Community-acquired pneumonia (adult)

A/Professor John Ferguson
Microbiologist and Infectious Diseases Physician
Hunter Area Pathology Service
Newcastle, NSW, Australia
jferguson@hnehealth.nsw.gov.au

May 2018
http://idmic.net
Overview

1. Epidemiology
2. Prevention
3. Clinical assessment
4. Laboratory diagnostics
5. Antimicrobial therapeutics
Bir Hospital Division of Medicine annual report

Common causes for admission

– COPD with exacerbation  573
– Community acquired pneumonia  286
– TB/Empyaema/Pneumothorax  430
– CLD  334
– Poisoning  517
– Heart failure/valvular disease  429
Figure 1: Age-specific incidence of community-acquired pneumonia
Error bars=95% CIs. Modified from reference 8 with permission of Oxford University Press.
• Childhood pneumonia is the leading single cause of mortality in children < 5 years.
• incidence < 5yr estimated at 0.29 episodes per child-year in developing and 0.05 episodes per child-year in developed = 156 million episodes /yr ;151 million in developing world.
• Of all community cases, 7–13% are severe enough to be life-threatening and require hospitalization.
• Pneumonia is responsible for about 19% of all deaths in < 5 children
Predisposing host conditions

- Alterations in the level of consciousness, anesthesia, and alcohol abuse
- Smoking tobacco
- Alcohol consumption
- Hypoxemia
- Acidosis
- Toxic inhalations
- Pulmonary edema
- Uremia
- Malnutrition
- Administration of immunosuppressive agents
- Mechanical obstruction of a bronchus
- Being elderly, there is a marked increase
- Cystic fibrosis
- Bronchiectasis
- Chronic obstructive pulmonary disease (COPD)
- Previous episode of pneumonia or chronic bronchitis
- Immotile cilia syndrome
- Kartagener’s syndrome (ciliary dysfunctions)
- Young's syndrome (azoospermia, sinusitis)
Aetiology of CAP

• *Streptococcus pneumoniae*, viral pneumonia and tuberculosis main pathogens associated with adult pneumonia.

• *Staphylococcus aureus*: increasing significance, in children and adults
Other bacterial causes

- *Legionella* species: rare (virtually no data Nepal)
- *Klebsiella* and other aerobic Gram negatives (Enterobacteriaceae): rare
- *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*: largely self limited illness
- *Haemophilus influenzae* is responsible for well less than 5% of cases of CAP (but often isolated from sputum in COPD)

*Chlamydophila pneumoniae* was previously known as *Chlamydia pneumoniae*
THE ETIOLOGY OF FEBRILE ILLNESS IN ADULTS PRESENTING TO PATAN HOSPITAL IN KATHMANDU, NEPAL

Clinical characteristics of patients presenting with fever to a hospital in urban Nepal

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Winter (n = 370)</th>
<th>Summer (n = 506)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (range)</td>
<td>27 (14–85)</td>
<td>25 (14–89)</td>
</tr>
<tr>
<td>Female</td>
<td>196 (53%)</td>
<td>213 (42%)</td>
</tr>
<tr>
<td>Recruitment rate (no./day)</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Clinical diagnosis at presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteric fever</td>
<td>92 (27%)</td>
<td>260 (58%)</td>
</tr>
<tr>
<td>Lower respiratory tract infection</td>
<td>106 (31%)</td>
<td>24 (6%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>34 (10%)</td>
<td>25 (6%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>49 (14%)</td>
<td>34 (8%)</td>
</tr>
<tr>
<td>Meningitis/encephalitis</td>
<td>4 (1%)</td>
<td>15 (3%)</td>
</tr>
<tr>
<td>Place of enrollment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency room</td>
<td>112 (30%)</td>
<td>286 (61%)</td>
</tr>
<tr>
<td>Outpatient clinic</td>
<td>252 (68%)</td>
<td>177 (38%)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>6 (2%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Admission</td>
<td>60 (16%)</td>
<td>80 (17%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brahmin</td>
<td>70 (19%)</td>
<td>111 (23%)</td>
</tr>
<tr>
<td>Chetttri</td>
<td>94 (26%)</td>
<td>112 (23%)</td>
</tr>
<tr>
<td>Newar</td>
<td>109 (29%)</td>
<td>115 (24%)</td>
</tr>
<tr>
<td>Tibeto-Burmese</td>
<td>25 (7%)</td>
<td>21 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>71 (20%)</td>
<td>122 (25%)</td>
</tr>
<tr>
<td>Pathogen</td>
<td>Winter</td>
<td>Summer</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>Bloodstream isolates</td>
<td>37 (10%)</td>
<td>100 (20%)</td>
</tr>
<tr>
<td><em>Salmonella enterica</em> serotype Typhi</td>
<td>21 (6%)</td>
<td>39 (8%)</td>
</tr>
<tr>
<td><em>Salmonella enterica</em> serotype Paratyphi A</td>
<td>7 (2%)</td>
<td>50 (10%)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>4 (1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>2 (1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>2 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>1 (0.3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>0 (0%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Urinary antigen tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>31 (8%)</td>
<td>20 (4%)</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em> serogroup 1</td>
<td>1 (0.3%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Serologic diagnoses</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Rickettsia typhi</em></td>
<td>32 (9%)</td>
<td>65 (13%)</td>
</tr>
<tr>
<td><em>Orientia tsutsugamushi</em></td>
<td>12 (3%)</td>
<td>16 (3%)</td>
</tr>
<tr>
<td><em>Leptospira</em> species</td>
<td>9 (2%)</td>
<td>27 (5%)</td>
</tr>
<tr>
<td>Dengue virus</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>HIV</td>
<td>6 (2%)</td>
<td>5 (1%)</td>
</tr>
</tbody>
</table>

*HIV = human immunodeficiency virus.*
Pneumococcal disease. The majority of patients with pneumococcal disease were diagnosed with pneumonia at the time of presentation. However, 25% of these patients were thought to have enteric fever. Compared with all others in the cohort, patients with pneumococcal disease were older (median age = 40 years versus 25 years; $P < 0.001$) and more likely to have a history of chronic lung disease ($RR = 2.7$, graphic changes consistent with pneumonia. However, radiographic infiltrates were occasionally present among patients presenting with scrub typhus (25%), murine typhus (5%), and leptospirosis (6%), and were notably absent from patients with culture-confirmed enteric fever. The two positive L. pneumophila urinary antigen test results may be falsely positive given that neither patient had a clinical presentation consistent with pneumonia.
Viral pneumonia

- Full text on website
- All ages, more so very young and the elderly

Panel: Viruses linked to community-acquired pneumonia in children and adults

- Respiratory syncytial virus
- Rhinovirus
- Influenza A, B, and C viruses
- Human metapneumovirus
- Parainfluenza viruses types 1, 2, 3, and 4
- Human bocavirus*
- Coronavirus types 229E, OC43, NL63, HKU1, SARS
- Adenovirus
- Enteroviruses
- Varicella-zoster virus
- Hantavirus
- Parechoviruses
- Epstein-Barr virus
- Human herpesvirus 6 and 7
- Herpes simplex virus
- Mimivirus
- Cytomegalovirus†
- Measles†

*Mostly in children. †Mostly in developing countries.

Lancet 2011 Review- Murdoch
H1N1 pneumonia; 36/M requiring ventilation
### VIROLOGY - PCR TESTS

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLU A type H3 PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>H1N1(A)-Swine PCR</td>
<td>Detected</td>
</tr>
<tr>
<td>Influenza A PCR</td>
<td>Detected</td>
</tr>
<tr>
<td>Influenza B PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>RSV PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Picornavirus PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Parainfluenza 1 PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Parainfluenza 2 PCR</td>
<td>Not Detected</td>
</tr>
</tbody>
</table>

### HAEMATOLOGY - FULL BLOOD COUNT

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
<th>Film</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>3.7 L (4.0 - 11.0)</td>
<td></td>
<td>Neut : 2.6 D</td>
<td>Aty Lymphs :</td>
</tr>
<tr>
<td>RBC</td>
<td>4.12 L (4.50 - 6.50)</td>
<td></td>
<td>Lymph : 0.8 D</td>
<td>Smear cells :</td>
</tr>
<tr>
<td>HGB</td>
<td>124 L (130 - 180)</td>
<td></td>
<td>Mono : 0.3</td>
<td>Plasma cell :</td>
</tr>
<tr>
<td>HCT</td>
<td>0.357 L (0.380 - 0.490)</td>
<td></td>
<td>Eos : 0.0</td>
<td>Hairy cells :</td>
</tr>
<tr>
<td>MCV</td>
<td>86.7 (80.0 - 100.0)</td>
<td></td>
<td>Baso : 0.0</td>
<td>Abn Lymph :</td>
</tr>
<tr>
<td>MCH</td>
<td>30.1 (27.0 - 32.0)</td>
<td></td>
<td>Bands :</td>
<td>Abn Mono :</td>
</tr>
<tr>
<td>MCHC</td>
<td>347 (310 - 360)</td>
<td></td>
<td>Meta :</td>
<td></td>
</tr>
<tr>
<td>RDW</td>
<td>13.6 (9.0 - 14.5)</td>
<td></td>
<td>Myelo :</td>
<td></td>
</tr>
<tr>
<td>PLT</td>
<td>160 (150 - 400)</td>
<td></td>
<td>Promyelo :</td>
<td></td>
</tr>
<tr>
<td>MPV</td>
<td>8.8 (7.2 - 11.1)</td>
<td></td>
<td>Blasts :</td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>Analyser WBC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comment</td>
<td>&lt;F8&gt;: Slight leucopaenia. Occasional reactive lymphocyte present.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ICU: 82 year old female

ICU
• Acute onset ARDS like picture – cough, dyspnoea onset over 4-5 days
• Cultures and urinary antigens negative for *Legionella* LP1 and pneumococcus
• Normal procalcitonin (c/w viral infection)
• Antibiotics: penicillin+gentamicin+azith
### VIROLOGY - PCR TESTS

**Specimen:** Scr. swab(s)  
**Location:** Nose/Throat

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A PCR</td>
<td>Not Detected</td>
<td>H1N1(A)-Swine PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Influenza B PCR</td>
<td>Not Detected</td>
<td>Influenza A PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td>FLU A type H3 PCR</td>
<td>Not Detected</td>
<td>Influenza B PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RSV PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Picornavirus PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parainfluenza 1 PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parainfluenza 2 PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parainfluenza 3 PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adenovirus PCR</td>
<td>Not Detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metapneumovirus PCR</td>
<td>Detected</td>
</tr>
</tbody>
</table>

**COMMENT:**

Human Metapneumovirus RNA DETECTED.
HIV and community-acquired pneumonia

Less advanced disease (CD4 < 200)
- *Strep. pneumoniae*, *Haemophilus*, *Staph. aureus*
- *M. tuberculosis*
- *Escherichia coli*, *Serratia species*

More advanced disease (CD4 < 50-100)
- Pneumocystis
- Toxoplasmosis
- *Non-tuberculous mycobacteria*, *Rhodococcus equi*
- *Pseudomonas*
- *Cryptococcus*
- *Cytomegalovirus*

Not *Candida* species! Mucocutaneous disease only; pneumonia very rare if ever. Laboratory should always check that ‘Candida’ isolated from sputum is not in fact cryptococcus (this organism has a capsule that is easily seen under an india ink stain)
Overview

1. Epidemiology

2. Prevention:
   • Immunisation
   • Wood fire smoke avoidance, smoking

3. Clinical assessment

4. Laboratory diagnostics

5. Antimicrobial therapeutics
Immunisation

Adults

- *Streptococcus pneumoniae* Pneumovax-23- considerable data on prevention in adults; however immunity not durable (polysaccharide vaccine)

Children

- Use of conjugate PCV vaccines in children also prevents a large proportion of invasive disease due to the same/related serotypes in adults
- **Pertussis** and **Measles** immunisation remain critical for pneumonia prevention
Overview

1. Epidemiology
2. Prevention
3. Clinical assessment
   1. Is it pneumonia?
   2. Severity assessment
4. Laboratory diagnostics
5. Antimicrobial therapeutics
Is it pneumonia?

- **Infective syndromes to consider**
  - Acute on chronic obstructive lung disease - a minority have consolidation
  - Acute bronchitis (often viral)
  - Upper respiratory infections (assume viral)
  - Tuberculosis (several patterns)

- **Non-infective syndromes:**
  - Asthma
  - Cardiac failure
  - Pulmonary embolus
  - Pulmonary hemorrhage
  - Pneumothorax

N.B. potential for diagnostic error is high with respiratory infection
CAP Severity assessment

1. **CORB Severity Score**
   - C onfusion (new or worsening)
   - O 2 saturation ≤ 90% or pO2 < 60mm
   - R espiratory rate ≥30
   - B P – hypotension D<60

   2 or more factors present = severe pneumonia

2. CAP requiring ventilatory support- assume ‘severe’ CAP

3. Severe sepsis presentations:
   • chest source always requires consideration

Also SMART-COP, CURB65

---

**Related Article**

Severe CAP

• Broader spectrum treatment indicated for severe CAP; unproven whether it improves outcomes

• Australian approach:
  – Pneumococcal cover (benzylpenicillin)
  – Aerobic gram negative cover (initial gentamicin)
  – Legionella/other atypical organisms (azithromycin)

• Doxycycline : as good for atypical cover as azithromycin – additional spectrum for Q fever.
Overview

1. Epidemiology
2. Prevention
3. Clinical assessment
4. Laboratory diagnostics
5. Antimicrobial therapeutics
Diagnostics

- FBC- low WCC (+/- low platelets) may indicate viral or atypical cause
- Sputum gram stain: good rapid test, provided white cells+++ and no squamous epithelial cells
  - predictive of pneumococcal or staphylococcal cause; also pointer to Gram negative infection
- Sputum culture:
  - Isolation of predominant *Staph. aureus* or Gram negative aerobe may indicate non-pneumococcal cause
- Blood cultures- important in severe CAP; provides documentation of cause and allows for later direction of treatment based on susceptibilities/ identification
- [Urinary antigens - pneumococcus and Legionella LP1]
- [Respiratory viral PCR detection, Legionella PCR]
Bacteraemic (severe) CAP: NSW 2008-2013, adults; BACTEC

<table>
<thead>
<tr>
<th>Organism group</th>
<th>Count</th>
<th>Group</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>GNEG (enterobacteriaceae)</td>
<td>54</td>
<td>GNEG</td>
<td>98</td>
<td>21%</td>
</tr>
<tr>
<td>GNEG (H influenzae)</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (pseud aerug)</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph (MRSA)</td>
<td>21</td>
<td>S. aureus</td>
<td>96</td>
<td>21%</td>
</tr>
<tr>
<td>Staph (MSSA)</td>
<td>75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep (other)</td>
<td>9</td>
<td>Streptococcal</td>
<td>265</td>
<td>58%</td>
</tr>
<tr>
<td>Strep (pneumo)</td>
<td>221</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep A</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep B</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep C/G</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>459</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Predominance of Gram positive pathogens (79%)
Cf: bacteraemic HAP, 2008-2013, Adult

<table>
<thead>
<tr>
<th>Organism group</th>
<th>ICU-JHH</th>
<th>Not ICU</th>
<th>Total</th>
<th>Gram neg</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobe</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>GNEG (A baumannii)</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (Acinetobacter other)</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (enterobacteriaceae)</td>
<td>17</td>
<td>14</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (H influenzae)</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (other)</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (pseud aerug)</td>
<td>7</td>
<td>3</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNEG (Steno)</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph (MRSA)</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph (MSSA)</td>
<td>3</td>
<td>15</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep (pneumo)</td>
<td>9</td>
<td></td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep C/G</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>30</strong></td>
<td><strong>54</strong></td>
<td><strong>84</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Sputum: diagnostic value

“Microscopic examination of sputum samples before antibiotics were administered and performance of culture within 24 h of receipt of such treatment yielded the correct diagnosis in >80% of cases of pneumococcal pneumonia”
Potential problems with sputum

- Specimen not possible - early pneumonia or poorly cooperation/illness
- Delay in transport to lab or high temperatures
  - Particularly a problem for pneumococcal or TB isolation
- Poor quality samples - shown by presence of squamous epithelial cells and absence of neutrophils
- Growth of colonising respiratory flora in chronic lung disease patients - e.g. *Haemophilus, Moraxella, Pseudomonas, E. coli* etc. creates diagnostic confusion
MICROBIOLOGY - RESPIRATORY CULTURE  
Sputum

Macro: Bloodstained sample

Result status - VALIDATED BY M.O.

GRAM STAIN

Polymorphs: Profuse
Squam/epith: Scanty
Organisms: Gram positive cocci - Profuse

CULTURE: Oropharyngeal flora - Scanty

1. Meth-res. S. aureus - Profuse

8th July 07 admitted with CAP
- Sudden onset “flu-like symptoms” day prior to presentation
- Developed cough and haemoptysis
- Rx - penicillin and doxycycline with clinical improvement

<table>
<thead>
<tr>
<th>PEN</th>
<th>ERY</th>
<th>DA</th>
<th>FOX</th>
<th>VA</th>
<th>FUC</th>
<th>RIF</th>
<th>GM</th>
<th>CIP</th>
<th>SXT</th>
<th>MUP</th>
<th>DO</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>
19th July reviewed in respiratory clinic

- Worsening cough and haemoptysis
- SOB on minimal exertion
- RR 22, Sats 78% on RA, Febrile 39°
- Extensive crackles over both upper zones

- Medical history
  - Asthma - well controlled on salbutamol
- Nil significant family history
- Social history
  - Manager of bakery
  - Smoker 20/day for 20 years and recently stopped
  - No IV drug use
- Nil sick contacts
Progress

- Admitted 19/7: IV vancomycin 1g 12-hrly
- HDU 21/7 with type 2 respiratory failure – BIPAP
- 23/7-30/7 CXR worsening
  - Vancomycin increased to 1g TDS on 23/7
  - Oral rifampicin and fusidic acid added 28/7
  - TTE 27/7 – mild TR and MR, no vegetations
- CT Chest 26/7 cavitation RUL and suggestive of loculated empyema
- 31/7 RUL Lobectomy
  - Intubated 6 days and required inotrope support
  - Lung tissue culture MRSA
29th August

Convalesc.
influenza
CFT titres
negative
The emergence and global dissemination of multidrug-resistant Gram-negative bacteria from the Indian subcontinent has received much attention. Less attention, however, has been given to reports describing the emergence in the past 5 years of two community-associated meticillin-resistant Staphylococcus aureus (MRSA) lineages from the Indian subcontinent—sequence types (ST)772 and ST22. Both lineages express Panton-Valentine leucocidin (PVL), which is associated with skin and soft tissue infections. ST772 and ST22 MRSA expressing PVL have become increasingly prevalent in India and have caused outbreaks and infections elsewhere in the world, which are often epidemiologically linked to India. Findings from a whole-genome sequencing study have shown that, within the ST22 population, PVL-producing ST22 strains are distinct from the well known nosocomial UK EMRSA-15 clone. Thus earlier studies using pulsed-field gel electrophoresis and multilocus sequence typing most likely incorrectly assigned PVL-producing ST22 strains as UK EMRSA-15-like. Early reports of PVL-positive ST22 strains were of meticillin-susceptible S aureus. Reports from India indicate that PVL-producing ST22 MRSA strains are now common in hospitals and the community. Outbreaks outside of India have been reported in England, Germany, Japan, and Australia. In 2010, ST22 PVL-producing MRSA was the most common multiresistant PVL-producing MRSA strain in England. Of concern is that ST222 strains that produce PVL are typically resistant to ciprofloxacin, erythromycin, gentamicin, and trimethoprim—a degree of multidrug-resistance rarely seen in community-associated MRSA. Strains from this lineage often cause recurrent abscesses, have proven difficult to eradicate, and have enhanced biofilm formation compared with other S aureus strains, and health-care staff have been implicated as vectors in nosocomial outbreaks. ST772 meticillin-susceptible S aureus was first described in Bangladesh and in India in 2004. ST22 and ST772 PVL-producing MRSA strains are now replacing ST239 MRSA as the predominant lineage in Indian hospitals. The infiltration and displacement of endemic hospital-acquired and community-associated MRSA in health-care settings in India echoes the experience seen with other community-associated MRSA strains in other countries such as the USA300 strain in North America. ST772 PVL-producing MRSA has caused an outbreak in Ireland, and in England the number of cases rose from ten in 2007 to 61 in 2009, and by 2010 was one of the most common multidrug-resistant PVL-positive MRSA lineages in England. As with Gram-negative bacteria in the Indian subcontinent, the widespread use of antibiotics, poor public
Overview

1. Epidemiology
2. Prevention
3. Clinical assessment
4. Laboratory diagnostics
5. **Antimicrobial therapeutics**
How long to treat?

- Mild/moderate (outpatient) – 3 days
- Hospitalised – 3-5 days if improving by then
- Longer directed therapy:
  - Gram negative pneumonia (2 weeks)
  - Staphylococcal pneumonia (up to 4-6 weeks)
  - Suspected or proven *Legionella*
- Early switch to oral treatment is safe
**Interventions:** Patients who had substantially improved after three days’ treatment with intravenous amoxicillin were randomly assigned to oral amoxicillin (n = 63) or placebo (n = 56) three times daily for five days.

**Outcome:** No significant difference in outcome on any measure.
## Failure of treatment

<table>
<thead>
<tr>
<th>Reason for failure</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect diagnosis</td>
<td>pulmonary embolism, pulmonary oedema, pulmonary eosinophilia, Wegener’s granulomatosis, drug allergy, lung cancer</td>
</tr>
<tr>
<td>Resistant organism/infection</td>
<td><em>Mycoplasma pneumoniae, Chlamydia psittaci, Coxiella burnetii, Staphylococcus aureus, β-lactamase-producing Haemophilus influenzae (unusual)</em></td>
</tr>
<tr>
<td></td>
<td>unrecognised pulmonary tuberculosis</td>
</tr>
<tr>
<td></td>
<td><em>Pneumocystis carinii</em></td>
</tr>
<tr>
<td>Inadequate dose or route of</td>
<td>oral erythromycin for <em>Legionella</em> infection</td>
</tr>
<tr>
<td>administration</td>
<td></td>
</tr>
<tr>
<td>Complication</td>
<td>empyema, abscess, pulmonary embolism, fever related to drug therapy</td>
</tr>
<tr>
<td>Underlying disease</td>
<td>lung cancer, cardiac failure, immunodeficiency</td>
</tr>
</tbody>
</table>

Also:

- Viral pneumonia
- Cryptococcal pneumonia
- Organising pneumonia syndromes
Gram positives

Coloured scanning electron micrograph of *Streptococcus pneumoniae*
Figure 4. The relationship between time above MIC\textsubscript{90} in serum and bacteriological success for $\beta$-lactam antibiotics in the treatment of acute otitis media (circles) and acute maxillary sinusitis (squares) caused by \textit{S. pneumoniae} (filled symbols) and \textit{H. influenzae} (open symbols).\textsuperscript{19,39,40}

Each study point represents a different ‘double tap’ otitis media study where cultures of middle ear fluid were performed before and after treatment to determine efficacy.
Penicillin at appropriate dose attains necessary concentrations in lung and blood to be effective in pneumonia due to strains of pneumococci that have elevated MICs to penicillin.

Figure 5. Concentrations of penicillin achieved in human serum after intravenous administration of a range of doses compared with the MIC values of penicillin-susceptible (MIC ≤ 0.06 mg/L), penicillin-intermediate (MIC > 0.06, < 1.0 mg/L) and penicillin-resistant (MIC 1.0–4.0 mg/L) S. pneumoniae. Reproduced from reference 44 with permission of Chest.
**Streptococcus pneumoniae:** betalactam therapy

- Community-acquired pneumonia
  - evidence that treatment failures do NOT occur with benzylpenicillin or amoxycillin provided dosing is appropriate.
  - Trial evidence fails to indicate superiority of IV over oral

- Ampicillin/amoxycillin
- Penicillin-G (benzylpenicillin).
- Oral penicillin-V (phenoxyethyl penicillin) NOT recommended

**AVOID** ceftriaxone in CAP- unless documented penicillin allergy- **cefuroxime** sufficient then

**AVOID** cephalexin/cephalothin/cefazolin –high level pneumococcal resistance possible
Other potential pneumococcal agents: rates of (high-level) resistance*

- Doxycycline: 23%
- Erythromycin: 15%
- Co-trimoxazole: 89% (52% in another study)
- Vancomycin: all pneumococci susceptible; reserve for MRSA pneumonia – high dosing required (loading dose)

**AVOID quinolones for CAP** – best to reserve their use for proven Gram negative infection or MDR-TB etc

Gram negatives
• 45/M
• Smoker
• Febrile
• WCC 19.3
• *Klebsiella pneumoniae* from blood cultures
Aminoglycosides in Gram negative lung infection

• Represent a good empiric option for pneumonia where Gram negatives are suspected, provided local susceptibility is high (above 75%) e.g.
  – Neonate
  – HIV infected
  – Severe pneumonia case – until re-evaluation 48 hrs
Aminoglycosides: Lung Penetration

- pH concerns: sputum pH 6.5 reduces action of aminoglycosides
- Alveolar lining fluid (ALF) studies:
  - In the rat model, the ratio of AUC in ALF to that seen in serum for gentamicin was 0.67 and 0.76 in non-inflamed and inflamed lung respectively.
  - In humans, peak netilmicin levels of 14.7 mg/L were seen in ALF after 120 minutes, 41% of the 30 minute plasma concentration.
Aminoglycosides: clinical efficacy in pneumonia

Monotherapy with isepamicin for Gram negative pneumonia attended by 95% cure or improvement on an intention to treat analysis in 125 patients. This compared with 97% efficacy in 60 patients managed with twice daily amikacin.

Antibiotic Guidelines 2015 Australia

Short term empirical therapy with gentamicin
- **Initial dose**: based on age
- **Number of empiric doses**: based on renal function
- **NO** monitoring is required for patients receiving short course treatment
- Few indications for > 3 days treatment

<table>
<thead>
<tr>
<th>Patient age</th>
<th>Initial dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 years</td>
<td>7.5 mg/kg up to 320 mg</td>
</tr>
<tr>
<td>10 – 29 years</td>
<td>6 mg/kg up to 560 mg</td>
</tr>
<tr>
<td>30 – 60 years</td>
<td>5 mg/kg up to 480 mg</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>4 mg/kg up to 400 mg</td>
</tr>
<tr>
<td>&gt;10 years with severe sepsis (sepsis syndrome)</td>
<td>7 mg/kg up to 640 mg</td>
</tr>
</tbody>
</table>

**Recommended doses**: these should be rounded to the nearest 40mg increment

**Recommended dosing interval**:

<table>
<thead>
<tr>
<th>Creatinine clearance (mL/min)</th>
<th>Dosing interval</th>
<th>Maximum number of empiric doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>24 hrs</td>
<td>3 (at 0, 24 and 48 hours)</td>
</tr>
<tr>
<td>40 – 60</td>
<td>36 hrs</td>
<td>2 (at 0 and 36 hours)</td>
</tr>
<tr>
<td>30 – 40</td>
<td>48 hrs</td>
<td>2 (at 0 and 48 hours)</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Give initial dose once, then seek expert advice</td>
<td></td>
</tr>
</tbody>
</table>

The dosing interval for subsequent empirical dosing is based on the patient’s renal function, since elimination of aminoglycosides is by renal excretion. Empiric therapy should be charted in the regular section of the NIMC with days blocked out as below to prevent >3 doses being administered.
CAP: suggested local research topics

- How much diagnostic error occurs with CAP at Bir Hospital?
- What is the value of sputum Gram stain smear as performed here?
- What is the incidence of staphylococcal pneumonia?
- How is CAP treated and for how long?
- What guidelines if any are clinicians following for CAP management?
- Audits of severe CAP to describe its epidemiology, clinical presentation, microbiology and outcome
- Randomised trials to establish:
  - Adequacy of narrow spectrum treatment – e.g. penicillin vs ceftriaxone
  - Short course treatment - 3 vs 7 days for CAP that is improving at 3 days
- The role of pneumococcal vaccination in prevention of adult CAP
COPD patients

• Usually colonised with *Haemophilus influenzae* (non-typeable) +/- *Moraxella* +/- pneumococcus

• Exacerbations – majority if not all are due to prior respiratory viral infections; most do not exhibit CXR consolidation

• During a viral exacerbation, overgrowth of colonisers occurs- lab reports these and it drives unnecessary antibiotic treatment

• Exacerbations have a self limited time course – up to 2 weeks; placebo controlled antibiotic trials indicate that antibiotics provide minimal additional benefit
Approach for acute on chronic airflow patients

- In admitted cases, AVOID prolonged antibiotics- MAX 3 days; chose penicillin/amoxycillin OR doxycycline to target pneumococcus and maximise supportive care

- In presence of CXR-proven consolidation, treat as per CAP – narrow spectrum – penicillin +/- doxycycline

- Outpatient cases – AVOID antibiotics

- Maximise non-antibiotic management measures- e.g. treat coincident asthma, oxygen, physiotherapy, cease smoking
COPD: suggested local research topics

• How much diagnostic error occurs with COPD exacerbations at Bir Hospital? E.g. missed cardiac failure, asthma, other diagnosis
• How are outpatient COPD exacerbations treated and for how long?
• What guidelines if any are clinicians following for COPD management?
• Audits of inpatients with exacerbation of COPD to describe management and outcome
• Microbiological studies of prior viral causes of exacerbations
• Randomised trials to establish:
  – Value of antibiotics in admitted cases – narrow spectrum vs placebo.
  – Value of antibiotics in non-admitted cases – narrow spectrum vs placebo
  – Value of certain interventions to reduce smoking or other causative factors
Ground glass changes in PCP infection
Pneumocystis pneumonia

- Primary and Secondary prevention- cotrimoxazole three times weekly

- Diagnosis
  - Clinical
  - CXR
  - (Immunofluorescence or PCR)

- Treatment
  - Mild-moderate disease: cotrimoxazole same dose oral/iv (1st line) OR
    - clindamycin + primaquine (2) OR dapsone+trimethoprim (2)
  - Severe disease (< 70mm o2 or < 94% o2 saturation)
    - Cotrimoxazole (15mg/kg TMP component daily IV in three divided doses for 21 days)
    - Corticosteroids (40mg prednisolone bd 5 days; then 40mg daily 5 days, 20mg for 11days)
Pneumonia key points

1. Prevention: immunisation- pneumococcal (and influenza) vaccination
2. Make the diagnosis (always consider differential, including staphylococcal disease).
3. Explicitly assess severity – CORB score or similar
4. Appropriate empiric antibiotic therapy- must provide pneumococcal cover
   - mild/moderate – penicillin-G or amoxycillin (cefuroxime for allergic patient)
   - severe – broader spectrum to include atypical, aerobic Gram negative
5. Re-evaluate patient severity and response at 48-72hrs
6. Develop and implement guidelines for management of pneumonia:
   • SHORT durations of treatment in accord with evidence
   • AVOID quinolones and third generation cephalosporins as first line agents