Cough is common in children and is one of the most frequent reasons for consulting a health professional. Around one-third of children are reported to have had a cough during any particular month, a significant proportion of whom will have a chronic cough. It is therefore not uncommon for parents to report symptoms of chronic cough in their child and seek advice from their GPs. Some of these children get referred to the hospital paediatricians for expert advice and management; however, this can present a challenge to health professionals. Studies have shown that up to 40 per cent of school-age children continue to cough 10 days after the onset of a common cold and 10 per cent of preschool children continue to cough 25 days after a respiratory tract infection.

It is important that health professionals consider a list of differential diagnoses when faced with a child with chronic cough (acute cough usually lasts less than three weeks). Potential causes include: asthma, cystic fibrosis, foreign body aspiration, anatomical abnormalities of the airways and other disor-
ders such as gastro-oesophageal reflux disease and sinusitis.\textsuperscript{1,5}

Children with chronic cough should always be referred for paediatric assessment. The assessment should include details of:

- how and when did the cough start
- quality of cough (eg productive or not, paroxysmal, with or without a ‘whoop’)
- whether the cough has a waxing and waning course or getting progressively worse
- whether it is an isolated symptom, any trigger factors noted (eg exercise, feeding, exposure to cold, on lying flat).\textsuperscript{4}

Table 1 lists some of the potentially serious disorders that may be detected in a child presenting with chronic cough.\textsuperscript{4} A chest X-ray should be performed to rule out a serious underlying condition.\textsuperscript{4}

It is not uncommon for children with chronic cough to receive asthma therapies to minimal or no benefit. Recurrent or nocturnal wet cough in the absence of wheezing is very common, particularly in preschool children, and is most unlikely to be due to asthma.\textsuperscript{6,7}

Studies have shown that children with chronic wet cough often have bronchitis and this is evident on bronchoscopy. Protracted bacterial bronchitis (PBB) is defined as persistence of isolated wet cough lasting more than four weeks and responding to antibiotic treatment.\textsuperscript{5} It remains an under-recognised condition often not familiar to or readily accepted by health professionals. Children with chronic wet cough accompanied by purulent bronchial secretions frequently have a bacterial infection of the lower airway.\textsuperscript{7}

Different terms have been used to describe the clinical phenotype of PBB such as ‘chronic bronchitis’ or ‘protracted bronchitis’ or ‘pre-bronchiectasis’.\textsuperscript{1}

Current clinical management of cough, with antibiotics being seldom prescribed when the aetiology is considered most likely to be viral, may result in low-grade bacterial infections being untreated and sometimes lead to the development of PBB.\textsuperscript{1} The greatest risk of PBB stems from its probable role in

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical presentation</th>
<th>Investigation</th>
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<tr>
<td>Cystic fibrosis</td>
<td>troublesome cough, repeated chest infections, prolonged diarrhoea, failure to thrive</td>
<td>sweat test, assessment of pancreatic function, genetic testing</td>
</tr>
<tr>
<td>Immune deficiencies</td>
<td>may be inherited or infection related (eg HIV), failure to thrive, frequent, unusual or recurrent severe infections, chronic cough, rashes, etc</td>
<td>differential white cell counts, immunoglobulin levels and subsets, functional antibody responses and lymphocyte subset analysis</td>
</tr>
<tr>
<td>Anatomical disorder (eg bronchomalacia) or lung malformation (eg cystic congenital thoracic malformation)</td>
<td>inherited condition, may have been detected on antenatal scans, stridor, feeding difficulties, failure to thrive, need for respiratory support in neonatal period, cough, etc</td>
<td>bronchoscopy and CT scan</td>
</tr>
<tr>
<td>Retained inhaled foreign body</td>
<td>usually young child, may or may not have history of choking, chronic cough, chest signs may be prominent on one side of chest</td>
<td>CXR and high-resolution CT scan; rigid bronchoscopy can be both diagnostic and/or therapeutic</td>
</tr>
<tr>
<td>Primary ciliary disorders</td>
<td>may be associated with dextrocardia/situs inversus, sinusitis, chronic cough, failure to thrive, etc</td>
<td>screening fractional nasal nitric oxide, saccharine test, cilial ultrastructure and function, culture of ciliated epithelium</td>
</tr>
<tr>
<td>Pertussis and pertussis-like illness</td>
<td>troublesome spasmodic cough after initial respiratory infection that slowly resolves over 3–6 months; vomits clear tenacious mucus; older child may complain of difficulty in catching breath</td>
<td>CXR, positive serology or culture (for Bordetella pertussis, parapertussis, adenovirus, influenza, parainfluenza) may be helpful in reducing requirements for further investigation</td>
</tr>
</tbody>
</table>

Table 1. Potentially serious causes of chronic cough in children; adapted from British Thoracic Society guidelines
Prescribing in children

Key points

- protracted bacterial bronchitis is commonly misdiagnosed as asthma
- diagnosis is clinical and is achieved by presence of wet cough lasting >4 weeks
- it is primarily a neutrophilic disease and presence of respiratory bacterial pathogens has been demonstrated in bronchoalveolar lavage
- a prolonged course of oral antibiotics of 2–3 weeks is suggested as the initial therapy
- treatment is likely to result in symptom resolution and may minimise the risk of developing bronchiectasis

Structurally damaging the airways, evident from radiological studies with high-resolution computed tomography or bronchography, and with the potential to lead to bronchiectasis.1

Bacterial isolates in children with PBB

The presence of bacteria in the lower airway in PBB was demonstrated more than a decade ago following bronchoalveolar lavage (BAL) on 23 children with chronic cough lasting for at least a month. These children did not have evidence of asthma. Neutrophilia was reported in the BAL, suggestive of an underlying persistent airway infection.3,5,8 Similar BAL results of neutrophilia co-existent with typical respiratory bacteria, such as Haemophilus influenzae, Moraxella catarrhalis and Streptococcus pneumoniae were described in subsequent studies conducted in Australia.5,9

Presence of bacteria in BAL was also demonstrated in a US study of 197 children aged 0 to 3 years, and purulent bronchitis was seen at bronchoscopy in 56 per cent of cases. The bacterial cultures were positive in 91 cases (46 per cent) with the following bacteria seen: nontypable H. influenzae (49 per cent), Strep. pneumoniae (20 per cent), M. catarrhalis (17 per cent), Staphylococcus aureus (12 per cent) and Klebsiella pneumoniae in one patient.7 The positive bacterial cultures occurred more frequently in children with purulent bronchitis than those with non-purulent bronchitis.7

In another study of 33 children10 aged between 4 and 38 months, significant bacterial cultures (in BAL) were found in 48 per cent of children, while respiratory viruses were detected in 22 per cent of cases and mixed bacterial-viral infection in 12 per cent.

Diagnosing PBB

The first step is to confirm the history from the parents with specific information being sought on cough and wheeze. The duration of symptoms should be clarified to determine whether the cough has been actually persistent and chronic, rather than two or three different episodes that occurred back to back and with some symptom-free period in between.

Prolonged cough in children can be classified into two main types – specific and nonspecific.11,12 Specific prolonged cough refers to the presence of signs and symptoms, including the presence of a ‘moist’ or ‘productive’ cough, which increases the likelihood of an underlying disorder causing the cough, of which PBB is one of the commonest ones. Nonspecific cough, also known as a ‘dry’ cough, has minimal or nonexistent secretions and a lack of other signs and symptoms.

Once a clinical suspicion of PBB arises it may be appropriate here to refer to paediatric services to establish the diagnosis and to exclude other possible serious causes. The threshold for suspecting PBB will be lower in children who have co-existing structural or functional abnormalities of the airways.1,5

A chest X-ray may be performed in some cases and will be found to be normal in most instances.4 A sputum culture may also be sent in older children.4 Diagnosis may be confirmed by bronchoscopy with BAL followed by bacterial study; however, such an invasive approach may not be deemed necessary or may not be readily available in most cases.

A reasonable alternative approach to avoid invasive bronchoscopy but permit early institution of management is to prescribe a course of appropriate oral antibiotics, but it should be explained to parents that this may not allow for a definitive diagnosis.3,5

Drug treatment

The mainstay of treatment of children with PBB is with prolonged antibiotic therapy; the British Thoracic Society (BTS) advises using four to six weeks of oral antibiotics.4 In the absence of a bacterial culture a prolonged course of either amoxicillin or a macrolide antibiotic is suggested in most children with PBB.13 The expected benefits include resolution of cough and parental report about improvement in symptoms.14

Since PBB was first described, it has been incorporated into paediatric cough management guidelines in the USA, UK and Australia with current guidelines recommending the use of antibiotic therapy for children with PBB.14,15 A paediatric formulation such as the BNF for Children should always be consulted before prescribing antibiotics.
Use of co-amoxiclav

In an Australian randomised controlled trial with 50 children (median age 1.9 years) seen with chronic wet cough of more than three weeks’ duration, 25 children were assigned to receive either two weeks of twice-daily oral co-amoxiclav (22.5mg per kg per dose) or placebo.

The primary end-point noted was ‘cough resolution’ defined as >75 per cent reduction in the validated verbal category descriptive (VCD) cough score within 14 days of treatment compared with baseline scores, or cessation of cough for more than three days.

Significantly higher cough resolution rates (48 per cent) were noted in children who received co-amoxiclav compared with those on placebo (16 per cent). The median VCD score (post-treatment) of 0.5 in the co-amoxiclav group was significantly lower than in the placebo group of 2.2. There was no significant difference in the BAL data between the two groups.

This study provided the first high-level evidence for the inclusion of antibiotics in paediatric cough-specific guidelines as treatment for PBB. Although the BTS suggests a four- to six-week course of antibiotics in clinical practice a two- to three-week course may be tried at the first consultation with a plan to review the child at the end of the antibiotic therapy.

Use of macrolide antibiotics

In a Cochrane review, macrolide antibiotics such as azithromycin were not found to be superior to co-amoxiclav in treating children with chronic cough. However, these antibiotics do have a role in treating children with PBB, especially in children who may be allergic to the penicillin group of antibiotics.

Azithromycin also has a dosing benefit as it needs to be administered only once a day. It can be prescribed for three days per week over a period of three weeks. When compared to 42 doses of co-amoxiclav (two-week course), only nine doses of oral azithromycin will need to be administered (three-week course) and is useful in a young child where adherence might be an issue.

Other macrolide antibiotics, including erythromycin and clarithromycin, are equally effective but multiple doses need to be given to children.

Conclusion

Cough is common in children and is considered to be persistent if lasting for more than three weeks. PBB presents with wet, moist, productive cough and these symptoms should warrant a detailed clinical assessment.

It is commonly misdiagnosed as asthma, although the two conditions may co-exist. As such, PBB is often initially treated with asthma therapies to no benefit, and great care should be taken to avoid such children being mislabelled as ‘asthmatic’. Minimal investigations are necessary and a trial of a prolonged course of oral antibiotics is useful.

Further research relating to PBB is necessary and Sheffield Children’s NHS Foundation Trust is currently undertaking the biggest study in the world.

References


Declaration of interests

None to declare.

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