Key points

❯ Hospital-acquired pneumonia has a major impact in terms of mortality and morbidity.

❯ Empirical treatment approach is still the best course of action.

❯ Prevention is of critical importance.

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Hospital-acquired pneumonia

Educational aims

❭ To improve knowledge of HAP management.
❭ To better understand the epidemiological basis for the correct empirical therapy of HAP.

Summary

HAP still has a major impact in terms of mortality and morbidity among hospitalised patients. Early appropriate antibiotic therapy is associated with a reduction in mortality and improved outcome. Although, in most cases, an empirical approach is still the rule, taking into account the risk factors, the severity of illness and length of stay before the pneumonia onset can better target antibiotic therapy. The patient's follow-up course, in terms of microbiological, clinical and radiological monitoring, is important. Prevention strategies are of critical importance and are based on the understanding of the epidemiology and pathogenesis of HAP. Routine efforts for the prevention of HAP should be directed towards obtaining effective surveillance and infection-control programmes, including staff education, use of proper isolation techniques and infection-control practices. This review aims to increase understanding of these points to allow improved knowledge and treatment of HAP.

Glossary

Hospital-acquired pneumonia (HAP) is defined as a pulmonary infection developing during hospitalisation, 48 hours or more after admission, and not present or incubating at the time of admission.
Ventilator-associated pneumonia (VAP) is defined as a pneumonia that arises more than 48–72 hours after endotracheal intubation.
Healthcare-associated pneumonia (HCAP) is defined as a pneumonia in any patient who has been hospitalised in an acute care hospital for 2 or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent *i.v.* antibiotic therapy, chemotherapy or wound care within the past 30 days of the current infection; or attended a hospital or haemodialysis clinic. Patients with HCAP require therapy for multidrug-resistant (MDR) pathogens [1].

Table 1   Main recommendations for the management of modifiable risk factors for HAP and VAP

Host related
Adequate nutrition, enteral feeding via orogastric tubes
Reduction/discontinuation of immunosuppressive treatments
Prevent unplanned extubation (restraints, sedation)
Kinetic beds
Incentive spirometry, deep breathing and pain control

Device/treatment related
Minimise use of sedatives and paralytics
Avoid gastric overdistention
Avoid intubation and reintubation
Expeditious removal of endotracheal and nasogastric tubes
Semirecumbent positioning
Drain condensate from ventilator circuits
Endotracheal tube cuff pressure (>20 cmH$_2$O prevents leakage of bacterial pathogens around the cuff into lower respiratory tract)
Continuous aspiration of subglottic secretions
Use of heat moisture exchangers (reduces ventilator circuit colonisation but not VAP incidence)

Environment related
Attention to infection-control procedures, i.e. staff education, hand washing, patient isolation
Microbiological surveillance programme

Epidemiology

The incidence of HAP is ~0.5–2.0% among all hospitalised patients and is the second most common nosocomial infection, yet the first in terms of mortality (ranging 30–>70%). These figures further increase in patients with VAP, which alone represents >80% of overall HAPs in the USA [2, 3].

The incidence in different hospitals and different wards of the same hospital varies considerably. The main risk factors are age, type of hospital and type of ward [4]. Patients aged <35 years are less prone to develop HAP than elderly patients; the incidence of HAP may vary between 5 and 15 episodes per 1,000 discharges. In large teaching hospitals, the incidence is higher than in district hospitals, possibly relating to differences in patient complexity. HAP is quite uncommon in paediatric and obstetric wards, and clearly most common in surgical wards and intensive care units (ICUs), particularly in ventilated patients in whom the incidence may be >35 episodes per 1,000 patient days [5–7].

Another important epidemiological variable and risk factor for aetiology and outcome is the time of onset. Late-onset HAP (≥5 days after admission) is more likely to be associated with difficult-to-treat pathogens, such as MDR microorganisms, which are formed in early-onset HAP (occurring within the first 4 days of hospitalisation). The new American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines state that patients with early-onset HAP who have received prior antibiotics and have had prior hospitalisation within the past 90 days or who are elderly residents of long-term care facilities (*i.e.* those with healthcare-associated pneumonia (HCAP)) are at a greater risk of colonisation and infection with MDR pathogens and should be treated similar to patients with late-onset HAP [1].

Pathogenesis and risk factors

The understanding of the pathogenesis of HAP is a fundamental step for the comprehension of risk factors involved in nosocomial pneumonia [8]. Colonisation of the oropharynx by enteric Gram-negative bacteria rises with the increasing severity of underlying conditions, and occurs in a large majority of critically ill patients within a few days of admission. Oropharyngeal and gastric colonisation, and the subsequent aspiration of their contents into the lungs in patients with impaired mechanical, cellular and humoral defences leads to the possible development of HAP. Other possible mechanisms of lung infection in these patients include the passage of enteric bacteria or their products from the gut to the lung, haematogenous spread from a distant site of infection and direct inoculation into the airways of intubated patients from ICU personnel. Inadequate hand washing may, in fact, facilitate the spread of bacteria [9].

Critical risk factors comprise the following: prolonged (>48 hours) mechanical ventilation, with pneumonia developing in 9–40% of patients [10, 11]; duration of hospital or ICU stay; severity of underlying illness; Acute Physiology and Chronic Health Evaluation (APACHE) score; presence of acute respiratory distress syndrome (ARDS); and comorbidities. Risk factors for the early development of HAP in ventilated patients have been evaluated in a prospective study [12]. The results of a multivariate analysis indicated cardiopulmonary resuscitation (odds ratio (OR) 5.1) and continuous sedation (OR 4.4) as the main risk factors for early development of pneumonia, whereas prior antibiotic use was protective (OR 0.29). Another prospective study indicated low serum albumin at admission, high maximum positive end-respiratory pressure, upper respiratory tract colonisation by Gram-negative bacilli, smoking and duration of mechanical ventilation as independent risk factors for pneumonia [13]. In addition, it was shown that antibiotic use prior to admission to the ICU was associated with a lower incidence of pneumonia [13].

The ATS/IDSA guidelines state that routine prophylaxis of HAP with oral or parenteral antibiotics reduces the incidence of ICU-acquired VAP,

Table 2 Main aetiology of HAP according to time of onset of the pneumonia

No known risk factors for MDR pathogens (early onset)
Streptococcus pneumoniae#
Haemophilus influenzae
Methicillin-sensitive Staphylococcus aureus
Antibiotic-sensitive enteric Gram-negative bacilli
    Escherichia coli
    Klebsiella pneumoniae
    Enterobacter spp.
    Proteus spp.
    Serratia marcescens

Risk factors for MDR pathogens (late onset)
Pathogens listed above plus
    MDR pathogens
    Pseudomonas aeruginosa
    Klebsiella pneumoniae (ESBL)
    Acinetobacter spp.
    Methicillin-resistant Staphylococcus aureus
    Legionella pneumophila

ESBL: extended spectrum β-lactamases. #: taking into account the resistance prevalence in each country.

Table 3 Main risk factors for specific pathogens of HAP

Pathogen	Risk factors
Staphylococcus aureus	*Coma, head trauma, recent influenza, history of i.v. drug use, diabetes mellitus, renal failure*
Methicillin-resistant Staphylococcus aureus	*Antibiotics before onset of pneumonia, prolonged mechanical ventilation*
Pseudomonas aeruginosa	*Prolonged ICU stay, steroids, antibiotics, structural lung diseases (bronchiectasis, cystic fibrosis), malnutrition*
Anaerobes	*Witnessed aspiration, recent abdominal surgery*
Acinetobacter spp.	*Antibiotics before onset of pneumonia plus mechanical ventilation*

but it is not recommended for routine use, particularly in patients with a high risk for MDR pathogens [1]. Prophylaxis of gastric bleeding with H_2-antagonist or sucralfate is acceptable and strict control of hyperglycaemia is indicated. Table 1 summarises the main recommendations for modifiable risk factors management.

Aetiology

The spectrum of pathogens involved in HAP, VAP and HCAP is certainly different from that of community-acquired pneumonia and is influenced by the presence of at least three main factors [14]: 1) severity of illness; 2) presence of risk for specific pathogens; and 3) time to onset of pneumonia.

The pathogens that are most frequently involved in HAP are aerobic Gram-negative bacilli (*Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Acinetobacter* spp., *etc.*) and *Staphylococcus aureus*. These bacteria can be considered the "core" pathogens in HAP, along with *Streptococcus pneumoniae*. The role of a polymicrobial aetiology of HAP has been proposed in ~50% of cases [15, 16]; however, CUNHA [17] has questioned the aetiological role of multiple-pathogen recovery in respiratory secretion specimens. Table 2 shows the main aetiology according to pneumonia time of onset, and the main risk factors for specific pathogens are outlined in table 3.

Diagnosis

The clinical diagnosis of HAP is often difficult to establish. The new ATS/IDSA guidelines suggest the use of clinical and bacteriological strategy [1]. Table 4 summarises the major points and recommendations of the guidelines.

As stated in the guidelines, any delays in the initiation of appropriate antibiotic therapy may be related to an increased mortality and, thus,

therapy should not be postponed for the purpose of performing diagnostic tests.

Treatment

Antibiotic selection for empirical therapy of HAP should be primarily based on the risk for MDR pathogen infection. Figure 1 summarises the indication of the ATS/IDSA guidelines [1].

Patients with HCAP should be treated for potentially MDR pathogens, and antibiotic class change is indicated in the presence of recent antibiotic treatment. Combination therapy should be used if patients are likely to be infected by MDR pathogens, and monotherapy can also be used in severe pneumonias in the absence of such a risk.
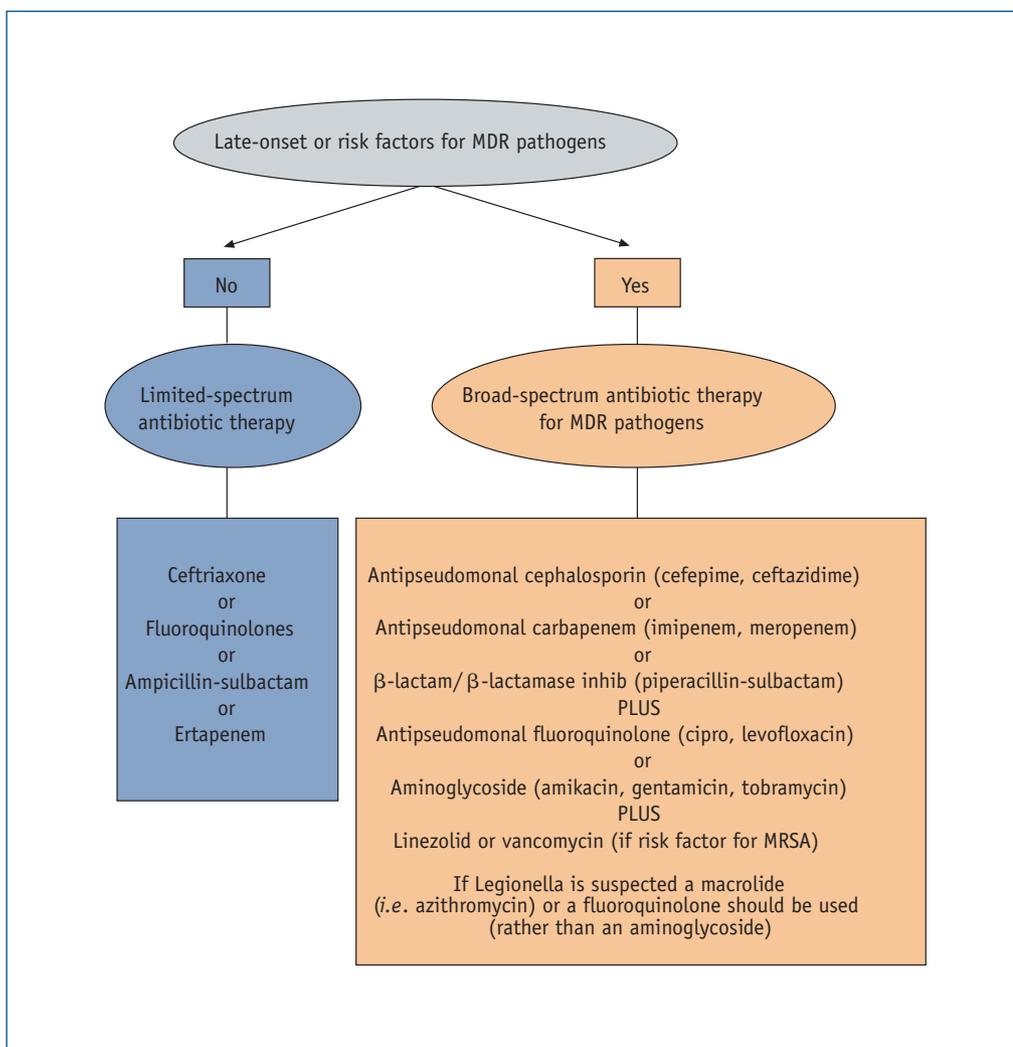
A short course of therapy (*e.g.* 7 days) can be appropriate, provided that the patient has a good clinical response and *P. aeruginosa* is not involved as aetiological agent [1].

Table 4   Major points and recommendations for the diagnosis of HAP#

Medical history and physical examination
Chest radiograph (posteroanterior and lateral)
Blood gas analysis
Blood cultures
Thoracentesis if pleural effusion
Endotracheal aspirate, bronchoalveolar lavage or protected brush sample for culture before antibiotic (negative results do not rule out viral or Legionella infections)
Extrapulmonary site of infection should be investigated

#: the most accurate clinical criteria for starting empirical antibiotic therapy: presence of a new or progressive radiographic infiltrate plus at least two of three clinical features (fever >38°C, leukocytosis or leukopaenia and purulent secretions).

Figure 1
Algorithm for empirical antibiotic approach for HAP, VAP and HCAP.

Educational questions

1. Late-onset HAP means:
   a) Pneumonia related to mechanical ventilation.
   b) Pneumonia diagnosed after at least 10 days of mechanical ventilation.
   c) Pneumonia that arises 5 days or more after admission.

2. Healthcare-associated pneumonia should be considered as a risk for:
   a) Infection with MDR pathogens.
   b) *Streptococcus pneumoniae* infection.
   c) *Haemophilus influenzae* infection.

3. A short course of therapy (*e.g.* 7 days) can be appropriate:
   a) Provided that the patient has a good clinical response and *Pseudomonas aeruginosa* is not involved as an aetiological agent.
   b) Provided that the patient has an aetiological diagnosis of *Streptococcus pneumoniae* infection.
   c) In early-onset pneumonia.

4. Antibiotic monotherapy can be used:
   a) In early-onset pneumonia and also in severe pneumonias in the absence of risk for MDR pathogens.
   b) Only in early-onset pneumonia.
   c) Only in mild VAP.

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Suggested answers

1. c
2. a
3. a
4. a