PRINCIPLES OF ANTIBIOTIC USE

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dcasip.medicine.duke.edu
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Objectives

Understand why antibiotics are “special” medications
The 4 Moments of Antibiotic Decision-Making
Antimicrobial Stewardship Programs
“Action” strategies in different clinical settings
We Love Antibiotics

<table>
<thead>
<tr>
<th>Inpatient</th>
<th>Long-term Care</th>
<th>Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>At any given time, 65% of inpatients at DUMC are receiving at least one antibiotic</td>
<td>Up to 70% of residents in a nursing home receive one or more courses of systemic antibiotics when followed over a year</td>
<td>423-553 antibiotic prescriptions per 1000 people in the US per year</td>
</tr>
<tr>
<td>There are &gt;31,000 antibiotic orders (new starts) placed at DUMC annually</td>
<td>40-75% of antibiotic prescriptions are inappropriate</td>
<td>30% are unnecessary, (representing 47 million prescriptions/year)</td>
</tr>
<tr>
<td>DUMC spends &gt;$10 million on antimicrobial agents each year</td>
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</tbody>
</table>
Why We Love Antibiotics

Wonder Drug
Antibiotics are time-tested placebos

Active intervention
Antibiotic Rx is easy:
- Avoids doing a structured exam or long DDx
- Avoids time-consuming discussions
- i.e. Easier to treat than diagnose or educate

Experiences
Identifying Infected vs. Not Infected is hard

Tangible
“Just in case” perceived to be lower risk than “watchful waiting”

Insurance
Why we HAVE TO improve Antibiotic Use

Antibiotics are unlike any other drug, in that the use of the agent in one patient can compromise its efficacy in another.

A lot of antibiotic prescriptions are unnecessary or sub-optimal.

We are running out of antibiotics.

Antibiotic misuse harms patients.

Improving antibiotic use has many benefits for patients and society.

Slide adapted from Arjun Srinivasan, MD (CDC)
Antimicrobial Use Impacts: Infection Prevention, HAIs, AND Patient Outcomes

Drug-resistance (MRSA, VRE, CRE, FQR-EC)

*C. difficile* infection

Infection treatment success/failure
- Complications
- Readmissions
- Mortality
- Length of Stay

Adverse Safety Events
- Allergic reactions
- Drug toxicity events
- Acute Kidney Injury

Healthcare Resources and Cost
- (all of the above)
- Pharmacy budget; ICU days
One in Five Inpatients get an Antibiotic Adverse Drug Event

1488 patients followed for 30 days after antibiotic initiation

Followed 90 days for CDI and MDRO acquisition

General medical inpatients who had at least 24h of antibiotics during admission

20% of patients experienced at least one antibiotic-associated ADE

Making the Right Decision Is Important

Prospective study of febrile adult patients
30 day follow up
All cause mortality 20% vs 11.8% in febrile patients prescribed inappropriate vs. appropriate empiric abx (p=0.01; OR 1.88; 95% CI 1.29-2.72)
Length of stay >2 days longer if inappropriate empiric antibiotics prescribed (p = 0.002)

Wrong Antibiotic = Increased Mortality

655 ICU admissions with underlying infections
- 62% pneumonia
- 34% BSI

Inadequate antimicrobial therapy independently associated with increased mortality
- RR 4.26

<table>
<thead>
<tr>
<th>Sometimes, You Don’t Need An Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Don’t routinely prescribe antibiotics for <strong>acute mild-to-moderate sinusitis</strong> unless symptoms last for seven or more days, or symptoms worsen after initial clinical improvement</td>
</tr>
<tr>
<td>Don’t order antibiotics for <strong>adenoviral conjunctivitis</strong></td>
</tr>
<tr>
<td>Don’t routinely provide antibiotics before or after <strong>intravitreal injections</strong></td>
</tr>
<tr>
<td>Don’t prescribe oral antibiotics for <strong>uncomplicated acute tympanostomy tube otorrhea</strong></td>
</tr>
</tbody>
</table>

www.choosingwisely.org
AU represents a modifiable risk

AU in Nursing Homes is highly variable and correlated with AEs

Daneman et al. JAMA IM 2015;175 (8): 1331-1339
What is optimal antibiotic therapy…?

Right Diagnosis
Right Drug
Right Dose
Right Timing
Right Duration

Improve therapeutic choices (underuse)
Reduce unnecessary use (overuse)
Why “Good” Antibiotics Fail

Drug-related
- suboptimal dosing
- poor penetration

Patient-related
- comorbidities
- organ dysfunction
- immunocompromised host

Pathogen-related
- resistance
- virulence
- high inoculum
- biofilms

Site-related
- undrained abscesses
- foreign body

The “4 Moments” of Antibiotic Decision-Making

1. Does the patient have an infection that requires antibiotics?
2. Have I ordered appropriate cultures before starting antibiotics?
   What empirical antibiotic therapy should I initiate?
3. A day or more has passed.
   Can I stop antibiotics?
   Can I narrow therapy?
   Can I change from IV to oral therapy?
4. What duration of antibiotic therapy is needed for this patient’s diagnosis?

Tamma PD et al. JAMA. 2019;321(2):139-140.
The “Six Ds” of Antimicrobial Stewardship

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Make and document the right diagnosis.</td>
</tr>
<tr>
<td>Debridement/Drainage</td>
<td>Drainage of abscesses and removal of necrotic tissue of foreign material when required.</td>
</tr>
<tr>
<td>Drug</td>
<td>Use the right drug empirically according to suspected or confirmed diagnosis, risk factors for resistant pathogens, allergy, or major side effects.</td>
</tr>
<tr>
<td>Dose</td>
<td>Use right dose according to diagnosis, site of infection, or renal/hepatic dysfunction.</td>
</tr>
<tr>
<td>Duration</td>
<td>Use drugs for an appropriate duration.</td>
</tr>
<tr>
<td>De-escalation</td>
<td>Re-evaluate diagnosis and therapy routinely and de-escalate therapy to narrow-spectrum and/or oral agents when appropriate.</td>
</tr>
</tbody>
</table>

General Indications for Antibiotics

Prophylaxis: prevent infection
- EASY! Guidelines and ordersets

Empiric: when you suspect infection but don’t exactly know with what pathogen
- Not easy. Local guidelines help (based on local micro data).

Directed: pathogen known
- Moderately easy. Follow and interpret patient-specific micro data.
Choice of Empiric Antimicrobials

What class of pathogen am I likely to be treating?
- (Bacterial? Viral? Fungal? Other?)

If bacterial, what organisms are most likely?
- (Gram positive? Gram negative? Anaerobe?)

What information can I get to guide treatment?
- Microbiology data?

Do I need to order any other diagnostic tests?

How sick is my patient? How risky would it be if I miss?

Is my patient “special”? – allergy, ADEs, immune status

Have I ordered appropriate cultures before starting antibiotics?

What empirical antibiotic therapy should I initiate?
De-escalation

De-escalation is a core principle of Antimicrobial Stewardship.

Target/narrow antibiotic therapies after more clinical data returns

Stop therapy when infection has been ruled out

A day or more has passed.

Can I stop antibiotics?
Can I narrow therapy?
Can I change from IV to oral therapy?
Clinical information trickles in over time.

This means clinicians have to reassess regularly.

This also means they get interrupted with ‘real-time’ notifications and need to respond.

This a complex process: unpredictable, unknowns, uncertainty.

Putting the puzzle together completely takes attention, follow up on details, ability to make decisions in the setting of unknowns, AND an eye on the long-term goals.
DIAGNOSIS

Microbiologic Culture
- “Gold standard”
- Requires sampling of site of infection prior to therapy
- Allows determination of antimicrobial susceptibility

Growth?
- Stain (Prelim ID)
- Definitive ID
- Susceptibility testing
DIAGNOSIS: Stain

Direct Visualization

Gram stain
- Often provide clues to etiology (may allow presumptive diagnosis in some cases)
- Gram Positive
- Gram Negative
- Non-staining

Shape
- Cocci
- Rods

Aerobic/Anaerobic

www.laboratoryinfo.com
Quick and Dirty Anti-bacterial Classification

Gram positive – skin, lung, guts, devices
Gram negative – guts, urine, some lung
Atypical – lung, STIs
Anaerobes – gas- and abscess-forming, bad odors
Antifungals – guts, devices, immunosuppressed + abx-exposed hosts
GRAM POSITIVE ORGANISMS

Gram positive cocci
- *Staphylococcus aureus*
- Coagulase negative staphylococcus
- *Streptococcus pneumoniae*
- *Streptococcus* sp.
- *Enterococcus* sp.

Gram positive rods
- *Bacillus* sp. (aerobes)
- *Clostridium* sp. (anaerobes)

Gram positive – skin, lung, guts, devices
# Antibiotics with Gram Positive (+) Activity

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>S. aureus</th>
<th>MRSA</th>
<th>VRE</th>
<th>E. faecalis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nafcillin/Oxacillin</td>
<td></td>
<td></td>
<td></td>
<td>Ampicillin</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam, Piperacillin/Tazobactam</td>
<td></td>
<td></td>
<td></td>
<td>Ampicillin/Sulbactam, Piperacillin/Tazobactam</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td></td>
<td></td>
<td></td>
<td>Ceftaroline (only)</td>
</tr>
<tr>
<td>Carbapenems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Fluoroquinolones)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td></td>
<td></td>
<td></td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Clindamycin+/-</td>
<td></td>
<td></td>
<td></td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Linezolid</td>
<td></td>
<td></td>
<td></td>
<td>Linezolid</td>
</tr>
<tr>
<td>Daptomycin</td>
<td></td>
<td></td>
<td></td>
<td>Daptomycin</td>
</tr>
<tr>
<td>Telavancin</td>
<td></td>
<td></td>
<td></td>
<td>Telavancin</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td></td>
<td></td>
<td></td>
<td>TMP-SMX</td>
</tr>
<tr>
<td>Dalvabancin, Oritavancin</td>
<td></td>
<td></td>
<td></td>
<td>Dalvabancin, Oritavancin</td>
</tr>
</tbody>
</table>
GRAM NEGATIVE ORGANISMS

Gram negative cocci
- Neisseria meningitidis
- Neisseria gonorrhoeae

Gram negative rods (enteric)
- E. coli
- Klebsiella sp.
- Enterobacter sp.
- Proteus sp.
- Serratia sp.

Gram negative rods (non-enteric, non-lactose fermenters)
- Pseudomonas aeruginosa
- Stenotrophomonas maltophilia
- Acinetobacter sp.

Gram- negative: guts, urine, some lung
## Antibiotics with Gram Negative (-) Activity

<table>
<thead>
<tr>
<th>Antibiotic Class</th>
<th>E. coli</th>
<th>K. pneumoniae</th>
<th>Enterobacter</th>
<th>P. aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Ampicillin)</td>
<td>(Ampicillin)</td>
<td>(Ampicillin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Amp/sulb)</td>
<td>(Amp/sulb)</td>
<td>(Amp/sulb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pip/Tazo</td>
<td>Pip/Tazo</td>
<td>Pip/Tazo</td>
<td>Pip/Tazo</td>
<td>Pip/Tazo</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Cephalosporins</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;, 4&lt;sup&gt;th&lt;/sup&gt;, 5&lt;sup&gt;th&lt;/sup&gt; gen.</td>
<td>Ceftaz/Cefepime</td>
<td></td>
</tr>
<tr>
<td>Carbapenems</td>
<td>Carbapenems</td>
<td>Carbapenems</td>
<td>Carbapenems</td>
<td>Imip, Mero, Dori</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Aztreonam</td>
<td>Aztreonam</td>
<td>Aztreonam</td>
<td>Aztreonam</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Aminoglycosides</td>
<td>Aminoglycosides</td>
<td>Aminoglycosides</td>
<td>Amino-glycosides</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>Fluoroquinolone</td>
<td>Fluoroquinolone</td>
<td>Fluoroquinolone</td>
<td>Cipro and Levo</td>
</tr>
<tr>
<td>Trimeth/Sulf</td>
<td>Trimeth/Sulf</td>
<td>Trimeth/Sulf</td>
<td>Trimeth/Sulf</td>
<td></td>
</tr>
</tbody>
</table>
Antibiotics with Anti-anaerobic Activity

<table>
<thead>
<tr>
<th>Class</th>
<th>Agents (Route)</th>
<th>B. fragilis susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-lactam</td>
<td>amoxicillin/clav (PO)</td>
<td>90-97%</td>
</tr>
<tr>
<td>beta-lactamase inhibitor combinations</td>
<td>ampicillin/subl (IV)</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>piperacillin/tazo (IV)</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>cefotetan (IV)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>cefoxitin (IV)</td>
<td>83-90%</td>
</tr>
<tr>
<td>Carbapenem</td>
<td>doripenem (IV)</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td></td>
<td>ertapenem (IV/IM)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>meropenem (IV)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>imipenem (IV)</td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>moxifloxacin (IV/PO)</td>
<td>66-70%</td>
</tr>
<tr>
<td>Other</td>
<td>clindamycin (IV/PO)</td>
<td>66-70%</td>
</tr>
<tr>
<td></td>
<td>metronidazole (IV/PO)</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td></td>
<td>tigecycline (IV)</td>
<td>81-96%</td>
</tr>
</tbody>
</table>

*B. fragilis* is the most common group of gut anaerobes. Then GPCs (*Clostridium* spp.)

Also consider: mouth, vaginal sources

Gas- and abscess-forming, bad odors

*C. difficile* is a special case (oral vancomycin).
NON-STAINING PATHOGENS

- Not stained by Gram’s method (Intracellular)
  - *Legionella* sp.
  - *Chlamydia*
  - *Rickettsia*

- Mycobacteria
  - *M. tuberculosis*
  - Non-tuberculous mycobacteria

Ziehl-Neelsen Stain of TB
Atypicals

Macrolides:
- Azithromycin
- Clarithromycin

Tetracyclines:
- Doxycycline
- Minocycline

<table>
<thead>
<tr>
<th>Community-acquired pneumonia</th>
<th>Pathogens</th>
<th>CXR pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical pneumonia</td>
<td>Bacterial: S. Pneumoniae H. Influenzae</td>
<td>Lobar, dense</td>
</tr>
<tr>
<td>Atypical pneumonia</td>
<td>Viral: influenza, RSV Bacterial: Legionella Mycoplasma Chlamydia</td>
<td>Diffuse, patchy</td>
</tr>
</tbody>
</table>
Mechanisms of Action of Antibiotics

- **DNA replication**
- **Nucleotide biosynthesis**
- **Protein synthesis**
- **Topo-isomerase**
- **RNA transcription**
- **Cell wall synthesis**
- **β-lactams**
  - Cephalosporins
  - Carbapenems
- **Cell wall integrity**
- **Cytoplasmic membrane integrity**
- **Protein synthesis**
- **mRNA**
- **Sulfonamides**
  - TMP-SMX
- **Fluoroquinolones**
- **Metronidazole**
- **Penicillins**
- **Rifampin**
- **Tetracyclines**
- **Aminoglycosides**
- **Macrolides**
- **Oxazolidinones**
- **Glycylcyclines**
- **Streptogramins**
- **Lincosamides**

Cell membrane and cell wall

Beta-lactams: Interfere with cell wall synthesis
- **Penicillins**: Oxacillin, ampicillin, piperacillin
- **Cephalosporins**: 1°, 2°, 3°, 4°, 5° cephalosporins
- **Carbapenems**: Imipenem, meropenem, ertapenem, doripenem
- **Monobactams**: Aztreonam

Peptide antibiotics disrupt cell membrane integrity
- **Glycopeptide**: Vancomycin, oritavancin, telavancin, dalbavancin
- **Cyclic Lipopeptide**: Daptomycin
ANTIBACTERIALS: MECHANISMS

Interference with ribosomal function

- **Aminoglycosides:**
  - Gentamicin, tobramycin, amikacin
- **Tetracyclines:**
  - Tetracycline, minocycline, doxycycline
  - Omadacycline, eravacycline
- **Glycylcyclines:**
  - Tigecycline
- **Macrolides:**
  - Erythromycin, azithromycin, clarithromycin
- **Chloramphenicol**
- **Lincosamides:**
  - Clindamycin
- **Oxazolidinone:**
  - Linezolid, Tedizolid
Antimetabolites

- Sulfonamides
- Trimethoprim-sulfamethoxazole

Inhibition of DNA-directed RNA polymerase

- Rifampin, rifapentine, rifabutin

Degradation of DNA

- Metronidazole

Inhibit of DNA gyrase (bactericidal)

- **Quinolones:**
  - Ciprofloxacin, levofloxacin, moxifloxacin
DIAGNOSIS

Antigen tests

- Very useful for following (and sometimes diagnosing) viral infections: HIV, HBV, HCV, EBV, CMV
- Occasionally useful for other pathogens (e.g., cryptococcus)
DIAGNOSIS

Serology

- For bacterial infections, generally not useful in early diagnosis (usually requires acute and convalescent tests)
- For viral infections, IgM may allow early diagnosis (e.g., HepA)
DIAGNOSIS

PCR and other “molecular” tests
- Increasingly used allows diagnosis of non-culturable pathogens (e.g., norovirus) and faster identification (e.g., pertussis, MRSA in blood);
- Subject to false positives due to sensitivity (e.g. C. difficile)
Patients are individuals.

Drug interactions
Age
Allergies
Pregnancy, breast feeding
Toxicity (idiosyncratic reactions)
Dose adjustment for renal and/or hepatic dysfunction
Ability to absorb an oral antibiotic
Immune status

Adherence:
- Cost
- Taste
- Frequency of administration
- Pill size
- Duration of therapy
- Multiple drug therapy
- Adverse effects
- Current symptoms
Pathogens are tricky.

Antibiotic = A drug that kills or inhibits the growth of bacterial pathogens

Resistant = Somewhat arbitrary designation that implies that an antimicrobial will not inhibit bacterial growth at clinically achievable concentrations

Susceptible = Somewhat arbitrary designation that implies that an antimicrobial will inhibit bacterial growth at clinically achievable concentrations
Key Terms

MIC = Minimal inhibitory concentration. Lowest concentration of antimicrobial that inhibits growth of bacteria. Commonly used in clinical lab.

MBC = Minimal bactericidal concentration. Concentration of an antimicrobial that kills bacteria. Used clinically only in special circumstances.

Breakpoint = The MIC that is used to designate between susceptible and resistant.
Methods for Testing Resistance: Minimal Inhibitory Concentration

Known quantity of bacteria placed into each tube

Lowest concentration of an antimicrobial that results in the inhibition of visible growth of a microorganism

Increasing antibiotic concentration

0.25 µg/mL
0.5 µg/mL
1.0 µg/mL
2.0 µg/mL
4.0 µg/mL
8.0 µg/mL
16 µg/mL

Durations

- Most guideline-recommended antibiotic durations are based on...
- Qualified with “it depends…”
- Duration questions are ~70% of ID consults.

Trials comparing short- vs. longer-course antibiotics have shown short-course is just as effective.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Antibiotic Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>3-5 days</td>
</tr>
<tr>
<td>Long</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Nosocomial pneumonia (HAP/VAP)</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>≤ 8 days</td>
</tr>
<tr>
<td>Long</td>
<td>10-15 days</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>5-7 days</td>
</tr>
<tr>
<td>Long</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>4 days</td>
</tr>
<tr>
<td>Long</td>
<td>10 days</td>
</tr>
<tr>
<td>Acute exacerbation of chronic bronchitis (AECB) and COPD</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>≤ 5 days</td>
</tr>
<tr>
<td>Long</td>
<td>≥ 7 days</td>
</tr>
<tr>
<td>Acute bacterial sinusitis</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>5 days</td>
</tr>
<tr>
<td>Long</td>
<td>10 days</td>
</tr>
<tr>
<td>Cellulitis</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>5-6 days</td>
</tr>
<tr>
<td>Long</td>
<td>10 days</td>
</tr>
<tr>
<td>Chronic osteomyelitis</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>42 days</td>
</tr>
<tr>
<td>Long</td>
<td>84 days</td>
</tr>
</tbody>
</table>

5 is the new 7.
WHAT IS ANTIMICROBIAL STEWARDSHIP?
“coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the selection of the optimal [antibiotic] drug regimen including dosing, duration of therapy, and route of administration.”

-- *Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS)*

Antimicrobial Stewardship Program

Decision support for prescribers of antimicrobials.

Coordinated program

Multidisciplinary teams
- MD, PharmD, RN, micro, IP, IT

Multi-level interventions:
- Educational
- Systems-based vs. 1:1
- Technology
- Active vs. Passive

Goals of Antimicrobial Stewardship

Primary:
- Improve quality and increase safety through appropriate use of antimicrobials
  - Improve therapeutic choices (underuse)
  - Reduce unnecessary use (overuse)

Secondary:
- Decrease emergence of resistance

Desirable “side effects” from an ASP:
- Decrease costs for health system
- Satisfy regulatory requirements

The goal is NOT to decrease antibiotic use…
It’s to IMPROVE antibiotic use!
Regulators are coming here.

AS, antimicrobial stewardship; ASP, antimicrobial stewardship programs
Resources for Inpatient Stewardship

IDSA/SHEA guidelines on Implementing an ASP: CID 2016;62(10):e51–e77

CDC Core Elements Document(s):
https://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf

The Joint Commission Standard:
https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf
<table>
<thead>
<tr>
<th>Strength of Rec</th>
<th>Strategies</th>
</tr>
</thead>
</table>
| Strong         | Preauthorization/restriction  
Prospective audit & feedback  
CDI-focused intervention  
PK monitoring (AG)  
IV/PO switch  
Duration-focused intervention |

| Weak           | Facility-specific guidelines  
Syndrome-specific intervention  
Time-out/Auto Stop  
Computerized Decision Support  
PK monitoring (Vanco)  
Alternate dosing for Beta Lactams  
Penicillin allergy assessments  
Stratified antibiograms  
Cascaded reporting of susceptibilities  
Rapid diagnostics: virus, blood culture  
Serial procalcitonin in ICU sepsis  
Fungal markers in Hem malignancy  
Febrile Neutropenia guidelines  
Antifungals in immunocompromised  
DOT>DDD AU data |

| Good Clinical Practice | Cost > purchasing data  
Choose clinical outcome metrics wisely  
Promote AS in SNFs, NICUs, terminally ill |

| Rec Against | Antibiotic Cycling  
Didactic education alone |

"Action" for inpatient ASPs

LOTS of potential AS strategies suggested in Guidelines

Must be tailored to institutional need and priorities

AVOID: overtaxed ASP personnel

CID 2016;62(10):e51–e77
“Actions” for Inpatient Stewardship

Preauthorization/restriction (before prescribing)
- Can be time/personnel intensive
- Must think through unintended consequences and process snafus
- Not for all hospitals – local culture plays a role
- Best if for targeted agents (not every antibiotic order…)

Post-prescription audit and feedback (after prescribing)
- Front-line stewardship “experts” actively review patients on antibiotics and give feedback to prescribers 1:1
- Time intensive, but effective
- Better for personal relationships
- Need ID “back up” for tough cases
“Tracking” Antibiotic Use

NHSN AU Option is optional/voluntary for acute care hospitals

- ONLY uses electronic data from EHRs (no manual surveillance and no subjective components)

Rate: Days of therapy (DOT) per 1,000 days present

- DOT = calendar days of treatment regardless of number of doses
- Separate drugs counted separately
- Denominator is DIFFERENT than patient days

Data is stratified by Agent, Route, Unit location

Certain agent groups/locations have a benchmark – “SAAR”

- Standardized Antibiotic Administration Ratio: Observed/Expected based on NHSN baseline + limited risk adjustment with information from annual survey
- Example group: “Agents primarily used for resistant gram positive infections”
- Only med/surgical units and ICUs (no benchmarks for specialized areas)

Benchmarking AU between Hospitals

Ongoing area of research, more data emerging

What you want to measure:
- Prescribing practices and decision-making

What you get:
- Tonnage or measure of abx exposure – not “appropriate” abx

Problems:
- Case mix
- Hospital size
- Clinical service lines (e.g. surgical specialties, types of ICUs, moms/babies)
- Assume more = bad (not always true clinically)

Should be viewed as a starting point for further investigation and explanation.

Stenehjem. CID 2016;63(10):1273–80
CMS: ASP required in Long-term Care

CMS Requirement for Long-term Care ASPs Nov 2017*
*deferred citations for 18 months

Barriers to Implementation of AS in LTC:
Knowledge/Evidence
Expertise
Different stakeholders + processes of care than acute care
Personnel and turnover
Resources for LTC Stewardship

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<th>Table 1</th>
<th>Resources for Antibiotic Stewardship in LTC</th>
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Special Article

Template for an Antibiotic Stewardship Policy for Post-Acute and Long-Term Care Settings

Robin L.P. Jump MD, PhD a,b,*, Swati Gaur MD, MBA, CMD c, Morgan J. Katz MD d, Christopher J. Crnic MD, PhD c,f, Ghinwa Dumyati MD, MSc, Muhammad S. Ashraf MBBS b, Elizabeth Frentzel MPH 1, Steven J. Schweon RN, MPH, MSN, CIC, HEM 1, Philip Sloane MD, MPH 1, David Nace MD, MPH, CMD 1 on behalf of the Infection Advisory Committee for AMDA—The Society of Post-Acute and Long-Term Care Medicine.

CDC Core Elements

AHRQ Guide

CMS Standard Interpretive Guidance

Duke Center for Antimicrobial Stewardship and Infection Prevention
Examples of Stewardship “Action” in LTC

Antibiotic use protocols – “Minimum Criteria” for Abx starts

Test/diagnostic stewardship
- UA/culture
- C. difficile

Durations/length of therapy
- UTI
- Pneumonia
- Cellulitis

“Active monitoring” as an alternative to empiric antibiotics in patients who have a clinically undifferentiated problem (e.g. “not at baseline”)
Example: Antibiotic Use Protocol

Target: nursing assessment
Identifies “red flag” symptoms
Includes “notes” that identify key areas for baseline knowledge
Provides next steps alternative (other than an antibiotic)

AHRQ Toolkit: “Minimum Criteria for Common Infections”
• This is an active process
• More frequent vital signs
• Oral hydration
• Assess for pain, changes in medicine, other reasons like a bad night’s sleep
• (or disagreement with a loved one)
Careful Observation Order Set

- Obtain vital signs (BP, Pulse, Resp Rate, Temp, Pulse Ox) every ____ hours for ____ days.
- Record fluid intake each shift for ______ days.
- Notify physician if fluid intake is less than ______ cc daily.
- Offer resident _____ ounces of water / juice every _____ hours.
- Notify physician, NP, or PA if condition worsens, or if no improvement in _____ hours.
- Obtain the following blood work ________________________________.
- Consult pharmacist to review medication regimen.
- Contact the physician, NP, PA with an update on the resident’s condition on ________.
Potential Policies & Procedures

- Concerns about stinky or cloudy urine should lead to increased hydration and perhaps, watchful waiting/careful observation.
- Automatic review of all medication changes by outside providers.
- Send residents to the Emergency Room with a note clearly stating what you are (and are not) worried about.
Potential Policies & Procedures

- Clear criteria for collecting a urine sample
- Documented protocol for proper sample collection and handling
- Communication tools when nurses call a covering provider
- Proactively talk to residents and their family members—on admission and during change of status
Resources for Outpatient Stewardship

No regulatory requirements (yet)
- Drafted for TJC, open for public comment

4 “Core Elements”

Type of outpatient practice setting is highly varied
- Adult/pediatric
- Specialty clinics
- Retail clinics
- Urgent Care

https://www.cdc.gov/antibiotic-use/community/pdfs/16_268900-A_CoreElementsOutpatient_508.pdf
“Action” in Outpatient Stewardship

Most literature in Primary or Urgent Care

Peer comparison + data feedback

- Most commonly done for upper respiratory infection
- Identify diagnoses (e.g. viral URI) for which antibiotics should not be given. Benchmark % given abx with peers
  - HEDIS measures (primary care and pediatrics)

Suggested alternatives

Accountable justification

“Nudge” letter/poster

Education combined with the above

Gerber. JAMA 2013;309(22):2345-2352
Meeker. JAMA 2016; 315(6)562-570
Summary
Antibiotics are life-saving medicines that are often misused.
Antimicrobial decision-making is complex.
Optimized antimicrobial use through antimicrobial stewardship protects patients from unintended consequences.
Antimicrobial use affects individuals AND populations. Healthcare exposed populations are the most at risk.
Antimicrobial Stewardship Programs should be supported in all US healthcare facilities and is a key component of infection prevention.
THANK YOU! Rebekah.Moehring@duke.edu