

# 7

# Infections of the respiratory tract

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## Overview

This chapter deals with infections of structures that constitute the upper and lower respiratory tract. The general population commonly experiences upper respiratory tract infections, which are often seen in general practice. Lower respiratory tract infections are less common but are more likely to cause serious illness and death. Diagnosis and specific chemotherapy of respiratory tract infections present a particular challenge to both the clinician and the laboratory staff. Successful preventive strategies are available for several respiratory infections.

## 7.1 Pathogenesis

### Learning objectives

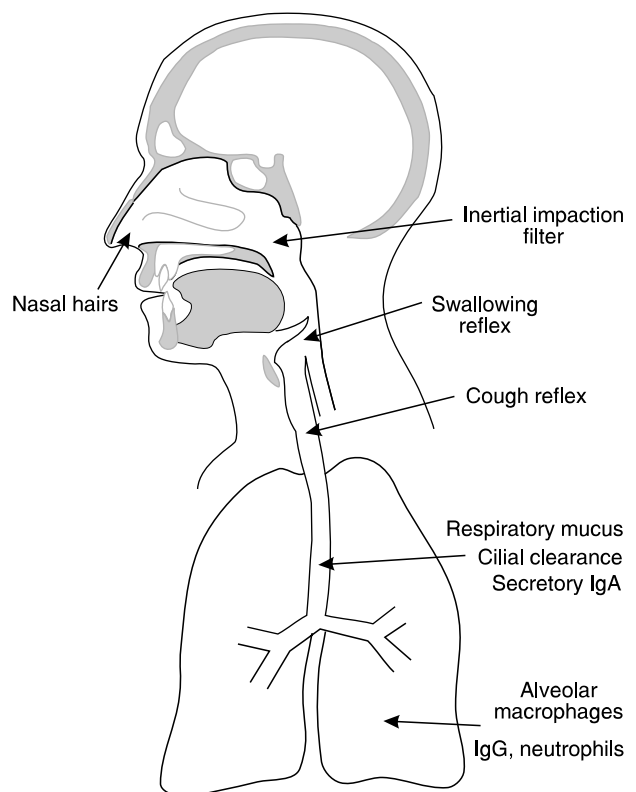
You should:

- understand the mechanisms by which respiratory infections occur
- know how pathogens overcome host defences
- understand what factors increase vulnerability to respiratory infections.

The principal function of the respiratory tract is gas exchange. It is therefore constantly exposed to the gaseous environment, including particulate organic material, such as bacteria, viruses and spores (Ch. 3). Although the entire respiratory tract is constantly exposed to air, the majority of particles are filtered out in

the nasal hairs and by inertial impaction with mucus-covered surfaces in the posterior nasopharynx (Fig. 11). The epiglottis, its closure reflex and the cough reflex all reduce the risk of microorganisms reaching the lower respiratory tract. Particles small enough to reach the trachea and bronchi stick to the respiratory mucus lining their walls and are propelled towards the oropharynx by the action of cilia (the 'mucociliary escalator'). Antimicrobial factors present in respiratory secretions further disable inhaled microorganisms. They include lysozyme, lactoferrin and secretory IgA.

Particles in the size range 5–10 µm may penetrate further into the lungs and even reach the alveolar air spaces. Here, alveolar macrophages are available to phagocytose potential pathogens, and if these are overwhelmed neutrophils can be recruited via the inflammatory response. The defences of the respiratory tract are a reflection of its vulnerability to microbial attack. Acquisition of microbial pathogens is



**Fig. 11** Defences of the respiratory tract.

primarily by inhalation, but aspiration and mucosal and haematogenous spread also occur. Individuals with healthy lungs rarely have any bacteria beyond the carina.

Respiratory pathogens have developed a range of strategies to overcome host defences. Influenza virus, for example, has specific surface antigens that adhere to mucosal epithelial cells. The virus also undergoes periodic genetic reassortment resulting in expression of novel adhesins to which the general population has no effective immunity. *Streptococcus pneumoniae* and *Haemophilus influenzae* both produce an enzyme (IgA protease) capable of disabling mucosal IgA. Both these species, other capsulated bacteria and mycobacteria are all resistant to phagocytosis. Penetration of local tissues is usually required before damage occurs, although viruses causing the common cold appear to be an exception. In some lower respiratory tract infections, the host response is the principal cause of damage.

Human behaviour can also increase the risk of respiratory infection. Tobacco smoking has this effect by reducing the efficiency of ciliary function and by causing the production of more viscous respiratory secretions. Tracheal intubation for prolonged periods in the critically ill bypasses the upper respiratory tract and provides a conduit for microbial access directly into the lungs.

## 7.2 Diagnosis

### Learning objectives

You should:

- know which features indicate that a specific area of the respiratory tract is infected
- know how to assess respiratory compromise
- know how to identify the pathogen.

### Clinical features

The features of different respiratory tract infections largely depend on the structures where inflammation is localised and the extent to which function is altered. So, infection of the nasopharynx will result in a nasal discharge, bronchitis in cough and sputum production, and pneumonia in cough and sputum, but also in increased respiratory rate and chest radiograph changes.

Most upper respiratory tract infections are caused by viruses and are self-limiting. A specific aetiological diagnosis would not alter treatment and would be costly. The role of the physician is limited to reassuring the

patient and recognising the more serious bacterial infections that require specific antimicrobial chemotherapy or more extensive supportive treatment.

Lower respiratory tract infection should always be taken seriously since it is more likely to cause serious morbidity or even death.

### Laboratory tests

History, physical examination, X-rays and laboratory investigations focus on two issues: the degree of respiratory compromise and the identity of the causal pathogen. Since a wide range of candidate pathogens may have to be considered, the number of likely candidates should be reduced as far as possible by searching for clues in the history, examination and preliminary results. A history of tobacco consumption, recent travel, occupation, pets, and contacts with similar symptoms should be sought.

Diagnostic specimens can be obtained from the respiratory tract with deceptive ease, but their value is often limited by contamination by the indigenous flora of the oral cavity. To prevent contamination of lower respiratory tract specimens, the upper respiratory tract must be bypassed. Chest X-rays are a fundamental part of evaluation of lower respiratory tract infections and provide evidence of the distribution and extent of disease more reliably than signs elicited by auscultation. Postero-anterior views are most commonly used, but a lateral view can provide valuable additional information.

Blood gas analysis should be performed if there is any suspicion of acute respiratory compromise. The key indicators of disease severity in pneumonia are raised respiratory rate (> 30 beats/min), hypoxia, hypercapnia, bilateral or recently enlarging radiographic opacities, shock, renal failure and confusion.

## 7.3 Management

### Learning objectives

You should:

- know when chemotherapy is indicated
- know how to choose the most suitable drug
- know how to prevent infection and the spread of infections.

### Chemotherapy

The antimicrobial therapy of respiratory tract infection depends not only on the likely microbial cause of

infection but also on the primary site involved and the severity of disease. The commoner upper respiratory tract infections are rarely life threatening and in many cases are self-limiting. It is therefore possible to manage many of these infections without specific chemotherapy, thereby avoiding all the possible adverse effects. However, even apparently trivial infections such as pharyngitis may require specific antibiotic treatment in some cases. The problem is in knowing who and when to treat with antimicrobial agents.

Lower respiratory infections are less of a problem in this respect, since infection is much more likely to cause significant morbidity and mortality. Antibiotics should be used as early as possible in the course of infection. The problem here is in knowing which of a wide range to choose. It is often necessary to make a 'best guess' or presumptive choice in severely ill patients, based on the most likely microbial agent. The initial choice of chemotherapy may have to be substantially modified in the light of laboratory results. Patients with pneumonia who are ill enough to require hospitalisation usually require parenteral antibiotics. A syndrome-based choice of therapy has become the preferred approach, since antibiotic choice and decisions on the need for hospital admission and active supportive care do not have to wait for a laboratory-based aetiological diagnosis.

### Prevention

The ease with which respiratory infections can be spread and their associated morbidity has led to the development of specific preventive approaches. Influenza can be prevented by immunisation with a live attenuated vaccine. The changes in epidemic strains of influenza virus necessitate periodic changes in vaccine composition and revaccination of high-risk groups such as the elderly and patients with cardiac or renal failure. Pneumococcal infection can also be prevented by vaccination. Like influenza, changes in prevailing infective strains (capsular polysaccharide types) require alterations in the composition of the polyvalent vaccine. Again, vaccination is restricted to high-risk groups. Infection with *Mycobacterium tuberculosis* can be prevented by vaccination with a live-attenuated strain (BCG; bacillus Calmette–Guérin), although protection against pulmonary infection may be only partial in some populations. In hospitals, the spread of respiratory infection from known cases of influenza and pneumonia can be prevented by infection control procedures. These are referred to as 'additional precautions' and include nursing the patient in a separate side ward, away from other patients and non-immune staff. Filter-type masks and aprons are also

worn by staff and other visitors. At a personal level, covering the mouth when coughing or sneezing is a simple but effective means of preventing the spread of respiratory pathogens.

## 7.4 Diseases and syndromes

### Learning objectives

You should:

- know the major infections of the respiratory tract
- know the factors contributing to their occurrence
- understand the basis of their clinical management.

The main infectious diseases of the respiratory tract are listed in Table 9.

### Pharyngitis

Pharyngitis is an inflammation of the throat, resulting in pain on swallowing and swollen, red pharyngeal mucosa. It is most often caused by a respiratory virus (rhinovirus, coronavirus, adenovirus, influenza virus, parainfluenza viruses, respiratory syncytial virus), Epstein–Barr virus or coxsackievirus.

Aetiological clues include:

- conjunctivitis: adenovirus
- constitutional symptoms (lethargy and malaise) and tonsillar exudate: Epstein–Barr virus
- posterior palatal ulcers: coxsackievirus
- abrupt onset, 'doughnut' pharyngeal lesions and beefy uvula: *Streptococcus pyogenes* (group A streptococcus)
- grey pharyngeal pseudomembrane in unvaccinated subject: *Corynebacterium diphtheriae*.

### Bacterial pharyngitis

Bacterial pharyngitis is less common and its single most frequent cause is *S. pyogenes*. Other rare bacterial causes include *Neisseria gonorrhoeae*, *Mycoplasma pneumoniae*, *C. diphtheriae* and *Arcanobacterium haemolyticum*. Peak incidence is between autumn and spring in temperate climates, and during the rainy season in the tropics. Transmission is more rapid among groups sharing crowded living quarters and is by droplet spread or direct transmission.

### Viral pharyngitis

Viral pharyngitis is a self-limiting condition that does not usually require a specific aetiological diagnosis.

**Table 9** Infectious diseases of the respiratory tract

Infection	Features
Pharyngitis	Acute inflammation of the throat, resulting in pain on swallowing and swollen, red pharyngeal mucosa
Common cold	Self-limiting rhinitis, causing nasal discharge, nasal obstruction, discomfort and sneezing
Influenza	Acute, usually self-limiting, viral infection with respiratory and systemic features
Otitis media	Acute inflammation of the middle ear
Otitis externa	Inflammation of the external auditory meatus
Acute sinusitis	Inflammation of the maxillary, frontal, ethmoid or sphenoidal sinuses
Laryngitis	Inflammation of the larynx, with hoarseness and loss of voice
Bronchitis	Cough and sputum production; can be acute or chronic
Pneumonia	
Acute, community-acquired	Occurs prior to or immediately after hospital admission; cough, chest signs and fever
Acute, hospital-acquired	Occurs in vulnerable patients in hospital; onset gradual and symptoms unreliable for diagnosis
Chronic	Insidious onset, prolonged course; usually diagnosed by radiological findings
In AIDS	See Ch. 18
Pulmonary tuberculosis	Coughing and sneezing occur, fever, night sweats, weight loss and coughing blood; chest X-ray demonstrates lung changes
Empyema	Accumulation of purulent fluid in the pleural space
Croup	See Ch. 16
Epiglottitis	See Ch. 16
Bronchiolitis	See Ch. 16

### Diagnosis

When Epstein–Barr virus infection (**infectious mononucleosis**) is suspected, full blood count, blood film and Paul–Bunnell test for heterophile antibodies should be requested. This is not sensitive in Asians; in this group IgM to viral capsid antigen should be sought. The investigation most frequently requested for pharyngitis is detection of *S. pyogenes*. This species is detected either by culture on blood agar and subsequent latex agglutination reaction for group-specific polysaccharide, or by direct antigen detection. Neither method can distinguish oropharyngeal colonisation from true infection, but only culture allows antibiotic susceptibility testing. Suspicion of infection with *N. gonorrhoea*, *Mycoplasma* spp., *Arcanobacterium* sp. or *Corynebacterium* spp. should be communicated to the laboratory so that specialist, non-routine culture media can be used.

### Treatment

An oral penicillin or erythromycin is used to treat streptococcal pharyngitis. Treatment may not alter the course of the primary pharyngeal infection, but it should reduce the risk of major non-infective sequelae such as rheumatic heart disease, poststreptococcal glomerulonephritis and Sydenham's chorea. The need for antibiotic treatment of streptococcal pharyngitis has been questioned in developed countries, since the non-infective sequelae of streptococcal infection are all rare; but the recent increase in streptococcal infection in Europe and North America may change this view.

The other complications of streptococcal pharyngitis include scarlet fever (less common than in the past in developed countries), streptococcal toxic shock syn-

drome (both caused by toxin) and **quinsy** (paratonsillar abscess). In quinsy, there may be secondary infection with oral anaerobic bacteria, but these are often penicillin sensitive. Drainage of purulent foci is required.

### Common cold

The common cold is a frequent occurrence, especially in young children and their parents during the autumn–spring period. The condition is caused mainly by rhinoviruses. The size of the rhinoviral group, and the causal role of other respiratory viruses in a minority of common colds, has prevented the development of an effective vaccine. There is a nasal discharge, nasal obstruction and sneezing. Pharyngitis and cough may be present, but fever and myalgia are both rare features. There is no reason to use antimicrobial agents, and treatment should be restricted to alleviation of symptoms.

### Influenza

Epidemic and endemic influenza occurs, caused by influenza virus groups A–C. Some of the features of a common cold may be present, but systemic and respiratory symptoms are more pronounced. Fever, lethargy and myalgia are all common. The influenza virus is an RNA virus with a segmented genome. Two major surface antigens are used in typing epidemic strains: haemagglutinin and neuraminidase. The different types of influenza virus noted in successive epidemics are the result of genetic reassortment which causes an antigenic shift. Minor changes in antigenic makeup occur between epidemics. These are referred to as antigenic drift. Antigenic shift results in influenza epidemics because it renders

pre-existing specific immunity to influenza virus antigens obsolete. High mortality rates have been recorded during influenza epidemics as a result of cardio-respiratory failure or secondary bacterial pneumonia (caused by *Staphylococcus aureus* or *S. pneumoniae*).

### Diagnosis

Diagnosis is usually clinical, with serology reserved for epidemiological studies and pandemic surveillance.

### Treatment

Treatment is aimed at symptomatic relief and at complications if they occur. However, amantidine treatment may be of benefit if commenced early during infection with epidemic type A strains.

New treatments for influenza infection, such as the neuraminidase inhibitor oseltamivir, may reduce the duration of symptoms in a proportion of patients.

A vaccine is available, but it is only effective against previously isolated strains. The vaccine is therefore offered to those at high risk of complications, i.e. the elderly, those with cardiac or respiratory disease, those with renal failure, the inhabitants of residential institutions and those in high-risk occupations (e.g. health care).

## Otitis media

Otitis media is an acute inflammation of the middle ear. It is most frequent in the younger child, whose eustachian tube is shorter and more horizontal. It is also more prone to blockage by hypertrophic lymphoid tissue at the proximal end, as a result of prior respiratory tract infection. Purulent fluid accumulates behind a tense, red tympanic membrane and may discharge externally after rupture of the membrane. Infection is most often caused by *S. pneumoniae* or *H. influenzae*. Fever and local pain are common features. Common complications include secretory otitis media and impaired hearing. Much rarer complications are meningitis and mastoiditis.

### Diagnosis

Diagnosis is mainly clinical. Auroscopic examination of both tympanic membranes should be performed. Aetiological diagnosis is possible only if purulent exudate from the middle ear is cultured, either following discharge via the eardrum or following tympanocentesis.

### Treatment

Antimicrobial treatment is with an antibacterial agent (e.g. oral ampicillin or erythromycin for 7–10 days). Some authorities recommend decongestant therapy as an alternative in uncomplicated acute otitis media.

## Otitis externa

Inflammation of the external auditory meatus is most often caused by the hyphae-forming fungus *Aspergillus niger*.

Diagnosis is by culture of fungus from exudate.

Aural toilet and treatment with a topical agent such as aluminium acetate may be sufficient. Topical antibiotic preparations should be avoided. A rare, sometimes life-threatening variant, called malignant otitis externa, occurs in diabetics and is caused by *Pseudomonas aeruginosa*. Therapy with agents effective against *Pseudomonas* spp. should be used.

## Acute sinusitis

Infection of the axillary, frontal, ethmoid or sphenoidal sinuses with bacteria from the nasopharynx follows impaired drainage of sinus secretions as a result of a prior upper respiratory tract infection or similar cause. The bacteria most commonly implicated are *S. pneumoniae* and *H. influenzae*. Infection causes the sinus to fill up with mucus, which alters the resonance of the voice and causes a feeling of local discomfort.

### Diagnosis

Diagnosis is mainly from the symptoms, but special radiographic views may show filling of a maxillary sinus. Representative bacteriological specimens are difficult to obtain.

### Treatment

Treatment is with decongestants to improve drainage. Surgical procedures may be required in more severe or persistent cases. Some authorities argue that oral antibiotics (e.g. ampicillin or erythromycin) should be used in addition.

## Laryngitis

Laryngitis is caused by one of the 'respiratory' viruses and is a self-limiting condition of hoarseness and loss of voice. It may also be a feature of a common cold or influenza. No specific therapy is required.

## Bronchitis

There are three related conditions: acute bronchitis (in the strict sense), tracheobronchitis and acute exacerbation of chronic bronchitis.

*Acute bronchitis.* This condition involves a cough, sputum production (which is usually white to cream in colour) but no radiographic changes on chest X-ray. Infection is with *M. pneumoniae*.

*Tracheobronchitis.* Here, acute bouts of coughing are not accompanied by significant sputum production. Infection is caused by influenza virus, and features of systemic infection such as fever and myalgia may be present.

*Acute exacerbation of chronic bronchitis.* A chronic productive cough changes to become productive of larger

quantities of newly purulent sputum. This may be the result of infection with one of the respiratory viruses, *S. pneumoniae* or *H. influenzae*.

### Diagnosis

In practice, there is considerable overlap between these three conditions. Sputum culture is of limited diagnostic value. Some authorities recommend culture only when there is no response to treatment after 48 hours.

### Treatment

Some patients will benefit from a few days' treatment with an antibacterial agent (e.g. oral ampicillin or erythromycin), but many patients will not experience any benefit from therapy.

Patients at risk of cardiac or respiratory failure should be vaccinated against pneumococcal infection and influenza.

### *Pneumonia: acute, community-acquired*

Acute pneumonia has its onset either prior to or immediately after admission to hospital. It is one of the most common infectious causes of death worldwide. Patients with acute pneumonia usually have a cough, chest signs and fever. The cough may or may not be productive of purulent sputum. Chest signs are variable and prone to subjective interpretation. They may indicate areas of consolidation, fluid in the air spaces or even the presence of an effusion or cavity. The most important consequence of acute pneumonia is impairment of respiratory function, which should be assessed as a first priority. The identity of the likely infective agent will determine choice of antimicrobial therapy. A careful history, thorough examination and appropriate chest X-rays should provide some clues to the likely causative agent.

Four main clinico-pathological patterns of acute pneumonia are recognised:

- lobar pneumonia
  - pulmonary consolidation demarcated by border of segment or lobe

- most often caused by *S. pneumoniae*
- also caused by *S. aureus*, *S. pyogenes* (group A streptococcus) and *Legionella pneumophila*

- bronchopneumonia
  - patchy consolidation around the larger airways
  - caused by *S. pneumoniae*, *H. influenzae*, *S. aureus* and *L. pneumophila*
- interstitial pneumonia
  - fine areas of interstitial infiltration in lung fields
  - usually no sputum production at presentation
  - caused by *Legionella* sp., *Mycoplasma* spp. or virus
  - initial treatment is with erythromycin
- aspiration pneumonia
  - follows aspiration of oral or gastric contents
  - damage usually caused by chemical or mechanical insult
  - chest X-ray changes either in lower right lobe or, if supine, apex of right lower lobe
  - bacterial damage caused by oral streptococci or anaerobes.

### Aetiological clues

The causative organism can be suggested by the type of symptom observed (Table 10).

### Diagnosis

The choice of presumptive therapy may be narrowed by sputum Gram stain results. Culture and antibiotic susceptibility results take too long to affect the initial choice of treatment but may be reason for subsequent modification, particularly if the response to initial therapy has been poor. Sputum specimens should be obtained with the minimum of contamination by oral flora. A deep cough sputum specimen collected first thing in the morning is best. This should be preceded by a gargle with sterile water. A physiotherapist may help if the patient has difficulty producing a specimen. A rigid, screw-top container should be used, and the patient instructed how to avoid contamination of its outer surface.

Specimen contamination by the oral flora can be avoided altogether by more invasive methods that

**Table 10** Features of pneumonia caused by different bacteria

Organism	Symptoms
<i>Streptococcus pneumoniae</i>	Sudden onset pleuritic pain, fever, rusty sputum, cold sores
<i>Klebsiella pneumoniae</i>	Thick, viscous red sputum, alcoholic patient
<i>Staphylococcus aureus</i>	Pneumonia following influenza
<i>Streptococcus pneumoniae</i>	Pneumonia in the chronic bronchitic
<i>Haemophilus influenzae</i>	Pneumonia in the chronic bronchitic
<i>Mycoplasma pneumoniae</i>	Non-productive cough, pharyngitis in young adult with family contacts; ambulant despite positive chest X-ray
<i>Legionella pneumophila</i>	Non-productive cough, confusion, diarrhoea, middle-aged male, smoker, exposure to air conditioning or hotel shower
<i>Mycobacterium tuberculosis</i>	Upper lobe consolidation, hilar lymphadenopathy, vagrant or alcoholic
<i>Chlamydia psittaci</i>	Close contact with parrot or similar type of bird

bypass the mouth. These include transtracheal aspiration, bronchoscopy with protected specimen collection device and transbronchial or transthoracic biopsy. All these techniques require time, skill and special equipment and may cause unwanted side effects. Blood culture should be performed if the patient has a fever.

Preliminary result based on Gram stain can be provided in minutes after the laboratory receives the specimen. If the smear is full of neutrophil polymorphs and a single type of organism (e.g. Gram-positive diplococcus), the result may make a timely contribution to clinical decision-making. Large quantities of saliva or the presence of buccal epithelial cells in the smear suggest that it is unsuitable for further bacteriological evaluation. It is important to alert the diagnostic laboratory to the possibility of *Mycoplasma*, *Legionella* or *Mycobacterium* spp. because these organisms all require non-routine procedures for detection. Some laboratories offer direct or indirect immunofluorescent detection of *Legionella* and *Chlamydia* spp. *Legionella* and mycoplasmas can be cultured, but there is a low rate of detection compared with serological methods. However, the delay necessary for a second serum titre makes the information obtained of less use in patient management.

### Treatment

Presumptive therapy of acute pneumonia is often chosen on a 'best guess' basis and now follows a syndrome-based approach that does not depend on being able to name the microbial cause of infection before choosing the most suitable antimicrobial agents. It is rarely practical to cover all possible pathogens with a presumptive chemotherapeutic regimen. Agents should be chosen for their action against the most likely pathogens and given by the route and dose that guarantees maximum antimicrobial effect. In practice, this usually means by the intravenous route. Response to presumptive therapy should be monitored carefully. However, the response may not be immediate, and some patients die from acute pneumonia despite optimal antimicrobial therapy. It may, therefore, be difficult to decide whether a particular antibiotic has had the desired effect or not. Radiographic improvement may lag behind clinical response by several days.

### Prevention

Pneumococcal pneumonia can be prevented by vaccinating with a polyvalent vaccine to capsular polysaccharides. Protection is only partial because of changes that occur in the relative prevalence of particular pneumococcal capsular types (around 84 at present). Vaccination is, therefore, limited to those at greatest risk: the elderly, those with chest or heart disease, chronic renal failure and prior to splenectomy.

*Legionella* infection can be prevented by public health measures to reduce the risk of exposure by bio-ciding or heating water sources likely to act as a source of contaminated aerosols, e.g. evaporative condensers and air-conditioning cooling towers.

### *Pneumonia: acute, hospital-acquired*

Pneumonia is the third most common hospital-acquired (nosocomial) infection but the most common one to cause death. It affects smokers, patients with prior chest disease or following operations (especially thoracic and upper abdominal), and ventilated critically ill patients. The last group has the highest relative risk.

Nosocomial pneumonia is most often caused by *P. aeruginosa*, *S. aureus* and the Enterobacteriaceae. Rarely *Legionellas* or respiratory viruses are implicated. There is a particular association between *S. aureus* pneumonia and traumatic head injury.

The mechanically ventilated patient is prone to colonisation of the lungs by bacteria from the stomach and mouth. These organisms enter the trachea along the outside of the tracheal tube. Occasionally, bacteria from the mechanical ventilator and other respiratory support devices get into the lungs via the lumen of the tracheal tube.

### Diagnosis

Onset of nosocomial pneumonia is typically more gradual than community-acquired infection. In the critically ill, the usual signs of pneumonia—purulent sputum, fever, raised leucocyte count and radiographic infiltrates—may each signify the presence of non-infective processes. Clinical diagnosis is therefore unreliable, and bacteriological examination of tracheal secretions will only demonstrate the extension of upper respiratory tract bacterial flora into the trachea. Protected collection techniques (e.g. bronchoalveolar lavage with a protected bronchoscopy catheter) are the preferred method for collection of satisfactory bacteriological specimens in untreated patients.

### Management

Antimicrobial chemotherapy must be tailored to the needs and susceptibility patterns of the hospital or unit in question. Regular epidemiological review of laboratory results should be used to plan presumptive therapy. Many patients who develop nosocomial pneumonia are already debilitated and may not respond to optimal antimicrobial therapy. A number of preventive strategies have therefore been developed. As yet, no preventive strategy offers complete protection against nosocomial pneumonia, and antibiotic prophylaxis has been the most disappointing.

### *Pneumonia: chronic*

Chronic pneumonia has a more insidious onset and prolonged course than acute pneumonia. There is no single symptom complex, so the diagnosis is often based on radiological findings. Fever is variable but, where present, may be accompanied by night sweats and shaking attacks (rigors). Features of chronic sepsis such as weight loss and anorexia may also be present. Cough may be productive of purulent sputum, occasionally bloodstained (haemoptysis).

Not all causes of chronic pneumonia are infective. Other causes include neoplasms and connective tissue disease. The most common infective cause is pulmonary tuberculosis. Other infective causes include atypical mycobacteria, other bacteria and fungi.

#### **Diagnosis**

A careful history and clinical examination are important. Investigation should include a full workup for acute pneumonia. Sputum examination should be accompanied by a request for acid-fast stain (Ziehl–Neelsen or auramine–phenol), silver stain and cytology. This will help to exclude mycobacteria, fungi and neoplasms. The chronicity of the condition should allow completion of diagnostic tests before commencing specific antimicrobial chemotherapy. Since some conditions may require months of chemotherapy, it is important to do everything possible to obtain a specific diagnosis before committing the patient to a prolonged course of treatment.

### *Pulmonary tuberculosis*

While chronic pneumonia is a common presentation of *M. tuberculosis*, there are several other presentations of pulmonary tuberculosis:

- acute bronchopneumonia
- pulmonary cavitation
- miliary tuberculosis
- primary complex of focal, peripheral lung disease and hilar lymphadenopathy may be noticed as an incidental finding on a chest radiograph.

Pulmonary tuberculosis is common throughout the developing world. In more developed countries, its incidence has fallen over the 20th century until recently, the reversal being caused by a combination of the acquired immunodeficiency syndrome (AIDS) and urban poverty. Primary infection follows airborne transmission from an individual with pulmonary tuberculosis. Given adequate host defences, exposure results in formation of a primary complex. The thick, lipid-containing cell wall of mycobacteria renders the organisms resistant to phagocytosis. The inhaled bacteria are, therefore, walled

off by fibrosis to form a granuloma with central caseating necrosis. Immunity is mediated by the cellular immune system. Primary tuberculous pneumonia only occurs if cell-mediated immunity is inadequate to resist the initial infective challenge. Secondary pneumonia may occur following reactivation of the primary focus, often at the left or right apex.

#### **Diagnosis**

Fever, night sweats, weight loss and haemoptysis are all clinical features of pulmonary tuberculosis. The radiographic appearance supports one of the clinical presentations listed above. In addition to the routine Gram stain, sputum should also be subjected to acid-fast stain (either Ziehl–Neelsen or auramine–phenol). Three consecutive early morning specimens should be stained in this way. Sputum specimens should be treated as a potential infection hazard, with proper warning given to ward, portering and laboratory staff. The results of acid-fast stain can be provided the same day, but culture, identification and susceptibility results take several weeks because of the slow growth rate of mycobacteria. Patients who produce little or no sputum and children require either bronchoscopy or gastric aspiration to obtain diagnostic specimens. Nucleic acid amplification (polymerase chain reaction) tests can provide a much more rapid confirmation of *M. tuberculosis* infection in sputum smear-positive disease. Rapid, automated analysers have shortened the time to culture-based confirmation and generation of susceptibility testing. However, it may still require several weeks to demonstrate the presence of multidrug-resistant *M. tuberculosis*. Bacterial gene sequencing at the 16S ribosomal locus is widely used to confirm the identity of presumed *M. tuberculosis* isolates.

#### **Treatment**

Current treatment regimens employ several antimycobacterial agents to guarantee sufficient antibacterial activity in different cellular and extracellular locations: inside phagocytic cells, in granulomata and in collections of respiratory secretions. Many different regimens have been evaluated. The most effective regimens currently in use employ up to four agents in an intensive induction period of 2–4 weeks, followed by a maintenance period of 5–9 months with fewer agents. Patients are a potential source of secondary infection if acid-fast bacilli are found in sputum at the time of diagnosis. Current treatment regimens should render them non-infectious within days. Poor compliance with recommended maintenance therapy can be the cause of relapse. Commonly used antituberculous agents are rifampicin, isoniazid, ethambutol, pyrazinamide and streptomycin.



### Prevention

Prevention is by intradermal inoculation of a live attenuated strain of mycobacterium (BCG) after non-reactivity has been demonstrated by tuberculin skin test. Since the main reservoir of disease in developed countries is adults with untreated pulmonary tuberculosis, secondary spread can be prevented by contact tracing and treatment. In some countries, cattle are a significant additional reservoir. Pasteurisation of milk, meat inspection and establishment of a national tuberculosis-free cattle stock are all important approaches to prevention of zoonotic tuberculosis.

### Empyema

Empyema is the accumulation of purulent fluid in the pleural space. It is caused by direct extension from underlying pneumonia, infection resulting from penetrating thoracic trauma or haematogenous spread from a distant focus. Infection may be caused by a variety of bacteria including *S. aureus*, the Enterobacteriaceae, streptococci and obligate anaerobes.

### Diagnosis

Pleural effusion and a gas–fluid interface may be evident on chest radiograph (a lateral view is a more sensitive means of detection), and there will also be dullness to percussion over the affected area.

The collection of purulent fluid requires drainage for diagnostic and therapeutic purposes. Anaerobic culture should be requested, preferably by communication with the laboratory prior to undertaking the drainage procedure. A thoracic surgical opinion should be sought early.

### Treatment

Presumptive antibiotic therapy depends on the results of Gram stain but should include an agent active against obligate anaerobes, e.g. metronidazole.

## 7.5 Organisms

A checklist of the organisms discussed in this chapter is given in Box 2. Further information is given on the pages indicated.

### Box 2 Organisms that infect the respiratory tract

<b>Bacteria</b>	<b>see page</b>	<b>Fungi</b>	<b>see page</b>
<i>Streptococcus pneumoniae</i>	245	<i>Aspergillus niger</i>	269
<i>Staphylococcus aureus</i>	243		
<i>Corynebacterium diphtheriae</i>	246–7	<b>Viruses</b>	
<i>Klebsiella pneumoniae</i>	248	Rhinoviruses	260
<i>Pseudomonas aeruginosa</i>	249–50	Coronaviruses	258
<i>Haemophilus influenzae</i>	251	Coxsackieviruses	260
<i>Legionella pneumophila</i>	252	Adenoviruses	257
<i>Mycoplasma pneumoniae</i>	254	Influenza virus	259
<i>Chlamydia</i> spp.	255	Parainfluenza viruses	259
<i>Streptococcus pyogenes</i>	244	Respiratory syncytial virus	259
<i>Mycobacterium tuberculosis</i>	253–4	Epstein–Barr virus	257
<i>Mycobacterium</i> spp.	253–4		
<i>Arcanobacterium haemolyticum</i>	73		

## Self-assessment: questions

### Multiple choice questions

- Match the organism with the most appropriate means of subverting host defences:
 

a. <i>Haemophilus influenzae</i>	i. IgA protease
b. Influenza virus	ii. Phagocytosis-resistant cell wall
c. <i>Mycobacterium tuberculosis</i>	iii. Adhesion to epithelial receptors
d. <i>Streptococcus pneumoniae</i>	
- Cigarette smoking results in:
  - Increased mucus viscosity
  - Impaired ciliary action
  - Reduced particle clearance from airways
  - Increased risk of Legionella infection
  - Susceptibility to mycoplasma infection
- Pharyngitis:
  - Is usually caused by a virus
  - Always benefits from antibiotic treatment
  - Can be caused by bacteria other than *Streptococcus pyogenes*
  - Of bacterial origin can be distinguished from viral pharyngitis on clinical signs alone
  - Can lead to glomerulonephritis
- Non-infective sequelae of streptococcal pharyngitis include:
  - Scarlet fever
  - Rheumatic heart disease
  - Sydenham's chorea
  - Glomerulonephritis
  - Quinsy
- The common cold can be caused by:
  - Coronavirus
  - Epstein-Barr virus
  - Mycoplasma* sp.
  - Respiratory syncytial virus
  - Rhinovirus
- The following respiratory pathogens are likely to be isolated from sputum specimens without special request:
  - Streptococcus pneumoniae*
  - Staphylococcus aureus*
  - Legionella pneumophila*
  - Mycobacterium tuberculosis*
  - Klebsiella pneumoniae*
- Failure of pneumonia to respond to antimicrobial therapy may be because of:
  - Incorrect diagnosis
  - Inappropriate choice of antibiotic
  - Wrong route of administration
  - Reliance on radiological changes
  - Host factors
- Common bacterial causes of nosocomial pneumonia include:
  - Staphylococcus aureus*
  - Streptococcus pneumoniae*
  - Pseudomonas aeruginosa*
  - Mycobacterium tuberculosis*
  - Klebsiella pneumoniae*
- Pulmonary tuberculosis may present as:
  - Bronchopneumonia
  - Pulmonary cavitation
  - Chronic pneumonia
  - Acute lobar pneumonia
  - Miliary disease
- The key diagnostic features of chronic pneumonia are:
  - Cough
  - Fever
  - Purulent sputum
  - Breathlessness
  - Radiographic changes

### Case history questions

#### History 1

A 3-year-old boy attended the clinic because he was irritable, off his food and had a sore left ear. His GP noticed that he had a moderately inflamed throat and a red, immobile left eardrum. The GP prescribed an oral medication that was not an antibiotic and gave the mother a bacteriology swab to take away. The mother remarked that her 1-year-old daughter also had a sore throat.

- What condition does the boy have?
- What did the GP prescribe?
- What do you think the swab was for?
- Does the little girl have the same condition?

## History 2

A 16-year-old student was admitted to an intensive care unit following a severe head injury in a road traffic accident. Four days after admission, he was still in need of mechanical ventilation and had developed a fever and raised leucocyte count. One of the nurses had noticed that the patient had purulent and slightly bloodstained tracheal secretions and had sent them to the diagnostic laboratory. The Gram stain report said: 'Gram-positive cocci: further identification and sensitivities to follow'. Intravenous flucloxacillin was commenced, and fucidic acid added 2 days later when further results reached the intensive care unit. The patient had a further serious infection with *Pseudomonas aeruginosa* 2 weeks later but survived and eventually left hospital after almost a year.

1. What was the first infection?
2. Why was flucloxacillin chosen?
3. How reliable is tracheal suction as a specimen collection technique?

## Data interpretation

Table 11 is the report relating to a 57-year-old male smoker with fever, confusion, diarrhoea and non-productive cough.

1. Given the clinical features in this case, what possible bacterial cause of this infection has not been mentioned on this report?

**Table 11** Report for data interpretation

Test	Results	
Bronchoalveolar lavage fluid		
Microscopy	Leucocytes +++ Epithelial cells + Monocytes + Gram stain mixed bacteria Acid-fast stain: no acid-fast bacilli seen Mycobacteria: culture results will be issued on a separate report	
Culture	Mixed bacteria including <i>Moraxella catarrhalis</i> , <i>Pseudomonas aeruginosa</i> and viridans group streptococci	
Antibiotic susceptibilities of <i>M. catarrhalis</i> and <i>P. aeruginosa</i>		
Amoxicillin	R	
Augmentin	S	
Doxycycline	S	
Co-trimoxazole	R	S
Gentamicin	S	S
Ciprofloxacin	S	S
Timentin	S	S

R, resistant; S, sensitive.

2. Does a negative report rule out the possibility of the species mentioned in your answer to 1?
3. What is the explanation for the presence of each of the bacteria mentioned in this report?
4. What other microbiological investigations might help you to establish an aetiological diagnosis in this case?

## Objective structured clinical examination (OSCE)

A 48-year-old man with fever and a productive cough was admitted after he became increasingly short of breath. He had a temperature of 38.5°C, a pulse of 120 beats/min and a respiratory rate of 22 breaths/min. Chest examination revealed reduced expansion on the right, dullness to percussion, quiet breath sounds and dullness to percussion in the right midzone and green-coloured sputum. Chest X-ray showed a clearly demarcated opacity occupying the right middle lobe. Blood gases on arterial blood collected while the patient was breathing room air confirmed a hypoxia and respiratory acidosis.

You are asked the following:

1. Does this patient have a lobar pneumonia?
2. Is his pneumonia most likely to be caused by *Streptococcus pneumoniae* infection?
3. Do other bacteria such as *Legionella pneumophila* cause lobar pneumonia?
4. Will bacteriological investigations assist the immediate management of this infection?
5. Should ceftriaxone be used as a first choice of antibiotic in resistant *Streptococcus pneumoniae* infection?

## Short notes questions

Write short notes on the following:

1. Why the lungs are usually free from bacterial contamination in healthy individuals
2. Methods you know for obtaining diagnostic microbiology specimens from the lower respiratory tract; describe how to prevent contamination with the oral flora
3. Influenza and its complications
4. The clinical presentation of acute bronchitis and its treatment

## Viva questions

1. Are viral upper respiratory tract infections important?
2. What microbiological tests would you use to diagnose an acute, community-acquired

pneumonia? How would the results influence your choice of antibiotic treatment?

3. In acute, community-acquired pneumonia, a specific aetiological diagnosis is now thought to be less

important as a guide to immediate clinical management. What key features will determine your immediate course of action?

## Self-assessment: answers

### Multiple choice answers

1. a. and i.  
b. and iii.  
c. and ii.  
d. and i.
2. a. **True**.  
b. **True**.  
c. **True**.  
d. **True**.  
e. **False**. *Mycoplasma* infection typically affects young adults.
3. a. **True**. It is usually self-limiting. Suspected Epstein–Barr virus (infectious mononucleosis) should be investigated.  
b. **False**. Antibiotics are ineffective against viral pharyngitis and do not always benefit patients with bacterial pharyngitis.  
c. **True**. *Neisseria gonorrhoeae*, *Mycoplasma pneumoniae* and *Corynebacterium diphtheriae* are rarer causes.  
d. **False**. Bacterial and viral pharyngitis cannot be reliably distinguished on clinical grounds.  
e. **True**. A potential risk with streptococcal infection.
4. a. **False**. Scarlet fever is a manifestation of infection caused by an erythrogenic strain of *Streptococcus pyogenes*.  
b. **True**. Probably caused by bacterial antigens.  
c. **True**. It is closely linked with rheumatic fever.  
d. **True**. Related to bacterial antigens.  
e. **False**. Quinsy is a paratonsillar abscess.
5. a. **True**.  
b. **False**. Epstein–Barr virus causes infectious mononucleosis (glandular fever) in which pharyngitis may be a feature.  
c. **False**. *Mycoplasma* infection causes pharyngitis, bronchitis and interstitial pneumonia but does not cause the common cold.  
d. **True**.  
e. **True**.
6. a. **True**.  
b. **True**.  
c. **False**. *Legionella pneumophila* requires special culture media, direct immunofluorescence or serological tests.
- d. **False**. *Mycobacterium tuberculosis* usually requires a special request for acid-fast stain and special media.
- e. **True**.
7. a. **True**. Signs and symptoms of pneumonia can be variable and open to interpretation.  
b. **True**. Presumptive therapy is required and as response may not be immediate it is difficult to assess the choice of antibiotic.  
c. **True**. Route should be chosen to give maximum effect; this usually means intravenous.  
d. **True**. Radiological improvement is slow.  
e. **True**. Concomitant illness and a history of smoking or chest infections affect response.
8. a. **True**. Particularly associated with traumatic head injury.  
b. **False**. More typically associated with community-acquired disease.  
c. **True**. A common cause.  
d. **False**. More typically associated with community-acquired disease. Nevertheless, there are growing concerns that multidrug-resistant *M. tuberculosis* can spread within hospitals to affect other patients and staff.  
e. **True**.  
Secondary spread of less-common pathogens does occasionally occur through airborne transmission in hospitals where infection control practice is inadequate.
9. a. **True**.  
b. **True**. Seen on chest radiograph.  
c. **True**. Pulmonary tuberculosis is the most common cause of chronic pneumonia.  
d. **False**. Acute lobar pneumonia is usually caused by *Streptococcus pneumoniae* and bacterial species (not including mycobacteria).  
e. **True**. Lesions resemble millet seeds.
10. a. **False**. Cough may occur but is not diagnostic.  
b. **False**. When present, fever may be accompanied by night sweats and rigors.  
c. **False**. If a cough occurs, it may produce a purulent sputum, occasionally bloodstained.  
d. **False**.  
e. **True**. Chronic pneumonia has no consistent presentation or collection of symptoms. Diagnosis is usually based on radiographic appearance.

## Case history answers

### History 1

1. This patient has acute otitis media.
2. It was initially treated with an oral decongestant.
3. The swab was provided so that the mother could send in a specimen of pus from the affected ear if rupture of the tympanic membrane occurred.
4. The sister probably had the same upper respiratory tract infection that predisposed the boy to secondary otitis media. The mother was advised that her daughter did not require 'prophylactic' antibiotics.

### History 2

1. The first infection was a hospital-acquired (nosocomial) pneumonia, and since he was mechanically ventilated, it could also be referred to as a ventilator-associated pneumonia.
2. Flucloxacillin was given because *Staphylococcus aureus* infection was suspected; an organism more common in patients with head injury. (The fusidic acid was added 2 days later when the presence of *S. aureus* was confirmed.)
3. Tracheal aspirates from mechanically ventilated patients are prone to contamination with bacteria from the upper trachea and are, therefore, not representative of the smaller airways. Specialised bronchoscopic techniques are preferred as a means of specimen collection in ventilated patients in intensive care, but these techniques are only available in some centres.

## Data interpretation answer

1. *Legionella* spp.
2. No. Neither culture-based methods nor nucleic acid amplification is the most sensitive means of diagnosing Legionnaires' disease. The urinary antigen test is currently the most sensitive means of confirming *L. pneumophila* infection.
3. The bacteria reported here could have been carried on the tip of the bronchoscope after contamination during passage through the oropharynx. *M. catarrhalis* and viridans group streptococci are oropharyngeal commensals. *P. aeruginosa* is a coloniser of the oropharynx in a proportion of hospital patients, the percentage increasing with length of hospital stay, severity of underlying disease and exposure to broad-spectrum antibiotics.
4. Legionnaires' disease can be diagnosed using a combination of serology, culture-based methods, nucleic acid amplification by the polymerase chain reaction and urinary antigen test. Serological tests for other respiratory pathogens should also be performed.

## OSCE answer

1. Yes. He has a right middle lobe pneumonia.
2. Yes. This is the most common cause of community-acquired lobar pneumonia.
3. Yes. Other bacterial species including *L. pneumophila* can cause lobar pneumonia.
4. Yes. A sputum Gram stain showing neutrophils and many Gram-positive diplococci will increase the suspicion that this is a *S. pneumoniae* infection. The result should be available within minutes of receiving the sample in the laboratory.
5. No. Moderate penicillin resistance does not result in a significant increase in risk of penicillin treatment failure for *S. pneumoniae* infection unless the patient has meningitis. In this case, ceftriaxone would be a satisfactory choice of agent. But for lobar pneumonia, high-dose intravenous benzylpenicillin remains the treatment of choice.

## Short notes answers

1. Review the anatomical, physiological and other defences of the respiratory tract.
2. Start with a list. A tabular answer would be acceptable.
3. Remember to mention pathogenesis, surface antigen variation, epithelial damage and subsequent staphylococcal pneumonia.
4. Three brief paragraphs on acute bronchitis (strict sense), tracheobronchitis and acute exacerbation of chronic bronchitis. If recommending antimicrobial therapy, justify in terms of pathogens and likely outcome.

## Viva answers

1. Yes. They are the commonest infective reason for medical consultation and antibiotic prescription. You should mention the common cold and pharyngitis as a minimum. Mention local data on specific viral pathogens, epidemiology, public health issues and complications, if available.
2. Microscopy and culture of respiratory secretions, nucleic acid amplification tests (polymerase chain reaction (PCR)), serology, urinary antigen test for *Legionella pneumophila*. Only a clear-cut Gram or acid-fast stain result and a urinary antigen test can have immediate impact on antibiotic choice. PCR takes longer but will produce a specific result. Culture is even slower and often produces inconclusive results. Serology is rarely helpful in acute management as a rise in antibody titre may not occur until the patient has begun to recover.

3. The severity of respiratory infection is now taken as the main guide to whether the patient (i) needs hospital admission, and (ii) requires intensive respiratory care. Key features used to make these

decisions are respiratory rate, blood urea, falling  $P_{aO_2}$  (arterial partial pressure of oxygen), falling blood pressure and involvement of both lungs or multiple lobes on chest radiograph.