Disclosures

• None
Objectives

• Describe chronic cough and its common etiologies
• Present guideline approach to chronic cough in pediatrics
• Translate guidelines to clinical practice of pediatric pulmonologists and primary care providers
Chronic Cough in Pediatrics

• 3 year old previously healthy female presents to your office for the 4th time in 6 weeks with complaint of cough

• Cough is one of most common reasons for medical visits
• An effective cough is important to maintaining respiratory health
• When persistent, prolonged, unexplained cough can be distressing to patient and family

Impact of Chronic Cough

• Impaired quality of life
• Multiple physician visits
• Adverse effects from inappropriate use of medications, testing
• May miss or delay diagnosis of a serious underlying condition

Chronic Cough Guidelines in Pediatrics

• Identify etiology using a systematic approach
• Early diagnosis
• Reduce morbidity
• Improve Quality of Life
• Minimize effects of inappropriate use of testing or medications
• Reduce costs

Chronic Cough Guidelines in Pediatrics

- 2006 American College of Chest Physician (ACCP) CHEST Guidelines – updated 2017

Guidelines for Evaluating Chronic Cough in Pediatrics

ACCP Evidence-Based Clinical Practice Guidelines

Anne B. Chang, MBBS, PhD; and William B. Glomb, MD, FCCP

Causes of Chronic Cough

- Asthma
- Cystic Fibrosis
- Allergic Rhinitis
- Sinusitis
- Respiratory infections
- Post infectious cough
- Foreign body inhalation
- Protracted Bacterial Bronchitis (PBB)

- Airway lesions
- Vocal cord dysfunction
- Otogenic Causes
- GERD
- Cardiac Disease
- Side effects of medications
- Environmental pulmonary toxins, pollutants
- Functional Respiratory Disorder
Post Viral Cough

• Presence of cough after acute viral illness
• Not much known about natural course after 25 days
• Child can acquire a new respiratory illness in the interim and original coughing illness can appear prolonged
  – 5-8 respiratory viral illnesses a year before age 4 years
  – 2-5 respiratory illnesses a year in teens and preteens

• Consider other etiologies, especially pertussis and mycoplasma

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Protracted Bacterial Bronchitis (PBB)

- First described in 2006
  1. Presence of chronic wet cough
  2. Response with cough resolution to antibiotics (amoxicillin-clavulanate) within 2 weeks of use
  3. Lower airway infection with respiratory pathogen density $>10^4$ cfu/mL in bronchoalveolar lavage fluid in the absence of Bordetella pertussis, Mycoplasma pneumoniae or chlamydia infection

- Microbiologic diagnosis
  - Typical pathogens *haemophilus influenza*, *moraxella catarrhalis*, *streptococcus pneumoniae*

PBB Diagnosis

• Newer described clinical diagnostic criteria
  – Not feasible nor warranted to have every child with chronic cough undergo bronchoscopy
  – Does not require microbiologic criteria, but rather an absence of other causes of chronic wet cough

1. Presence of chronic wet cough
2. Response with cough resolution to antibiotics (amoxicillin-clavulanate) within 2 weeks of use
3. Absence of other causes of chronic wet cough

PBB Treatment

- Generally 2 - 4 week course of antibiotics
  - In many children 2 weeks may be sufficient
  - Rarely some children need >4 weeks of antibiotics
  - Shorter courses advocated in consideration of antibiotic stewardship
  - In practice, treat for 2 weeks, reassess, extend course x 2 weeks if symptoms have not resolved
  - If no improvement after 4 weeks, further diagnostics to look for underlying disease (CT chest, Bronchoscopy, BAL)

Airway etiologies

• Tracheomalacia
  – May have associated vascular anomaly
  – Malacia also associated with impaired mucociliary clearance

• Mass lesion
  – Upper airway cyst
  – Partial web
  – Tracheal stenosis
  – Hemangioma
Otogenic causes

• “Arnold Ear Cough Reflex”
  – Stimulation of external auditory meatus stimulates auricular branch of vagus nerve
• Case reports (rare) of chronic cough
  – Wax impaction
  – Cholesteatoma
  – Acquired aberrant sensory referral post-cardiac transplant

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Cough as Side Effect

- ACE inhibitors
- Inhaled medications (asthma medications)
- Complication of vagal nerve stimulator

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Pollutants

- Second hand smoke
- Indoor biomass combustion (wood burning stove)
- Other pollutants
Functional Respiratory Disorder

- **Tic cough** “Habit cough”
  - Definition of Tic
    - Repetitive movement or phonic production that involves discrete muscle groups
    - Fragments of normal motor actions or vocalizations that are misplaced in context
  - Suppressibility, distractibility, suggestibility, variability, premonitory sensation
  - Treatment
    - Behavioral interventions
    - Pharmacologic interventions

Chang AB, Glomb WB. *Chest.* 2006 129.1_suppl.260S
Functional Respiratory Disorder

• **Somatic Cough** “Psychogenic cough”
  – Transfer of psychologic distress into a physical symptom
  – Must meet DSM-5 criteria
    
    A. One or more somatic symptoms that are distressing or result in significant disruption of daily life.
    
    B. Excessive thoughts, feelings, or behaviors related to the somatic symptoms or associated health concerns as manifested by at least one of the following:
      1. Disproportionate and persistent thoughts about the seriousness of one’s symptoms.
      2. Persistently high level of anxiety about health or symptoms.
      3. Excessive time and energy devoted to these symptoms or health concerns.
    
    C. Although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically more than 6 mo).

  – Treatment
    • Reassurance, counseling, relaxation techniques, referral to a psychologist, psychotherapy, hypnosis, suggestion therapy

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Chronic Cough Guidelines in Pediatrics

- ACCP guideline defines pediatric patient as 14 years and younger
- Patients 15+ years should be managed utilizing adult guidelines for cough
- May be more appropriate to use a different algorithm in different clinical scenarios (3rd world country with high TB prevalence)

Chronic Cough Defined

- Presence of a daily cough for >4 weeks

- Expected Cough
- Specific Cough
- Non-specific Cough

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Chronic Cough Defined

• Expected cough
  – Even normal children cough

• Small number of children have viral induced cough that lasts >4 weeks
  – No studies specifically looking at reasons for those children to have prolonged viral cough nor their outcomes

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Chronic Cough Defined

• Specific Cough
  – cough is symptom or sign of an underlying respiratory or systemic disease
  – etiology and necessity of further investigations is usually evident from the presence of these symptoms and signs – “Cough pointers”

• Non-Specific Cough
  – No identified etiology
  – Absence of cough pointers
  – Most commonly a “non-serious” etiology
  – Many spontaneously resolve – based on placebo arms of RCTs
# Cough Pointers

<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-</td>
<td>• Abnormal cough characteristics (brassy, plastic bronchitis, paroxysmal with/without</td>
</tr>
<tr>
<td>converting enzyme inhibitors, illicit drug use)</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>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>
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<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>

Systemic

- Cardiac anomalies
- Digital Clubbing
- Failure to thrive
- Medications or Drugs associated with chronic cough (ACE inhibitors, illicit drugs)
- Neurodevelopmental abnormality
- Fever
- Immune deficiency
- Feeding difficulties
- History of contacts (TB)

Pulmonary

- Chest pain
- Daily moist or productive cough
- Hemoptysis
- Abnormal cough characteristics (brassy, plastic bronchitis, paroxysmal with/without posttussive vomiting, staccato, cough from birth)
- Recurrent pneumonia
- Hypoxia/cyanosis
- History of previous lung disease or predisposing causes (neonatal lung disease, foreign body aspiration)
- Exertional dyspnea
- Dyspnea at rest or tachypnea
- Chest wall deformity
- Auscultatory findings (stridor, wheeze, crackles)
- Chest radiograph abnormalities
- Pulmonary function test abnormalities

Cough Pointers

• High sensitivity and specificity of identifying etiology if a cough “pointer” can be identified

• Recognition of cough pointers is dependent on accurate identification
  – History
  – Medical providers’ experience and expertise
Cough History

• Time frame
• Quality – wet, dry, honking, brassy, staccato, paroxysmal, producing casts
  – Better associated with identifying etiology in children as compared to adults

• Many cough descriptions are subjective
• Nocturnal cough reporting is unreliable
What if No “Cough Pointer”?
Presence of 'specific cough pointers'

- Yes
  - CXR and Spirometry (if >3-6 years old)* abnormal

- No
  - See figure 3

Is the cough characteristic?

- Yes
  - See figure 2

- No
  - Non-specific cough
    - Watch, wait and review
      - usually post viral cough or acute bronchitis
      - rarely but examine for foreign body inhalation, asthma, upper airway disorders, adverse events of medications, functional disorders, parasitic, mycoplasma, GERD, ear problems

- No
  - Evaluate
    1. Tobacco smoke and other pollutants
    2. CHF's activity, parental expectations and concerns
    3. Treat any obvious illness above

- Review in 1-2 weeks
  - ‘specific cough pointers’ present
    - resolved
      - persistent cough
    - discharge
      - Discuss options with parents

Watch, wait and review approach

- Review in 2 weeks
  - Cough resolving?
    - Yes
      - ICS (400μg/day budesonide equivalent)
    - No
      - Consider trial of therapy

Trial of therapy

- Dry cough
  - Review in 2-3 weeks
    - Cough resolving?
      - Yes
        - Cease ICS
        - Review points 1-3
      - No
        - Protracted bronchitis
          - Cease ICS
          - Review points 1-3
          - (see fig 3)

- Wet cough
  - Anti-microbials (10 days)
  - Review in 1-2 weeks
    - Cough resolving?
      - Yes
        - Protracted bronchitis
        - Cease ICS
        - Review points 1-3
      - No
        - (see fig 3)
Initial Evaluation of Unexplained Chronic Cough

- Chest Radiograph &
- **Spirometry** (if developmentally appropriate)
  - If suspect asthma, add testing to evaluate airway hyperresponsiveness

Abnormal CXR or spirometry or Cough Pointer

**Figure 3.** Approach to a child ≤ 14 years of age with chronic specific cough (ie, cough associated with other features suggestive of an underlying pulmonary and/or systemic abnormality). Children > 14 years of age should be managed as outlined in adult guidelines, but there is no good evidence concerning where the age cutoff for treatment should be. TB = tuberculosis; TEF = tracheoesophageal fistula.

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S Figure 3
Bronchiectasis or Recurrent pneumonia

- **Etiologies**
  - Cystic fibrosis
  - Primary ciliary dyskinesia
  - Previous severe pneumonia
  - Immunodeficiency
  - Structural airway lesions
  - Congenital lung lesions
  - Missed foreign body
  - TEF/ H-fistula

- **Diagnostics**
  - Sweat test
  - Bronchoscopy
  - Cilia biopsy
  - Immune workup
  - HRCT chest
  - “Ba” swallow
Aspiration

• Etiologies
  – Primary and secondary
  – Neurologically abnormal
  – Altered swallow
  – Weak cough reflex
  – Neuromuscular disease
  – Laryngeal abnormalities
  – Tonsil adenoid hypertrophy
  – TEF/H-fistula
  – Severe GERD

• Diagnostics
  – “Ba” swallow
  – Bronchoscopy & Lavage
  – Video fluoroscopy
  – pH monitor
  – Lung milk scan/salivagram
Chronic or less common infections

- TB
- Non-tuberculosis mycobacteria
- Mycoses
- Parasites

Diagnostics
- Mantoux (aka TST, PPD)
- Bronchoscopy & lavage
- HRCT chest
Interstitial Lung Disease

• Etiologies
  – Rheumatic diseases
  – Cytotoxics
  – Drugs
  – Radiation

• Diagnostics
  – Autoimmune markers
  – HRCT chest
    • Inspiratory & expiratory images
  – Lung biopsy

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Figure 3
Airway abnormality

- Tracheo-bronchomalacia
- Other intraluminal lesions
- Extrinsic compression lesions

Diagnostics
- Bronchoscopy & lavage
- CT chest
- MRI chest

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Figure 3
Other less common pulmonary conditions

- Primary and secondary tumours
Cardiac

• Etiologies
  – Pulmonary hypertension
  – Cardiac edema

• Diagnostics
  – Referral to pediatric cardiology
  – Echo
  – Cardiac catheterization
No Cough Pointers

Normal CXR and Normal Spirometry

• What next?
Evaluation of Chronic Cough

• Consider further investigations to confirm and guide treatment
  – CT chest
  – CT sinus
  – Flexible bronchoscopy & Bronchoalveoar lavage
  – Skin prick allergy testing
  – Immune studies
  – Sweat test
  – PCD testing
  – Cardiopulmonary exercise testing
  – Mantoux or other testing for infectious etiologies
  – Cardiac, GI tests (or referral to subspecialty colleagues)
Evaluation of Chronic Cough

• Tests should be individualized and chosen in accordance with clinical setting and the child’s signs and symptoms
• Consider adverse effects of possible tests
CT scans

- Chest CT is **Gold Standard** for evaluating small airway structural integrity
  - Bronchiectasis
  - Interstitial changes
  - Congenital abnormalities

Chang AB, Glomb WB. *CHEST* 2006 129.1_suppl.260S
• One study of CT chest for chronic productive cough
  – 43% yield for bronchiectasis
• One study of CT sinus for chronic cough
  – 66% abnormal But…
  • rhinorrhea, nasal congestion, sniffing, and postnasal drip had no significant relationship with paranasal sinus CT scan abnormality
  • 50% asymptomatic children have incidental sinus abnormality
CT disadvantages

- Often requires sedation in youngest children
- Risks to higher radiation exposure
  - Age and dose dependent increased lifetime cancer mortality risk

- Prior consultation with a pediatric pulmonologist is encouraged
  - Radiation exposure risks
  - Ensure most appropriate CT ordered
    - Conventional, high resolution (HRCT), contrast and spiral CTs all have different indications

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Flexible Bronchoscopy & Bronchoalveolar Lavage (BAL)

Indications

• Suspicion of foreign body
• Radiographic changes
• Suspicion of airway abnormality
• Microbiologic studies and lavage
• Poorly controlled conditions
Flexible Bronchoscopy & Bronchoalveolar Lavage (BAL)

• Series of 3 studies with yield ranging from 6-56% in identifying significant abnormalities
  – Study with 56% abnormalities were predominantly tracheobronchomalacia

• Multiple BAL studies
  – Some children identified with asthma-type inflammatory changes
  – But some children with known asthma did not demonstrate these changes
  – Lipid laden macrophages for aspiration controversial

Chang AB, Glomb WB. *CHEST* 2006 129.1_suppl.260S
Other Evaluations

• Pertussis
  – “whoop”, post tussive emesis, known exposures
• TB, other “atypical” infections if seeing patients in endemic areas

• Skin prick testing usually doesn’t aid in diagnosing etiology of chronic cough

Management

• Primary driver of management pathway should be based on
  – Cough etiology when known or
  – Clinical history and characteristics of cough when etiology is unclear

• Irrespective of diagnosis, discuss and manage
  – Patient/parental expectations and fears
  – Cough burden and impact on quality of life
  – Environmental influences

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Non-Specific Cough

- Watch, wait and review
  - Usually post viral cough or acute bronchitis
  - Rarely, but examine for foreign body, asthma, upper airway disorders, adverse effects of medication, functional disorders, pertussis, mycoplasma, GERD, ear problems

- Evaluate
  - Tobacco smoke and other pollutants (manage with elimination)
  - Child’s activity, parental expectations and concerns (manage expectations, fears)
  - Treat any obvious illness above

- Review in 1-2 weeks
  - At that time can continue watch, wait and review or start a trial of therapy

Chang AB, Glomb WB. CHEST 2006 129.1 suppl.260S
Empiric Treatment

• In some circumstances may need to trial empiric therapy
  – Diagnostic hypothesis based on cough features
  – Define a limited duration to confirm or refute the hypothesis
  – Re-evaluate and stop or continue intervention accordingly

• Guidelines discourage empiric treatment if symptoms of upper airway cough, asthma, gastroesophageal reflux are not identified

OTC Cough Medications

• AAP statement – no cold and cough medications for children under 6 years old
• Systemic reviews demonstrate little, if any benefit
• Increased morbidity and mortality
Antihistamines

- Adult data shows improvement in acute and chronic cough
- Some data in teenagers, young adults that antihistamine plus nasal medications improve symptoms
- No data in pediatrics for chronic cough
  - No significant improvement in acute cough
- Consider 1 week trial of antihistamines
- Consider 1-2 weeks of nasal corticosteroids
Asthma Therapy

• No benefit of Beta-2 agonists or anticholinergic agents in isolated cough
• Some subjects have benefitted from low dose inhaled corticosteroids
• No data for systemic steroids
• No data for leukotriene antagonists

• Trial inhaled corticosteroids for 2-4 weeks. If cough resolves, consider withdrawal and reassessment
Antimicrobials

• Improvement if known bacterial etiology
• No benefit in cough associated with acute respiratory illness

• Trial antibiotics 1-2 weeks, reassess.
  – Extend if needed for PBB
GERD Therapy

• Difficult to elucidate whether cough worsens reflux or whether reflux causes cough

• No improvement with motility agents
• No improvement with feeding positions
• Unclear data for acid suppressant or antacid treatments
• Unclear results of thickening liquid
• No data for fundoplication
Time Limited Empiric Trials of Therapies

- Antihistamines: 1 week
- Topical nasal corticosteroids: 1-2 weeks
- Inhaled corticosteroids: 2-4 weeks
- Antimicrobials: 1-2 weeks

- No benefit:
  - Beta-2 agonists
  - OTC cough medications
Our pulmonary team is here to help
Summary of Guidelines
GRADE Framework for evidence based medicine

• Quality of evidence rating based on:
  – Risk of bias, Inconsistency, Indirectness, Reporting bias, Imprecision
    A - High
    B - Moderate
    C - Low or very low

• Strength of recommendation rating based on:
  – Quality of evidence, Balance of benefits and harms, Patients’ values and preferences, Availability of resources
    Grade 1 - Strong
    Grade 2 - Weak
Summary of Guideline Recommendations

• We suggest defining chronic cough as the presence of daily cough of at least 4 weeks in duration (Ungraded, Consensus Based Statement).

• We suggest that an assessment of the effect of cough on the child and the family be undertaken as part of the clinical consultation (Ungraded, Consensus Based Statement).

• Exacerbating factors such as Environmental Tobacco Smoke exposure should be determined and interventional options for the cessation of exposure advised or initiated (Level: low; Benefit: substantial)
Summary of Guideline Recommendations

- We recommend taking a systematic approach (such as using a validated guideline) to determine the cause of the cough (Grade 1A).
- We recommend using pediatric-specific cough management protocols or algorithms (Grade 1B).
- Etiologic factors and treatments in children are sometimes different from those in adults. (Level: low; Benefit: substantial)
- When pediatric-specific cough recommendations are unavailable, adult recommendations should be used with caution. (Level: expert opinion; Benefit: intermediate)

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Summary of Guideline Recommendations

• We recommend basing the management or testing algorithm on cough characteristics and the associated clinical history, such as using specific cough pointers like presence of productive/wet cough (Grade 1A).

• We recommend that a chest radiograph and, when age appropriate, spirometry (pre- and post-β₂ agonist) be undertaken (Grade 1B).

Chang AB, Giomb WB. CHEST 2006 129.1_suppl.260S
Summary of Guideline Recommendations

• In children with specific cough, further investigations may be warranted, except when asthma is the etiologic factor.
  (Level: expert opinion; Benefit intermediate)

• For children 6-14 years of age with chronic cough and asthma clinically suspected, we suggest that a test for airway hyperresponsiveness (AHR) be considered (Grade 2C).

• Children with chronic productive purulent cough should always be investigated to document the presence or absence of bronchiectasis and to identify underlying and treatable causes such as cystic fibrosis and immune deficiency. (Level: low; Benefit: substantial)

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Summary of Guideline Recommendations

• We recommend not routinely performing additional tests (eg, skin prick test, Mantoux, bronchoscopy, chest CT); these should be individualized and undertaken in accordance with the clinical setting and the child’s clinical symptoms and signs (Grade 1B).

• We suggest undertaking tests evaluating recent *Bordetella pertussis* infection when pertussis is clinically suspected

  (Ungraded, Consensus Based Statement)
Summary of Guideline Recommendations

• In children with chronic cough, the etiology should be defined and treatment should be etiologically based. (Level: expert opinion; Benefit: substantial)

• In children with cough, cough suppressants and other OTC cough medicines should not be used on patients, especially young children, who may experience significant morbidity and mortality. (Level: good; Benefit: none)

• An empirical approach aimed at treating upper airway cough syndrome due to a rhinosinus condition, gastroesophageal reflux disease, and/or asthma should not be used unless other features consistent with these conditions are present (Grade 1A).

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
Summary of Guideline Recommendations

• We suggest that if an empirical trial is used based on features consistent with a hypothesized diagnosis, the trial should be of a defined limited duration in order to confirm or refute the hypothesized diagnosis. (Ungraded, Consensus Based Statement).

• In children who have started therapy with a medication, if the cough does not resolve during the medication trial within the expected response time, the medication should be withdrawn and other diagnoses considered. (Level: low; Benefit: intermediate)

Chang AB, Glomb WB. CHEST 2006 129.1_suppl.260S
References

Thank You

• Questions?

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