Rational Antibiotic Use in the Management of Respiratory Tract [RTI] and Urinary Tract [UTI] Infections

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Disclosures

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Tomorrow’s Antibiotics: The Drug Pipeline

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.

Number of Antibacterial New Drug Application (NDA) Approvals vs. Year Intervals*

*Intervals from 1980–2009 are 5-year intervals; 2010–2012 is a 3-year interval. Drugs are limited to systemic agents.

Data courtesy of FDA’s Center for Drug Evaluation and Research (CDER).
Objectives

- Describe and discuss Upper and Lower RTIs, and diagnostic approaches.
- Review rational use on antibacterial agents for RTIs.
- Describe and discuss asymptomatic bacteriuria vs simple UTIs vs complicated UTIs, and diagnostic approaches.
- Review rational use of antibacterial agents for UTIs.
Definitions

• Upper RTI: Common cold [viral], Pharyngitis*, Croup [Acute laryngotracheobronchitis], Acute laryngitis*, Otitis externa / media* / Mastoiditis, Acute sinusitis*, Epiglottitis

• Lower RTI: Acute bronchitis *[mainly viral], Acute exacerbations of COPD, Bronchiolitis, Acute pneumonia [ bacterial / CAP / ABP ], Empyema, Lung abscess, Chronic pneumonia, Cystic fibrosis
Microbial etiology

• Acute bronchitis
  ▫ Influenza A/B*
  ▫ Rhinoviruses
  ▫ Coronavirus
  ▫ Adenoviruses
  ▫ Respiratory Syncytial Virus
  ▫ Human metapneumovirus
  ▫ Parainfluenzavirus
  ▫ Measles virus
  [ <10% bacterial ]
  ▫ Mycoplasma pneumoniae
  ▫ Chlamydia pneumoniae
  ▫ Bordetella pertussis*

• Acute bacterial pneumonia
  ▫ Streptococcus pneumoniae*
  ▫ Hemophilus influenzae
  ▫ Mycoplasma pneumoniae
  ▫ Chlamydia pneumoniae
  ▫ Legionella pneumophila
  ▫ Staphylococcus aureus
  ▫ Enteric GNRs

• HCAP / HAP / VAP
  ▫ Pseudomonas aeruginosa
  ▫ MRSA
  ▫ Multi-drug resistant organisms
Diagnosis

**Acute bronchitis**
- Dry or productive cough for 3 weeks or less, mostly wintertime, low-grade fevers
- Initially with rhinitis, nasal congestion, malaise, sore throat
- Occasionally with wheezing
- < 7% with abnormal CXR
- WBC or CRP do not reliably discriminate viral from bacterial infections
- Serum Procalcitonin is not elevated with viral infection
- Molecular diagnostics [PCR]

**Acute pneumonia**
- Cough, sputum production, dyspnea, chest pain, fever, fatigue, sweats, headache, nausea, myalgia, abdominal pain, occasional diarrhea
- Typically abnormal CXR
- Sputum gram stain / culture
- Blood cultures [HCAP, HAP, VAP, immunocompromised]
- Serum procalcitonin [and CRP] are usually elevated with bacterial infection
- Serum Ab [Mycoplasma] and Urine Ag [Legionella] tests
- Molecular diagnostics [PCR]
Chest Radiography
Management considerations

- Acute bacterial pneumonia pathogens differ from those associated with HCAP, HAP, VAP and Aspiration pneumonia
- Viral pneumonias cannot be reliably distinguished from bacterial pneumonia based on physical examination, WBC or CXR
- Despite exhaustive effort, an etiology for CAP is achieved only ~ 50% of the time
- Older series indicated 25% mortality, while modern series show about 10-15% mortality from pneumococcal bacteremia [so vaccinate!]
Rational antibiotic use in RTIs

- Acute bronchitis is a viral infection 90% of the time, and can be treated symptomatically.
- Empiric antibiotic choices include macrolides, fluoroquinolones, beta-lactams [PCN, Cephs], vancomycin, doxycycline, and clindamycin – but treatment hinges on the clinical situation [IDSA/ATS guidelines].
- CAP can typically be treated for 5 - 10 days.
- Prior treatment with fluoroquinolones, cephalosporins or clindamycin can predispose to Clostridium difficile infection.
- Infections untreatable with antibiotics can sometimes be treated surgically.
Pulling the trigger on antibiotic Rx

- Treat the symptoms [or defer an antibiotic prescription] if the syndrome is likely to be viral
- See if a rapid diagnostic test [PCT, Multiplex PCR, CXR, POC testing] is available
- Pathogen identification and susceptibility test results allows for de-escalation of therapy [inpt.]
- Spectrum coverage, host factors, collateral damage, and costs factor into choosing an agent(s)
- Consultation with ID is recommended if bacterial resistance and patient allergies severely limits antibiotic choices
Definitions / Urinary Tract Infections

• Asymptomatic bacteriuria [ASB]: Presence of significant bacteriuria with no symptoms referable to the urinary tract
  ▫ F: $\geq 100K$ CFU/ml of the same organism in 2 consecutive voided specimens, or 1 fresh catheter sample
  ▫ M: $\geq 100K$ CFU/ml in 1 voided specimen, or fresh catheter sample

• Simple UTI: [\sim\text{cystitis}, \sim\text{pyelonephritis}] Ascending infection in younger females, typically due to E coli [rarely yeast], $\geq 1000$ CFU/ml with symptoms
Complicated UTI [~Nosocomial]

• Typically associated with indwelling catheters (97%), anatomical or functional abnormalities, surgery or instrumentation
• Nosocomial: Acquired in any institutional setting providing health care
• CA-UTI: ≥1000 CFU/ml in symptomatic pt
• Symptoms: Fever/rigors, altered mentation, flank pain, CVA tenderness, pelvic discomfort, new or worsening incontinence / malaise / lethargy
• SCI patients: Increased spasticity, autonomic dysreflexia, sense of unease
Epidemiology of CA-UTI

- Accounts for 40% of nosocomial infections in US hospitals annually
- The incidence of bacteriuria in indwelling catheter systems with a closed drainage system is 3 - 8% / day
- Serial urine cultures growing the same isolate implies a focal nidus of infection, while different isolates implies contamination or incorrect collection technique
- CA-bacteriuria comprises a large reservoir of antibiotic-resistant organisms, and is a frequent target of inappropriate antimicrobial therapy
Diagnosis / Nosocomial UTI

- Urinalysis [Dipstick and Microscopic]: Typically all that’s needed to diagnose uncomplicated UTI [cystitis] in the outpatient setting.
- CA-UTI: Symptoms [no other recognized cause], Urine culture $\geq 100K$ CFU/ml, or UCx with 1K-100K CFU/ml and (+) dipstick [Nitrite(+), LE(+)], pyuria or bacteria seen on Gram stain.
- Urine cultures can be helpful in looking for patterns of infection, and susceptibility testing.
Treatment issues

• Problems arise when the organism is multi-drug resistant, or the patient has numerous drug allergies or adverse reactions

• Treatment can often be for 1-5 days for cystitis, but may be closer to 5-10 days for complicated UTIs

• Removal [or replacement] of the catheter helps reduce the bioburden [biofilm]

• Recurrent UTIs merit work up for anatomical or functional problems

• Oral agents are tried first, but IV agents may be needed for difficult cases
Antibiotic agents for UTI

- **Oral:** Ciprofloxacin, Levofloxacin, penicillins, cephalosporins, SXT / TMP-SMZ / Bactrim, Nitrofurantoin [only if the GFR $\geq 50$ mls/min], fosfomycin
- **IV:** Extended-spectrum penicillins [Zosyn], cephalosporins, aztreonam, carbapenems, aminoglycosides, fluoroquinolones, linezolid
- ? bladder irrigation
- ? antibiotic - impregnated or antibiotic - coated catheters
Accepted Prevention Strategies

• Reduce exposure to catheterization at the outset
• Try alternative catheter methods [condom, supra-pubic, intermittent] rather than Foley
• Closed catheter drainage system, and positioning
• Use of multiple infection control techniques and strategies simultaneously [“bundling”]
• Methenamine hippurate [Hiprex] / mandelate [Mandelamine] are bladder antiseptics that may be helpful in patients without an indwelling catheter, do not have a neurogenic bladder, and a GFR $\geq 50$ mls/min
Marginal Prevention Strategies

• Enhanced meatal care
• Cranberry products: No published data in catheterized adults without neurogenic bladder
• Bladder irrigation with saline or antibiotics
• Antimicrobial drugs in the drainage bag
• Prophylactic antibiotics at the time of catheter removal or replacement
• ? Routine catheter change
• Mannosides
• Bacterial interference
Antibiotic Stewardship

• Optimizing antibiotic selection for a given syndrome, taking into account pathogen, as well as host factors, and their interaction
• Avoiding empiric approaches, and striving for a microbiologic diagnosis
• Look for clinical decision support tools online or with your EMR [eg. VirtuWell / HPMG]
• De-escalate regimens as soon as possible
• Emphasize non-antibiotic approaches to prophylaxis [infection control, vaccination, etc]