Rational Use of Antibiotics: A Case Based Approach

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Outline

- Case based approach to illustrate principles of rational antibiotic use
Patient AG

- 65-yr male
- History: Cough, fever x 10 days; wheezing & breathlessness x 2 days
- Past h/o: BA x 10 yrs; DM x 2 yrs
- Exam: Pulse - 102/min; BP - 120/80 mmHg; RR - 40 /min
- RS: Bilateral scattered wheeze; crepitations right mammary, interscapular & infrascapular regions
Severity Assessment: CURB-65 Score

- **Confusion** (abbreviated mental test score ≤ 8 or new disorientation in person, place, or time);
- **Urea** > 7 mmol/l;
- **Respiratory rate** ≥ 30/min;
- Low **Blood pressure** (systolic blood pressure < 90 mm Hg or diastolic blood pressure ≤ 60 mm Hg);
- **Age** ≥ 65 years

- **AG Score**: 2
Severity Assessment & Site of Care

Key Bacterial Pathogens in CAP

- S. pneumoniae: 66%
- Other: 12%
- Legionella spp.: 4%
- M. pneumoniae: 7%
- H. influenzae: 12%

- Study cohorts: N = 127
- Total patients: N = 33,148
- Total patients reporting data: N = 6866

A Specific Pathogens Detected

Patients with a Positive Result (%)

Viral pathogen only (22%)
Viral–viral co-detection (2%)
Bacterial–viral co-detection (3%)
Bacterial pathogen only (11%)
Fungal or mycobacterial detection (1%)

Pathogen Detected

- Human metapneumovirus
- Respiratory syncytial virus
- Parainfluenza virus
- Coronavirus
- Mycoplasma pneumoniae
- S. aureus
- Adenovirus
- Legionella pneumophila
- Enterobacteriaceae
- Other
### Initial Empiric Antibiotics

<table>
<thead>
<tr>
<th></th>
<th>American (IDSA/ATS)</th>
<th>British (NICE/BTS)</th>
<th>European*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preferred</td>
<td>Alternative</td>
<td>Preferred</td>
</tr>
<tr>
<td>Outpatient without</td>
<td>Macrolide</td>
<td>Doxycycline</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>comorbidities; low</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient with</td>
<td>β-lactam plus</td>
<td>Respiratory</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>comorbidities or high</td>
<td>macrolide</td>
<td>fluoroquinolone</td>
<td></td>
</tr>
<tr>
<td>rate bacterial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>resistance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient not in ICU;</td>
<td>β-lactam* plus</td>
<td>Respiratory</td>
<td>Aminopenicillin with or without macrolide</td>
</tr>
<tr>
<td>moderate severity</td>
<td>macrolide</td>
<td>fluoroquinolone</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient in ICU;</td>
<td>β-lactam* plus</td>
<td>β-lactam* plus</td>
<td>Third-generation cephalosporin* plus macrolide</td>
</tr>
<tr>
<td>high severity</td>
<td>macrolide</td>
<td>respiratory</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>fluoroquinolone</td>
<td></td>
</tr>
</tbody>
</table>

Local or adapted guidelines should be used to adapt for different epidemiology. IDSA = Infectious Diseases Society of America. ATS = American Thoracic Society. NICE = National Institute for Health and Care Excellence. BTS = British Thoracic Society. ICU = intensive care unit. *Preferred β-lactam drugs include cefotaxime, ceftriaxone, and ampicillin. 
†Respiratory fluoroquinolone limited to situations in which other options cannot be prescribed or are ineffective (e.g., hepatotoxicity, skin reactions, cardiac arrhythmias, and tendon rupture). ‡Preferred β-lactam drugs include cefotaxime, ceftriaxone, or ampicillin-sulbactam. §β-lactamase-stable β-lactams include co-amoxiclav, cefotaxime, cefotaxime fosamil, ceftriaxone, cefuroxime, and piperacillin-tazobactam. ¶Third-generation cephalosporin (e.g., cefotaxime, ceftriaxone).

*Table: Empirical antibiotics suggested for community-acquired pneumonia*
Patient AG: Antibiotics

• Piperacillin-Tazobactam + Azithromycin + Oseltamivir

• Rationale: “Consider influenza virus infection as possible cause of any febrile respiratory illness requiring hospitalization during influenza season; consider testing for influenza & starting empiric antiviral therapy”

### Microbiological Investigations

<table>
<thead>
<tr>
<th></th>
<th>Outpatient</th>
<th>Inpatient, low severity</th>
<th>Inpatient, no ICU, moderate severity</th>
<th>Inpatient, ICU, high severity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sputum culture</strong></td>
<td>None routinely</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Blood culture</strong></td>
<td>None routinely</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td><strong>Legionella urinary antigen</strong></td>
<td>None routinely</td>
<td>None routinely</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Pneumococcal urinary antigen</strong></td>
<td>None routinely</td>
<td>None routinely</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Invasive respiratory tract sample culture</strong></td>
<td>None routinely</td>
<td>None routinely</td>
<td>None routinely</td>
<td>Yes*</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>None routinely</td>
<td>None routinely</td>
<td>None routinely</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

**Community-acquired pneumonia**


http://dx.doi.org/10.1016/S0140-6736(15)60733-4
Labs: Microbiology

- Sputum Gram stain: Many pus cells, few epithelial cells, occ GNC groups
- Sputum culture: Yeast
- Blood culture: No growth
- Influenza virus PCR (N-P swab): Influenza A – Negative; Influenza B – Positive
Antibiotic Duration

• 5 – 7 days
• Criteria for stopping antibiotics
  – Afebrile x 48 hrs.
  – Clinically stable
    • BP >90 mm Hg syst
    • Pulse <100/min
    • RR <24/min
    • O2 sat >90%
    • paO2 >60 mm Hg on room air
• Longer duration for empyema, lung abscess, unusual pathogens

Prevention

• Smoking cessation

• Vaccination
  – Annual flu vaccine
  – Pneumococcal vaccine: 1 dose PCV-13, followed by 1 dose PPSV-23 after 1 year
Patient S

• 69-yr female, no known co-morbidities
• History: Fever with rigors, dysuria, frequency, hematuria x 3 days
• Exam: Temp 103 °F; pulse 124/min; RR 32/min; BP 130/80 mm Hg mm Hg syst.; has bilateral costo-vertebral angle tenderness
How accurate are symptoms of UTI?

- Dysuria, frequency: PPV >90% for LUTI
- Fever, rigors, CVA tenderness indicates UUTI
- Cloudy urine, malodorous urine, bloody urine
  - High sensitivity, poor specificity
  - Visual appearance prone to error
- Worsening incontinence
- Systemic symptoms
  - Altered mental status, delirium
  - MOSF, hypotension
Algorithm for Evaluating Women With Symptoms of Acute UTI

Woman With ≥1 Symptoms of UTI

Risk Factors for Complicated Infection? Yes

Consider Urine Culture to Establish Diagnosis
Consider Initiating Empirical Treatment

No

Back Pain or Fever?

Yes

Probability of UTI Moderate (~60%) and Probability of Pyelonephritis Unknown
Consider Urine Culture to Establish Diagnosis
Consider Empirical Treatment

No

Vaginal Discharge?

Yes

Low to Intermediate Probability of UTI (~20%)
Pelvic Examination (including Cervical Cultures When Appropriate) and Urine Culture to Establish Diagnosis

No

Most Elements of the History (and Physical Examination) Positive?

Yes

High Probability of UTI (~90%)
Consider Empirical Treatment Without Urine Culture

No

Perform Dipstick Urinalysis

Dipstick Results Positive?

Yes

High Probability of UTI (~80%)
Consider Empirical Treatment Without Urine Culture

No

Low to Intermediate Probability of UTI (~20%)
Consider Urine Culture or Close Clinical Follow-up and Pelvic Examination (including Cervical Cultures When Appropriate)

*JAMA.2002; 287: 2701-2710.
Urinalysis

Absence of pyuria (leukocyte esterase) & bacteriuria (nitrite) rules out UTI
Performance characteristics of leukocyte esterase and nitrite tests, alone or in combination, for detection of bacteriuria and/or pyuria

<table>
<thead>
<tr>
<th>Test, colony count</th>
<th>Performance characteristics</th>
<th>Predictive values</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Positive</td>
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<tr>
<td>Leukocyte esterase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq 10^5$ cfu/mL</td>
<td>68–98</td>
<td>59–96</td>
<td>19–86</td>
</tr>
<tr>
<td>$\geq 10^4$ cfu/mL</td>
<td>64–77</td>
<td>59–83</td>
<td>16–52</td>
</tr>
<tr>
<td>$\geq 10^3$ cfu/mL</td>
<td>62–79</td>
<td>55–84</td>
<td>3–81</td>
</tr>
<tr>
<td>Nitrite</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq 10^5$ cfu/mL</td>
<td>19–45</td>
<td>95–98</td>
<td>50–78</td>
</tr>
<tr>
<td>$\geq 10^4$ cfu/mL</td>
<td>8–39</td>
<td>97–98</td>
<td>27–81</td>
</tr>
<tr>
<td>$\geq 10^3$ cfu/mL</td>
<td>0–50</td>
<td>48–98</td>
<td>0–82</td>
</tr>
<tr>
<td>Leukocyte esterase and nitrite</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq 10^5$ cfu/mL</td>
<td>35–84</td>
<td>98–100</td>
<td>84</td>
</tr>
<tr>
<td>$\geq 10^3$ cfu/mL</td>
<td>0–45</td>
<td>62–98</td>
<td>0–66</td>
</tr>
<tr>
<td>Leukocyte esterase and/or nitrite</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq 10^5$ cfu/mL</td>
<td>67–100</td>
<td>67–98</td>
<td>40–95</td>
</tr>
<tr>
<td>$\geq 10^4$ cfu/mL</td>
<td>74–79</td>
<td>66–82</td>
<td>42–54</td>
</tr>
<tr>
<td>$\geq 10^3$ cfu/mL</td>
<td>71–84</td>
<td>41–83</td>
<td>49–81</td>
</tr>
</tbody>
</table>

**NOTE.** The criteria used to assess the clinical importance of isolates and the laboratory methods used varied between studies; the data are presented only as an overview of reported performance characteristics of the tests. All numbers are rounded to the nearest whole number. cfu, colony-forming units.

Urine Culture

• Bacteriuria is **NOT** a disease
  – Does not establish diagnosis
  – Rarely an indication for antibiotics

• Sample
  – Gold standard: bladder urine obtained by SPA
  – Contamination rates similar for MSCC and MS sample*

• Significant bacteriuria
  – \( >10^5 \) cfu/ml, single organism
  – SPA \( >10^2 \) cfu/ml
  – Symptomatic women \( >10^2 \) cfu/ml

• Antibiotic susceptibility

Contamination rates similar for midstream urine collected with cleansing (MSCC) vs. without cleansing (MS) in women being tested for urinary tract infection

Asymptomatic Bacteriuria

• Significant bacteriuria (± pyuria) in the absence of symptoms
• No improvement in symptomatic UTI or survival with treatment
• No role for routine screening or treatment
• Screening & treatment recommended only for:
  1. Pregnancy
  2. Urologic procedures in which mucosal bleeding is anticipated
Imaging

• To detect complications, anatomic abnormality
• Indications
  – Severe sepsis
  – Persistent symptoms after 72 hrs appropriate Rx
  – DM
  – Immune suppression
  – Obstructive uropathy
  – Recurrent UTI
Patient S: Investigations

- Haemoglobin 11.3 g/dl
- Total WBC 17900/mm$^3$ (N90%)
- Platelets 199000/mm$^3$
- Urea 136 mg/dl; creatinine 6.76 mg/dl
- Electrolytes: Na 124; K 5.4; HCO3 16
- Urinalysis: Leukocytes 2+; Nitrite 2 +
- USG abdomen & pelvis: No sig abnormality
Patient S: Empiric Antibiotics

• Meropenem
• Rationale:
  – *E. coli* most common bacterial pathogen
  – ESBL rates ≈80% in *E. coli*
  – Antibiotics for severe ESBL infections: carbapenems, BL-BLI
  – Early, appropriate therapy for sepsis, septic shock
<table>
<thead>
<tr>
<th>Drug</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefoper + sulbact</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Gentamicin</td>
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</tr>
<tr>
<td>Netilmicin</td>
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</tr>
<tr>
<td>Tigecycline</td>
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</tr>
<tr>
<td>Colistin</td>
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</tr>
<tr>
<td>Piperacillin/Tazo</td>
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</tr>
<tr>
<td>Cefpodoxime</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

Blood Culture
Treatment

• Acute uncomplicated cystitis in women
  – Antibiotics: TMP-SMX, Ciprofloxacin, Nitrofurantoin
  – Duration: 3 - 7 days\textsuperscript{1}

• Pyelonephritis
  – Antibiotics:
    • Initial empiric choice: AG, FQ, 3\textsuperscript{rd} gen cephalosporins, BL-BLI, Ertapenem
    • De-escalate after culture & susceptibility reports
  – Duration: 7 days of treatment equivalent to longer treatment in terms of clinical & microbiological failure, including in bacteremic patients\textsuperscript{2}

Conclusions

• Accurate diagnosis essential for appropriate antibiotic treatment
• Initial empiric based on likely pathogen, antibiotic susceptibility
• De-escalate when DST available
• Use short antibiotic courses
Thank You!