate rapid release
# Antibiotic Stewardship vs Infection Control

<table>
<thead>
<tr>
<th>Patient safety</th>
<th>Infection Control</th>
<th>antibiotic Stewardship Program</th>
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</thead>
<tbody>
<tr>
<td><strong>Optimize environment and protocols within the hospital to prevent infections</strong></td>
<td></td>
<td><strong>Optimize antibiotic therapy</strong></td>
</tr>
<tr>
<td>Treatment?</td>
<td><strong>Not responsible for diagnosis and treatment</strong></td>
<td><strong>Not responsible for diagnosis and treatment</strong></td>
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</table>
What Antibiotic Stewardship is NOT?

▪ It is not a mechanism to restrict or prevent antibiotics among patients with infections or suspected infections that need antibiotics.

▪ If there is an issue in any facility where antibiotic stewardship programs are impeding urgent antibiotic release for patients with sepsis or septic shock, this should be assessed and modified.
Antibiotic Stewardship Programs and Public Health

- Antibiotic stewardship interventions have been proven to improve individual patient outcomes, reduce the overall burden of antibiotic resistance, save healthcare dollars, and ultimately save lives.
Appropriate Antibiotic Use & Challenges in the ED

- ED’s role in appropriate antibiotic use
  - Diagnose sepsis and serious bacterial infections
  - Start empiric antibiotic therapy
  - Obtain appropriate cultures prior to treatment (e.g. blood cultures)
  - Prescribe antibiotics for discharged patients

- ED’s challenges in stewardship
  - Hard to capture all ED clinicians
  - Need for quick decision making
  - Lack of follow-up
  - Patient satisfaction & demand

May et al. 2013 Annals of Emergency Medicine
Antibiotic Stewardship and Sepsis

- No single template for a program to optimize antibiotic prescribing in hospitals

- Complexity of medical decision making and variability in the type and care among U.S. hospitals require flexibility in implementation
  - Adapting to ED is especially challenging

- Antibiotic stewardship has been successful in many different healthcare settings (i.e. long term care facilities, telemedicine)

Antibiotic Stewardship: Hospital Core Elements

- Leadership Commitment
- Accountability
- Drug Expertise
- Action
- Tracking
- Reporting
- Education

Antibiotic Stewardship: Outpatient Core Elements

- Commitment
- Action for policy and practice
- Tracking and reporting
- Education and expertise

https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html
ED and Antibiotic Stewardship

- Engaging ED as first stop in inpatient care
  - Have an ED clinician sit on the hospital antibiotic stewardship program
  - Leverage the ED pharmacist (<5% of EDs have a dedicated pharmacist)
  - Guide ED empiric treatment with clinical pathways, clinical decision support, antibiotic order forms
  - Collect cultures prior to starting antibiotics to help the inpatient team optimize therapy
  - Optimize antibiotic dosing

Objectives

▪ Review importance of antibiotic stewardship

▪ Discuss how antibiotic stewardship and sepsis treatment align

▪ Discuss public health and sepsis prevention and identification activities
Sepsis: Challenges to Diagnosis and Treatment

- Difficult to diagnose, no specific pathogen or clinical test for sepsis

- Lack of sepsis diagnostic specificity and the importance of initiating early antibiotic therapy likely contributes to inappropriate broad spectrum use of antibiotics

- A pathogen is not identified in most cases of sepsis and septic shock

- Viral infections also contribute to a significant amount to sepsis

- Sepsis can mimic other types of conditions
Sepsis: Challenges to Diagnosis and Treatment

**Diagnosing sepsis is subjective and highly variable: a survey of intensivists using case vignettes**

Chanu Rhee, Sameer S. Kadri, Robert L. Danner, Anthony F. Suffredini, Anthony F. Massaro, Barrett T. Kitch, Grace Lee, and Michael Klompas

- 5 case vignettes of patients with **suspected or confirmed infection** and **possible organ dysfunction** distributed to 94 academic intensivists
  - Respondents classified cases as SIRS alone, sepsis, severe sepsis, septic shock, or none of the above

Rhee et al, Crit Care 2016
Antibiotic Stewardship and Sepsis: ED

- Front line practitioners are important for addressing antibiotic resistance

- Broad spectrum antibiotic use is often the most appropriate initial regimen for life-threatening infections
  - Ensuring the **most appropriate empiric treatment** is a major focus of stewardship
  - Appropriate culture and diagnostics performed in the ED ensures antibiotics are tailored
Sepsis and Septic Shock vs Infections

- Imperative for early antibiotic administration in sepsis and septic shock
  - Antibiotics and source control are the backbone of sepsis treatment

- However, among patients with infections (without signs of sepsis) – further work can be performed prior to initiation of antibiotics
  - Getting a ‘true’ history of allergies from a family member or medical records if possible
  - Making sure appropriate tests are performed to localize the source of infection, including cultures if needed

http://jamanetwork.com/journals/jama/fullarticle/2598892
Sepsis Treatment: Antibiotic Stewardship

- The initial choice of an antibiotic in the ED is perhaps the most important dose the patient receives
  - Should be based on suspected infection, host factors and prior antibiotic exposure

- The antibiotic choice in the ED has significant influence on what therapy is continued in the inpatient setting
  - Represents an important opportunity for antibiotic stewardship

Pulia et al. 2016 Emergency Medicine Clinics of North America
Sepsis Treatment: Antibiotic Stewardship

- ED plays an important role in obtaining cultures prior to administration of antibiotics that allows for tailoring of antibiotic therapy during hospitalization

Pulia et al. 2016 Emergency Medicine Clinics of North America
Specimen Collection

- **Swabs are discouraged** since swabs usually have insufficient material for gram stain and culture;
  - if swabs must be used be sure quantity is adequate for both culture and gram stain

- **Do not culture chronic superficial wounds or sinus drainage** since superficial cultures correlate poorly with deep cultures

- **Stool:**
  - Multiple specimens per day are not indicated
  - Formed stools in general should not be submitted

https://www.cdc.gov/getsmart/healthcare/implementations/clinicianguide.html
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Sepsis Prevention Framework

**Pathogens**
- Identifiable Pathogen Prevention
  - Support vaccine development + promotion
  - Antimicrobial stewardship
  - Disease surveillance
  - Outbreak response
  - Infection prevention for HAIs

**Host Susceptibility**
- Demographics (e.g., Age, SES, access to care)
- Health Behaviors (e.g., smoking)
- Microbiome
- Immune and Genetic Factors
- Comorbidities (e.g., COPD, CHF, Cancer, Diabetes)
- Healthcare Factors (e.g., indwelling devices)

**Infection**
- Pathogen not identified in >50% sepsis

**Sepsis**

**Death**
Sepsis Questions: Public Health Perspective

- Who develops sepsis or infections that often lead to sepsis?

- How many persons get sepsis each year in the United States? How many die?

- How can CDC work to improve education for healthcare providers, patients and caregivers about sepsis?

- How can other research – microbiome disruption, patient skin or nasal disinfection, improved management of medical devices, etc. – contribute to sepsis prevention?
Vital Signs: Sepsis (August, 2016)
Thank You!

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Questions? Contact the E-QUAL team at equal@acep.org