Recognition and management of children with protracted bacterial bronchitis

Chronic moist cough in children can be associated with serious pathologies. Protracted bacterial bronchitis remains a clinical diagnosis causing persistent moist cough, disturbed sleep, exercise intolerance and significant levels of morbidity. Management involves minimal investigations and prolonged courses of antibiotics.

Protracted bacterial bronchitis is a clinical diagnosis, defined as 'an isolated chronic moist cough persisting continuously for more than 4 weeks without any clinical findings suggestive of an alternative diagnosis and resolution of symptoms in the majority when antibiotic therapy is given for at least 2 to 3 weeks' (Chang et al, 2008). When treatment fails, more detailed investigations and a treatment approach similar to that for non-cystic fibrosis bronchiectasis are required. A systematic review encompassing 989 children with non-cystic fibrosis bronchiectasis identified an underlying disorder in 63% of children but in almost a third no identifiable pathology was found (Brower et al, 2014). Whether unrecognized, untreated or frequently recurring protracted bacterial bronchitis leads to development of chronic suppurative lung disease and subsequent bronchiectasis (Chang et al, 2008; Verhagen and de Groot, 2015) is a question that can only be answered by long-term prospective studies.

The concept of protracted bacterial bronchitis is not new although over the years it has been described by different terminologies such as chronic bronchitis of childhood, protracted bronchitis, persistent endobronchial infection or pre-bronchiectasis, all aiming to reflect the clinical phenotype (Marchant et al, 2008a; Craven and Everard, 2013). Until recently, protracted bacterial bronchitis has remained underrecognized and largely undiagnosed, with cases of protracted bacterial bronchitis presenting with chronic moist cough being attributed to other aetiologies. This under-recognition may be because health professionals are not familiar with the condition or there may be a reluctance to accept the diagnosis (Paul and Hilliard 2014). This often leads to these children being inappropriately treated as having 'asthma' with minimal or no improvement in clinical condition. The idea of treating relatively well looking children with just a moist cough with prolonged courses of antibiotics may also lead to under-recognition and non-acceptance of the condition.

However, increased availability of advanced diagnostic procedures such as bronchoscopy and demonstration of different bacteria in bronchoalveolar lavage samples has led to a better understanding of the persistence of a low grade bacterial infection in the conducting airways in an otherwise well child (Craven and Everard, 2013; Paul and Hilliard, 2014). Inclusion of this condition in the British Thoracic Society guidelines 'Recommendations for the assessment and management of cough in children' should lead to an increased awareness of the condition (Shields et al, 2008).

This article outlines the recognition and management of children with protracted bacterial bronchitis and discusses the management of the small number of cases who fail to respond to or relapse after courses of oral antibiotics.

Differential diagnosis of moist cough in children

Chronic cough is a common presentation in children; some of these cases can be associated with serious pathologies. This can be an extremely distressing symptom and has a major impact on a child's activities of daily living, sleep and school performance. It is also associated with a high burden of recurrent medical attendances, parental stress and anxiety (Marchant et al, 2008b). A chronic moist cough is always abnormal and represents excessive airway secretions, and it is the most useful clinical marker in predicting specific cough (Chang et al, 2005). However, a chronic dry cough may represent a dry phase of an otherwise usually moist cough, or the airway secretions may be too little to influence the cough quality.

Chronic and especially recurrent or persistent moist cough secondary to some of the causes listed in *Table 1* could indicate that bronchiectasis has developed, although the aim should be to detect early and aggressively treat to prevent or reverse bronchiectasis, challenging the belief that bronchiectasis is irreversible (Eastham et al, 2004). It is important to rule out serious causes of

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chronic cough in children and a thorough focused history will help differentiate protracted bacterial bronchitis from other serious causes (Paul and Hilliard, 2014). While reviewing a child with chronic cough, it is important to enquire about the duration of cough, whether the cough is dry or moist and the presence of other associated features, e.g. nasal symptoms, other infections, wheeze or hypoxia.

Blood inflammatory markers are likely to be normal in most cases and it is important that unnecessary investigations are avoided. Chest radiographs may be useful in cases where the cause of chronic cough remains unclear from the history and is likely to give some indication of other serious pathologies such as undiagnosed cystic fibrosis (may show evidence of bronchiectasis, hyperinflation, lobar collapse) or foreign body aspiration (may show signs of air trapping, hyperinflation of one lung or lobe, or the actual [radio-opaque] foreign body) (Paul and Hilliard, 2014).

A prospective multicentre cohort study from Australia used an evidence-based cough algorithm to manage the chronic cough of 346 newly referred children. This study used validated cough outcome measures and *a priori* definitions and timeframes to define cough resolution so as to overcome potential biases of single centre studies. The top four diagnoses in their cohort were protracted bacterial bronchitis (142/346 (41%) of children), asthma, bronchiectasis, and 'resolved without specific diagnosis' (Chang et al, 2012). Chronic moist cough in childhood should therefore be carefully evaluated and child-specific evidence-based algorithms used. It is important that secondary care clinicians working with children have a structured approach when presented with a child with chronic cough. A list of possible aetiologies for children presenting with moist cough is listed in *Table 1*.

Epidemiology of protracted bacterial bronchitis

Protracted bacterial bronchitis is not a new condition but is increasingly recognized as being a re-emerging condition (Craven and Everard, 2013). In the 1950s, the number of cases of non-cystic fibrosis-related bronchiectasis declined (and there was probably a decrease in the number of cases of protracted bacterial bronchitis) (Pasteur et al, 2010) secondary to widespread use of antibiotics, improved living conditions and vaccination. As well as these factors, excessive focus on asthma as the cause of chronic respiratory symptoms and stringent antibiotic prescribing policies in primary care since the 1990s to reduce the prescription of antibiotics in children may have shifted the focus away from protracted bacterial bronchitis as a cause of chronic cough in children and masked the true prevalence of this condition. It is not unrealistic to presume that a number of low grade bacterial chest infections would have been labelled as viral infections and managed with antipyretics and reassurance (Ashworth et al, 2005; Arnold and Bush, 2006). However, the number of cases of protracted bacterial bronchitis now appears to be rising again, hence the condition is considered to be re-emerging.

Table 1. Children presenting with chronic moist cough where further investigations are suggested

Pointers to serious pathologies	Possible underlying aetiology
Daily moist or productive cough	Protracted bacterial bronchitis
	Cystic fibrosis
	Immune deficiencies
	Primary ciliary disorders
	Recurrent pulmonary aspiration
	Retained inhaled foreign body
Cough characteristics (cough with choking, cough quality, cough starting from birth)	Congenital airway or lung abnormalities
Exertional dyspnoea	Compromised lung function of any chronic lung or cardiac disease
Chest pain	Asthma
	Functional pleuritis
Symptoms of upper respiratory tract infection (may coexist or be a trigger for an underlying problem)	Upper airway cough syndrome
	Primary ciliary disorders
Feeding difficulties (including choking and/or vomiting)	Compromised lung function
	Primary aspiration
Failure to thrive	Compromised lung function
	Immunodeficiency
	Cystic fibrosis
Neurodevelopmental abnormality	Primary or secondary aspiration risk
Abnormal findings on chest auscultation (wheeze, crackles, differential breath sounds)	Asthma
	Bronchitis
	Congenital lung disease
	Foreign body aspiration
	Airway abnormality
Digital clubbing	Chronic suppurative lung disease
	Cystic fibrosis
Haemoptysis	Acute or chronic infection
	Foreign body
Recurrent pneumonia	Immunodeficiency
	Congenital lung problem
	Airway abnormality
Immune deficiency	Atypical and typical respiratory infections
Cardiac abnormalities (also think of associated airway problems, pulmonary oedema, Kartagener's syndrome or immunodeficiency)	Any cardiac illness

adapted from Chang and Glomb (2006); Donnelly et al (2007); Marchant et al (2008b); Shields et al (2008); Paul and Hilliard (2014); Srivastava and Bhatt (2014)

Typically preschool children are the age group affected by protracted bacterial bronchitis. In the younger child, protracted bacterial bronchitis is often secondary to an infective event and is most common in the first 2 years of life (respiratory cilia take longer to recover from the initial infection) (Priftis et al, 2013). A study of 104 children with protracted bacterial bronchitis reported that children affected are typically preschool boys, with prolonged moist cough and parent-reported wheeze, who have attended child care (Wurzel et al, 2014). The prevalence of protracted bacterial bronchitis in childhood is not exactly known; the use of different terminologies to identify different meanings in the spectrum of protracted bacterial bronchitis also makes it very difficult to gauge its true prevalence (Kompare and Weinberger, 2012). However, when the symptom of chronic cough was evaluated in a structured manner, between 23 and 41% of children with chronic cough turned out to have protracted bacterial bronchitis (Asilsoy, 2008; Marchant et al, 2008a; Chang et al, 2012).

Protracted bacterial bronchitis is a chronic respiratory infection that can occur in the 'well child' as well as those with pre-existing airway disease. The prevalence of protracted bacterial bronchitis in children with airway malacias is considerably higher than in children with normal airways (Wurzel et al, 2014). A study from the USA involving 70 children with protracted bacterial bronchitis found that tracheomalacia, bronchomalacia or both were present in 52 (74%) children (Kompare and Weinberger, 2012). A hypothesis for this is that airway collapse interferes with normal cephalad mucous flow, thus decreases the effectiveness of coughing and predisposes to bacterial stasis (Fahy and Dickey, 2010). It is unclear, however, what cause and effect relationship exists between airway malacia and protracted bacterial bronchitis – Moreno et al (2014) found that 28% of children with malacia had protracted bacterial bronchitis and 76% of children with protracted bacterial bronchitis had airway malacia. This also raises a question about the potential for chronic airway damage from protracted bacterial bronchitis.

Pathophysiology of protracted bacterial bronchitis

Bacterial lower respiratory tract infections can be differentiated into two discrete clinical entities – infections that affect the respiratory zone of the lung *vs* infections that affect the conducting airways (Priftis et al, 2013). The larger respiratory zone contributes to 95% of lung volume and includes respiratory bronchioles, alveolar ducts and alveolar sacs. The smaller conducting zone includes the trachea, bronchi and terminal bronchioles; it does not contribute to gaseous exchange and is the anatomical dead space.

The pathophysiology of protracted bacterial bronchitis involves bacterial biofilm formation (in contrast to the rapidly dividing planktonic state seen in acute pneumonia affecting the respiratory zone) (Priftis et al, 2013). Biofilm is a highly-organized multicellular community, encased in an extracellular polymeric matrix. Bacteria within biofilm tend to have a reduced growth rate and increased resistance not only to the host's immune system but also to antibiotics – antibiotics targeting the bacterial cell wall are ineffective because of the reduced replication rate. In addition, the polymeric matrix presents a physical barrier to cellular effectors of immunity and is highly recalcitrant to removal (Bakaletz, 2012). This pathophysiological mechanism may explain why routine 7- or even 14-day courses of antibiotics are often ineffective in treating children with protracted bacterial bronchitis.

Bronchoscopy and bronchoalveolar lavage cultures taken from children with confirmed protracted bacterial bronchitis have provided an insight into the common bacterial pathogens. Typically non-typable *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* have been grown separately or in combination in various studies (Kompare and Weinberger, 2012; Marchant et al, 2012; Priftis et al, 2013; Narang et al, 2014). *H. influenzae* was the commonest organism isolated and polymicrobial growth was common in up to 35% of patients (Marchant et al, 2012; Priftis et al, 2013).

Bronchoalveolar lavage samples from children with protracted bacterial bronchitis also have significant airway neutrophilia (Kompare and Weinberger, 2012; Marchant et al, 2012; Wurzel et al, 2014). Levels of inflammatory mediators such as interleukin 8 (IL-8) and active matrix metalloproteinase 9 (MMP-9) were both significantly higher ($P<0.005$) in patients with protracted bacterial bronchitis than in controls (children whose cough resolved naturally) (Marchant et al, 2008a). CD56 and CD16 (natural killer cells) levels were also higher in children with protracted bacterial bronchitis (Wurzel et al, 2014). This suggests that protracted bacterial bronchitis is associated with airway neutrophilia and a marked inflammatory mediator response with evidence of innate immune system activation.

Clinical presentation of protracted bacterial bronchitis

In a study of 81 children with protracted bacterial bronchitis from the UK, the most common initiating event was an acute lower respiratory tract infection (42%), with pneumonia accounting for a further 30% (Donnelly et al, 2007). The same study revealed the initial history given by parents included persistent cough (95%), shortness of breath (43%), wheezing (48%), noisy breathing and exacerbation with upper respiratory tract infections (Donnelly et al, 2007). In another study of 104 children from Australia, the median cough duration in protracted bacterial bronchitis was 28 weeks (Wurzel et al, 2014).

The cough has been typically described as a 'moist' or a 'smoker's cough' (Donnelly et al, 2007). A retrospec-

tive study reviewing the presence of airway malacia in children diagnosed with protracted bacterial bronchitis noted that none had fever or a toxic appearance associated with their respiratory symptoms (Kompare and Weinberger, 2012). This suggests that children with protracted bacterial bronchitis suffer from respiratory symptoms but otherwise generally look well in themselves. This could partly account for the time delay from symptom onset to diagnosis – the 'watch and wait' ideology.

Infective exacerbations are an important feature of protracted bacterial bronchitis. While infective (bacterial or viral) exacerbations of respiratory diseases such as asthma or cystic fibrosis are well known, viral–bacterial co-infection is also a common feature of protracted bacterial bronchitis. One study reported that viruses were detected in nasopharyngeal aspirate of 85% of patients with protracted bacterial bronchitis (Wurzel et al, 2014). During an infective exacerbation, children will often experience an increase in symptoms for a period of time and then regress back to the baseline level (Craven and Everard, 2013). The secondary superimposed infection is thought to cause the release of planktonic bacteria from the established biofilm (likely in response to the associated inflammation) as seen in patients with cystic fibrosis (Høiby, 2002).

History and examination

The diagnosis of protracted bacterial bronchitis remains a clinical one. The first and most vital step is to confirm the history from parents. Specific information should be sought on the duration of cough and noisy breathing, the nature of the cough (i.e. dry or moist), that the cough is actually persistent and chronic (i.e. not different episodes occurring back to back with symptom-free periods in between), and therapies used so far (e.g. inhaled bronchodilators or steroids for asthma, often without any actual benefit) including whether any antibiotics have been used (Paul and Hilliard, 2014).

A study from the UK with 47 children (median age 26 months) identified bacterial bronchitis in 43% of children with persistent wheeze having received optimal treatment for asthma (24% were receiving oral steroids) (Saglani et al, 2006).The same study also identified coexisting gastro-oesophageal reflux and positive bacterial cultures in a significant number of children, the most likely explanation being aspiration leading to disruption of the normal epithelium and colonization by organisms such as *H. influenzae* (Saglani et al, 2006). Even when DNA-based methods were used, strikingly similar core respiratory microbiota were seen in common childhood airway pathologies and this is likely shaped by natural aspiration and impaired clearance of the same airway microbes (Van der Gast et al, 2014). However, longitudinal and interventional studies are required to define the relationships between microbiota, treatments and disease progression.

Once the history raises a clinical suspicion of protracted bacterial bronchitis, the child should be referred to a paediatrician to establish the diagnosis and explain the condition to the parents. It is also important to exclude other possible causes which will be largely dependent on the history and examination while investigations will help rule out other conditions. Other coexisting conditions such as airway malacias make the child prone to frequent respiratory exacerbations and it is important to decide whether the deteriorating respiratory symptoms are the result of the primary illness or whether protracted bacterial bronchitis is exacerbating the primary illness. This is difficult and actions will largely be based on an individual clinical assessment, but protracted bacterial bronchitis should be considered in any child with troublesome respiratory symptoms.

The history should be followed by a detailed clinical examination. The physical examination including auscultation of the chest will usually be normal although this is necessary to rule out other differential diagnoses. Rattles (heard with or without stethoscope) and felt as vibrations on palpation of the chest are often found during an acute episode – this noise is often mislabelled as wheeze by parents and some health professionals (Craven and Everard, 2013).

Investigations and diagnosis

The patterns of symptoms found in protracted bacterial bronchitis are not unique to the condition and are commonly seen in all differentials of protracted bacterial bronchitis (*Table 1*). When evaluating patients with respiratory symptoms, one suggestion is to use the acronym SPUR (severe, persistent, unusual, recurrent) to prompt consideration of further investigations for underlying causes of respiratory symptoms (Jesenak et al, 2011). In addition, symptoms being unresponsive to treatment, such as a cough not responding to inhaled or oral corticosteroids, should trigger consideration of an alternative diagnosis.

Protracted bacterial bronchitis is a clinical diagnosis made on assessment of response to treatment of moist cough with antibiotics. A reasonable approach, suggested in the literature and from the authors' clinical experience, is to explain the clinical diagnosis and give a trial of oral antibiotics. It is important, however, to explain to parents that this approach may not confirm a definitive diagnosis but minimizes the risk from invasive investigations such as bronchoscopy and associated general anaesthesia (Kompare and Weinberger, 2012; Craven and Everard, 2013).

Investigations should generally be reserved for cases where the child remains unresponsive to prolonged course of antibiotics or if there have been more than two relapses of protracted bacterial bronchitis (Donnelly et al, 2007; Paul and Hilliard, 2014). Chest radiographs may be performed in children with protracted bacterial bronchitis and are generally normal although some may show peri-

bronchial thickening (Marchant et al, 2008b; Chang et al, 2012). However, chest radiographs can provide useful information in children with chronic cough if the diagnosis is unclear (Donnelly et al, 2007; Bakaletz, 2012). High-resolution computed tomography may be helpful where coexistent anatomical or lung malformations (e.g. congenital cystic adenomatoid malformation) or retained foreign bodies are suspected (Donnelly et al, 2007; Shields et al, 2008). A sputum culture or cough swab may be sent in older children but microbiological yield is usually low (Shields et al, 2008; Chang et al, 2012).

Diagnosis of protracted bacterial bronchitis can be confirmed by bronchoscopy with bronchoalveolar lavage followed by microbiological studies; however, such an invasive approach may not be necessary in most cases. Moreover, the technical expertise and facilities for paediatric general anaesthesia and bronchoscopy are often only available in specialist centres (Paul and Hilliard, 2014). Bronchoscopy with bronchoalveolar lavage may be considered in cases where relapse is seen after three courses of prolonged oral antibiotics or if there is a strong insistence from parents for a definitive diagnosis at the very outset (Craven and Everard, 2013).

A retrospective review of 50 children with protracted bacterial bronchitis in the UK suggested that multiple lobes should be sampled for bronchoalveolar lavage at bronchoscopy (as per the European Respiratory Society guidance) as organisms are likely to be missed if a sample is taken from a single lobe only (Narang et al, 2014). The bronchoalveolar lavage sample sent for microbiological studies is likely to grow bacterial species, non-typable *H. influenzae* and *S. pneumoniae* being most commonly documented in studies (Kompare and Weinberger, 2012; Marchant et al, 2012; Priftis et al, 2013; Wurzel et al, 2014). Microbiological confirmation will allow use of antibiotics to which the isolate is sensitive and is likely to allow better resolution in resistant cases already treated with usual antibiotics. Bronchoscopy will also help document the presence or otherwise of airway malacia.

In children requiring repeated courses of antibiotics, further investigations should be considered. This includes total immunoglobulins G, A, M and E, specific antibodies against *H. influenzae* B (Hib) and *S. pneumoniae*, sweat tests and ciliary studies. In a retrospective study of 81 children with a clinical diagnosis of protracted bacterial bronchitis, further investigations were carried out in children who required more than two courses of antibiotics. One-third of these children had specific antibody levels against Hib, tetanus and *S. pneumoniae* measured. Suboptimal specific antibody levels were commonly seen, but almost all levels returned to normal after revaccination (Donnelly et al, 2007). In contrast, Lim et al (2012) found that 14 out of 24 (58%) children with chronic moist cough failed to mount an adequate antibody response to booster immunization against Hib and *S. pneumoniae*, consistent with specific polysaccharide antibody deficiency. This raises the question of whether ineffective vaccine-related antibody status or missed vaccinations can increase susceptibility to developing protracted bacterial bronchitis. However, the *H. influenzae* detected in previously immunized children with protracted bacterial bronchitis are often the non-typable strains (Craven and Everard, 2013), which are not covered by the Hib vaccine.

Treatment

Treatment with prolonged courses of oral antibiotics is required to eradicate the formation of bacterial biofilm in children with protracted bacterial bronchitis, thus allowing time for regeneration of epithelium in the absence of infection (Chang et al, 2012). There is a lack of evidence regarding the optimal duration of antibiotic therapy that will allow mucociliary clearance (Craven and Everard, 2013). The British Thoracic Society recommends the use of oral antibiotics in children with protracted bacterial bronchitis for 4–6 weeks (Shields et al, 2008). A review by Craven and Everard (2013) suggested using an empirical course of oral antibiotics for 6–8 weeks.

A double-blind randomized controlled study from Australia involving 50 children with protracted bacterial bronchitis (moist cough of at least 3 weeks' duration) showed that antibiotic therapy with co-amoxiclav for 2 weeks led to resolution of cough in 48% of children compared to only in 16% in children who received a placebo (Marchant et al, 2012). The authors' practice is to use 3 weeks of oral antibiotics followed by a review at the end of the antibiotic therapy.

As most cases of protracted bacterial bronchitis are treated on clinical suspicion, the most commonly used empirical antibiotic is oral co-amoxiclav (Marchant et al, 2012). A Cochrane review of treatment of acute lower respiratory tract infections (Laopaiboon et al, 2015) found no significant difference in the incidence of clinical failure on days 10–14 with azithromycin, amoxicillin or co-amoxiclav but a subgroup analysis showed that trials with acute bronchitis participants had significantly lower levels of clinical failure in those taking azithromycin. Azithromycin has a definite dosing benefit (administered only once a day) and fewer adverse effects (Laopaiboon et al, 2015). Although azithromycin is not more effective in treating lower respiratory tract infections it is particularly useful in those with a penicillin allergy and in younger children for dosage benefit (9 doses of azithromycin *vs* 63 doses of co-amoxiclav for a 21-day course) (Paul and Hilliard, 2014).

It is important to ensure that the childhood immunizations are up to date, even more so in children with predisposing risk factors for developing protracted bacterial bronchitis. Patients who had been vaccinated were 50 times less likely to isolate a pneumococcal vaccine conjugate serotype from bronchoalveolar lavage (Priftis et al, 2013).

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Management of children with protracted bacterial bronchitis who fail to respond to initial treatment

Persistent moist cough and failure to respond or relapse after three courses of oral antibiotics (of 2–3 weeks' duration) should lead to consideration of a high-resolution computed tomography scan and bronchoscopic assessment (Paul and Hilliard, 2014). A high-resolution computed tomography scan will identify bronchiectatic changes in the lungs and help decide on further management. Evidence of chronic suppurative lung disease or airway malacias may be found during bronchoscopic assessment, and bronchoalveolar lavage samples should be taken from multiple lobes and sent for microbiological and cytological studies (Narang et al, 2014). The choice of intravenous antibiotics should be guided by the growth of organisms and sensitivities of the bronchoalveolar lavage sample; the duration may vary between 4 and 6 weeks. A good response to intravenous antibiotics reduces the likelihood of developing bronchiectasis in the long term although it does not exclude the possibility completely (Goyal et al, 2014).

Treatment of recurrent episodes of protracted bacterial bronchitis is still based on extrapolation of treatment approaches to chronic suppurative lung disease and established non-cystic fibrosis bronchiectasis. This includes maintenance azithromycin therapy for up to 24 months which leads to decreased pulmonary exacerbations in children with non-cystic fibrosis bronchiectasis or chronic suppurative lung disease. However, this can cause increased carriage of azithromycin-resistant bacteria, the clinical consequences of which are uncertain, and will need careful monitoring and further study (Valery et al, 2013; Gao et al, 2014). While many knowledge gaps and management challenges remain, the future is improving for patients with bronchiectasis (Grimwood et al, 2014).

Prognosis

Untreated cases may very rarely have natural resolution of their cough but the vast majority will require prolonged courses of antibiotics to treat troublesome symptoms. The natural history of untreated or frequently recurrent protracted bacterial bronchitis remains unknown. Long-term prospective follow-up studies are needed to determine whether untreated or frequently recurrent protracted bacterial bronchitis, chronic suppurative lung disease and bronchiectasis are different conditions with overlapping symptoms or reflect severity as part of a spectrum (Chang et al, 2008).

The outcome for children with protracted bacterial bronchitis treated with antibiotics is generally good. A retrospective long-term review of 44 children with confirmed diagnosis of protracted bacterial bronchitis found that 33 (75%) children achieved complete resolution with antibiotics and 10 had incomplete resolution with prolonged courses of antibiotics (Pritchard et al, 2015). Five children were treated or investigated for other respiratory conditions, three of whom were diagnosed with asthma and started on corticosteroids (Pritchard et al, 2015). Another review of 81 children with a clinical diagnosis of protracted bacterial bronchitis (only a minority had bronchoalveolar lavage) found that 41 (51%) children were symptom free after two courses of antibiotics, although 13% of 41 children with protracted bacterial bronchitis required ≥6 courses of antibiotics (Donnelly et al, 2007). Children with specific polysaccharide antibody deficiency were more likely than children with normal antibody responses to require intravenous antibiotics and to have abnormal chest radiographs (Lim et al, 2012).

While a watch and wait approach is justifiable when managing children with chronic dry cough without any cough pointers, the same does not apply for children with chronic moist cough (Chang et al, 2015). Emerging evidence from randomized controlled trials supports treatment of initial episodes of protracted bacterial bronchitis with at least 2-week-long courses of oral antibiotics (Marchant et al, 2012) and failure to respond to a 4-week course of appropriate antibiotics increases the likelihood of bronchiectasis being detected on high-resolution computed tomography (Goyal et al, 2014).

KEY POINTS

- Protracted bacterial bronchitis should be considered in any child who has an isolated chronic moist cough persisting continuously for more than 4 weeks.
- Airway malacia is associated with protracted bacterial bronchitis.
- Prolonged courses of antibiotics are necessary to treat protracted bacterial bronchitis.
- Recurrent episodes of protracted bacterial bronchitis should lead to a thorough investigation for possible underlying serious causes of chronic moist cough in children.

Conclusions

Protracted bacterial bronchitis remains an underrecognized condition which may not be familiar to health professionals. Clinical suspicion is vital to the diagnosis of protracted bacterial bronchitis. A thorough history and assessment is necessary, but only minimal investigations are usually needed. A trial of a prolonged course of oral antibiotic therapy is often beneficial although this conservative approach may not allow definitive confirmation of the diagnosis. Further research is necessary to define the specific aetiology of this condition and optimize treatment strategies. This article heightens awareness of this important condition, which can have serious outcomes if not recognized and treated in a timely manner. **BJHM**

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