Pneumonia due to viral and atypical organisms and their sequelae

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Most children presenting with pneumonia in the industrialised world will have a viral or ‘atypical’ organism. The clinical features of these ‘atypical’ pneumonias may be indistinguishable from bacterial pneumonia. New diagnostic techniques such as the polymerase chain reaction may help in diagnosis and choice of treatment, where appropriate. The pathological and clinical features of infection with each agent are discussed, together with their sequelae.

World-wide, pneumonia is estimated to cause the deaths of 4 million children under 5 years annually. Most of these deaths occur in the non-industrialised world where bacterial organisms are largely responsible. However, in industrialised countries, where mortality is much lower, viruses account for most lower respiratory infections. In a recent survey of children admitted to hospital with pneumonia, 75% of infections diagnosed were viral or ‘atypical’ infections (Mycoplasma or Chlamydia). In the industrialised world, a great reduction in mortality from childhood pneumonia has been achieved in the last 60 years. In the US, deaths from pneumonia in children have fallen by 97% since 1939.

Many children with viral lower respiratory infection present clinically with bronchiolitis. However, there may be typical features of pneumonia and it is often impossible to distinguish clinically or radiologically between viral and bacterial pneumonia. Viruses such as influenza can directly infect the lower respiratory tract but can also predispose to a secondary bacterial bronchopneumonia. The clinical presentation of viral lower respiratory infection may be very atypical. For instance, post mortem evidence shows that children dying from sudden infant death syndrome more frequently have histological evidence of viral pneumonia than controls.

Viral or atypical organisms may lead to a more severe form of pneumonia in the following groups: (i) bronchopulmonary dysplasia; (ii) immune deficiency or immunosuppression; (iii) congenital heart disease; (iv) asthma; and (v) cystic fibrosis and other disorders of mucociliary clearance such as primary ciliary dyskinesia.

Although it is difficult to distinguish clinically between viral and bacterial causes of pneumonia, inflammatory markers may be helpful. Recent work...
suggests that one such marker, procalcitonin, has a similar sensitivity to C-reactive protein (sensitivity 86%) but is more specific for bacterial pneumonia in children (specificity 88%). This is a controversial question, with one estimate of the sensitivity of procalcitonin as low as 50%. However, a low sensitivity may be due to children receiving prior treatment with antibiotics.

Immunofluorescence of respiratory secretions (e.g. nasopharyngeal aspirate, tracheal aspirate or broncho-alveolar lavage) can be performed against a ‘panel’ of respiratory viruses and is highly specific. This offers the possibility of near patient testing and early treatment with specific antiviral agents such as the neuraminidase inhibitors against influenza. The use of the polymerase chain reaction (PCR) can increase the rate of diagnosis of treatable causes of pneumonia from 13% to 31%.

Specific viral pathogens and their clinical syndromes

Influenza

Influenza viruses of types A, B and C cause disease in man. Type A is responsible for influenza pandemics and can cause severe disease in the young. Types B and C do not cause pandemics and cause less severe disease.

On the surface of the influenza virion are the glycoproteins haemagglutinin (H) and neuraminidase (N; see Table 1). Haemagglutinin allows the virion to bind to the host cell membrane. Neuraminidase allows the budding virion to cleave itself from the host cell and go on to infect other cells. Influenza virus maintains its infectivity in the community by undergoing antigenic drift and shift, due to changes in the protein structure of haemagglutinin. In the case of antigenic drift, these changes consist of a small number of amino acid substitutions only. When non-immune individuals encounter the modified virus, this leads to an epidemic. Less frequently, a much greater change in the antigenic structure of the virus occurs, with many more susceptible individuals in the community. This is called antigenic shift and leads to pandemics of influenza where many young adults are affected.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Genome</th>
<th>Size (nm)</th>
<th>Envelope</th>
<th>Surface glycoproteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Negative sense RNA</td>
<td>80–120</td>
<td>Yes (host cell derived)</td>
<td>Neuraminidase (N), haemagglutinin (H)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Double stranded DNA</td>
<td>50–60</td>
<td>No</td>
<td>Protein capsid with surface fibres</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>Negative sense RNA</td>
<td>120–300</td>
<td>Yes (host cell derived)</td>
<td>F (fusion), G and SH proteins</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>Negative sense RNA</td>
<td>150–200</td>
<td>Yes (host cell derived)</td>
<td>Haemagglutinin-neuraminidase fusion protein</td>
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<tr>
<td>Rhinovirus</td>
<td>Positive sense RNA</td>
<td>20–30</td>
<td>No</td>
<td>Protein capsid with ‘canyon’ binding site</td>
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</table>
In 1957, a pandemic caused by so-called ‘Asian ‘flu’ – influenza A (H2N2) – lead to an estimated 69,400 deaths in the US8. School-age children were particularly vulnerable. Amongst 5–20 year olds, mortality was 2–3 times greater than in any other age group9. This epidemic represented the only time in the last 60 years when there has been a rise in mortality from pneumonia in the US, amongst children of all ages4.

During an epidemic season, influenza can account for an excess of 19 admissions per 1000 infants at high risk10. Influenza can cause severe infection in patients with cystic fibrosis11, although chest radiograph abnormalities are mainly those of bronchiectasis and sputum retention (Fig. 1). Children immunosuppressed following transplantation are also vulnerable12.

Influenza is spread by aerosol transmission. Particles of up to 10 µm in diameter are most effective. The presence of specific secretory IgA antibodies to influenza, on the nasal mucosa, is protective. Infection leads to cell death, primarily in the upper airway. Direct viral infection of the lung parenchyma occurs, characterised by haemorrhage and a

Fig. 1 Chest radiograph of a child with cystic fibrosis, taken during a pulmonary exacerbation, associated with influenza A virus infection. A good clinical response was seen to treatment with inhaled zanamivir and intravenous anti-pseudomonal antibiotics.
relative lack if inflammatory cells. Influenza virus has specific effects which may lead to secondary bacterial infection. Mucociliary clearance is impaired and bacterial adherence to respiratory epithelium is enhanced. Furthermore, influenza infection impairs T-cell, neutrophil and macrophage function.

Influenza has an incubation period of 18–72 h. The child may present with fever, myalgia and rigors. Fever usually lasts for around 3 days. Cough and pharyngitis are usually present initially, but may be overshadowed by the systemic symptoms. Younger children may develop croup. In children with a primary viral pneumonia, the fever may fail to settle and the cough becomes more prominent. In contrast, where influenza is complicated by bacterial pneumonia, the fever may settle initially but then re-crudesce. Between 4–8% of otherwise healthy individuals aged 5–50 years will develop pneumonia as a result of influenza infection.

Influenza may be diagnosed by direct immunofluorescence or viral culture of respiratory secretions. Retrospectively, paired acute and convalescent serology, using the complement fixation test can be helpful. A 4-fold rise in titre between the acute and convalescent specimens is diagnostic.

Influenza vaccine is recommended in the UK for all patients with chronic respiratory disease. This includes children with cystic fibrosis and asthma. The vaccine is usually given in an inactivated parenteral form, though a live aerosolised form has been developed. The parenteral form has an efficacy of 68% in the prevention of serologically proven influenza in healthy adults. Rates of hospitalisation and complications such as pneumonia are not affected by immunisation. There is no evidence that immunisation reduces the frequency of exacerbations in patients with asthma or cystic fibrosis.

Amantadine has been available for many years. It is only effective against influenza A. The license extends to children, although the appropriate dose for children under 10 years is unclear.

Zanamivir is the first of a new class of antiviral drugs – the neuraminidase inhibitors – to receive a license. Zanamivir is not absorbed when given orally and so inhalation is used. It shortens the duration of influenza symptoms by approximately 24 h. A reduction in complications such as pneumonia has not been demonstrated. In the UK, the National Institute for Clinical Excellence (NICE) has recommended the use of zanamivir for at-risk adults during an influenza epidemic, provided they present within 36 h of the onset of symptoms and can start treatment within 48 h.

Long-term sequelae of influenza are thought to be less common than with adenovirus pneumonia. However, bronchiectasis and obliterative bronchiolitis have been reported, when influenza infection occurs in the preschool child.
Adenovirus

Organisms of the adenovirus sub-genera B, C, E and F cause respiratory and enteric infection in children. The virion can interact with the host cell in one of three ways. The reproductive cycle of the virus may be completed, leading to cell lysis and death. Alternatively, the virus may cause chronic infection in tissues such as the tonsil. In experimental animals, oncogenic transformation may occur when adenovirus DNA is incorporated in the host cell genome.

Adenovirus is thought to cause around 10% of respiratory disease in children\(^2\), though infection may be subclinical. In young adults, the incubation period is 4–5 days. The spectrum of illness varies from mild pharyngitis and tracheitis in older children and adults to severe bronchiolitis in infants. Extrapulmonary disease such as conjunctivitis, gastroenteritis, intussusception, haemorrhagic cystitis and encephalitis can occur. Children may have both respiratory and non-respiratory disease as a feature of their illness. Fatal adenovirus pneumonitis has been reported in transplant recipients\(^2\)

There is no antiviral agent of proven efficacy against adenovirus, though the use of intravenous ribavirin has been reported\(^2\). Specific immunoglobulin has been used in adenovirus infection, complicating severe combined immune deficiency\(^2\). A live oral vaccine is available, but its use is restricted to military recruits.

![Fig. 2 Expiratory CT scan of a child with obliterative bronchiolitis following adenovirus infection, showing the ‘mosaic’ appearance. Hyperinflation (H) is seen in the left lower lobe (black) and an area of normal lung (grey) in the right lower lobe (N).](image-url)
Adenovirus may be cultured from throat swab, stool, conjunctival scrapings and urine. Rapid identification (though not serotyping) from respiratory secretions is possible by immunofluorescence. Serological diagnosis may be helpful retrospectively.

Adenovirus DNA has been found in the respiratory secretions of infants who develop bronchopulmonary dysplasia more frequently than in those with normal lungs. This has led to speculation that it may have an aetiological role in the development of bronchopulmonary dysplasia.

Pulmonary infection with adenovirus serotypes 3, 7 and 21 can lead to the development of obliterative bronchiolitis which may be accompanied by traction bronchiectasis. This is best diagnosed on high resolution computerised tomography (CT), where patchy areas of hyperinflation on the expiratory film produce the so-called ‘mosaic’ appearance (Fig. 2). Bronchiectasis may occur in over a quarter of children with adenovirus pneumonia.

In one study, adenovirus DNA was demonstrated, by the PCR, in the respiratory secretions of 78% of children with stable asthma. In contrast, adenovirus DNA was found in only one control patient. This has led to speculation that the chronic form of infection described above may have a role in the aetiology of asthma.

**Respiratory syncytial virus (RSV)**

Respiratory syncytial virus infection has been discussed extensively elsewhere in this issue and is not considered further here.

**Human metapneumovirus (hMPV)**

This newly discovered virus is closely related taxonomically to RSV. It has been isolated from nasopharyngeal aspirate samples taken from children with respiratory tract infections. The clinical features are thought to be similar to RSV, including bronchiolitis and pneumonia. The virus may account for approximately 10% of unexplained respiratory infections in children during the winter season. Seroprevalence studies in The Netherlands show that 25% of infants aged 6–12 months have antibodies to the virus and that by 5 years virtually all children are seropositive. The virus appears to have been circulating in the human population for at least half a century.

**Parainfluenza**

The glycoproteins on the envelope of parainfluenza viruses (Table 1) bind to sialic acid residues found on the surface of respiratory epithelial cells. Parainfluenza viruses types 1, 2 and 3 (but most commonly 3)
cause respiratory disease in children. Parainfluenza virus type 3 is
demic throughout the year, with a peak in spring; types 1 and 2 cause
autumn epidemics. The virus shows a tropism for the ciliated epithelial
cells, lining the large airways. Release of the virus, following replication,
occurs from the apex of the cells into the mucus layer. The presence of
a fusion protein can lead to formation of a syncytium of epithelial cells,
as with RSV.

In a similar fashion to RSV, parainfluenza type 3 causes respiratory
infection in infants under 6 months, who have maternally-derived
antibody. Commonly, these infants present with bronchiolitis. In older
children, croup is the most common clinical syndrome.

Pneumonia is uncommon in healthy children. However, fatal
pneumonia, with viral dissemination, has been reported (with type 3) in a
child with severe combined immune deficiency29. Bone marrow transplant
patients are also vulnerable, with pneumonia developing in almost half of
patients in whom the virus is isolated30. Children with bronchopulmonary
dysplasia, prematurity, congenital heart disease or asthma are also more
likely to develop lower respiratory infection and to require more
supportive therapy such as oxygen31. Secondary bacterial infection is
thought to occur in approximately one-third of children with lower
respiratory infection due to parainfluenza32.

Rapid diagnosis and assignment to type 1, 2 or 3 is possible by immuno-
fluorescence of respiratory secretions. Viral culture and paired sera may
also be helpful.

No specific antiviral agent has been shown to be effective, though
intravenous ribavirin has been used in the immunosuppressed33. A live
attenuated nasal vaccine is in development34.

Long-term sequelae of parainfluenza infection is uncommon. However,
bronchiolitis obliterans with organizing pneumonia has been reported35.

Rhinovirus

The structure of rhinovirus virion is summarised in Table 1. The virion
contains a so-called ‘canyon’ site in its capsid which binds to the host
cell receptor, intracellular adhesion molecule 1 (ICAM-1)36. Figure 3
shows an electron micrograph of the virus in cells in tissue culture.

One hundred rhinovirus immunotypes have been demonstrated and so
individuals remain susceptible to new antigenic variants throughout life.
Transmission is through the presence of infectious secretions on hands,
with transfer to conjunctiva or nasal mucosa.

Rhinovirus grows best at temperatures of around 33°C and so it
preferentially infects the nasal mucosa (which is cooled by inspired air).
However, rhinovirus infection can trigger lower respiratory illness,
particularly exacerbations of asthma. A community study in Southampton, UK, found that viruses, primarily rhinovirus, were found in 80% of reported episodes of wheeze, in school-aged children with asthma. The mechanism of this effect has been the subject of much research interest. Biopsy studies have shown that there are increased numbers of bronchial lymphocytes and eosinophils, following experimental infection in volunteers. Studies in vitro have shown raised levels of cytokines and an up-regulation of the receptor ICAM-1.

Other vulnerable groups may develop lower respiratory symptoms. In a prospective study of children with cystic fibrosis, 28% of exacerbations were associated with a viral infection, over half of which were rhinovirus. Infants with bronchopulmonary dysplasia may also have a severe lower respiratory illness with rhinovirus. One study found that the frequency of intensive care admission was similar with rhinovirus and RSV, though fewer infants with rhinovirus needed ventilation.

Immunofluorescence and serology are not available for diagnosis of rhinovirus infection as the large number of antigenic types makes this impracticable. Infection may be diagnosed by means of tissue culture of respiratory secretions at 33°C.

Nosocomial infection can be prevented by careful hand washing and this is important for those caring for vulnerable children in hospital. The prospects for a vaccine have been limited by the large number of serotypes. Current research into specific treatments has looked at the possibility of competitive inhibition of the binding of rhinovirus to ICAM-1 on the host cell membrane.
Measles

Measles is one of the most contagious of the communicable diseases and is spread by direct contact with respiratory secretions. Children with measles are most infectious during the late prodromal phase and cease to be infectious 48 h after the appearance of the rash. The introduction of immunisation has resulted in a dramatic reduction in the incidence of infection in the UK, although sporadic outbreaks in non-immunised groups do occur.

The virus can infect respiratory epithelium in the upper or lower respiratory tract. Following mucosal infection, a primary viraemia occurs, with spread of the virus within the monocyte, throughout the reticulo-endothelial system. The onset of the prodrome corresponds to the period of secondary viraemia, when the virus is released from the monocytes. Following this, the respiratory mucosa throughout the respiratory tract becomes infected.

The incubation period is 10–14 days. There follows a prodromal phase of fever, coryza and extreme misery. Towards the end of the prodrome, Koplick’s spots appear on the mucosa on the inside of the cheek, followed shortly afterwards by a erythematous maculopapular rash.

Respiratory involvement is universal, and acute respiratory complications include laryngotracheobronchitis, bronchiolitis and measles-associated pneumonia. The latter can result from direct viral invasion of the respiratory tract or from secondary infection with other bacteria or viruses. Both disruption of mucosal surfaces and the immunosuppression associated with measles virus, predispose to secondary infection which is thought to occur in over half of children with measles associated pneumonia. Streptococcus pneumoniae is the commonest secondary bacterial infection, whilst parainfluenza and adenovirus are the most frequent viruses. During recovery from measles, cell-mediated immunity is suppressed. Measles infection is known to be associated with the later development of bronchiectasis.

Diagnosis is usually made clinically. However, immunofluorescence of nasal secretions and PCR will both provide a rapid confirmation. Sero-logical tests including complement fixation, haemagglutination inhibition and ELISA are helpful, where a rising titre can be demonstrated.

As bacterial secondary infection is common, routine antibiotic treatment for all children with measles has been practised in many endemic regions. However, this practise is not supported by a recent Cochrane Review of studies (most of poor methodological quality) in over 1400 children with measles. This review found no difference in mortality, in children treated with antibiotics, compared to controls.

Treatment with vitamin A has been shown to be beneficial, although children with measles may not have clinical evidence of vitamin A
deficiency. Vitamin A 200,000 IU given orally, once daily for 2 days reduces the risk of death from measles by 64%. Recovery from pneumonia is more rapid and fewer children develop laryngotracheobronchitis. Measles immunisation is highly effective in preventing measles and reduces mortality in immunised children by between 40–75%. However, paradoxically, when deaths from measles are excluded, this reduction is virtually unchanged. This suggests that immunisation has a non-specific beneficial effect, perhaps through immune sensitisation.

Cytomegalovirus (CMV)

CMV is a DNA virus – one of the largest viruses to infect man. CMV infection may present as a pneumonitis. In otherwise healthy individuals (usually young adults), this may occur as a complication of CMV mononucleosis and causes only mild symptoms. However, in immunosuppressed patients, such as renal transplant recipients, the infection can have a significant mortality.

CMV antigen can be demonstrated in peripheral blood mononuclear cells by means of immunofluorescence and allows rapid diagnosis. PCR can be used to detect CMV DNA in body fluids. Culture of urine and broncho-alveolar lavage specimens may be diagnostic, though gives less rapid results.

Ganciclovir and foscarnet are effective, though toxic, antiviral agents. Where possible, transplanting CMV-positive donor organs or bone marrow to a CMV-negative recipient should be avoided.

Epstein-Barr virus (EBV)

EBV is a double stranded DNA virus, approximately 200 nm in diameter, surrounded by an envelope. By early adulthood, over 90% of healthy individuals will have serological evidence of past EBV infection.

Pulmonary manifestations of EBV in otherwise healthy individuals are rare. Dramatic tonsillar enlargement can lead to severe upper airways obstruction. In patients with cystic fibrosis, EBV has been shown to cause a deterioration in nutrition and pulmonary function which lasts over 6 months after diagnosis of the infection.

The glandular fever screening test, which detects heterophile antibodies, is readily available and is positive in 90% of cases.

Varicella (chicken pox)

Like CMV and EBV, varicella is a herpes virus. It is an enveloped DNA virus 150–200 nm in diameter.
Infection is usually mild when it occurs in early childhood. Hospitalisation of children with varicella is rarely necessary. In the small number of children severe enough to be admitted to hospital, pneumonitis is common. In the immunosuppressed, varicella can be associated with life threatening multi-organ involvement. In children with cystic fibrosis, pulmonary exacerbation can occur, without the typical radiological appearances of varicella. The deterioration in pulmonary function can take up to 18 months to resolve.

Severe infection should be treated with intravenous acyclovir. Immunisation is now available, but is not part of the primary immunisation schedule in the UK.

**Specific atypical pathogens and their clinical syndromes**

*Mycoplasma pneumoniae* and *Ureaplasma urealyticum*

The mycoplasmas are among the smallest free-living organisms which are pathogenic in man. They are deformable rods which pass through bacterial filters and are not seen on Gram staining.

Although infection is endemic in most communities, epidemics occur in 4–7 year cycles. School children are primarily affected. There is an autumn peak, thought to correspond to children returning to school.

*U. urealyticum* is found in the female genital tract and can cause respiratory infection in the new-born. An association between respiratory infection with *U. urealyticum* and the development of chronic lung disease of prematurity has been demonstrated in studies, performed over a decade apart. This is in spite of many innovations in neonatal care. Morbidity due to this infection is seen throughout the first year of life.

Mycoplasma can be isolated from children with asthma more frequently than controls and mycoplasma has been suggested as a precipitating factor for wheeze. Prevalence in children with CF is low, possibly related to difficulties in isolating the organism in the presence of other pathogens. Severe infection has been reported in Down’s syndrome.

The incubation period for *M. pneumoniae* is 2–3 weeks. Classically, a dry cough develops over 1–2 days, with low grade fever. The cough may be debilitating and can be confused with pertussis. Chest pain can occur. Younger children may have upper respiratory infection only. Where pneumonia develops, clinical examination may be unremarkable. Classically, diffuse involvement on the chest radiograph is described. However, in a study of children admitted to hospital with pneumonia, most children with mycoplasma had lobar consolidation on the chest radiograph (see Table 2). Mycoplasma was the commonest single pathogen causing pneumonia in this study.

Traditionally, cold agglutinins are used for rapid diagnosis. These are not specific for mycoplasma infection as they occur also in CMV and...
EBV infection. Neither are they 100% sensitive. Complement fixation tests are helpful retrospectively. New techniques such as PCR can be applied to blood or nasal secretions. However, it may be necessary to combine PCR and serology to achieve maximum sensitivity.

Erythromycin or one of the newer macrolides such as clarithromycin are both effective treatments for mycoplasma pneumonia. Erythromycin reduces the carriage of *U. urealyticum* in the respiratory tract of infants. However, macrolides have not been shown to be effective in preventing the development of chronic lung disease. A large randomised trial is needed.

**Table 2** Numbers of children with pneumonia, having different radiological appearances

<table>
<thead>
<tr>
<th>Organism</th>
<th>Lobar consolidation</th>
<th>Alveolar consolidation</th>
<th>Non-alveolar changes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><em>Mycoplasma</em></td>
<td>11</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td><em>Pertussis</em></td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><em>Chlamydia</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Virus</em></td>
<td>14</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td><em>No diagnosis</em></td>
<td>29</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

From a prospective study of 89 children. Radiological appearances are subdivided by type of pathogen. Three children had co-infection with both viral and bacterial pathogens. Reproduced from Clements et al with permission of the BMJ Publishing Group.

**Chlamydia trachomatis, Chlamydia pneumoniae and Chlamydia psittaci**

Chlamydia is an obligate intracellular parasite. Three species of chlamydia are pathogenic in man.

*C. trachomatis* can cause pneumonia in the new-born. This occurs in around 16% of infants of mothers who carry the organism in the birth canal. Infants may present up to 8 weeks of age with cough and tachypnoea. Diagnosis relies on culture of nasal secretions or microscopy of conjunctival scrapings, if conjunctivitis co-exists. Treatment is with erythromycin. At follow-up to 8 years, there is a higher prevalence of wheezing in children who had pneumonia due to *C. trachomatis* before 3 months of age.

*C. pneumoniae* is a common cause of community-acquired pneumonia in school-age children, accounting for 10% of cases in one study (31% in secondary school age children). The incubation period is approximately 21 days. Symptoms may initially be upper respiratory, followed by prolonged cough. Treatment is with erythromycin or another macrolide, although the cough may persist for months after treatment. There has been recent interest in a possible role of *C. pneumoniae* in the pathogenesis of coronary artery disease. Patients hospitalised with coronary artery disease are more likely to be seropositive for *C. pneumoniae* than age-matched.
controls and \textit{C. pneumoniae} has identified, by PCR, in atheromatous plaques.

\textit{C. psittaci} is a zoonosis, acquired from birds (virtually any species). It causes a spectrum of clinical illness varying from mild ‘flu-like symptoms, through to a mononucleosis like syndrome or an atypical pneumonia. Diagnosis is by serological testing and treatment is with erythromycin (or a tetracycline antibiotic in children over 12 years).

\textit{Legionella pneumophila}

\textit{Legionella} is a Gram-negative, aerobic organism. The organism survives in warm water (up to 60°C) and has been found in the humidification system for incubators in a neonatal nursery. Transmission is by inhalation of an aerosol or by ingestion of contaminated water. Legionnaire’s disease can vary in severity from a mild illness with cough and fever, to a severe, life-threatening pneumonia. Around 10% of children in hospital will have serological evidence of past infection. Seroprevalence is higher in children with asthma than in controls. Diagnosis is serological or by culture of the organism. \textit{Legionella} is an intracellular pathogen and effective antibiotics include macrolides, quinolones and co-trimoxazole.

\textit{Coxiella burnetti} (Q fever)

This rickettsial infection is a zoonosis. The animal reservoir includes domestic animals such as cattle and sheep. Urine, faeces and particularly birth products, such as placenta, are infectious. Infection is by the aerosol route. In one study, serological evidence of acute infection was found in a third of school-age children with an influenza-like illness. When the organism causes pneumonia, fever is universal and is accompanied by dry cough. Clinical features are non-specific and diagnosis is serological. Erythromycin, which is often the first line antibiotic in atypical pneumonia, may not be effective and rifampicin can be added or a quinolone substituted.

\textbf{Key points for clinical practice}

- Viral and ‘atypical’ organisms are the most common cause of pneumonia in children in the industrialised world
- The clinical and radiological appearances may be indistinguishable from bacterial pneumonia
- Vulnerable groups of infants or children may have a more severe clinical illness
- Where no organism has been isolated and pneumonia has failed to respond to first line antibiotics within 48 h, empiric therapy with a macrolide will cover many atypical organisms
References

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