Review diagnosis, aetiology, and severity in adult community-acquired pneumonia

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Introduction

Lower respiratory tract infections, excluding tuberculosis (TB) are the third most common cause of death worldwide and the most common cause of death in low-income countries.[1] Community-acquired pneumonia (CAP) is responsible for a large proportion of these deaths. Prompt administration of antibiotics and best supportive care can reduce the risk of death and the choice of antibiotic should be guided by an appreciation of the likely aetiological agent.[2] Once CAP has been diagnosed, severity scores can help identify those patients at greatest risk of complications.[3,4] In this article we review the guidance on clinical and aetiological diagnosis and severity assessment.

Diagnosis and definition of CAP

For the purpose of this review, CAP refers to pneumonia in a patient who has not been recently hospitalised and who is not known to have an inherited or acquired immunodeficiency (e.g. HIV) or active cancer. Various definitions for pneumonia exist and the diagnostic criteria used will depend on the context in which the patient is assessed. The 'gold standard' definition is a clinical syndrome compatible with lower respiratory tract infection associated with consolidation seen on a plain X-ray, together with the identification of a respiratory pathogen from a clinical specimen. The X-ray changes reflect the pathological hallmark of pneumonia, which is large numbers of neutrophils in the alveoli and/or terminal bronchioles. This infiltrate can extend to involve a whole lobe (lobar pneumonia) or multiple segments of several lobes (as in bronchopneumonia).[5]

However, access to X-rays and a laboratory varies, and in a community setting many patients are diagnosed with pneumonia without an X-ray or microbiological support. In practice, the clinical challenge is to distinguish the small fraction of patients that have pneumonia (with its high mortality risk) from the larger population with uncomplicated lower respiratory tract infections (which confer a much lower mortality risk). Where an X-ray is not available no one clinical sign or symptom can predict the presence of pneumonia, but the most accurate diagnosis is achieved by combining a number of simple clinical features: an example of such an algorithm is show is Figure 1.

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Microbiological aetiology of CAP[2]

Generalisations regarding frequency of individual aetiological agents in CAP are difficult because study methodologies have varied and the data are biased by the disproportionate number of studies from Europe and the United States, and the very limited number of studies from Africa. Notwithstanding these factors, *Streptococcus pneumoniae* is the most frequent isolate in all geographical areas and in all patient groups with a frequency of approximately 40% of all cases of CAP in adults. The frequency of other bacterial pathogens is even more difficult to extrapolate from widely differing estimates but *Chlamydia pneumoniae* (13%), *Haemophilus influenza* (5–10%), *Mycoplasma pneumonia* (1–10% but dependent on cyclical epidemics), *Legionella* species (0.5–20%), *Staphylococcus aureus* (0.8–9%), and gram-negative enteric organisms (1–2%) make up the majority of the rest of the bacterial causes. Viruses are responsible for between 9–13% of CAP and the major pathogen here is influenza (A and B), which outside of pandemic years has a seasonal pattern. Various patient factors such as age, alcohol, diabetes, and residing in a nursing home have been investigated to see if they predict differing frequencies of aetiological agents but no consistent difference in the occurrence of causative pathogens has been found to be associated with any factor. Presenting clinical symptoms (e.g. diarrhoea) have been investigated to try to identify patterns predictive of individual pathogens and none has been found to be reliable. Microbiological confirmation of the pathogen responsible for CAP relies on laboratory processing that, when available, takes several days and so practically all initial treatment is empirical. Since no clinical features can reliably predict the pathogen the initial choice of antibiotic should always aim to cover

Figure 1 Diagnostic criteria for CAP without access to a chest X-ray

- Symptoms of an acute lower respiratory tract illness (cough plus another lower tract symptom, e.g. dyspnoea, pleuritic pain).
- New focal chest signs on examination (e.g. brochial breathing).
- One of: sweating; fever; shivers; myalgia; or pyrexia > 30ºC.
- No other explanation for the illness.

Adapted from: British Thoracic Society guidelines for the manaagement of communtity-acquired pneumonia in adults: update 2009. *Thorax* 2009; 64 (Suppl III): iii1–55.[2]

Streptococcus pneumoniae. If atypical pathogens such as *Chlamydia pneumoniae* are suspected then the antibiotic regimen should be expanded perhaps by the addition of a macrolide antibiotic.

A note on tuberculosis

In areas with a high burden of TB and in particular where HIV rates are also high, the diagnostic algorithm shown in Fgure 1 will inevitably capture some cases of TB.[6] Even when X-rays are available there is much overlap between the radiological manifestations of CAP and pulmonary TB. In general, CAP may manifest with a more acute onset of symptoms whereas TB often has an element of chronicity; however, these distinctions will not be consistently reliable. In practice, if CAP is suspected, treatment should be initiated and if the clinical condition does not improve as expected, the possibility of TB should be entertained and sputum smears performed.

Assessing the severity of CAP

Risk of death from CAP is associated with multiple clinical factors and some of the most important are listed in Figure 2. Studies of pneumonia in Africa have validated the importance of some of these factors and identified additional prognostic features specific to the region (see Figure 3a). In an attempt to improve the outcome of patients with CAP a number of different clinical algorithms have been devised to delineate those at greatest risk of death. The PSI[4] (pneumonia severity index) and the CURB65 score[3] (confusion, urea, respiratory rate, blood pressure, and age greater than 65 score) are the most widely used and have similar operational characteristics with CURB65 having slightly greater specificity and the PSI greater sensitivity. In a resource-poor setting both scores are difficult to apply as they require prompt access to blood tests. However, without a value for serum urea, using only the patient's age, presence, or absence of confusion, the respiratory rate, and the blood pressure at the time of presentation, similar predictions can be made about the risk of death (see Figure 3b). The practical utility of these scoring systems is in deciding who can be safely treated at home with oral antibiotics (CRB 0) and who should be admitted for hospital care or considered for intensive care admission (CRB 4). All scoring systems should be used in conjunction with sound clinical judgement and not relied upon alone, such that some patients with intermediate CRB scores (2–3) can be treated at home where as others will need to be observed in hospital.

Figure 2 Associations with 30-day mortality from CAP

- Older age (in adults).
- Co-morbidity (especially: cancer, liver, kidney or neurological disease, heart failure, alcohol).[4]
- Raised respiratory rate.
- Confusion.
- Hypotension.
- Hypoalbuminaemia.
- Hypoxia.
- High or low white cell count.
- Bilateral X-ray changes.
- Positive blood culture.
- No pyrexia in the elderly.

Adapted from: British Thoracic Society guidelines for the management of communtity-acquired pneumonia in adults: update 2009. *Thorax* 2009; 64 (Suppl III): 1–55.

Figure 3a) Indicators of severity derived from African studies on CAP: factors associated with a five-times or greater risk of death

1. Age >55.
2. Use of traditional healer.
3. Diastolic blood pressure<60 mmHg, respiratory rate >30/min.
4. Pulse >120 beats/min.

Adapted from French N, Gilkes C. Pneumococcal disease. In: *Manson's Tropical Diseases*. 21st edition. Saunders 2003.[7]

Figure 3b) Practical clinical prediction scores with and without access to blood urea

C new onset of confusion (mini mental score < 8)

U >7 mmol/L
R >30/min

B Blood pressure: <90 mmHg systolic and/or <60 mmHg diastolic
Age >65 years

CURB65 score	**CRB65 score**
Stratified mortality	
0 or 1 = 1.5%	0 = 1.2%
2 = 9.2%	1 or 2 = 8.15%
3 or more = 22%	3 or 4 = 31%

Derived from: Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; 58: 377–82.[3]

Pneumonia and HIV

CAP is common in those with advanced immune suppression from HIV. The spectrum of bacterial pathogens is similar to the non-HIV-infected population but other opportunistic pathogens assume a greater significance, in particular *Pneumocystis jiroveci*.[8] *Streptococcus pneumoniae* remains the commonest bacterial pathogen and evidence suggests standard severity scoring algorithms are valid in the context of HIV.[9] The British HIV Association recently published new guidelines for HIV testing in which

they suggested all those with CAP should be offered HIV testing.[10] The UK has a relatively low prevalence of HIV and this advice is therefore even more pertinent in those African countries that have a higher prevalence. The World Health Organization suggests all those with a diagnosis that is more common in the context of HIV, for example pneumonia, should be offered an HIV test at the point of care.[11]

Conclusion

CAP is common and carries a significant risk of death. The spectrum of causative agents responsible is predictable and should guide empirical therapy. TB and *Pneumocystis jiroveci* assume greater significance as causes of CAP in populations with a high rate of HIV infection but the spectrum of bacterial pathogens remains similar. The mortality risk can be estimated by simple clinical scoring systems that can help identify those with more or less severe disease.

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