Community Acquired & Nosocomial Pneumonias

IDSA/ATS 2007 & 2016 Guidelines

José Luis González, MD
Clinical Assistant Professor of Medicine
Outline

• Intro - Definitions & Diagnosing
• CAP treatment
• VAP & HAP treatment
• De-escalating empiric therapy
• Use of biomarkers
• Summary
Definitions

• No gold standard
• Pneumonia: new lung infiltrate w/ clinical evidence of infectious origin:
Definitions

- No gold standard

- Pneumonia: new lung infiltrate w/ clinical evidence of infectious origin:
  - New onset fever
  - Purulent sputum
  - Leukocytosis
  - Decline in oxygenation
Pneumonias: Most common causes
Pneumonias: Most common causes

- S. pneumo, h. flu, m. catarrhalis
- Atypicals
- Viruses +/- causative agents
- Triaging:
Pneumonias: Most common causes

• S. pneumo, h. flu, m. catarrhalis
• Atypicals
• Viruses +/- causative agents

• CURB-65, PORT/PSI score, SMART-COP, REA-ICU, simplified minor criteria
IDSA / ATS 2007 Guidelines for CAP Tx

• Outpatient
  • No recent tx or comorbidities:
IDSA / ATS 2007 Guidelines for CAP Tx

- Outpatient
  - No recent tx or comorbidities: macro or doxy
IDSA / ATS 2007 Guidelines for CAP Tx

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  • Recent tx or comorbidities: FQ OR (macro AND β-lactam)
IDSA / ATS 2007 Guidelines for CAP Tx

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• Inpatient
  • Non-ICU:
IDSA / ATS 2007 Guidelines for CAP Tx

• Outpatient
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  • Recent tx or comorbidities: FQ OR (macro AND ß-lactam)

• Inpatient
  • Non-ICU: FQ or both (macro AND ß-lactam)
IDSA / ATS 2007 Guidelines for CAP Tx

• Outpatient
  • No recent tx or comorbidities: macro or doxy
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• Inpatient
  • Non-ICU: FQ or both (macro AND β-lactam)
  • ICU:
IDSA / ATS 2007 Guidelines for CAP Tx

• Outpatient
  • No recent tx or comorbidities: macro or doxy
  • Recent tx or comorbidities: FQ OR (macro AND β-lactam)

• Inpatient
  • Non-ICU: FQ or both (macro AND β-lactam)
  • ICU: β-lactam AND either (macrolide or FQ)
IDSA / ATS 2007 Guidelines for CAP Tx

- **Outpatient**
  - No recent tx or comorbidities: macro or doxy
  - Recent tx or comorbidities: FQ OR (macro AND β-lactam)

- **Inpatient**
  - Non-ICU: FQ or both (macro AND β-lactam)
  - ICU: β-lactam AND either (macrolide or FQ)

- 3 RCTs showed non-inferiority of β-lactam monotherapy in non-ICU pts
• Switch to PO as soon as tolerable
• Tx \geq 5\text{ days}
• Osteltamivir not recommended for pts w/ sxs >48h
• Guide therapy if etiology is IDd
Steroids as Adjunctive Treatment

- Multi-center, RCT: clinical stability **3.0 vs 4.4 days** (HR 1.33 95%CI 1.15-1.5) w/ 10mg prednisone x 7d
- Multi-center RCT: reduced risk of tx failure **(OR 0.34 95% CI 0.14-0.87)** w/ prednisolone 0.5mg/kg x 12h x 5d
- Differing results in sepsis literature w/ use of steroids
- Cochrane Review showed reduced mortality in patients w/ severe pneumonia using steroids
IDSA/ATS 2016 Guidelines
Management of Adults with Hospital-acquired and Ventilator-associated Pneumonia

• Use of Gradings of Recommendations Assessment, Development & Evaluation (GRADE)
• No more HCAP
• Encouraging development of hospital-specific antibiograms
Definitions

• Healthcare-Associated Pneumonia

• HAP:
  • pna not incubating at time of hospital admission and
  • occurring 48° post admission

• VAP:
  • pna occurring 48° post endotracheal intubation
Sputum Samples

• Non-invasive sampling > invasive sampling (wk, lq)
• Hold abx if Cxs result < threshold CFUs (BALs) (wk, vlq)

• Tx based on microbiologic evidence rather than empirically (wk, vlq)
  BAL < \(10^4\) CFUs   ETA < \(10^5\) CFUs   Induced sputum < \(10^6\) CFUs

• Only 30% of resp infections due to MRSA in pts w/ +MRSA screen
• Meta-analysis: poor concordance between gram stains and final cultures
Ventilator-Associated Pneumonia

Empiric Treatment
Organisms

• Gram Negative Bacilli

• Staphylococcus Aureus: MRSA vs MSSA

• Pseudomonas Aeruginosa: single agent vs double-coverage
VAP: Gram negative bacilli & MSSA

- Cefepime 2g IV q8h
  or
- Piperacillin-Tazobactam 4.5g IV q6h
  or
- Levofloxacin 750 IV qDay / Ciprofloxacin 400mg IV q8h
  or
- Meropenem 1g IV q8h / Imipenem 500mg IV q6h
VAP: When to treat for MRSA (sr, lg)

- IV abx within 90 days prior
- Renal replacement therapy
- Hospitalized 5d prior to intubation
- Septic shock @ time of VAP
- ARDS preceding intubation
- >10-20% or unknown MRSA rate (satisfied @ LAC)
# LAC-USC Medical Center
**Jan 2017-Dec 2017**

## Gram Positives

<table>
<thead>
<tr>
<th>Isolate Type</th>
<th># of Isolates</th>
<th>Amoxicillin</th>
<th>Clindamycin</th>
<th>Cefoxitin</th>
<th>Cefotaxime</th>
<th>Ceftriaxone</th>
<th>Daptomycin</th>
<th>Erythromycin</th>
<th>Gentamicin Synergy</th>
<th>Levofloxacin</th>
<th>Linezolid</th>
<th>Oxacillin</th>
<th>Pefloxacin</th>
<th>TMP/SMX</th>
<th>Trimethoprim</th>
<th>Vancomycin</th>
<th>Nitrofurantoin</th>
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<tr>
<td>MRSA</td>
<td>747</td>
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<td>67</td>
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<td>13</td>
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**Rate of MRSA susceptibility: 36%**

**Rate of VRE faecalis: 36%**

## URINE ISOLATES

<table>
<thead>
<tr>
<th>Isolate Type</th>
<th># of Isolates</th>
<th>Amoxicillin</th>
<th>Clindamycin</th>
<th>Cefoxitin</th>
<th>Cefotaxime</th>
<th>Ceftriaxone</th>
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**Rate of VRE faecalis: 2%; VRE faecium 68%**

* Meningitis, ** Non-meningitis; TMP/SMX: Trimethoprim/Sulfamethoxazole; MRSA: methicillin-resistant S. aureus; MSSA: methicillin-susceptible S. aureus; VRE: vancomycin resistant Enterococcus, 30 isolates tested
Treating for MRSA

- Vancomycin 15 mg/kg IV q8-12h
  or
- Linezolid 600 mg IV q12h
VAP: When to treat with 2 antibiotics for pseudomonas (wr, lq)

- IV abx within 90 days prior
- Renal replacement therapy
- Hospitalized 5d prior to intubation
- Septic shock @ time of VAP
- ARDS preceding intubation
- >10% resistance rates to single agent being considered (satisfied @ LAC)
### LAC-USC Medical Center
#### Jan 2017 - Dec 2017

### Gram Positives

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<tr>
<th></th>
<th># of isolates</th>
<th>Ampicillin</th>
<th>Cefaclor</th>
<th>Cefepime</th>
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Rate of MRSA: 33% - VRE faecium 58%

### Gram Negatives

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</tbody>
</table>

Rate of ESBL E coli: 28% - ESBL Klebsiella: 14%; CFE E coli: 2 isolates; CFE Klee pneumoniae: 0 isolate; 6 isolates tested; 8 isolates tested
Agents with activity against pseudomonas

- Cefepime 2g IV q8h
  
or
  - Piperacillin-Tazobactam 4.5g IV q6h
    
or
  - Levofloxacin 750 IV qDay / Ciprofloxacin 400mg IV q8h
    
or
  - Meropenem 1g IV q8h / Imipenem 500mg IV q6h
Hospital-Acquired Pneumonia

Empiric Treatment
HAP: Gram negative bacilli & MSSA

- Cefepime 2g IV q8h
  - or
- Piperacillin-Tazobactam 4.5g IV q6h
  - or
- Levofloxacin 750 IV qDay / Ciprofloxacin 400mg IV q8h
  - or
- Meropenem 1g IV q8h / Imipenem 500mg IV q6h
HAP: When to treat for MRSA *(sr, vlq)*

- IV abx within 90 days prior
- Septic shock
- Need for vent support due to pna
- >20% or unknown MRSA rate *(satisfied @ LAC)*
Treating for MRSA

• Vancomycin 15 mg/kg IV q8-12h
  or
• Linezolid 600 mg IV q12h
HAP: When to treat with 2 antibiotics for pseudomonas (sr, vlq)

- IV abx within 90 days prior
- Septic shock
- Need for vent support due to pna
- Structural lung disease (bronchiectasis or CF)
- High qual. Gram stain w/ numerous predominant GNB
Agents with activity against pseudomonas

- Cefepime 2g IV q8h
  or
- Piperacillin-Tazobactam 4.5g IV q6h
  or
- Levofloxacin 750 IV qDay / Ciprofloxacin 400mg IV q8h
  or
- Meropenem 1g IV q8h / Imipenem 500mg IV q6h
<table>
<thead>
<tr>
<th>VAP</th>
<th>HAP</th>
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<tr>
<td><strong>MRSA</strong></td>
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| IV abx within 90 days prior  
>10-20% or unknown MRSA rate  
Renal replacement therapy  
Hospitalized 5d prior to intubation  
Septic shock @ time of VAP  
ARDS preceding intubation | IV abx within 90 days prior  
>20% or unknown MRSA rate  
Septic shock  
Need for vent support due to pna |
| **Pseudomonas** | **Pseudomonas** |
| IV abx within 90 days prior  
>10% resistance rate to single agent being considered  
Renal replacement therapy  
Hospitalized 5d prior to intubation  
Septic shock @ time of VAP  
ARDS preceding intubation | IV abx within 90 days prior  
Septic shock  
Need for vent support due to pna  
Structural lung dz (bronchiectasis or CF)  
Gram stain w/ +++ predominant GNB |
Use Pharmakokinetic Data for Dosing (wk, vlq)

- 3 RCTs and 4 observational trials:
  - improved clinical cure rate
  - Reduced mortality
  - Reduced length of ICU stay
Duration of treatment

- How long do you treat?
Duration of treatment

• VAP: 7 days (st, mq)
  • 1 meta-analysis 508pts (7-8d tx vs 10-15d) showed no diff in:
    • Mortality, recurrent pna, duration of vent, hosp stay
  • Another 883pts (7-8d vs 10-15d) showed no diff in:
    • Mortality, recurrent pna, duration of vent, length of ICU stay
    • Subgroup of pseudomonas & Acinetobacter = slight increase in recurrence

• HAP: 7 days (st, vlq)
  • No studies on HAP duration of therapy; recs based on VAP
Empiric vs Targeted therapy
Empiric vs Targeted therapy

• Targeted > Empiric (st, lq)

• For pts w/ confirmed pseudomonas w/ known susceptibilities; ok to use monotherapy unless pt is: (wk, vlq)
  • In septic shock
  • At high risk of death
HAP & VAP: Should therapy be de-escalated?
HAP & VAP: Should therapy be de-escalated?
(wk, vlq)

- 6 trials: 1 RCTs, 5 observational trials
- When pooled, no diff in mortality
- 2nd RCT: some worse outcomes but pna subgroup = no diff
- Reasonable to de-escalate to single broad spectrum agent in pts who:
  - Have negative cultures
  - Are clinically improving
Ventilator Associated Tracheobronchitis

• Ventilated patient with:
  • Fever
  • New/increased sputum production
  • + endotrach aspirate cx (ETA $\geq 10^6$ CFUs)

• And no radiographic evidence of pneumonia

• Do not treat (wk, lq)
Biomarkers: Procalcitonin (PCT)

• Initiation
  • LAC says: yes
  • IDSA/ATS says: no (st, mq)
    • → no studies comparing patient outcomes
    • 6 studies w/ significant sources of bias: 67% sens, 83% spec

• Discontinuation
  • Meta-analysis of 14 trials: no diff in mortality or tx failure
  • 3 other RCTs: shorter duration of abx tx (9 vs 12d) w/o diff in outcomes
Procalcitonin Algorithm
@ LAC-USC
Cochrane Database Review

• 26 trials, (18 new trials in 2017 review)
• lower mortality rate 8.6% vs 10.0% (OR 0.83, 95% CI .70-.99, P=0.037)
• Treatment failure not significantly different
• 2.4 day reduction in abx exposure (5.7 vs 8.1d, 95% CI -2.71 to -1.15, P<0.001)
• Lower risk of abx SEs (16.3% vs 22.1%, OR 0.68, 95% CI 0.57-0.82, P <0.001)
Summary

• HAP & VAP occur 2 days post inciting event
• Obtain non-invasive cultures for HAP and VAP only
• Use antibiogram
• Use pharmacokinetic data
• De-escalate if pt improves, once sensitivities result. Ok to use PCT
References


2. LAC + USC Antibiogram; accessed 12/5/2017


