Chronic cough in Pediatrics

GLEM, October 5th, 2018

Céline Kempeneers
Department of Pediatrics, Pediatric Respirology
Burden of chronic cough in children

• Cough:
  - Most common presenting symptom in primary care\(^1\)

• Chronic cough associated with:
  - Unrecognized impaired quality of life (QoL)\(^2,3\)
    - Child: Ability to sleep, play, attend school
    - Parents: Distress and anxiety
  - Lead to multiple physicians visits\(^4\):
    - 80% referred children: \(\geq 5\) visits in 12 months
    - 53% referred children: \(\geq 10\) visits in 12 months
  - Inappropriate use of medications (+ side effects)\(^5\)

\(^1\) Irwin, *Chest* 2006; \(^2\) Chang *Chest* 2012; \(^3\) Cornford *Fam Pract* 1993; \(^4\) Marchant, *Chest* 2008; \(^5\) Thomson *J Pediatr Child Health* 2002
Chronic cough: frustrating

• What is normal? => discrepancy between clinicians and parents\(^1\)
  o Frequency:
    - Normal children: cough 11 times/day\(^2\) (up to >30 times a day)
    - Chronic bronchitis: 500-1000 times/day
    - URTI: increased cough frequency and severity
  o Duration:
    - Chronic cough: > 3\(^3\), > 4\(^4\), > 8\(^5,6\) weeks
  o Differenciating:
    - Acute recurrent cough
      - Normal preschool children: 6-10 respiratory infection a year\(^6\)
    - Chronic cough
  • Many causes

Chronic cough in children: Increasing interest

2017

General Practice

Belgium

Liège

Use of Management Pathways or Algorithms in Children With Chronic Cough
CHEST Guideline and Expert Panel Report
Anne B. Chang, MBBS, PhD, MPH; John J. Oppenheimer, MD; Miles M. Weinberger, MD, FCCP; Bruce K. Rubin, MD; Cameron C. Grant, MBChB, PhD; Richard S. Irwin, MD, Master FCCP; on behalf of the CHEST Expert Cough Panel

Chronic cough postacute respiratory illness in children: a cohort study
Kerry Ann E O’Grady,1 Benjamin J Drescher,1 Vikas Goyal,1,2 Natalie Phillips,3

Management of Children With Chronic Wet Cough and Protracted Bacterial Bronchitis
CHEST Guideline and Expert Panel Report
Anne B. Chang, MBBS, PhD, MPH; John J. Oppenheimer, MD; Miles M. Weinberger, MD, FCCP; Bruce K. Rubin, MD; Cameron C. Grant, MBChB, PhD; Kelly Weir, BSPhThy, MSPThy, PhD, CPSP; and Richard S. Irwin, MD, Master FCCP; on behalf of the CHEST Expert Cough Panel

Fifteen-minute consultation: a structured approach to the management of chronic cough in a child
Cherry Alviani,1 Gary Ruiz,1 Atul Gupta1,2

Prolonged Cough in Pediatric Population First Line Care, Belgian Guidelines
Sophie Leconte1,2,*, Stéphanie Valentin1, Estelle Dromelet1 and Michel De Jonghe1
1Centre académique de médecine générale, Université catholique de Louvain, Bruxelles, Belgium
2Institut de Recherche santé et société, Université catholique de Louvain, Bruxelles, Belgium

VIGNETTE DIAGNOSTIQUE DE L’ÉTUDIANT
Mise au point d’une toux chronique

R. Louis (1)
• Personal interest in chronic cough/asthma misdiagnosis

Chronic cough and wheeze in children: do they all have asthma?

M. Seear, D. Wensley

DOI: 10.1183/09031936.97.10020342
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Cough: physiopathology

• Important airway protective reflexes
• Control: voluntary + involuntary
• Receptors:
  • Localisation: pharynx, larynx, tracheobronchial tree
  • Stimulation: change in temperature, chemical, mechanical stresses
• Response: cough
  − Deep inspiration
  − Closure of the glottis
  − Contraction of respiratory muscles
  − Open of the glottis
  − Expulsion of air, mucous, potential foreign body

**Cough Mechanisms**

[Diagram showing the stages of cough: irritation, inspiration, compression, expulsion.]

Glottis closes

Muscles contract (rectus, obliques, intercostals) forcing diaphragm up.

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Cough: Definitions

1/10 healthy children: prolonged (> 3 weeks) acute cough after URTI

<table>
<thead>
<tr>
<th>Cough definition</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>A forced expulsive manoeuvre which starts against a closed glottis, associated with a characteristic sound.</td>
</tr>
<tr>
<td>Acute cough</td>
<td>A recent onset cough lasting less than 3 weeks.</td>
</tr>
<tr>
<td>Prolonged acute cough</td>
<td>Cough lasting at least 3 weeks, which is ‘relentlessly progressive’ and may warrant early investigations.</td>
</tr>
<tr>
<td>Recurrent cough</td>
<td>Repeated (greater than two per year) cough episodes that each last more than 14 days.</td>
</tr>
<tr>
<td>Chronic cough</td>
<td>A non-resolving daily cough lasting longer than 4–8 weeks. There is no exact consensus on the duration in children.</td>
</tr>
<tr>
<td>Specific cough</td>
<td>A cough with a specific underlying cause.</td>
</tr>
</tbody>
</table>
Chronic cough in Pediatrics: Etiologies
Box 1 Conditions causing chronic cough.\textsuperscript{4,5}

Infections:
- Viral respiratory tract infections
- Postinfectious illness (including Mycoplasma, pertussis and chlamydia)
- Tuberculosis

Atopic conditions:
- Asthma
- Allergic rhinitis

Chronic suppurative lung disease:
- Cystic fibrosis
- Primary ciliary dyskinesia
- Immune deficiencies
- Other causes of bronchiectasis
- Protracted bacterial bronchitis

Inhaled foreign body

Airway lesions:
- Compression, for example lymph nodes, vascular ring
- Airway malacia

Upper airway disease:
- Upper airway cough syndrome (formerly known as postnasal drip syndrome)
- Adenotonsillar hypertrophy
- Rhinosinusitis or rhinitis
- Nasal polyps

Recurrent aspiration (from oesophageal or swallowing problems):
- Gastro-oesophageal reflux disease (GORD)
- Neuromuscular disease
- Tracheo-oesophageal fistula

Interstitial lung disease

Other:
- Environmental exposure to tobacco smoke or other chemical irritants
- Psychogenic cough
- Cardiac disease
- Medication related (e.g. ACE inhibitors)
Chronic cough: 5 most frequent diagnoses

% of cohort

- Protracted Bacterial Bronchitis
- Asthma
- Bronchiectasis
- Natural resolution
- Tracheomalacia

- Whole cohort
- 0-2 years
- >2 to 6 years
- >6 to 12 years
- >12 years

Chang 2012
3 studies: aetiology of chronic cough

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Number</th>
<th>Average age of child when studied (years)</th>
<th>Definition of chronic cough (greater than)</th>
<th>Average length of coughing at referral</th>
<th>Evaluations undertaken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marchant JM et al</td>
<td>Australia</td>
<td>108 children referred to tertiary respiratory centre</td>
<td>Median 2.6 years</td>
<td>3 weeks</td>
<td>Median 6 months</td>
<td>CXR, FEV1, ENT assessment, bronchoscopy/BAL, Sweat test, IgGs, allergy tests, HRCT, pH studies, mycoplasma/pertussis tests</td>
</tr>
<tr>
<td>Khoshoo V et al</td>
<td>USA</td>
<td>40 children referred to pulmonary clinic</td>
<td>Mean 7.8 years</td>
<td>8 weeks</td>
<td>18 weeks</td>
<td>CXR, FEV1, ENT assessment, bronchoscopy/BAL, Sweat test, IgGs, allergy tests, HRCT, pH studies, mycoplasma/pertussis tests</td>
</tr>
<tr>
<td>Asilsoy S et al</td>
<td>Turkey</td>
<td>108 children referred to Children's Hospital &amp; Research Centre</td>
<td>Mean 8.4 years</td>
<td>4 weeks</td>
<td>4.16 months</td>
<td>CXR, FEV1, ENT assessment, bronchoscopy/BAL, IgGs, allergy tests, HRCT, gastroesophageal scintigraphy, mycoplasma/pertussis tests</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Marchant JM et al</td>
<td></td>
<td>PBB – 40%</td>
<td>Natural Resolution – 22%</td>
<td>Bronchiectasis – 6%</td>
<td>Asthma – 13%</td>
<td>UACS – 3%</td>
</tr>
<tr>
<td>Khoshoo V et al</td>
<td></td>
<td>GORD – 27%</td>
<td>UACS – 23%</td>
<td>Asthma – 13%</td>
<td>UACS – 20%</td>
<td>PBB – 23%</td>
</tr>
<tr>
<td>Asilsoy S et al</td>
<td></td>
<td>GORD – 5%</td>
<td>Multiple aetiologies – 20%</td>
<td>Bronchiectasis – 3%</td>
<td>UACS + asthma – 7%</td>
<td>PBB + asthma – 12%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Others – 2%</td>
</tr>
</tbody>
</table>

1 Shields, Pediatr Respir Rev 2013
### TABLE 1 | Prospective Studies That Have Described Various Etiologies of Chronic Cough in Children (Key Questions 1 and 2)

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Country</th>
<th>Setting</th>
<th>Method of Assessment</th>
<th>Inclusion Criteria, Exclusion</th>
<th>No. Enrolled/No. Complete/Age</th>
<th>Top 3 Most Common Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aslany et al. 2008</td>
<td>Turkey</td>
<td>Single center, pediatric inpatients</td>
<td>ACCP guideline(^1)</td>
<td>&gt;4 wk cough; Exclusion: none reported</td>
<td>108/108 Mean = 8.4 y, Range = 6-14 y</td>
<td>Asthma/asthma-like n = 27 (25%), PBB = 25 (23%), UACS = 22 (20%)</td>
</tr>
<tr>
<td>Chang et al. 2012</td>
<td>Australia</td>
<td>Multicenter, Respiratory inpatients</td>
<td>Modified ACCP(^2) and TSANZ(^2) guidelines</td>
<td>Age &lt;18 y cough &gt;4 wk duration, newly referred; Exclusion: chronic respiratory illness</td>
<td>346/346 Mean = 4.5 y, SD = 3</td>
<td>Asthma = 55 (16%), Resolved without specific diagnosis = 48 (14%)</td>
</tr>
<tr>
<td>Dani et al. 2002</td>
<td>India</td>
<td>Single center, pediatric inpatients</td>
<td>Sequential routine investigations: full blood count, erythrocyte sedimentation rate, Mantoux test, sputum, throat swab, chest radiograph Further investigations (eg, HIV, CT imaging, bronchoscopy, barium swallow) when indicated</td>
<td>Consecutive, immune-competent, age 1-12 y Chronic cough &gt;3 wk, unknown etiology; Exclusion: heart disease</td>
<td>94 Age NR</td>
<td>Asthma = 35 (37%), Tuberculosis = 21 (22.3%), Pulmonary eosinophilia = 9 (9.5%), Sinusitis = 9 (9.5%)</td>
</tr>
<tr>
<td>Gadik et al. 2015</td>
<td>Turkey</td>
<td>Single center, pediatric or allergy inpatients</td>
<td>ACCP guideline(^3)</td>
<td>Age &lt;17 y, persistent cough &gt;4 wk; Exclusion: known chronic respiratory, neuromuscular, growth, cardiac problems; genetic syndromes; prematurity</td>
<td>563/563 Mean age = 5.4 y, SD = 3.8</td>
<td>Asthma = 140 (25%), Asthma-like = 107 (19%), PBB = 67 (12%)</td>
</tr>
<tr>
<td>Karabel et al. 2014</td>
<td>Turkey</td>
<td>Single center, respiratory inpatients</td>
<td>ACCP guideline(^4)</td>
<td>&gt;4 wk cough; Exclusion: neuromuscular, cardiac, syndromes, respiratory tract infection last 4 wk</td>
<td>270/270 Mean = 6.5 y, range = 7 mo-17 y</td>
<td>Asthma = 73 (27%), Asthma-like = 42 (15.5%), GERD = 27 (10%)</td>
</tr>
<tr>
<td>Khosho et al. 2009</td>
<td>USA</td>
<td>Single center, pediatric inpatients</td>
<td>Chest radiograph, bronchoscopy, PFT with methacholine, sweat test, pH-or impedance-metry, skin testing, Ig levels Others also had: Barium meal or swallow, CT chest/sinus, laryngoscopy, Mantoux test</td>
<td>&gt;8 wk cough, born full term, neurodevelopmentally normal, no smoke exposure, no history of febrile or respiratory illness, no cardiac illness; Exclusion: asthma, RAD, cystic fibrosis (unless able to do PFT/airway hyperreactivity)</td>
<td>40/40 Mean age = 7.8 y, range = 5-12 y</td>
<td>GERD = 11 (27.5%), Asthma/cough variant asthma = 11 (27.5%), Allergy = 9 (22.5%)</td>
</tr>
<tr>
<td>Marchant et al. 2006</td>
<td>Australia</td>
<td>Single center, respiratory inpatients</td>
<td>Modified ACCP 1998(^5) guideline</td>
<td>&gt;3 wk cough, age &lt;18 y, newly referred; Exclusion: NR</td>
<td>108/103 Median = 2.6 y, IQR = 1.2-6.9</td>
<td>PBB = 43 (40%), Resolved without specific diagnosis = 24 (22%), Bronchiectasis = 6 (5.6%)</td>
</tr>
<tr>
<td>Rehman et al. 2009</td>
<td>Pakistan</td>
<td>Single center, pediatric inpatients</td>
<td>Locally designed algorithm with Mantoux test</td>
<td>Age 6-59 mo &gt;4 wk cough; Exclusion: use of ACE inhibitors</td>
<td>172/161 Summary NR</td>
<td>Asthma = 61 (38%), Postviral = 21 (13%), Tuberculosis = 14 (9%)</td>
</tr>
<tr>
<td>Usta et al. 2014</td>
<td>Turkey</td>
<td>Single center, pediatric allergy inpatients</td>
<td>British Thoracic Society guideline</td>
<td>Exclusion: NR</td>
<td>156/156 Mean = 8.4 y, SD = 2.6</td>
<td>Postnasal drip + asthma = 30 (19%), Postnasal drip = 29 (19%), Asthma = 19 (12%), PBB = 19 (12%)</td>
</tr>
<tr>
<td>Yilmaz et al. 2014</td>
<td>Turkey</td>
<td>Single center, pediatric asthma, allergy inpatients</td>
<td>CHEST guidelines but evaluated by allergists skin prick test (house dust mites, pollen, alternaria, animal dander, latex), full blood count</td>
<td>Age &lt;18 y, chronic cough &gt;4 wk (non-specific isolated dry cough); Exclusion: specific cough pointer present, wet cough, chest radiograph or PFT results abnormal, characteristic cough pattern, chronic respiratory illness, use of ICS, LTRA, ACE inhibitor</td>
<td>119/109 Median = 5 y, IQR = 3.5-9</td>
<td>Resolved without prescription = 23 (21%), Rest were treated with ICS for 2 wk: 24 (22%) responded, 62 (57%) partially responded</td>
</tr>
</tbody>
</table>
BTS guidelines: Recommendations for the assessment and management of cough in children.

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Cause</th>
<th>Potential investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequently recurring viral bronchitis</td>
<td>Viral infections</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Crowd ed living conditions, ETS and</td>
<td>Chest radiography</td>
</tr>
<tr>
<td></td>
<td>attendance in child care nursery</td>
<td>Examine during a period when symptom-free</td>
</tr>
<tr>
<td>Postviral cough</td>
<td>Viral respiratory infections, Chlamydia and Mycoplasma infections</td>
<td>None, chest radiography, serology</td>
</tr>
<tr>
<td>Pertussis and pertussis-like illness</td>
<td>Bordetella pertussis, parapertussis, adenovirus, influenza, parainfluenza</td>
<td>Consider trial of asthma therapy (some mild asthmatics have prolonged recovery from each viral infection)</td>
</tr>
<tr>
<td>Cough variant asthma</td>
<td>Asthma</td>
<td>Nil</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest radiograph, positive serology or culture may be helpful in reducing requirements for further investigation</td>
</tr>
<tr>
<td>Allergic rhinitis, postnasal drip and sinusitis – cough likely due to concomitant tracheobronchial inflammation</td>
<td>Causes of allergic rhinitis</td>
<td>None, 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</td>
</tr>
<tr>
<td>Psychogenic cough</td>
<td>Underlying stress</td>
<td>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</td>
</tr>
</tbody>
</table>

ETS, exposure to environmental tobacco smoke; FeNO, fractional exhaled nitric oxide concentration; BDR, bronchodilator responsiveness; BHR, bronchial hyperreactivity.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis</td>
<td>Sweat test, nasal potential difference, assessment of pancreatic function, genotyping</td>
</tr>
<tr>
<td>Immune deficiencies</td>
<td>Differential white cell counts, immunoglobulin levels and subsets, functional antibody responses and lymphocyte subset analysis</td>
</tr>
<tr>
<td>Primary ciliary disorders</td>
<td>Screening FnNO, saccharine test, ciliary ultrastructure and function, culture of ciliated epithelium</td>
</tr>
<tr>
<td>Protracted bacterial bronchitis</td>
<td>Chest radiography, sputum for culture, exclusion of other causes in this table. Response to 4–6 weeks antibiotic and physiotherapy</td>
</tr>
<tr>
<td>Recurrent pulmonary aspiration:</td>
<td>Barium swallow, videofluoroscopy, 24 h pH studies, milk isotope scan, fat-laden macrophage index* on bronchovascular 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</td>
</tr>
<tr>
<td>Laryngeal cleft or 'H' type tracheo-oesophageal fistula</td>
<td></td>
</tr>
<tr>
<td>Post-TOF repair with swallowing incoordination</td>
<td></td>
</tr>
<tr>
<td>Neuromuscular or neurodevelopmental disorder</td>
<td></td>
</tr>
<tr>
<td>GOR, hiatal hernia</td>
<td></td>
</tr>
<tr>
<td>Retained inhaled foreign body</td>
<td>Chest radiography and HRCT scan may show focal lung disease</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Chest radiography, Mantoux, early morning gastric aspirates and gamma interferon tests</td>
</tr>
<tr>
<td>Anatomical disorder (eg, bronchomalacia) or lung malformation (eg, cystic congenital thoracic malformation)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bronchoscopy and CT scan</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>Spirometry (restrictive defect), chest radiography and HRCT scan, lung biopsy</td>
</tr>
<tr>
<td>Specific pointers to diagnosis</td>
<td>Suggested specific diagnosis</td>
</tr>
<tr>
<td>-------------------------------------------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Sudden onset cough</td>
<td>Inhaled foreign body</td>
</tr>
<tr>
<td>Barking/brassy cough</td>
<td>Airway malacia</td>
</tr>
<tr>
<td>Paroxysmal cough with classic inspiratory ‘whoop’</td>
<td>Pertussis syndrome</td>
</tr>
<tr>
<td>Wheezing episodes/atopy/exertional dyspnoea/chest hyperinflation/pectus deformity</td>
<td>Asthma</td>
</tr>
<tr>
<td>Rhinitis, allergic salute, throat clearing</td>
<td>Allergic rhinitis</td>
</tr>
<tr>
<td>Choking with feeds/chesty post feeds/neurodevelopmental abnormality</td>
<td>Recurrent aspiration</td>
</tr>
<tr>
<td>Wet cough, poor growth, features of malabsorption, nasal polyps, purulent sputum, finger clubbing</td>
<td>Bronchiectasis (various causes, eg, cystic fibrosis, primary ciliary dyskinesia)</td>
</tr>
<tr>
<td>Recurrent infections, wet cough</td>
<td>Immune deficiency</td>
</tr>
<tr>
<td>Progressive cough, weight loss, fever, night sweats and haemoptysis</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Dry cough and breathless</td>
<td>Interstitial lung disease</td>
</tr>
<tr>
<td>Abnormal cardiac examination, exertional dyspnoea, hypoxaemia</td>
<td>Cardiac disease</td>
</tr>
<tr>
<td>Honking, bizarre cough/cough disappears in sleep</td>
<td>Psychogenic cough</td>
</tr>
<tr>
<td>Mucopurulent drainage, chronic nasal obstruction, facial pain or pressure</td>
<td>Sinusitis</td>
</tr>
<tr>
<td>Medication history (ACE inhibitors/illicit drugs)</td>
<td>Drug reaction</td>
</tr>
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</tr>
</tbody>
</table>

BAL, bronchoalveolar lavage; CXR, chest X-ray; HRCT, high-resolution CT.

**Fifteen-minute consultation**: A structured approach to the management of chronic cough in a child.
Protracted Bacterial Bronchitis (PBB)

• Persistent and recurrent bacterial infection of the conducting airways
• Pathogens:
  – Haemophilus Influenzae
  – Streptococcus pneumoniae
  – Moraxella Catarrhalis

Clinical features

- Usually <6 years old, median age 3 years
- Chronic wet cough
  - Changing posture
  - At night
  - At exercise
- « Short of breath at exercise »
- Rattling breathing (can be reported as wheeze)
- Lack of energy

Chang 2008, Craven 2013
Diagnostic criteria

• Pediatric condition
• Chronic (>4 weeks) wet cough with or without rattling breathing
• Resolution with 2-4 weeks oral antibiotic
• Absence of alternative specific cause of cough

=>Diagnostic:
  – Clinical + response to Ab OR
  – Bronchoscopy

Diagnostic

- **Response to Antibiotics:**
  - Partial / transient with short courses (5-7 days)
  - Resolution with long courses (min 10-14 days)

- **Chest X-Ray:** often normal / peribronchial wall thickening

- **CT scan:** exclude bronchiectasis

- **Cough swab:** low sensitivity

- **Bronchoscopy:**
  - Secretions
  - Oedematous collapsable bronchi

- **BAL:** positive culture for typical pathogens, neutrophilic inflammation

  *Chang 2008, Craven 2013*
Pathophysiology: The Vicious Circle

- Single or repeated pulmonary insult
- Impaired primary/secondary defense system
- Stasis

⇒ Bacteria thrive in the airways

**Insult of the airways => impaired mucociliary clearance**
- Bacterial/viral infection in early childhood
- Tracheobronchomalacia
- Aspiration
- Asthma
- Immunodeficiency
- Neuromuscular disease
- Significant medical intervention/chemotherapy
- Poor social conditions

- **Bacteria secrete biofilm**
  - Attachment
  - Access to nutrients
  - Decrease Ab penetration

- **Vicious circle**: self-perpetuating respiratory inflammation and infection
  ⇒ bronchiectasis

Natural history of PBB

Progression of disease process

- Protracted bronchitis
- CSLD
- Radiological bronchiectasis
PPB: Investigations

• **First stage:**
  - Chest x-ray
  - Cough swab/ sputum analysis

• **Recurrent episodes of PBB:**
  => Further antibiotic courses
  => > 3/year: Reconsider diagnosis:
  - Other causes of chronic wet cough?
  - Predisposing factors for PBB? (aspiration!)
  - CSLD/bronchiectasis?
  - Immunodeficiency?

• **Investigations:**
  => Bronchoscopy, BAL
     => CT scan
  ⇒ further investigations for bronchiectasis

Donnelly 2007, Chang 2008, Craven 2013, Kantar 2017
Chronic cough in Pediatrics: Algorithms
## TABLE 2  Summary of Pediatric Chronic Cough Guidelines on the Use of Routine Tests

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Country</th>
<th>Society</th>
<th>Suggested Routine Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang et al(^{12})/2006</td>
<td>Australia</td>
<td>Thoracic Society of Australia and New Zealand</td>
<td>Yes Spirometry(^{a}) and chest radiography</td>
</tr>
<tr>
<td>Chang and Glomb(^{6})/2006</td>
<td>United States</td>
<td>American College of Chest Physicians</td>
<td>Yes Spirometry(^{a}) and chest radiography</td>
</tr>
<tr>
<td>Gibson et al(^{28})/2010</td>
<td>Australia</td>
<td>Australian Lung Foundation</td>
<td>Yes Spirometry(^{a}) and chest radiography</td>
</tr>
<tr>
<td>Kohno et al(^{29})/2006</td>
<td>Japan</td>
<td>Japanese Respiratory Society</td>
<td>No</td>
</tr>
<tr>
<td>Leconte et al(^{30})/2008</td>
<td>Belgium</td>
<td>Primary care</td>
<td>No Tests based on clinical suspicion</td>
</tr>
<tr>
<td>Lu(^{31})/2014</td>
<td>China</td>
<td>Multiple societies</td>
<td>Yes (based on translated article) Chest radiography</td>
</tr>
<tr>
<td>Shields et al(^{11})/2008</td>
<td>England</td>
<td>British Thoracic Society</td>
<td>Yes Spirometry(^{a}) and chest radiography</td>
</tr>
<tr>
<td>Zacharasiewicz et al(^{32})/2014</td>
<td>Austria</td>
<td>Austrian Society of Pediatrics, Austrian Society Pneumology</td>
<td>Yes Spirometry(^{a}) and chest radiography</td>
</tr>
</tbody>
</table>

\(^{a}\)Spirometry if age appropriate (usually when aged > 5 years but in some centers, spirometry can be undertaken in children > 3 years).
Fifteen-minute consultation: A structured approach to the management of chronic cough in a child.
BTS guidelines: Recommendations for the assessment and management of cough in children.

1. Specific pointers identified from history, examination, chest x ray, spirometry (>5 years)
   - Yes: Wheezing episodes, other atopy → Asthma
   - No: Isolated cough, otherwise well child
     - Yes: (Clearing throat, allergic salute) → Post nasal drip/allergic rhinitis
     - No: Is the cough truly troublesome?
       - Yes: Persistent endobronchial infection
         - CF
         - PCD
         - PBB
         - ID
       - No: (Wet/productive cough)
         - Yes: (Choking with feeds, chesty after feeds) → Recurrent aspiration
         - No: (Brassy or barking cough)
           - Yes: Tracheo/bronchomalacia, airways compression
           - No: Cough bizarre, disappears when asleep, "la belle indifference" → Psychogenic cough
             - Yes: (Dry cough, breathless restrictive spirometry) → Interstitial lung disease
             - No: (Progressive cough, weight loss, fevers) → TB

2. isolate cough, otherwise well child

3. Is the cough truly troublesome?
   - Yes: Test for BDR or home PEFR monitoring
     - Yes: Trial anti-asthma medication
       - Yes: Stop anti-asthma medication
         - Yes: Consider further investigations, and follow-up
       - No: Stop anti-asthma medication
         - Yes: Restart anti-asthma medication only if cough relapses

4. Reassure, observe, follow-up
Chronic (>4 weeks duration) wet or productive cough

Identify any specific cough pointers, perform chest radiograph and (if possible) spirometry

Specific cough pointers present
Investigate accordingly

Specific disorder diagnosed
Treatment based on diagnosis

No specific diagnosis

Specific pointers absent

Attempt sputum culture
Trial treatment for PBB

Wet cough persists (check adherence)
Investigate for an underlying cause

Recurrence
Further antibiotic course
Consider further investigations

Wet cough resolved
Diagnose PBB

No recurrence

ERS statement on protracted bacterial bronchitis in children
Chronic cough in Pediatrics: Evaluation in Practice
Chronic cough: detailed history

1. How and when the cough started?
2. Is the cough an isolated symptom?
3. What triggers the cough?
4. Does the cough disappear when the child goes to sleep?
5. What is the nature and quality of the cough?
6. What treatments has the child been tried on and how beneficial were they?
7. What other medication is used? e.g. ACE inhibitors
8. Is there a family history of respiratory, allergic or infectious disease?
9. Does the child smoke? Do the parents smoke? Is there evidence of any environmental pollutant at home?
10. How disruptive is the cough?
11. Is there evidence of Obstructive Sleep Apnoea? How large are the tonsils?

1 Shields, Pediatr Respir Rev 2013
Chronic cough: clinical examination

- Full clinical systematic examination
- General health
- Height and weight centile
- Nutritional status
- Chest examination
- ENT examination
- Cardiovascular examination

…Ask the child to cough!
Chronic cough: red flags

Important:

• Wet/dry cough
  • Wet: mucous hypersecretion
  • Dry: airway irritation/non-airway cause
• Neonatal onset/Sudden onset
• Growth/general status
• Swallowing difficulties
• Dyspnoea
• Recurrent infections
• Progressively more severe cough
• Cough disappear at night

+ Abnormal physical examination!

Box 1. List of some red flag symptoms and signs in chronic cough.

- Coughing started suddenly with a choking episode or an inhaled foreign body is suspected
- Coughing is relentlessly progressive
- There are already specific pointers for an underlying diagnosis including
  - Weight loss, night sweats suggestive of TB
  - Haemoptysis
  - Signs of chronic lung disease or ill-health already present (poor growth, finger clubbing, chest wall abnormality and abnormal lung sounds)
- Coughing with a background history of recurrent pneumonia
- Cough starting in neonatal period
- Swallowing difficulties
  - With craniofacial abnormality
  - With neuromuscular disorder
- Dyspnoea – chronic or exertional
- Wet cough lasting more than 3-4 weeks

1 Shields, Pediatr Respir Rev 2013
Chronic cough: red flags

**TABLE 1**  
Extended List of Cough Pointers (Modified From Previous Papers)\(^6,12,23\)

<table>
<thead>
<tr>
<th>Systemic</th>
<th>Pulmonary</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cardiac abnormalities</td>
<td>• Chest pain</td>
</tr>
<tr>
<td>• Digital clubbing</td>
<td>• Daily moist or productive cough</td>
</tr>
<tr>
<td>• Failure to thrive</td>
<td>• Hemoptysis</td>
</tr>
<tr>
<td>• Medications or drugs associated with chronic cough (angiotensin-converting enzyme inhibitors, illicit drug use)</td>
<td>• Abnormal cough characteristics (brassy, plastic bronchitis, paroxysmal with/without posttussive vomiting, staccato, cough from birth)</td>
</tr>
<tr>
<td>• Neurodevelopmental abnormality</td>
<td>• Recurrent pneumonia</td>
</tr>
<tr>
<td>• Fever</td>
<td>• Hypoxia/cyanosis</td>
</tr>
<tr>
<td>• Immune deficiency (primary or secondary)</td>
<td>• History of previous lung disease or predisposing causes (eg, neonatal lung disease, foreign body aspiration)</td>
</tr>
<tr>
<td>• Feeding difficulties</td>
<td>• Exertional dyspnea</td>
</tr>
<tr>
<td>• History of contacts (eg, tuberculosis)</td>
<td>• Dyspnea at rest or tachypnea</td>
</tr>
<tr>
<td></td>
<td>• Chest wall deformity</td>
</tr>
<tr>
<td></td>
<td>• Auscultatory findings (eg, stridor, wheeze, crackles)</td>
</tr>
<tr>
<td></td>
<td>• Chest radiograph abnormalities</td>
</tr>
<tr>
<td></td>
<td>• Pulmonary function test abnormalities</td>
</tr>
</tbody>
</table>
Chronic cough: baseline investigations

- Chest radiograph
- Spirometry with or without test of bronchodilatator responsiveness (BDR)
- Sputum analysis
- (Allergy testing)

Complete investigations if red flags
Chronic cough in Pediatrics: Management
Chronic cough: management

• Treatment of specific diagnosis if found
• Remove from exposure to aeroirritants
• Non-specific isolated cough in an otherwise well child:
  • Parental reassurance
  • FU after 6-8 weeks: cough resolved? No specific pointers?
• Empirical trial:
  – Not recommended, unlikely beneficial (Cochrane review)
  – If trial: time-limited
• Anti-asthma: ICS, beta-2 agonist, leukotriene receptors antagonists
• Anti-allergic rhinitis: anti-histamines
• Anti-gastro-oesophageal reflux treatment
• Trial of anti-asthma therapy:
  • Attempt to document bronchial hyperresponsiveness (spirometry + BDR, response to salbutamol)
  • Adequate doses, clear outcome, defined period 8-12 weeks then stop
    – No response: asthma unlikely
    – Response and early relapse of cough: cough-variant asthma likely
Chronic cough in Pediatrics: Take Home messages
Take Home Messages

• Definition chronic cough in children: > 4 weeks¹
• Delayed diagnosis may cause respiratory morbidity
• Early diagnosis of underlying chronic disease:
  • Appropriate management: cough may resolve
  • Improved QoL
• Use of cough algorithms: can lead to earlier diagnosis

• => Recommendations¹:
  • Use of pediatric-specific cough management protocols or algorithms
  • Basing management on clinical history, physical examination, cough characteristics, red flags
  • Baseline investigations:
    − Chest X-Ray, spirometry (+ BDR)
    − To consider: sputum analysis, allergy testing, bronchoscopy, Chest CT, Mantoux
  • Empirical treatment trial:
    − Based on features consistent with hypothesized diagnosis
    − Limited duration, aim to confirm or refute diagnosis