Community Acquired Pneumonia (CAP)

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Conflicts of interest

Research Grants:
DFG, EU, BMBF
Bayer, Grifols, Insmed

Fees for Lectures:
Astellas, AstraZeneca, Boehringer, Basilea, Bayer,
Berlin-Chemie, Grifols, Infectopharm, Mundipharma,
MSD, Novartis, Pfizer

Advisory Board:
AstraZeneca, Boehringer, Bayer, GSK, Insmed,
Novartis, Pfizer
34-year-old female, GP visit after two days of symptoms

- 2 days ago cough without sputum production started
- Fever of 38.9°C
- From yesterday increasing dyspnoea
- Yesterday evening temperature 39.1°C, chills
- Until now symptomatic therapy with antipyretics (paracetamol)
34-year-old female, GP visit after two days of symptoms

• History
  – Asthma bronchiale from childhood on
    • Regular therapy with fluticasone/salmeterol 50/250 1 puff bid
  – No further abnormalities known yet

• Profession
  – Grammar school teacher

• Family anamnesis
  – Married, two children (6 and 8 years old)
  – Mother and 6-year-old daughter with asthma as well
  – 6-year-old daughter with otitis media a week ago
Who is a “patient at risk”?
Setting

Steroid Use in Asthma - A Risk Factor for CAP?

McKeever T. Chest 2013; 144: 1788-94

- Primary care data from The Health Improvement Network in the UK
- People with asthma with pneumonia or lower respiratory tract infection
- Age- and sex-matched control subjects.
- The highest strength of ICS (≥1,000 µg) had a 2.04 increased risk of pneumonia or LTRI compared with no prescription for ICS within the previous 90 days
34-year-old female, GP visit after two days of symptoms

Clinical signs and symptoms

- Pt. well orientated
- Dyspnoea at rest (RR 24/minute), not cyanotic
- Cough without sputum production
- Auscultation:
  - Rales at left lower lobe dorsal
- HR 116/min, RR 85/52 mmHg, 38.9°C
Severity assessment

- **C** onfusion
- **R** espiratory rate > 30/min
- **B** lood pressure (RRsyst < 90 mmHg or RRdiast < 60 mmHg)
- > 65 (in CURB U=Urea > 7 mmol/L)

- 0 points treatment outside the hospital
- 1 point consider hospitalization
- > 2 points admit to hospital
Who is a “patient at risk”?

Age

Ewig S et al. Thorax 2009; 64: 1092-9
Who is a “patient at risk”? 

**Age**

- Comparison of patients with CAP aged 18 to <65 yrs with those aged 65 yrs in the CAPNETZ database were analysed for potential differences in baseline.
- 7,803 patients were studied:
  - 52.3% aged <65 yrs
  - 18 to <30 yrs 6.4%
  - <40 yrs 17.1%
  - <50 yrs 29.4%
- Co-morbidity 46.6% in the younger versus 88.2% in the older patient group.
- 74.0% of the younger patients presented with CURB-65 score of 0.
- *Streptococcus pneumoniae* and *Mycoplasma pneumoniae* were the most frequent pathogens in the younger patients.
- Short-term mortality was very low (1.7% versus 8.2%) and even lower in patients without co-morbidity (0.3% versus 2.4%).
- Long-term mortality was 3.2% versus 15.9%, also lower in patients without co-morbidity (0.8% versus 6.1%).

34-year-old female, GP visit after two days of symptoms

Biochemistry

- WBC 12,800/µL, Hct 34.6%, Platelets 142,000/µL
- Sodium 135 mmol/L, Glucose 12.6 mmol/L, BUN 33 mmol/L
- CRP 320mg/L, PCT 1.5 µg/L
- paO₂ 65mmHg, paCO₂ 32mmHg, pH 7.4, HCO₃ 17.4, SaO₂ 92%
Severity assessment

Clin Infect Dis 2007; 44: S27-72

• Major criteria
  – Mechanical ventilation
  – Septic shock (catecholamines)

• Minor criteria
  – Respiratory rate >30/min.
  – pO₂/FiO₂ < 250
  – Multilobular infiltrates in chest x ray
  – Altered mental status
  – BUN > 20 mg/dL
  – Thrombocytopenia (< 100,000/mm³)
  – Hypothermia (< 36.0°C)
  – Hypotension (Fluid resuscitation necessary)
34-year-old patient with CAP
CAP
paCO$_2$ as risk factor

- Retrospective observational study in 453 hospitalized CAP patients in two US hospitals
  - 188 (41%) Pts. with normal PaCO$_2$
  - 194 (42%) Pts. with PaCO$_2$ <35 mm Hg
  - 70 (15%) Pts. with PaCO$_2$ >45 mm Hg
- Hypocapnic pts. with increased 30d mortality (OR=2.84) and increase of ICU admittance (OR=2.88) compared with normocapnic patients
- Hypercapnic pts. with increased 30d mortality (OR=3.38) and ICU admittance (OR=5.35)
- These differences remain after exclusion of COPD pts

Laserna E et al CHEST 2012; 142(5):1193–1199
Biomarker
Blood glucose level

- 6,891 patients with community acquired pneumonia included in the German CAPNETZ study between 2003 and 2009.
- In patients without known diabetes, an elevated glucose level at admission was a predictor of 28- and 90-day mortality in CAP
  - glucose on admission 6–<11 mmol/L
    - HR for death at 90 days 1.55 (P<0.001)
  - admission glucose levels ≥14 mmol/L
    - HR for death 6.04 (P<0.001)
  - Pts with previously diagnosed diabetes had an increased overall mortality as compared to patients without diabetes (HR 2.47; P<0.001)
    - This outcome was not significantly affected by admission glucose levels (P=0.18).

Lepper P et al. BMJ 2012 May 28;344:e3397
# Biomarker Procalcitonin

<table>
<thead>
<tr>
<th></th>
<th>Risk Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate Analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (&gt; 0.228 ng/mL)</td>
<td>9.94 (5.22-18.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRB-65 (&gt;1)</td>
<td>6.56 (3.95-10.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Multivariate analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (&gt; 0.228 ng/mL)</td>
<td>7.75 (3.78-15.87)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRB-65 (&gt;1)</td>
<td>4.32 (2.58-7.25)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Krüger S et al. ERJ 2008; 31: 349-55
### Who is a “patient at risk”?

#### Etiology

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Outpatients (%)</th>
<th>Hospitalised Patients, not-ICU (%)</th>
<th>ICU-Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em></td>
<td>38</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td><em>M. pneumoniae</em></td>
<td>8</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>13</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td><em>C. pneumoniae</em></td>
<td>21</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>1,5</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>0</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Legionella spp.</td>
<td>0</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td><em>C. burnetti</em></td>
<td>1</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>RS-Virus</td>
<td>17</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>«unknown»</td>
<td>50</td>
<td>41</td>
<td>45</td>
</tr>
</tbody>
</table>

Prevalence of pathogens identified in patients with CAP with HIV or COPD

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>HIV</th>
<th>COPD</th>
<th>COPD</th>
<th>No COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with pathogen identified(^a)</td>
<td>Episodes with pathogen identified(^a)</td>
<td>Patients with pathogen identified(^b)</td>
<td>Range (%)</td>
</tr>
<tr>
<td>Gram-positive bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>57.8–81.8</td>
<td>429–51.4</td>
<td>37.5–66.3</td>
<td>26.9–57.0</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>6.5</td>
<td>3.3</td>
<td>1.1</td>
<td>0.8–3.2</td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram-negative enteric bacilli(^b)</td>
<td>7.8</td>
<td>7.1–42.9</td>
<td>16.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>3.2–9.1</td>
<td>6.7–14.3</td>
<td>1.1–4.2</td>
<td>1.7–3.8</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>5.9</td>
<td>6.7</td>
<td>2.1–7.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>5.8</td>
<td>6.7</td>
<td>1.1–2.6</td>
<td>1.1–1.3</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>5.9</td>
<td>6.7</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>5.9</td>
<td>6.7</td>
<td>2.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>9.1–10.8</td>
<td>3.3</td>
<td>2.1–12.5</td>
<td>1.7–3.8</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>5.9</td>
<td>6.7</td>
<td>2.1–6.3</td>
<td>4.1–4.5</td>
</tr>
<tr>
<td>Coxiella burnetii</td>
<td>5.9</td>
<td>6.7</td>
<td>2.1</td>
<td>1.5–3.4</td>
</tr>
<tr>
<td>Virus</td>
<td></td>
<td></td>
<td>4.2–13.7</td>
<td>2.8–12.5</td>
</tr>
</tbody>
</table>
34-year-old female, Intermediate Care Unit

- Pneumococcal urine antigen positive
- Blood culture positive for *S. pneumoniae*
- Therapy:
  - 2g Ceftriaxon od. + 500 mg Clarithromycin bid intravenously
- Oxygen supplementation
- Low dose low molecular heparin
<table>
<thead>
<tr>
<th>Source</th>
<th>Outcome</th>
<th>β-Lactam Plus Macrolide or Fluoroquinolone Monotherapy</th>
<th>β-Lactam Monotherapy</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>No. (%)</td>
<td>No. of Patients</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Gleeson et al, 1999</td>
<td>30-d Mortality</td>
<td>544</td>
<td>46 (8.4)</td>
<td>3430</td>
</tr>
<tr>
<td>Houck et al, 2001</td>
<td>30-d Mortality</td>
<td>312</td>
<td>26 (8.3)</td>
<td>1741</td>
</tr>
<tr>
<td>Garcia-Valezquez et al, 2005</td>
<td>In-hospital mortality</td>
<td>918</td>
<td>56 (6.1)</td>
<td>270</td>
</tr>
<tr>
<td>Paul et al, 2007</td>
<td>30-d Mortality</td>
<td>282</td>
<td>27 (7.4)</td>
<td>271</td>
</tr>
<tr>
<td>Bratzler et al, 2008</td>
<td>30-d Mortality</td>
<td>338</td>
<td>57 (16.9)</td>
<td>4463</td>
</tr>
<tr>
<td>Blasi et al, 2008</td>
<td>End of therapy mortality</td>
<td>375</td>
<td>19 (5.7)</td>
<td>452</td>
</tr>
<tr>
<td>Tessmer et al, 2008</td>
<td>30-d Mortality</td>
<td>946</td>
<td>42 (4.4)</td>
<td>908</td>
</tr>
<tr>
<td>Rodriguez et al, 2013</td>
<td>30-d In-hospital mortality</td>
<td>3239</td>
<td>74 (23.0)</td>
<td>2001</td>
</tr>
<tr>
<td>Garin et al, 2014</td>
<td>30-d Mortality</td>
<td>289</td>
<td>10 (3.4)</td>
<td>291</td>
</tr>
<tr>
<td>Postma et al, 2015</td>
<td>30-d Mortality</td>
<td>566</td>
<td>NR</td>
<td>506</td>
</tr>
<tr>
<td>Bratzler et al, 2008</td>
<td>30-d Mortality</td>
<td>5045</td>
<td>318 (6.3)</td>
<td>4463</td>
</tr>
<tr>
<td>Blasi et al, 2008</td>
<td>End of therapy mortality</td>
<td>363</td>
<td>33 (9.1)</td>
<td>452</td>
</tr>
<tr>
<td>Ewig et al, 2011</td>
<td>30-d Mortality</td>
<td>365</td>
<td>NR</td>
<td>1703</td>
</tr>
<tr>
<td>Postma et al, 2015</td>
<td>90-d Mortality</td>
<td>665</td>
<td>NR</td>
<td>506</td>
</tr>
</tbody>
</table>
Who is a “patient at risk”? 
Co-morbidity

- Observational, retrospective study of consecutive patients hospitalized with CAP at the Veterans Hospital of Louisville, KY, USA
- 500 patients admitted to ICU
- Clinical failure was defined as development of respiratory failure or shock
- AMI* was diagnosed based on abnormal troponin levels and ECG
- AMI was present in 15% of patients with severe CAP (13/86)
- AMI was present in 20% of patients that developed clinical failure (13/65)
- Significant associations of AMI with PSI score and with clinical failure (p=0.036)

<table>
<thead>
<tr>
<th>Variable</th>
<th>AMI (n = 29)</th>
<th>No AMI (n = 471)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to clinical stability, mean days ± SD</td>
<td>4.59 ± 2.73</td>
<td>3.1 ± 2.25</td>
<td>0.008</td>
</tr>
<tr>
<td>Length of hospital stay, mean days ± SD</td>
<td>9.9 ± 7.90</td>
<td>6.3 ± 7.68</td>
<td>0.01</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>15 (61.7)</td>
<td>52 (11.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality in hospital</td>
<td>8 (27.6)</td>
<td>32 (6.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality within 30 days after hospital admission</td>
<td>9 (31.0)</td>
<td>45 (9.6)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

NOTE: Data are no. (%) of patients, unless otherwise indicated

* AMI = acute myocardial infarction

Ramirez J. Clin Infect Dis 2008; 47: 182-87
Who is a “patient at risk”?  
Co-morbidity

- 1,343 in-patients and 944 out-patients with CAP
- Cardiac complications (new or worsening heart failure, new or worsening arrhythmias, or myocardial infarction) in 358 in-patients (26.7%) and 20 out-patients (2.1%)
- Most events (89.1% in in-patients, 75% in out-patients) were diagnosed within the first week, more than half of them were recognized in the first 24 hours
- Incident cardiac complications were associated with increased risk of death at 30 days

34-year-old female, Intermediate Care Unit
Day 3

- CRP and PCT decreased quickly
- Respiratory Rate at rest 16/minute
- Temperature: 37.8°C
- SaO2 (2 L oxygen supplementation) 96%
- Biochemistry
  - BUN 19 mmol/L
  - Glucose 9.8 mmol/L
C-reactive protein (CRP): Correlation with appropriateness of therapy

- Patients with inappropriate antibiotic treatment have a slower decline in CRP levels in first week of follow-up

34-year-old female, Intermediate Care Unit
Day 3

• Patient transferred to a normal ward
• Clarithromycin stopped
• Ceftriaxon switched to Amoxyclav 875/125 mg bid orally
• Early mobilisation out of bed
The ProCAP study – Antibiotic duration

Christ-Crain M et al, AJRCCM 2006; 174(1):84-93
CAP
Duration of Treatment

- Intervention group:
  - After 5 days stop of antibiotic therapy, if
    - Temperature < 37.8°C for 48 hours
    - Maximally one sign of clinical instability

- Control group:
  - Treatment duration due to physicians decision

Uranga A. et al.. JAMA Intern Med. 2016 Sep 1;176(9):1257-65
### CAP

#### Duration of Treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Group</th>
<th>Intervention Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No. of participants</td>
<td>150</td>
<td>162</td>
<td></td>
</tr>
<tr>
<td>Clinical success, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 10</td>
<td>71 (48.6)</td>
<td>90 (56.3)</td>
<td>.18</td>
</tr>
<tr>
<td>At day 30</td>
<td>132 (88.3)</td>
<td>147 (91.9)</td>
<td>.33</td>
</tr>
<tr>
<td>CAP symptom questionnaire score, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 5</td>
<td>23.7 (11.4)</td>
<td>27.2 (12.5)</td>
<td>.10</td>
</tr>
<tr>
<td>At day 10</td>
<td>18.8 (9.0)</td>
<td>17.9 (7.6)</td>
<td>.69</td>
</tr>
<tr>
<td>Per-Protocol Analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No. of participants</td>
<td>137</td>
<td>146</td>
<td></td>
</tr>
<tr>
<td>Clinical success, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 10</td>
<td>67 (50.4)</td>
<td>86 (59.7)</td>
<td>.12</td>
</tr>
<tr>
<td>At day 30</td>
<td>126 (92.7)</td>
<td>136 (94.4)</td>
<td>.54</td>
</tr>
<tr>
<td>CAP symptom questionnaire score, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 5</td>
<td>24.3 (11.4)</td>
<td>26.6 (12.1)</td>
<td>.16</td>
</tr>
<tr>
<td>At day 10</td>
<td>18.1 (8.5)</td>
<td>17.6 (7.4)</td>
<td>.81</td>
</tr>
</tbody>
</table>
- Prospective, multicentre, randomised, controlled, open-label intervention trial in 15 hospitals in the Netherlands
- Critically ill patients aged at least 18 years, admitted to the ICU,
  In the
  - Procalcitonin-guided group
    - non-binding advice to discontinue antibiotics was provided if procalcitonin concentration had decreased by 80% or more of its peak value or to 0.5 μg/L or lower
  - Standard-of-care group, patients were treated according to local antibiotic protocols.
Procalcitonin guided antibiotic therapy

• Between Sept 18, 2009, and July 1, 2013, 1575 were randomly assigned to
  – procalcitonin-guided group (761)
    • In 538 patients (71%) in the procalcitonin-guided group antibiotics were discontinued in the ICU
    – standard-of-care (785).
  • Median consumption of antibiotics was 7.5 in the PCT-guided group versus 9.3 daily defined doses in the SOC group
    – between-group absolute difference 2.69, p<0.0001
  • Median duration of treatment was 5 days in the PCT guided group and 7 days in the SOC group
    – between-group absolute difference 1.22, p<0·0001).
  • 28 day mortality was 149 (20%) in the PCT-guided group and 196 (25%) in the SOC group (   
    – between-group absolute difference 5.4%, p=0.0122) according to ITT analysis
34-year-old female, normal ward
When to discharge from the hospital?

- Heart rate ≤ 100/min,
- Respiratory rate ≤ 24/min,
- Systolic blood pressure ≥ 90 mmHg
- Temperature ≤ 37.8 °C,
- Eating and drinking not altered
- Normal mental status
- No hypoxemia (PO₂ ≥ 60 mm Hg, SaO₂ ≥ 90%)
» Pneumonia so? « asked the Senator and looked from one doctor to another »yes, indeed – Pneumonia«, answered Doktor Langhals with serious and correct bowing.

Thomas Mann. Die Buddenbrooks, IX. Teil, 1. Kapitel
• 82 year old male, nursing home resident, confusion starting two days ago
• Anamnesis
  – Diabetes mellitus for 15 years
  • Insulin dependency
  – Myokardial infarction 3 years ago
  – During the last 6 month two times hospital admitted with complicated UTI due to benign prostata hypertrophy
• Clinical Examination
  – Patient not oriented, dizziness
  – Respiratory rate at rest 20/minute, no cyanosis
  – Productive cough, Sputum colour: dark yellow
  – Auscultation:
    Rales ubiquitios.
  – HR 116/min, BP 170/50 mmHg, Temp. 36,1°C orally
Who is a “patient at risk”?  
Setting

• Admittance at the emergency department

• Additional Results
  – Biochemistry
    • WBC 16,900/µl, Hct 54,0%, Platelets 86,000/µl
    • Sodium 135 mmol/l, Glucose 236 mg/dl, BUN 33 mmol/l, Creatinine 1,5 mg/dl
    • CRP 216 mg/l
    • paO2 55 mmHg, paCO2 30 mmHg, pH 7,37, HCO3 17,4, SaO2 89%
  – Chest x-ray
Severity assessment

Clin Infect Dis 2007; 44: S27-72

- **Major criteria**
  - Mechanical ventilation
  - Septic shock (catecholamines)

- **Minor criteria**
  - Respiratory rate >30/min.
  - \( pO_2/FiO_2 < 250 \)
  - Multilobular infiltrates in chest x ray
  - Altered mental status
  - BUN > 20 mg/dL
  - Thrombocytopenia (< 100,000/mm³)
  - Hypothermia (< 36.0°C)
  - Hypotension (Fluid resuscitation necessary)
Setting: Nursing Home

Polverino E. Thorax 2010; 65: 354-59
• CAPNETZ Data Base (Pat. > 65 years)
• Patients with ‘classical’ CAP vs patients with HCAP
• No difference in etiology
  – *S. pneumoniae* dominant
• Multiresistant Pathogens rare (<5%)
  – *Staphylococcus aureus* was the only one more prevalent in HCAP
• Short- and long-term mortality higher in HCAP
• No association between mortality and MDR


<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Short-term mortality</th>
<th>Long-term mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with CAP≥65 years (n = 2569)</td>
<td>Patients with NHAP≥65 years (n = 518)</td>
</tr>
<tr>
<td><em>Streptococcus pneumonia</em></td>
<td>17/244 (7.0)</td>
<td>8/29 (27.6)</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>2/34 (5.9)</td>
<td>0/0</td>
</tr>
<tr>
<td><em>Legionella spp.</em></td>
<td>5/95 (5.3)</td>
<td>2/12 (16.7)</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>1/29 (3.4)</td>
<td>0/1 (0.0)</td>
</tr>
<tr>
<td><em>Enterobacteriaceae</em></td>
<td>7/67 (10.4)</td>
<td>4/11 (36.4)</td>
</tr>
<tr>
<td><em>Pseudomonas spp.</em></td>
<td>2/22 (9.1)</td>
<td>1/3 (33.3)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>2/17 (11.8)</td>
<td>4/10 (40.0)</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em></td>
<td>1/8 (12.5)</td>
<td>0/1 (0.0)</td>
</tr>
<tr>
<td><em>Influenza A</em></td>
<td>5/55 (9.1)</td>
<td>1/8 (12.5)</td>
</tr>
</tbody>
</table>
## Risk for MDR pathogens

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic heart failure</td>
<td>Enterobacteriaceae</td>
</tr>
<tr>
<td></td>
<td>*(i.e. <em>Klebsiella pneumoniae</em>, <em>Escherichia coli)</em></td>
</tr>
<tr>
<td>CNS-Disease (Dysphagia)</td>
<td>S. aureus (MSSA)</td>
</tr>
<tr>
<td></td>
<td>Enterobakterien</td>
</tr>
<tr>
<td></td>
<td>*(z. B. <em>Klebsiella pneumoniae</em>, <em>Escherichia coli)</em></td>
</tr>
<tr>
<td></td>
<td>Anaerobier</td>
</tr>
<tr>
<td>Severe COPD (GOLD IV and/or frequent exacerbations), Bronchiectasis</td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>Bedridden, enteral nutrition via PEG</td>
<td>S. Aureus</td>
</tr>
<tr>
<td></td>
<td>Enterobacteriaceae</td>
</tr>
<tr>
<td></td>
<td>P. aeruginosa</td>
</tr>
</tbody>
</table>
# Evaluation for MDR pathogens

<table>
<thead>
<tr>
<th>Exposition</th>
<th>Risk Factors</th>
<th>Modifying Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission of MDR pathogens</td>
<td>Strong: recent hospitalisation, Possible: Chronic Hemodialysis, Nursing Home</td>
<td>number, duration, Setting (f.e. ICU), Intervention (f.e. invasive MV)</td>
</tr>
<tr>
<td>Antimicrobial pre treatment</td>
<td>„Collateral damage“ of antimicrobial therapy</td>
<td>Antibiotic spectrum numbers, Dosis and Duration</td>
</tr>
</tbody>
</table>

Ewig S. et al.. Pneumologie 2016; Mar;70(3):151-200
• Admitted to the respiratory intermediate critical care unit

• Therapy:
  – 2g Ceftriaxon od + 500mg Clarithromycin bid
  – Oxygen supplementation
  – Low molecular heparin

• Further course
  – Deterioration of the clinical condition, development of multi organ failure
    • pO2 48 mmHg, start with High Flow oxygen
    • Creatinine 2.8 mg/dl
    • Platelets 68.000/µl

• Transfer to the Medical ICU
Klebsiella pneumoniae

• Diagnostics
  – Blood Cultures (two pairs)
    • positive for K. pneumoniae
  – Sputum Culture
    • Positive for K. pneumoniae and C. albicans
  – Urine Legionella Antigen
    • negative

- Ampicillin          R
- Piperacillin        R
- Cefazolin           R
- Ceftriaxon          R
- Ceftazidim          R
- Ciprofloxacin       R
- Moxifloxacin        R
- Cotrimoxazol        S
- Gentamicin          S
- Ertapenem           S
- Meropenem           S
- Colistin            S
ESBL Therapy

• Carbapenemes, Carbapenemes, Carbapenemes .....
Tazobactam for ESBL and Carbapenemases?
• Slow improvement of vigilance
• Normalisation of biochemistry parameters
• SaO2 (2 l Oxygen suppl.) 96%
• Respiratory rate at rest 16/minute
• Temperature: 37.0°C
• Discharge to RICU at day 6, to normal ward at day 10
# Fall 4

15.02.

27.02.
CAPNETZ
31.03.2016

- 11,044 patients
  - 8,082 hospitalized patients
  - 3,062 outpatients
- 28 day mortality 8.2%
  - 0.5% in outpatients
  - 11.5% in hospitalised patients
  - 2.2% in patients < 65 years
  - 11.8% in the elderly
- 6-Month mortality 13.8%
  - 5.6% of the patients died after hospital discharge
CAP – Long Term Mortality

- 6,078 adults with CAP were prospectively recruited and matched (age, sex, and site of treatment) with 5 control subjects without CAP (n = 29,402, 56% outpatients).
- Over a median of 9.8 years, 2,858 patients with CAP died compared with 9,399 control subjects (RR 30 per 1,000 py; aHR 1.65; P,0.001).
- Pts < 25 years old had the lowest absolute RR (4 per 1,000 py; aHR, 2.40).
- Pts > 80 years old had the highest absolute rate difference (92 per 1,000 py; aHR, 1.42).

Eurich DT et al. AJRCCM 2015; 192: 597-604
Eurich DT et al. AJRCCM 2015; 192: 597-604

- All CAP Patients
- Inpatients Only
- Outpatients Only
- Exclude Events within 30 Days
- Exclude Events within 90 Days

Time-Varying Elixhauser Comorbidities
- Comorbidity Subgroups
  - Diabetes
  - Heart Failure
  - COPD
  - >= 3 Comorbidities
  - No Comorbidities
- Exclude Prior History of CAP

HR:
- Reduced Risk
- Increased Risk
- HR values for different conditions and scenarios are shown on the graph.
CAP – Long Term Mortality

- 2 community-based cohorts:
  - CHS, n = 5888; age ≥ 65 y; enrollment period 1989–1994
  - ARIC, n = 15,792; age 45–64 years; enrollment period 1987–1989.
- Follow up through 31.12. 2010
- Matching of each participant hospitalized with CAP to 2 controls.
- Of 591 pneumonia cases in CHS, 206 had CVD events over 10 years after pneumonia hospitalization.
- CVD risk among pneumonia cases was highest during the first year after hospitalization and remained significantly higher than among controls through 10 years.

# CAP – Long Term Mortality

<table>
<thead>
<tr>
<th>Time Intervals After Pneumonia</th>
<th>Pneumonia Cases</th>
<th>Controls</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of CVD Events/ No. at Risk (%)</td>
<td>No. of CVD Events/ No. at Risk (%)</td>
<td>Unadjusted</td>
</tr>
<tr>
<td><strong>0-30 d</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>54/508 (10.6)</td>
<td>6/1092 (0.5)</td>
<td>4.70 (3.42-5.98)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>28/177 (15.8)</td>
<td>2/396 (0.5)</td>
<td>6.28 (3.46-9.10)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>26/331 (7.9)</td>
<td>4/696 (0.6)</td>
<td>3.95 (2.58-5.22)</td>
</tr>
<tr>
<td><strong>31-90 d</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>11/384 (2.9)</td>
<td>9/1084 (0.8)</td>
<td>3.32 (2.55-4.10)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>3/122 (2.5)</td>
<td>2/393 (0.5)</td>
<td>4.46 (2.77-6.69)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>8/262 (3.1)</td>
<td>7/691 (1.0)</td>
<td>2.80 (1.96-3.65)</td>
</tr>
<tr>
<td><strong>91 d-1 y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>22/345 (6.4)</td>
<td>55/1063 (5.2)</td>
<td>2.39 (1.85-3.11)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>9/113 (8.0)</td>
<td>13/207 (6.2)</td>
<td>3.16 (2.00-4.12)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>13/232 (5.6)</td>
<td>42/678 (6.2)</td>
<td>2.03 (1.42-2.88)</td>
</tr>
<tr>
<td><strong>1-2 y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>28/322 (8.7)</td>
<td>53/985 (5.4)</td>
<td>3.05 (2.42-3.89)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>7/67 (8.0)</td>
<td>22/367 (6.0)</td>
<td>2.23 (1.46-3.04)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>21/159 (13.4)</td>
<td>31/516 (5.0)</td>
<td>1.96 (1.44-2.67)</td>
</tr>
<tr>
<td><strong>2-3 y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>9/209 (4.3)</td>
<td>38/885 (4.4)</td>
<td>1.75 (1.39-2.12)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>2/68 (2.9)</td>
<td>12/323 (3.7)</td>
<td>1.85 (1.22-2.49)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>7/141 (5.0)</td>
<td>27/562 (4.8)</td>
<td>1.70 (1.25-2.14)</td>
</tr>
<tr>
<td><strong>3-4 y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>14/182 (7.7)</td>
<td>35/811 (4.3)</td>
<td>1.74 (1.37-2.12)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>7/63 (11.1)</td>
<td>17/292 (5.8)</td>
<td>1.79 (1.54-2.34)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>7/119 (5.9)</td>
<td>18/519 (3.5)</td>
<td>1.72 (1.24-2.19)</td>
</tr>
<tr>
<td><strong>4-5 y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pneumonia</td>
<td>12/143 (8.4)</td>
<td>32/736 (4.3)</td>
<td>1.70 (1.31-2.10)</td>
</tr>
<tr>
<td>With organ dysfunction</td>
<td>3/54 (5.6)</td>
<td>6/255 (2.4)</td>
<td>1.82 (1.15-2.48)</td>
</tr>
<tr>
<td>Without organ dysfunction</td>
<td>9/89 (10.1)</td>
<td>26/481 (5.4)</td>
<td>1.64 (1.15-2.13)</td>
</tr>
</tbody>
</table>
CAP – Long Term Mortality

- 392 patients with pneumococcal pneumonia
- Fortyeight (12.2%) patients died within 1 month of admission.
- 32.2% of the 1-month survivors died within 10 years
- The death rate increased proportionally with the height of the admitting PORT score (P < .001)

Sandvall B et al. CID 2013:56; 1145-6.
CAP at discharge from hospital
What to consider

- E80 smoking cessation
- E81 check for PPI therapy, stop if not indicated
- E82 check for antipsychotic/antidepressive therapy. Stop if not indicated
- E83 in COPD patients check for ICS use. Stop if not indicated
- E84 check for influenza-/pneumococcal vaccination. Add if not present
- E87 check for dysphagia. Start logopaedy and physiotherapy if necessary
21.02.2016

• 21 year old female from Somalia, fever for 48 hours
• Anamnesis (Translator)
  – Migration started a year ago
  – Migration route via Libya and Italy, several times imprisoned in Libya
  – Arrived in a refugee center in Hannover a week ago
  – Pregnancy cannot be ruled out
• Clinical status
  – Oriented patient
  – Little dyspnoe at exercise, but not at rest (Respiratory rate 12/minute), not cyanotic
  – Cough without sputum production
  – Auscultation:
    • Rales lower lobes
    – RR 84/min, BP 115/65 mmHg, Temp. 38,5°C
CAP Diagnosis in Outpatients

E1 Chest X-ray if pneumonia is suspected

E2 Thoracic ultrasound may be used if chest x-ray is not available

E3 CRP-POCT recommended. If increased (> 50 mg/l), CAP probable

Ewig S. et al.. Pneumologie 2016
E13 In patients with mild pneumonia no microbiological diagnosis is recommended

Ewig S. et al.. Pneumologie 2016
Severity assessment

- C onfusion
- R espiratory rate > 30/min
- B lood pressure (RRsyst < 90 mmHg or RRdiast < 60 mmHg)
- > 65 (in CURB U=Urea > 7 mmol/L)

- 0 points  treatment outside the hospital
- 1 point  consider hospitalization
- > 2 points  admit to hospital
GP prescribed:

- Amoxyclav 875/125 bid
CAP in outpatients
Treatment

• E23 In patients with mild CAP without co-morbidities a monotherapy with high dose Amoxicillin should be started

• Alternativly (Penicillin hypersensitivity) a fluorquinolone (Moxifloxacin, Levofloxacin), or a Makrolid (Azithromycin, Clarithromycin, second choice), or a Tetracyclin (Doxycyclin) could be used
CAP in Outpatients
Treatment

- E24 Patients with mild CAP and co-morbidities should be treated with a Aminopenicillin/Betalaktamase-Inhibitor-Combination
- Alternativly a flourquinolone (Moxifloxacin, Levofloxacin) could be used
- In severe COPD and/or bronchiectasis a treatment with Amoxicillin/Ciprofloxacin or Levofloxacin is possible
Community-acquired pneumonia as medical emergency: predictors of early deterioration

Martin Kolditz, Santiago Ewig, Benjamin Klapdor, Hartwig Schütte, Johannes Winning, Jan Rupp, Norbert Suttrop, Tobias Welte, Gernot Rohde

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4771 patients included in CAPNETZ 2007-2012

Exclusion:
- 1256 patients with ambulatory management
- 88 patients with missing data for emergency CAP definition

3429 patients included in analysis

Emergency CAP within 72 h:
- 140 patients (4%)
  - 30-day mortality 24 (17%)

Emergency CAP within 7 d:
- 173 patients (5%)
  (Additional 33 patients)
  - 30-day mortality 46 (27%)

No emergency CAP within 7 d:
- 3254 patients (95%)
  - 30-day mortality 65 (2%)

Presenting with immediate need of MV/VS*:
- 99 patients (68%)
  - 30-day mortality 8 (8%)
  - Invasive MV/VS* 29 (31%)
  - 30-day mortality 7 (24%)
  - Non-invasive MV* 66 (69%)
  - 30-day mortality 1 (2%)

Need of MV/VS* between day 4 and 7:
- 21 patients (64%)
  - 30-day mortality 10 (48%)

Death between day 4 and 7 without MV/VS*:
- 12 patients (36%)

Need of MV/VS* without immediate MV/VS*:
- 35 patients (25%)
  - 30-day mortality 6 (17%)

Death within 72 hours without MV/VS*:
- 10 patients (7%)
23.02.2016

- Erneute Vorstellung in der Notaufnahme wegen deutlicher Verschlechterung
- Klinischer Befund
  - Orientierte Patientin
  - Luftnot unter geringster Belastung (Ruhe Atemfrequenz 30/Minute), keine Zyanose
  - Husten ohne Sputumproduktion
  - Auskultation:
    - Verschärftes Atemgeräusch + mittelblasige Rg´s ubiquitär
    - HF 116/min, RR 85/52 mmHg, Temp. 38,9°C aurikulär
- Labor
  - Leuko 12.800/ µl, Hct 34,6%, Thrombo 142.000/µl, CRP 320mg/l
  - Natrium 135 mmol/l, Glucose 12.6 mmol/l, Harnstoff-N 33 mmol/l
  - paO2 55mmHg, paCO2 32mmHg, pH 7,40, HCO3 17,4, SaO2 86%
Schweregradbeurteilung in der Notaufnahme

• Major Kriterien
  – Beatmung
  – Katecholamine wegen Kreislaufschock

• Minor Kriterien
  – Atemfrequenz ≥ 30/min.
  – pO2/FiO2 < 250
  – Multilobuläre Infiltrates im Röntgenbild
  – Desorientiertheit
  – BUN > 20 mg/dl
  – Thrombozytopenie (< 100.000/mm³)
  – Hypothermie (< 36.0°C)
  – Hypotension (Volumenersatz notwendig)

Ewig S. et al. Pneumologie 2016
23.02.2016

- Behandlungsbeginn mit 2g Ceftriaxon 1x tgl + 500mg Clarithromycin 2x tgl. iv
- Schnelle Verschlechterung
- Intubation und Beatmung am selben Tag
- Trotz hohem PEEP und Bauchlagerung weitere Verschlechterung
  - pO2 42 mmHg, pCO2 56 mmHg, pH 7.23 mit FiO2 1.0 und PEEP 18 cm H2O
- Beginn einer v/v ECMO Therapie
Wie wird eine schwere CAP therapiert?

• E27 Patienten mit schwerer Pneumonie sollen initial kalkuliert eine intravenöse Kombinationstherapie aus einem β-Laktam mit breitem Spektrum (Piperacillin/Tazobactam, Cefotaxim oder Ceftriaxon) und einem Makrolid erhalten.

• Bei klinischer Stabilisierung und fehlendem Nachweis eines atypischen bakteriellen Erregers soll die Makrolidtherapie nach 3 Tagen beendet werden.

• Die Monotherapie mit einem Fluorchinolon (Moxifloxacin, Levofloxacin) ist eine mögliche Alternative, dies gilt jedoch nur für Patienten ohne septischen Schock.

• Starke Empfehlung, Evidenz B.
Welche anderen supportiven Maßnahmen sind indiziert?

• In den systematischen Reviews und Metaanalysen wurde wiederholt darauf hingewiesen, dass bei schwerer Pneumonie systemische Steroide die Letalität möglicherweise vermindern können und zur Beantwortung der Frage größere prospektive Studien notwendig sind.
Welche anderen supportiven Maßnahmen sind indiziert?

- E49 Patienten mit im Rahmen der Pneumonie zunehmender Obstruktion bei chronisch obstruktiver Lungenerkrankung (COPD oder Asthma) sollen systemische Steroide adjuvant entsprechend den üblichen Therapiestandards für 5 bzw. 7 Tage erhalten.
- Starke Empfehlung, Evidenz B.
Corticosteroids as adjunctive treatment in severe Influenza

- H1N1 in South Korea 2009/2010 were enrolled.
- Patients with and without adjuvant corticosteroid treatment were retrospectively compared by
  - (1) a retrospective cohort study
  - (2) a propensity-matched case–control study.
- 245 patients were enrolled in the cohort study, 107 (44%) received CS
  - 90-day mortality 58% with and 27% wo CS (P<0.001).
- In the case–control study, 90-day mortality 54% (35 of 65) with and 31% (20 of 65) wo CS (P= 0.004)

• Mikrobiologie:
  – Blut Kulturen: negative
  – Sputum Kulturen: negativ
  – Urin Antigen: Pneumokokken/Legionellen negativ
  – Influenza Screening: negativ
  – HIV Schnelltest: negativ
  – Schwangerschaftstest: negativ
<table>
<thead>
<tr>
<th>Erreger</th>
<th>Typische Anamnese</th>
<th>Verfahren</th>
<th>Referenz</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bakterien</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>junger Patient, ambulant, manchmal Ausbrüche, epidemiologische Situation</td>
<td>NAT</td>
<td>[171]</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>epidemiologische Situation, Reisen mit Hotelaufenthalt</td>
<td>Urinantigen, NAT</td>
<td>siehe Text</td>
</tr>
<tr>
<td><em>Chlamydomphila psittaci</em></td>
<td>Tierkontakt (Papagelen, Sittiche, Tauben)</td>
<td>NAT, NAT</td>
<td>[160]</td>
</tr>
<tr>
<td><em>Coxiella burnetii</em></td>
<td>epidemiologische Situation, Tier (Schaf) Kontakte</td>
<td>NAT</td>
<td>[172]</td>
</tr>
<tr>
<td><em>Burkholderia pseudomallei</em></td>
<td>Reisen nach Südostasien (Meliodose) Reisen</td>
<td>Kultur</td>
<td>[160]</td>
</tr>
<tr>
<td><strong>Respiratorische Viren</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Influenza A/B</em></td>
<td>epidemiologische Situation (Saison, Epidemie &amp; Pandemie)</td>
<td>NAT</td>
<td>siehe Text</td>
</tr>
<tr>
<td><em>Parainfluenzaviren</em></td>
<td>epidemiologische Situation</td>
<td>NAT</td>
<td>siehe Text</td>
</tr>
<tr>
<td><em>Adenoviren</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>RSV</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Mers-Coronavirus</em></td>
<td>epidemiologische Situation, Kontakt zu Infizierten</td>
<td>NAT, in der Regel in spezialisierten Zentren</td>
<td>[173]</td>
</tr>
<tr>
<td><strong>Pilze</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Cryptococcosis neoforms var. gattii</em></td>
<td>Aufenthalt in trockenen Zonen/ Regionen der südl. USA, Mittel und Südamerika</td>
<td>kulturell unter S3-Sicherheitsbedingungen</td>
<td>[174]</td>
</tr>
<tr>
<td><em>Histoplasmosis</em></td>
<td>Aufenthalt in gefährdeten Regionen der USA (Ohio, entlang der Flüsse Mississippi und Missouri und St. Lawrence River) und Mittelamerika</td>
<td>kulturell Serologie, NAT</td>
<td>[175, 176]</td>
</tr>
<tr>
<td><em>Cryptothyrium capsulatum</em></td>
<td>Aufenthalt in trockenen Zonen/ Regionen der südl. USA, Mittel und Südamerika</td>
<td>kulturell Antigen-Test, NAT</td>
<td>[177]</td>
</tr>
</tbody>
</table>
25.02.2016

- Mikrobiologie:
  - Blut Kulturen: negative
  - Sputum: Gram Färbung negativ
  - Urin Antigen: Pneumokokken/Legionellen negativ
  - Influenza Screening: negativ
  - HIV Schnelltest: negativ

- Myoplasmen PCR positiv
- Mycoplasmen IGM 1:256
25.02.2016

• Umstellung der Antibiotikatherapie auf Moxifloxacin 400 mg 1x tgl.
• Langsame Erholung, ECMO nach 5 Tagen beendet, Extubation nach 9 Tagen, Antibiotikatherapie nach 10 Tagen