



Investigation of the child with recurrent pneumonia

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In this series, we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

Incidence and definitions

Pneumonia occurs often in Australian children and is an important reason for hospitalisation, especially in those aged less than 5 years. The incidence of pneumonia in Australian children is five to eight cases per 1000 children per year.¹ A subset of these children will present with recurrent pneumonia, which is defined as two or more episodes in a year or three or more episodes ever, with radiographic clearing between episodes.²

The true incidence of recurrent pneumonia is unknown, although retrospective studies of hospitalised patients report an incidence of 6 to 9%.³⁻⁵ A systematic approach to recurrent pneumonia will identify those children who potentially have more serious conditions while not over-investigating those with recurrent viral illnesses or unrecognised asthma.

The child with recurrent 'chest infections' can be a significant diagnostic challenge. Healthy preschool children have an average of six upper respiratory tract infections each year.⁶ This has been attributed to the delay in maturation of the immune system, day-care attendance, parental smoking and environmental pollution, greater sibling number and shorter breastfeeding duration. Viruses or atypical bacteria are the main aetiological agents, and the child usually has a self-limiting or easily managed condition.^{7,8}

In a number of cases, however, serious underlying pathology, either structural or systemic, predisposes the child to recurrent infections, which if undiagnosed or diagnosed late may lead to progressive and/or irreversible lung damage. The aim of this article is to assist the physician in identifying those children who require further investigation.

IN SUMMARY

- Recurrent pneumonia is defined as two or more episodes in a year or three or more episodes ever, with radiographic clearing between episodes.
- A systematic approach to recurrent pneumonia will identify those children with potentially more serious conditions while not over-investigating those with recurrent viral illnesses or unrecognised asthma.
- A persistent wet cough is abnormal in childhood (a recurrent wet cough is, however, common in children under the age of about 5 years, who have frequent viral lower respiratory tract infections and/or asthma).
- An estimated 6 to 9% of children hospitalised with pneumonia have had a previous episode: most of these children have an identifiable predisposing condition.
- A delay in diagnosis of the underlying cause of recurrent pneumonia may be associated with a significant decline in lung function and bronchiectasis.
- Children with focal disease, failure to thrive, comorbidities or chronic suppurative symptoms require specialist assessment.

Causes of recurrent pneumonia

Although there are several review articles on recurrent pneumonia in childhood,⁹⁻¹⁴ there are only a few recent or sufficiently large primary studies of children with recurrent pneumonia,^{3-5,15,16} especially from developed countries.^{3,5} Determining the incidence and aetiology is further complicated by the lack of adequate radiological follow up. Most recommendations for the management of childhood pneumonia advise against obtaining a follow-up film if the child is clinically well.¹⁷⁻¹⁹ In the absence of documented radiological resolution, recurrent pneumonia may therefore be misdiagnosed as persisting pneumonia (defined as the persistence of radiographic abnormalities for more than three months),² which may have a more focal cause.

Table 1 summarises the current literature on the causes of recurrent pneumonia in children.

Clinical evaluation

History

It is important to determine the onset, duration, severity and outcome of all previous episodes of pneumonia in addition to the current one. Cough is one of the most common symptoms in children presenting to Australian GPs. Most childhood coughing illnesses resolve within two weeks (acute cough). Chronic cough (lasting more than four weeks) or a productive (wet) cough usually indicates an underlying condition. A wet cough lasting longer than four weeks or purulent sputum is always abnormal in childhood and should be investigated.

Feeding difficulties such as choking, gagging, or coughing with food suggest direct aspiration due to oropharyngeal inco-ordination, whereas vomiting or regurgitation after meals suggests gastro-oesophageal reflux (GOR). A nocturnal cough may indicate asthma or GOR. The finding of abdominal distension, steatorrhoea and failure to thrive in the context of respiratory symptoms is suggestive of cystic fibrosis, while an acute choking event implicates an inhaled foreign object. Recurrent skin, upper respiratory or gastrointestinal infections in infancy are common presentations of immunodeficiency.

The age of the child, his or her general health and the site of the pneumonia can be helpful clues to the possible aetiology. As previously mentioned, preschool children can have as many as six acute respiratory illnesses in a year,⁶ and up to one-third

Investigating recurrent pneumonia in children

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An underlying cause is found in most children with recurrent pneumonia and may include recurrent viral infections (with or without a history of asthma), pulmonary aspiration (usually in the neurologically impaired child), immune defects and congenital lung anomalies. Children with focal disease, failure to thrive, comorbidities or chronic suppurative symptoms are most likely to have a significant predisposing condition and require specialist assessment.

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of these cases have lower respiratory tract involvement.⁸ *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are increasingly recognised as causes of recurrent respiratory illnesses, including community-acquired pneumonia,^{7,20} and co-infection with two or more pathogens is present in up to one-third of cases.^{20,21}

A personal or family history of asthma or other atopic conditions such as allergic rhinitis and eczema is an important association. A past

continued

Table 1. Recent studies of recurrent pneumonia in children

Authors and setting	Demographics	Main findings*
Carbezuelo et al, ³ Spain, tertiary hospital, 1994-2003	1644 children hospitalised with pneumonia; 106 (6.4%) children met recurrent pneumonia diagnostic criteria; age: 1 month to 14 years	Cause identified in 92 patients (86.7%) <ul style="list-style-type: none"> • Asthma 30.4% • Congenital heart defects 29.3% • Aspiration 27.1% • Immune disorder 9.7% • Pulmonary anomalies 2.1%
Ciftci et al, ⁴ Turkey, tertiary hospital, 1997-2002	788 children hospitalised with pneumonia; 71 (9%) children met recurrent pneumonia diagnostic criteria; age: 3 months to 12 years	Cause identified in 60 patients (85%) <ul style="list-style-type: none"> • Asthma 32% • Gastro-oesophageal reflux 15% • Immune disorders 10% • Congenital heart disease 9% • Lung anomalies 6% • Cystic fibrosis 3%
Owayed et al, ⁵ Canada, tertiary hospital, 1987-1997	2952 children hospitalised with pneumonia; 238 (8%) children met recurrent pneumonia diagnostic criteria; age: 2.5 months to 15.6 years	Cause identified in 220 patients (92%) <ul style="list-style-type: none"> • Aspiration 48% • Immune disorders 10% • Congenital heart disease 9% • Asthma 8% • Lung anomalies 8%
Lodha et al, ¹⁵ India, tertiary hospital, 1996-2000	2264 children with various respiratory conditions; 70 children met recurrent pneumonia diagnostic criteria; age: 3 months to 12 years	Cause identified in 59 patients (84%) <ul style="list-style-type: none"> • Aspiration 24.2% • Immune disorders 15.7% • Asthma 14.2% • Lung anomalies 8.6% • Primary ciliary dyskinesia 7.1%
Heffelfinger et al, ¹⁶ Haiti, tertiary hospital, 1998	103 children met recurrent pneumonia diagnostic criteria; age: 7 months to 7.75 years	<ul style="list-style-type: none"> • Asthma 79% • Tuberculosis 2% • IgA deficiency 1% • HIV infection 0%

* Percentages given for each individual cause are the percentages of the total cohort and not just of those in whom a cause was identified.

history of prematurity and chronic neonatal lung disease, congenital abnormality of the respiratory tract such as tracheo-oesophageal fistula, congenital heart disease or neurological impairment should be determined. In addition, an environmental history, including day-care attendance, exposure to environmental tobacco smoke and pollutants, household crowding, number of siblings and contacts with possible infected family members provides insight into possible risk factors (Table 2).

Examination

Failure to thrive and poor development are important signs suggesting serious underlying pathology. The classic signs of acute pneumonia are:

- fever
- tachypnoea (generally a respiratory rate >60 breaths/min in neonates to 6-month-old infants; >40 breaths/min in 6- to 12-month-old infants; >35 breaths/min in preschool children; >30 breaths/min in primary school-aged children; and >20 breaths/min

in high school-aged children)

- use of accessory muscles
- dullness to percussion
- reduced air entry
- crackles.

The presence of wheeze is highly suggestive of asthma but certain infections, such as *M. pneumoniae* infection, and structural abnormalities of the airways can also present this way. Digital clubbing (Figure 1) suggests bronchiectasis and requires investigation. Nasal polyps may indicate asthma, cystic fibrosis or primary

Table 2. Determining key clinical features

Questions to answer in the history	Comments
At what age did the symptoms begin?	Recurrent pneumonia due to immunodeficiency syndromes or congenital lung lesions usually presents in early infancy
What is the child exposed to in his or her environment – e.g. tobacco smoke, school/day-care attendance, number of siblings, etc?	Such environmental exposure may be associated with recurrent upper respiratory tract infections. Persistent bacterial bronchitis is often under-recognised or misdiagnosed as recurrent pneumonia. Recurrent viral respiratory tract infections and asthma may be misdiagnosed as recurrent pneumonia
Has the child had intermittent episodes of wheeze, eczema, allergic rhinitis or food allergies, or does he or she have a family history of allergy or asthma?	Asthma is commonly associated with the diagnosis of recurrent pneumonia
Has the child had an acute choking episode?	An inhaled foreign body is a common cause of intraluminal obstruction, especially in children aged 6 months to 3 years. However, most episodes are not observed and hence a high index of suspicion for foreign body inhalation is required
Does the child have neurological impairment or feeding difficulties and gagging episodes?	A child with developmental delay or structural abnormalities such as history of tracheo-oesophageal fistula may have direct or reflux aspiration
Does the child have a wet cough that has lasted more than four weeks?	A purulent cough, especially if associated with expectorated sputum, indicates suppurative lung disease and affected children need urgent evaluation
Questions to answer in the examination	
Is the child thriving?	If the child is not thriving, consider cystic fibrosis or immune deficiency and refer to a specialist
Does the child have clubbed fingers or toes?	Suppurative lung disease needs urgent evaluation to prevent bronchiectasis and irreversible loss of lung function
Is wheeze present?	Asthma is the most common underlying cause of recurrent pneumonia
Does the child have a chest deformity such as a pectus carinatum/excavatum or Harrison's sulcus?	Such deformity implies chronic respiratory pathology
Do the clinical signs recur on the same side?	Recurrence on the same side implies a structural cause
Is dextrocardia present?	Dextrocardia is found in 50% of cases of primary ciliary dyskinesia

ciliary dyskinesia. Rashes resembling eczema or *Candida* may be associated with T-lymphocyte abnormalities. Dextrocardia suggests primary ciliary dyskinesia (Table 2).

Investigations

Children with recurrent pneumonia may require more extensive investigation than those with a single episode. Initially, a chest x-ray, full blood count with differ-

ential, C-reactive protein measurement and blood cultures can be performed.

The chest x-ray may show focal or bilateral disease. Recurrent focal disease implies a structural cause and a bronchoscopy is indicated. Patchy areas of atelectasis may be due to mucous plugging in a child with asthma.

In the co-operative child over the age of 5 years, spirometry may help diagnose asthma by either demonstrating a 12%

improvement in FEV₁ after administration of a bronchodilator or a 15% drop in FEV₁ with bronchial challenge testing. If the child is unable to perform spirometry, a therapeutic trial of anti-inflammatory therapy over two to four weeks may help establish the diagnosis.

Table 3 outlines investigations for recurrent pneumonia (which should be guided by the specific history). A high resolution CT scan (HRCT) is indicated in



Figure 1. Digital clubbing associated with bronchiectasis in a young child with cystic fibrosis.

both focal and diffuse disease to exclude structural causes, assess mediastinal lymphadenopathy, and determine the extent and severity of the lung disease. A general anaesthetic is usually required for very young children undergoing HCRT. In some cases a flexible bronchoscopy, for the purpose of assessing airway structure and/or obtaining bronchoalveolar lavage fluid for culture, can be performed under the same anaesthetic. An approach to investigating the child with recurrent pneumonia is given in the flowchart on page 22.

Underlying causes of recurrent pneumonia

Affecting a single lobe or area

Pneumonia recurring in the same area of the lung suggests focal pathology and requires bronchoscopic evaluation. Intraluminal causes, such as mucoid impaction, are most common in children (Table 4).

Inhaled foreign body

An inhaled foreign body is an uncommon cause of recurrent pneumonia (found in only four of 70 children in a study from India),¹⁵ but the most common cause of intraluminal obstruction in children. In most cases the child presents acutely with a history of choking; however, missed and/or unsuspected foreign body inhalation can occur with late presentation

Table 3. Investigations for recurrent pneumonia

Initial investigations

- Chest x-ray
- Full blood count and differential
- Blood culture
- Sputum culture
- Mycoplasma serology

Possible investigations after specialist assessment

- Radiological tests
 - Chest high resolution CT scan
 - Modified barium swallow (video fluoroscopy)
- Haematological tests
 - C-reactive protein
 - IgE and skin prick allergy test
 - Immunoglobulins (IgA, IgM, IgG and IgG subclasses)
 - T- and B-cells and T-cell subsets
 - Neutrophil function
 - Specific antibody production to polysaccharide and protein antigens (response to pneumococcal vaccination and tetanus toxoid)
 - Total haemolytic complement (CH50) and C3 and C4
 - Alpha-1 antitrypsin levels and phenotype
- Pulmonary function test with or without bronchodilator responsiveness
- Sweat test
- Mantoux test
- Bronchoscopy
- Multichannel impedance/pH manometry
- Nasal brushings for assessment of ciliary structure and function
- Nasal nitric oxide

associated with wheezing, cough or recurrent pneumonia.²²

Most inhaled foreign bodies are organic, commonly nuts, vegetables and seeds, and as such are radiolucent. Organic substances can induce a chemical pneumonitis, intense granulation and persistent

Table 4. Underlying causes of recurrent pneumonia

In a single area/lobe of the lung

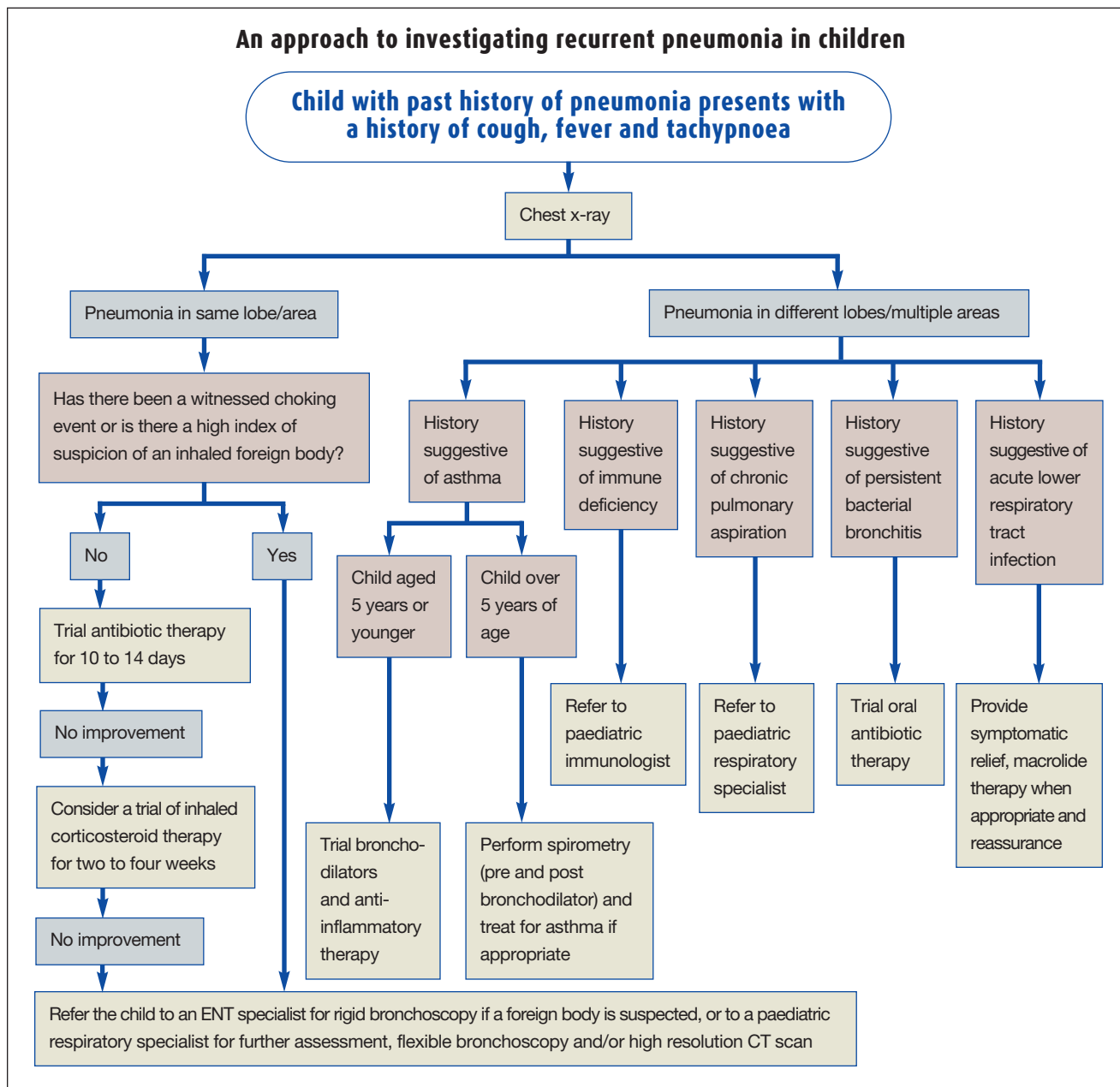
- Intraluminal obstruction
 - Inhaled foreign body
 - Mucoid impaction
 - Endobronchial tumour: bronchial carcinoid, mucoepidermoid tumour
- Extraluminal compression
 - Enlarged lymph nodes: infection, tumour, sarcoidosis
 - Enlarged or aberrant vessels
- Structural abnormalities of airways or lung parenchyma
 - Airway anomalies: bronchomalacia/stenosis, bronchogenic cyst
 - Parenchymal anomalies: congenital lobar emphysema, congenital cystic adenomatoid malformation, pulmonary sequestration
 - Middle lobe syndrome

In multiple areas/lobes of the lung

- Recurrent acute lower respiratory tract infections/persistent (protracted) bacterial bronchitis
- Asthma
- Chronic pulmonary aspiration
- Congenital heart disease
- Mucociliary disorders
 - Cystic fibrosis
 - Ciliary dyskinesia
- Immunodeficiency
 - B-lymphocyte disorders
 - T-lymphocyte disorders
 - Combined B- and T-lymphocyte disorders
 - Complement defects
 - Phagocytic defects
 - Hyposplenism

localised airway damage. Inorganic objects such as buttons and pins are often radio-opaque. Any child with a suspected inhaled foreign body needs referral for a rigid bronchoscopy by an ENT surgeon.

continued



Middle lobe syndrome

Middle lobe syndrome is a distinct clinical and radiological entity defined as persistent atelectasis (more than one month’s duration) and/or recurrent consolidation (two or more episodes) of the right middle lobe or lingula.²³ Middle lobe syndrome involves recurrent cycles of atelectasis, infection and inflammation with eventual bronchiectasis (Figures 2a and b).

The right middle lobe is vulnerable to

atelectasis for several reasons. The origin of its bronchus is narrow and has an acute take-off angle, its proximity to hilar lymph nodes renders it susceptible to extrinsic compression when they enlarge, and there is decreased collateral ventilation. Most cases of middle lobe syndrome are attributed to asthma.

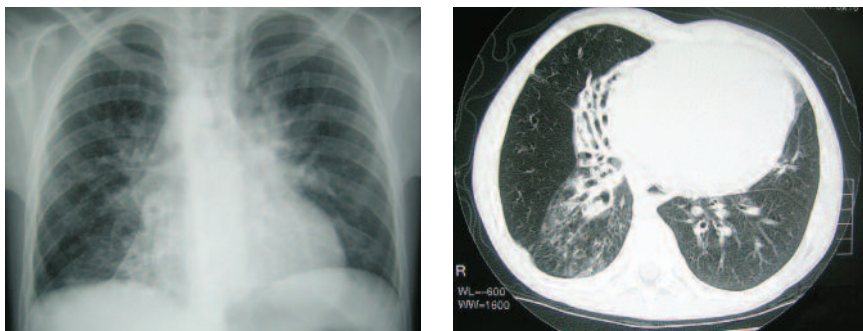
Management of middle lobe syndrome includes bronchodilators, inhaled corticosteroids, daily physiotherapy and

prolonged antibiotic treatment (for four to six weeks). Children with persisting atelectasis require an HRCT to assess the presence of bronchiectasis and hilar lymphadenopathy and bronchoscopy to exclude an inhaled foreign body.

Endobronchial tumours

Endobronchial tumours are rare in childhood. Children with these tumours usually present with symptoms of ‘asthma’ or

continued



Figures 2a and b. a (left). Chest x-ray of a child with right middle lobe syndrome associated with bronchiectasis. b (right). Chest high resolution CT scan of the same child showing bronchiectasis in the right middle lobe and adjacent lower lobe.

secondary pulmonary infection. These tumours include bronchial carcinoid and mucoepidermoid tumours, which are low-grade malignant neoplasms. Prognosis is excellent if these tumours are diagnosed and resected early.^{24,25} Benign endobronchial tumours include hamartomas, haemangiomas, papillomas, inflammatory pseudotumours, leiomyomas and mucous gland tumours. Bronchoscopy confirms the presence of the tumour and allows endobronchial biopsy. Complete surgical resection is curative, although clinical follow up is recommended.^{24,25}

Congenital lung lesions

Other causes of recurrent pneumonia occurring in the same area of lung are extrinsic compression of an airway usually due to enlarged lymph nodes or vascular rings and slings. Congenital anomalies of the airway, pulmonary vasculature or lung parenchyma such as sequestration and cystic pulmonary airway malformations often present with recurrent infection. Evidence of extrinsic compression can be detected by direct visualisation during bronchoscopy and further delineated by HRCT. Suspected vascular rings and slings are best investigated with echocardiography and contrasted chest CT or magnetic resonance angiography.

Affecting multiple lobes

Many underlying conditions are associated

with recurrent pneumonia occurring in multiple areas, as shown in Table 4.

Recurrent acute lower respiratory tract infections

Several viruses are frequently associated with lower respiratory infections, especially in infants. These include respiratory syncytial virus, human metapneumovirus, influenza virus and rhinovirus.^{8,20} Atypical bacteria such as *M. pneumoniae* and *C. pneumoniae* are also associated with recurrent respiratory tract infections in children.^{7,26}

Symptomatic relief, macrolide therapy when appropriate and reassurance are all that are required for children with recurrent acute lower respiratory tract infections. Smoking cessation should be discussed with parents when relevant.

Persistent bacterial bronchitis

Persistent or protracted bacterial bronchitis is an important cause of chronic cough in otherwise healthy children and may be the unforeseen result of reduced prescribing of antibiotics for respiratory illnesses. The diagnosis is made when a chronic wet cough (lasting for more than one month) resolves after appropriate antibiotic therapy. *Haemophilus influenzae* and *Streptococcus pneumoniae* are the most commonly isolated organisms and treatment should be directed towards these (usually a two to four-week course of

antibiotics). Treatment may need to be extended until after the cough clears to prevent progression to bronchiectasis in a subgroup of patients.

Asthma

Children diagnosed with 'recurrent pneumonia' with diffuse patchy changes or even lobar collapse on chest x-ray may have unrecognised asthma.¹⁵ Often a history of recurrent episodes of cough, wheeze or breathlessness with upper respiratory tract infections, exercise or weather changes, or hay fever and eczema is present. Occasionally only a family history of asthma is documented.

A trial of bronchodilators and anti-inflammatory therapy may be beneficial, especially in younger patients unable to perform spirometry. In older children, assessment of bronchodilator responsiveness and/or demonstration of airway hyper-responsiveness will help establish the diagnosis.

In some circumstances a child may have both asthma and an underlying immune deficiency.²⁷ This should be considered if the child appears to have poorly controlled asthma despite reasonable anti-inflammatory therapy.

Immunodeficiencies

Most children with recurrent pneumonia do not have an immunodeficiency. If present, most immune disorders associated with recurrent respiratory infections are due to an IgG subclass or IgA deficiency.²⁸ Clinical features of immunodeficiencies include recurrent upper respiratory tract infections, acute otitis media, sinusitis and bronchiolitis.

Children with significant immune defects usually present with more than four bacterial infections in a year, unexplained bronchiectasis, recurrent or severe infections of the skin and gastrointestinal tract, lymphadenopathy or failure to thrive.²⁸ The younger the child, the more severe the immune defect is likely to be. Often a family history of consanguinity or

recurrent infections and early deaths is present as many immunodeficiencies are inherited.

Aspiration

Chronic pulmonary aspiration is the repeated passage of food, gastric refluxate or oropharyngeal secretions into the airways resulting in respiratory pathology.²⁹ It can be the result of swallowing dysfunction, GOR or failure of adequate airway protective reflexes. Chronic pulmonary aspiration is often associated with comorbidities such as chronic lung disease, neurodevelopmental disorders, tracheo-oesophageal abnormalities or craniofacial malformations, and is commonly worse during viral upper respiratory tract infections.

A history of coughing, gagging or choking during feeds, particularly thin fluids, suggests direct aspiration and requires a swallowing assessment (feeding

videofluoroscopy) and consultation with a speech pathologist. Vomiting, irritability during feeds, epigastric pain and nocturnal cough in children suggests GOR.

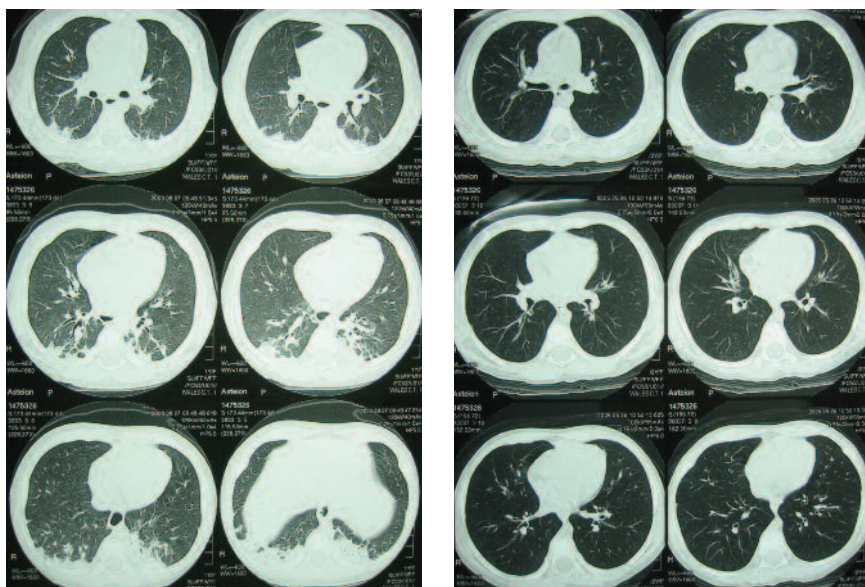
Although there is no current gold standard test for pulmonary aspiration, multichannel intraluminal impedance/pH monitoring may become the preferred investigation for evaluating proximal reflux and possible aspiration.²⁹ Chest x-rays are not sufficiently sensitive to detect early lung injury due to aspiration. They may show hyperinflation, segmental infiltrates or bronchial thickening during an acute event but will not reveal bronchiectasis until it is well established. HRCT will detect early lung pathology including air trapping, centrilobular thickening ('tree in bud') and bronchiectasis. Figures 3a and b show chest HRCT scans of a patient with chronic pulmonary aspiration before and six months after fundoplication.

Mucociliary disorders

Cystic fibrosis is the most common life-limiting genetic condition in Caucasians. In Australia approximately one in 3000 babies is born with this disorder. The primary defect in cystic fibrosis is abnormal ion and water transport across epithelial cells. In the lung this results in abnormally thick mucus that predisposes to chronic airway infection and inflammation. Newborn screening detects about 90 to 94% of affected babies and, therefore, the diagnosis may be missed at birth.

A history of neonatal jaundice, poor weight gain, steatorrhoea or chronic cough suggests cystic fibrosis, although recurrent pneumonia in infancy may be the only manifestation. A positive sweat test confirms the diagnosis; it is recommended that this be performed by experienced personnel.³⁰ In older children, isolation of *Pseudomonas aeruginosa* in sputum or

continued



Figures 3a and b. a (left). Chest high resolution CT scan of a young patient with chronic pulmonary aspiration showing basal atelectasis. b (right) Follow-up chest high resolution CT scan of the same patients six months after fundoplication showing complete resolution.

bronchiectasis should raise clinical suspicion of cystic fibrosis.

Primary ciliary dyskinesia is a rare genetic condition characterised by impaired mucociliary clearance and recurrent sino-pulmonary infections. It affects one in 15,000 to 30,000 individuals³¹ and is most often inherited as an autosomal recessive condition. It may present in the newborn period with unexplained tachypnoea and/ or respiratory distress, neonatal

pneumonia or persistent rhinitis. In childhood, recurrent lower respiratory tract infections, chronic purulent rhinitis, sinusitis and otitis media or 'atypical asthma' are common clinical features. Situs inversus is present in 50% of cases of primary ciliary dyskinesia (Figure 4), but only 23% of patients with situs inversus have primary ciliary dyskinesia.³²

Primary ciliary dyskinesia is the underlying cause for about 6% of cases of recurrent pneumonia in children.^{5,33} Its diagnosis is often delayed and as many as 30% of patients have established bronchiectasis at the time of diagnosis.³⁴ The condition can be diagnosed on nasal brushings, even in neonates. Light microscopy determines ciliary beat frequency and pattern and electron microscopy assesses ciliary ultrastructure. Nasal nitric oxide is very low in primary ciliary dyskinesia. Specialist respiratory care can prevent deterioration in lung function.³⁵

Management

The management of the child with recurrent pneumonia is beyond the scope of the

article, but involves treatment of the acute pneumonia and the underlying cause, with specialist referral where appropriate.

Summary

Most children with recurrent pneumonia will have an identifiable underlying cause. Asthma and recurrent viral or atypical infections are common, especially in early childhood, and should be considered. Any child who has a wet cough for longer than eight weeks is at risk of developing bronchiectasis and requires specialist review. Aspiration, immunodeficiency, mucociliary disorders and structural lung abnormalities are the most common causes of recurrent pneumonia. Pathology in the same area or lobe indicates a focal process. Evaluation involves a step-wise approach in which common conditions are screened for initially, with subsequent referral of the child to specialist care to prevent chronic lung disease and loss of lung function. **MT**

A list of references is available on request to the editorial office.

DECLARATION OF INTEREST: None.

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Figure 4. Chest x-ray showing situs inversus in a patient with primary ciliary dyskinesia who presented with recurrent pneumonia.

Investigation of the child with recurrent pneumonia

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