Childhood pneumonia: an update in the post-COVID-19 era

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Abstract

Community acquired pneumonia is the leading global cause of death in childhood. Whilst COVID-19 infection does not typically cause severe illness in children the subsequent social isolation, along with changes in hygiene practices led to reduced levels of respiratory viruses and bacteria during the pandemic. This caused a significant change in the seasonality of community acquired pneumonia. Viruses are still the most common cause of community acquired pneumonia, however bacteria can cause more severe disease and it can be difficult to distinguish clinically between them. Generally, children with pneumonia can be managed at home with antipyretics, oral hydration and oral antibiotics, however a small subset need admission to hospital. Complications from pneumonia include pleural effusion, empyema, necrotizing pneumonia and pneumatocele. This article aims to direct physicians on the diagnosis and management of community acquired pneumonia and highlight the key changes since the COVID-19 pandemic.

Keywords Chest infection; childhood; paediatric; pneumonia; post-pandemic

Introduction

Pneumonia is a lower respiratory tract infection involving the bronchi to the alveoli. An inflammatory response occurs in response to infection causing fluid and exudate to accumulate in the alveoli affecting gas exchange. Pneumonia can be caused by any infective agent; bacteria, virus and fungus. Paediatric pneumonia is a significant burden across health services with pneumonia being the leading cause of death in children worldwide.

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The COVID-19 pandemic resulted in widespread quarantine and social isolation that resulted in an epidemiological change to paediatric pneumonia. In a peculiar juxtaposition with adult patients, paediatric pneumonia rates dropped.[1] There was also a reduction in PICU admissions by over 3700 in the UK and Ireland, 41% reduction from respiratory illness and a 60% reduction in bronchiolitis.[2] The assumed cause of this phenomenon is two-fold;

1. Children infected with Severe Acute Respiratory Syndrome *Coronavirus 2* (SARS-CoV-2) are not severely affected in the same way as adults. Even children with underlying respiratory co-morbidities remained relatively unscathed during the pandemic. Based on the findings from a study from Cincinnati Children's Hospital Medical Centre, it has been postulated that children have a different immune response to SARS-CoV-2 than adults. First, children had more robust and durable antibody responses against SARS-CoV-2. Secondly, there was a rapid induction of mucosal immunity in the nasal tract, which might contribute to the mild course of disease in infants and young children by containing viral replication in the nose.[3]
2. During the pandemic there was a significant reduction in non-SARS-CoV-2 respiratory viruses circulating due to public health measures including school closures, wearing of face masks, social distancing and travel restrictions.[1] However, post-lockdown, the viruses have made a return and there has been a shift in the seasonality of these illnesses.

Signs and symptoms

Paediatric presentation of pneumonia has not changed since the COVID-19 pandemic. Symptoms of pneumonia include cough, pyrexia, malaise, shortness of breath and chest pain. In young children, symptoms can be inconspicuous such as reduced feeding. These lower respiratory tract symptoms may be associated with upper respiratory tract symptoms, particularly in viral cause, such as rhinorrhoea and a sore throat.

Typical signs of pneumonia in children include tachypnoea, increased work of breathing, and tachycardia. On examination, signs of increased work of breathing may be evident e.g. tracheal tug, subcostal recession, intercostal recession and use of accessory muscles. On auscultation, reduced air entry, wheeze and coarse crepitations may be present. The percussion note over the affected area of lung will often be dull, or stony dull if there is an associated parapneumonic effusion. If a child is hypoxic (SpO_2 less than 94%) but no signs are heard on auscultation further investigation is warranted. If a child is showing signs of severe disease, they should be admitted to hospital (Table 1).

Chronic disease should be considered as part of the differential diagnosis, particularly if recurrent presentation. These would include congenital heart disease, chronic lung disease of prematurity, cystic fibrosis, bronchiectasis and immunodeficiency.

Pathophysiology

Infection within the lower respiratory tract causes pneumonia by triggering inflammation and cell death of the epithelium of the bronchi and alveoli. This in turn causes further inflammation and exudate to accumulate in the alveoli which affects gas exchange causing hypoxia. Hypoxia leads to tachypnoea and increased

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Signs of severe disease by age group[4]

Infants	Older child
O_2 sats <92%, cyanosis	O_2 sats <92%, cyanosis
Respiratory rate (RR) >70 breaths/min	RR >50 breaths/min
Significant tachycardia for level of fever	Significant tachycardia for level of fever
Capillary refill >2 s	Cap refill >2 s
Difficulty breathing	Difficulty breathing
Intermittent apnoea, grunting	Difficulty breathing, grunting
Not feeding	Signs of dehydration

Table 1

work of breathing and use of accessory muscles. Trapped secretions and inflammation lead to wheeze and cough.

Pneumonia can be classified based on radiological appearance. Opacity is a radiological term to describe an area of density on an X-ray (appears white). Bronchopneumonia appears on X-ray as bilateral opacification (consolidation) (Figure 1). In bronchopneumonia, the chest X-ray appears patchy with peri-bronchial thickening and ill-defined air-space opacities most commonly at the base. Lobar pneumonia is diffuse consolidation involving one entire lobe of the lung (Figure 2) and this can lead to collapse of that lobe. This may be difficult to pick up because rather than being a large consolidation, the lobe has completely collapsed and therefore no air is getting in (in a sense it may appear to have disappeared). The adjacent lobe will often fill the space left behind but overall, the lung should appear reduced in volume compared with the contralateral lung. For example, the 'Sail Sign' is collapse of the lower left lobe behind the heart (Figure 3). Round pneumonia on X-ray is depicted as an encircled area of consolidation localized to one area of the lung (Figure 4).

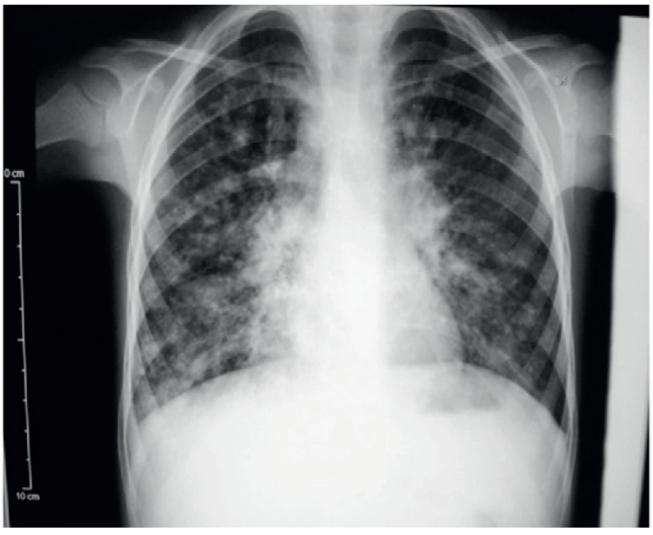

Figure 1 Bronchopneumonia. The chest X-ray shows patchy, ill-defined air space consolidations with peri-bronchial thickening. This is in keeping with bronchopneumonia. Reproduced from reference 5 with permission from Elsevier.

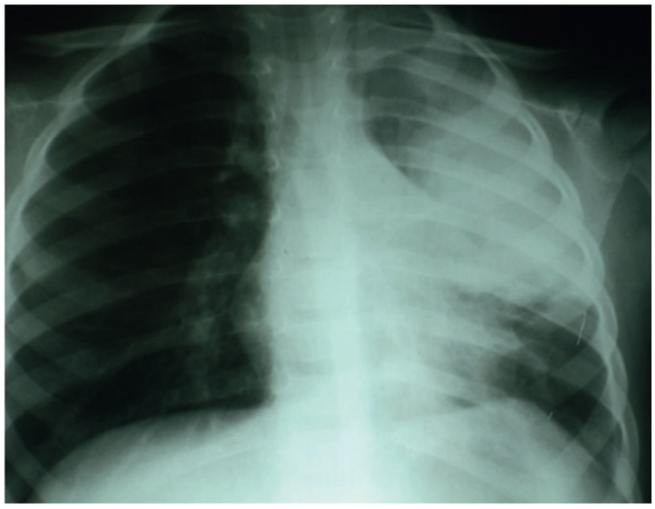

Figure 2 Lobar pneumonia. The chest X-ray shows diffuse consolidation involving one entire lobe of the lung (the left upper lobe). Reproduced from reference 5 with permission from Elsevier.

Round pneumonia is more common in the lower lobes and is associated with children under the age of 8 years. It is hypothesized that adults do not develop round pneumonia as adults have well developed Pores of Kohn and Canals of Lambert which allows infection to disseminate into the lobe and cause lobar pneumonia.[6]

Rarely, severe forms of pneumonia may result in the formation of lung abscess, a complete breakdown of tissue and formation of pus-filled pockets in focal areas of the lung. Also, the

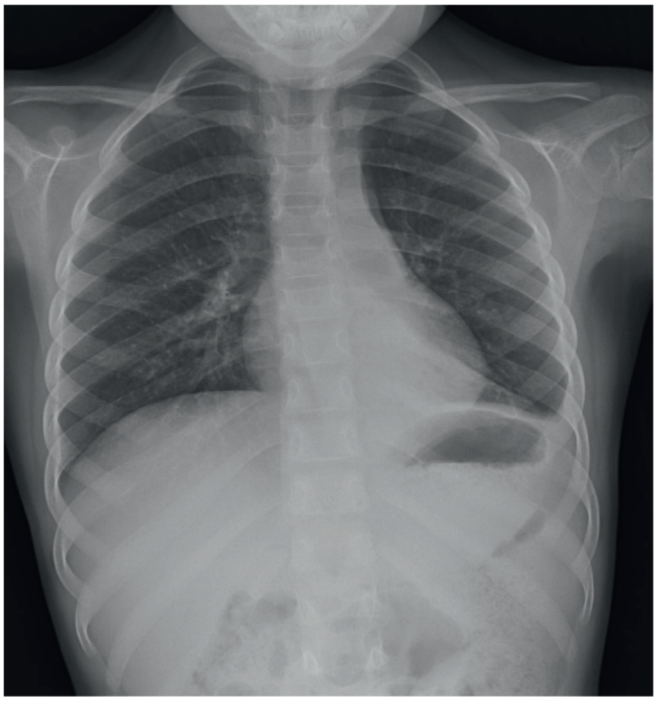

Figure 3 Sail Sign. The chest X-ray shows a discrete line behind the left heart. Inferior to this is a dense consolidation in a triangular shape. This represents the collapsed left lower lobe and there is then associated volume loss in the left lung overall. This is known as the 'sail sign'.

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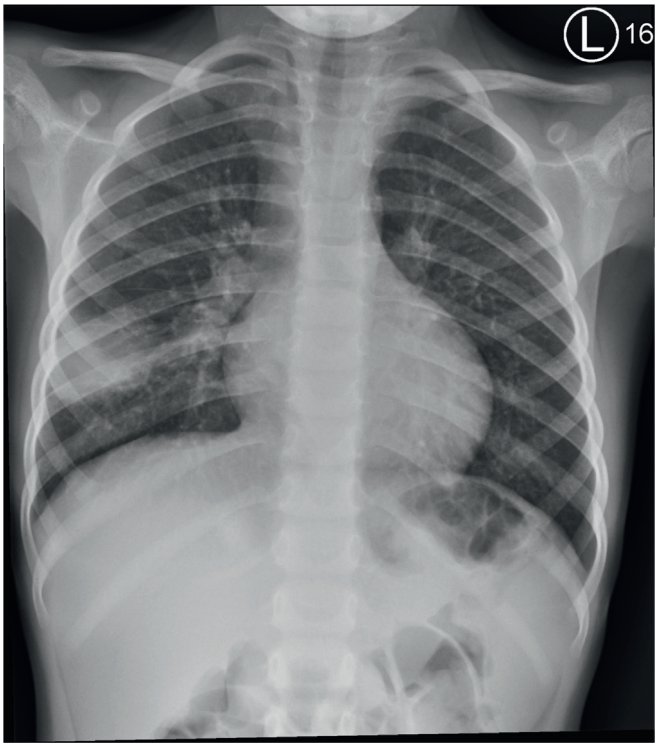

Figure 4 Round pneumonia. The chest X-ray shows an encircled area of consolidation localized to one area of the lung.

infection may spread to the pleural space forming a fibrinopurulent exudate filling this space known as empyema (see later for more details on complications of pneumonia).

In lobar pneumonia, there are 4 main histological changes that occur:

1. Congestion — alveolar oedema and vascular congestion occurs in the first 24 hours. Bacteria and neutrophils are present.
2. Red hepatization — the airspaces within the lungs gather exudates containing red blood cells, neutrophils and fibrin. This occurs within day 2—4 of infection.
3. Grey hepatization — this stage occurs 2—3 days later. Red blood cells begin to breakdown and there is accumulation of haemosiderin.
4. Resolution — this occurs over the course of 3 weeks. Infiltrates are reabsorbed and lung parenchyma is restored.

Pathogens

Community acquired pneumonia (CAP) can be caused by viruses, bacteria and fungi. Viruses account for over 50% of pathogens. Bacterial infections are more likely to cause serious infection and require hospital admission.

Viruses

Common viruses include Respiratory Syncytial Virus (RSV), Influenza, Parainfluenza, Rhinovirus, Metapneumovirus, Coronavirus and Adenovirus. In the neonatal population, TORCH infections are a potential cause of congenital pneumonia such as cytomegalovirus (CMV) and herpes simplex virus (HSV).

Since COVID-19 there has been a change in the typical seasonal pattern of respiratory tract pathogen transmission. Prior to the COVID-19 pandemic, RSV and Influenza were mainly seasonal illnesses with RSV rates rising from September through to early spring with a peak in January. However in 2021, as a consequence of the public's re-emergence from 'lockdown' and a population of infants naïve to RSV, there was a peak of RSV infection in July and more children were hospitalized over the summer months.[7]

COVID-19

SARS-CoV-2 is a new strain of Coronavirus. COVID-19 was the name given to the disease caused by SARS-Cov-2. SARS-Cov-2 is highly contagious and causes symptoms similar to other respiratory viruses. Symptoms include malaise, pyrexia, fatigue, myalgia, ageusia and anosmia. Most children infected are well enough to be managed at home. Special considerations are required for those children with co-morbidities including complex neuro-disability, raised body mass index (BMI), immunodeficiency, pre-existing respiratory disease, complex genetic or metabolic conditions or multiple congenital abnormalities.[8] It should be noted that severe illness is rare, and children account for 0.5% of COVID-19 deaths[9] and only 1% of hospitalizations.[10]

Bacteria

Streptococcus pneumoniae is the most common pathogenic bacteria to cause pneumonia. Pneumococcal conjugate vaccine (PCV) was first licenced in 2000 and since then diseases due to subtypes included in the vaccine have dropped to negligible levels in those vaccinated.[11] Other common bacterial pathogens include *Haemophilus influenza*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Moraxella catarrhalis* and *Mycoplasma pneumoniae*.

Children who culture gram-negative bacteria such as *Pseudomonas aeruginosa* or *Burkholderia cepacia* are more likely to have impaired immune responses. These are typically seen in children with cystic fibrosis but are pathogenic in many other chronic lung conditions.

M. pneumoniae is an atypical pathogen that is more likely to cause bronchopulmonary pneumonia. Other causative agents of atypical pneumonia include *Legionella pneumoniae* and *Chlamydia pneumoniae*. These organisms are usually intra-cellar and are difficult to culture. Post the COVID-19 pandemic, in a similar trend to that seen in the change of viral seasonality, there has been an increased incidence of *M. pneumoniae*-related pneumonia in children. The WHO attributed these cases to an immunity gap in a cohort of children who were isolated, resulting in large outbreaks once exposure to these pathogens returned.[7]

Tuberculosis should be considered in children with risk factors such as travel to endemic countries or positive contact. Children with tuberculosis present with a chronic cough, weight loss, fever, fatigue and night sweats. Chest X-ray may show hilar lymphadenopathy with focal consolidation. Miliary TB can show diffuse nodularity.

Viral-bacterial co-infection is commonly seen and may be a result of viruses enabling bacterial colonization and enhancing bacterial infection. Viruses disrupt the respiratory epithelium and alter the immune response increasing risk of bacterial co-infection. Bacterial co-infection is more likely to have poorer

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outcomes including admission to intensive care and increased duration of mechanical ventilation.

Fungi

Fungal infections are a rare cause of CAP but are important to consider especially in the immunocompromised patient. *Aspergillius Fumigatus*, *Pneumocystic jirovecii* and *Candida albicans* are common fungi involved in pneumonia. Infections are more difficult to treat and have a higher mortality rate. Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity reaction to *A. fumigatus*. It more commonly affects patients with asthma and cystic fibrosis. Patients can present with wheeze and dyspnoea, but also productive cough, fever and malaise.

Table 2 lists the common pathogens causing pneumonia in children.

Diagnosis

Microbiological tests

Swabs from the pharynx can be used for Polymerase Chain Reaction (PCR) testing of viruses. PCR involves isolation of DNA or RNA from the sample. DNA or RNA primers for a known pathogen amplify positive sequences with each replication cycle. The more DNA or RNA in the sample that is positive for the pathogen, the lower the number of replication cycles it takes to detect the DNA/RNA (this is reported as the CT (cycle threshold) count). PCR testing is highly sensitive but can result in a false positive diagnosis. Rapid, point of care (POC) testing for common viruses is possible using PCR techniques. The use of this technology has expanded since the COVID-19 pandemic and is accessible in many emergency departments. This can provide a quick diagnosis of a limited number of viruses such as SARS-Cov-10, RSV and Influenza. However, availability varies between hospitals and these tests have low sensitivity.

Gram stain and culture is used to identify bacteria. These tests can be performed on sputum, bronchoalveolar lavage or cough swabs. Sputum samples are difficult to obtain in children as most swallow their sputum. Cough swabs (where a swab is held in the oral cavity while the child coughs) are easier to obtain but less sensitive. Bronchoalveolar lavage is commonly performed if a child is intubated in the intensive care environment or via flexible bronchoscopy if the child is being investigated for chronic symptoms.

Urinary antigens for *S. pneumoniae* and *legionella* can be identified; however, they are not commonly used due to lack of specificity.

Blood tests

Useful haematological investigations include a blood culture, c-reactive protein (CRP), full blood count (FBC) and anti-streptolysin O titre (ASOT). Blood cultures should be routinely taken if sepsis is suspected in a child and ideally taken pre-antibiotic administration, however if antibiotics have already been commenced, this shouldn't stop blood cultures being obtained.

CRP is a frequently used inflammatory marker. It is a sensitive marker for both viral and bacterial infections however, it does not allow the clinician to differentiate between these. A very high result that is consistently elevated would be suggestive of an undertreated bacterial infection. A high white cell count (WCC) is not specific for bacterial infection though the differential, specifically neutrophils are typically elevated in bacterial infection. Lymphocytes are elevated in COVID-19 along with other viral infections. ASOT may be useful to identify streptococcal infections, but this test is not specific for pneumonia.

Imaging

Chest x-rays are commonly performed on adults presenting with signs of pneumonia however they are not performed routinely in the paediatric population. This is because chest x-rays are neither sensitive nor specific and do not usually change management of the patient. Chest x-rays vary in quality and are often open to interpretation. If a chest X-ray is performed, the British thoracic society (BTS) do not recommend routine follow up chest X-ray unless there are complications.[4] Ultrasound is not routinely performed to diagnose pneumonia. Nevertheless, more studies are showing that ultrasound is a safe, non-invasive means of diagnosis compared to X-ray.[4]

CT scans are not routinely used to evaluate pneumonia in the paediatric population. However, one may be required if the patient is not responding to antibiotics and to evaluate for complicated pneumonia.

Management

It is important to consider whether a child needs an acute hospital admission for management of their illness. A lower threshold should be used in children with chronic lung disease, immunodeficiency, neuromuscular disorders, congenital heart disease, infants under 3 months and those who were born at less than 32 weeks. Distance from hospital and carers' ability should also be taken into consideration. Children should be admitted if they require oxygen or if they have significant dyspnoea. General

Common pathogens causing pneumonia in children[5]

Age	Viruses	Bacteria
<20 days	HSV, CMV	*E. coli*, Group B Strep, Listeria
3 weeks—3 months	Adenovirus, RSV, Parainfluenza, Influenza	*Chlamydia trachomatis, S. pneumoniae, Pertussis, H. Influenzae, S. aureus, Moraxella catarrhalis*
4 months—5 years	Adenovirus, Rhinovirus, Influenza Parainfluenza, RSV, Varicella Zoster	*S. pneumoniae*, Mycoplasma *H. influenza, S. aureus*
>5 years	Influenza, Epstein Barr virus, Rhinovirus, Adenovirus	*S. pneumoniae*, Tuberculosis, Mycoplasma, *S. aureus*

Table 2

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management includes ensuring adequate oxygenation. Oxygen saturations should be aimed at greater than 94%. Signs of dehydration and hypovolaemia should be treated appropriately. Fever can be managed with antipyretics.

Antimicrobials

If a child does not require hospital admission but has signs and symptoms of pneumonia, antibiotics should still be considered as bacterial and viral infections cannot easily be distinguished from each other. Empiric antibiotic choices should follow local guidance to cover for the most common bacteria. Typically, the recommended first line antibiotic of choice is amoxicillin. Clarithromycin is an alternative in children with penicillin allergy or if *M. pneumoniae* infection is suspected.

The combination of wheeze in association with coryzal symptoms is indicative of a viral process and antibiotics may be withheld in this circumstance. However, should the patient's symptoms not improve then antibiotics should be prescribed.

Evidence of pulmonary infiltrates on chest radiograph is more indicative of a bacterial cause but not every child with mild symptoms of pneumonia warrants imaging and so this information is not always readily available, particularly in the primary care setting where most children first present.

Care givers should be given advice with regards to fever management and the importance of hydration. They should also be advised of warning signs including cyanosis, apnoea, dehydration and increased work of breathing. If symptoms are persisting for greater than 48 hours post antibiotic therapy or they are concerned about their child, then they should attend the emergency department.

If the child is clinically unwell and requires hospital admission, intravenous antibiotics should be considered. Again, antibiotic choice should follow local guidance but would typically include cover for *S. pneumoniae* with amoxicillin or a cephalosporin. If intravenous fluids are required, fluid balance should be monitored along with urea and electrolytes as these children are at an increased risk of syndrome of inappropriate anti-diuretic hormone (SIADH).

COVID-19

Children with mild to moderate infection with COVID-19 do not routinely need admission to hospital.[8] For children admitted with pneumonia where COVID-19 is felt to be the cause, National Institute of Clinical Excellence (NICE) advises the use of remdesivir (an inhibitor of viral RNA polymerase). Intravenous remdesivir is indicated in children from 4 weeks old if they weigh over 3 kg, have pneumonia and require supplemental oxygen, or if they weigh more than 40 kg and are at serious risk of severe illness.[12]

NICE also recommends the use of corticosteroids in the management of COVID-19. Indications include patients that require the use of supplemental oxygen during hospital admission. The course of corticosteroids is for 10 days but this can be reduced if the patient has side effects or are well enough to be discharged from hospital.

It should also be noted that these children are at an increased risk of pulmonary embolism, and this should be considered in a child who has an increasing oxygen requirement, hypovolaemia or tachycardia.[8]

Physiotherapy

Chest physiotherapy is not routinely recommended in the management of pneumonia in children as it may prolong fever and exacerbate breathing difficulties. However, chest physiotherapy should be continued in children who routinely use physiotherapy for airway clearance. If a child becomes acutely unwell and mucous plugging is suspected, assisted airway clearance may be beneficial.

Complications

Most children make a full recovery from pneumonia however around 3% will end up with a complication. Complications can include parapneumonic effusion, empyema, abscess formation, necrotizing pneumonia and pneumatocele.

Empyema and pleural effusion

Parapneumonic pleural effusions are a result of the accumulation of fluid in the intrapleural space. This is a result of inflammation affecting cell membrane permeability allowing exudate to accumulate. This occurs in 1% of CAP but up to 40% of patients admitted to hospital with pneumonia.[13] An effusion should be suspected if pyrexia is persistent for over 7 days or 48 hours with adequate antibiotic therapy. Empyema is the result of the accumulation of neutrophils and bacteria in the effusion. On examination, there is dullness to percussion. A chest X-ray should be performed if an effusion is suspected (Figure 5) and ultrasound can be used to estimate the volume and complexity of fluid and the presence of thickening or septations.

There is a lack of evidence and therefore no clear guidance on what is the most effective treatment. Often the decision comes down to the particular clinician or centre's own experience and the local expertise available.

Some centres advocate for the early use of Video assisted thoroscopic surgery (VATS) to debride the pleural space before leaving in pleural drains. This can shorten length of antibiotic duration. Other centres use pleural drains in conjunction with fibrinolytic agents (urokinase) to break down the connective tissue within the effusion when it has become loculated.

Pleural fluid can be sent for direct microscopy, culture, lactate dehydrogenase and PCR. This can allow for more targeted antibiotic therapy. However, as in most cases antibiotics will already have been administered, cultures from pleural fluid are notoriously difficult to grow and are often 'falsely' negative.

The mainstay of treatment for all patients with parapneumonic effusion is intravenous antibiotics. Local trust antimicrobial guidelines should be followed and antibiotics should cover for *S. pneumoniae* infection. In the post-COVID era, *S. pyogenes* has become a more common pathogenic cause of pleural effusion. Holdstock et al. showed increased rates of GAS (Group A Streptococcus/*S. pyogenes*) isolated in children presenting with pleural effusion. There was also an increase in the number of children requiring intrapleural drainage. The group hypothesized that this was due to a resurgence of viral upper respiratory tract infection post-lock-down and a waning immunity to GAS.[14]

Empiric antibiotic choices include cephalosporins, macrolides and clindamycin. Clindamycin acts to reduce exotoxin

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production from the causative bacteria and is commonly discontinued once the fever resolves. Combination therapy with two of these agents is often preferred and a prolonged course of up to 6 weeks is often required.

Necrotizing pneumonia and lung abscess

Necrotizing pneumonia is the liquefaction of the lung parenchyma resulting in gangrene. There is loss of parenchymal architecture and eventual replacement by small air or fluid filled cavities. The most common bacteria associated with necrotizing pneumonia is *S. pneumoniae*. Abscess formation is a collection of pus within the lung parenchyma.

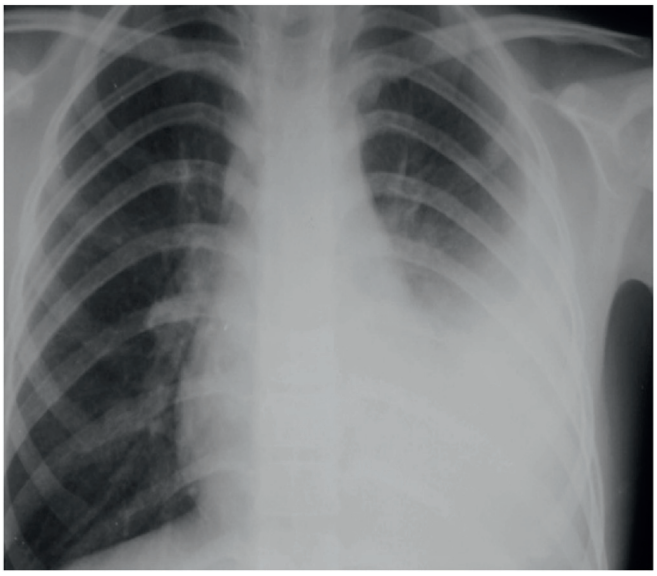

Figure 5 Pleural effusion. This chest X-rays show dense consolidation in the lower zone of the left lung. The costophrenic angle has been completely obscured (blunted) by consolidation and therefore there is presumed fluid accumulation. Reproduced from reference 5 with permission from Elsevier.

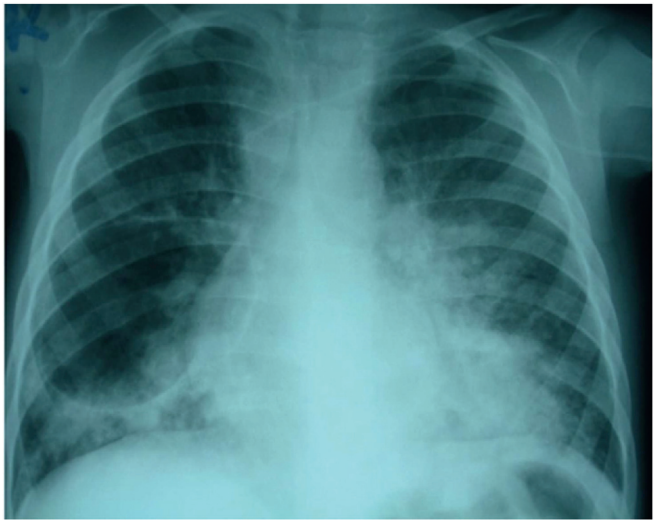

Figure 6 Pneumatocele. This chest X-ray shows a well circumscribed circular region in the right lung which is filled with air. Reproduced from reference 5 with permission from Elsevier.

Both necrosis and abscess formation should be assessed by a CT scan. Abscess with pleural effusion may require drainage. Both necrosis and abscesses require a prolonged course of antibiotics. Long term complications include chronic cough, bronchiectasis and scarring.

Pneumatocele

Pneumatoceles are air-filled cysts within the lung parenchyma. As the bronchus becomes narrowed by infection and inflammation, a ball-valve mechanism occurs resulting in dilation of the alveoli with air unable to escape the cystic space. Pneumatoceles can be confused for abscess formation on chest X-ray, however pneumatoceles usually resolve without intervention. It is therefore important to distinguish between the two (Figure 6).

Conclusion

While the general principles and presentation of paediatric pneumonia have not changed, the COVID-19 pandemic did alter the epidemiology. While rates of pneumonia initially plummeted, there has been a resurgence in both viral and bacterial causes with changes to previously long standings trends regarding aetiology and seasonality. It is important we react to these changes to ensure that patients are receiving the most effective treatment as quickly as possible. ◆

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Practice points

- Carefully examine all children with a fever for signs of pneumonia. Tachypnoea, fever and cough are the most sensitive signs. Dull percussion note is a specific marker of pneumonia
- Sicker children or those with complications such as parapneumonic effusion will benefit from intravenous antibiotics and clindamyci
- Since the pandemic, the effects of seasonality on viral infection has waned and there has been an increase in some types of bacterial infection e.g. Group A Streptococcus

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