Acute Respiratory Infections in Adults and Children Over 5 Years of Age

Author: Dr Colin Mathews (ASH physician)

Topic Reviewers: Dr Paul Torzillo; Dr Andrew Bell; Top End DMOs; Dr Penny Roberts-Thomson (Nguiu); Malcolm Auld (RAN, Bonya Clinic); Rin Riemersma (RAN, Finke); Leone Radnedge (RAN, Utopia)

Introduction

Respiratory tract infections (RTI), including pneumonia, represent a high proportion of the burden of ill health and death throughout the world.

In developed countries, such as the United States, figures show that RTIs are the seventh most important cause of morbidity and sixth commonest cause of death (the mortality rate being 10%) with the cost to the country being over 20 billion dollars annually.[1,2,3]

In Australia it has been reported that pneumonia occurs in 200 per 100 000 adults and accounts for 2% of hospital admissions each year, the mortality being 7–10%. One organism alone, the pneumococcus, affects 50–100 per 100 000 at the extremes of life and has a case fatality rate of 12–14%.[4,5,6]

RTIs are more important in under-developed countries and among Indigenous populations, and are claimed to be the commonest cause of morbidity and mortality.[7,8,9]

In Aboriginal people lung disease, mainly acute respiratory infections, result in 12% of hospital admissions for males and 9% for females, this being a five-fold greater morbidity and increased mortality compared to the non-Indigenous population. For the pneumococcus the rate of infection is as high as 1500 per 100 000 for children under two years, but remains at about 100 per 100 000 for the 15–64 year age group.[10,11]

A number of different pathogenic organisms are implicated in acute respiratory infections (ARI), which involve the upper respiratory tract, causing colds, influenza, sinusitis, pharyngitis and the lower respiratory tract resulting in bronchitis and pneumonia.

The incidence of RTIs caused by the various pathogens differs from area to area and from time to time. Precise figures implicating specific causative agents are difficult to obtain for various reasons. At the best, there is delay in making the diagnosis because it takes several days to culture an organism from pathology samples and several weeks to get information on serology tests.

In practice, most serious attempts at categorising agents are deficient due to a large group of ‘No pathogen identified’.

These may be due to patients receiving early antibiotic treatment, having inadequate sputum, inappropriate sampling or the limitations of the procedures currently used.

Significant issues in the Northern Territory and remote Indigenous communities

- Persistent high rates of invasive pneumococcal disease and the overwhelming likelihood that this is the major pathogen involved in community acquired pneumonia (CAP).
- The implications of a probable increase in intermediate level penicillin resistance in invasive pneumococcal isolates.
- The importance of the frequency of underlying disease, including chronic lung disease/bronchiectasis.
- Confusion engendered by the fact that people with underlying lung disease often wheeze with pneumonia.
- The lack of accurate clinical predictors of pneumonia in adults leading to a high possibility of incorrect diagnoses and assessments in this area. Health workers are encouraged to seek early medical consultation.
- The use of predictors of severity and poor outcome as the basis for immediate medical consultation.
- The disproportionately high morbidity and mortality from ARI in the Indigenous population.
- The lack of ready access to hospital-based investigations, such as X-rays, experienced by many patients because of their remote location or, at times, a reluctance to submit to a system foreign to their culture.
- The difficulties involved in decisions to transfer patients to a larger centre, including the assessment of severity and urgency, the reluctance to leave the 'safety' of home and the organisation and cost of evacuation.
- The pressing need for more effective and greater utilisation of preventive measures, including interventions for environmental health factors, smoking and vaccinations.[4,10]
- In the Northern Territory, the rates of pneumococcal disease are also higher in the non-Indigenous population than in the rest of Australia.

As noted, these diseases are worldwide and many of the problems needing attention are also relevant elsewhere.

There may also be some other poorly understood contributing factors in local respiratory illnesses. As some Alice Springs physicians report; 'Experience and common sense suggest there are defective immune responses. We see people who attend early in their illness, receive appropriate management (confirmed by pathology results), have the right temperature and white cell responses but get progressively worse and die' (pers. comm.).

Clinical aspects

Typically patients with RTI present with the general features of infection (fever, sweating, lethargy, anaemia) and the specific symptoms involving the respiratory tract (nasal discharge, facial pain, cough, sputum production, chest pain, dyspnoea). There is usually a short period between the onset of illness and the manifestations implicating the respiratory tract, and in epidemics the incubation period is usually short.[12] These comments do not apply to some chronic disorders, particularly tuberculosis, which is dealt with in a separate chapter.

It is common for patients to seek care early in the illness and it may be possible to assess the severity and expected course at this stage. In the Northern Territory, however, distance from help and cultural

differences frequently delay the presentation during which time the disease may progress to become less responsive to therapy.

Disease severity

Significant factors indicating severe disease are[2,13,14]:

- Body temperature <36?C
- Respiratory rate > 30/min
- Pulse rate >120/min
- Systolic blood pressure <90 mm Hg
- Altered mental status
- Evidence of multi-lobar disease
- Indication of extra-pulmonary infection
- Hospital admission in the previous year
- Reduced oxygen saturation
- Associated conditions

Other circumstances, many of which affect Indigenous populations and are particularly significant in the Northern Territory, alter the pattern of disease leading to higher susceptibility and greater severity. These include[11,16]:

- Environmental exposures: Air pollutants, camp fires, smoking, petrol fumes, Infections associated with overcrowding
- Co-morbidities: Asthma, allergy, chronic lung disease, diabetes,[17] renal failure, alcohol, chronic liver disease, neoplastic disease, immunosuppression

Comments on allergy

There is thought to be less allergy in Aboriginal than Caucasian patients, but it is so common in the latter group it is part of remote practice. However, Dr John Weiner, visiting allergist, advised he sees a number of Aboriginal people from the bush who are allergic to couch grass causing asthma. Prof Anne Woolcock, Australia’s (late) asthma guru, wrote in several articles about increasing dust mite allergy in north Queensland Aboriginal communities.

Complications

Most RTIs are treated and respond to appropriate antibiotics, or spontaneously resolve (viral). Some progress to complications, and there may also be long-term consequences.

Short-term complications[12]

- Lungs: abscess, atalectasis
- Pleura: pneumothorax, effusion, empyema
- Other sites: pericardial, cerebral, hepatic

Long-term consequences[18,19]

- Bronchiectasis
- Chronic airway limitation, and other lung function abnormalities

Aetiological agents

A number of pathogens are implicated in RTIs and their distribution varies in time, place and setting. There are different ways of classifying these infections and their manifestations and it is useful to consider more than one approach.

A. Classification by causative organism

- **'Typical' pathogens**: Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, other gram negative bacilli
- **'Atypical' pathogens**: Mycoplasma pneumoniae, Chlamydia pneumoniae and C. psittaci, Legionella species
- **Aerobic bacteria**: Staphyloccus aureus, Pseudomonas aeruginosa, Bordetella pertussis (Mycobacterium tuberculosis)
- **Anaerobic bacteria**: Bacteroides fragilis, Streptoccus anginosus, Fusobacteria
- **Rickettsiae**: Coxiella burneti (Q fever), louse borne, murine and scrub typhus
- **Viruses**: Influenza, para-influenza, rhino- and corona- viruses, herpes simplex and zoster, cytomegalovirus

B. **Classifications by clinical syndrome** [2,6,12,15]

- Community-acquired pneumonia: Typical and atypical agents, aerobic bacteria, C. burneti
- Aspiration pneumonia: Typical and anaerobic bacteria
- Hospital acquired pneumonia: Typical, aerobic and anaerobic bacteria
- Acute bronchitis: Typical and atypical agents, P. aeruginosa, B. pertussis. Viruses group 3 d i
- Otitis media: Typical agents. C. Pneumoniae, Streptococcus pyogenes

C. Distribution patterns

Although some organisms causing pneumonia lead to classical features, such as pneumococci typically causing lobar consolidation, none of the signs or symptoms are specific for a particular organism. It is therefore difficult or impossible to differentiate the causative organism on clinical grounds (as mentioned earlier, this difficulty extends into hospital and research medicine.)

In practice, it is appropriate to focus on the most important pathogen, S. pneumoniae, which is probably the commonest cause of infection and is certainly the leading cause of death from CAP in Central Australia. The protocol is based on this but is modified for the Top End in the wet season where melioidosis is the major cause of mortality from ARI.[6,37] [Editor: For details see melioidosis chapter.]

Comments about specific organisms

Pneumococci It is generally agreed that these are the most significant pathogens causing CAP throughout the world, in Australia and in our region, where the highest rate of infection in any community has been demonstrated. It is important that treatment protocols and preventative measures be directed against this organism.

There are many serotypes with variations of importance in time and place. Furthermore, the frequency and pattern of antibiotic use influences the patterns of sensitivity, which in turn dictates the appropriate medication and vaccine for specific groups. [6,8,10,20,21]

Haemophilus influenzae Worldwide, this is historically the second most important CAP pathogen and it is interesting that in the two small studies from north Queensland and Alice Springs, greater numbers of this organism were recorded. Thompson suggests that this may relate more to colonisation than invasion and further assessment comparing

blood culture and bronchoscopy specimens with sputum samples would be appropriate.[22,23]

Melioidosis and acinobacter Local variations are exemplified by the significance of these bacteria in the Top End, with their resulting severe disease and high mortality. (See chapter on meloiodosis).[37]

Staphylococcus While numbers of this pathogen invading the lung are small the complications and mortality are high and it is important that this infection be identified promptly.

Atypical agents Although the studies included have revealed relatively few infections with these organisms, they are becoming more important in developed areas. There is an impression that they are uncommon in north Australia, but they are not routinely investigated. Although Thompson found no positive serology for atypicals and there were only two cases of chlamydia in the series in Alice Springs, there have been reports of two cases of Legionella longbeachae and up to five cases of mycoplasma a month during 2001. Recent studies have demonstrated a better patient outlook if antibiotics covering these agents are included in treatment, even if there is no positive evidence of their presence. However, in the protocol, these concerns need to be balanced against the need to focus on the best antibiotic regimen for the predominant pneumococcal disease.[22–25]

Diagnosis of respiratory tract infection

In children, studies have indicated useful predictive values for clinical features in making the diagnosis of pneumonia. By contrast, in adults there is little data to help. Fever, tachycardia, changes in alertness, etc. may occur in many disorders and even more specific findings such as dyspnoea and cough, are present in other conditions e.g. asthma, cardiac failure and metabolic acidosis. The constellation of findings helps to make a diagnosis of pneumonia, but when in doubt it is advisable to seek help and often to treat because of the potential harm of untreated infections.[15,29,30,31]

Management

When a diagnosis of pneumonia is made (or strongly suspected) antibiotic use is mandatory. The appropriate treatment depends on the actual or likely organism, the usual antibiotic for those bacteria and the pattern of antibiotic resistance. Each of these aspects varies in time and place and advice on the local situation, which may be subject to review.[8,31,32]

The rapid emergence of antibiotic resistance in all pathogenic organisms in all infections is of major concern for the ongoing management of illness. Contributing to this state has been inappropriate use of antimicrobials, both from prescribing practices of the medical profession and poor compliance to treatment regimens by patients.

To minimise the effects of this situation, greater efforts need to be made to apply evidence-based measures in diagnosing and treating patients, using correct doses, administration measures and courses, and withholding drugs if advisable. However, many decisions are difficult when managing seriously ill patients infected with unknown organisms and sensitivity patterns, and empirical treatment may be needed.

However, in many cases, resistance is only partial and not all in vitro (laboratory) findings are translated into in vivo responses. Therefore, larger doses of a standard antibiotic may be used effectively in people with a normal immunity profile. Thus, penicillin can still be used for pneumococcal and other infections, and newer broad-spectrum antibiotics kept for the future or for other pathogens.[8,31,32]

Practical antibiotic regimens

It is clear that in each location, the initial treatment must be on empirical grounds, with management of the individual patient being modified according to the clinical course of the disease and the availability of information, such as laboratory results and radiological findings.

Regimens also differ according to the severity of the disease and whether it is acquired in the community or hospital (or institution). Other factors, such as cost and practicality, are also important.[1,28,32,33]

Following are examples of CAP protocols and some results, which may have some relevance to the decisions made here:

An article from Post-Graduate Medicine in November 1999 recommended:

a. For chest infection with typical organisms: amoxycillin, alternatives being amox/clavulanate, macrolides or cephalosporins including cefuroxime and third generation agents.

b. For CAP, which may include atypical organisms: beta-lactams, new generation macrolides or doxycycline, alternatives being cephalosporins or fluoroquinolones.

This is a fairly typical example of advice for developed countries.[15]

In Pakistan in the early 1990s the WHO recommended oral co-trimoxazole for non-severe pneumonia, with clinical failures receiving oral Amoxycillin. A study of children in two communities showed a cure rate of 91% and 92% despite the fact that in vitro resistance to the drug was shown to be up to 45% during the same period.

This is an example of an undeveloped country using an economical regimen that appeared effective.[34]

[Editor: Cure rates in community trials will vary depending on the proportion of cases that were caused by susceptible organisms. Of prime importance in this would be the proportion that was caused by viral infection and hence not responsive to antibiotic treatment.]

A study of the empirical treatment of CAP in the Royal Prince Alfred and Gosford hospitals compared the efficacy of a penicillin-based protocol with third generation cephalosporins. The penicillin protocol was:

Clinical condition	**Treatment**
For mild to moderate CAP	IV Benzyl penicillin and oral macrolide
For those with COAD	IV Ampicillin and oral macrolide
For severe CAP	IV Benzyl penicillin, Erythromycin and Gentamicin
For penicillin sensitivity	IV Cephalothin

Adherence to the protocol was not good, but retrospective analysis indicated the outcomes were the same in each group. This is an example of Australian practice, though the study was considered of poor design with selection and adherence bias.[13]

The protocol for CAP in the Top End (NT) published in December 2000 is:

	No risk factors	**Risk factors**
Mild pneumonia	penicillin	penicillin
Moderate pneumonia	penicillin	ceftriaxone + gentamicin
Severe pneumonia	ceftriaxone	(ceftriaxone or ceftazidime or meropenem) + gentamicin

Note: For atypical pneumonia, add or substitute erythromycin or ciprofloxacin. Risk factors include alcohol or kava excess, diabetes, chronic renal disease, chronic lung disease, steroid therapy.[33]

The current recommended initial therapy for patients admitted to Alice Springs Hospital is:[14]

Moderate pneumonia	IV Penicillin 1.2 g 6-hourly Roxithromycin 300 mg daily
Moderate pneumonia with risk factors	IV Penicillin 1.2 g 4-hourly O Roxithromycin 300 mg daily IV Gentamicin (5 mg/kg) daily for 2/7
Severe pneumonia	IV Penicillin 1.2 g 4-hourly IV Erythromycin 1 g 6-hourly and IV Gentamicin (5 mg/Kg) daily for 2/7
Critically ill patients Admit to ICU	IV Ceftriaxone 2 g daily IV Erythromycin 1 g 6-hourly IV Gentamicin (5 mg/kg) daily for 2/7

The local hospital regimens are given for information and to show that penicillin is also a drug of first choice for in-patients.

Parenteral vs oral antibiotics

There has been an ongoing debate amongst CARPA practitioners about the recommendation to treat all pneumonia with parenteral penicillin. There is

no data to inform this debate but there is a wealth of clinical experience and common sense.

There is benefit in standardising treatment (both drug and method of giving it) for pneumonia across the CARPA region. This includes making it easier to give IM injections if people expect them.

The case for only recommending parenteral penicillin is that:

- It can be given once a day, except for severe cases.
- It can be linked to reviewing the patient daily, and this may be skipped otherwise.
- High penicillin levels can be achieved, adequate to cover the increasing frequency of intermediate resistance in the pneumococcal isolates.
- It is currently accepted practice by ‘most’ community people.
- It ensures some level of compliance, at least if the people return to the clinic.
- It helps to ensure that cases with under-recognised severity receive more adequate treatment.

The case against only recommending parenteral penicillin is that:

- It is painful.
- Many community-based staff feel they can assess if a person is likely to take oral antibiotics as needed.
- Some patients may feel offended at not being ‘trusted’ to take oral antibiotics.
- It may be over-treating many people.
- It may be ‘disempowering’ for some patients if they feel like they have less control over their treatment that oral treatment might offer.

Further investigation

If a system for transporting specimens to the hospital laboratory is practical, blood and sputum tests for moderately ill patients are recommended.

In other settings, the diagnosis of pneumonia is dependent on the demonstration of consolidation on chest X-ray. In remote areas, the diagnosis is clinical but, under some circumstances, late referral for X-rays may be indicated. If considered, the decision should be made in consultation with a doctor.

‘Simple’ pneumonia usually improves in two days and settles in six days. If symptoms become worse in the first week or persist beyond that time, further action may be needed.

Clinical features which indicate complications — such as effusion, collapse, bronchiectasis, antibiotic resistance or other diagnoses — include:

- Increasing shortness of breath
- Coughing blood (apart from rusty sputum in the first few days)
- Chest pain (other than early pleurisy)
- Shift of the trachea from the mid-line
- Reduced breath sounds on one side
- Persistence or late onset of bronchial (tubular) breath sounds

Post-acute management

It is prudent to consider background factors that may have contributed to the illness and predispose to slow convalescence or recurrence such as:

- Poor housing conditions and overcrowding
- Poor nutrition, excess alcohol
- Active (or passive exposure to) smoking
- Other co-morbidities

Of these factors, nutrition, smoking, excess alcohol and petrol sniffing are all amenable to individual level intervention as described elsewhere in the CARPA manual and reference book.

It is important that the patient's immunisation status is checked and appropriate vaccination given, especially for pneumococcus and influenza.[4,35,36]

References

Note: A number of references have been taken from several large documents & for convenience, these are abbreviated in the list below.

PD1A 2000–Pneumococcal Disease in Australia. MJA 3rd October 2000, Vol 173 Supplement.
ICARI.1997 International Conference Acute Respiratory Infections Canberra. 7–10 July 1997

1. Andreson D. & Collignon P. Antibiotics for CAP. MJA 2 April 2001; 174 (7). Editorial.
2. Bryan S. Acute CAP Diagnosis and Treatment. Journal of Sth Carolina Med Association Jan 2001.
3. Garabaldi A. Epidemiology of CAP. Am J Med June 1985; 78(6B).
4. Indigenous Paediatric Respiratory Workshop Alice Springs August 2001. Comments.
5. Tsirgiotis & Ruffin CAP: A perspective for family practice. Aust Fam Physician July 2000; 29(7).
6. Jenkins C. How to treat CAP. Australian Doctor September 1997.
7. Hunter's Tropical Medicine and Emerging Infections Diseases 8th Edition 2000, edited by G. Thomas Strickland.
8. PDIA Gilbert GL. Retreat of the Pneumococcus.
9. Mathews C. Unpublished PNG.
10. Torzillo et al. Invasive pneumococcal disease in Central Australia. MJA 20 February 1995; 162.
11. Australian Lung Foundation COPD 2001. Case Statement.
12. Harrison's Principles of Internal Medicine 2000. CAP Outpatient Management.
13. Dobbin C. et al. The efficiency of an antibiotic protocol in CAP. MJA 2 April 2001; 174(7).
14. Segasothy M. Department of Medicine Communications, ASH.
15. Singh & Arrieta. Of bugs and drugs. Post Grad Med November 1999; 106(6).
16. Atkins & Meikle. Central Australia Respiratory Outreach Project. Report, May 2001.
17. Patel S. et al. Frequent hospital admissions for bacterial infections among aboriginal people with diabetes in Central Australia. MJA 19 August 1991; 155.
18. Chang A. 2001. Chest Infections from 3–12 months in CARPA reference Book. Alice Springs: CARPA, 2003.
19. Woodcock A & Hensely M. Chronic Respiratory Consequences of ARI ICARI, 1997.
20. McIntyre et al. Pneumococcal Disease in NSW. PD1A 2000.
21. Krause et al. Invasive Pneumococcal Disease in NT. PD1A 2000.
22. Alice Springs Hospital. Infection Control Unit Annual & Monthly Reports, 2000, 2001.
23. Thompson J. CAP in NE Australia: A hospital based study. Aust NZ J Medicine 1997; 27.
24. Torzillo P. Communication 1998. Alice Springs.
25. Segasothy M. Personal Communication. ASH.
26. Semin. Respiratory Infection September 1994; 9(3). Macdonald et al. CAP: The future microbiology laboratory.
27. Colacino J. Rapid diagnosis for viral respiratory disease. ICARI, 1997.
28. Thomson R. Laboratory diagnosis of respiratory infections. Current Opinion in Infectious Diseases 1999.

29. Klugman K. Antimicrobial Resistance. ICARI 1997.
30. Collignon & Turnidge, Antibiotic resistance in Strep. pneumoniae. PD1A 2000.
31. Turnidge et al. Rapidly emerging antimicrobial resistance in S. pneumoniae. MJA 15 February 1999; 170.
32. Paterson & Playford. Controversies in Health. MJA 6 April 1998; 168.
33. Currie et al. Antibiotic protocol for adult CAP in the Top End. NT Disease Control Bulletin, December 2000; 7(4).
34. Qazi S. Antibiotic strategies in developing countries. ARI Experiences in Pakistan. ICARI 1997.
35. Lehmann D. Efficiency & effectiveness of pneumococcal vaccines. PD1A 1997.
36. Lehmann D. Application of polysaccharide pneumococcal vaccine. ICARI 1997.
37. Currie et al. Melioidosis, The Top End prospective study. NT Disease Control Bulletin. December 2000; 7(4).