LRI Children's Hospital

Management of Chronic Cough in Children UHL Children's Medical Guideline

Staff relevant to:	Clinical staff within the UHL Children's Hospital
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1. Introduction and scope

Cough is a common presenting symptom in children. Chronic cough is variously defined as cough lasting for more than 4 weeks [1] or 8 weeks [2] but for the purposes of this guidance, we have agreed upon the more recent European definition of **cough lasting more than 4 weeks**.

Chronic cough is common and can be a symptom of various diseases and the remit of this guidance is to provide a diagnostic pathway so that serious underlying diseases are not missed. This guideline is to be used in the Leicester children's hospital for children referred for chronic cough from primary care or secondary care.

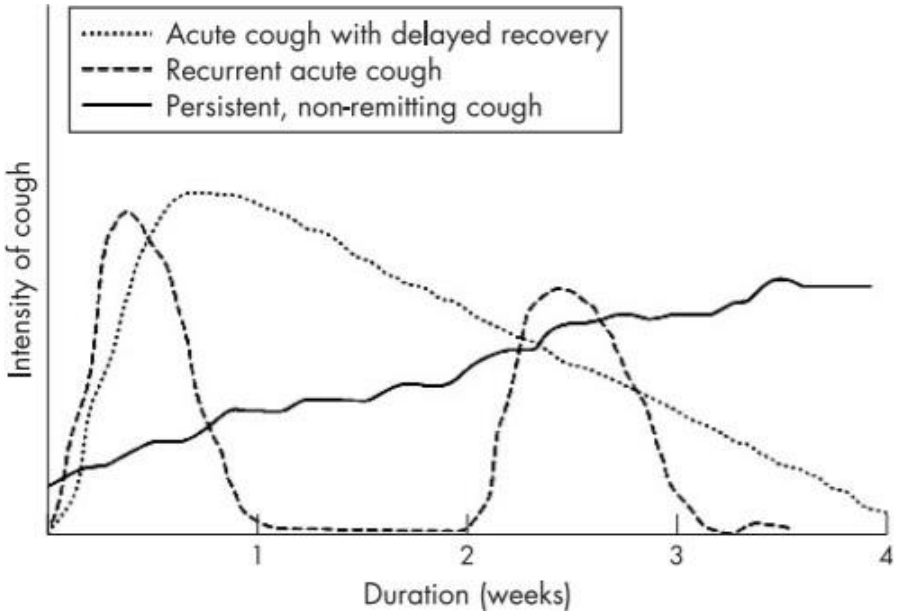
2. Clinical Assessment of a child presenting with chronic cough

2.1 Presentation:

- Many children who are referred for chronic cough, in fact have *recurrent episodes of acute cough*, typically lasting 1-3 weeks. This is a common occurrence, typically in winter, and usually in pre-school age group. In the absence of red flag symptoms (-see below), these children can be safely discharged with reassurance. In some situations, there is a delayed recovery of acute cough (~10% of post-viral cough can persist more than 3 weeks). The hallmark is improvement of symptoms with time in absence of specific treatment.

- On the other hand *persistent, non-remitting cough* (i.e. symptom severity does not improve or worsens over the course of the illness) is usually an indicator of underlying disease and investigations should be fast tracked [Figure 1].
- The other pattern to be aware of is episodic exacerbations of cough where cough does not completely disappear between episodes. These children should be managed as chronic cough.

Figure 1: Diagram representing patterns of cough over time. From Shields et al [2]



2.2 Nature of cough: one of the key diagnostic discriminators is the nature of the cough,

- A wet, or chesty cough is associated with airway secretions, and is associated with airway or parenchymal infection such as bronchitis, bronchiectasis etc.
- A dry cough is associated with many other problems (see diagnostic algorithm). DO NOT make a diagnosis of asthma in isolated cough, unless proven by objective measurements.

2.3 Other key clinical questions:

Further history and physical examination is necessary to identify specific markers of the various differential diagnoses. The broad diagnostic pathway is as given below (figure 2). There are a few red flag presentations which deserve further evaluation.

RED FLAGs (🚩) indicate need for further evaluation

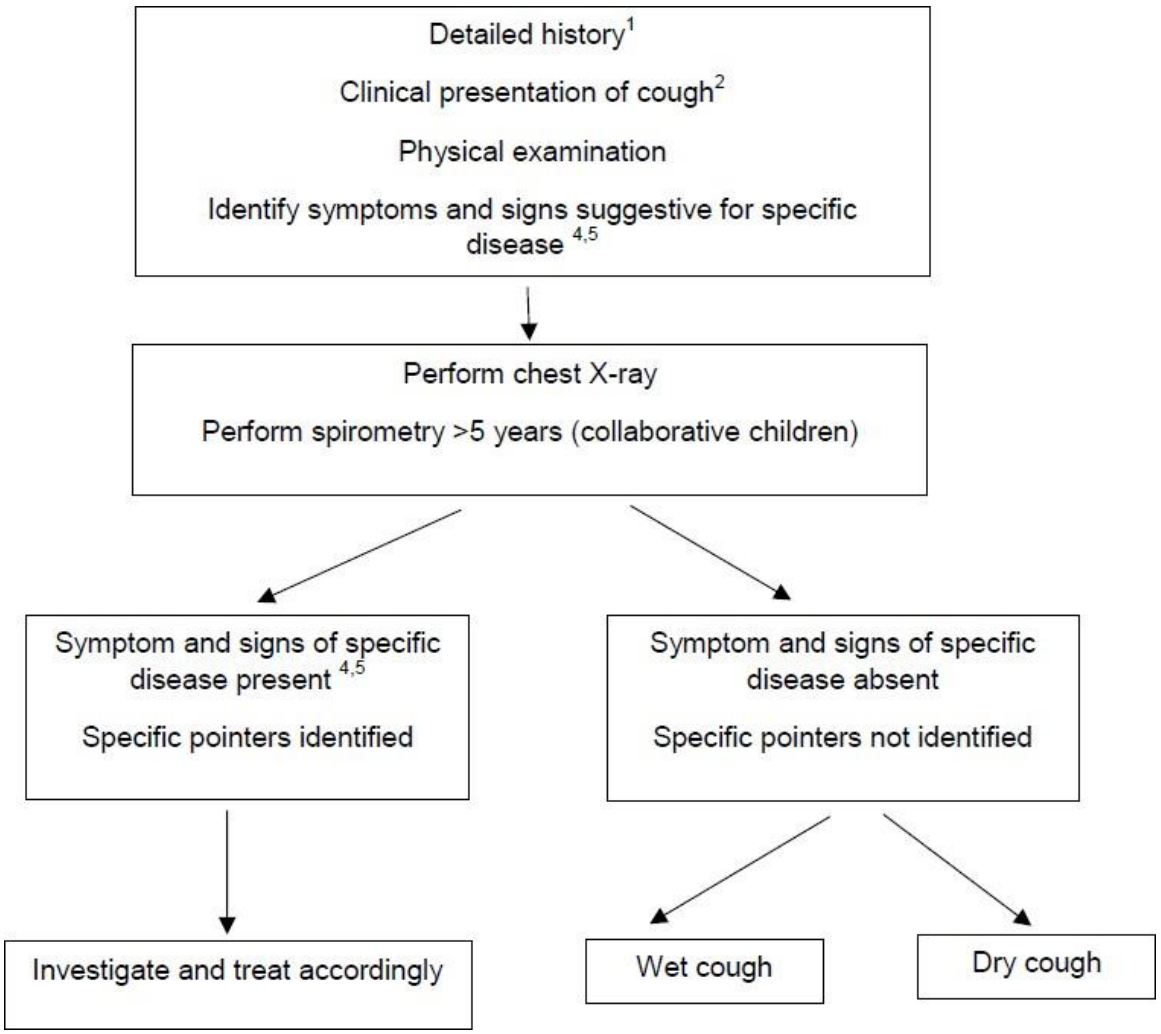
- Onset
  - Neonatal onset – PCD, congenital airway disorders 🚩
- Diurnal variation
  - Disappears when asleep – habit cough
  - Early morning dry cough – asthma
  - Cough on change of posture (e.g. waking up) – bronchiectasis, GORD

- Associations (in combination with wet cough)
    - Choking episode at onset - previous inhaled foreign body
    - Choking/gagging/vomiting with feeds – Unsafe swallow
    - Vomiting/heartburn – may be present (not universally) with GORD
    - Persistent nasal discharge – post nasal drip
        - neonatal onset of nasal discharge – PCD
    - GI symptoms: neonatal meconium ileus, steatorrhoea or malabsorption – CF
    - Other site infections (e.g. skin, GI, ear) or atypical infections – primary immunodeficiency
    - Severe illness usually needing positive pressure at onset – post infective sequelae esp. bronchiolitis obliterans
- Recurrent hospitalisations
    - Pneumonia: more than 2 chest infections with radiological changes
    - Need for HDU/intensive care during these admissions
- If sputum is produced – ask for colour, consistency, amount per day
- Presence of haemoptysis
- Birth history – If child was born outside UK, may not have had new-born screening for CF. Preterm birth, respiratory support at birth,
- Developmental history – motor/speech/ global (e.g. cough related to aspiration, weak cough leading to airway infections)
- Growth history (faltering) – CF, immunodeficiency, other chronic disease
- Immunisation history – This history is needed to interpret vaccine specific antibodies. Has BCG been given if at risk group?
- Family history: History of atopy, F/H of immunological problems, CF, PCD, consanguinity, Smoking history (relevant even if claimed to be outside home), Pets at home
- History for TB: travel, parental country of birth, BCG? Other systemic symptoms e.g. fever, night sweats, weight loss

2.4 Examination:

- Growth centiles – growth faltering. Severe growth faltering is a red flag sign
- Clubbing
- Work of breathing (non-specific, but warrants closer examination)
- Ask the child to Huff and cough (wet vs dry)
- Crackles
- Wheeze
- Differential air entry
- ENT examination - rhinitis, nasal polyps (can be associated with CF or PCD), otitis media, tonsillar enlargement.
- Cardiac examination

Figure 2: Pathway for evaluation of chronic cough in children. From Morice et al (3)



3. Differential diagnoses:

The above mentioned history and physical examination should be sufficient to form a differential diagnosis which could include:

3.1 Chronic dry cough

a. Associated with preschool wheeze/ Asthma
b. Postnasal drip associated with rhinitis
c. Habit cough (disappears completely when asleep, attention seeking nature)
d. Tracheomalacia / Post Tracheo-Oesophageal fistula (TOF) repair (Brassy barking nature – TOF cough)

3.2 Chronic wet cough

a. Recurrent viral infections
b. Protracted bacterial bronchitis (PBB -see below)

c. Recurrent or persistent airway infections (various etiologies – Immunodeficiency, recurrent aspiration, CF, PCD, Post infective bronchiolitis obliterans)
d. Non CF Bronchiectasis (Various etiologies- recurrent PBB, Immunodeficiency, recurrent aspiration, post infective – e.g. pertussis, TB, complication of foreign body aspiration or obstruction of airway)

4. Management of children presenting with chronic cough

4.1 Chronic dry cough

4.1.1 Investigations:

Diagnosis is often based on clinical assessment. There are a few investigations that are helpful. Consider the following investigations:

a. Spirometry with bronchodilator reversibility, Exhaled fractional Nitric Oxide (FeNO): over 5 years of age, if suspicion of asthma – please refer to asthma guideline [4, 6].
b. FBC (for eosinophil count, lymphocyte count)
c. Vitamin D levels
d. Total IgE and specific IgE to aeroallergens, skin prick test to aeroallergens (refer to allergy clinic) may be useful if allergic rhinitis/ postnasal drip is suspected
e. Consider serology for atypical organisms, including Bordetella pertussis, mycoplasma. If there is a high suspicion of atypical pneumonia, discuss with microbiology about sending atypical pneumonia screen from PCR of respiratory samples.
f. Consider chest radiograph, especially in presence of red flags.
g. Therapeutic trials are indicated as below

Management of dry cough:

General – applicable to all patients with relevant history

- Smoking cessation, including avoidance of second hand tobacco smoke (Step right out programme [5])

Differential diagnosis of dry cough (and management) may include

a. Preschool wheeze or asthma (note: isolated dry cough in children should not trigger a diagnosis of asthma: cough variant asthma is vanishingly rare in children. Presence of wheeze on auscultation by clinician (during exacerbations) is necessary to make this diagnosis.
    i. Trial of steroid inhaler
    ii. Inhaler technique

iii. Asthma action plan
iv. Paediatric asthma clinic referral if previous HDU/intensive care admissions or persistent sub-optimal control.(6)

b. Allergic rhinitis/postnasal drip
   i. Trial of antihistamines e.g. cetirizine
   ii. Trial of intranasal steroids e.g. Avamys
c. Tracheobronchomalacia
   i. Referral to respiratory team if high index of suspicion (If recurrent stridor refer to ENT team, in addition)
d. Habitual cough
   i. Psychosocial approach to management

UHL practice point: Consider appropriate referral (Allergy clinic, asthma service, tertiary respiratory clinic, ENT clinic) if therapeutic trials above are not successful.

5 Chronic Wet cough

A large proportion of referrals for chronic wet cough, in reality have recurrent episodes of acute / subacute cough associated with a viral respiratory tract infection. In the absence of red flags, these children can be safely discharged back to primary care, with reassurance (see 2.1 and fig 1).

UHL practice point: Children, who are not discharged as above, should be referred to a tertiary paediatric respiratory clinic within UHL.

Suggested point of referral to tertiary respiratory paediatric team. Please refer for stage 1 investigations (section 5.1.1) and start stage 1 management (sec 5.1.2) at this point, while awaiting tertiary respiratory review.

A large proportion of chronic wet cough in children is due to protracted bacterial bronchitis (PBB: for a review, see ERJ and Gilchrist). Investigations and management of children with chronic wet cough takes into account exclusion of other possible etiologies (investigations), while treating protracted bacterial bronchitis, which is the commonest differential diagnosis

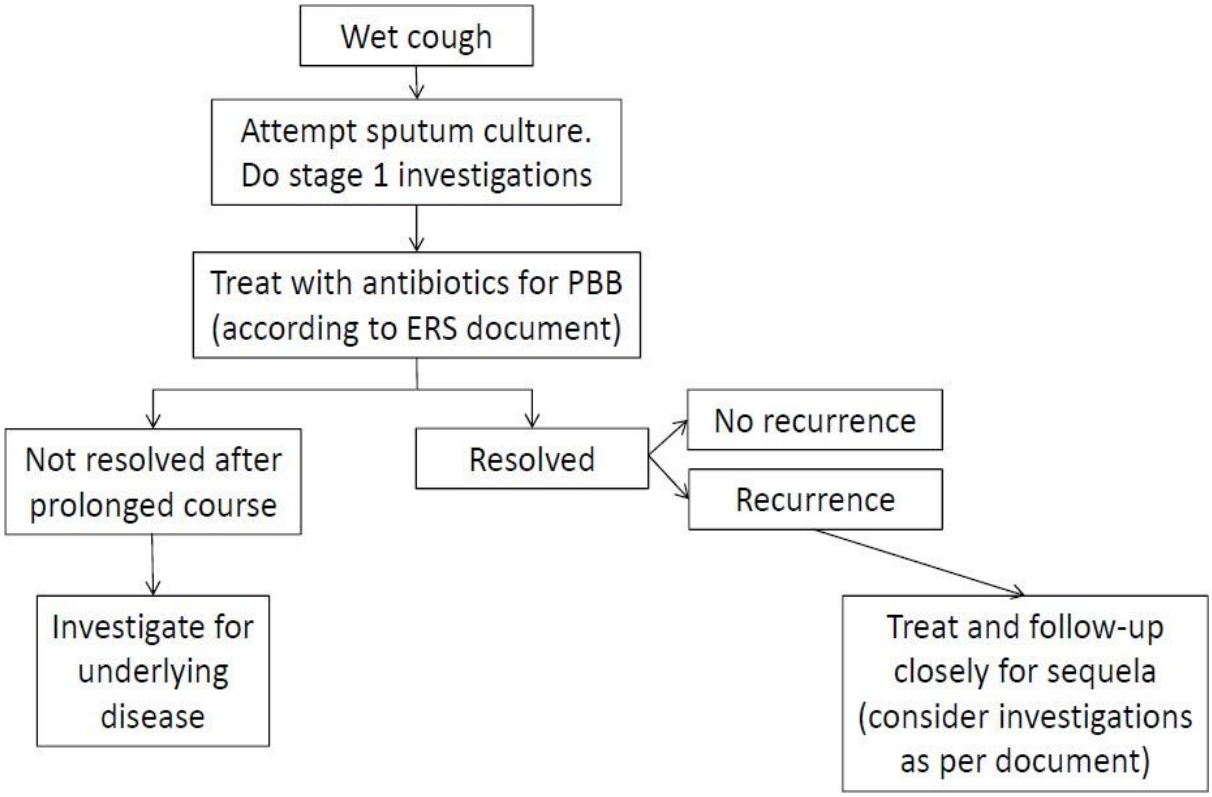
PBB is defined as per the box below

Figure 3: Diagnostic criteria for PBB (From Gilchrist [7]).

Diagnostic criteria	
PBB-micro	I. Chronic wet cough (>4 weeks) II. Lower airway infection (>10^4 colony forming units per ml on BAL) III. Cough resolution following 2 weeks antibiotics
PBB-clinical	I. Chronic wet cough (>4 weeks) II. Absence of symptoms or signs of other causes of wet cough III. Cough resolution following 2 weeks antibiotics
PBB-extended	PBB-micro or PBB-clinical but cough only resolves after 4 weeks antibiotics

The pathway for management of chronic wet cough is summarized in figure 4.

Figure 4: Pathway for management of chronic wet cough in children.
(Modified from Morice et al [3])



5.1 Stage 1

5.1.1 Investigations:

- Chest x-ray: usually normal in PBB. Look for areas of lobar, segmental or subsegmental atelectasis. Look for pronounced bronchial markings which may indicate bronchiectasis (not sensitive or specific)
- Spirometry with bronchodilator reversibility and fractional exhaled nitric oxide if over 5 years old: usually normal in PBB. Contact Paediatric respiratory physiology to arrange spirometry (email paedphysiologyrequests@**uhl-tr.nhs.uk**)
- Immunology work up including:
    - Full blood count noting absolute lymphocyte and eosinophil count
    - Immunoglobulins
    - Functional antibodies for H. influenza, pneumococcus and tetanus
    - Lymphocyte subsets
- Vitamin D
- Sweat chloride – send an email to SweatTest@uhl-tr.nhs.uk with patient details. Fill a biochemistry form for sweat chloride and send FAO Dr Maddocks, special biochemistry, chemical pathology dept, UHL (through internal post).
- Microbiology – sputum culture. There is very little evidence for utility of cough swabs in this scenario
- Virology – if there are symptoms suggesting current URTI
- Tests for mycobacterial infection[8] (e.g. Quantiferon/ Mantoux) if high index of suspicion. Refer to TB clinic if positive.

5.1.2 Treatment of PBB:

- A long course of oral antibiotics (usually 2 weeks of co-amoxiclav) is given. If long course of oral antibiotics are started for presumed PBB at a non-respiratory clinic, please notify respiratory team. If there is history of IgE mediated allergy to penicillin, alternatives such as oral second or third generation cephalosporin, trimethoprim-sulfamethoxazole, or a macrolide is used [1] (with input from microbiology team).
- Antibiotic therapy can be extended up to a maximum of 4 weeks if symptoms improve [1] but do not disappear. Evaluate on a two-weekly basis whether symptoms improving (phone call).

UHL practice point: Please email the details of children started on long course of oral antibiotics and where stage 1 investigations are done to Children's respiratory mailbox: Childrensrespiratory@uhl-tr.nhs.uk.
These children are booked to respiratory MDT virtual clinic at 6-8 weeks.
Children's respiratory nursing team will contact parents at 2 weeks (and 4 weeks if necessary) after commencement of antibiotics to decide on continuation of further therapy as per the guideline. If further prescription is necessary, it will be sent via Trustmed pharmacy.
If there is good response to antibiotics, and no concerns on stage 1 investigations, child is given an open appointment valid for 1 year following the virtual clinic review (discharge at the 1 year point if no further episodes).

- If good response, but further episode of wet cough, re-trial second course of prolonged antibiotics as above.
- In the absence of any specific diagnosis on stage 1 investigations, a second episode of chronic wet cough in 1 year or third episode of chronic wet cough should trigger **stage 2** investigations and management (5.1.4).
- No response or partial response to prolonged course of oral antibiotics:
    - Microbiology: This is especially important if there is no/ partial response to prolonged course of antibiotics, and the child is unable to expectorate sputum. Induced sputum and/or broncho-alveolar lavage (see stage 2 investigations) for airway microbiology should be considered.
    - Consider management of underlying problems as per 5.1.3
    - In some cases, this may be because of a 'reporting' fallacy. Parent may report as 'wet' cough, when it is in reality a dry cough. This may need a careful evaluation from an experienced respiratory clinician or paediatrician, especially if the child doesn't or is unable to cough at request in clinic.
    - If the above points are not applicable, trigger **stage 2** investigations and management.

5.1.3 Management of specific situations:

If stage 1 investigations are abnormal, consider the following:

- Abnormal Immunology results:
    - Obtain advice from immunology department (Generic email address: paedsimmunology@uhl-tr.nhs.uk . See also 'PID guideline[9]'
    - Consider prophylactic antibiotics
    - Referral to immunology clinic for follow-up if relevant
- Cystic Fibrosis:
    - High sweat chloride – repeat sweat chloride and refer to CF clinic
    - Intermediate sweat chloride levels (30-60 mmoL/L) – repeat sweat test. Consider other tests, including faecal elastase (pancreatic function), genetic tests for CF. Refer to CF clinic if further suspicion of CF.
- Unusual bacteria in sputum:
    - Unusual organisms such as pseudomonas in sputum should trigger investigations to etiologies such as CF, PCD or non-CF bronchiectasis.
    - Antimicrobial therapy should be tailored to the organism.
- Abnormal chest X Ray:
    - Persistent collapse/ consolidation: repeat chest radiograph after a course of antibiotics (as per stage 1). If still persistent or strong suspicion of bronchiectasis, further investigations such as Bronchoscopy and HRCT chest should be considered (see 5.1.5).
- Restrictive spirometry:
    - Underlying bronchiectasis and/or bronchiolitis obliterans must be considered. Bronchoscopy and HRCT chest should be considered (See 5.1.5). If bronchiolitis obliterans is a differential diagnosis, inspiratory and expiratory sequences of HRCT should be done. Ask for contrast enhanced CT chest if there is airway narrowing/compression on bronchoscopy.

5.2 Stage 2:

Stage 2 investigations are indicated if symptoms are not controlled with above management. The conditions picked up in stage 2 investigations are not necessarily less prevalent than in stage 1, however the investigations tend to be more invasive or 'niche'. If a condition below is strongly suspected (see red flags in section 2.3), it may be requested in stage 1, but consult the relevant specialist (respiratory paediatrician, gastro-enterologist, ENT, S&LT, immunologist). Alternatively, a trial of therapy may be instituted before investigations (e.g. treatment for gastro-oesophageal reflux) at the direction of treating consultant.

5.2.1 Investigations:

- pH and/or Impedence study – to rule out gastro-oesophageal reflux. If a bronchoscopy is being planned, it is our practice to insert the probe at the time of the anaesthetic

- Assessment of safety of swallowing – Refer to speech and language therapy team.
    - Clinical assessment by S&LT team may be sufficient. Unsafe swallow is managed as per S&LT team.
    - In some cases unsafe swallow may be because of anatomical problems (e.g. laryngeal cleft), and ENT assessment of upper airway is indicated (usually done joint with lower airway bronchoscopy by respiratory team in the context of chronic cough).
    - Formal videofluoroscopy is done in some cases following consultation between S&LT team and respiratory paediatrician. Silent aspiration, titration of therapy (feed thickeners), and evaluation of unclear cases are some indications of videofluoroscopy.

- Extended immunology tests – are done in consultation with immunology team (generic email address paedsimmunology@uhl-tr.nhs.uk), if unusual features are present in presentation, microbiology, or basic immunology tests.

- Bronchoscopy/bronchoalveolar lavage – to look for airway anatomy (look for tracheobronchomalacia, pits of H-type TOF, other abnormal anatomy), consistency and amount of secretions. Send for microbiology (include extended microbiology and mycobacteria – specify CF organisms), virology and cytology (For BAL differential count) as a minimum. In the presence of ongoing wet cough, consider course of antibiotics followed by HRCT (see below).

- Tests for PCD – refer to national PCD diagnostic lab at Leicester.

  UHL practice point: email referrals to national PCD diagnostic service to: **kellychamberlain@nhs.net and** l.causon@nhs.net

- HRCT chest (ask for inspiratory and expiratory phase). Look for bronchiectasis, bronchiolitis obliterans. Ask for contrast enhanced CT if there is airway malacia on bronchoscopy.
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5.2.2 Management of specific conditions:

Consider referral to specific clinics if not done already:

UHL practice point: If there are specific diagnoses, refer to one of the following services as appropriate

- Central England PCD management service – Leicester hosts the PCD management service for Central England. Contact l.causon@nhs.net with details of the patient
- Bronchiectasis clinic
- Respiratory- Immunology clinic

Children without the above mentioned diagnoses, with persistent or recurrent symptoms tend to be managed in the complex respiratory clinic (Code- RESPCOM)

Consider referral to physiotherapy if persistent wet cough. Consider prophylactic antibiotics [(1)].

6 Education and Training

None

7 Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
1. Red flag symptoms appropriately picked up? 2. Followed the appropriate decision tree for the patient 3. Investigations are done appropriately and in a timely manner 4. Appropriate follow-up arranged	1. Audit of children referred to UHL with chronic cough	Dr. Manjith Narayanan, Dr. David Lo	Once in 2-3 years	At departmental audit meeting. Systemic risks or lack of resources on monitoring audit will be reported at board level.

8. Supporting Documents and Key References

1. Kantar A et al. ERS statement on protracted bacterial bronchitis in children. Eur Respir J 2017; 50: 1602139

2. Shields MD et al. Recommendations for the assessment and management of cough in children. Thorax 2008; 63: 3, doi:10.1136

3. Morice AH, Millqvist E, Bieksiene K, et al. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. Eur Respir J 2019: DOI: 10.1183/13993003.01136-2019

4. NICE asthma guideline: https://www.nice.org.uk/guidance/ng80

5. Step right out programme https://www.leicester.gov.uk/media/181017/tobacco-section-march-2016.pdf

6. Asthma and wheeze UHL Children's Guideline August 2020

7. Gilchrist FJ. An approach to the child with a wet cough. Paed respiratory reviews 2019 75-81

8. Tuberculosis UHL Children's Hospital Guideline July 2020

9. Investigating Suspected Primary Immunodeficiency UHL Children's Medical Guideline August 2019

9. Key Words

Children, Respiratory, Chronic cough, wet cough, chesty cough, dry cough, Airway, Asthma, Spirometry, protracted bacterial bronchitis, bronchiectasis.

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) M Narayanan - Consultant	**Executive Lead** Chief Medical Officer
Details of Changes made during review: **New guideline** **July 2021 v1.1** **Paed physiology contact details changed**	