Community-acquired pneumonia in adults

The recommended empirical therapy in adults for the common condition community-acquired pneumonia is combination therapy with a narrow spectrum beta lactam antibiotic, to treat typical pathogens, and a macrolide antibiotic or doxycycline, to treat atypical pathogens.

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Community-acquired pneumonia (CAP) – defined as pneumonia occurring in an immunocompetent patient who has not been in hospital for at least 14 days – is a common and potentially serious illness. It affects all ages but its incidence increases with age, particularly above the age of 50 years. Mortality is around 8% but ranges from below 1% in the outpatient setting to above 20% in patients requiring intensive care therapy.

Pathogenesis and aetiology

The respiratory tract below the larynx is normally sterile despite the continual introduction of potential pathogens during inhalation and microaspiration. This sterility is due to host defences such as innate and acquired immunity and mucociliary transport systems. When these factors are impaired or the amount of aspiration overcomes the defences, pneumonia is more likely. Table 1 lists the factors that are associated with an increased risk of CAP.

Although there are many potential causes of CAP, a specific pathogen is found in only a few cases outside of trials of CAP. Table 2 lists the more common and some of the important but less common pathogens in CAP.

Managing the patient with CAP

When considering the diagnosis of CAP, it may be helpful to separate the management process into a series of questions:

- Is it really CAP?
- How severe is the pneumonia?
- Is hospitalisation appropriate?
- What therapy should be commenced?
- Are there any special considerations?

IN SUMMARY

- **Community-acquired pneumonia (CAP) is defined as pneumonia occurring in an immunocompetent patient who has not been in hospital for at least 14 days.**
- **CAP can be difficult to differentiate clinically from many other illnesses, the most common being viral respiratory tract infections. Chest x-ray infiltrate is the feature that best identifies patients as having pneumonia.**
- **Patients with normal chest x-rays are unlikely to benefit from taking antibiotics.**
- **Features of CAP that suggest the need for hospitalisation are severe breathlessness, confusion, inability to maintain oral intake, hypotension, hypoxia and multilobar or bilateral changes on chest x-ray.**
- **Treatment recommendations for CAP are controversial but existing Australian guidelines to use combination antibiotic therapy aimed at typical and atypical pathogens are appropriate.[1]**

Table 1. Factors associated with an increased risk of CAP

Age above 50 years
Alcoholism
Asthma
Cardiac failure
Cerebrovascular disease
Chronic obstructive pulmonary disease
Dementia
Immunosuppression
Indigenous background
Institutionalisation
Seizure disorders
Smoking

Table 2. Pathogens in CAP

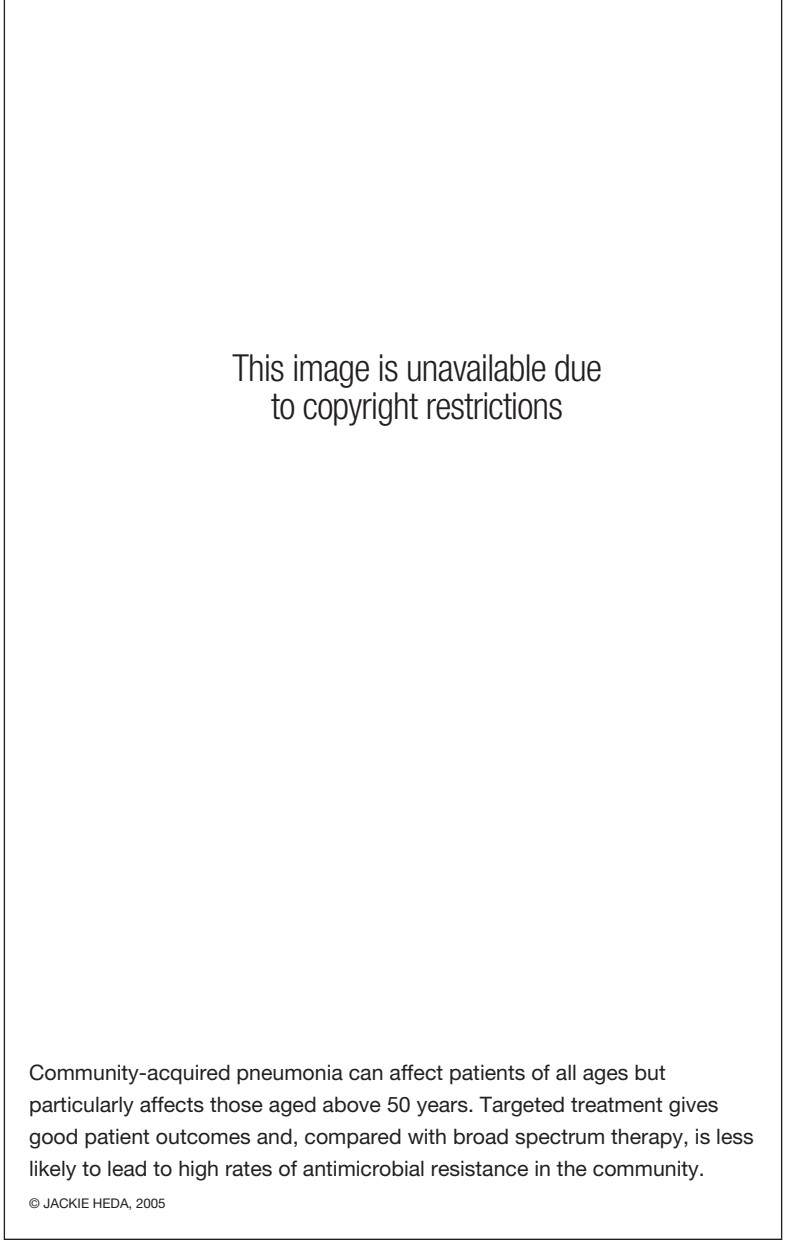
More common pathogens

Streptococcus pneumoniae
Chlamydophila pneumoniae
Chlamydophila psittaci
Mycoplasma pneumoniae
Haemophilus influenzae
Moraxella catarrhalis
Respiratory viruses

Less common but important pathogens

Legionella species
Staphylococcus aureus
Gram-negative bacilli
Pathogens specific to tropical northern Australia:
Acinetobacter baumannii, Burkholderia pseudomallei

Community-acquired pneumonia



Community-acquired pneumonia can affect patients of all ages but particularly affects those aged above 50 years. Targeted treatment gives good patient outcomes and, compared with broad spectrum therapy, is less likely to lead to high rates of antimicrobial resistance in the community.

Is it really CAP?

Acute respiratory illness is one of the most common presentations in general practice. Only a small proportion of patients will have pneumonia, and it requires skill to separate those few who may need antibiotics from the majority who do not.

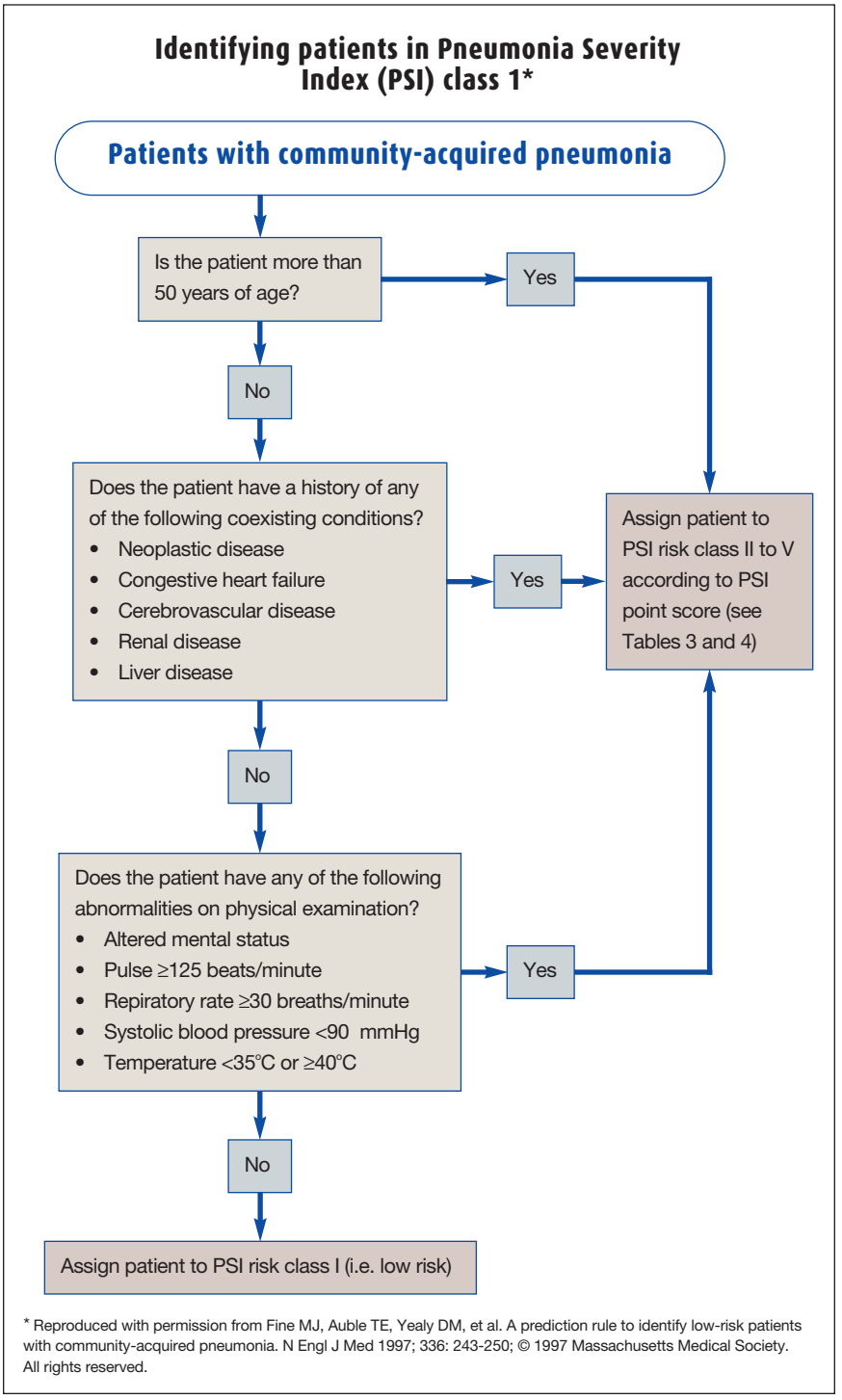
The unnecessary use of antibiotics for upper respiratory tract syndromes that resemble pneumonia is an important driver of cost and antibiotic resistance.

Suggestive symptoms

Patients with CAP are likely to have at least two of the following symptoms: fever or hypothermia, rigors, sweats, new or increased cough (with or without sputum), chest discomfort and new onset of dyspnoea. However, some patients present only with fever, and in the elderly, confusion or hypothermia may be the only initial clue.

Suggestive signs

On respiratory examination, tachypnoea above 20 breaths per minute is an important clue and the patient may have dullness to percussion, focal crackles or bronchial breath sounds. The absence of these signs, however, does not exclude a diagnosis of CAP.



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Investigations

The key to the diagnosis of CAP is the presence of a new infiltrate on chest x-ray (Figure 1). The decision to order an x-ray is a matter for clinical judgement. Rarely, patients with pneumonia may have a normal x-ray very early in their illness or if they are volume depleted. Generally, patients with a normal chest x-ray will not benefit from antibiotics.

How severe is the pneumonia?

In primary care, several features can help identify those patients requiring more attention. These include:

- advanced age
- major comorbidities – such as renal impairment, cardiac failure, chronic liver disease, cerebrovascular or other neurological disease, malignancies and immunosuppression
- certain physical signs – such as tachypnoea (30 or more breaths per minute), hypotension (systolic pressure less than 90 mmHg or diastolic ≤60 mmHg) and acute confusion
- an oxygen saturation below 90%, if pulse oximetry is available
- presence of bilateral or multilobar involvement on chest x-ray.

Pneumonia Severity Index and CURB-65

As the management of CAP is a significant contributor to overall healthcare expenditure, particularly for inpatients, there has been a lot of interest in developing systems that identify those patients warranting admission and those that can safely be discharged.

The best known system is the Pneumonia Severity Index (PSI), developed by Fine and colleagues.[2] In this system an initial set of clinical parameters is applied to the patient (Step 1; see the flowchart on this page). Then, if the patient is not at low risk (low risk equals class I according to the PSI), a 20-point protocol that requires access to pathology results is applied (Step 2; Table 3). These features

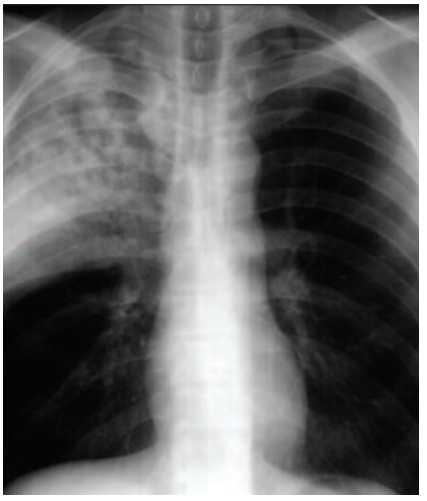

Figure 1. Classic lobar pneumonia

are used to calculate a score that reflects the patient's mortality over 30 days; 30-day mortality rises with the PSI class (Table 4). This system was developed and validated in North America and is now being increasingly used in Australia. A retrospective review of CAP patients at the Austin Hospital, Melbourne, showed very similar 30-day mortality to the figures published by Fine *et al*. The PSI has now been adopted by the Australian antibiotic guidelines (*Therapeutic guidelines: antibiotic, version 12, 2003*) to help guide empirical antibiotic therapy.[1] This decision was based on expert opinion rather than evidence.

CURB-65 is an alternative system promoted by the British Thoracic Society.[3] This simpler system assigns a point each to:

- Confusion
- Urea above 7 mmol/L
- Respiratory rate 30 breaths/min or above
- Blood pressure: systolic below 90 mmHg or diastolic ≤60 mmHg
- age 65 years or above.

Increasing number of points on this six-point score (range 0 to 5) is associated with higher 30-day mortality. CURB-65 can be cut back to CRB-65 for primary carers where access to the urea result is delayed (then a five-point score, range 0 to 4). It should be noted that nursing home patients were excluded from the study used to derive the C(U)RB-65 system. The categorisation of CURB-65 and CRB-65 scores into mortality risk groups is given in Tables 5 and 6, along with 30-day mortality data and suggested management strategies.

Is hospitalisation appropriate?

Based on low 30-day mortality, patients in PSI class 1 or with a CRB-65 score of 0 usually can be safely treated at home with

Table 3. Pneumonia Severity Index (PSI): point scoring system for non-class I patients[2]*

Characteristic	Points assigned†
Demographic factors	
Age: men	Age (yr)
women	Age (yr) minus 10
Nursing home resident	+10
Comorbid illness	
Neoplastic disease	+30
Liver disease	+20
Congestive heart disease	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical examination findings	
Altered mental state	+20
Respiratory rate ≥30 breaths/minute	+20
Systolic blood pressure <90 mmHg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125 beats/minute	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Urea ≥11 mmol/L	+20
Sodium <130 mmol/L	+20
Glucose ≥14 mmol/L	+10
Haematocrit <30%	+10
pO_2 arterial blood <60 mmHg or O_2 saturation <90%	+10
Pleural effusion	+10

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† A total point score for a given patient is obtained by summing the patient's age in years (age minus 10 in women) and the points for each applicable charateristic.

Table 4. PSI risk classes and 30-day mortality data[2]

PSI risk class (number of points)	30-day mortality (%)
I	0.1
II (≤70)	0.6
III (71 to 90)	0.9
IV (91 to 130)	9.3
V (>130)	27.0

continued

Table 5. CURB-65 system of CAP severity[3]

CURB-65 risk group	CURB-65 score*	30-day mortality (%)	Suggested management
1	0 or 1	1.5	Usually safe to manage at home
2	2	9.2	Likely to need admission
3	3 to 5	22	Manage as severe

*CURB-65 = Assign one point for each feature present: confusion, urea >7 mmol/L, respiratory rate ≥30 breaths/min, blood pressure – either systolic <90 mmHg or diastolic ≤60 mmHg, age ≥65 years.

oral antibiotics. Other patients warrant assessment in the emergency department. From there, it is generally appropriate to admit patients in PSI class 3 or above or a CURB-65 score of 2 or more. However, it should be remembered that these systems are guides only and supposedly low risk patients may still require admission for reasons such as social isolation, vomiting or medical concern.

We occasionally see previously well adults with clinically obvious severe pneumonia. Marked tachypnoea, hypotension, hypoxia and extensive multilobar involvement on chest x-ray are clues. Importantly, these patients often require admission to the intensive care unit and the severity of their disease may be underestimated by both CURB-65 and PSI.

In the emergency department, patients found clinically and on chest x-ray to have CAP should have testing done to calculate their PSI or CURB-65 scores to help guide subsequent management decisions. These investigations should include full blood evaluation, urea and electrolytes measurement, glucose measurement and assessment of oxygenation (pulse oximetry, or arterial blood gases if more severe).

To determine aetiology, send a sputum sample from a productive cough for Gram stain and culture and obtain blood cultures before starting antibiotics. The Gram stain should be chased up immediately, as the presence in a good quality sputum sample of clumps of Gram-positive cocci (suggestive of *Staphylococcus*) or large numbers of Gram-negative rods prompts different initial treatment to the more common finding of Gram-positive cocci in pairs seen in pneumococcal infection (Figure 2).

In patients with more severe disease, urine should be sent for *Legionella* antigen testing. Other tests that are being increasingly used are the pneumococcal urinary antigen test and respiratory virus PCR on swabs of the nose and throat. The former has a sensitivity of about 80% and a specificity above 90%, and takes only 15 minutes to perform. Newer PCR tests for atypical agents such as *Legionella, Mycoplasma* or *Chlamydophila* (formerly *Chlamydia*) are also available but are incompletely validated. Acute serology is unlikely to give a diagnosis in isolation (except possibly for *Mycoplasma*), but serology may be helpful during convalescence (on serum samples taken at least three weeks later). Seroconversion for *Legionella* may take as long as six to 12 weeks, particularly in more severe cases.

Table 6. CRB-65 system of CAP severity[3]

CRB-65 risk group	CRB-65 score*	30-day mortality (%)	Suggested management
1	0	1.2	Usually safe to manage at home
2	1 or 2	8.2	Assess in hospital
3	3 or 4	3.1	Urgent hospital referral

*CRB-65 = Assign one point for each feature present: confusion, respiratory rate ≥30 breaths/min, blood pressure – either systolic <90 mmHg or diastolic ≤60 mmHg, age ≥65 years.

What therapy should be commenced?

Streptococcus pneumoniae remains the most common cause of CAP and despite the vast amount of literature regarding antibiotic resistance in this pathogen, there is yet to be a reported case of clinical failure when CAP is treated with simple beta lactam antibiotics such as penicillin. This is different to the situation with infections of the central nervous system (CNS), where failures have occurred with beta lactam therapy because the blood–brain barrier results in lower levels of antibiotic in the CNS.

In retrospective studies of confirmed cases of pneumococcal CAP, mortality is lower when a beta lactam is combined with another antibiotic. Whether this lowered mortality is due to the treatment of an undiagnosed second 'atypical' pathogen, to an anti-inflammatory effect of macrolide antibiotics or to some other mechanism is unclear. The Australian antibiotic guidelines now recommend dual therapy combining a narrow spectrum beta lactam and an 'atypical' agent such as a macrolide or doxycycline for all classes of CAP.[1]

Choice of empirical therapy for CAP is a contentious area, with vast differences in the recommendations of North American (USA and Canada) authorities compared to British, European and

Australian guidelines. While authorities in North America rely heavily on the use of respiratory fluoroquinolones such as levofloxacin (unavailable in Australia) and moxifloxacin (Avelox), Australian authorities believe that their high cost and excessively broad spectrum coverage warrant limitation of their use. Given that the fluoroquinolones are the only widely useful orally active antibiotics effective against a wide range of Gram-negative bacteria such as *Pseudomonas* and many of the Enterobacteriaceae, this approach is appropriate to maintain low rates of resistance to these agents. Resistance to quinolones among respiratory pathogens is being increasingly seen in the USA and Canada.

Given these considerations, we recommend the following of the current Australian antibiotic guidelines for the treatment of CAP, as detailed in *Therapeutic guidelines: antibiotic, version 12, 2003*. Suggested empirical therapy for CAP in nontropical parts of Australia is given in Table 7.[1] Therapy should be given for seven days in mild to moderate cases but may need to be longer in more severe cases or with pathogens such as *Legionella*. It is also important to remember prevention and to follow the guidelines regarding vaccination for influenza

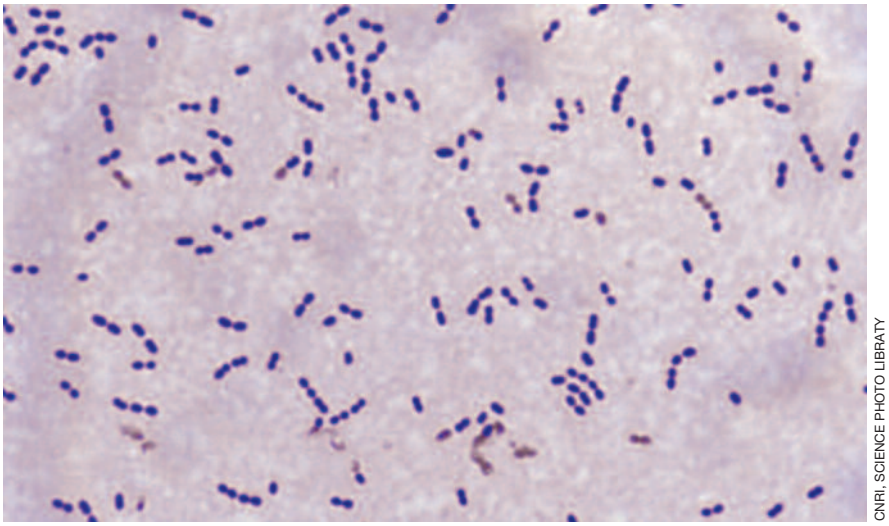

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Figure 2. Sputum containing Gram-positive cocci in pairs, typical of pneumococcal infection.

Table 7. Empirical therapy for CAP in non tropical parts of Australia[1]*

PSI class†	Typical cover	Atypical cover	Alternatives
I and II	Oral amoxycillin 1 g 8-hourly for 7 days	Either oral doxycycline 200 mg stat then 100 mg daily for 5 days or oral roxithromycin (Biaxsig, Rulide) 300 mg daily for 7 days	Oral cefuroxime (Zinnat) 500 mg 12-hourly for 7 days if penicillin allergic. Oral moxifloxacin (Avelox) 400 mg daily for 7 days if immediate penicillin hypersensitivity‡
III and IV§	Intravenous benzylpenicillin (BenPen) 1.2 g 6-hourly until clinical stability achieved; then change to oral therapy.‖ Consider adding gentamicin if Gram-negative organisms identified in sputum or blood	Either oral doxycycline 200 mg stat then 100 mg daily for 5 days or oral roxithromycin 300 mg daily for 7 days	Intravenous ceftriaxone (Rocephin) 1 g daily if penicillin allergic (until clinical stability achieved; then change to oral therapy).‖ Oral/intravenous moxifloxacin 400 mg daily for 7 days if immediate penicillin hypersensitivity‡
V§	Either intravenous ceftriaxone 1 g daily or intravenous benzylpenicillin 1.2 g 6-hourly (until clinical stability achieved; then change to oral therapy‖) plus intravenous gentamicin 4 to 6 mg/kg/day	Either intravenous azithromycin (Zithromax) 500 mg daily or intravenous erythromycin (Erythrocin IV) 0.5 to 1 g 6-hourly	Intravenous moxifloxacin 400 mg daily if immediate penicillin hypersensitivity‡

* Antibiotics that are essentially equivalent to those listed in this table may be used instead. † PSI class = Pneumonia Severity Index class. ‡ As a single agent. § Total duration of treatment depends on clinical response but is generally 7 to 14 days but up to 21 days in confirmed *Legionella* cases. ‖ Clinical stability = a sustained response in temperature and respiratory rate for about 24 hours.

(Fluad, Fluarix, Fluvax, Vaxigrip) and pneumococcus (Pneumovax 23).

Are there any special considerations?

- Staphylococcal pneumonia is an uncommon cause of CAP. It is hard to diagnose without a good quality sputum sample, does not respond to standard therapy, tends to present with more severe illness, has a higher mortality and may be associated with recent influenza infection.
- CAP due to Gram-negative bacteria is uncommon and has a higher mortality than CAP due to Gram-positive bacteria. It is usually seen in nosocomial pneumonia or in alcoholic patients, nursing home residents or patients with chronic lung conditions such as bronchiectasis. Again, sputum sample testing (especially Gram stain) is required for diagnosis.
- Severe CAP in residents of tropical northern Australia may be due to *Acinetobacter baumannii* or *Burkholderia pseudomallei* (melioidosis). It is more commonly seen in alcoholic patients and diabetic patients and should be treated with aminoglycosides and broad spectrum beta lactam antibiotics. For further details of appropriate therapy, see the *Therapeutic guidelines: antibiotic, version 12*.
- Unusual viral infections such as severe acute respiratory syndrome (SARS) or the so-called 'bird flu' (influenza H5N1) may present as CAP. Awareness of current outbreaks of these infections and the patient's travel history are needed for consideration of such diagnoses. Also, clusters of illness in healthcare workers should arouse suspicion.
- Tuberculosis should be considered in patients with appropriate epidemiological risk factors (for example, older Australians or overseas-born patients) plus cough and fever lasting longer than one to two weeks and failure to respond to conventional therapy.
- CAP may be associated with HIV infection. Pneumococcal pneumonia is more common in patients infected with HIV, and opportunistic infections such as *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*) may present with a slowly progressive atypical pneumonia.
- If the patient is not improving, check that the prescribed medication is actually being taken and, if given orally, is being absorbed. The diagnosis

should be reconsidered, reviewing available diagnostic data. Specialist support may be required as progressive pneumonia has a high mortality. Antibiotic resistance *per se* is not necessarily the problem.

Conclusion

For a condition as common as CAP, it is surprising that its treatment is so controversial. The recommended empirical therapy in Australia for most patients is combination therapy with a narrow spectrum beta lactam (such as amoxycillin or benzylpenicillin [BenPen]) plus another antibiotic (such as doxycycline or roxithromycin [Biaxsig, Rulide]) to treat atypical pathogens. This gives good patient outcomes and, when compared with more broad spectrum therapy, is less likely to lead to high rates of antimicrobial resistance in the community. MT

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1. Therapeutic guidelines: antibiotic, version 12. Melbourne: Therapeutic Guidelines; 2003. p.165-175.
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Further reading

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