Infectious Diseases Guideline Updates - Community Acquired Pneumonia and Asymptomatic Bacteriuria

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Objectives for Pharmacists
• Compare differences between the 2007 and 2019 ATS/IDSA CAP guidelines
• Identify guideline-recommended empiric therapies for the outpatient treatment of CAP
• Discuss updates to the IDSA Asymptomatic Bacteriuria Guidelines
• Identify patients for whom screening and treatment of asymptomatic bacteriuria is recommended

Objectives for Technicians
• Discuss updates to the ATS/IDSA CAP guidelines
• List guideline-recommended empiric therapies for the outpatient treatment of CAP
• Discuss updates to the IDSA Asymptomatic Bacteriuria Guidelines
• List indications for screening and treatment of asymptomatic bacteriuria

Patient Case
JD is a 67-year-old male who presents to urgent care with clinical and radiographic evidence of CAP. He has no significant PMH and does not meet criteria for hospital admission. Of the following regimens, which would NOT be appropriate for empiric treatment of his CAP?

A) Amoxicillin PO 1 gram TID
B) Doxycycline PO 100 mg BID
C) Azithromycin PO 500 mg x 1 day, then 250 mg for 4 days

2019 ATS/IDSA CAP Guidelines

CAP Controversies
Pathogenic Cause of Pneumonia

Historically
• Streptococcus pneumoniae
• Haemophilus influenzae
• Mycoplasma pneumoniae
• Staphylococcus aureus
• Legionella species
• Chlamydia pneumoniae
• Moraxella catarrhalis

Now
• Streptococcus pneumoniae
• Respiratory viruses
• Unknown causes

2007 ATS/IDSA Criteria for Severe CAP

One major criterion OR three or more minor criteria

Minor Criteria:
• Respiratory rate >30 breaths per min
• PaO₂/FiO₂ ratio <250
• Multisite infiltrates
• Confusion and/or delirium
• Unintentional weight loss >10% in 1 month
• Creatinine (serum creatinine ≥3 mg/dL)
• Chronic heart failure with oxygen requirement ≥2 L/min

Major criteria:
• Septic shock requiring fluid resuscitation
• Respiratory failure requiring mechanical ventilation

HCAP Has Been Abandoned

• Accepted in 2007 ATS/IDSA guidelines
• HCAP was defined for those patients who had any one of several potential risk factors for antibiotic-resistant pathogens:
  • Residence in a nursing home and other long-term care facilities
  • Hospitalization for >2 days in the last 90 days
  • Receipt of home infusion therapy
  • Chronic dialysis
  • Home wound care
  • Family member with a known antibiotic-resistant pathogen

• These factors do not predict high prevalence of antibiotic-resistant pathogens in most settings
  • Recommend abandoning this categorization

New Risk Factors for Resistant Pathogens

Add empiric coverage of Methicillin-resistant Staphylococcus aureus (MRSA) or Pseudomonas aeruginosa in adults with CAP if locally validated risk factors for either pathogen are present

Individual risk factors
• Previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection
• Hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days

Diagnostics

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>2007 ATS/IDSA Guideline</th>
<th>2019 ATS/IDSA Guideline</th>
</tr>
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</table>
| Sputum culture | Primarily recommended in patients with severe disease | Now recommended in inpatients who:
 • Are classified as severe disease
 • Are empirically treated for MRSA or P. aeruginosa
 • Have risk factors for MRSA or P. aeruginosa |
| Blood culture | | |
Diagnostics

Do NOT routinely test urine for pneumococcal antigen in adults with CAP, except in adults with severe CAP.

Do NOT routinely test urine for Legionella antigen in adults with CAP except:

• In cases where indicated by epidemiological factors, such as association with a Legionella outbreak or recent travel
• In adults with severe CAP

Procalcitonin

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>2007 ATS/IDSA Guideline</th>
<th>2019 ATS/IDSA Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procalcitonin</td>
<td>Not covered</td>
<td>Empiric antibiotic therapy should be initiated in adults with clinically suspected and radiographically confirmed CAP regardless of initial serum procalcitonin. Use of procalcitonin to de-escalate antibiotics NOT addressed</td>
</tr>
</tbody>
</table>

Empiric Outpatient Treatment

Healthy adults without comorbidities

- Amoxicillin 1 g three times daily
- Doxycycline 100 mg twice daily
- Macrolide only in areas with pneumococcal resistance to macrolides <25%

Adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia

- Amoxicillin/clavulanate OR a cephalosporin (cefpodoxime 200 mg twice daily or cefuroxime 500 mg twice daily)
- Macrolide or doxycycline
- Respiratory fluoroquinolone

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Empiric Inpatient Treatment

Inpatients (non-severe) without risk factors for MRSA or P. aeruginosa

- β-lactam (ampicillin/subactam, cefotaxime, cephradine or cefazolin)
- PLUS
- Macrolide
- OR
- Respiratory fluoroquinolone

Inpatients (severe) without risk factors for MRSA or P. aeruginosa

- β-lactam + macrolide
- OR
- β-lactam + respiratory fluoroquinolone

Contraindications to both macrolides and fluoroquinolones:

• Combination therapy with a β-lactam and doxycycline 100 mg twice daily

Rate of macrolide-resistant Streptococcus pneumonia in 2014

Atypical Coverage Still Recommended

Garin et al. 2014
- Randomized control trial in 580 patients with CAP
- Could not rule out the possibility that β-lactam monotherapy was inferior to β-lactam/macrolide therapy for patients with CAP

Nie et al. 2014
- Systematic review and meta-analysis
- β-lactam/macrolide therapy reduced mortality in patients with CAP compared with patients treated with β-lactam monotherapy

Empiric Inpatient Treatment- MRSA

<table>
<thead>
<tr>
<th>Prior Respiratory Isolation of MRSA</th>
<th>Related Hospitalization and Potential Antibiotics and Locally Validated Risk Factors for MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsevere pneumonia</td>
<td>Add MRSA coverage (vancomycin or linezolid) and obtain cultures/nasal PCR to allow de-escalation or confirmation of need for continued therapy</td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td>Same as above</td>
</tr>
</tbody>
</table>

De-escalation

In patients empirically treated for MRSA or P. aeruginosa:
- Deescalate to standard CAP therapy if cultures do not reveal a drug-resistant pathogen and the patient is clinically improving at 48 hours
- Switching from parenteral to oral antibiotics
  - No specific time frame given
  - Either the same agent or the same drug class should be used

Imaging

In adults with CAP whose symptoms have resolved within 5 to 7 days, do NOT routinely obtain follow-up chest imaging
- Positive yield from repeat imaging ranges from 0.2% to 5.0%

Duration

Antibiotic therapy should be continued until the patient achieves stability and for no less than a total of 5 days
- Resolution of vital sign abnormalities [heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature], ability to eat, and normal mentation
Aspiration Pneumonia

Do NOT routinely add anaerobic coverage for suspected aspiration pneumonia unless lung abscess or empyema is suspected

- Recent studies have shown that anaerobes are uncommon in patients hospitalized with suspected aspiration pneumonia. Many of these patients have resolution of symptoms within 24 to 48 hours and require only supportive treatment, without antibiotics.

Corticosteroids

Do NOT routinely use corticosteroids in adults with nonsevere CAP, severe CAP, or influenza pneumonia

- There are no data suggesting benefit of corticosteroids in patients with nonsevere CAP with respect to mortality or organ failure and only limited data in patients with severe CAP.
- Recommendations do not apply to clinically appropriate use of steroids for comorbid diseases.

Endorse Surviving Sepsis Campaign recommendations on the use of corticosteroids in patients with CAP and refractory septic shock.

Influenza

Test for influenza when influenza viruses are circulating in the community.

Antiviral treatment in adults with CAP who test positive for influenza in the inpatient or outpatient settings regardless of duration of illness before diagnosis.

Standard antibiotic treatment for adults with clinical and radiographic evidence of CAP who test positive for influenza in the inpatient and outpatient settings.

Patient Case

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Summary of Differences between the 2019 and 2007 ATS/IDSA CAP Guidelines

1) Obtain sputum and blood cultures for severe CAP and for patients with risk factors or in those receiving empiric treatment for MRSA or P. aeruginosa.
2) Macrolide monotherapy is now a conditional recommendation for outpatients based on resistance levels.
3) Abandon HCAP as an indication for broad spectrum antibiotics.
4) Stronger evidence for β-lactam/macrolide combination in severe CAP.
5) Procalcitonin not recommended to determine need for initial antimicrobial therapy.
6) Recommend against corticosteroid use, although it may be considered in patients with refractory septic shock.
7) Recommend against routine follow-up chest imaging.
Patient Case
MC is a 72-year-old female who presents to the emergency room from a skilled nursing facility with altered mental status. She has been more lethargic over the past several days and “not her usual self” according to the skilled nursing facility staff. She does not meet SIRS criteria on admission. The team requests a urinalysis with the following results:

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Leukocyte esterase</th>
<th>WBC</th>
<th>Nitrite</th>
<th>Epithelial cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many</td>
<td>Trace</td>
<td>7</td>
<td>Positive</td>
<td>3</td>
</tr>
</tbody>
</table>

Patient Case
MC is too altered to report if she is having any urinary symptoms. The team orders antibiotics for empiric treatment of a UTI. How do you proceed?

Asymptomatic Bacteriuria
• Asymptomatic bacteriuria (ASB) is the presence of 1 or more species of bacteria growing in the urine at ≥10^5 colony-forming units [CFU]/mL, irrespective of the presence of pyuria, in the absence of signs or symptoms attributable to urinary tract infection (UTI)
• Common finding in some healthy female populations and in many women or men with abnormalities of the genitourinary tract that impair voiding
• Classic symptoms of UTI include focal genitourinary symptoms such as urinary frequency, urgency, dysuria, and costovertebral angle tenderness

Prevalence of ASB for Different Populations

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence (%)</th>
<th>Population</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Women</td>
<td></td>
<td>Persons with kidney transplants</td>
<td></td>
</tr>
<tr>
<td>Pre-menopausal</td>
<td>1.0 – 5.0</td>
<td>Fat month post transplant</td>
<td>23 – 34</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1.0 – 5.0</td>
<td>1 mo. – 1 yr. post transplant</td>
<td>10 – 17</td>
</tr>
<tr>
<td>Post-menopausal (50-70 yrs)</td>
<td>2.8 – 3.6</td>
<td>Persons with spinal cord injuries</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>15.0 – 16.0</td>
<td>Intermittent catheter-use</td>
<td>23 – 49</td>
</tr>
<tr>
<td>Men</td>
<td>6.7 – 11</td>
<td>Spinal/recto-penile cath</td>
<td>57</td>
</tr>
<tr>
<td>Persons with Diabetes</td>
<td></td>
<td>Persons with indwelling catheter</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>10.0 – 16.0</td>
<td>Short-term (per catheter)</td>
<td></td>
</tr>
<tr>
<td>Men (≥ 75 yrs)</td>
<td>3.6 – 19</td>
<td>Long-term</td>
<td>2/100 – 2/200</td>
</tr>
<tr>
<td>Elderly persons in LTCF</td>
<td></td>
<td>Children</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>25 – 50</td>
<td>Boys</td>
<td>≤ 1</td>
</tr>
<tr>
<td>Men</td>
<td>15 – 30</td>
<td>Girls</td>
<td>1 – 2</td>
</tr>
</tbody>
</table>

Who Should NOT Be Screened for ABS?
• Infants and children
• Healthy premenopausal, nonpregnant women or healthy postmenopausal women
• Older, community-dwelling persons who are functionally impaired
• Older persons residing in long-term care facilities
• Patients with diabetes
• Renal transplant recipients who have had renal transplant surgery <1 month prior
• Patients with nonrenal solid organ transplant
• Patients with spinal cord injury
• Patients with a short-term indwelling urethral catheter (<30 days) or long-term indwelling catheters
• Patients undergoing elective urologic surgery
• Patients planning to undergo surgery for an artificial urinary sphincter or pelvic prosthesis implantation
• Patients living with implanted urologic devices
Pregnant Women
Screen for and treat ASB in pregnant women
- Randomized studies from the 1960s to 1980s uniformly reported that antimicrobial treatment decreased the incidence of pyelonephritis from 20%–35% to 1%–4%.
- 2015 prospective study in Netherlands suggested that nontreatment of ASB may be an acceptable option for selected low-risk women.
- Antimicrobials probably reduce the risk of pyelonephritis and may reduce the risk of low birth weight.
- May also reduce the risk of preterm labor.
- Recommend 4 to 7 days of antimicrobial therapy.

Older, Functionally or Cognitively Impaired Patients
Careful observation rather than antimicrobial therapy in patients:
- With delirium (acute mental status change, confusion) and without local genitourinary symptoms or other systemic signs of infection.
- Who experience a fall.
- Treatment of ASB in patients with delirium has not been shown to have any beneficial impact in clinical outcomes compared to no treatment, including reducing severity or duration of delirium and reducing risk of sepsis, death, or hospitalizations.

Patients With Neutropenia
No recommendation for or against screening for or treatment of ASB
- High risk neutropenia (absolute neutrophil count <100 cells/mm³ 2-7 days' duration following chemotherapy).
- Current management for patients with high-risk neutropenia typically includes prophylactic antimicrobial therapy.
- Recent retrospective review of patients admitted to hospital with febrile neutropenia occurring within 4 weeks of chemotherapy reported that only 2.8% had UTI (2.9% of those with ANC ≤100 cells/mm³), and only 1 of 198 patients had bacteremia from a urinary source.

Patients With Catheters
- Short-term catheter-associated bacteriuria does not appear to increase the risk for sepsis or death.
- Tambyah et al. reported that 235 of 1497 (14.9%) evaluable newly catheterized patients developed bacteriuria (defined as ≥10³ CFU/mL) at a mean of 6.4 ± 6.1 days.
- Only 15 of the 194 (7.7%) patients with bacteriuria who could be interviewed reported subjective symptoms.
- No recommendation for or against screening for and treating ASB at the time of catheter removal.

Patients Undergoing Endourological Procedures
Screen for and treat ASB prior to surgery in patients who will undergo endoscopic urologic procedures associated with mucosal trauma
- High risk of sepsis for patients undergoing invasive endourologic procedures in the presence of bacteriuria.
- Perioperative antimicrobials probably reduce the risk of sepsis by approximately 6% and of UTIs by approximately 9%.
- Obtain urine culture prior to procedure, target antimicrobial therapy, recommend 1 to 2 doses rather than prolonged therapy.

Patient Case
MC is too altered to report if she is having any urinary symptoms. The team orders antibiotics for empiric treatment of a UTI. How do you proceed?
Patient Case
MC is too altered to report if she is having any urinary symptoms. The team orders antibiotics for empiric treatment of a UTI. How do you proceed?

Have an informed discussion with the team. As patient does not have systemic signs of an infection, recommend careful observation rather than antimicrobial therapy.

Summary of 2019 IDSA ASB Guidelines

• Just say NO to screening and treating ASB! Except for:
  • Pregnant women
  • Patients Undergoing Endourological Procedures
• No recommendation given for neutropenic patients

Questions?