Community Acquired Pneumonia Update 2019

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Disclosures: Insmed
Objectives
Update Clinical Aspects of CAP

• CAP Epidemiology
• Bugs, Guidelines & Antimicrobial Selection
• *S. pneumoniae* Pneumonia focus
  – Invasive Disease
  – Dual Therapy (Macrolide) for Invasive Pneumococcal Pneumonia
  – Resistance & Clinical outcomes
• Recent concepts: Procalcitonin, CAP marks Risk for CV complications
CAP Epidemiology

• Incidence
  – 4.5 million case/ yr (80% managed as outpatients)
  – Hospitalization: 650/100,000

• Key Risk Factors: Aging, Comorbidity (eg, DM, CVA, CHF, COPD)
  – Smoking, EtOH, Opiate abuse
  – Crowding/Low Income
  – Respiratory Virus Infection (Influenza) → Bacterial pneumonia
  – (Immunocompromise)

• Cost: $10 - 40 billion/year
  – 20% hospitalized, account for ~80% cost
  – Pts > 65 account for 60% of hospitalized CAP

• Mortality Estimates
  – Outpatient 5%, Hospitalized 12%, ICU 30%
  – #1 Cause of death of all Infectious Diseases (US)
Age Impact on CAP Incidence

 Ramirez JA et al. CID 2017;65(11):1806-12
Comorbidity Impact
Incidence of Hospitalization for CAP

Ramirez JA et al. CID 2017;65(11):1806-12
**CAP Epidemiology**

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  - 4.5 million cases/yr (80% managed as outpatients)
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  - Outpatient 5%, Hospitalized 12%, ICU 30%
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Pneumonia Spectrum

• **CAP: Community Acquired Pneumonia**
  
  • **HCAP (Healthcare associated pneumonia)**
    – Prior hospitalization of ≥ 2 days (within 90 days)
    – Resided in nursing home or long-term care facility
    – Received recent IV antibiotics (within 30 days)
    – ↑ Risk for insufficient initial antibiotic coverage

• HAP (hospital-acquired pneumonia)
  – Pneumonia that occurs > 48 hours from time of admission

• VAP (ventilator-associated pneumonia)
  – Pneumonia 48–72 hours after endotracheal intubation

966 Pathogen Detected
853 of 2259 patients (+ CXR)

Majority (62%):
No pathogen detected
Respiratory viruses > bacteria
S. pneumoniae most common bacterial isolate

Jain et al. NEJM 2015
CAP Clinician Conundra

- Multiple organism etiologies w/ different antibiotic susceptibility
- No culture/susceptibility data in outpatient setting (inpatient delay ~48hrs)
- Causative organisms remains unknown > 50% cases
- Era of antimicrobial resistance
**CAP Guideline Evolution**

- Infectious Disease Society of America (IDSA) 1998, 2000, 2003
- Canadian (2000) and BTS (2001) also…

- Evolution of CAP guidelines produced risk stratification based on characteristics that predict organism & link with rational empiric antibiotic choices
Key Guided Decisions for Hospital CAP...

• Diagnosis by chest x-ray

• Abx ASAP at site of presentation (ER/clinic)

• Trend: Shorter duration of antibiotic Rx
  – Mod-Severe CAP \(\Rightarrow\) 3 days IV abx, Total 5-8 days (except MRSA, \(P\, aeruginosa\))

• Early Switch IV to Oral
  – Criteria: GI tract fxn, Temp & WBC improving
  – Prevents complication a/w IV (infection/phlebitis)
  – Meta-analysis—9 studies (Rhew et al: Arch Int Med 2001)
  – Supportive data continues to accumulate…
# Severity, Site of Care, Evaluation

<table>
<thead>
<tr>
<th>Severity</th>
<th>Site of Care</th>
<th>Suggested Micro Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild CURB-65 0, PSI I or II</td>
<td>Outpatient Clinic</td>
<td>Generally not needed</td>
</tr>
<tr>
<td>Moderate CURB-65 1 or 2 PSI III or IV</td>
<td>Inpatient</td>
<td>Blood Cultures Pneumococcal Urine Ag Legionella Urine Ag Respiratory Viral Panel</td>
</tr>
<tr>
<td>Severe CURB-65 &gt; 3 PSI IV or V</td>
<td>ICU</td>
<td>Blood Cultures Pneumococcal Urine Ag Legionella Urine Ag Respiratory Viral Panel Consider: BAL (ie, fungi, multiplex PCR [virus, bacteria, resistance genes])</td>
</tr>
</tbody>
</table>

## CAP: Duration of Abnormalities

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Duration (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia &amp;/or hypotension</td>
<td>2</td>
</tr>
<tr>
<td>Dyspnea, Fever, Hypoxemia</td>
<td>3</td>
</tr>
<tr>
<td>Cough</td>
<td>14</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14</td>
</tr>
<tr>
<td>Chest X-ray changes</td>
<td>30</td>
</tr>
</tbody>
</table>

Reducing Antibiotic Use in LRTI

Specific levels of serum Procalcitonin, an inflammatory biomarker, can be used to identify non-bacterial respiratory tract infections & reduce antibiotic use…

- True
- False
- Uncertain
Reducing Antibiotic Use in LRTI

Specific levels of serum Procalcitonin, an inflammatory biomarker, can be used to identify non-bacterial respiratory tract infections & reduce antibiotic use…

- True
- False
- Uncertain
Procalcitonin: Reducing Antibiotic Use in LRTI

• 13 kD protein, normally not detectable in serum
• Bacterial infection: Procalcitonin released into serum w/in 3-6 hours vs CRP & ESR, delayed ~24 hours
  – Potent stimuli: Endotoxin (gram negatives), IL-1, TNF
  – Gram positive bacteria less potent but markedly greater than viruses/mycoplasma
• Virus infection: Interferon-\(\gamma\) release suppresses procalcitonin
LRTI: Procalcitonin Guided Therapy

Cochrane Meta Analysis 2011, updated 2017 supports Procalcitonin Guided Treatment (international)

• High quality data from 26 RCT both severe & not RTI
• Withhold antibiotics & shorten antibiotic duration
• Lower risk for mortality
• Fewer antibiotic related AE’s (ie, C diff)

Why isn’t procalcitonin algorithm widely used US?

• Sporadic skepticism remains in the US
• Recent: Failed to reduce antibiotic use in 14 US ED’s
  Huang DM, et al. NEJM 2018;379(3):236-49

Test not available at UIHC at the point of care
(eg, ESR, CBC, D-Dimer)
Who Here Adheres to CAP Guidelines?

Outpatient CAP?

Hospitalized CAP?
Positive Impact of Guideline Adherence

Outpatient CAP
• ↓ Number admissions w/o ↑ adverse events

Inpatient CAP (80% cost)
• ↓ Length of stay and Cost
• ↓ Mortality
  – 1st 48 hours & 30 day time points
  – General ward & ICU cases

Bugs...

**Outpatient:**

*S. pneumoniae, M. pneumoniae, H. influenzae, C. pneumoniae, Respiratory viruses*

**Inpatient:**

**Non-ICU:** *S. pneumoniae, M. pneumoniae, C. pneumoniae, H. influenzae, Legionella spp, Aspiration, Respiratory viruses*

**ICU:** *S. pneumoniae, S. aureus (CA-MRSA), Legionella spp, GNB, H. influenzae*

**Outpatient IDSA/ATS Therapeutic Guidelines**

<table>
<thead>
<tr>
<th>Outpatient bacterial CAP w/ following:</th>
<th>Therapeutic recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>No RF for DRSP</td>
<td>Macrolide (azithro-, clarithro-, or erythromycin*) [Strong, I] OR Doxycycline [Weak, III]</td>
</tr>
<tr>
<td>Co-morbidities†; Immunosuppression; Antimicrobials use past 3 months; RF for DRSP</td>
<td>Respiratory quinolone (moxi-, gemi-, levofloxacin) [Strong, I] OR Macrolide + Amox‡ or Amox-clav§ [Strong, I] Alternative β-lactam: ceftriaxone, cefpodoxime, cefuroxime Alternative to macrolide: Doxycycline [Moderate, III]⁺</td>
</tr>
</tbody>
</table>

*Erythromycin is less effective against *H influenzae*.

†Chronic heart, lung, liver, or renal disease; DM; EtOHism; Malignancy; asplenia.

‡1 g 3 times daily.

§2 g 2 times daily.

⁺Regions where macrolide resistant (MIC ≥ 16) *S. pneumoniae* rates >25%
# Inpatient IDSA/ATS Therapeutic Guidelines

<table>
<thead>
<tr>
<th>Inpatient CAP</th>
<th>Therapeutic recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-ICU</td>
<td>Respiratory quinolone (moxi-, gemi-, levofloxacin)* [Strong, I] OR β-lactam plus macrolide [Strong, I]</td>
</tr>
<tr>
<td>ICU</td>
<td>β-lactam (ceftriaxone, cefotaxime, or amp/sulb) PLUS either Respiratory quinolone [Level I] OR Macrolide [Level II]</td>
</tr>
</tbody>
</table>

**Special Concerns:**

- *P. aeruginosa*—Anti-pneumococcal, anti-pseudomonal β-lactam (pip/tazo, cefepime, mero- or imipenem) plus Cipro- or levofloxacin (750mg) OR Above β-lactam plus aminoglycoside and azithromycin or respiratory quinolone

- CA-MRSA—Vancomycin or Linezolid

*Quinolone alone exhibited 2x ↑mortality compared to β-Lactam & macrolide combination for PSI class V in VA population.*

S. pneumoniae…

- Most common bacterial cause: Hospitalized CAP Decreasing w/ increased vaccination
- Detectable by sensitive/specific Urine Ag Test
- Invasive Pneumococcal Disease (IPD)
  - CAP w/ +blood culture, Menningitis, Empyema
  - At risk: children, >65, Co-morbidity & Immune impaired
  - Case fatality 10-40% among adults
  - Dual antibiotic (macrolide) therapy…

Kyaw et al. NEJM 2006; Bender et al. Clin Infect Dis 2008
Macrolide Benefit?

- Macrolide benefit = Antibiotic benefit… also achieved by tetracyclines or quinolones
- No benefit: all supportive data retrospective & suspect
- Macrolides a/w better outcomes
Dual Antibiotics w/ Macrolide for IPD (Adults)

- Supported by retrospective studies showing lactam/macrolide more potent than other combinations
- Multiple data point to beneficial Macrolide effect
  - Atypical org (M. pneumonae, C. pneumoniae, L. pneumophila) unrecognized co-pathogen (all age groups)
    - Quinolone & Tetracycline outcomes not as good as Macrolides (in vitro = not different)
    - Macrolides decrease release of toxin by S pneumoniae (pneumolysin)
  - Animal model ⇒ Macrolide advantage demonstrable even w/ Macrolide resistant organisms
  - Anti-inflammatory effect of Macrolides well documented
- Best outcomes: Hospitalized CAP w/RF for sepsis, respiratory failure (anti-inflammatory advantage not required CAP no RF)

When I’m Admitted to ICU w/ CAP...

ASAP...

IV azithro (anti-pneumolysin)

followed by

IV ceftriaxone
What is the clinical impact of Drug Resistant S. pneumoniae (DRSP)?
Antibiotic Resistance Impact on CAP Outcomes

- Difficult to show correlation between MIC & outcome
- Clinical failures more often associated with…
  - Host factors: Extremes of age, Immunosuppression, Debilitating Disease, Multi-comorbidity
  - Intrinsic organism virulence such as capsule subtype
- Mortality Rates associated with…
  - Multi-lobar involvement, Severity = ICU (hypotensive, ↓ O2)
  - Renal disease & multiple co-morbidity

**S. pneumoniae Pneumonia...**

- **Most common bacterial cause:** 30-60% hospitalized Community Acquired Pneumonia (CAP)
- **Invasive Pneumococcal Disease (IPD)**
  - Pneumonia w/ +blood culture, Meningitis, or Empyema
  - Case fatality 10-40% among adults
  - At risk: Children, >65, & patients w/ chronic illness...
- **Vaccine (23 valent, Pneumovax) reduces IPD incidence in adults**
  - Covers about 80% of strains causing pneumonia
  - Noninvasive pneumonia (mortality <5%) rate unaffected
- **Protein conjugated vaccine (13 valent, Prevnar) reduces IPD in children**
  - ↓ Nasopharynx carriage
  - Reduces IPD in adult caregivers (herd immunity)

Kyaw et al. *NEJM* 2006; Bender et al. *Clin Infect Dis* 2008
# Chronic Illness and Risk for Invasive Pneumococcal Disease

Asthma and Smoking added to list of indications in 2009

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Cases /100,000 Persons</th>
<th>Fold Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy adults</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>51</td>
<td>5.8</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>63</td>
<td>7.1</td>
</tr>
<tr>
<td>Chronic heart disease</td>
<td>94</td>
<td>10.6</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>100</td>
<td>11.3</td>
</tr>
<tr>
<td>Solid cancers</td>
<td>300</td>
<td>34.1</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>423</td>
<td>48.1</td>
</tr>
<tr>
<td>Hematologic cancers</td>
<td>503</td>
<td>57.1</td>
</tr>
</tbody>
</table>

All above = Indications for Pneumonia Vaccine

Asthma and Smoking added to list of indications in 2009

Kyaw et al: JID 2005;192:377-86
**S. pneumoniae Pneumonia...**

- Most common bacterial cause: 30-60% hospitalized Community Acquired Pneumonia (CAP)
- Invasive Pneumococcal Disease (IPD)
  - Pneumonia w/ +blood culture, Meningitis, or Empyema
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Kyaw et al. *NEJM* 2006; Bender et al. *Clin Infect Dis* 2008
Polysaccharide Vaccine (23 valent) Effective...

- In at risk group: Prevents Invasive Pneumococcal Pneumonia (IPD) by 60-80%, which carries high case fatality rate

- Hospitalized CAP: Reduced mortality (40-70%), complications, & Length of Stay.

- Protein Conjugate Vaccine (Prevnar 13) approved for immunosuppressed adults December 2011

The 13-valent Protein Conjugate Vaccine (Prevnar) should be routinely given to all adults \( \geq 65 \) years…

- True
- False
- Uncertain
Pneumococcal Pneumonia Prevention

The 13-valent Protein Conjugate Vaccine (Prevnar) should be routinely given to all adults $\geq 65$ years…

- True
- False
- Uncertain
## ACIP Adult Vaccine Recommendations
**PCV13 (New) vs PPSV 23 (Current)**

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Underlying medical condition</th>
<th>PCV13 Recommended</th>
<th>PPSV23 Recommended</th>
<th>Revaccination 5 yrs after first dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunocompetent persons</strong></td>
<td>Chronic heart disease(^\d)</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease(^\d)</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cerebrospinal fluid leak</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cochlear implant</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alcoholism</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic liver disease, cirrhosis</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cigarette smoking</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td><strong>≥ 65</strong></td>
<td></td>
<td>✅</td>
<td>✅</td>
<td>If prior to 65</td>
</tr>
<tr>
<td><strong>Persons with functional or anatomic asplenia</strong></td>
<td>Sickle cell disease/other hemoglobinopathy</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Congenital or acquired asplenia</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td><strong>Immunocompromised persons</strong></td>
<td>Congenital or acquired immunodeficiency(^\d)</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human immunodeficiency virus infection</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic renal failure</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nephrotic syndrome</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leukemia</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hodgkin disease</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Generalized malignancy</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iatrogenic immunosuppression(^\d)</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Solid organ transplant</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple myeloma</td>
<td>✅</td>
<td>✅</td>
<td></td>
</tr>
</tbody>
</table>

≥ 65 yo should get PCV13 at the next vaccine opportunity
- Naïve: PCV13 then PPSV23 6-12 months later
- Prior PPSV23: PCV13 ≥ 1 year after PPSV23
Sequential Administration & Interval
ACIP Recommendations

*Minimal interval = 8 weeks and
PPSV23 can be done >6-12 months post PCV13 if window missed

MMWR Sept 19 2014
Both PCV13 & PPSV23 should be given routinely, in series, to all $\geq 65$ years

Other recommendations for PCV13 & PPSV23 have not changed
BTW...Influenza Vaccine Effective Also

- Compiled data (15 trials): 80% effective against lab-confirmed influenza when vaccine matches circulating strain(s)
- Elderly (>65) exhibit less reliable response to vaccine
  - Account for ~90% influenza related deaths
  - 50-60% reduction: pneumonia, hospital admits, and death
- Herd immunity effect: Health care worker vaccination >50% → significant reduction in patient mortality during flu season (eg, 22->14%)

Long Term Consequences of CAP?

Hospital CAP survivors > 2.5x one year mortality cp to age, sex-matched controls

• Holds up even when those w/ significant co-morbidities removed

• Possible explanation: CAP accelerates CV disease
  - Inflammation (eg IL-6, IL-10) destabilizes atheromatous plaques
  - Statin Rx a/w improved CAP outcomes (not proven when tested prospectively)
  - Risk may persist 5-10 years
  - Pathogen associated mechanisms…

Yende et al. *Am J Respir Crit Care Med* 2008
Restrepo & Reyes. *Respirology* Jan 2018
CV Complications d/t *S. pneumoniae*
Conclusions

Reviewed/updated clinical aspects of CAP:

- Epidemiology, Guidelines, Antimicrobial selections
- Viruses more common than previously suspected
- *S. pneumoniae* Pneumonia
  - Invasive Disease (IPD)
  - Dual (w/ macrolide) Therapy for Invasive Pneumococcal Pneumonia
  - Vaccination ↓ IPD…Pneumococcal (& Flu) vaccine work!
- Recent concepts: Procalcitonin (maybe), Hospital CAP → Long term consequences,
Selected References

• **CAP Review**

• **PCV13 for ≥65 years**

• **LRTI: Procalcitonin Guided Abx Stewardship**
  - Schuetz P, et al: PCT to initiate or d/c antibiotics in acute RTI. *Cochrane Database of Systematic Reviews* 2017; (10)CD007498
CAP Hospitalization

- Data → 20% CAP patients require hospitalization, but... MD practice: >50% admitted

- Prospective PSI studies:
  - MDs tend to err toward admitting low risk patients
  - MD judgment supersedes the PSI recommendations: 30% - 50% low-risk patients hospitalized
  - Reduced number of low-risk patients hospitalized = good outcome

Marrie et al: *JAMA*. 2000
**CAP--Site of Treatment (Out or In)**

- Determining site of treatment (outpatient or inpatient) remains the single most important clinical decision\(^1\)
- The Fine PSI or PORT prediction rule uses clinical RF to stratify patients into 5 severity classes & determine site of Rx\(^2\)

### PSI 2-step process
**Step 1: Does the patient fall into Risk Class I?**

**CAP is present**

- **\(\leq 50\) years**
  - No comorbid disease*
  - Vital signs normal
  - Mental status normal
  - **Risk Class I**
  - **Outpatient**

- **\(>50\) years**
  - Comorbid disease
  - Vital signs not normal
  - Mental status not nl
  - **Risk Class II-V**
  - **Step 2**

* Comorbid diseases include neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, or renal disease.

Step 2: Use Pneumonia Severity Index (PSI) numerical risk factor scoring system to classify patients into Risk Classes II–V.

**Risk factors**
- **Age:** men (+age in years); women (+age in years - 10)
- **Nursing Home Placement:** (+10)
- **Comorbidities:** neoplastic disease (+30), liver disease (+20), congestive heart failure (+10), cerebrovascular disease (+10), renal disease (+10)
- **Physical Findings:** altered mental status (+20), respiratory rate ≥30 m (+20), systolic blood pressure <90 mm Hg (+20), temperature <35°C or ≥40°C (+15), pulse ≥125 m (+10)
- **Lab / Radiology:** arterial pH <7.35 (+30), blood urea nitrogen ≥30 mg/dL (+20), sodium <130 mEq/L (+20), glucose ≥250 mg/dL (+10), hematocrit <30% (+10), PaO2 <60 mm Hg (+10), pleural effusion (+10)

**Risk Classes**
- **Risk Class II (≤70):** Outpatient
- **Risk Class III (71-90):** Outpatient/brief inpatient
- **Risk Class IV (91-130):** Inpatient
- **Risk Class V (>130):** Inpatient

## Who Should Be Hospitalized? -- PSI Outcome & Recommendations

<table>
<thead>
<tr>
<th>Risk Class</th>
<th>Points</th>
<th>%Mortality</th>
<th>Recommend</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td>0.1</td>
<td>Outpatient*</td>
</tr>
<tr>
<td>II</td>
<td>&lt;70</td>
<td>0.6</td>
<td>Outpatient*</td>
</tr>
<tr>
<td>III</td>
<td>71-90</td>
<td>0.9-2.8</td>
<td>Brief Inpatient*</td>
</tr>
<tr>
<td>IV</td>
<td>91-130</td>
<td>8.2-9.3</td>
<td>Inpatient</td>
</tr>
<tr>
<td>V</td>
<td>&gt;130</td>
<td>27-29.2</td>
<td>Inpatient</td>
</tr>
</tbody>
</table>

*Exceptions/Updates…  Adapted from Metlay & Fine: *Ann Int Med* 2003
Low Risk PSI Score…
Mitigating Factors for Outpatient Rx

• O2 saturation < 90% on ambient air
• Inability to take oral medications
• Frail physical conditions
• Unstable living situation
• Active co-morbidities requiring treatment
• Unreliable patient

Halm & Teirstein: NEJM 2002
IDSA/ATS: Site of Care (In or Out)
Severity of Illness Assessment

• Use index to identify candidates for outpatient Rx [Strong, I]
  – Pneumonia Severity Index (I-III vs. IV & V)…
  – Confusion, Uremia, Respiratory Rate, Low BP, and ≥ 65 = CURB-65 Index

• Subjective factors (eg, reliability, resources, etc) over rule decision based on index calculation [Strong, I]

• ICU admit criteria more quantitative [Moderate, II]
  – Goal: reduce # admitted to gen floor, then w/in 48 hrs transfer to ICU
## What tests?

- **Outpatient**: Chest x-ray…other tests optional
- **Inpatient**: When test yield is reasonable & results likely to change antibiotic selection…

<table>
<thead>
<tr>
<th>Indication</th>
<th>Blood Cult.</th>
<th>Sputa GS/C</th>
<th>Leg. UAT</th>
<th>S. pn. UAT</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU Admission</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X (QC)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X (tap)</td>
</tr>
<tr>
<td>EtOH abuse history</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Outpatient antibiotic failure</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cavitary Infiltrates</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X (TB,F)</td>
</tr>
<tr>
<td>Asplenia</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchiectasis/Severe COPD</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent travel (past 2 weeks)</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X (varies)</td>
</tr>
</tbody>
</table>

Prednisone Speeds CAP Recovery?

- Non-ICU Hosp CAP N=785, 7 Swiss tertiary hospitals
- DBRPC, Prednisone 50 mg x7days
- Endpoint: Stable VS x24hrs
- Results favored Prednisone
  - Median Time to Clin Stability: 3.0 vs 4.4 d, $P<0.0001$
  - Time to Hosp D/C: 6 vs 7 days, $P=0.012$
  - Pneumonia Associated Complications: 11 vs 22, NS
  - Prednisone a/w more inpatient hyperglycemia

Blum et al. *Lancet* 2015
Prednisone: Additional Supportive Data

- Beneficial anti-inflammatory effect
- Meta-analysis 13 RCT; 40-50 mg prednisone x 5-10 D
- Reduced mortality severe (ICU), but not non-severe
- Reduced time to cure, LOS, ICU days, respiratory failure, pneumonia complications
- Severe & non-severe pneumonia: reduced clinical failure: death from any cause & x-ray progression
- Elevated BS, but does not outweigh benefits

Procalcitonin Guided Therapy

**ProREAL: Arch Int Med 2012; 172(9): 715-721**

- Prospective, Multi-center (14), International (Swiss[10], France[3], US[1]), Observational, Quality Control
- Office, ER, Hospital Settings from Sept 2009-Feb 2011
- LRTI: CAP, Acute Exacerbation COPD, & Acute Bronchitis
- No Exclusion Criteria…Real Life Setting
- Web-based Procalcitonin Threshold ($\leq$ 25 ng/L) Protocol
  - Withhold Antibiotics
  - Stop Antibiotics
  - Strict adherence expected, but criteria to over-rule (initiate or continue antibiotics in extreme illness)
- N = 1759 (Swiss 1361, US 295, French 103)
- Evaluated 30 days:
  - Duration of Antibiotics: Compliant vs. Non-Compliant
  - Adverse Outcomes: Withheld antibiotics initially & Shortened course
ProREAL Results

- Adherent vs Non: Abx Duration ↓ 1.51 D (7.4 → 5.9, P < 0.001)
- At 30 days: No increased Adverse Events when antibiotics withheld or discontinued early