Antibiotic Stewardship in Practice
Understanding the growing threat of antibiotic resistance

Objectives
Antibiotic Stewardship in Practice

- Understand the growing threat of antibiotic resistance
- Review literature and current guidelines for treatment and proper selection and use of antimicrobial agents to limit the development of resistance
- Review methods and tools available to assist providers with the implementation of antibiotic stewardship in your practice
- Review common medical conditions associated with high rates of inappropriate antimicrobial use

Emerging Infectious Disease
Streptococcus pneumoniae penicillin susceptibility

2010 date: < 40% are susceptible = BIG PROBLEM

Antibiotic Use
Appropriate VS Inappropriate Use

- Empiric use when there is a reasonable clinical suspicion of infection
- Choose antibiotics active against the most likely organism(s)
- Choose antibiotics known to penetrate involved tissue
- Use correct doses of antibiotics – don’t underdose
- Know when bacteriostatic antibiotics are adequate; or when bactericidal drugs are necessary.
- In serious, potentially life-threatening infections:
  - start broad, then de-escalate after cultures back
- Stop antibiotics when infection resolved or when evidence accumulates against existence of infection
  - Ex: 3 day course vs. 7 day course

Misuse of Antibiotics
Sequela to Antibiotic Resistance

- Incomplete, delayed, or failed resolution of infection
- Prolonged or unnecessary hospitalizations
- Increased incidence of antibiotic side effects
- Development of multi-drug resistant strains of bacteria
- Increased health care costs

Antibiotic Stewardship
Why is it important?

http://wwwnc.cdc.gov/eid/images/02-0123-F1.jpg
Impacts of antimicrobial resistance

- Treatment failures
- Morbidity and mortality
- Risk of hospitalization
- Length of hospital stay
- Need for more expensive and broad spectrum antibiotics

Understanding antimicrobial resistance

- Multiple resistance mechanisms
  - Genetic diversity
  - Nucleotide substitution
  - DNA rearrangements
  - Gene acquisition
  - Transformation
  - Transduction
  - Conjugation
  - Mobile genetic elements
  - Gene cassettes
  - Integrons
  - Insertion sequence elements and transposons
  - Plasmids

- What this means:
  - Bacterial organisms are actually genetically modifying themselves to be more resistant to the drugs we use to kill them.
  - Examples:
    - MRSA
    - ESBL (KP, E. coli)
    - CRE
    - …

Causes of resistance

- Genetic plasticity
- Growing biomass of microorganisms
- Excessive antibiotic use
- Lax infection control policy
- Not utilizing local/regional antibiogram data

Providers have some control…

New antibiotics??

Where’s the R&D for new antimicrobials?

What happens when we run out?

New Antibiotics as of 2012
Clinical Diagnosis of infection should be made using MULTIPLE DATA points

- PNEUMONIA
  - Fever
  - Leukocytosis
  - Purulent sputum
  - New infiltrate
  - Cough, chest pain, dyspnea
  - Hypoxia
  - Sputum gram stain shows many WBCs, few epithelial cells

- URINARY TRACT INFECTION
  - Dysuria
  - Urinary frequency
  - Fever
  - Pelvic or flank pain
  - Pyuria
  - Number of epithelial cells in UA
  - Sputum gram stain shows many WBCs, few epithelial cells

- URINARY TRACT INFECTION
  - ODOR: foul smelling
  - Surrounding erythema
  - indurated, tender
  - Purulent drainage
  - Fever
  - Leukocytosis

WOUND INFECTIONS

- Common Medical Conditions:
  - These are associated with high rates of antibiotic mis-use
  - Rhinosinusitis
  - Bronchitis
  - Urinary Tract Infections
  - Pharyngitis
  - Cutis Media

Infection should NOT be made based on culture results only

- Why?

Interpreting Culture Reports

First step: Distinguish between colonization and contamination

- Colonization – present but is not causing symptoms of clinical disease
- Contamination – environmental contamination and not present in or on patient

EVERY POSITIVE CULTURE SHOULD BE VIEWED WITH RESPECT TO MULTIPLE DATA POINTS

CHOOSE EMPIRIC TREATMENT

- Head and Neck
  - Remember: Most URI, pharyngitis, sinusitis, bronchitis have viral etiology
  - If symptoms are high clinical suspicion for bacterial etiology, organisms include:
    - Strepococcus viridans group, Lancefield group, staphylococcus, peptostreptococcus, Mobilis, anaerobacterium, lactobacili spp, eikenella, etc.
  - Antibiotics for use:
    - First: Beta lactam/beta lactamase inhibitor combos
    - Second: Clindamycin
    - Third: 2nd generation cephalosporins
    - Fourth: 4th generation quinolones (moxifloxacin)
    - Levoquin is not desired to be good choice D/T high rates of resistance

Tools

Antibiograms

Local and Regional Trends
Antibiograms
What are they?
- Antibiograms aggregate information for an entire institution or testing facility over a period of several months or a year.
- They display the organisms present in clinical specimens sent for laboratory testing, and the susceptibility of each organism to an array of antibiotics.
- Antibiograms are routinely prepared by hospital laboratories but are not routine in the private laboratory testing facilities until recently. (i.e. LabCorp, Quest, etc.)

How we can get them and use them?
- Sensitivities of community-acquired and hospital-acquired organisms and hospital-acquired organisms vary from region to region.
- Knowledge of the general sensitivities aid in choosing appropriate antibiotics and early appropriate antibiotics and early institution of therapy.
- Community-level aggregate antibiogram information can enable providers and epidemiologists in that community to track antimicrobial resistance levels and to raise awareness of the resistance problem and the need to use optimal empiric therapy, and may be used to identify opportunities to both reduce inappropriate antimicrobial usage and to ascertain success of such efforts.

Using Antibiogram Data
Local and Regional Susceptibility Data
- Antibiograms run specific bacterial isolates against multiple agents using at least 2 antimicrobials from at least 3 different classes of antibiotics.
- Data set collection is then compiled for multiple isolates and checked for trends.
- Common trends can be detected using antibiogram surveillance methods providing important data to assist providers in prescribing practices.

Tools to assist

Sanford Guide to Antimicrobial Therapy
- Top resource for clinicians reference (regardless of location).
- National antibiogram compilation.
  - 2013-2014 will have regional/state data for those states participating in antibiogram studies.
  - 34 states so far.
  - South Carolina is one of them!!
- Extensive organism list.
- Extensive disease/condition list.
- Tables/Tools are excellent resources.

Using an antibiogram
Sanford (book or app)
Antibiogram Spectrum of Activity = what it works against!

- NOT GOOD for MSSA, MRSA
- Intermediate against Virtan Strep.

Antibiogram data availability

- South Carolina’s Careful Antibiotic Use (CAUse) campaign
- Partnership with laboratories and testing facilities throughout the state to provide disease-specific and organism-specific resistance trends allowing providers to use the best evidence-based prescribing practices
- Education materials available for patients as well to help educate on why or why not they need a specific antibiotic.

Resources and References

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Strategies to incorporate antibiotic stewardship into your practice

- Education – keep up to date
  - CDC Get Smart: http://www.cdc.gov/getsmart/index.html
  - SCDHEC CAUse: http://www.statelibrary.sc.gov/sc-careful-antibiotic-use
  - IDSA: http://www.idsociety.org/Stewardship_Policy/
  - Patient education is important as well
- Adherence – use the guidelines
  - They’re published everywhere, but CDC, Guidelines.gov, and IDSA has most current and up-to-date

Conclusion

- We must be diligent in our pursuit of awareness of increasing antibiotic resistance in order to make a difference in the lives of our patients.
- Antibiotic stewardship is one practice strategy that applies to all spectrums of medical care – outpatient, inpatient, and community.
- Development of novel antibiotics has significantly declined; therefore, we must employ appropriate diagnostic and careful prescribing practices.
Colds and the Flu

Steph Throat

Urinary Tract Infections

Mononucleosis

Common Medical Conditions Associated with High Rates of Inappropriate Antimicrobial Use

+ Rhinosinusitis
  - Viral etiology (97%-+, but antibiotics usually prescribed)
  - Bronchitis
  - Acute vs. Chronic (ACECD)
  - Otitis Media
  - AOM recommendations (> 2 yrs)
  - Pharyngitis
  - Pediatrics vs. adults
  - Urinary Tract Infection
  - VS. Asymptomatic bacteriuria

+ Make an Impact…
Treat when appropriate.
Treat when necessary.

Common Acute Upper Respiratory Infections

- Rhinosinusitis
- High dose amoxicillin or trimethoprim-sulfamethoxazole (most patients)
- Amoxicillin-clavulanate (or a fluoroquinolone, or 2nd, 3rd-generation cephalosporin) recommended for patients who fail first line therapy, or have received antibiotics within previous 4-6 weeks.
- Duration: 10-14 days OR for 7 days after resolution of symptoms to insure complete response
- ADJUNCTS:
  - Intranasal corticosteroids appropriate for bacterial (and viral) sinusitis shown to reduce symptom severity and duration.

+ Rhinosinusitis
- Symptom duration > 7-10 days, or double worsening present?
- Consider bacterial etiology in > 50% of patients with > 10 day duration.

SINUSITIS

Acute bacterial sinusitis cannot be differentiated from viral rhinosinusitis in the first 3-4 days of illness...

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- No specific diagnostic test
- Symptoms similar – viral vs. bacterial difficult
- ~ 0.5-2.0% = acute bacterial rhinosinusitis
- “Gold Standard” – sinus puncture and aspiration
- We do this HOW OFTEN?
- Guidelines recommend differentiating acute bacterial from viral rhinosinusitis using:
  1) symptoms
  2) physical symptoms
  3) duration of the presence of symptoms
- Physical signs not specific for bacterial vs. sinus – DURATION is key

- Patients > 10 days duration of illness OR
- Unusually severe presentation of extra-sinus manifestations
- Orbital OR Facial cellulitis
- Common pathogens:
  - Streplococcus pneumoniae
  - Haemophilus influenzae
  - Moraxella catarrhalis
- Less common pathogens (chronic):
  - Staphylococcus aureus (MRESA?)
  - Pseudomonas aeroginosa (esp with chronic cases with ANY history of pneumonia)
  - Anaerobes

- Rhinosinusitis
- Symptom duration > 7-10 days, or double worsening present?
- Consider bacterial etiology in > 50% of patients with > 15 days duration.

+ Rhinosinusitis
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Rhinosinusitis

The “common cold”

Sinusitis

Ace bacterial sinusitis cannot be differentiated from viral rhinosinusitis in the first 3-4 days of illness...

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Rhinosinusitis

DURATION OF SYMPTOMS OF VIRAL URI (good patient info...)

Bronchitis

Cough – 3rd most common chief complaint

Bronchitis

What we know....

- Self-limiting, but with long duration (avg. 3 weeks)
- Studies demonstrate high rates of antibiotic prescriptions for acute bronchitis despite the fact that we know most cases are viral in origin.
- Antibiotics for acute bronchitis demonstrates no clinically significant benefits

What that means....

- Lack of benefit + potential adverse events (including increasing antibiotic resistance): routine treatment of acute bronchitis with antibiotics NOT APPROPRIATE
- Bordatella pertussis: < 1% of cases (think IMMUNIZATION)
- Mycoplasma pneumoniae and Chlamydia pneumoniae – atypical, self-limiting; require special testing, not recommended

Bronchitis

Uncomplicated Acute Bronchitis –

< 5 yrs: VIRAL ETIOLOGY > 99%

- Symptomatic treatment:
  - Antitussives
  - Bronchodilators (if indicated)
- Antibiotic therapy ONLY indicated with:
  - Associated sinusitis
  - Heavy growth on throat culture for Streptococcus pneumoniae, Streptococcus sp. (Group A), H. influenzae
  - NO improvement in 1 week.
  - TREATMENT: Amoxicillin; avoid quinolones

Uncomplicated Acute Bronchitis –

> 5 yrs: VIRAL ETIOLOGY ~ 90%

- PURULENT SPUTUM ALONE NOT INDICATION FOR ANTIBIOTIC TX
- COUGH LAST ~ 2 WKS
- FEVER/CHILLS: CXR

OTHER:

- Symptomatic treatment:
  - Antitussives
  - Bronchodilators (if indicated)
Bronchitis Treatment Guidelines

- Acute Exacerbation of Chronic Bronchitis (ABECB)
- Separate group of suspected pathogens:
  - Viruses – 20-50%
  - C. pneumoniae – 5%
  - M. pneumoniae - <1%

Symptoms:
- Increased dyspnea
- Increased sputum viscosity/purulence
- Increased sputum volume

Treatment Guidelines

Mild-Moderate Disease:
- NO antimicrobial tx or
- Amoxicillin 500 po TID 7-10d
- Dicyclline 100mg po BID 10d
- TMP-SMX 1 DS tab po BID 10-14d
- NOTE: No fluoroquinolones!

Severe Disease:
- Amox/Clav 875/125mg po BID 10d
- Azithromycin 500mg po daily 3d
- Clarithromycin ER 1000mg po daily 7-14d
- 2nd or 3rd generation Cephalosporins (use a reference for dosing)
- NOTE: No fluoroquinolones!

Hospitalized Patients:
- Studies reveal benefit in patients hospitalized with severe disease

Have you seen this?
Children vs. Adults

Acute Otitis Media – Children (>2yrs)

- FACTS:
  - AOM = most common reason for antibiotic prescriptions
  - High rate of spontaneous resolution (80%) WITHOUT antibiotic treatment; antibiotics not shown to reduce complications
  - Recommendations – observation without antibiotics option for treating children > 2 yrs with non-severe cases
  - What we know:
    - Majority (>85%) children will improve in 48-72 hours
    - Follow-up phone call should be made to assess status in 2-3 days
    - Wait-and-see prescriptions written at initial visit to be filled in 2-3 days if no improvement
    - Some studies have shown this reduces antibiotic use by ~50%

- Antibiotic Treatment Guidelines (BACTERIAL ETIOLOGY)
  - High dose Amoxicillin
  - Severe cases (fever > 39°C/102.2°F; severe pain, treatment failure w/ Amox)
  - Consider risk for PCN-resistant Streptococcus:
    - Recent antibiotic use (>30d)
    - Age > 2 yrs
    - Childcare attendance

- NOTE: AOM UNLIKELY IN ADULTS
- STRONGLY CONSIDER WITH SEVERE EAR PAIN AND FEVER
- ALLERGIES IF PCN ALLERGIES PRESENT – BEST TREATMENT NOT AVAILABLE; IMPORTANT TO DOCUMENT ACTUAL REACTIONS – MAY NEED TO UTILIZE
Pharyngitis

“Sore throat”

Children vs. adults

Pharyngitis

- FACTS:
  - 30-40% pediatric pharyngitis = bacterial
  - <10% adults adult (>19 yr old) = bacterial

- FACTS:
  - Excessive antibiotic use in acute pharyngitis r/t perceived risk of complications of Streptococcus pyogenes
  - Neisseria gonorrhoea (risk: >16 yr) in <1% cases pharyngitis

Complications of Pharyngitis

Serious but rare: Streptococcus pyogenes

- Acute rheumatic fever
- Acute glomerulonephritis - greater risk in <17 yrs
- Local complications – peritonsillar, retropharyngeal abscesses: evidence does not support the use of antibiotic treatment to prevent further complications such as glomerulonephritis
- NOTE: meta-analysis literature review – antibiotic treatment of culture-confirmed Strep = little impact on duration of symptoms/return to activity and no evidence that it reduces risk of spread

Pharyngitis: Assessment & Treatment

- Rapid Strep Testing:
  - Recommended to help guide antibiotic use and avoid inappropriate use of antibiotics for viral pharyngitis
- Throat Cultures:
  - Children: recommended as confirmatory testing with negative rapid strep testing
  - Not recommended in adult population (RST: high sensitivity in adult population)

- TESTING – BOTH RAPID AND CULTURE-CONFIRMED TESTING IN CHILDREN associated with reduced utilization of antibiotics to treat pharyngitis
- RARE IN ADULTS SO RAPID TESTING HELPS PROVIDER/PATIENT AGREE ON PLAN FOR TREATMENT

Pharyngitis: Treatment Notes

- ANTIBIOTICS RECOMMENDED ONLY FOR CHILDREN WITH ACUTE PHARYNGITIS WITH RAPID ANTIGEN TESTING OR CULTURE RESULTS PROVIDING EVIDENCE OF A STREPTOCOCCAL INFECTION
- ASIM recommends use of CENTOR Clinical Prediction Rule for rapid strep testing and/or empiric antibiotic treatment

- CENTOR CRITERIA
  - Who will benefit from rapid strep testing?
  - Who will benefit from empiric treatment?
  - Scores help determine
  - American Society of Internal Medicine (ASIM)
  - Infectious Diseases Society of America (IDSA)

- Each counts as one point
  - Subjective/objective fever
  - Absence of cough
  - Tender anterior cervical lymph nodes
  - Tonsillar exudate
  - TOTAL SCORE

- Treatment strategies for adult
  - Centor criteria score 3 or 4 ➔ empiric treatment for adults - 40% patients will still receive inappropriate antibiotic therapy
  - Centor criteria score 1-2 ➔ rapid antigen testing in adults
  - Centor criteria score ≤ 1 ➔ antibiotics

Pharyngitis: Treatment Notes

- RAPID STREP TESTING ➔ avoids inappropriate use of antibiotics for viral pharyngitis
- Throat Cultures ➔ confirmatory testing in children

Testing – both rapid and culture-confirmed testing in children associated with reduced utilization of antibiotics to treat pharyngitis.

Pharyngitis

- FACTS:
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Pharyngitis treatment notes

- Large survey -> 10,000 physicians interviewed
- Perceptions that patients expected antibiotic prescription
- Patients’ expectations for abx rx ranked 11th of 13 options for reason to see provider
  - Top 3 reasons for van:
  - Find cause
  - Pain relief
  - Information re: course of illness
- First line treatment options are still the BEST choice
  - Pen/amox/penegra
- 100% Streptococcal pyogenes: in-vitro susceptibility

Urinary Tract Infections

Diagnosing UTI
- Treating UTI
- Resistance in UTI Treatment

Urinary Tract Infections

- Dysuria, Frequency, hesitancy
- Women - dysuria + freq w/o vaginal discharge = 96%
- Confirmation by urinalysis with culture and sensitivity testing recommended to avoid overuse of antibiotics

Resistance in UTI Treatment

- E. coli
  - Responsible for > 90% UTI
  - NOW associated with high resistance rates
  - ESBL E. coli NOW widespread community-acquired infection
  - ESBL E. coli resistant to penicillins, cephalosporins, fluoroquinolones, and trimethoprim-sulfamethoxazole
- Regional resistance rate for E. coli in 2010
  - 49% ampicillin
  - 27% trimethoprim-sulfamethoxazole
  - 39% fluoroquinolones
  - 7% Nitrofurantoin

Impact of vaccines

- Hib (Conjugate H. influenzae type B)
- Prevnar 13 (13-valent conjugate pneumococcal
- Routine use of these vaccines has significantly reduced the incidence of these infections in children, which can lead to serious invasive infections such as meningitis and bacteremia. Subsequently, they seem to have reduced the incidence of otitis media and bacterial sinusitis in children.

References

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- [http://scantibiogramproject.net](http://scantibiogramproject.net)