

## British Thoracic Society Guidelines

Recommendations for the assessment and management of cough in children

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## SUMMARY OF GUIDELINES FOR COUGH IN CHILDREN

### **Acute Cough** (Figure 1)

#### *Diagnosis*

- The vast majority of children with acute cough have a viral respiratory tract infection.
- An attempt should be made to arrive at a specific clinical diagnosis (Table 1).
- The absence of fever, tachypnoea and chest signs appears to be most useful for ruling out future complications in children with cough in primary care.

#### *Investigations*

- Most children with cough due to a simple URTI will not need any investigations.
- Children in whom an inhaled foreign body is a likely cause of cough should have an urgent bronchoscopy.
- A chest radiograph should be considered in the presence of lower respiratory tract signs, relentlessly progressive cough, haemoptysis or features of an undiagnosed chronic respiratory disorder (Table 2).

#### *Treatments*

- Over the counter medications are as effective as placebo for acute cough with head colds in children.
- Bronchodilators are not effective for acute cough in non-asthmatic children
- Antibiotics are generally not effective or recommended for treating acute coughs due to simple 'head colds'.
- Macrolide antibiotics should be given early (first 1-2 weeks) to children with pertussis.
- Antihistamines and intranasal steroids are beneficial for children with an allergic cough in the pollen season.

#### *Education*

- There may be benefits from educating the community and medical profession about the natural history of cough with head cold. For the majority of children the cough will have resolved by 14 days, however, for an important minority the cough will take 3-4 weeks to resolve. Giving this information to parents may reduce the need for subsequent doctor consultations providing the cough is subsiding and provided that warnings are given about when to reconsult (eg on-going fever, tachypnoea)

### **Prolonged acute cough** (Figure 2)

There is a 'grey' area between acute and chronic cough (cough lasting > 8 weeks), sometimes called 'subacute cough'. Much coughing in children lasting > 3 weeks is related to transient viral or pertussis like infections. Therefore a period of observation (3 to 8 weeks) may be needed to determine if further investigations will be required. If the cough is abating and the child is otherwise well no further tests may be required, however, it will be important to follow up the child in 6-8 weeks time to ensure that the cough has resolved. If the cough is progressive or if a retained inhaled foreign body is likely earlier investigations are required. Most acute coughs associated with upper respiratory infections should be abating in the second week whereas a relentlessly progressive cough becomes increasingly severe (frequency and severity) beyond 2-3 weeks. In this situation diagnoses that should be considered include pertussis, retained inhaled foreign body, expanding mediastinal neoplasm, lobar collapse secondary to mucous plug and TB (often with accompanying weight loss). A chest radiograph will usually be needed.

**Recurrent cough:** a recurrent cough without a cold is taken as repeated ( $\geq 2$ /year) cough episodes, apart from those associated with head colds, that each last more than 7-14 days. If the periods of resolution are short frequently recurrent cough will be difficult to distinguish from persistent chronic cough.

### **Chronic Cough** (Figure 3)

- The management of chronic coughing relates to first making an accurate underlying diagnosis and then applying specific treatment for that condition (Tables 4,5).
- Most chronic coughs in childhood are not due to the same conditions as occur in adults. The use of adult based cough algorithms is unsuitable for application in children.
- The initial assessment should be used to identify pointers suggestive of specific disorders (Tables 3,4,5)
  - A detailed history should be taken and all children with cough should have a full clinical examination.
  - A chest radiograph is indicated for most children.
  - Spirometry with or without tests of bronchodilator responsiveness (BDR) or bronchial hyperreactivity (BHR) should be attempted in children old enough to perform the manoeuvres.
  - An attempt should be made to observe the cough and to obtain a sample of sputum.
  - A 'wet' moist productive cough is an alert that there is chronic over production of mucus and great care should be taken before such children are labeled as 'asthmatic'. Protracted bacterial bronchitis or a more serious condition such as CF should be considered
  - Allergy testing (skin prick or RAST specific testing) may be helpful in determining if a child is atopic and in the correct background that would make problem coughing more likely to be due to asthma.
- In otherwise well children with non-specific isolated dry coughing with no specific disease pointers empirical trials of anti-asthma, anti allergic rhinitis or anti gastro-oesophageal reflux therapy are unlikely to be beneficial and are generally not recommended.

However, as it can be difficult to rule out asthma as a cause of coughing in young children a trial of anti-asthma therapy (typically inhaled corticosteroids) may be used. In such a trial the treatment should be effectively delivered in adequate doses with clear cut outcomes recorded.

A definite period of time should be set e.g. 8-12 weeks after which the trial of anti-asthma medication should be stopped. If the child has responded to anti-asthma therapy and the treatment has subsequently been stopped cough variant asthma is suggested by an early relapse that again responds to therapy. If there is no response the treatment should be stopped as asthma is unlikely and the cough is unresponsive to asthma medication. This is important so that children with simple recurrent viral bronchitis or post-viral cough do not end up on long term high doses of inhaled corticosteroid.

- Psychotherapy regimes may be helpful in treating psychogenic coughing
- An attempt should be made to remove children with chronic cough from exposure to aero-irritants such as environmental tobacco smoke
- Non-specific isolated dry coughing in an otherwise well child should be differentiated from those with more serious conditions.

'Red flag' alert symptoms/signs include:

- a. neonatal onset,
- b. cough with feeding,
- c. sudden onset cough,
- d. chronic moist cough with phlegm production,
- e. associated night sweats/weight loss,
- f. continuous unremitting or worsening cough,
- g. signs of chronic lung disease.

## **GUIDELINES FOR COUGH IN CHILDREN**

### **Introduction to guidelines**

All children experience head colds and many consult their doctor because of associated coughing (1). Cough with colds remedies are among the most commonly used medications in children in Western societies despite evidence suggesting ineffectiveness of medication to treat cough as a symptom. The aetiology of coughing in children will cover a wide spectrum of respiratory disorders in children and finding and treating the underlying cause is important.

Community based surveys show that parental reported cough as an isolated symptom has a high prevalence (2,3). Reported cough without colds has a prevalence of 28% in boys and 30% in girls (4). The recognized under diagnosis of asthma led to the importance of cough as a symptom being stressed. However, there is increasing evidence that children are inappropriately treated for asthma based on cough as the sole symptom (5, 6).

Coughing in children can be distressing and has a major impact on a child's sleep, school performance and ability to play. It may similarly disturb other family member's sleep and be disruptive for school teachers. Considerable parental anxiety is generated in families with a child with problem coughing (7,8).

The reported severity of a child's cough may relate to how it affects parents and teachers. Recent evidence has highlighted that parental reporting of the frequency and severity of a child's cough is unreliable compared to objective measures and this is especially true for nocturnal cough. Indeed it has been suggested that cough as reported in surveys and as a clinical trial outcome should either not be used or be interpreted with caution (9-12). This limits the certainty that can be placed on most of the published literature that has not used objective cough measurements

### **The need and purpose of BTS recommendations on the management of cough**

These guidelines are needed because childhood coughing is a common problem that generates much anxiety, has numerous different causes and is often wrongly diagnosed and inappropriately treated. Differences between childhood and adult cough suggest the need for separate guidelines. The 'big three' causes of adult chronic cough (cough variant asthma, postnasal drip and gastro-oesophageal reflux) are not necessarily valid for children (13).

The aim is to produce guidelines that are relevant to the clinical management of cough in children up to 12 years without known lung disease both in primary and secondary care. Both adult and childhood conditions and treatments will need to be considered when dealing with teenagers. No attempt has been made to provide a comprehensive list of all causes of coughing.

These guidelines cover acute, chronic and recurrent coughing. We have used the approach that an attempt should be made to arrive at a specific diagnosis for cause of cough (specific cough). We have covered the commonly encountered situation of a child who does not appear to have a specific pointer to a cause or to have significant underlying serious disease but has problem cough (non specific isolated cough).

### **Methodology for generation of the guidelines**

There is currently a lack of evidence on which to make evidence based statements for the diagnosis, investigation and treatments included in this guideline. Most of the features of a cough and investigations have not been formally evaluated for their predictive value in the diagnosis of a specific

condition. In the Cochrane Library database three recent systematic reviews of treatment of prolonged non-specific cough in children (inhaled anti-cholinergics, theophyllines, cromones) found no eligible RCT studies and in a further review (gastro-oesophageal reflux treatment) 3 paediatric studies were found but none could be included in the meta-analysis (14-17).

In order to make opinion and consensus based statements based on the known literature that would be useful the following methodology was used;

**Step one.** MD Shields performed a database literature search (Medline, Embase, Cochrane Library and Google Scholar) initially using terms: “cough” AND “child”. Exclusions included Non-English speaking and pertussis vaccine development papers. Also excluded were papers on specific diseases including asthma, cystic fibrosis and pneumonia that already have published management guidelines. Abstracts of papers were then reviewed and relevant papers obtained. The relevant studies to the UK population were largely performed in Europe, N.American, Australia and N.Zealand and S.Africa.

Specific searches of the databases were subsequently made adding terms “gastroesophageal reflux”, “cough variant asthma”, “Isolated” OR “non-specific cough” AND “randomised controlled trial” OR “placebo”

**Step two.** MD Shields produced a framework document.

**Step three.** The framework document was sent to the other team members (A Bush, S McKenzie, M. Everard, R. Primhak) who modified the document and added their opinions until consensus was obtained.

**Step four.** General practitioners (V. McGovern, T. Carroll and N. White [GP trainee]) and paediatricians (N Kennedy and D O’Donoghue, J Hughes [both trainees]) provided further comments on improving the usefulness of the guidelines.

## Terms used in this guideline

**Cough:** For the purposes of this document the following definition is used: “cough is a forced expulsive manoeuvre, usually against a closed glottis and which is associated with a characteristic sound”

**Acute cough:** a recent onset of cough lasting less than 3 weeks

**Chronic cough:** a cough lasting more than 8 weeks .

The main reason to classify cough on this time basis is that 3-4 weeks allows most simple infective causes of cough to have resolved and identifies those children with chronic cough that might require further investigations.

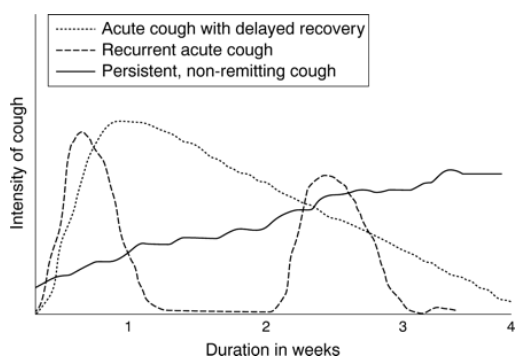
### **Prolonged acute cough:**

Clearly there is a ‘grey’ area between acute and chronic cough, sometimes called ‘subacute cough’ (18). An example of such a situation would be a child with pertussis or post viral cough whose cough may be slowly resolving over a 3-8 weeks period. If a cough is resolving an additional period of time may be required to elapse before performing further investigations. Most acute coughs associated with upper respiratory infections should be abating in the second and third week. However, if the cough is not waning by the third week and is becoming more severe in frequency and intensity (‘relentlessly progressive’) earlier investigations may be warranted (Table 2).

**Recurrent cough:** a recurrent cough without a cold is taken as repeated ( $\geq 2$ /year) cough episodes, apart from those associated with head colds, that each last more than 7-14 days (19,20). If the periods of resolution are short frequently recurrent cough will be difficult to distinguish from persistent chronic cough.

Figure 1 illustrates types of cough intensity over time (21).

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**Post viral cough:** is taken as a cough originally starting with an upper respiratory tract infection but lasting more than 3 weeks.

**Specific cough:** a specific cough is one in which there is a clearly identifiable cause.

***Non-specific isolated cough:*** the term ‘non-specific isolated cough’ has been used to describe children who typically have a persistent dry cough, no other respiratory symptoms (isolated cough), are otherwise well with no signs of chronic lung disease and have a normal chest radiograph.

## ACUTE COUGH IN CHILDREN

### 1. INTRODUCTION

#### Recommendation 1.1

The vast majority of children with acute cough have a respiratory tract infection and an attempt should be made to arrive at a specific clinical diagnosis (Table 1) (22).

Acute cough is usually caused by viral upper respiratory tract infection (URTI) likely with associated bronchitis in children but may arise from lower respiratory tract infections, hayfever, an inhaled foreign body or be the first presentation of a chronic disorder. Symptomatic URTI with cough in school children typically occurs between 7-10 times per year (23,24).

Prospective studies of acute cough in young children in general practice suggested that about 50% had recovered by 10 days and 90% by 25 days and therefore 10% still had problems in the 3<sup>rd</sup> to 4<sup>th</sup> week. This was supported by a recent systematic review of the natural history of acute cough in which it was estimated that about one quarter will still be unwell with cough at two weeks (25,26).

### 2. INVESTIGATIONS

#### Recommendation 2.1

Most children with cough due to a simple URTI will not need any investigations.

The absence of fever, tachypnoea and chest signs appears to be most useful for ruling out future complications in children with cough in primary care.

In a prospective cohort study of 222 children 0-4 years of age in primary care with acute cough the presence of fever, tachypnoea and chest signs were associated with increased risk of subsequently developing a complication (any new symptom or sign suggestive of a deterioration). Reconsultations occurred in 10% of cases which were mostly due to persisting symptoms and reported serious complications were rare with two hospital admissions for bronchiolitis and one for pneumonia (27, 28).

#### Recommendation 2.2

Children in whom an inhaled foreign body is a likely cause of cough should have an urgent rigid bronchoscopy

#### Recommendation 2.3

A chest radiograph should be considered in the presence of lower respiratory tract signs, a cough that is relentlessly progressive beyond 2-3 weeks, haemoptysis or features of an undiagnosed chronic respiratory disorder (Table 2)

While the cough associated with acute head cold may take 2-4 weeks to fully resolve usually the cough severity and frequency is abating after the second week. Occasionally a child is seen with an acute onset cough and relentlessly progressing in frequency and severity beyond 2-3 weeks. In this situation diagnoses that should be considered include retained inhaled foreign body, expanding mediastinal neoplasm, lobar collapse secondary to mucous plug and TB (often with accompanying weight loss). Table 2 summaries some of the indications for performing a chest radiograph in acute cough.



**Table 1.** Questions to be addressed to arrive at a specific diagnosis for acute cough.

Question	Features	Likely common diagnoses
Is this an acute upper respiratory infection?	Coryzal symptoms	Simple head cold with cough suggesting presence of some degree of tracheitis and / or bronchitis
Is this a croup syndrome?	Stridor with an associated 'barking' or 'croupy cough'. In milder cases only the barking cough may be present	<ul style="list-style-type: none"> <li>• Viral croup</li> <li>• Recurrent spasmodic croup</li> <li>• Bacterial tracheitis<sup>1</sup></li> </ul>
Are there any features to suggest a lower respiratory tract illness?	Tachypnoea*, respiratory distress with increased work of breathing, chest signs (crackles/wheeze) and fever	<ul style="list-style-type: none"> <li>• pneumonia<sup>2</sup></li> <li>• bronchiolitis<sup>3</sup></li> <li>• asthma<sup>4</sup></li> </ul>
Is there anything to suggest an inhaled foreign body?	Very sudden onset or witnessed choking episode	Inhaled foreign body. Bronchoscopy is indicated on history alone to diagnose and remove it.
Is there anything to suggest acute pollinosis (hay fever)?	Cough with other features of 'hayfever' in pollen season. This cough is often described as a 'clearing the throat' cough.	Allergic rhinitis cough  True coughing may suggest allergic tracheobronchial inflammation
Is there anything to suggest that this is a presentation of a chronic respiratory disorder?	Failure to thrive, finger clubbing, over inflated chest, chest deformity, features of atopy	See chronic cough section

\* The respiratory rate varies with age and tachypnoea is defined as a respiratory rate > 60/min for < 2 months, > 50/min for 2 to 12 months, and > 40/min for > 1 year of age.

<sup>1</sup> Bacterial tracheitis is an uncommon but life threatening condition in which children have a high temperature and progressive upper airways obstruction. The croupy cough helps to distinguish it from epiglottitis. These children usually need their airway secured and intravenous antibiotics to cover Staphylococcus aureus, Haemophilus Influenza B and streptococcal infections.

<sup>2</sup> Pneumonia is suggested if there is cough, fever and signs of respiratory distress in the absence of stridor or wheeze.

<sup>3</sup> Bronchiolitis is suggested in an infant with cough associated with crepitations with or without audible wheeze during the winter RSV season

<sup>4</sup> Asthma is suggested if cough is associated with wheezing

**TABLE 2** Suggested indications for performing a chest radiograph in a child with acute cough

Indication	Features	Likely common diagnoses
Uncertainty about the diagnosis of pneumonia.	<ol style="list-style-type: none"> <li>1. Fever and rapid breathing in the absence of wheeze/stridor.</li> <li>2. Localising signs in chest*</li> <li>3. Persisting high fever or unusual course in bronchiolitis.</li> <li>4. Cough and fever persisting beyond 4-5 days.</li> </ol>	Pneumonia. N.B. chest radiograph is not always indicated- use to resolve uncertainty or in more severe cases **
Possibility of an inhaled foreign body	Choking episode may not have been witnessed but cough of sudden onset or presence of assymmetrical wheeze or hyperinflation	Inhaled foreign body. Expiratory film may help in acute bronchial obstruction, but normal chest radiograph does not exclude foreign body. Bronchoscopy is the most important investigation.
Pointers suggesting that this is a presentation of a chronic respiratory disorder	<ol style="list-style-type: none"> <li>1. failure to thrive</li> <li>2. finger clubbing</li> <li>3. over inflated chest</li> <li>4. chest deformity</li> </ol>	See chronic cough section
Unusual clinical course	<ol style="list-style-type: none"> <li>1. Cough is relentlessly progressive beyond 2-3 weeks.</li> <li>2. Recurrent fever after initial resolution.</li> </ol>	Pneumonia. Enlarging intrathoracic lesion TB Inhaled foreign body Lobar collapse
Is there true haemoptysis? ***		Acute pneumonia Chronic lung disorder eg CF Inhaled Foreign Body TB Pulmonary Haemosiderosis Tumour, AV malformation

\*Dull percussion, reduced air entry, crackles or bronchial breathing.

\*\* Community Acquired Pneumonia Guidelines (38-40)

\*\*\* true haemoptysis needs to be differentiated from spitting out blood secondary to nose bleeds, cheek biting, pharyngeal and oesophageal or gastric bleeding.

### **3. TREATMENTS: cough with simple head colds**

While parents report benefit from various over the counter preparations for treating children's cough there is little evidence of a specific pharmacologic effect.

#### **Recommendation 3.1**

Over the counter medications are as effective as placebo for acute cough with head colds in children

A systematic review of 6 RCTs and a further recent RCT found that over the counter antitussives, antihistamines and antihistamine-decongestant combinations were as effective as placebo with the potential for causing side-effects. (29, 30).

#### **Recommendation 3.2**

Bronchodilators are not effective for acute cough in non-asthmatic children

RCTs of salbutamol versus placebo has no beneficial effect for acute cough in non asthmatic children (31, 32).

#### **Recommendation 3.3**

Antibiotics are generally not effective or recommended for treating acute coughs due to simple 'head colds'

While there is evidence for increased parental satisfaction with receiving an early antibiotic prescription for children with coughing with 'head colds' systematic review of the evidence shows that antibiotics are not beneficial and may be associated with side effects. This included children with acute bronchitis and green coloured sputum in the absence of signs of possible pneumonia (33-35)

#### **Recommendation 3.4**

There may be benefits from educating the community and medical profession about the natural history of cough with head cold.

For the majority of children the cough will have resolved by 14 days, however, for an important minority the cough will take 3-4 weeks to resolve. Giving this information to parents may reduce the need for subsequent doctor consultations providing the cough is subsiding (27,28,36) and provided that warnings are given about when to reconsult (eg on-going fever, tachypnoea)

#### **Recommendation 3.5**

Parents should be warned that information obtained from the internet on cough may be unreliable.

According to one study of the 19 website pages identified in the year 2000 ten contained more incorrect than correct information and only 1 appeared to be mostly correct (37).

### **4. TREATMENTS: cough with specific diagnosis**

#### **Recommendation 4.1**

Evidence based guidelines exist for treatments of the common specific causes of acute cough and should be referred to.

- Community Acquired Pneumonia guidelines (38,39,40).
- Croup (41)
- Bronchiolitis (42-44)

- Asthma (45)

### **Recommendation 4.2**

Macrolide antibiotics should be given early to children with pertussis

If pertussis has been diagnosed – macrolide antibiotics, if given very early (in the first 1 to 2 weeks) in the course of the disease, can alter slightly the clinical course but their main role is to reduce the period of infectivity (46). However, the early stages of pertussis can be difficult to distinguish from simple head colds making this recommendation hard to carry out in practice other than in the situation when coughing starts after a known exposure. Azithromycin and clarithromycin are equally effective but have fewer side effects than erythromycin (47-49)

Anecdotal evidence suggested using salbutamol or steroids might reduce the cough spasm severity in pertussis but this was not confirmed in RCTs (50,51). A recent Cochrane review concluded that there was insufficient evidence (poor study quality) to draw conclusions about the efficacy of steroids, salbutamol, antihistamines at symptomatic relief of coughing in pertussis. There were no statistically significant differences in coughs per 24 hours or duration of hospitalization between these interventions and placebo (52)

### **Recommendation 4.3**

Antihistamines and intranasal steroids are beneficial for children with an allergic cough in the pollen season.

A RCT has shown that antihistamines are beneficial for reducing cough frequency and intensity during the pollen season (53). Intranasal steroids may have an efficacy advantage over antihistamines (54).

## CHRONIC COUGH IN CHILDREN

### 1. INTRODUCTION

Most coughing in children is related to transient infections. Therefore a period of observation (3 to 8 weeks) may be needed to determine if further investigations will be required. Indeed, in one study about 50% of children with apparent persistent nocturnal cough improved in the 2 weeks after presentation irrespective of how long the cough had been going on before the time of assessment (55). If the cough is abating no further tests may be required whereas if the cough is progressive or if a retained inhaled foreign body is likely earlier investigations are required.

A recurrent cough without a cold is taken as repeated ( $\geq 2$ /year) cough episodes apart from those associated with head colds that each last more than 7-14 days. If the periods of resolution are short recurrent cough will be difficult to distinguish from persistent chronic cough. In addition, many children with asthma syndromes or more serious underlying illnesses such as cystic fibrosis have recurrent cough with flare ups during disease exacerbations. Therefore in these guidelines children with prolonged acute cough, chronic cough and recurrent cough are not specifically separated. Clinical experience suggests that most children with chronic cough have recurrent viral bronchitis (recurrent cough) or post viral syndromes (subacute cough) and are otherwise healthy. In a two year prospective cohort study rhinovirus (32%), pertussis (17%) and RSV (11%) were the most frequent respiratory pathogens detected from children with prolonged coughing episodes but other infections have been associated with prolonged cough including Mycoplasma, Chlamydia and adenovirus (56,57).

#### Classifications

Generally, cough in children can be placed in one of three overlapping categories (58) by a good history and thorough physical examination.

These three categories are:

1. **Normal child:** recent objective audio-recording studies suggest that normal children (currently free from upper respiratory tract infections) have on average 11 coughs each day with some experiencing more than 30 episodes per day (59,60). Cough frequency and severity increases during upper respiratory tract infections and some children experience recurrent upper respiratory tract infections (eg 8-10 episodes predominantly in the winter) with each new infection being associated with coughing that may last more than 7 days (e.g. recurrent viral bronchitis). It is therefore difficult and requires experience to be sure when a child is normal (61,62).
2. **Specific cough:** after a detailed clinical assessment pointers often suggest a specific diagnosis and requirement from additional investigations (Tables 4,5)
3. **Non-specific isolated cough:** clinical experience and epidemiological studies indicate that a significant number of children are otherwise well with no underlying serious illness and appear to have a “non-specific isolated persistent cough”. This term has been used when an isolated dry cough persists with no other chest signs or symptoms in an otherwise completely well child, in whom appropriate investigation has revealed no abnormality (58, 63). “Non-specific isolated persistent cough” should not be thought of as a diagnosis in itself but rather as a label. As these children truly have increased cough frequency and severity (64) there is likely a specific but as yet unidentified cause. Although the precise diagnosis is not available it is possible that they have mild forms of the specific diagnoses listed in Table 4 or very occasionally a more serious underlying condition (Table 5).

Recent evidence would suggest that only a small proportion of children with non-specific isolated persistent cough have asthma. They have different risk factors from classical asthma and only a small number subsequently develop asthma with wheezing. Bronchial hyper- reactivity (BHR) is associated with the symptom of wheeze but not isolated dry or nocturnal cough and is not predictive of response

to asthma treatment or the development subsequently of asthma (65-68). In addition, studies of airway inflammation that include induced sputum and BAL fluid suggest that only a small minority of children with unexplained isolated cough have evidence of eosinophilic airways inflammation (69-71). Some of these children have heightened cough receptor sensitivity (72). The role of GOR as a cause of isolated cough in otherwise well children is unclear. Gastro-oesophageal reflux is a frequent finding in infancy with or without vomiting and is only sometimes associated with cough symptoms.

## **2. EVALUATION**

When evaluating a child with a chronic cough the key aims are to decide if:

- a diagnosis can be easily made clinically or is it necessary to perform further investigations to make a diagnosis or rule out certain more serious conditions
- there are any effective treatments available or is reassurance and support all that is needed

### ***POINTERS IN THE HISTORY (TABLE 3)***

There is limited published evidence but much experience on which to make statements on how the characteristics of a cough relate to the underlying cause.

Traditionally cough is characterized by its time of onset (neonatal, infancy and childhood), nature (dry or productive), its quality (brassy, croupy, honking, paroxysmal or staccato), the timing (persistent, intermittent, nocturnal and on awaking), triggering factors (cold air, exercise, feeding, seasonal, starts with a headcold), alleviating factors (bronchodilators, antibiotics) and presence of associated symptoms (eg wheezing, shortness of breath).

#### **Recommendation 2.1**

A detailed history should be taken and should address the following questions:

- 1] how and when did the cough start?
- 2] what is the nature and quality of the cough?
- 3] is the cough an isolated symptom?
- 4] what triggers the cough?
- 5] is there a family history of respiratory symptoms, disorders and atopy.
- 6] what medications is the child on, what treatments has the child had for the cough and what effect they have had on the cough frequency and severity?
- 7] Does the cough disappear when asleep (suggests psychogenic or habit cough)
- 8] Does the child smoke cigarettes or exposed to environmental smoke?

#### **Recommendation 2.2**

Cough starting in the neonatal period requires further investigation. All neonates and infants with an unexplained persistent cough should be observed feeding by an experienced nurse.

Chronic cough starting in the neonatal period usually indicates significant disease, and especially if it starts in the first few days or weeks of life. Possible diagnoses include:

- Aspiration - tracheoesophageal fistula or laryngeal cleft. A moist cough following feeding, irritable and arching after feeds or choking on feeds require further investigations.
- Congenital malformation - compression of airway or tracheobronchomalacia,
- Cystic Fibrosis,
- Primary ciliary dyskinesia, especially if there is chronic persistent rhinitis from birth
- Lung infection in-utero or in perinatal period eg. CMV, RSV, chlamydia.

**Recommendation 2.3**

Determine if the cough is wet and productive or dry

It is worth determining if the cough is productive (wet / moist with sputum production versus dry). Reporting of this feature compares well with amount of phlegm seen at bronchoscopy (73). A cough that sounds wet or productive implies either an increase in airway secretions or abnormalities in its clearance mechanisms. It may be difficult to be sure if a young child has a productive cough as most young children and especially those less than 5 years of age do not expectorate sputum but tend to swallow it. They often vomit and the sputum colour can be seen in the vomitus.

Dry non-productive cough may be suggestive of allergens in an allergic child, viral infections, TB or inhaled irritants.

- Children with isolated dry cough who appear otherwise healthy and have a normal chest radiograph could have one of the conditions listed in Table 4. Children with stable asthma cough more frequently than controls and an increase in coughing heralds the onset of an exacerbation in those asthmatic children whose parents report cough to be a significant feature in their exacerbations (74). Many of the conditions listed in Table 5 can be difficult to distinguish from asthma.
- Children with persistent productive (moist or wet) cough which may or may not be associated with ill-health and recurrent pneumonia or pulmonary infiltrates on chest radiograph should be investigated to determine if they have bronchiectasis or any of the specific suppurative lung conditions that eventually lead to bronchiectasis (Table 5).

Cough productive of casts is unusual and suggests the rare plastic bronchitis (75)

**Recommendation 2.4**

Determine whether the cough occurs in paroxysmal spasms and is associated with an inspiratory 'whoop'

Paroxysmal spasmodic cough with or without an inspiratory 'whoop' is the major feature of the pertussis syndromes with B.Pertussis being the most likely organism (56,57, 76-78). Post tussive vomiting often occurs.

Pertussis may be underdiagnosed in children and adolescents. In a community based survey parents reported cough lasting longer than 2 weeks in the past 12 months in 22% of children 5-14 years of age with 18% of these meeting the case definition for pertussis (77). In a second study 37% of school aged children with cough lasting more than 2 weeks had serological evidence of recent Bordetella pertussis. Pertussis should be considered in any child coughing for more than 2 weeks (especially if associated with whooping or vomiting) even if the child has been previously immunized (78).

A staccato like cough in infancy has been described in Chlamydia infections (79)

**Recommendation 2.5**

Determine if the cough is brassy, croupy or bizarre and honking.

A brassy, barking or croupy cough is suggestive of tracheal or glottic irritation and children appeared distressed with the cough (80-86). A 'seal-like' barking or brassy cough which is particularly severe with concomitant viral upper respiratory infection occurs in children with tracheal compressive lesions or in those with tracheomalacia including the so called 'TOF cough' following repair of a tracheoesophageal fistula.

A disruptive bizarre honking cough in a child who exhibits 'la belle indifference' suggests a psychogenic cough (87-92). Although the literature generally lumps the bizarre honking psychogenic

cough with habit coughs clinical experience would suggest that habit coughs occur as a dry non-irritative repetitive coughing often persisting long after a head cold has already resolved. Psychogenic and habit coughs generally increase when parents or teachers are present. Traditionally these coughs are described as not being present at night. However, a recent case report using a cough monitor suggests that some do have increased cough at night (90).

The condition of 'psychogenic cough' is not well defined but the diagnosis implies that there is no underlying organic cause for the coughing. The underlying cause may relate to the secondary gain produced by the coughing e.g. school absence. There is little information on how accurate clinical characteristics (Table 3) are at identifying children with a non-organic cause of coughing.

Suggestive features of non-organic coughing include:

- Bizarre honking disruptive coughing
- Cough that obviously increases with attention and decreases with involvement and concentration in some activity or sleep
- Child exhibits 'la belle indifférence' to the disruptive coughing

### **Recommendation 2.6**

Children with true haemoptysis require further investigation including a chest radiograph. It is important to ensure that a child truly has haemoptysis. Apparent haemoptysis may be related to nose bleeds, cheek biting, haematemesis or factitious illness.

Causes of haemoptysis include:

- Pneumonia / lung abscess
- Chronic lung disease with bronchiectasis eg Cystic Fibrosis
- retained inhaled foreign body
- TB
- pulmonary haemosiderosis
- tumour
- pulmonary arteriovenous malformation
- pulmonary hypertension

### **Recommendation 2.7**

Determine if the cough is an isolated symptom

Children with coughing associated with wheezing or breathlessness should have the following conditions considered;

- asthma
- retained inhaled foreign body
- recurrent pulmonary aspiration
- airways compression or tracheobronchomalacia
- bronchiolitis obliterans or interstitial lung disease
- neonatal chronic lung disease
- cardiac disease with either congestive heart failure or large left to right shunts

Other atopic disorders such as eczema or allergic rhinitis makes an asthma diagnosis more likely. It is important to remember that parents may report associated shortness of breath with the bout of coughing and that this is different from true breathlessness when a child is not actually coughing.



### **Recommendation 2.8**

Determine what triggers the cough

- Children with asthma may cough with exercise (especially in cold air), excitement and at night.
- Children with psychogenic coughs typically have increased cough when given attention by others and the cough disappears when the child is asleep.
- Swallowing or post prandial cough suggests possibility of recurrent pulmonary aspiration.

### **Recommendation 2.9**

Determine if there is a family history of respiratory disorders

- A strong family history of asthma and other atopic disorders puts a child into the background that makes an asthma diagnosis more likely.

A history of TB or elderly relative with a cough is important for the diagnosis of TB.

### **Recommendation 2.10**

Determine what medication the child is on

- Children treated with angiotensin converting enzyme inhibitors may develop persistent cough (93, 94).
- It is important to record what treatments have been used for the cough and what effect these have had.

**Table 3 Questions to address in cough evaluation**

<b>Question</b>	<b>Examples</b>	<b>Diagnosis</b>
How did the cough start?	Very acute onset	retained inhaled foreign body
	Head cold	an infective cause eg post viral
When did the cough start?	Neonatal onset (especially if in first few days of life)	<ul style="list-style-type: none"> <li>• Aspiration</li> <li>• Congenital malformation</li> <li>• Cystic Fibrosis</li> <li>• Primary ciliary dyskinesia</li> <li>• Lung infection in-utero</li> </ul>
What is the quality of the cough?	Productive ('moist or wet')	Chronic suppurative lung disease (bronchiectasis) eg CF
	Paroxysmal spasmodic cough with or without an inspiratory 'whoop' and vomit	Pertussis or pertussis-like illness
	Haemoptysis	<ul style="list-style-type: none"> <li>• CF</li> <li>• Other bronchiectasis</li> <li>• retained inhaled foreign body</li> <li>• TB</li> <li>• tumour.</li> <li>• pulmonary haemosiderosis</li> <li>• pulmonary arteriovenous malformation</li> </ul>
	'Bizarre honking cough' in a child exhibiting 'la belle indifference' to the cough and which increases with attention	Psychogenic cough
	Dry repetitive cough, disappears with sleep	Habit cough
	Brassy, barking or 'seal like'	Tracheal or glottic cause eg tracheo- and /or bronchomalacia
	Cough producing casts of the airways	Plastic bronchitis
Is the cough relentlessly progressive?		Inhaled foreign body Lobar collapse TB Rapidly expanding intrathoracic lesion
Is the cough an isolated symptom?	Isolated cough (otherwise well)	Non-specific isolated cough Recurrent viral bronchitis Psychogenic cough
	Associated wheezing present	1] asthma 2] retained inhaled foreign body 3] recurrent pulmonary aspiration 4] airways compression or tracheobronchomalacia 5] bronchiolitis obliterans or interstitial lung disease 6] neonatal chronic lung disease and rarely 7] cardiac disease with either congestive heart failure or large left to right shunts
	Associated ill-health, recurrent pneumonia or pulmonary infiltrates	Cystic Fibrosis Immune deficiencies Primary ciliary disorders Recurrent pulmonary aspiration Retained inhaled foreign body Tuberculosis Persistent bacterial bronchitis Anatomical disorder
	Associated shortness of breath and restrictive lung defect	Interstitial lung disease
What triggers the cough?	Exercise, cold air, early morning	Asthma
	Lying down	Post nasal drip, GOR disease
	Feeding	Recurrent pulmonary aspiration

### **3. POINTERS IN THE CLINICAL EXAMINATION**

#### **Recommendation 3**

All children with cough should have a full clinical systematic examination including an assessment of the child's general health, height and weight centile, nutritional status and ENT examination.

Digital clubbing will be missed unless specifically sought, and asymmetric auscultatory signs also point to the need for further investigation.

A normal clinical examination does not exclude significant pathology. It is worth asking the child to cough or 'huff' as part of the examination as this may help identify children with a loose wet cough. ENT examination should include the external auditory meatus looking for wax or a foreign body which may cause chronic cough possibly through stimulation of the auricular branch of the vagal nerve (95). Rarely mannerisms associated with unusual stereotypic coughs would suggest Tourette's syndrome (96). However, the diagnosis of Tourette's syndrome cannot be made on a single tic, including isolated cough.

Cough can be a manifestation of congestive heart failure with pulmonary oedema which will occur most commonly in infancy.

### **4. INVESTIGATIONS**

#### **Recommendation 4.1**

A chest radiograph is indicated for most children with chronic cough.

A chest radiograph will give a good 'overview' of the state of the lungs and may give indications for further investigations. A chest radiograph may not be indicated if a mild specific disorder is definitively diagnosed (asthma / allergic rhinitis or if a pertussis-like illness is clearly resolving). However, a normal chest radiograph does not always exclude significant pathology such as bronchiectasis and further imaging may be needed.

#### **Recommendation 4.2**

Spirometry with or without tests of bronchodilator responsiveness (BDR) or bronchial hyperreactivity (BHR) should be attempted in children old enough to perform the manoeuvres.

Spirometry also gives a good 'overview' of the state of lung volumes and airways calibre.

Unfortunately the presence of BHR in children with isolated cough is not predictive of response to asthma treatment or the development subsequently of asthma (68,97,98).

#### **Recommendation 4.3**

An attempt should be made to observe the cough and to obtain a sample of sputum. This will be difficult in young children and may require help of an experienced physiotherapist. The sample can be sent for microbiological assessment (culture and sensitivity, virology including using PCR) and for differential cytology.

#### **Recommendation 4.4**

Allergy testing (skin prick or RAST specific testing) may be helpful in determining if a child is atopic and in the correct background that would make problem coughing more likely to be due to asthma.

The presence or absence of pointers suggesting specific and serious lung disease will determine the requirements for more detailed investigations (Tables 3,4,5 )

In an otherwise healthy child with chronic dry or recurrent cough the investigations may be initially limited to those for conditions in Table 4 but careful follow up is required to ensure no signs of more serious disease develop. A child presenting with chronic productive cough and signs of chronic respiratory disease will require assessment for the conditions listed in Table 5.

## **5. TREATMENT OF CHRONIC COUGH**

### **Recommendation 5.1**

The use of adult based cough algorithms are unsuitable for application in children. Marchant et al found that in fewer than 10% was asthma, GOR or upper respiratory disorder a cause of cough at a tertiary referral unit (99). The 'big three' causes of adult chronic cough (cough variant asthma, postnasal drip and gastro-oesophageal reflux) are not necessarily valid for children (13).

### **Recommendation 5.2**

An attempt should be made to remove children with chronic cough from exposure to aero-irritants such as environmental tobacco smoke

Children cough more if they are passive smokers and this is usually secondary to parental smoking. There is considerable evidence that exposure to environmental irritants such as cigarette smoke and home pollutants (such as nitrogen dioxide and pm10 particles) is associated with increased coughing. Although there is little information showing that removal from these aero-irritants is helpful it seems sensible to try and remove the child from such exposures (100-103). The adolescent who develops a recurrent or persistent cough should be suspected of cigarette smoking.

## **6. TREATMENTS: cough with a specific diagnosis**

### **Recommendation 6.1**

The management of chronic coughing relates to first making an accurate underlying diagnosis and then applying specific treatment for that condition.

Evidence based guidelines and review articles exist for treatments of the specific disorders associated with cough and should be referred to.

- Asthma
- Cystic Fibrosis
- Immune deficiencies
- Primary Ciliary Dyskinesia
- Tuberculosis

### **Recommendation 6.2**

Children with protracted bacterial bronchitis should first have other underlying conditions excluded and sputum cultured before this diagnosis is made. A trial treatment of physiotherapy and a prolonged course (e.g. 4-6 weeks) of appropriate antibiotics may be tried

There have been considerable concerns about using the term ‘chronic bronchitis’ in children with worries that asthma and more serious underlying conditions may be missed. Juvenile chronic bronchitis with persistent endobronchial infection (recently labeled persistent bacterial bronchitis) has been described for many decades (104-112). Children have chronic or recurrent cough with sputum production. This term should only be used after underlying causes have been excluded (Table 5). Despite these concerns there appears to be a group of children who have persistent productive cough in whom other underlying diagnosis have been excluded and for whom antiasthma therapy has failed. For these children a trial of intensive physiotherapy and prolonged course of an appropriate antibiotic may be useful. A recent Cochrane Review of antibiotics for prolonged moist cough in children found 2 suitable but not high quality studies that suggest beneficial effects from using antibiotics in this situation – but cautioned that antibiotics also have their own side-effects (113-115). In a recent study using an adult-based algorithm approach to the child with chronic cough (majority with wet cough) the most common final diagnosis was ‘protracted bacterial bronchitis’ and this condition may therefore be more common than previously thought (99). Further research is needed to determine how frequent this condition is and whether it is a precursor to bronchiectasis or chronic obstructive pulmonary disease in adulthood.

## **7. TREATMENTS: *non-specific isolated cough in an otherwise well child.***

The evidence base for treating children with non-specific persistent isolated cough (which includes post-viral cough, recurrent viral bronchitis) is sparse and no treatments seem particularly effective. Parental reassurance is required and usually with the passage of time the cough eventually subsides. If the impact of the cough is mild and there are no diagnostic pointers in an otherwise well child a period of observation with no diagnostic tests or treatments should be considered.

### **Recommendation 7.1**

Whenever specific workup is not pursued as part of the management plan this should be time limited (eg 6-8 weeks) and a comprehensive review performed to ensure that the cough is resolved and no specific pointers have developed.

### **Recommendation 7.2**

In otherwise well children with non-specific isolated coughing with no specific disease pointers empirical trials of anti-asthma, anti allergic rhinitis or anti gastro-oesophageal reflux therapy are unlikely to be beneficial and are generally not recommended.

### **Asthma therapy**

Anti-asthma therapy has not been shown to be effective for children with non-specific persistent isolated cough (either not effective or insufficient evidence)

- Two RCTs have compared inhaled corticosteroids (beclomethasone, fluticasone) with placebo for treating children with isolated non-specific cough. A small beneficial effect was observed only for the study using very high dose fluticasone but the author advises caution regarding the potential for side effects (55,98).
- There is currently insufficient evidence (no RCTs) to support the use of inhaled anticholinergics (14) in the treatment of persistent non-specific cough in children.
- There is currently insufficient evidence (no RCTs) to support the use of theophyllines in the treatment of persistent non-specific cough in children (15).
- There is currently insufficient evidence (no RCTs) to support the use of inhaled cromones (16) in the treatment of persistent non-specific cough in children.

- One RCT was unable to show a therapeutic advantage of Ketotifen over placebo for treating infants and young children less than 3 years with chronic cough (or wheeze) (116).
- There is currently insufficient evidence (no RCTs) to support the use of leukotriene receptor antagonists in the treatment of persistent non-specific cough in children (117).

It can be difficult to determine whether a child with non-specific isolated coughing has underlying cough predominant asthma and therefore might respond well to anti asthma therapy. Therefore many practitioners now recommend a 'trial of anti-asthma therapy' for young children with isolated coughing (conditions listed in Table 1) as a test for asthma. This practice is less than ideal but results from an imprecise definition of asthma and lack of suitable available tests to confirm an asthma diagnosis in young children.

### **Recommendation 7.3**

If a trial of anti-asthma therapy is used to diagnose problem coughing as being caused by asthma the treatment should be effectively delivered in adequate doses and clear cut outcomes recorded.

A definite period of time should be set e.g. 8-12 weeks after which the trial of anti-asthma medication should be stopped

Before embarking on a 'therapeutic trial' of asthma medication it is worth first attempting to document bronchial hyper responsiveness (e.g. peak flow variability during a period of home monitoring, FEV1 response to acute administration of bronchodilator, or an acute bronchoconstriction to a simple exercise test).

When using a 'trial of medication' to make a diagnosis of cough variant asthma it is important that the treatment is effectively delivered in adequate doses and that clear outcomes are recorded by parents. The response to short acting bronchodilators should be recorded to determine if they provide short term relief of coughing. In order to clearly confirm or exclude an asthma diagnosis inhaled corticosteroids are likely required (example: BDP or BUD 400 mcg per day for the defined period of 8-12 weeks). Alternatively for those with chronic cough (regular daily or nocturnal) a therapeutic trial of oral steroid (example: prednisolone 1-2 mg / Kg for 3-5 days) is an effective tool to resolve symptoms quickly and point to a diagnosis of asthma (118).

If a child has frequently recurrent cough lasting greater than 2 weeks with 'head colds' but completely recovering in-between that might be due to asthma a longer period of treatment (e.g. 8 -12 weeks) would be required to determine whether the cough frequency and severity of the episodes has been reduced.

If the child has responded to anti-asthma therapy and the treatment has subsequently been stopped cough variant asthma is suggested by an early relapse that again responds to therapy. If there is no response the treatment should be stopped as asthma is unlikely and the cough is unresponsive to asthma medication. This is important so that children with simple recurrent viral bronchitis or post-viral cough do not end up on long term high doses of inhaled corticosteroid.

### **Postnasal drip and rhinosinusitis therapy**

It has been suggested that allergic rhinitis and sinusitis are associated with cough that results from postnasal drip and irritation of the larynx although the evidence behind this is lacking (119,120). The typical adult symptoms of sensation of secretions dripping down the posterior pharynx from the back of the nose and frequent 'throat clearing' type of cough may be difficult to elucidate from a child. Children with chronic allergic rhinitis may have a transverse nasal crease due to the 'allergic salute' from frequent nose rubbing. When a true harsh self propagating cough is present it is unlikely that

treatment of nasal secretions will be beneficial as it is likely that the same pathological process occurs in both the nose and the laryngotracheobronchial tree. In adults a major diagnostic criterion is response to treatment. Sinusitis has been described in association with allergic rhinitis and asthma in children (121-123)

#### **Recommendation 7.4**

In children with a throat clearing type of cough and signs of allergic rhinitis allergen avoidance and a trial of therapy is indicated.

Allergen avoidance, oral antihistamines and intranasal corticosteroids are the cornerstones of management (124).

#### **Recommendation 7.5**

Empirical Gastro-oesophageal reflux (GOR) therapy is not indicated for non-specific cough in children. Although non-controlled studies have found improvement of cough with GOR therapy a recent Cochrane Review showed that there was a lack of data on which to base recommendations for the empiric treatment of GOR in children with cough (125-127).

#### **Recommendation 7.6**

In arriving at a diagnosis of psychogenic or habit cough the physician should first be sure that organic causes are unlikely and that the suggestive features are present.

Suggestive features of non-organic coughing include:

- Bizarre honking disruptive coughing
- Cough that obviously increases with attention and decreases with involvement and concentration in some activity or sleep
- Child exhibits 'la belle indifférence' to the disruptive coughing

Habit or 'tic' like coughs are generally less disruptive.

#### **Recommendation 7.7**

Psychotherapy such as behaviour modification regimes may be helpful in treating psychogenic coughing (87-92).

**Table 4.** Patterns, causes and potential investigations of chronic or frequently recurrent cough in otherwise healthy children.

	Pattern	Cause	Potential Investigations
Frequently recurring viral bronchitis	Episodic, frequent in winter, associated with 'head colds', may occur back-to-back'	Viral infections. Crowded living conditions, ETS and attendance in child care nursery	Nil chest radiograph Examine during a period when symptom free
Postviral cough	Troublesome cough (day and night) following a respiratory infection and slowly resolving over next 2-3 months	Viral respiratory infections, chlamydia and mycoplasma infections	Nil, chest radiograph, serology. Consider trial asthma therapy (some mild asthmatics have prolonged recovery from each viral infection).
Pertussis and Pertussis-like illness	Troublesome spasmodic cough after initial respiratory infection which slowly resolves over 3-6 months. Vomiting clear tenacious mucus. Older child may complain of difficulty catching breath	B. Pertussis, parapertussis, adenovirus, influenza, parainfluenza	Nil chest radiograph, +ve serology or culture may be helpful in reducing requirements for further investigation
Cough variant asthma	Isolated cough (no wheezing) due to asthma. Confidence in diagnosis increased when strong atopic background present and cough responds rapidly to anti-asthma medication but relapses when stopped	Asthma	Nil, chest radiograph, Is airways obstruction present and reversible? BHR or BDR tests, Is there eosinophilic inflammation? Induced sputum, allergy tests, FeNO, Response to asthma medication.
Allergic rhinitis, post nasal drip and sinusitis – cough likely due to concomitant tracheobronchial inflammation.	Not fully accepted as a cause of cough. Cough when 'head hits the pillow' or constant throat clearing by day. May have transverse nasal crease of 'allergic salute'	Causes of allergic rhinitis	ENT examination, often no investigations needed, chest radiograph, allergy tests. Response to anti rhinitis treatment within two weeks.  CT scan of sinuses
Psychogenic cough	Usually an older child/adolescent. A] tic-like 'habit cough' persisting after head cold or during times of stress B] Bizarre disruptive honking cough with child exhibiting 'la belle indifference'. Cough goes away with concentration or sleep	Underlying stress.  Bizarre honking cough usually serving a purpose with some secondary gain.	It is important to do investigations to assure the doctor and parent that no major disease is being missed. However, it is important not to keep performing futile investigations that may reinforce the underlying problem.

ETS – exposure to environmental tobacco smoke  
 FeNO – fractional exhaled nitric oxide concentration  
 BDR – bronchodilator responsiveness  
 BHR – bronchial hyper reactivity  
 TOF – tracheo-oesophageal fistula



**Table 5.** Potentially serious lung disorders with chronic coughing. Most should have a chest radiograph and an attempt to obtain sputum for microbiology. A high resolution CT scan may be indicated to determine extent of disease eg focal versus generalised

Condition	Investigations
Cystic Fibrosis	Sweat test, nasal potential difference, assessment of pancreatic function, genotyping
Immune deficiencies	Differential white cell counts, immunoglobulin levels & subsets, functional antibody responses, and lymphocyte subset analysis
Primary ciliary disorders	Screening FnNO, saccharine test, ciliary ultrastructure and function, culture of ciliated epithelium
Protracted Bacterial Bronchitis	chest radiograph, sputum for culture, exclusion of other causes in this Table. Response to 4-6 weeks antibiotic and physiotherapy. HRCT scan
Recurrent pulmonary aspiration <ul style="list-style-type: none"> <li>• laryngeal cleft or 'H' type tracheo-oesophageal fistula</li> <li>• Post TOF repair with swallowing incoordination</li> <li>• Neuromuscular or neurodevelopmental disorder</li> <li>• GOR, hiatal hernia.</li> </ul>	Barium swallow, videofluoroscopy, 24 h pH studies, milk isotope scan, fat laden macrophage index* on bronchalveolar lavage if bronchoscopy indicated. Oesophagoscopy with biopsy may be indicated.  NB: there is little evidence that GOR alone is a cause of cough in otherwise healthy children.
Retained inhaled foreign body	chest radiograph and HRCT scan may show focal lung disease. Rigid bronchoscopy is both diagnostic and therapeutic and is almost always indicated if the history is suggestive of inhaled retained foreign body.
Tuberculosis	chest radiograph, Mantoux, early morning gastric aspirates and urine for specific culture
Anatomical disorder eg bronchomalacia or lung malformation eg. cystic congenital thoracic malformation.	Bronchoscopy and CT scan.
Interstitial lung disease	Spirometry (restrictive defect), chest radiograph and HRCT, lung biopsy

FnNO: fractional nasal nitric oxide.

\* fat laden macrophages in BAL may not be a specific test for recurrent pulmonary aspiration.

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