Antibiotic Prescribing Practices

Get Smart About Antibiotics Week

CDC and SHARPS

November 17-21 2014
Did You Know?

- Up to 50% of antibiotic use in hospitals is either unnecessary or inappropriate.
- Antimicrobial overuse increases the development of drug-resistant organisms.
- Antibiotic resistance is one of the world’s most pressing public health threats.
Evolution of Antimicrobial Resistance

- *S. aureus* → Penicillin-resistant *S. aureus* [1950s]
- Penicillin-resistant *S. aureus* → Methicillin-resistant *S. aureus* (MRSA) [1970s]
- Methicillin-resistant *S. aureus* (MRSA) → Vancomycin-resistant enterococci (VRE) [1990s]
- Vancomycin-resistant *S. aureus* (VISA) [1997]
- Vancomycin-resistant enterococci (VRE) [2002]
Antimicrobial Resistance

Examples of How Antibiotic Resistance Spreads

- Animals get antibiotics and develop resistant bacteria in their guts.
- Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.
- Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.
- Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.
- George gets antibiotics and develops resistant bacteria in his gut.
- George stays at home and in the general community. Spreads resistant bacteria.
- George gets care at a hospital, nursing home or other inpatient care facility.
- Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.
- Patients go home.
- Resistant bacteria spread to other patients from surfaces within the healthcare facility.

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.
YOU ARE THE NEXT CLASS OF DRUG-RESISTANT BACTERIA. AS HUMAN CONTINUE TO ABUSE AND OVERUSE ANTIBIOTICS, YOUR RANKS WILL SWELL. SO, GO OUT THERE AND MUTATE! AND REMEMBER: THAT WHICH DOES NOT KILL US MAKES US STRONGER!!!
Methicillin-resistant *Staphylococcus aureus*

- CA-MRSA in children’s hospitals account for ~40-75% of all *S. aureus* isolates
Vancomycin -Resistant Enterococcus (VRE)

- VRE: Emerged in the United States in early 1990s
- Increase in prevalence:
  - % of enterococcal isolates from hospitalized patients that were VRE:
    - 1990-1997: <1%
    - 1999: 25%
    - 2003: 28.5%
Gram Negative Resistance

- Resistant gram negative bacteria are increasingly prevalent and equally important as resistant gram positive bacteria
- Increase in prevalence:
  - % of isolates that were resistant has increased over the past two decades
  - *K. pneumoniae, E. coli,* and *Pseudomonas aeruginosa*
Gram Negative Extended Spectrum B-Lactamases (ESBL)

- Enzymes that **inactivate** penicillins, cephalosporins and aztreonam
- Found in GNR
  - *E. coli*
  - *Klebsiella*
  - *Proteus mirabilis* and other gram negative
- ESBL producers are resistant to multiple drugs
- Labs can test to detect ESBL production for these organisms
Gram Negative AmpC B-Lactamases

- Preferentially hydrolyze cephalosporins
  - Resist inhibition by B-lactamase inhibitors
  - When hyperproduced they cause resistance to penicillins, cephalosporins, and aztreonam
Gram Negative Carbapenemases

- Diverse enzymes that hydrolyze carbapenems and other B-lactams
  - *Klebsiella pneumoniae* is the most common in the U.S.
    - Increased laboratory identification of carbapenem resistant *Klebsiella pneumoniae* in Pinellas County, FL 2010
- Often associated with extensive (sometimes total) antibiotic resistance
- Transmissible enzymes are the concern, as they can be acquired by pathogens such as *Pseudomonas*, *Acinetobacter*, and other *Enterobacteriaceae*
Antibiotic Use → → Resistance

- All antibiotic use can lead to resistance
- Bacteria multiply quickly and can mutate quickly
- Sub-therapeutic concentrations select for resistant bugs
- Longer durations = more resistance
- Unexpected effects between antibiotic classes
Duration of Therapy

- Prolonged (>14 days) antibiotic use associated with MRSA colonization\(^1\)
- In outpatients, longer duration of therapy associated with isolation of resistant bacteria\(^2\)

\(^1\)Couderc C et al. CID 2014;59:206-15
\(^2\)Costelloe C et al. BMJ 2010;340:c2096
Unexpected Effects on Resistance: Fluoroquinolones

- FQ use associated with MRSA acquisition\(^1\)
- FQ use associated with colonization by MDR Gram-negative bacilli\(^2\)

\(^1\)Couderc C et al. CID 2014;59:206-15
Methods to Improve Antimicrobial Use

• Antimicrobial stewardship
  ▪ Prescriber education
  ▪ Restrict use of broad-spectrum antibiotics
  ▪ Prior approval to start/continue
  ▪ Standardized antimicrobial order forms
  ▪ Pharmacy substitution or switch
Methods to Improve Antimicrobial Use

Use hospital data:
- The prevalence of resistance can vary in each hospital unit
- Know the local antibiogram
- Know the patient population you are treating
Methods to Improve Antimicrobial Use

Colonized or Infected: What is the Difference?

- Patients who carry bacteria without evidence of infection (clinical signs of infection) are colonized.
- If an infection develops, it may be from bacteria that colonize the patient.
- Bacteria that colonize patients can be transmitted from one patient to another by the hands of healthcare workers.

Isolation is still required!
Treat infection, not colonization

- A major cause of antimicrobial overuse is treatment of colonization

  - Treat pneumonia, not the tracheal aspirate
  - Treat bacteremia, not the catheter tip or hub
    - Use proper aseptic technique for obtaining blood cultures to avoid false positives
  - Treat urinary tract infections, not the indwelling catheter
Methods to Improve Antimicrobial Use: "Antibiotic Time-outs"

• Empiric antibiotics are often started while diagnostic information is being obtained.

• Too often, providers do not revisit the selection of the antibiotic after more clinical and laboratory data (including culture results) become available.
Methods to Improve Antimicrobial Use: “Antibiotic Time-outs”

• An antibiotic “time out” prompts a reassessment of the continuing need and choice of antibiotics when the clinical picture is clearer and more diagnostic information is available. **ALL CLINICIANS** should perform a **review** of antibiotics **48 hours after antibiotics are initiated** to answer these key questions:
Methods to Improve Antimicrobial Use: “Antibiotic Time-outs”

1. Does this patient have an infection that will respond to antibiotics?
2. If so, is the patient on the:
   • right antibiotic(s),
   • right dose? (indication specific, dosed for renal &/or hepatic dysfunction)
   • right route of administration? (can you transition the patient from IV to PO)
3. Can a more targeted antibiotic be used to treat the infection (de-escalate)?
4. How long should the patient receive the antibiotic(s)?
Methods to Improve Antimicrobial Use: “Antibiotic Time-outs”

Make it part of your daily patient rounds
Choosing the Appropriate Antibiotic

- Efficacy - MICs and pharmacokinetics
- Route of administration
- Adverse effects
- Drug interactions
- Cost
- Narrowest spectrum
- Site of infection
- Optimal dosing
Antibiotic Duplication

... Avoiding Duplicate Therapy

Combinations of drugs may represent unnecessary overlap in antimicrobial spectra

Example: Zosyn® + metronidazole for intra-abdominal infection
Antibiotic De-escalation

"STUCK IN THE MIDDLE"
Unasyn, Cefuroxime, Septra, Cefoxitin

Broad Spectrum: Zosyn, Timentin,
Levofloxacin, Meropenem, Imipenem,
Cefepime, Cefotaxime, Ceftriaxone

Narrow Spectrum: Penicillin,
Ampicillin, Oxacillin, Cefazolin,
Linezolid, Clindamycin, Vancomycin

... De-escalating Therapy

Based on culture &/or susceptibility results:
Can you narrow the spectrum?
Can you transition IV → PO?
Are antibiotics necessary? (i.e. infection vs. colonization or negative cultures for >48-72 hours)
Some Examples of Antibiotics Used in Pediatrics

**Narrow Spectrum**
- amoxicillin
- PCN VK
- cephalexin

**Broad Spectrum**
- Cephalosporins
  - cefepime
  - ceftazidime
  - ceftriaxone
  - cefotaxime
  - cefdinir
- Beta lactamase inhibitors
  - amoxicillin/clavulanate
  - ampicillin/sulbactam
  - ticarcillin/clavulanate
  - piperacillin/tazobactam
Some Examples of Antibiotics Used in Pediatrics

- **Broad Spectrum Carbapenems**
  - imipenem/cilastatin
  - meropenem
  - ertapenem

- **Broad Spectrum Quinolones**
  - moxifloxacin
  - levofloxacin
  - ciprofloxacin
Select Duration of Antibiotics Wisely

- Finland published the treatment of pneumonia with Penicillin in the NEJM in 1945
  - Length of therapy was determined by:
    - Resolution of symptoms and signs
    - Treatment until temperature remained <100 F for 12 hours then given another 2-3 days of PCN

*Treatment of Pneumococcal Pneumonia with Penicillin. NEJM 1945;232 (26):747-755*
FIGURE 7. Course and Treatment in Case 40.

This patient had a severe pneumonia with involvement of the entire right lung on admission. He had been treated with sulfadiazine at home for about six days and had an adequate blood level of the drug on entry to the hospital. There was a steady drop in temperature after penicillin treatment was started, and clinical improvement followed.
Select Duration of Antibiotics Wisely

• Stop treatment when infection is cured or unlikely
  – Evaluate duration of treatment for tracheitis, pneumonia and sinusitis
  – Are antimicrobial agents always needed for staphylococcal skin abscess?
SUMMARY
Appropriate Antimicrobial Use

Avoid Antibiotic when not indicated

RIGHT DRUG
Against most likely pathogen
Resistance patterns
Patient risk factors
De-escalation

RIGHT DOSE
For indication/site of infection
Reduce risk of resistance
Avoid toxicity
Efficient kill

RIGHT DURATION
Shorter therapy
Reduce risk of resistance
Avoid toxicity
Cases
Selecting Antibiotics/Using the Antibiogram
Case #1

A 2 year old male with short gut is receiving TPN via Broviac line presents with fever and irritability. The blood culture is growing gamma hemolytic gram positive cocci in chains. What is your empiric antibiotic treatment?
Case #2

- An 8 month old female develops a large abscess involving the right thigh with erythema, swelling and tenderness that does not respond to cephalexin as an outpatient. She returns to the ED. She is admitted for an I & D. A wound culture is growing gram positive cocci in clusters. What is your empiric therapy?
Case #3

• A 10 year old male with resolved *S. pneumoniae* sepsis has been on a mechanical ventilator for 10 days for ARDS. He develops new onset fever and hypotension while on cefotaxim, a blood culture is sent from his CVL. The culture is growing *Serratia*. What is your antibiotic recommendation?
Case #4

• A premature neonate in the NICU has a blood culture positive for *Staphylococcus epidermidis* susceptible to everything tested including oxacillin. Because this seems unusual, you call the microbiology lab. How often does it really happen?
Case #5

- A 4 year old female with recurrent UTIs and VUR presents with urosepsis. On the wards, she is started on vancomycin and cefotaxime. She does not have meningitis. The following day she is transferred to the PICU after she develops hypotension and respiratory distress. The urine and blood culture grow *Enterobacter cloacae*. What are your antibiotic recommendations pending susceptibility results?
Case #6

- A 10 y/o male with spina bifida and neurogenic bladder has *Pseudomonas aeruginosa* growing in the urine. On admission he was started on gentamicin. What is the chance of the organism being susceptible to gentamicin?
Case #7

- A 3 year old female is admitted with pneumonia and a parapneumonic effusion. She is started on IV clindamycin. Pleural fluid from the chest tube is growing gram positive cocci in chains. She does not have meningitis. What is your empiric antibiotic choice?

The organism is identified as *S. pneumoniae* with MIC to PCN 1

- IV PCN infections outside CNS MIC: $\leq 2$ (S), 4 (I), $\geq 8$ (R)
- IV PCN CNS infections: MIC: $\leq 0.06$ (S), $\geq 0.12$ (R)
Case #8

• A 12 y/o male is admitted with an extensive right foot cellulitis without abscess. He is started on vancomycin. He is having very slow clinical improvement. The wound culture grows *Streptococcus pyogenes*. What is your antibiotic choice?
Case # 9

• 6 y/o female is admitted from the CF clinic with pulmonary exacerbation. She is empirically started on ceftazidime and tobramycin. She has had no clinical improvement. She undergoes a BAL. The lab calls to inform you that her BAL fluid is growing *Stenotrophomonas*. What is your antibiotic choice?
Case #10

- 3 month old male presents with 105 F fever, diarrhea and dehydration to the ED. He is admitted for IV fluid hydration. His blood culture is growing a gram negative rod. CSF culture is negative. The patient is empirically started on meropenem. The bacteria is identified as Salmonella (non-typhi). What is your antibiotic recommendation?
Case # 11

- 3 month old female presents with fever and lethargy. CSF is growing *Streptococcus pneumoniae*. What is your antibiotic management pending susceptibility results?
Case #12

- 35-week male is born without complication. On DOL #2 he develops respiratory distress and is transferred to the NICU. Ampicillin and gentamicin are started. The blood culture is growing small variable sized gram negative bacilli. His CSF has the same organism. What is your antibiotic recommendation?
Questions?

GET SMART
About Antibiotics Week
WWW.CDC.GOV/GETSMART
Evaluation of Pharmacokinetic/Pharmacodynamic Parameters as Related to Outcomes and Resistance

Introduction Presented by David S. Burgess, PharmD
## Summary Of Antimicrobial Pharmacodynamic Parameters

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Streptococcal Hemolysis

- **Alpha** (incomplete, green)
  - Viridans streptococci
  - *Streptococcus pneumoniae*
- **Beta** (complete, clear)
  - Group A (*Streptococcus pyogenes*)
  - Group B (*Streptococcus agalactiae*)
  - Group C and G
- **Gamma** (nonhemolytic)
  - *Enterococcus sp.*
  - Less commonly: *S. bovis, S. equinus,* some Viridans streptococci (Anginosus group, Mutans group, Mitis group, Salivarius group)