

Persistent Cough

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Objectives

- Describe the epidemiology and classification of cough
- Describe the common and uncommon causes in pediatrics and adults
- Describe the practical, cost-effective steps in diagnosis and management
- Understand the New 2006 Cough Guidelines

Disclosures

- Speakers' Bureau/Consultant/Ad Board
Greer Labs, TEVA, Respiratory Research,
CoCo Pharma, Merck, MEDA

Why do we cough?

- Cough is an important defense mechanism of the body that serves to clear the airway of excessive secretions and foreign matter
- It can be activated by
 - (1) Mechanical stimuli: foreign body, dust, talking
 - (2) Chemical stimuli: smoke, perfumes
 - (3) Thermal stimuli: cold air, hot air, cold water ingestion

What is the success rate with specific therapy in chronic cough?

- (A) 40-50%
- (B) 60-80%
- (C) 80-100%

What's the success rate?

- Cause of cough can be determined in 88 to 100% of cases
- Success rates with specific therapies range from 84 to 98%

Chest 1998;114(2):133s-181s

Thorax 1998;53:738-743

History

- Triggers: Talking, laughter, walking, running, strong smells, perfumes
- Timing: Daytime Vs nighttime
- Relationship with meals
- Preceding Events:
Viral URI, Recent Immigration from a developing country, foreign travel
- Analysis of cough sound: Peds Vs Adult
- Review of systems is very important

Analysis of cough sound

- Barking or brassy cough: Croup, tracheomalacia, habit cough
- Honking: Psychogenic
- Paroxysmal with or without whoop: pertussis and parapertussis
- Staccato: Chlamydia in infants

Physical Examination

- Thick, yellow postnasal drip visible in oropharynx: think chronic sinusitis
- Look into ears to rule out wax impaction and other causes (Arnold's Nerve)
- Look at nails for clubbing (CF, etc.)
- Check for thyroid masses
- Look for signs of atopy

Causes of acute cough

- Common cold
- Acute bronchitis
- Allergic rhinitis
- Acute bacterial sinusitis
- Pertussis in some communities
- COPD exacerbation

NEJM 2000;343(23):1715-1721

JAMA 2003;289(20):2701-2707

Cough vs. Airway Hyperreactivity

- Cough and Bronchial hyperreactivity (BHR) often coexist
- Cough and BHR are independent physiologic responses
- Inhibition studies
 - Lidocaine, oral codeine inhibit cough, not BHR
 - Cromolyn, atropine inhibit BHR, not cough

Choudry, Eur Resp J 1990;3:579-83,

Sheppard, Am Rev Resp Dis 1983; 127:691-4

Increased Cough Receptor Sensitivity

Cough Stimuli

Foreign Body
Dust/ cigarette smoke
Airway deformation
Mucous
Capsaicin
Nicotine
Histamine
Bradykinin
Prostaglandins($E_2, F_2\alpha$)

Neural mediators

Tachykinins, Neurokinin,
Substance P?, CGRP?

Types of nerve fibers

Rapidly adapting
receptors
Pulmonary C fibers
Bronchial C fibers

COUGH

Four basic steps for evaluating chronic cough

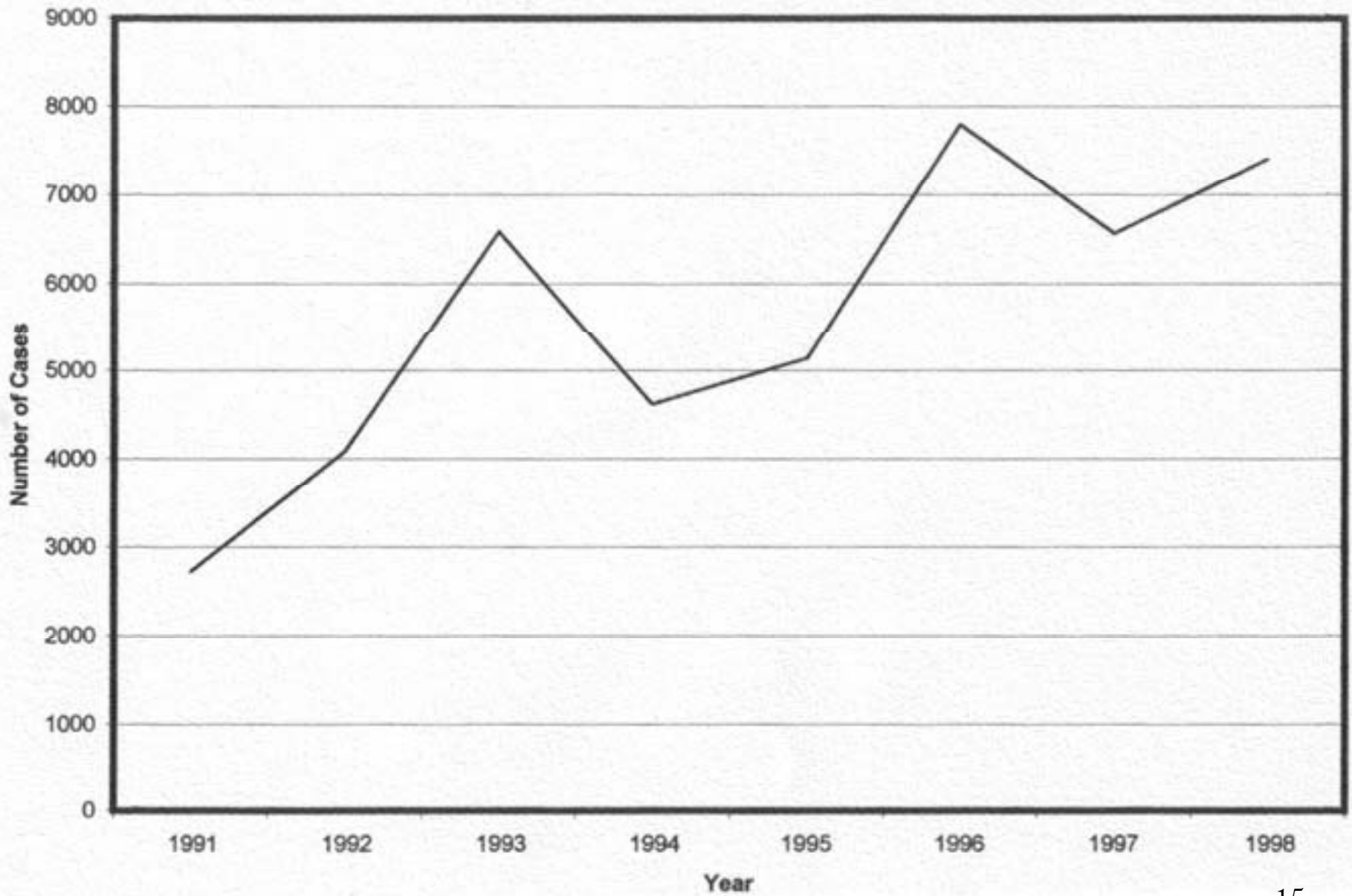
- Stop ACE-inhibitor
- Stop Smoking
- Chest XR
- Spirometry

Are we missing pertussis?

- 75 adults, cough for more than 14 days
- Pertussis diagnosis based on culture and PT or FHA titer
- 21% of adults had evidence of *B. pertussis* infection
- Clinical features and routine lab tests were of limited value in making the diagnosis

JAMA 1995;273:1044-1046

Cases of Pertussis in the US 1991-1998



Pertussis: Laboratory Diagnosis

- Leukocytosis with absolute lymphocytosis
- (Posterior) Nasopharyngeal swab and aspirate
- DFA testing: quick results but unreliable
- PCR: results in 48 h, false positives possible
- Culture of swab: takes 7 days for results
- Negative culture does not rule it out!
- Serology: IgG and IgA to fimbria, pertussis toxin and filamentous hemagglutinin (not standardized)
- Blood cultures: not useful

Pertussis

When to suspect & Whom to treat?

- Suspect and treat if a clear cut history of exposure
- Suspect and treat if cough and vomiting (?)
- Erythromycin is the drug of choice; however, unless administered early, it does not alter the course of the disease

NEJM 2000;343(23):1715-1721

JAMA 1995;273:1044-1046

Causes of chronic cough

- Postnasal drip syndromes (PNDS)/UACS
 - (1) Allergic rhinitis
 - (2) Nonallergic rhinitis
 - (3) Chronic bacterial sinusitis
- Asthma
- GERD
- Eosinophilic bronchitis
- Chronic bronchitis
- ACE-inhibitor induced cough

Chest 1999;116(2):279-84

Postnasal Drip Syndromes/Upper Airway Cough Syndromes How to treat

- Treat the cause: rhinitis, sinusitis
idiopathic (?)
- Antihistamine + decongestant (be cautious in elderly)
- Old vs new antihistamines
- Ipratropium (0.06%) nose spray
- Sinus Rinse/Rhinoflow/Water-Salt irrigation

NEJM 2000;343(23):1715-1721

How important is sinus imaging

- Consider doing in cough patients with postnasal drip unresponsive to treatment
- Consider doing in cough patients who are smokers
- Sinus XRay vs Sinus CT
- Sinus: Limited vs Full CT

Cough-variant asthma

What percentage of patients with asthma have cough as their sole presenting symptom?

- (A) 5%
- (B) 10-15%
- (C) 20-25%
- (D) 50-60%

Can asthma be a possibility if a pre- and post-bronchodilator spirometry is completely normal?

(A) Yes

(B) No

Methacholine Challenge test

In a setting of adult chronic cough patients:

- Positive predictive value:60-88%
- Negative predictive value:100%

Chest 1999;116(2):279-84

Methacholine Challenge test and allergy skin test correlative study in the diagnosis of asthma

- N= 175
- Allergy skin tests are simple, safe, inexpensive and reliable and there was an excellent correlation between these two tests
- More studies needed to clarify this further

Graif Y, Yigla M, Tov N, et al Chest 2002 Sep;122(3):821-5

Chronic cough completely
Relieved by a course of
Prednisone.

Is this diagnostic of asthma?

Chronic cough relieved by prednisone

Possibilities:

- (1) Allergic rhinitis
- (2) Asthma
- (3) Eosinophilic bronchitis
- (4) Others

Eosinophilic bronchitis

Asthma

- Sputum eosinophilia
- Airway hyperresponsiveness
- Treatment is inhaled or oral steroids

Eosinophilic bronchitis

- Sputum eosinophilia
- No airway hyperresponsiveness
- Treatment is inhaled or oral steroids
- Natural history unclear

A 40-year old reported with chronic cough for 1 year. He has a sticky sensation in the throat and a periodic hoarse voice.

Which of the following is a likely diagnosis?

- (A) Postnasal drip syndrome
- (B) Asthma
- (C) Acid reflux disease
- (D) Psychogenic

Causes of cough: single or multiple?

- Multiple causes were found in more than 60% when a large number of diagnostic tests are performed (US experience)
- Multiple causes were found in <26% when investigations were tailored to presenting features (European experience)

Reasons for misdiagnosis of chronic cough

- Failure to consider common extrapulmonary causes
- Insufficient dose of medication or duration of therapy

GERD

- Cough and hoarseness are the major complaints. Heartburn, sour taste and regurgitation are unusual.
- Silent reflux in 50-75% cases
- Mechanisms
- H₂-blocker therapy alone may fail
- Remember: Lifestyle modifications

Am J Gastroenterol 2000;95(8 Suppl):S9-14
Chest 2002;121:1132-40

If a patient with chronic cough and suspected GERD does not improve with 3 weeks treatment With a proton-pump inhibitor, the next step in The management should be

- (A) Refer for EGD
- (B) Refer for 24-hour esophageal pH monitor
- (C) Barium swallow
- (D) Continue the treatment aggressively

Therapeutic trials: When to expect a response?

- Smoking cessation: up to 4 weeks
- ACE-inhibitor discontinuation: up to 4 weeks
- Postnasal drip syndromes: up to 2-3 weeks
- Asthma: up to 6-8 weeks
- GERD: up to 8-12 weeks
- Eosinophilic bronchitis: up to 3-4 weeks

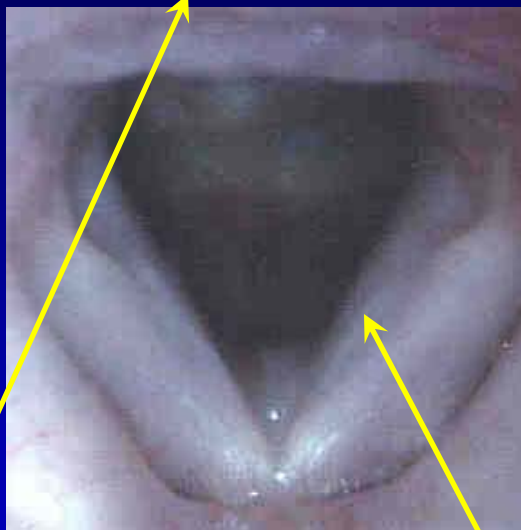
Don't give up too soon

Chest 1998;114(2):133s-181s

Reflux Tests

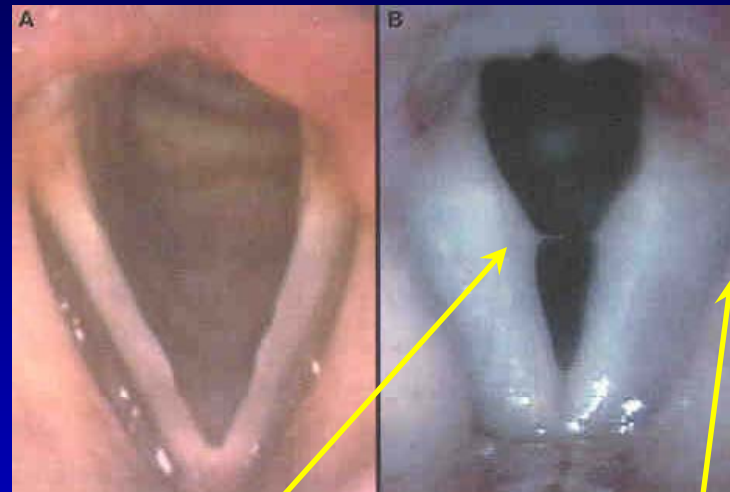
- Laryngoscopy
- 24-hour Esophageal pH monitor
- Multichannel Intraluminal Impedance and manometry
- Bravo pH Probe
- EGD
- Barium Swallow
- Motility studies
- Aeriflux

GERD/Laryngopharyngeal Reflux



Pseudosulcus vocalis

Posterior commissure hypertrophy



Vocal fold edema

Ventricular obliteration

Ear, Nose, Throat J 2002;82 (9 Suppl 2): 10-13

Sleep apnea and GERD

- The phreno-esophageal ligament (PEL) connects the diaphragm to the LES.
- During the sleep apnea syndrome, there is increased respiratory effort by the diaphragm.
- This extra effort is transmitted to the LES by the PEL.
- This further leads to opening of LES and possibly reflux.

Herr J. Chest 2001;120(3):1036-7

Sleep apnea and GERD

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Risks of proton-pump inhibitor therapy

- Community-acquired pneumonia
- Calcium malabsorption and hip fractures
- Vitamin B-12 malabsorption
(assess vitamin B-12 levels in patients on long-term PPI)
- Community-acquired *C diff.* infection
- Atrophic gastritis (PPI+ *H. pylori*)

Dose and duration- dependent!

Bradford GS, Taylor CT. Omeprazole and vitamin B-12 deficiency. Ann Pharmacother 1999, 33: 641-643

Yang YX, et al. Long-term PPI therapy and risk of hip fracture JAMA. 2006 Dec 27;296(24):2947-53

What is the clinical utility of flexible bronchoscopy

- Adds little to the diagnosis of chronic cough in the context of normal CXR or CT
- Useful to detect and assess endobronchial lesions (tumors, foreign bodies): very rare
- Always get a Chest CT before bronchoscopy
- If you are checking a Chest CT: include neck (speaker's experience)

How common is lung cancer in chronic cough?

- Very rare (0 to 2%)
- CXR has a negative predictive value of >95%, and a positive predictive value of 30 to 40%

Irwin et al. Chest 1998;114(2):133s-181s

Psychogenic (Habit) cough

- True incidence unknown
- Overdiagnosed by physicians
- Diagnosis of exclusion
- Patient education is the key

Ramanuja S, Kelkar P. Ann Allergy Asthma Immunol. 2009 Feb;102(2):91-5; quiz 95-7, 115.

When to use antitussives and protussives?

- Very rarely
- Incurable lung cancer
- Only for a short period in habit cough
- Guaiafenesin: ? decreases cough receptor sensitivity, mucolytic
Trial with good dose: 1200 mg
po bid

Drugs, 1993;46(1):80-91

Refractory Idiopathic Cough

Rule out all the possible causes first

Very challenging to treat

Experimental therapies:

Lidocaine nebulization, Water and salt irrigations of nose and sinus, Neurontin, Pamelor, Xanax, Baclofen, speech therapy evaluation and breathing exercises

Patient and family education and counselling

Am J Respir Crit Care Med 1995;152:2068-75

Zebras to watch for

- **“Clinically silent” suppurative airway disease**
- Congestive heart failure
- Cancer: bronchogenic, esophageal, metastasis
- Cystic fibrosis
- Interstitial lung disease
- Foreign bodies
- Pneumonia, Recurrent aspiration, pharyngeal dysf.
- Sarcoidosis

Chest 1995;108(4):991-7

Zebras to watch for cont...

- Pressure from an intrathoracic mass
- Primary ciliary dyskinesia (infertility)
- Lingual thyroid (hypothyroidism)
- Sleep apnea
- Vocal cord dysfunction
- Pulmonary tuberculosis
- Bronchiectasis

Ann Med 1989;21(6):425-7

Otolaryngol Head Neck Surg 2001;125:433-4

J Allergy Clin Immunol 2001;108(1):143

Take Home Points

- Individualize the treatment
- Flow diagrams/ Suggested reading
 - (1) Ramanuja S, Kelkar P. Ann Allergy Asthma Immunol. 2009 Feb;102(2):91-5; quiz 95-7, 115.
 - (2) Rank MA, Kelkar PS, Oppenheimer JJ. Ann Allergy Asthma Immunol. 2007;98:305-313
 - (3) Morice AH. ERJ 2004;24:481-492 (European)
 - (4) Irwin RS, et al. Chest 2006;129 (American)
 - (4) Morice AH, McGarvey L, Pavord I. Thorax 2006; 61:suppl 1 (British)

Thank you!

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