Management of Community- Acquired Pneumonia in Adults

1ST MEDICINE ANNUAL CME - CMCMAC 2016
CHRISTIAN MEDICAL COLLEGE ,VELLORE

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Dr. Dilip Mathai  MBBS MD PhD FCAMS  FRCP (Lond)
FICP FIDSA Hon. FFTM  RCPS (Glasg)

Professor of Medicine and Adult Infectious Diseases
Dean, Apollo Institute of Medical Sciences and Research
Apollo Health City, Jubilee Hills, Hyderabad, Telangana
dean@apolloimsr.edu.in
09443336984
Educational Objective

• Clinical Reasoning Skills / Diagnosing Strategies in CAP
• Pulmonary Pathophysiology and clinical correlation
• Planning for venue of care of patients with CAP
• Promote High Value Care Recommendations
Outline of presentation

• Epidemiology
• Understanding Typical vs Atypical organisms
• Utility of 12 tests for Diagnosis, Etiology, Management and Prognostication of Adult CAP
• Some examples from CMC
• Antibiotic use protocols
The 10 leading causes of death in the world

2012

- Ischaemic heart disease: 7.4 million
- Stroke: 6.7 million
- COPD: 3.1 million
- Lower respiratory infections: 3.1 million
- Trachea, bronchus, lung: 1.6 million
- HIV/AIDS: 1.5 million
- Diarrhoeal diseases: 1.5 million
- Diabetes mellitus: 1.5 million
- Road injury: 1.3 million
- Hypertensive diseases: 1.1 million

0 million | 2 million | 4 million | 6 million | 8 million | 10 million
Top 10 causes of death in low-income countries

2012

- Lower respiratory infections: 91
- HIV/AIDS: 65
- Diarrhoeal diseases: 53
- Stroke: 52
- Ischaemic heart disease: 39
- Malaria: 35
- Preterm birth complications: 33
- Tuberculosis: 31
- Birth asphyxia and...: 29
- Protein energy malnutrition: 27

Deaths per 100,000 population
Pneumonia : Still a challenge?

• Major healthcare and economic problem with a considerable effect on morbidity and mortality worldwide
• Incidence of CAP affecting 3–5 people per 1000 person-years, predominantly among the young and elderly.
• Even if discharged, patients are still at risk of returning to Emergency Departments or clinics and being readmitted with more severe disease.
• Important health-care related complication-second most common type of nosocomial infection and has the highest mortality
• Due to this high burden, physicians with patients suspected of pneumonia are constantly challenged to determine if the clinical syndrome is pneumonia rather than alternative diagnosis
12 Tests

1. Imaging
2. Pulse oximetry
3. Arterial Blood gases (ABG)
4. Complete Blood Count (CBC)
5. Serum Chemistry
6. Gram Staining
7. Sputum Culture
8. Blood Culture
9. Serological and Antigen testing
10. Procalcitonin
11. Thoracocentesis
12. Bronchoscopy
Evidence Based Medicine in CAP

• Burden of illness/relevance to practice
• Diagnosis
  a. History and physical examination
  b. Imaging studies (#1)
  c. Bacteriology and serology (# 6,7,8 and 9)
• Admission decision (#2,3,4 and 5)
• Empiric Antibiotic choice (#10,11, and 12)
• Treatment Duration
• Prevention
# Rating scheme for treatment recommendations

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Should always be offered</td>
</tr>
<tr>
<td>B</td>
<td>Should generally be offered</td>
</tr>
<tr>
<td>C</td>
<td>Optional</td>
</tr>
<tr>
<td>D</td>
<td>Should generally not be offered</td>
</tr>
<tr>
<td>E</td>
<td>Should never be offered</td>
</tr>
</tbody>
</table>
## Quality of evidence supporting the recommendations

| I | Evidence from at least one properly designed randomized control trial |
|II| Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytical studies or from multiple time-series studies or dramatic results from uncontrolled experiments |
|III| Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees |
First Grade
21 boys
16 girls
37 children
Management of Infectious Diseases

Manoj Jain
Dilip Mathai

JAYPEE
General Physician Vs Specialists

- Radiologist – Anatomy (Contour and texture)
- Cardiologist – limits to the understanding cardiac malfunctions, understands myocytes
- Nephrologist - Glomerulus – early kidney damage, dialysis technology, Transplant
- Neurologist – structure – EEG and EMG
- Gastroenterologist – Endoscopic diagnosis, intervention
- Rheumatologist – early arthritis/arthralgia of joints
- Hematologist – onco hematological, BMT
- Pulmonologist – endoscopy, biopsy, PFT
- Infectious disease – microbiology, antibiotics
Diagnosis

Dia’= through , ‘gnosis’=knowing

Diagnosis= through knowledge / to know thoroughly

Purpose :

• To locate a difficulty( internal disorder unpleasant symptoms)
• Discover the condition causing it
• Overcome it (to prevent recurrence)
Categorization into:

- Anatomical – cell, tissue, organ
- Physiological - alteration in function of cell, tissue or organ system
- Pathological - altered anatomy (histology) owing to altered physiology.
- Etiological - inducing agent (D/D)

How do we diagnose?
The diagnosis of pneumonia

• Constellation of suggestive clinical features such as tachypnea, fever, and respiratory rales or reduced breath sounds on auscultation
• Presence of consolidation or opacification in a chest radiograph (CXR) or in computerized tomography (CT) scan of the chest
• CXR is the main imaging approach in many settings; however, limitations for its use exist.
• Radiation exposure precludes CXR use in pregnant women.

• Frequently troublesome to acquire both posteroanterior and laterolateral projections in hospitalized patients especially among the critically-ill

• CXR can be a time consuming procedure and its interpretation has high inter-observer variability among radiologists
• Chest CT scan, considered the gold-standard imaging approach for pneumonia, has its own limitations: it is expensive; impractical, especially in the critically-ill; and, has higher radiation exposure than CXR
Evaluating Medical Information

See 1000 Cough patients

Order chest X-ray

Pneumonia present in 20 patients (20/750)

DO NOT Order chest X-ray

Pneumonia absent in 730 patients

Pneumonia absent in 220 patients

for 250 patients

for 750 patients

Pneumonia Present in 30 patients (30/250)
1. Imaging: a. Chest x ray

1. Chest x ray - primary investigation in diagnosing Pneumonia: Increased lung opacification with air bronchogram

2. Differentiates from other respiratory illnesses minimizing inappropriate use of antibiotics for viral infections and other conditions that do not require them.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>Lower lobe</td>
</tr>
<tr>
<td>Hematogenous</td>
<td>Miliary</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>Any lobe</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>Upper lobe</td>
</tr>
<tr>
<td>S.aureus</td>
<td>Pneumatocoele</td>
</tr>
</tbody>
</table>
1. Imaging: a. Chest x-ray

3. The extent of disease (lobar vs multilobar: multifocal areas of alveolar opacities), diffuse or localized, segmental, interstitial

4. Readily available, non-invasive test; Helps to identify 30% of patients with pneumonia having obstructions or underlying diseases such as neoplasms; and complications such as pleural effusion or abscesses.

5. Pneumonias due to varying aetiologies have been said to have their own characteristics on chest radiograph. However, there is a great degree of overlap between manifestations, so it is difficult to use radiographic findings to confirm the etiology.
1. Imaging: a. Chest x ray

6. Be aware of the possibility of false-negative results in patients who are substantially volume-depleted but have normal chest XR

7. Subtle pneumonia may be difficult to distinguish in patients with chronic lung disease, making comparison with old chest XR very important.

- Sometimes Other findings- Silhouette sign; Increased lung opacification abutting fissures etc.
- In all patients with suspected CAP, an attempt should always be made to obtain a chest radiograph
- If CXR not available, treat based on clinical presentation
- If patient improves with treatment no need for routine repeated CXR
- Repeat CXR if – Patient not improving / Need to rule out malignancy or alternative etiology / Patient worsens following initial improvement
- Resolution on Chest Radiograph – Lags behind clinical resolution in many cases.
- If lack of even partial radiographic resolution by 6 week – Consider alternative causes.
1. Imaging : b. CT Scan (Gold Std)

a. Differentiates for underlying bronchiectasis
b. Interstitial lung disease
c. Aspergillus infection
d. Extent of lung disease prognostication and for resolution ex; lymph nodes
e. Lung volume changes

- Thoracic CT – Do not perform routinely in suspected CAP
- Indications for Thoracic CT – Patients with Non resolving pneumonia or where complications of CAP are suspected
1. Imaging c. Use of lung ultrasound (LUS)

- Limited to the diagnosis of pleural effusions, thoracentesis and biopsy-guided procedures.
- In evaluating pulmonary conditions such as pneumonia and pneumothorax.
- The use of LUS has gained popularity in intensive care units (ICUs) and EDs in the last decade, and has become increasingly recognized as a potentially useful diagnostic approach for community-acquired pneumonia.
Diagnostic accuracy of LUS for pneumonia in adults. A Systematic Review and Meta-analysis:


• Maximum of 13 minutes to conduct
• 3.5–5 MHz micro-convex transducer probe
• for the diagnosis of pneumonia (CXR and CT) using LUS
• Pooled sensitivity 94% (95% CI, 92%-96%)
  specificity 96% (94%-97%)
• Pooled LR positive 16.8 (7.7–37.0)
  negative 0.07 (0.05–0.10)
• Area-under-the-ROC curve 0.99 (0.98–0.99)
• **Acute bronchitis** is a cough-predominant AR illness of < 3 weeks
• For > 40 years, trials have shown that antibiotics are not effective for acute bronchitis
• Despite this, between 1980 and 1999, the rate of antibiotic prescribing for Ac. Bronchitis was between 60% and 80% in the US.
• During the past 15 years, the (CDC) has led efforts to decrease antibiotic prescribing for acute bronchitis.

Since 2005, a Healthcare Effectiveness Data and Information Set (HEDIS) measure has stated that the **antibiotic prescribing rate for acute bronchitis should be zero.**
2. Pulse oximetry

1. Pulse oximetry and arterial blood gases helpful in assessing the severity of illness and the level of care
2. Oxygen saturation > 95%
3. Test is non invasive, simple to perform (70% - 100%)
4. May detect problems with ventilation and hypoxia before symptoms are observed clinically
   • People with oxygen saturation < 92% require admission to hospital
5. Test cannot distinguish between different forms of haemoglobin
6. Readings can be inaccurate owing to reduction in pulsatile blood flow—hypovolemia, hypotension, cold peripheries, arrhythmias; venous congestion—restriction of venous drainage, tricuspid regurgitation; bright ambient light; carboxyhemoglobin and methemoglobin; and nail varnish
3. Arterial Blood Gases

1. Arterial blood gas analysis – If pulse oximetric saturation not detectable or patient has underlying chronic lung disease like COPD

**Normal ranges**
- Arterial O2 tension (PO 2): 80 to 100 mm Hg
- Arterial carbon dioxide tension (PCO 2): 35 to 45 mm Hg
- pH: 7.35 to 7.45
- Bicarbonate (HCO 3): 20 to 28 mEq/L

2. Simple test to perform and interpret, however, arterial hematoma is possible if direct pressure is not applied to the puncture site for enough time
- Keep in mind the possibility of machine failure if values are not consistent with the clinical presentation; error in results may also occur if a venous sample is drawn instead of an arterial sample

3. Abnormal results can be caused by ventilation/perfusion mismatching resulting in hypoxemia or hypercapnia (uncompensated hypercapnia results in acidosis)
- Compensated chronic pulmonary disease or renal disease may alter baseline values
4. Complete Blood Count (CBC)

- CBC an indication of the possible presence of systemic infection as well as the state of the patient's overall health

**Normal ranges**

- Leukocyte count: 4,500 to 11,000/μL
  - Differential count:
    - Neutrophils—segmented: 1,800 to 7,800/μL
    - Neutrophils—bands: 0 to 700/μL
    - Lymphocytes: 1,000 to 4,800/μL
    - Monocytes: 0 to 800/μL
    - Eosinophils: 0 to 450/μL
    - Basophils: 0 to 200/μL

Haematocrit and erythrocyte indices are typically normal in patients with bacterial pneumonia
4. CBC

• In CAP, leukocyte count is 15,000 to 35,000/μL. Atypical pneumonia typically < 15,000/μL
• In juvenile neutrophil forms (a 'left shift') on differential cell count (normal in patients with atypical pneumonia). Elevated leukocyte count may indicate infection, especially if increased numbers of band forms (left shift) are present; leukopenia (<4,000/μL) or thrombocytopenia (<100,000/μL) indicates severe infection
• Leucocytosis in the absence of a left shift is often seen in patients who have recently undergone treatment with corticosteroids
5. Serum Chemistry

• Serum chemistry provides parameters for assessing severity (CURB, CRB-65)
• It serves as a useful baseline to calculate medication doses for treatment and monitor their side effects.
• Evaluating C-reactive protein (CRP) is useful if bacterial versus viral pneumonia is suspected.*
• High serum levels of C-reactive protein suggest the development of complications (pleural effusion) and worse prognosis.**
• C-reactive protein: > 1 mg/dL
• Readily available, relatively inexpensive, provides data points for severity scores (BUN for CURB system; BUN, sodium and glucose for PSI); however, test is nonspecific
• Blood glucose may be elevated due to underlying diabetes; hypoglycaemia is often a marker of overwhelming sepsis and a poor prognosis
5. Serum Chemistry

- Elevations in BUN may reflect underlying renal disease or dehydration; a high BUN is tallied as an adverse risk factor in severity scores.
- Sodium abnormalities may reflect alterations in hydration, effects of medication, or a variety of metabolic disorders; hypernatremia is associated with a worse prognosis in CAP.
- Medications, disorders, and other factors that may alter results include regular medication such as diuretics and syndrome of inappropriate antidiuretic hormone (SIADH).
- **In a prospective observational study of 540 inpatients with CAP, CRP levels showed consistent negative predictive values for survivors at 30 days (CRP <10 mg/L = 100% survivors, CRP <50 = 99.1% survivors, CRP <100 = 98.9% survivors, CRP <200 = 94.9% survivors). Admission CRP of less than 100 mg/L is associated with less need for mechanical ventilation and/or inotropic support and with fewer cases of complicated pneumonia as compared to higher values of CRP. The study concluded that C-reactive protein is an independent predictor of severity in community-acquired pneumonia. **Level of evidence: 2**

References:
* 10.1183/09031936.03.00080203 ERJ April 1, 2003 vol. 21 no. 4 702-705
12 Tests

1. Imaging
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12. Bronchoscopy
SPUTUM EXAMINATION

• Well expectorated
• Transported to laboratory within 2 hrs.
  - < 10 epithelial cells /LPF
  - > 25 PMNs/LPF

  ▪ Interpretation
    - Mixed organisms usually indicates contaminants
    - Gram positive diplococci predictive of S. pneumoniae
CRITICAL QUESTIONS

Does the patient have pneumonia?
What tests are required?

Is hospitalisation required & level?

What antibiotic should I choose?
Is oxygen required?
5. Serum Chemistry: CRB 65 scoring

- For all patients, clinical judgement supported by the CRB65 score should be applied when deciding whether to treat at home or refer to hospital.

**CRB65 score** - one point is awarded for each of the following features:
- Confusion - recent
- Respiratory rate 30 breaths/min or greater
- Blood pressure - systolic of 90 mmHg or less or a diastolic of 60 mmHg or less
- 65 years of age or older

- Patients who have a CRB65 score of 0 are at low risk of death and do not normally require hospitalisation for clinical reasons.
- Patients who have a CRB65 score of 1 or 2 are at increased risk of death, particularly with a score of 2, and hospital referral and assessment should be considered.
- Patients who have a CRB65 score of 3 or more are at high risk of death and require urgent hospital admission.

- PSI as a decision aid has been restricted to immunocompetent adults with CAP, with exclusion of children, pregnant women, patients with immunosuppression (e.g., HIV-infected patients), and those with hospital-acquired pneumonia.
## 5. Serum Chemistry: Pneumonia Severity Index

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – Men</td>
<td>Yrs.</td>
</tr>
<tr>
<td>Age – Women</td>
<td>Yrs. – 10</td>
</tr>
<tr>
<td>Nursing Home Resident</td>
<td>10</td>
</tr>
</tbody>
</table>

### Co-morbidity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplastic disease</td>
<td>10</td>
</tr>
<tr>
<td>Liver disease</td>
<td>20</td>
</tr>
<tr>
<td>CCF</td>
<td>10</td>
</tr>
<tr>
<td>Cerebro-vasc. Disease</td>
<td>10</td>
</tr>
<tr>
<td>Renal disease</td>
<td>10</td>
</tr>
</tbody>
</table>

### Examination

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered mental state</td>
<td>20</td>
</tr>
<tr>
<td>Resp. ≥ 30</td>
<td>20</td>
</tr>
<tr>
<td>Syst BP &lt; 90</td>
<td>20</td>
</tr>
<tr>
<td>Temp &lt; 35 or ≥ 40°C</td>
<td>15</td>
</tr>
<tr>
<td>Pulse ≥ 125</td>
<td>10</td>
</tr>
</tbody>
</table>

### Investigations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH &lt; 7.35</td>
<td>30</td>
</tr>
<tr>
<td>Urea ≥ 11 mmol/L</td>
<td>20</td>
</tr>
<tr>
<td>Na &lt; 130</td>
<td>20</td>
</tr>
<tr>
<td>Glucose ≥ 14</td>
<td>10</td>
</tr>
<tr>
<td>Hct &lt; 30%</td>
<td>10</td>
</tr>
<tr>
<td>PaO2 &lt; 60 mmHg or SaO2 (air) &lt; 90%</td>
<td>10</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>10</td>
</tr>
</tbody>
</table>
Differences between typical & atypical organisms

“Typical”
1. Has cell wall Ex: Streptococcus
2. Extracellular pathogens
3. Clinical onset: Rapid, abrupt (1-3 days)
4. Antibiotic action on cell wall
   • Suppurative

“Atypical”
1. No cell wall Ex. Mycoplasma
2. Intracellular
3. Slow, Insidious
4. Antibiotic inhibit protein synthesis
   • Non suppurative
# Infections caused by atypical organisms

<table>
<thead>
<tr>
<th>Typical</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Easy to isolate</td>
<td>5. Isolation is difficult</td>
</tr>
<tr>
<td></td>
<td>• Chronicity &amp; persistence</td>
</tr>
<tr>
<td></td>
<td>• Trophism</td>
</tr>
<tr>
<td></td>
<td>• Can occur in outbreaks</td>
</tr>
<tr>
<td></td>
<td>• Facultative or strict intracellular</td>
</tr>
<tr>
<td></td>
<td>• Multiply only in cells</td>
</tr>
<tr>
<td></td>
<td>• Virulence markers</td>
</tr>
</tbody>
</table>
### Difference between typical & atypical organisms continued

<table>
<thead>
<tr>
<th>Typical</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Affects lobar parenchyma</td>
<td>6. Bronchial / Tracheal</td>
</tr>
<tr>
<td>Unilateral or bilateral diffusion</td>
<td>Interstitial</td>
</tr>
<tr>
<td>7. Chronic form</td>
<td>7. Acute form</td>
</tr>
<tr>
<td>8. Antibiotic Resistance</td>
<td>8. Resistance is difficult to study</td>
</tr>
<tr>
<td></td>
<td>• Pharmacokinetics of antibiotics dosing vary</td>
</tr>
<tr>
<td>9. Diagnosed by gram stain, culture</td>
<td>9. by serology, PCR, Immunofluorescence</td>
</tr>
</tbody>
</table>
CLINICAL PRESENTATION

10. Typical pneumonia
Acute onset
High fever, rusty sputum
Pleuritic chest pain
Signs of lobar consolidation
X-ray- single lobe consolidation
WBC- increased

10. Atypical pneumonia
Subacute onset
Low grade fever
Systemic symptoms
Bilateral pneumonia
Symptoms out of proportion to signs

S. pneumoniae
Mycoplasma pneumoniae
Legionella pneumophila
Chlamydiae pneumoniae
6. Gram staining

• Debate on the usefulness of Gram staining and sputum culture in diagnosing CAP, as the majority of patients are started on empiric therapy.
• However, these tests often help to identify the causative pathogen, which allows narrowing of the original empiric broad-spectrum regimen to an agent specific to the target organism.
• Thus reducing cost, patient exposure to unnecessary antibiotics, and the potential for development of microbial resistance to broad-spectrum agents.
• Sputum is not present under normal conditions.
• Non invasive test that can be useful for identifying S pneumoniae and other pyogenic organisms. Gram stain helps to assess the clinical relevance of culture results, as it distinguishes material from the site of infection from oropharyngeal secretions.
• Saline inhalation and gentle chest percussion is helpful in patients who cannot readily produce a sputum sample. Invasive techniques such as needle aspiration and bronchial brushing should be avoided due to the high risk of complications and low reliability. Tracheal aspirates are easily obtained from patients who are intubated for mechanical ventilation and often provide valuable information because the sample comes directly from the site of infection and is protected from oropharyngeal contamination.
6. Gram staining

- Expectorated sputum is distinguished from saliva by the presence of more than 25 neutrophils and less than 10 squamous epithelial cells per high-powered field. Some clinical laboratories discard specimens that do not meet these criteria; others rely on the clinician to interpret the culture result in light of the Gram stain.

- Not a definitive test but may be helpful for directing initial antibiotic therapy if a predominant organism can be identified; also helpful in narrowing the antibiotic spectrum later if Gram stain and culture results together identify a pathogen.

- It should be noted that the utility of Gram stain and its usefulness in diagnosis is under debate. Certain organisms do not show up reliably on Gram stain (e.g., *H. influenzae*, *Legionella* species, *P. carinii*).

- Numerous Gram-positive diplococci along with polymorphonuclear leukocytes are representative of pneumococcal pneumonia. Other types of bacteria may be identified and are indicative of other etiologies. Antibiotic therapy can then be directed accordingly.

- A false-negative result is possible because representative sputum may be difficult for the patient to produce; false-positive results most often occur when the sample is examined by an inexperienced viewer. Previous antibiotic therapy will result in a high number of false-negative results.

- Be aware that atypical pneumonias may have a gradual onset and that patients with chronic disease may have been treated recently with antibiotics for other suspected disorders.
7. Sputum Culture

- Debate on the usefulness of sputum culture in diagnosing CAP, as the majority of patients are started on empiric therapy.
- Should show normal respiratory flora
- Results should be correlated with results from Gram stain, as cultures frequently show colonization and not a true etiology
- Expectorated sputum for culture purposes should contain more than 25 neutrophils and less than 10 squamous epithelial cells per high-powered field in order to ensure a representative sample of sputum (and not saliva)
- Test is the best way, in most cases, to identify an etiologic organism and to determine its susceptibility to various antibiotics; however, *S. pneumoniae* are Gram-positive diplococci that are difficult to maintain in culture due to autolysis
- False-negative rate of up to 50% (when Gram stain shows large number of organisms); in patients with proven *H. influenzae* infection, false-negative rate of up to 50%. Recent antibiotic therapy may alter results including creating false-negative results
- Yield - 34 to 86%
- Initial sputum for gram stain or culture – Obtain in all hospitalized patients
- Sputum examination for acid-fast bacilli (AFB) – Patients who fail to respond or suggestive clinico radiological features
- Pneumococcal antigen detection test or PCR / Legionella urinary antigen / Investigations for atypical pathogens and viruses – Desirable but not required routinely
8. Blood Culture

- Blood culture is recommended in patients with severe CAP and in immunocompromised patients with CAP;
- Case fatality rates for bacteremic pneumococcal pneumonia = 7 to 35%
- May help to determine or confirm the etiologic organism and may play a role in determining the length of treatment.
- **Blood cultures** – Not required in Outpatient setting
- Low sensitivity – Yield between 5% and 33%
ETIOLOGICAL AGENTS

**CAP (uncomplicated):**
- S. Pneumoniae
- Mycoplasma pneumoniae
- Legionella pneumophila
- Chlamydiae pneumoniae

**CAP (complicated):**
- Anaerobes
- Gram negative organisms

**HIV INFECTION**
1. S. pneumoniae
2. H. influenza
3. P. carinii
4. M. tuberculosis

**NOSOCOMIAL**
1. S. aureus
2. E. coli
3. Klebsiella
4. P. aeroginosa

POOR CORRELATION BETWEEN CLINICAL PICTURE X-RAY AND AGENT
9. Serological & Antigen testing

- Rapid test that can detect influenza, pneumococcal, and some *Legionella* antigens; however, not all strains are detected.
- Urine tests for detection of pneumococcal and *Legionella* serotype 1 antigens.
- Helpful in detecting infection due to these organisms when the results of other diagnostic testing are inconclusive, including after institution of antibiotics.
- A polymerase chain reaction test can detect all serotypes of *Legionella* species.
- Antigen detection of influenza in nasopharyngeal secretions is quite specific and may lead to the use of antiviral therapy instead of or in addition to antibiotics.
- Serologic antibody tests exist to help confirm a diagnosis of infection with pathogens such as *Legionella* species, *M pneumoniae*, and *Chlamydia* species, but they are generally not helpful in the acute stage of disease and are not routinely ordered.
### Serologic tests for atypical pathogens

<table>
<thead>
<tr>
<th>Atypical pathogens</th>
<th>Serologic test</th>
<th>Total No. of tests</th>
<th>No. of positivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. pneumoniae</td>
<td>Enzyme immunoassay</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C. pneumoniae</td>
<td>Urinary antigen test</td>
<td>100</td>
<td>36 (36%)*</td>
</tr>
<tr>
<td>L. pneumophilia</td>
<td>Urinary antigen test</td>
<td>100</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>200</strong></td>
<td><strong>36 (18%)</strong></td>
</tr>
</tbody>
</table>

1 : Enzyme immunoassay  
2 : Urinary antigen test  
* Based on IgM test results.
A. Acute Respiratory Infections:

1. Influenza - Swine flu and Bird Flu (Epidemic)
2. SARS (Epidemic)
3. Human Metapneumovirus (Epidemic)
4. Hanta Virus pulmonary syndrome (Epidemic)
5. Middle East Respiratory Syndrome (MERS)
Influenza H5N1/H7N9

- **Risks**: Poultry contact; limited human-human transmission; no "sustained" human-human transmission shown to date.
- Needs **hemagglutinin (HA) mutation** to promote binding to human epithelial cells. This will be the mutation likely to produce a global pandemic.
- **Only a few flu strains caused pandemics** in past 95 years: H1N1, H2N2, and H3N2.
Acute, Potentially Lethal Respiratory Tract Infection (RTI) Viruses in Travelers

**When to suspect:**

<table>
<thead>
<tr>
<th>MERS-Co-V</th>
<th>Influenza A H7N9</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unexplained severe lower RTI, with travel to Arabian Peninsula or neighboring countries within past 14 days</td>
<td>• Unexplained severe lower RTI, with travel to China within 10 days prior to onset of symptoms</td>
</tr>
<tr>
<td>• Diagnosis: Molecular test from CDC in most state labs</td>
<td>• Diagnosis: Molecular test from CDC available in most state labs</td>
</tr>
<tr>
<td>• Infection control: Strict precautions</td>
<td>• Infection control: Strict precautions</td>
</tr>
<tr>
<td>• Treatment: None; possibly interferon/ribavirin</td>
<td>• Treatment: Neuraminidase inhibitor (oseltamivir)</td>
</tr>
</tbody>
</table>
Initial antibiotic choice in 100 patients diagnosed to have CAP in CMC

1. Monotherapy

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; generation cephalosporins</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; generation cephalosporins</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; generation cephalosporins</td>
<td>17 (17%)</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; generation cephalosporins</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Penicillins</td>
<td>34 (34%)</td>
</tr>
<tr>
<td>Quinolones</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Macrolides</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Glycopeptides</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other : Augmentin</td>
<td>6 (6%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>45 (43.26%)</strong></td>
</tr>
</tbody>
</table>
# Initial antibiotic choice in 100 patients diagnosed to have CAP in CMC

2. Combination therapy

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>No. of patients (%)</th>
<th>Antibiotic class</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} CPS + MC</td>
<td>0 (0%)</td>
<td>PCN + FQ</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>1\textsuperscript{st} CPS + FQ</td>
<td>0 (0%)</td>
<td>PCN + AG</td>
<td>3 (2.88%)</td>
</tr>
<tr>
<td>1\textsuperscript{st} CPS + AG</td>
<td>0 (0%)</td>
<td>Other : 3\textsuperscript{rd} CPS+AG+MC</td>
<td>3 (2.88%)</td>
</tr>
<tr>
<td>2\textsuperscript{nd} CPS + MC</td>
<td>0 (0%)</td>
<td>Other : 3\textsuperscript{rd} CPS+CBP</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>2\textsuperscript{nd} CPS + FQ</td>
<td>0 (0%)</td>
<td>Other : 3\textsuperscript{rd} CPS+PCN+FQ</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>2\textsuperscript{nd} CPS + AG</td>
<td>0 (0%)</td>
<td>Other : 3\textsuperscript{rd} CPS+PCN+MC</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>3\textsuperscript{rd} CPS + MC</td>
<td>7 (8.65%)</td>
<td>Other : 3\textsuperscript{rd} CPS+PCN+AG</td>
<td>3 (2.88%)</td>
</tr>
<tr>
<td>3\textsuperscript{rd} CPS + FQ</td>
<td>1 (1.92%)</td>
<td>Other : PCN+ATT</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>3\textsuperscript{rd} CPS + PCN</td>
<td>11 (10.57%)</td>
<td>Other : FQ+ATT</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>4\textsuperscript{th} CPS + MC</td>
<td>0 (0%)</td>
<td>Other : 3\textsuperscript{rd} CPS+PCN+AG+MC</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>4\textsuperscript{th} CPS + FQ</td>
<td>0 (0%)</td>
<td>Other : 3\textsuperscript{rd} CPS+PCN+MC+CBP</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>4\textsuperscript{th} CPS + AG</td>
<td>0 (0%)</td>
<td>Other :</td>
<td>-</td>
</tr>
<tr>
<td>PCN + MC</td>
<td>5 (5.76%)</td>
<td>TOTAL</td>
<td>(59 (56.73 %))</td>
</tr>
</tbody>
</table>
Community Acquired Pneumonia - Treatment
CMC Hospital Protocol

• Ambulatory: Amoxycillin ± macrolide (if atypical organism suspected)

• Hospitalised: Crystalline penicillin 10 lakh units i.V q4h 7-10 days

• Hospitalised with (COPD, CCF, DM): Cefotaxime 1gm IV q8h 10-14 days

• Hospitalised in ICU: Cefotaxime 1gm IV q8h or Levofloxacin 500 mg p.o / IV + Erythromycin 1 gm p.o q6h or Azithromycin 0.5 gm IV od / od X 10-14 days
For effective action – MIC for an Abx < Susceptibility Breakpoint
### MIC Breakpoints for Streptococcus Pneumonia

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>S (MIC-&lt;microgram/ml&gt;)</th>
<th>I (MIC-&lt;microgram/ml&gt;)</th>
<th>R (MIC-&lt;microgram/ml&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>=0.06</td>
<td>0.12-1</td>
<td>&gt;2</td>
</tr>
</tbody>
</table>

Strep pneumo grown from sputum as well as has MIC against Penicillin of 1µg/ml

IV Penicillin 2mu 4hrly is effective treatment
Invasive Pneumococcal Disease in Children Aged Younger than 5 Years in India; A Surveillance Study


Alliance for Surveillance of Invasive Pneumococci (ASIP)
Antibiotic resistance – n=361

Key messages:
- high level of resistance to eryth and cotrimox

S = <2 mcgm/ml for blood; CSF 0.25 mcgm/ml
Drug – Body Issue

What the body does to the drug!

What the drug does to body!

Optimal times for beta lactam antibiotics above MIC for bacteriological cure are 40-50% of the dosing interval.
12 Tests

1. Imaging
2. Pulse oximetry
3. Arterial Blood gases (ABG)
4. Complete Blood Count (CBC)
5. Serum Chemistry
6. Gram Staining
7. Sputum Culture
8. Blood Culture
9. Serological and Antigen testing
10. Procalcitonin
11. Thoracocentesis
12. Bronchoscopy
10. Procalcitonin Levels

- Normal level: 0.15 ng/L or less
- **Comments**
  - A procalcitonin level greater than 0.25 ng/L is considered a biomarker of bacterial infection. *may lead to reduced antibiotic use in patients with respiratory tract infections, including CAP, without influencing mortality or length of hospital stay*
- **Evidence**
  - A systematic review of 14 RCTs included 4,221 adults with ARI, including 2,045 with radiograph-diagnosed CAP. It compared procalcitonin-guided therapy versus usual care. Procalcitonin-guided therapy was not associated with higher mortality or treatment failure. Total antibiotic use was significantly reduced as compared with usual care. Also, the procalcitonin group experienced a decrease in length of treatment, from 8 (5 to 12) to 4 (0 to 8) days.* [15] **Level of evidence: 1**
  - A systematic review of 8 RCTs, none blinded, evaluated procalcitonin-guided therapy versus usual care in 3,431 adults with a variety of acute respiratory illnesses, including 1,480 patients with CAP. As compared with usual care, there was a significant reduction in antibiotic use and duration of use in the procalcitonin group. There was no significant difference in the other outcome measures (mortality, ICU admission, and length of hospital stay). **[16] Level of evidence: 2**
  - A prospective observational study included 319 adults with CAP (n = 62), COPD, or asthma exacerbation, all receiving measurements of procalcitonin and CRP levels. For all patients, there was no difference in all-cause mortality but there was a significantly lower risk of treatment failure in the procalcitonin group (adjusted OR 0.82 [95% CI 0.71-0.97]). Patients with CAP had significantly increased procalcitonin levels compared with those with asthma or COPD (level of calcitonin in CAP group: 1.27 ng/mL; in COPD group: 0.05 ng/mL; in asthma group: 0.03 ng/mL).*** [17] **Level of evidence: 2**

***[17] Bafadhel M, Clark TW, Reid C et al. Procalcitonin and C-reactive protein in hospitalized adult patients with community-acquired pneumonia or exacerbation of asthma or COPD. Chest. 2011;139:1410-8
11. Thoracentesis

- Thoracentesis should be done in patients with confirmed pleural effusion (>5 cm high on the lateral view of an upright chest radiograph or >10 mm of fluid on a lateral decubitus view)
- When there is pleural fluid present and the patient is not responding as expected to appropriate treatment;
- When the effusion is enlarging or there are precipitating symptoms; when new fever or chest pain develop in a patient who had been improving; or when loculation is developing.
- The pleural cavity contains less than 20 mL of serous fluid
- Absence of pathogen or composition changes (normal protein level, cell count, glucose level, and pH)
- Allows the cause of the fluid accumulation to be identified and/or relieves the symptoms associated with the fluid accumulation
- May cause pneumothorax, fluid reaccumulation, pulmonary edema, bleeding, infection, or respiratory distress. Consequently, a chest radiograph is often obtained after the procedure to detect any complications
- Disorders and other factors that may alter results include previous antimicrobial therapy, malignancy, other inflammatory conditions (vasculitis), and CHF
12. Bronchoscopy

- Bronchoscopy with lavage, brushing, or biopsy might be considered in patients in whom unusual organisms (fungus, mycobacteria) are suspected or in patients with an atypical clinical course or who are not responding to appropriate initial therapy.

- Indication: Intubated and ventilated pt; airway obstruction from foreign body or tumor are. The role of bronchoscopy in the evaluation of patients with typical CAP is not clearly defined in the literature.

- Normally No obstructions or neoplasms and no pathogens on culture.

- Useful in determining exact etiology; however, there is a risk of complications such as worsened oxygenation and allergic drug reactions, and rarely, pneumothorax, hemoptysis, and pneumonia

- False-positive results are a possibility

- Other causes of an abnormal test result include bronchitis, mucus hypersecretion, bronchiolitis, tobacco use, malignancy, vasculitis, lung transplantation

- Previous antimicrobial therapy may mask infection in the cultured material
13. Other Special Tests

- Other special studies as indicated by the clinical presentation might include additional microbiologic studies for unusual pathogens (e.g., mycobacteria or fungi) or serologic markers of vasculitic syndromes (e.g., antineutrophil cytoplasmic antibodies or antinuclear antibodies)
RISK STRATIFICATION OF PNEUMONIA

History consistent with high risk:
   Age over 50 years
   History of cancer
   Congestive heart failure
   Cerebro vascular disease
   Renal or liver disease

Physical findings of high risk
   Altered mental status
   Tachycardia (>125 beats per minute)
   Tachypnea (>30 breaths per minute)
   Hypotension (<90 mmHg systolic)
   Temperature <35ºC (95F) >40ºC (104F)
Does this patient require oxygen?

Evidence of hypoxia:
• Pulse oximeter saturation < 90 %
• Cyanosed patient
• Restless patient
• Respiratory rate RR>30/min
• Dyspnea at rest

O2 ADMINISTRATION
- Nasal oxygen 1-2 L/min
- Mask oxygen 5 L/min
- Venturi mask oxygen
Which antibiotic is to be given?

**SUSPECTED PNEUMONIA**

**OUTPATIENT**
- Macrolides *or*
- Fluoroquinolones *or*
- Amoxycillin *or*
- Amoxycillin/clavulanate *or*
- Doxycyline

**IN-PATIENT**
- *Ward:*
  - Penicillin *or*
  - Cefotaxime
  - + Macrolide *or*
  - Fluoroquinolone
- *ICU:*
  - Cefotaxime
  - + Macrolide *or*
  - Fluoroquinolone
<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>250 mg bd 3-5 D</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>250-500 mg bd</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>500-750 mg OD</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>500 mg q8h</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>10 L IV q6h</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>1G q8h</td>
</tr>
<tr>
<td>Amoxyillin/clauv</td>
<td>500 mg q8h</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg bd</td>
</tr>
</tbody>
</table>
Ceftaroline Superior in Community-Acquired Pneumonia in Asia
24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID):
Abstracts O155 and eP425. Presented May 12, 2014

• 498 patients RCT  Phase 3 trial

• Microbiologically evaluable : 119 patients (57 +62) isolate identified at baseline, results were better with ceftaroline 600mgm BD than with ceftriaxone 2gms OD (87.7% vs 75.8%). This was consistent for Gram-positive and Gram-negative pathogens

• The most commonly isolated organisms were Streptococcus pneumoniae, Haemophilus parainfluenzae and Klebsiella pneumoniae
WHEN TO SHIFT FROM IV TO ORAL?

- < 72 hours
- Able to tolerate medicines orally
- Patient afebrile
  - Clinically better
RESPIRATORY INFECTIONS

Learning points

1. Diagnose pneumonia
2. Decide when to admit
3. Order and interpret tests
4. Choose appropriate antibiotics
5. Decide on O2 therapy
6. Know how to follow-up
Diagnostic strategy Pneumonia

- No teaching without a patient for a text
- Clinical reasoning  Clinical skills and diagnostic aptitude
- Avoid diagnostic errors  Encouraged to ‘see’ Than just ‘look’ Refine your powers of observation
- two approaches to reasoning –
  (system 1) the quick and intuitive approach “
  (system 2) slow, effortful and analytic” approach
- The two approaches are generally used interchangeably in a non–binary way, to the experience of the clinician Their familiarity with the clinical problem they are addressing.
- Intuitive spot diagnosis Single clinical cue
- More sophisticated pattern recognition Refinement strategies
- Restricted rule out, pattern fit recognition
- Deliberate reasoning

William Osler: A life in Medicine M Bliss 2007;
Heneghan C etal Diagnostic Strategies used in Primary Care BMJ 2009;338:946
History:

Mrs. TK, 48 yr old housewife from Kolkatta, hospitalized in CMC Vellore on 14th Nov 05 for evaluation of painful proximal muscle weakness and was diagnosed to have:

1. Dermatomyositis  
2. Hypothyroidism  
3. Osteopenia  
4. Essential hypertension

Started on the following medications:

T. Prednisolone 25mg tid  
T. Atenolol 50mg od  
T. Losartan hydrochloride 50mg od  
T. Azathioprine 125mg od  
T. Eltroxin 0.1mg od  
T. Alendronate 70mg od once a week
On 12th Dec 05 in Kolkatta, developed high grade fever, cough with sputum production treated with numerous antibiotics (to obtain names)

15 days later in Kolkatta due to worsening of symptoms and fluctuations in mentation despite treatment she was hospitalized

- CXR: extensive patchy opacities in Left lung field
- Bronchoalveolar lavage (BAL): Candida.albicans grown
- Azathioprine stopped; antimicrobials switched to
  
  Tab Linezolid 600mg bd + Inj. Meropenem 2gms IV bd +Tab.
  
  Itraconazole 200mg od
Returned to CMC Vellore on 25\textsuperscript{th} Jan 06, as fever with productive cough persisted with changes in mentation and for evaluation of non-resolving pneumonia.

**Differential Diagnoses:**

- Non-resolving pneumonia in immunocompromised host acquired from community or six weeks after hospitalization  \( \text{? MTB ? Fungal ? Nocardia} \text{?Anaerobic (aspiration due to muscle disorder )} \)
- Overlap Syndrome with SLE Lung + Dermatomyositis
- Dermatomyositis with underlying Lung malignancy
INVESTIGATIONS done at CMC Vellore on 25-1-2006

Hb : 7.8g/dl  
WBC count : 9800 mm$^3$  
Blood Gas  
  pH : 7.445  
  CO2 : 41.7mmHg  
  PO2 : 84.7mmHg  
  HCO : 28.2mmoles/  
  ABE : 4.2  
  O2 SAT : 96.5%  
C and P ANCA : Normal  
ANA : Positive  
ds DNA : Normal  
RF : Negative  
  CXR : L sided opacity  
Sputum AFB : Negative  
CRP : Negative  
  CT Thorax : bronchiectasis in the lower lobes. No interstitial fibrosis
COURSE IN HOSPITAL

Started on T. Fluconazole + T. Prednisolone + inj. Augmentin + inj. Meropenem

Repeat CXR was done which showed worsening
Microbiological investigations

Blood culture:

Non fermenting Gram negative bacilli – *Acinetobacter spp.*

Susceptible to: gentamicin
Resistant to : Ampi, Cefepime, Ctx, Cefpirome, Ctz, Cipro, Amik, Imi, Mero, Pip/Taz, Ticar/Clav

Sural nerve and muscle biopsy:

Right sural nerve and quadriceps muscle biopsy with no significant lesion.
Course in CMC Vellore

On admission (25-1-06)

07-02-06
After initial antibiotics (Mero, Augmen)
Confronting the Problem of Increasing Antibiotic Resistance
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