

# 1

# Healthcare-Associated Pneumonia: Epidemiology, Microbiology and Clinical Outcomes

MARCOS I RESTREPO AND ANTONIO ANZUETO

*Division of Pulmonary and Critical Care Medicine, South Texas Veterans Health Care System, Audie L Murphy Division; VERDICT, a HSR&D Center and the Department of Medicine, University of Texas Health Science Center, San Antonio, USA*

## Introduction

Pneumonia is one of the leading causes of hospitalisation and mortality in the United States [1]. Effective empiric treatment involves selecting an antibiotic with a spectrum of activity that includes the possible causative pathogen(s) [1]. Therefore, an evidence-based classification scheme that differentiates pneumonia based on the most likely causative organism(s) will help clinicians maximize the likelihood of providing the correct treatment and achieve favourable outcomes. Community-acquired pneumonia (CAP) is defined as signs, symptoms and radiographic evidence of pneumonia present in patients that come from the community which develop within 48 hours of hospital admission. In contrast, hospital-acquired pneumonia (HAP) is diagnosed as the presence of respiratory signs, symptoms and radiological evidence of pneumonia that begin after 48–72 hours of hospital admission. This classification is based in part due to differences in underlying etiologic pathogens, but despite the wide use of this dichotomous classification for pneumonia, data related to a variety of infectious processes indicate that these classifications may have significant limitations.

Healthcare reflects a continuum of care with many of the traditional ‘inpatient services’ now provided in outpatient settings. Some of these services include intravenous therapy at home, dialysis units and residence in long-term care facilities. In addition, invasive medical therapies are now routinely administered in nursing homes, rehabilitation centres or extended care facilities. Many surgeries or minor procedures are regularly performed in outpatient-based surgical centres, or ambulatory inpatient surgical areas. Thus, many patients who reside in the community have a constant exposure to inpatient settings, such as those that need chemotherapy, radiation therapy or haemodialysis [2]. Additionally, patients can move from hospital to a subacute care facility, and return to hospital, without ever truly residing in the ‘community’. Pneumonia that develops in these patients outside the hospital has been commonly categorized as CAP, even if those patients have been receiving healthcare in an outpatient facility or have a recent exposure to healthcare provided in facilities intimately related to inpatient care.

Thus, patients residing in long-term care facilities, individuals who have recently been hospitalised, and who have come in contact with the healthcare environment are an expanding part of the population. In these patients, infection is more common than in people residing in the community, and lower respiratory tract infection, including pneumonia, is the second most common infection [3]. In addition, nursing home-acquired pneumonia is the leading cause of mortality, hospitalisation and costs in older nursing home patients [4]. Muder reported that in the nursing home population the median rate of pneumonia is 365 per 1000 persons, compared to 34 per 1000 persons in those over 75 years of age who live in the community [5]. In addition, Vergis and colleagues [6] described a cohort of long-term care patients with pneumonia and compared them to patients without pneumonia closely matched for age, level of dependency and duration of institutionalisation. They found that an episode of pneumonia is associated with significant excess mortality that persists for up to two years. Other authors have demonstrated that pneumonia is the most common cause of infection when a resident of a long-term care facility has to be transferred to hospital for the treatment of infection [5]. These investigators showed that 10–18% of pneumonia related hospital admissions were nursing home residents [5].

All of these patients are commonly recognized in our traditional care model as subjects who develop infections in the ‘community’. This traditional care model indicates that community infections are usually caused by ‘community pathogens’ and that limited antibiotic therapy should be used for these infections. However, recent data indicate that these healthcare-associated infections have a unique epidemiology. The pathogens causing these infections may resemble those seen in hospital-acquired infections and are associated with higher morbidity, mortality and costs [7–15]. Accumulating evidence from other infectious diseases suggests that healthcare associated infections are distinct from those that are truly community acquired [7–15]. This is why these infections are now considered ‘healthcare-associated’ infections. The epidemiology, etiology and clinical outcomes of a new entity called Healthcare-Associated Pneumonia (HCAP) are reviewed in this chapter. Clarifying the epidemiology of these healthcare-associated infections, and HCAP specifically,

is crucial in efforts to design appropriate empiric antimicrobial treatment guidelines and improve patient outcomes.

## Healthcare-Associated Infections

Over the last several years, a number of investigators have documented that the pathogens responsible for healthcare-associated (HCA) infections are different from pathogens identified in patients from the community [7–15]. In fact, because of their contact with the healthcare environment, these patients may already be colonized with drug-resistant pathogens, bringing these organisms to the hospital at the time of admission. Tambyah and collaborators [9] showed, in one study of 383 patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infection, that 123 organisms (32%) were isolated from patients who had been in the hospital less than 48 hours, while only one was a true community-acquired isolate. From the patients that were in the hospital for less than two days, the remainder of isolates were found in patients that came from long-term care facilities (21, 17%); hospitalised or treated in an outpatient facility (94, 76%); or received dialysis, visiting nurse care and had undergone day surgery (7, 6%) [9]. Naimi and colleagues [8] showed, in a study of 1100 MRSA infections, that 85% were healthcare related. The definition of healthcare-associated infection included history of hospitalisation, surgery, dialysis or residence in a long-term care facility within a year of contracting the infection; or presence of a permanent indwelling catheter or medical device (e.g. gastrostomy, tracheostomy; and/or Foley catheter) [8]. In this cohort of healthcare-associated infection, Gram-negative multidrug-resistant (MDR) pathogens were frequently isolated [8].

Pop-Vicas *et al.* [7] demonstrated that MDR Gram-negative organisms collected within the first 48 hours of hospital admission were frequently identified as *Escherichia coli*, *Klebsiella* species and *Enterobacter cloacae*, but not *Pseudomonas aeruginosa*. Fifty-three per cent of these isolates were resistant to three antimicrobial groups and 12% were resistant to five antibiotic classes [7]. The risk factors for MDR pathogens included: elderly (>65 years of age), prior exposure to antibiotics and previous residence in a long-term care facility [7]. Thus, these data demonstrate that MDR pathogens such as, for example *P. aeruginosa* and *S. aureus*, are frequently found in healthcare-associated infections.

## Healthcare-Associated Pneumonia

### Definition

Healthcare-associated pneumonia (HCAP) was recently defined as a different infectious condition by the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) HAP consensus statement [16]. HCAP is now recognized as

an important cause of morbidity and mortality despite advances in antimicrobial therapy and better supportive care modalities [17–19]. HCAP includes pneumonias in any patient who is hospitalised in an acute care facility if the subject has any of the following characteristics: resided in a nursing home or long-term care facility; received intravenous antibiotic therapy, chemotherapy or wound care within the past 30 days; or attended a hospital or haemodialysis clinic [17–19]. In addition, these guidelines suggest that MDR pathogens should be considered in other nosocomial infections (current hospitalisation for more than five days and high frequency of antibiotic resistance in the community or in the specific hospital unit); or conditions not directly related to the hospitalisation, such as immunosuppressive disease and/or therapy (Table 1.1).

**Table 1.1** Definitions of ‘healthcare-associated’ infections in recent literature

ATS/IDSA [16] HCA-pneumonia	Kollef <i>et al.</i> [20] HCA-pneumonia	Friedman <i>et al.</i> [2] HCA-bloodstream infections
Patients with pneumonia on admission or within 2 days of admission and any of the following: (1) resided in a nursing home or long-term care facility; (2) home infusion therapy (received intravenous antibiotic therapy, chemotherapy); (3) wound care within the past 30 days; (4) hospitalisation for >2 days in the preceding 3 months; (5) chronic dialysis within 30 days; (6) family member with multi-drug resistant pathogen.	Patients with a first positive bacterial respiratory culture finding within 2 days of admission and any of the following: (1) admission source indicates a transfer from another health-care facility; (2) receiving long-term haemodialysis (ICD-9-CM codes); and (3) prior hospitalisation within 30 days who do not meet VAP definition.	Patients with positive blood culture obtained at the time of hospital admission or within 2 days of admission and any of the following: (1) received intravenous therapy at home; received wound care or specialized nursing care through a healthcare agency, family or friends; or had self-administered intravenous medical therapy in the 30 days before the bloodstream infection. Patients whose only home therapy was oxygen use were excluded; (2) attended a hospital or a haemodialysis clinic or received intravenous chemotherapy in the 30 days before the bloodstream infection; (3) hospitalised in an acute care hospital for >2 days in the 90 days before the bloodstream infection; (4) resided in a nursing home or long-term care facility.

ATS – American Thoracic Society; IDSA – Infectious Diseases Society of America;  
HCA – healthcare-associated; VAP – ventilator-associated pneumonia

## Clinical Characteristics

Limited information is available on the clinical characteristics of patients with HCAP. Kollef and colleagues [20] provided a comparison of patients with CAP, HCAP, HAP and ventilator-associated pneumonia (VAP). The reported data were from a retrospective cohort of 4543 patients with culture-positive pneumonia based on US inpatient databases. Of the 4543 patients, 2221 had CAP (48.9%), 988 had HCAP (21.7%), 835 had HAP (18.4%) and 499 had VAP (11%) [20]. Their definition of HCAP required patients to have positive bacterial respiratory tract cultures within two days of hospital admission and to have come from a healthcare facility, be receiving haemodialysis or have been hospitalised within the past 30 days. HCAP patients were significantly older than CAP patients (77 versus 65 years), but were similar in age to those with HAP. Half of the HCAP patients came from nursing homes, which was a far higher percentage than the percentage among patients with HAP and VAP residing in long-term care facilities. Illness severity was similar in both HCAP and VAP patients, but was higher than that seen in those patients with CAP and HAP [20].

## Microbiology

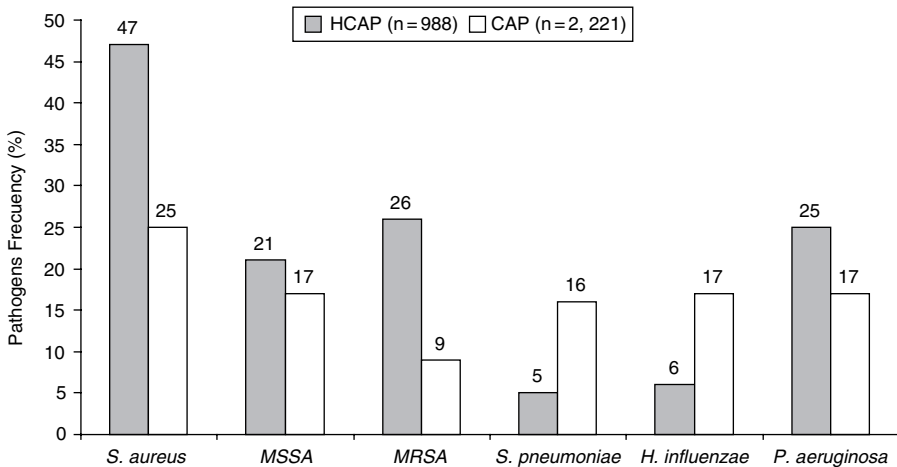
Most of the current microbiological data available are from patients with nosocomial infections in non-ventilated (HAP) or ventilated patients (VAP). The data on the pathogens that are isolated in patients with HCAP infections are more limited. However, given the frequent transfer of patients and healthcare workers between long-term and outpatient facilities and hospitals, the pathogens in these facilities are more likely to closely resemble those seen in nosocomial infections. Another limitation is that in most nursing home patients with HCAP there is no identifiable etiology [21]. This occurs in part because many patients are unable to produce sputum specimens suitable for analysis, and the difficulty of distinguishing colonization and infection in patients with adequate samples [5, 6, 18, 21].

Muder *et al.* [5] reviewed published studies and found that the most commonly identified healthcare pathogens included *S. pneumoniae* (0–39%), *S. aureus* (0–33%) and Gram-negative bacteria (0–51%). A potential relationship has been suggested between unrecognised aspiration of oral or gastric contents, the presence of dysphagia, increased oropharyngeal colonization and the subsequent development of pneumonia in older adults. In addition, isolation of *S. aureus* and Gram-negative bacilli (*E. coli* and *K. pneumoniae*) in the oropharynx could potentially lead to aspiration pneumonia [22]. Leibovitz and colleagues [23] showed that *P. aeruginosa* has been isolated from 34% of nasogastric tube fed older patients but from none of the orally fed control group. Other Gram-negative bacilli were isolated from 64% of tube fed patients and only 8% from the control group, suggesting that the oropharynx of tube fed patients could be a potential reservoir for *P. aeruginosa* and other Gram-negative bacilli [23]. In the study by Kollef *et al.* [20] *S. aureus* was a major pathogen in all pneumonia types, with its occurrence markedly higher in the non-CAP groups than in the CAP group. Kollef *et al.* [20], showed that the etiology of HCAP was different from HAP and VAP. However, HCAP differs from HAP or VAP to a lesser degree

than from CAP (e.g. more comparable *S. aureus* occurrences and mortality rates). These investigators also reported that *S. aureus* was a predominant pathogen in all types of pneumonia, including CAP.

There is a consensus in the literature that the most common pathogen for CAP is *S. pneumoniae* [24]. However, the results found by Kollef and collaborators [20] – that fewer patients admitted for CAP had *S. pneumoniae* infection than had *S. aureus* infection – probably reflected that the CAP patients were hospitalised [25, 26]. The high prevalence of *S. aureus* might be due to the relationship between this bacteria and severity of illness, in which the more severe CAP patients are the ones that tend to be hospitalised [1]. The occurrence of *S. aureus* in patients with HCAP was markedly higher than in patients with CAP. Compared with the HAP group, a greater proportion of patients in the HCAP group had *Pseudomonas* spp. and *S. pneumoniae* and a lower proportion had non-group *Streptococcus*. Compared with the VAP group, patients with HCAP were more likely to be infected by *S. pneumoniae* and less likely to have *Haemophilus* sp infection. Thus, HCAP is microbiologically different from CAP, HAP and VAP (Figure 1.1).

While most of the microbiology of healthcare-associated infections has not been focused strictly on pneumonia, data are available from pneumonia patients that were residents of long-term care facilities. El Solh *et al.* described, in a study of 95 elderly pneumonia patients, that those admitted from a nursing home had a higher frequency of enteric Gram-negative organisms and *S. aureus*, and a lower frequency of pneumococcus compared to those admitted from the community [27]. The same group of investigators showed, in a different study [28] of patients with severe pneumonia who had been admitted from a nursing home, that the frequency of MDR pathogens was increased in those who had recently received antibiotics and in those who also had a worse functional status (defined by the performance of activities of daily living).



**Figure 1.1**

Most common pathogens identified in HCAP patients compared to CAP patients.

CAP – community-acquired pneumonia; HCAP – healthcare associated pneumonia;  $p < 0.01$  for all comparisons with HCAP

Source: Adapted from Kollef *et al.* [20].

Recent data show that MRSA strains isolated from patients with healthcare-associated infections are distinct from those that are truly community acquired [8]. These bacteria isolates have different susceptibility to antibiotics [8]. In addition to the complexity introduced by evolving healthcare practices, the causative pathogens associated with CAP have also changed in prevalence in recent years. Although *S. pneumoniae* remains the most common causative pathogen, other pathogens (e.g. *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae* and *Legionella* spp.) exist, and their prevalence changes over time and varies by geographic location [1]. Furthermore, the emerging antimicrobial resistance of respiratory pathogens has complicated the management of these infections. These changes necessitate an evolving treatment strategy based on the most recent microbiologic and epidemiologic data [29].

## Outcomes

At the present time, a large proportion of hospitalised CAP patients may in fact have HCAP. Thus, our understanding of the outcome of this condition is not clearly defined. The recent data on HCAP strongly suggest that this is a new category of pneumonia with high mortality, length of stay and costs compared to CAP patients and even similar to HAP and VAP (Table 1.2). Kollef *et al.* [20] reported that mortality rates associated with HCAP (19.8%) and HAP (18.8%) were comparable ( $p > 0.05$ ); and both were significantly higher than that for CAP (10%, all  $p < 0.0001$ ) and lower than that for VAP (29.3%, all  $p < 0.0001$ ). Mean length of stay varied significantly with pneumonia category (in order of ascending values: CAP, HCAP, HAP and VAP; all  $p < 0.0001$ ). In addition, the length of hospital stay increased progressively for CAP, HCAP, HAP and VAP patients, and, in parallel with this, hospital costs increased for each of the four groups in the same order ( $p < 0.0001$ ). If HCAP patients were included in the CAP category according to the traditional classification schemes, these would have accounted for 31% of hospitalised CAP patients.

Multivariate analysis of the factors associated with pneumonia mortality indicated that *S. aureus* was the only pathogen that correlated with increased mortality. *S. aureus* not only increased mortality, but was also associated with increased length of hospital stay, and treatment costs observed in patients with HCAP, HAP and VAP. The clinical outcomes in patients with HCAP and HAP were comparable in terms of overall mortality. However, the mean length of hospital stay and treatment costs for HCAP patients was significantly lower in these groups of patients than in those with

**Table 1.2** Clinical outcomes and costs in patients with HCAP compared to CAP

Outcomes	HCAP (n = 988)	CAP (n = 2221)	p value
Mortality	19.8 %	10.0 %	<0.0001
Length of stay, mean (SD) days	8.8 (7.8)	7.5 (7.2)	<0.0001
Cost, mean (SD), total charges, \$	27 647 (37 974)	25 218 (40 577)	<0.0001

\* CAP – community acquired pneumonia; HCAP – healthcare-associated pneumonia;  
 $p < 0.01$  for all comparisons with HCAP

Source: Adapted from Kollef *et al.* [20]

HAP. This might reflect a difference in treatment for HCAP among clinicians who do not distinguish HCAP from CAP. Moreover, since treatment guidelines often do not recommend coverage for *S. aureus* in CAP, the association between the presence of *S. aureus* and mortality may reflect that subjects with such infections were more likely to have received antibiotics not effective against MSSA or MRSA. In other words, recovery of *S. aureus* may be a surrogate marker for the prescription of inappropriate antimicrobial therapy, a known predictor of poor outcomes in pneumonia [13]. Although the data reported by Koleff *et al.* [20] did not allow the investigators to separate colonization from infection, or to tell whether the isolated pathogen was actually causing the respiratory infection, the epidemiologic, bacteriologic and outcomes data were interesting, and help to better define the entity of HCAP.

It is important to take into consideration that the inclusion of HCAP in the nosocomial pneumonia guidelines and algorithms may suggest that empiric therapy for HCAP patients will not routinely include coverage against atypical pathogens, as is the case in CAP patients. This recommendation requires close monitoring, since outbreaks of atypical pathogen pneumonia can occur among nursing home residents, mainly *Legionella* spp. Conflicting data from two recent meta-analyses in patients with mild and moderate CAP showed that atypical coverage did not have an impact on patient's outcomes [30,31]. However, from the subgroup analysis, patients with *Legionella* infections tended to do worse if atypical coverage was not added [30,31]. In addition, there may be some patients with HCAP (such as those with a risk factor of recent antibiotic therapy for a short time or dialysis) who may not be at high risk of infection with MDR pathogens. In these patients the use of broad-spectrum antibiotics may be not necessary. Thus, in HCAP patients broad-spectrum antibiotics should initially be started, but later adjust based on the culture results.

## Summary

Healthcare-associated pneumonia is now identified as a unique entity that differs from CAP, and in many ways is similar to nosocomial pneumonia (either HAP or VAP). HCAP differs from CAP in both bacteriology and outcomes, and thus therapy for these two categories of pneumonia should be approached differently. This conclusion is based on the recently published American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) guidelines for the treatment of nosocomial pneumonia, which included patients with HCAP [16]. These guidelines suggested that HCAP patients should be treated differently from CAP patients, but similarly to HAP and VAP patients [16]. The guideline definition for HCAP included the following: hospitalisation for two days in the preceding 90 days; residence in a nursing home or extended care facility; recipients of home infusion therapy; long-term dialysis within 30 days; home wound care; and exposure to family members infected with MDR pathogens. The pathogens isolated in HCAP share more similarity with HAP and VAP than with CAP [16]. In the guidelines it was recommended that patients with HCAP be treated for potential MDR pathogens, including resistant Gram-negative organisms and MRSA. *S. aureus* was a major pathogen of all pneumonias with higher

rates in non-CAP pneumonias [16]. Compared to CAP, non-CAP was associated with more severe disease, higher mortality rate, greater length of stay and increased cost. The HCAP diagnosis implies that there is a need for confirmatory studies, and that future clinical practice guidelines and local critical pathways aimed at optimising and streamlining initial empiric antibiotic treatment for pneumonia would benefit from the separation of HCAP from CAP.

## Disclaimer

The views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs.

## References

1. Niederman, M.S., Mandell, L.A., Anzueto, A. *et al.* (2001) Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. *Am J Respir Crit Care Med*, **163**, 1730–1754.
2. Friedman, N.D., Kaye, K.S., Stout, J.E. *et al.* (2002) Healthcare-associated bloodstream infections in adults: a reason to change the accepted definition of Community-Acquired Infections. *Ann Intern Med*, **137**, 791–797.
3. Stevenson, K.B. (1999) Regional data set of infection rates for long-term care facilities: description of a valuable benchmarking tool. *Am J Infect Control*, **27**, 20–26.
4. Muder, R.R., Aghababian, R.V., Loeb, M.B., Solot, J.A. and Higbee, M. (2004) Nursing home-acquired pneumonia: an emergency department treatment algorithm. *Curr Med Res Opin*, **20**, 1309–1320.
5. Muder, R.R. (1998) Pneumonia in residents of long-term care facilities: epidemiology, etiology, management, and prevention. *Am J Med*, **105**, 319–330.
6. Vergis, E.N., Brennen, C., Wagener, M. and Muder, R.R. (2001) Pneumonia in long-term care: a prospective case-control study of risk factors and impact on survival. *Arch Intern Med*, **161**, 2378–2381.
7. Pop-Vicas, A.E. and D’Agata, E.M. (2005) The rising influx of multidrug resistant Gram-negative bacilli into a tertiary care hospital. *Clin Infect Dis*, **40**, 1792–1798.
8. Naimi, T.S., LeDell, K.H., Como-Sabetti, K. *et al.* (2003) Comparison of community- and healthcare-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA*, **290**, 2976–2984.
9. Tambyah, P.A., Habib, A.G., Ng, T.M., Goh, H. and Kumarasinghe, G. (2003) Community-acquired methicillin-resistant *Staphylococcus aureus* infection in Singapore is usually “healthcare associated”. *Infect Control Hosp Epidemiol*, **24**, 436–438.
10. Shorr, A.F., Tabak, Y.P., Killian, A.D. *et al.* (2006) Healthcare-associated bloodstream infection: a distinct entity? Insights from a large U.S. database. *Crit Care Med*, **34**, 2588–2595.
11. Engelhart, S.T., Hanses-Derendorf, L., Exner, M. and Kramer, M.H. (2005) Prospective surveillance for healthcare-associated infections in German nursing home residents. *J Hosp Infect*, **60**, 46–50.
12. Lesens, O., Hansmann, Y., Brannigan, E. *et al.* (2005) Healthcare-associated *Staphylococcus aureus* bacteremia and the risk for methicillin resistance: is the Centers for Disease

- Control and Prevention definition for community-acquired bacteremia still appropriate? *Infect Control Hosp Epidemiol*, **26**, 204–209.
13. McDonald, J.R., Friedman, N.D., Stout, J.E., Sexton, D.J. and Kaye, K.S. (2005) Risk factors for ineffective therapy in patients with bloodstream infection. *Arch Intern Med*, **165**, 308–313.
  14. Siegman-Igra, Y., Fourer, B., Orni-Wasserlauf, R. *et al.* (2002) Reappraisal of community-acquired bacteremia: a proposal of a new classification for the spectrum of acquisition of bacteremia. *Clin Infect Dis*, **34**, 1431–1439.
  15. Morin, C.A. and Hadler, J.L. (2001) Population-based incidence and characteristics of community onset *Staphylococcus aureus* infections with bacteremia in 4 metropolitan Connecticut areas, 1998. *J Infect Dis*, **184**, 1029–1034.
  16. American Thoracic Society/Infectious Diseases Society of America (2005) Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia. *Am J Respir Crit Care Med*, **171**, 388–416.
  17. Mylotte, J.M. (2002) Nursing home-acquired pneumonia. *Clin Infect Dis*, **35**, 1205–1211.
  18. Hutt, E. and Kramer, A.M. (2002) Evidence-based guidelines for management of nursing home-acquired pneumonia. *J Fam Pract*, **51**, 709–716.
  19. Tablan, O.C., Anderson, L.J., Besser, R. *et al.* (2004) Healthcare infection control practices advisory C: Guidelines for preventing healthcare-associated pneumonia, 2003: recommendations of CDC and the healthcare infection control practices advisory committee. *MMWR Recomm Rep*, **53**, 1–36.
  20. Kollef, M.H., Shorr, A., Tabak, Y.P. *et al.* (2005) Epidemiology and outcomes of healthcare-associated pneumonia: results from a large US database of culture-positive pneumonia. *Chest*, **128**, 3854–3862.
  21. Medina-Walpole, A.M. and Katz, P.R. (1999) Nursing home-acquired pneumonia. *J Am Geriatr Soc*, **47**, 1005–1015.
  22. Marik, P.E. and Kaplan, D. (2003) Aspiration pneumonia and dysphagia in the elderly. *Chest*, **124**, 328–336.
  23. Leibovitz, A., Dan, M., Zinger, J. *et al.* (2003) *Pseudomonas aeruginosa* and the oropharyngeal ecosystem of tube-fed patients. *Emerg Infect Dis*, **9**, 956–959.
  24. Mandell, L.A., Bartlett, J.G., Dowell, S.F. *et al.* (2003) Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. *Clin Infect Dis*, **37**, 1405–1433.
  25. Guest, J.F. and Morris, A. (1997) Community-acquired pneumonia: the annual cost to the national health service in the UK. *Eur Respir J*, **10**, 1530–1534.
  26. Marrie, T.J. (1994) Community-acquired pneumonia. *Clin Infect Dis*, **18**, 501–13; quiz 514–505.
  27. El-Solh, A.A., Sikka, P., Ramadan, F. and Davies, J. (2001) Etiology of severe pneumonia in the very elderly. *Am J Respir Crit Care Med*, **163**, 645–651.
  28. El Solh, A.A., Pietrantonio, C., Bhat, A., Bhora, M. and Berbari, E. (2004) Indicators of potentially drug-resistant bacteria in severe nursing home-acquired pneumonia. *Clin Infect Dis*, **39**, 474–480.
  29. Niederman, M.S. (2004) Review of treatment guidelines for community-acquired pneumonia. *Am J Med*, **117** (3A), 51S–57S.
  30. Shefet, D., Robenshtok, E., Paul, M. and Leibovici, L. (2005) Empirical atypical coverage for inpatients with community-acquired pneumonia: systematic review of randomized controlled trials. *Arch Internal Med*, **165**, 1992–2000.
  31. Mills, G.D., Oehley, M.R. and Arrol, B. (2005) Effectiveness of beta-lactam antibiotics compared with antibiotics active against atypical pathogens in non-severe community acquired pneumonia: meta-analysis. *BMJ*, **330**, 456.