Pneumonia
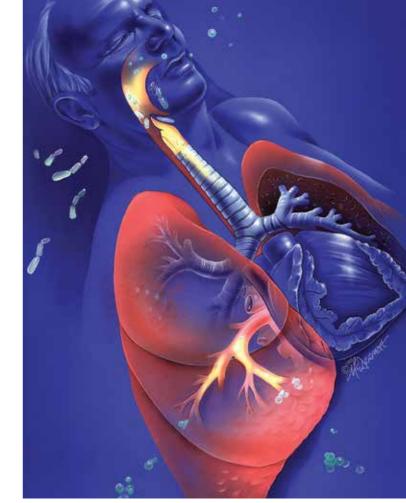## Who is at risk in your practice?

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GPs play an important role in the diagnosis, management and referral of patients with pneumonia and are uniquely placed to implement preventive measures such as smoking cessation and vaccination.

KEY POINTS

- Risk factors for pneumonia include increasing age, smoking and presence of chronic diseases, such as chronic lung disease, heart disease and diabetes.
- Preventive measures include influenza and pneumococcal vaccination and smoking cessation.
- GPs are at the front line of management of patients with pneumonia, including diagnosis, starting empirical outpatient antibiotic therapy and referring those who are very ill or at risk of deterioration to hospital.
- A chest x-ray is important for diagnosis of pneumonia.
- Most patients respond to empirical antibiotic therapy with amoxycillin, doxycycline or an appropriate macrolide antibiotic.
- Patients with nonresolving pneumonia require reassessment to confirm the diagnosis, identify the pathogen and look for complications or underlying disease such as malignancy.

O ver 100 years ago, William Osler described pneumonia as 'the old man's friend', allowing elderly patients a relatively rapid death without significant suffering. With improved nutrition, social welfare and the availability of immunisations and antibiotics, the death toll for pneumonia has reduced dramatically. However, lung infection remains a significant cause of morbidity and mortality in Australia, particularly in elderly people and those with chronic disease. The adult Australians at greatest risk of developing pneumonia, the role of preventive measures and practical aspects of the investigation, management and referral of patients with suspected pneumonia are discussed in this article. Practice points regarding management of patients with pneumonia are summarised in Box 1.[1,2] Five case histories illustrate a range of patients with pneumonia (Figures 1 to 5).

Epidemiology

Although upper respiratory tract infections and bronchitis account for most patients who present to GPs with new respiratory problems, pneumonia is the most likely new respiratory problem to result in patients being referred to hospital.[3,4] International data suggest approximately 30% of patients with pneumonia require hospitalisation; in 2013-14, pneumonia was the principal diagnosis for over 56,000 Australian hospital separations.[5,6] Notably, pneumonia is the most common associated cause of death in patients with chronic obstructive pulmonary disease (COPD) and contributes to a third of deaths due to dementia.[7] Given the ageing population, the burden of pneumonia is expected to increase.

What is pneumonia?

Pneumonia describes an inflammatory process involving the alveolar spaces, typically caused by infection. The differentiation between pneumonia and bronchitis, a lower respiratory tract infection that does not affect the lung parenchyma, can be difficult in clinical practice, particularly in patients with chronic lung disease in whom the baseline chest x-ray is abnormal. Pneumonia may be classified based on aetiology (bacterial, viral or fungal), location of organism acquisition (community-acquired, hospital-acquired or healthcare-associated) or pathophysiology (e.g. aspiration or

immunosuppression-related).

The classification of pneumonia as 'atypical' is generally discouraged as it incorrectly implies a distinctive clinical pattern.[8] Although certain clinical features occur more commonly with specific pathogens, this association generally does not allow accurate differentiation of causative organisms.

For the remainder of this article, the term pneumonia will be used to refer only to cases of presumed infectious aetiology, where a patient in the community or in a nursing home presents with symptoms that are either respiratory (e.g. cough, dyspnoea, chest pain) or systemic (e.g. fever, malaise, confusion) and new changes that are consistent with consolidation on chest x-ray.

What causes pneumonia?

There are more than 100 potential microbial causes of pneumonia. However, even with extensive microbiological investigation, no causative organism is identified in up to 50% of patients with pneumonia.[9] Most cases in which a microbial cause is identified are attributable to a handful of organisms (Box 2).[10-12] The spectrum of microbes varies with age, illness severity and geographical location, and can be dynamic in cases of outbreaks and epidemics. Specific pathogens can be associated with particular risk factors (Table 1). A medical, social, occupational and travel history may give clues to likely causative organisms.

Worldwide, *Streptococcus pneumoniae* is the most common identifiable cause of community-acquired pneumonia. More than 90 distinct serotypes have been described; most, if not all, are capable of causing serious disease in humans. Up to

50% of children and 20% of adults have asymptomatic colonisation of the nasopharynx with *S. pneumoniae*.[13,14] Independent risk factors for colonisation include crowded living conditions, low household income, smoking and recent antibiotic use. Organisms are presumably aspirated or aerosolised from the oropharynx or nasopharynx to the alveoli, where they cross the respiratory epithelium and begin the infective process. Conversion of asymptomatic colonisation to overt infection and invasive disease is not entirely understood but may be related to 'priming' of the airway by inflammation, for example caused by smoking exposure or viral infection.[15] Epidemiological data show definite seasonality and correlation of viral activity with invasive pneumococcal disease (IPD).[4,16] Indeed bacterial pneumonia is often secondary to a viral infection.

Viral pneumonia must not be underestimated, with many surveys identifying respiratory viruses as the second most common cause for patients to require hospitalisation.[11] Influenza remains the predominant viral cause of pneumonia and also predisposes to superimposed bacterial infection, particularly with *S. pneumoniae* but also with *Staphylococcus aureus*.[17] Other viral causes of pneumonia include respiratory syncytial virus, parainfluenza viruses, human metapneumovirus and coronaviruses. Bacterial and viral co-infection occurs frequently, commonly reported in 7 to 10% of those with positive microbiology, but may be found in up to 26%.[18]

The frequent failure to identify the organism responsible for pneumonia, along with the fact that neither radiological nor clinical features can reliably differentiate between the different aetiologies, has led to the practice of empirical antibiotic therapy (see below).

Who is at risk of pneumonia?

Although pneumonia can occur at any time of life, the incidence increases with age, with a marked increase after the age of 65 years.[19,20]

Indigenous Australians have a particularly increased risk of pneumococcal

pneumonia, with contributing factors including high rates of oropharyngeal colonisation, low vaccination uptake and high prevalence of other comorbidities, such as smoking and chronic lung disease.[21]

Active smoking is associated with a greater risk of severe sepsis, hospitalisation and death in comparison with nonsmoking.[22] Smoking has a profound effect on respiratory defence mechanisms, including alteration of mucociliary transport and inherent humoral and cellular defences. Moreover, smoking has been shown to increase adhesion of *S. pneumoniae*, *S. aureus* and *Haemophilus influenzae* to the oropharyngeal epithelium.[23] Passive smoking is also associated with increased risk.[24]

Although moderate alcohol consumption (two to four standard drinks daily) confers a modest protective effect, higher intake is associated with an increased risk of pneumonia and death. This has been attributed to impairment of local and systemic host immune mechanisms, as well as reduced alertness and favouring of aspiration.[25] Alcohol misuse together with tobacco smoking have been suggested to be the most preventable risk factors for IPD.[26]

Risk factors for aspiration pneumonia include increased age, poor oral hygiene, neurological disorders such as stroke and dementia, and oesophageal motility disorders such as gastro-oesophageal reflux disease.[27] Aspiration of oropharyngeal contents can also occur when the coordination of swallow and breathing is impaired, such as in COPD.[28]

A range of chronic diseases are associated with an increased risk of pneumonia including, but not limited to:[29]

- chronic respiratory disease (e.g. COPD, bronchiectasis)
- cardiovascular disease (e.g. coronary artery disease, congestive heart failure)
- cerebrovascular disease
- chronic kidney disease
- chronic liver disease
- malignancy
- diabetes
- dementia
- immunodeficiency.

TABLE 1. PNEUMONIA PATHOGENS ASSOCIATED WITH SPECIFIC RISK FACTORS

Risk factor group	Pathogens
Contact with young children	Viruses, *Bordetella pertussis*
'Flu' season	Influenza, *Streptococcus pneumoniae*, *Staphylococcus aureus* (including MRSA)
Recent travel	Viruses, *Legionella* spp., *Mycobacterium tuberculosis* (South-East Asia), *Burkholderia pseudomallei* (Far North Queensland), SARS virus, MERS virus (Middle East)
Exposure to animals	*Chlamydophila psittaci* (birds), *Coxiella burnetii* (farm animals)
Chronic lung disease	*Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Moraxella catarrhalis*
Nursing home residents	Enterobacteriaceae (Gram-negative bacteria), MRSA

Abbreviations: MERS = Middle East respiratory syndrome; MRSA = methicillin-resistant S. aureus; SARS = severe acute respiratory syndrome.

The risk of pneumonia in patients with multimorbidity, commonly defined as the presence of two or more chronic medical conditions, appears increased but the extent of the increase is difficult to quantify. Certain comorbidities may occur together, conferring an increased probability of community-acquired pneumonia ('risk stacking'). For instance, the common scenario of comorbid diabetes, chronic heart disease and COPD has been suggested to confer a hypothetical odds ratio of 7.5 or higher, which increases to more than 40 with the addition of ongoing smoking.[30] The presence of multiple health conditions is also associated with poorer prognosis; a prospective study showed that multimorbidity was an independent risk factor for death or hospitalisation within 90 days[31] (Figure 1).

Which adults should be offered vaccination?

Influenza vaccination reduces the likelihood of acquiring influenza, particularly when vaccine and circulating strains are well matched.[32] Adjusted analysis of case–control studies has shown that in community-dwelling patients aged 65 years and over, influenza vaccination reduces the risk of pneumonia, hospital admission and death.[33] Current Australian guidelines strongly recommend annual influenza
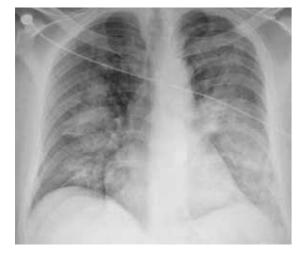

Figure 1. A 48-year-old man presented with malaise, rigors and delirium. He had minimal breathlessness and cough. Blood tests showed hyponatraemia. A chest x-ray showed bilateral consolidation. Urine antigen testing was positive for *Legionella pneumophila* serogroup 1. The patient's risk factors for pneumonia included heavy smoking and alcohol intake.

TABLE 2. AUSTRALIAN RECOMMENDATIONS ON PNEUMOCOCCAL VACCINATION USING 23VPPV IN ADULTS[34,38]

Risk of invasive disease	23vPPV vaccine recommendations*
Highest risk (category A)[†] • Asplenia • Immunosuppression • Chronic renal failure • Cochlear implant • CSF leak	• Three doses for all patients • Third dose to be given at: – age 65 years (non-Indigenous) or 50 years (Indigenous) OR – five years after second dose (whichever is later)
Increased risk (category B) • Chronic heart disease • Chronic lung disease • Diabetes mellitus • Down syndrome • Chronic liver disease • Tobacco smoking	• At least two doses for all patients • Two doses to be given if age 65 years or older (non-Indigenous) or 50 years or older (Indigenous) • A third dose for younger patients to be given at: – age 65 years (non-Indigenous) or 50 years (Indigenous) OR – five years after second dose (whichever is later)
Normal (healthy)	• Single dose if age 65 years or older (non-Indigenous) • Two doses if age 50 years or older (Indigenous)

Abbreviations: 23vPPV = 23-valent pneumococcal polysaccharide vaccine; CSF = cerebrospinal fluid.
* Minimum of five years between doses.
† Patients at greatest risk should also receive a single dose of 13-valent pneumococcal conjugate vaccine (13vPCV), preceding the 23-valent polysaccharide vaccine by two months. In patients who have had the polysaccharide vaccine, the 13vPCV dose should be given at least 12 months later. Stem cell transplant recipients should receive three doses of 13vPCV.

vaccination for all adults aged 65 years and older, Aboriginal and Torres Strait Islander people aged 50 years and older and patients at increased risk of complications, including adults with chronic illness or obesity and pregnant women.[34] Systemic adverse effects occur in 1 to 10% of patients and may mimic influenza, but patients should be reassured that the vaccine does not contain live virus and that fever, malaise and myalgia represent a normal immune response.

Pneumococcal vaccination is effective in reducing IPD.[35] Patients at highest risk of IPD are those with asplenia, haematological malignancy and transplant (Figure 2). Other conditions associated with an increased risk of IPD closely resemble general pneumonia risk factors.[34] Currently, 6 to 10% of patients requiring hospitalisation for community-acquired pneumonia have positive blood cultures or bacteraemia, and over half of these cases are caused by *S. pneumoniae*.[36] Recent evidence has demonstrated that pneumococcal vaccination also confers protection against nonbacteraemic pneumococcal pneumonia, with a 45% reduction in risk of disease caused by vaccine-related strains.[37]

Up to three doses of 23-valent pneumococcal polysaccharide vaccine are recommended for adults, depending on age, Indigenous status and the presence of conditions associated with increased risk of IPD. One or more doses of 13-valent pneumococcal conjugate vaccine are also recommended in those at greatest risk of IPD (Table 2).[34,38]

What other prevention measures should be encouraged?

Pneumonia prevention interventions include addressing individual patient factors as well as the socioeconomic determinants associated with increased risk.[38] Practical advice should include:

• hand hygiene
• cough etiquette
• avoiding sick contacts
• maintaining healthy nutrition
• maintaining good oral hygiene
• optimising chronic health conditions
• undertaking regular physical activity
• smoking cessation
• reducing alcohol intake.

How should patients be investigated and managed?

The combination of history taking and physical examination is insufficient to confidently rule in or rule out a diagnosis of pneumonia.[39] The elderly in particular may present without the classic symptoms that suggest pneumonia (cough, breathlessness and fever), and many present with confusion alone.[40] GPs are best placed to manage patients pragmatically at first presentation, including provision of antibiotics if pneumonia is clinically suspected. Guidelines emphasise the need to risk-stratify patients; those with severe illness

Figure 2. A 73-year-old man presented to hospital with fever, cough and breathlessness. He had a history of splenectomy in the 1970s, and could not recall when he last had a pneumococcal vaccination. A chest x-ray showed left upper lobe consolidation with air bronchograms, indicating pneumonia. Despite antibiotics and invasive cardiopulmonary support, the patient developed sepsis and died. Patients with haematological malignancy and asplenia are at highest risk of invasive pneumococcal disease and should have three doses of the 23-valent pneumococcal polysaccharide vaccine.

Figure 3. A 91-year-old man with known emphysema presented with a two-week history of breathlessness and cough productive of yellow-green sputum, unresponsive to amoxycillin. Pernasal swab for viral pathogens was positive for influenza type A virus. Sputum culture was positive for *Haemophilus influenzae*. A chest x-ray showed patchy changes at both bases, suggesting broncho-pneumonia. In patients with underlying lung disease, chronic scarring can make the chest x-ray difficult to interpret, and comparison with previous imaging is often helpful.

(e.g. altered mentation or abnormal vital signs) or comorbidities that confer worse clinical outcomes should be referred for inpatient management.[8,41]

Pulse oximetry allows simple and rapid assessment of oxygenation and is an essential component of clinical assessment of patients with suspected pneumonia. Peripheral capillary oxygen saturation (SpO_2) less than 92% on room air is associated with major adverse events and increased mortality; these patients should be referred immediately for inpatient care.[42]

Patients with suspected pneumonia who are assessed as suitable to manage in the community should be treated with oral antibiotics (see below). In addition, they should be advised to rest, avoid smoking, drink fluids and take simple analgesics/antipyretics. They should be counselled to present to a hospital emergency department if they do not improve.

Imaging

A chest x-ray is the most useful test for diagnosing pneumonia and should be performed in all patients with suspected pneumonia. Typical findings include patchy alveolar and/or interstitial infiltrates, with 'air bronchograms' (the hallmark finding of lung consolidation) and in some cases demarcation of fissures. Left lower lobe consolidation may appear as retrocardiac opacification, more easily seen on a lateral view. In patients with underlying lung disease, comparison with previous imaging may be helpful (Figure 3).

There is no need to perform CT of the chest initially. CT may be required if there is a clinical suspicion of pneumonia complicated by other pulmonary problems (e.g. pulmonary embolus, empyema, abscess or endobronchial obstruction). If patients are sufficiently ill for these

Figure 4. A 42-year-old woman was referred to the emergency department with a one-week history of cough and breathlessness not responsive to amoxycillin. Oxygen saturation was 87% on room air. A chest x-ray showed bilateral consolidation with involvement of the right middle lobe, indicated by loss of the right heart border and delineation of the horizontal fissure. The patient improved with empirical antibiotic therapy. At six-week follow up, the consolidation was completely resolved (not shown), and serology tests were positive for *Mycoplasma pneumoniae*. *Mycoplasma* spp. are common causes of pneumonia, particularly in younger adults, and patients require treatment with doxycycline or a macrolide such as clarithromycin.

diagnoses to be considered, they are likely to require hospitalisation.

Microbiological testing

Microbiological testing of respiratory secretions and blood is frequently not performed for patients with suspected pneumonia in primary care because empirical antibiotic therapy is highly successful. Important exceptions where we recommend collection of specimens for microbiological analysis include:

- patients with comorbid disease who may be infected with antibiotic-resistant or unusual organisms
- patients who do not respond to initial empirical antibiotic therapy
- patients with weight loss, haemoptysis and other risk factors for tuberculosis
- patients with suspected *Legionella* infection or influenza during outbreaks.

Sputum cultures from patients who have not yet commenced antibiotics are particularly valuable for identifying putative organisms and selecting antibiotics with the narrowest sensitivity spectrum. Sputum samples collected in the community are very useful if patients subsequently present to hospital because of clinical deterioration.

Antibiotic treatment

Antibiotic treatment should be based on local microbiology, suspected organisms and patient factors such as allergies and comorbidities. The Australian *Therapeutic Guidelines* recommend initial oral therapy with amoxycillin for five to seven days.[43] For patients with immediate penicillin hypersensitivity, doxycycline or an appropriate macrolide antibiotic are effective alternatives and have the added benefit of activity against *Mycoplasma pneumoniae*, which accounts for a significant proportion of cases of community-acquired pneumonia in young adults (Figure 4). For patients with COPD, who are more likely to be infected with *H. influenzae*, the pre-emptive addition of clavulanic acid may be appropriate. First-line empirical antibiotic options are listed in Table 3.[43,44]

Figure 5. A 35-year-old woman presented with a one-day history of pleuritic left chest pain, dyspnoea and fever. Urine was positive for pneumococcal antigen. Chest x-ray shows left lower lobe consolidation with a small pleural effusion. Consolidation is also present in the right lung. The effusion did not respond to drainage via a pleural catheter, and the patient underwent surgical decortication for complex parapneumonic pleural effusion.

When should patients be referred?

Pneumonia is an acute condition with significant morbidity and mortality. If patients do not respond within 48 hours of empirical therapy then referral to hospital is advised.[8] Failure of the patient to improve as expected can be due to a variety of reasons, including:

- local or systemic complications of pneumonia (e.g. pleural effusion, empyema, sepsis; Figure 5)
- complicating comorbidities (e.g. COPD, heart failure)
- incorrect diagnosis (e.g. undiagnosed malignancy)
- unusual or antibiotic-resistant pathogens (occurs in a minority of cases)
- an inhaled airway foreign body (in patients at high risk of aspiration).

How should patients be followed up?

GPs play a key role in the follow up of patients with pneumonia. Chest x-ray changes can persist for several weeks following clinical improvement.[45] All patients should have follow-up imaging at around six weeks to ensure resolution of consolidation. Persistent changes may reflect underlying disease such as malignancy or bronchiectasis.

Conclusion

The risk of acquiring pneumonia and subsequent prognosis are closely related to patient factors such as age, comorbidity and disability. GPs are at the front line, often being the first physician to assess patients with pneumonia and commence treatment. Patients should be promptly risk-stratified and referred for further investigation and/or hospitalisation if required. Follow-up imaging is important to confirm resolution of pneumonia. Finally, GPs have an invaluable role in identifying the patients who are most at risk and promoting preventive health measures, including optimising chronic health conditions, encouraging smoking cessation and providing vaccinations. MT

References

A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

TABLE 3. ANTIBIOTICS FOR EMPIRICAL OUTPATIENT TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN ADULTS*

Antibiotic	Comments
Amoxycillin 1 g orally, 8-hourly for 5 to 7 days	Consider addition of clavulanic acid, especially if Gram-negative organisms are suspected Liquid formulations are available and may be easier for some patients
Doxycycline 100 mg orally, 12-hourly for 5 to 7 days	Preferred if atypical pathogens suspected (e.g. *Mycoplasma, Chlamydophila, Legionella*) Avoid in pregnant women
Roxithromycin 150 mg orally, 12-hourly for 5 to 7 days	May be used if doxycycline is poorly tolerated and cover against atypical pathogens is required Interacts with many drugs and causes QT prolongation
Cefuroxime 500 mg orally, 12-hourly for 5 to 7 days	May be used in patients with penicillin allergy (excluding hypersensitivity) Provides little additional cover compared with amoxycillin, apart from Gram-negative organisms

* Adapted from *Therapeutic Guidelines* and the *Australian Medicines Handbook*.[43,44]

Pneumonia
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References

1. Rigotti NA, Munafo MR, Stead LF. Smoking cessation interventions for hospitalized smokers: a systematic review. Arch Intern Med 2008; 168: 1950-1960.
2. Toms C, Stapledon R, Waring J, Douglas P. Tuberculosis notifications in Australia, 2012 and 2013: Australian Mycobacterium Laboratory Reference Network. Canberra: Australian Government Department of Health. Available online at: http://www.health.gov.au/internet/main/publishing.nsf/Content/EE895A5F2FBD208FCA257E17007FDF29/$File/tb-notifications-2012-13.pdf (accessed July 2015).
3. Britt H, Miller GC, Henderson J, et al. General practice activity in Australia 2013-14. General practice series no. 36. Sydney: Sydney University Press; 2014.
4. Weinberger DM, Grant LR, Steiner CA, et al. Seasonal drivers of pneumococcal disease incidence: impact of bacterial carriage and viral activity. Clin Infect Dis 2014; 58: 188-194.
5. Guest JF, Morris A. Community-acquired pneumonia: the annual cost to the National Health Service in the UK. Eur Resp J 1997; 10: 1530-1534.
6. Australian Institute of Health and Welfare. Admitted patient care 2013-14: Australian hospital statistics. Canberra: AIHW; 2015.
7. Australian Institute of Health and Welfare. Multiple causes of death in Australia: an anaysis of all natural and selected chronic disease causes of death 1997-2007. Canberra: AIHW; 2012.
8. Levy ML, Le Jeune I, Woodhead MA, Macfarlaned JT, Lim WS; British Thoracic Society Community Acquired Pneumonia in Adults Guideline Group. Primary care summary of the British Thoracic Society Guidelines for the management of community acquired pneumonia in adults: 2009 update. Endorsed by the Royal College of General Practitioners and the Primary Care Respiratory Society UK. Prim Care Respir J 2010; 19: 21-27. Correction in Prim Care Respir J 2010; 19:108.
9. Cilloniz C, Ewig S, Polverino E, et al. Microbial aetiology of community-acquired pneumonia and its relation to severity. Thorax 2011; 66: 340-346.
10. Ruiz M, Ewig S, Marcos MA, et al. Etiology of community-acquired pneumonia: impact of age, comorbidity, and severity. Am J Resp Crit Care Med 1999; 160: 397-405.
11. Charles PG, Whitby M, Fuller AJ, et al. The etiology of community-acquired pneumonia in Australia: why penicillin plus doxycycline or a macrolide is the most appropriate therapy. Clin Infect Dis 2008; 46: 1513-1521.
12. Capelastegui A, España PP, Bilbao A, et al; Poblational Study of Pneumonia (PSoP) Group. Etiology of community-acquired pneumonia in a population-based study: link between etiology and patients characteristics, process-of-care, clinical evolution and outcomes. BMC Infect Dis 2012; 12: 134.
13. Hamaluba M, Kandasamy R, Ndimah S, et al. A cross-sectional observational study of pneumococcal carriage in children, their parents, and older adults following the introduction of the 7-valent pneumococcal conjugate vaccine. Medicine 2015; 94: e335.
14. Flamaing J, Peetermans WE, Vandeven J, Verhaegen J. Pneumococcal colonization in older persons in a nonoutbreak setting. J Am Geriatr Soc 2010; 58: 396-398.
15. Joseph C, Togawa Y, Shindo N. Bacterial and viral infections associated with influenza. Influenza and other respiratory viruses 2013; 7 Suppl 2: 105-113.
16. Watson M, Gilmour R, Menzies R, Ferson M, McIntyre P, New South Wales Pneumococcal Network. The association of respiratory viruses, temperature, and other climatic parameters with the incidence of invasive pneumococcal disease in Sydney, Australia. Clin Infect Dis 2006; 42: 211-215.
17. Cheng AC, Kotsimbos T, Reynolds A, et al. Clinical and epidemiological profile of patients with severe H1N1/09 pandemic influenza in Australia and New Zealand: an observational cohort study. BMJ Open 2011; 1: e000100.
18. Bello S, Minchole E, Fandos S, et al. Inflammatory response in mixed viral-bacterial community-acquired pneumonia. BMC Pulm Med 2014; 14: 123.
19. Welte T, Torres A, Nathwani D. Clinical and economic burden of community-acquired pneumonia among adults in Europe. Thorax 2012; 67: 71-79.
20. Baik I, Curhan GC, Rimm EB, Bendich A, Willett WC, Fawzi WW. A prospective study of age and lifestyle factors in relation to community-acquired pneumonia in US men and women. Arch Intern Med 2000; 160: 3082-3088.
21. Lim FJ, Lehmann D, McLoughlin A, et al. Risk factors and comorbidities for invasive pneumococcal disease in Western Australian Aboriginal and non-Aboriginal people. Pneumonia 2014; 11: 24-34.
22. Bello S, Menendez R, Torres A, et al. Tobacco smoking increases the risk for death from pneumococcal pneumonia. Chest 2014; 146: 1029-1037.
23. Piatti G, Gazzola T, Allegra L. Bacterial adherence in smokers and non-smokers. Pharmacol Res 1997; 36: 481-484.
24. Almirall J, Serra-Prat M, Bolibar I, et al. Passive smoking at home is a risk factor for community-acquired pneumonia in older adults: a population-based case-control study. BMJ Open 2014; 4: e005133.
25. Ruiz M, Ewig S, Torres A, et al. Severe community-acquired pneumonia. Risk factors and follow-up epidemiology. AM J Resp Crit Care Med 1999; 160: 923-929.
26. Grau I, Ardanuy C, Calatayud L, Schulze MH, Linares J, Pallares R. Smoking and alcohol abuse are the most preventable risk factors for invasive pneumonia and other pneumococcal infections. Int J Infect Dis 2014; 25: 59-64.
27. DiBardino DM, Wunderink RG. Aspiration pneumonia: a review of modern trends. J Crit Care 2015; 30: 40-48.
28. Cvejic L, Harding R, Churchward T, et al. Laryngeal penetration and aspiration in individuals with stable COPD. Respirology 2011; 16: 269-275.
29. Torres A, Peetermans WE, Viegi G, Blasi F. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. Thorax 2013; 68: 1057-1065.
30. Curcio D, Cane A, Isturiz R. Redefining risk categories for pneumococcal disease in adults: critical analysis of the evidence. Int J Infect Dis 2015; 37: 30-35.

31. Weir DL, Majumdar SR, McAlister FA, Marrie TJ, Eurich DT. The impact of multimorbidity on short-term events in patients with community-acquired pneumonia: prospective cohort study. Clin Microbiol Infect 2015; 21: 264. e7-264.e13.

32. Jefferson T, Di Pietrantonj C, Rivetti A, Bawazeer GA, Al-Ansary LA, Ferroni E. Vaccines for preventing influenza in healthy adults. Cochrane Database Syst Rev 2010; (7): CD001269.

33. Jefferson T, Di Pietrantonj C, Al-Ansary LA, Ferroni E, Thorning S, Thomas RE. Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev 2010; (2): CD004876.

34. Australian Technical Advisory Group on Immunisation. The Australian immunisation handbook. 10th ed. Canberra: Australian Government Department of Health; 2013.

35. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev 2013; (1): CD000422.

36. Saldias Penafiel F, O'Brien Solar A, Gederlini Gollerino A, Farias Gontupil G, Diaz Fuenzalida A. [Community-acquired pneumonia requiring hospitalization in immunocompetent elderly patients: clinical features, prognostic factors and treatment]. Archivos de bronconeumologia 2003; 39: 333-340.

37. Bonten MJ, Huijts SM, Bolkenbaas M, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 2015; 372: 1114-1125.

38. Almirall J, Bolibar I, Serra-Prat M, et al. New evidence of risk factors for community-acquired pneumonia: a population-based study. Eur Resp J 2008; 31: 1274-1284.

39. Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997; 278: 1440-1445.

40. Metlay JP, Schulz R, Li YH, et al. Influence of age on symptoms at presentation in patients with community-acquired pneumonia. Arch Intern Med 1997; 157: 1453-1459.

41. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007; 44 Suppl 2: S27-S72.

42. Majumdar SR, Eurich DT, Gamble JM, Senthilselvan A, Marrie TJ. Oxygen saturations less than 92% are associated with major adverse events in outpatients with pneumonia: a population-based cohort study. Clin Infect Dis 2011; 52: 325-331.

43. Respiratory tract infections [revised 2014 Oct]. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2015.

44. Anti-infectives [last modified July 2015]. In: Australian Medicines Handbook 2015 [Internet]. Adelaide: Australian Medicines Handbook Pty Ltd; 2015.

45. Mittl RL Jr, Schwab RJ, Duchin JS, Goin JE, Albeida SM, Miller WT. Radiographic resolution of community-acquired pneumonia. Am J Resp Crit Care Med 1994; 149: 630-635.