The Pathogenic Triad of Chronic Cough: Postnasal Drip Syndrome, Asthma, and Gastroesophageal Reflux Disease

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ABSTRACT

Chronic cough, lasting for 3 weeks or more, is one of the most common symptoms for which adult patients seek medical attention. The pathogenic triad of chronic cough is Postnasal Drip Syndrome (PNDS), Asthma, and Gastroesophageal Reflux Diseases (GERD) are the vast majority etiology of chronic cough in non-smoker adult with normal chest X-ray. The clinical investigations that should be performed are spirometry pre-post bronchodilator and bronchoprovocation testing for asthma; plain sinus radiograph and or computed tomographic imaging of the sinus for PNDS due to sinusitis; gastro-intestinal investigation 24 hours oesophageal pH monitoring and upper gastrointestinal endoscopy for GERD.

***Keywords**: chronic cough, postnasal drip syndrome, asthma, gastroesophageal reflux disease*

INTRODUCTION

Cough is an important physiologic defense mechanism that helps clear excessive secretions of mucus, foreign particles, and noxious aerosols from the airway. It is also the most common symptom for which adult patients seek medical attention from primary care physicians. In addition, referrals of patients with persistently troublesome chronic cough have been shown to account for up to 38% outpatient practice.[1,2,3]

The cough reflex, which is mediated through motor nerves, results from signals transmitted in sensory nerves from irritant cough receptors to the nervous system (CNS) cough center. Cough receptors are located throughout the respiratory tract and in extrapulmonary sites including the pleura and pericardium, auditory canals, paranasal sinuses, stomach, and diaphragm. Activation of this reflex occurs through receptor stimulation by inflammatory, mechanical, chemical, and thermal stimuli.[4,5]

CATEGORIES AND ETIOLOGY OF COUGH

Cough may be defined as acute or chronic based upon duration:

- Acute cough-duration of 3 weeks or less
- Chronic cough-duration of 3 weeks or more

The categories are not mutually exclusive because acute cough can persist and become chronic. Acute cough is most frequently due to the common cold followed by acute bacterial sinusitis, pertussis, and exacerbation of Chronic Obstructive Pulmonary Disease (COPD), allergic rhinitis, and asthma; less commonly, acute cough also can be associated with pulmonary embolism, congestive heart failure, and pneumonia. Chronic cough can be due to one cause, or simultaneously due to two or three diseases. The most common causes of chronic cough among non-smokers in adults are postnasal drip syndrome (PNDS), asthma, and gastroesophageal reflux disease (GERD). Smokers frequently have chronic cough due to chronic bronchitis but often do not seek medical attention because they have expectation of coughing as a side effect of smoking.[4,5,6]

Chronic Cough in Adults

Over the past 20 years, the importance and prevalence of postnasal drip syndrome (PNDS), asthma, and gastroesophageal reflux disease (GERD)

have all been established.[7] According to one clinical investigation by Pallombini et al, PNDS, asthma, and GERD, alone or in combination, were responsible for 93.6% of the cases of chronic cough.[8] Another review article by Irwin, PNDS, asthma, and GERD accounted for approximately 85% of all cases of chronic cough.[4] The relative frequency of the three varies with age. In adults in all ages, PNDS from rhinosinus disease is the most common cause, asthma the second, and GERD the third. In those 65 years old or older, GERD is second and asthma third. The remaining cases are due to various conditions, including chronic bronchitis caused by cigarette smoking or air pollution, angiotensin-converting enzyme (ACE) inhibitors, bronchiectasis, lung cancer, and aspiration from pharyngeal dysfunction.[9] We can view below the most common causes of chronic cough.[10,11]

Initial assessment and diagnostic evaluation of chronic cough

The patient's history may contain clues to the underlying disease. Postnasal drip, throat clearing, or nasal discharge and congestion point to PNDS. Intermittent shortness of breath, wheezing, and chest tightness are suggested for asthma. On the other hand, symptoms of heartburn, sour taste in the mouth, and persistent regurgitation are the classical symptoms of GERD. The absence of these or other characteristic symptoms does not rule out the three conditions as a cause of the chronic cough. Additional useful information would be whether the patient has a history of cigarette smoking or treatment with an ACE inhibitor. The character of the cough is not diagnostically helpful. Whether it is dry or wet, productive or unproductive, barking, honking, or paroxysmal, the same underlying disorders are found.[9,12]

A chest X-ray is clearly indicated in every patient with chronic cough. A normal film essentially rules out cancer, tuberculosis, bronchiectasis, and heart failure. In patients with PNDS, asthma, and GERD, the chest X-ray is usually normal. There is no consensus as to the best diagnostic strategy for chronic cough. Using a combination of anamnesis and physical examination suggest PNDS, asthma or GERD, the clinical investigations which should be performed are spirometry pre-post bronchodilator and bronchoprovocation testing for asthma; plain sinus radiograph or computed tomography imaging of the sinus for PNDS due to sinusitis; gastrointestinal investigation of 24 hours oesophageal pH monitoring (although not always available) and upper gastrointestinal endoscopy for GERD.[9,12,13]

The pathogenictriad of chronic cough.[4,8,9,10,11,12,14,15,16,17]

1. Postnasal Drip Syndrome (PNDS)

This rhinosinusitis syndrome should be one of the first conditions to be considered. Alone or in combination with asthma or GERD, PNDS is the most common cause of chronic cough in nonsmoking immunocompetent adults who have a normal chest X-ray. Clinical presentation of PNDS: cough, a feeling of something dripping into the throat, a need to clear the throat frequently, a tickle in the throat, nasal congestion or discharge, or history of recent upper respiratory illness. Allergy evaluation is probably most useful when there is a seasonal component to PNDS-induced cough, and/or the history strongly suggests an association with specific allergen exposure.

Treatment of PNDS due to allergic rhinitis: avoidance of offending allergen(s), sedating/non-sedating antihistamine plus decongestant is likely to be effective and nasal steroids as the drug of choice.

Treatment of PNDS due to sinusitis: antibiotics such as amoxicillin or combination of amoxycillin-clavulanic acid, cefadroxil, cefuroxime axetil, chlarithromycine, azythromycine, levofloxacine, moxifloxacine, or gatifloxacine, decongestant, and nasal steroid. Sinus

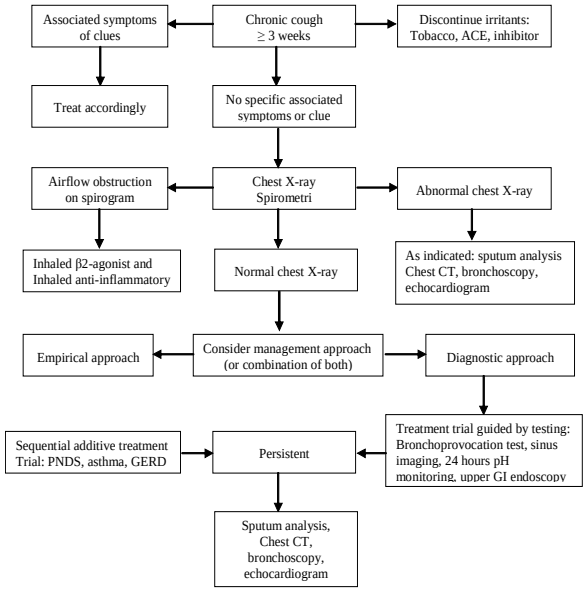
Table 1. Most common of chronic cough in patients investigated in specialist clinics [10,11]

Author	No patient (no female)	Improved	Diagnosis (% of total)			Most common other
			Asthma syndrome	GOR	Rhinitis	
Irwin et al	49 (27)	98%	25	10	29	Chronic bronchitis (12%)
Poe et al	109 (68)	96%	36	0	8	Post infectious (27%)
Poe et al	139 (84)	885	35	5	26	Idiopathic (12%)
Irwin et al	102 (59)	99%	24	21	41	Chronic bronchitis (5%)
Holfstein et al	228 (139)	91%	25	24	26	Post infectious (21%)
O'Connell et al	87 (63)	68%	6	10	13	Idiopathic (22%)
Smymios et al	71 (32)	97%	24	15	40	Chronic bronchitis (11%)
Mello et al	88 (64)	98%	14	40	38	Branchiectasis (4%)
Marchesani et al	92 (72)	91%	14	5	56	Chronic bronchitis (16%)
McGarvey et al	43 (29)	82%	23	19	21	Idiopathic (18%)
Palombini et al	78 (51)	-	59	41	58	Branchiectasis (18%)
Brithling et al	91 (-)	93%	31	8	24	Post viral (13%)
Simpson	86 (51)	92%	6	22	28	Post viral (13%)

surgery may be an option in patients who are refractory to medical therapy. The definitive diagnosis of chronic cough due to PNDS is made when cough ceases with specific rhinosinusitis therapy.

2. Asthma

Asthma is currently best understood as a chronic inflammatory disease of the airway presenting with characteristic symptoms of chest tightness, wheezing, dyspnea, cough, and associated physiologic abnormalities of variable airflow obstruction and airway hyperresponsiveness as directed by positive pre-post bronchodilator inhalation test and orbronchoprovocation testing with metacholine challenge test. All asthmatic patients experience cough as a symptom. When cough is the only asthma symptom, the disease is called *cough-variant asthma*.



Treatment of chronic cough due to asthma should be the same as for *classical asthma*: inhaled β2-agonist and inhaled anti-inflammatory agents (e.g. corticosteroids, nedrocomil sodium). The definitive diagnosis of chronic cough due to asthma is made when cough ceases with specific asthmatic therapy.

3. GERD

Although aspiration and irritation have been assumed as the main causes of chronic cough in patients with GERD, it is more likely that a vagally mediated reflux mechanism is responsible. Heartburn and regurgitation suggest a GERD-induced chronic cough, but these features maybe absent in "silent" GERD.

The most sensitive and specific test for GERD-induced chronic cough is 24-hour esophageal pH monitoring (unfortunately is not always present in referral hospital). Upper gastrointestinal endoscopy with mucosal biopsy is the gold standard in making diagnosis of GERD. PPI test may also be used to make a diagnosis of GERD if the result is positive.[18]

Treatment of GERD-induced chronic cough: combination of drug therapy with proton pump inhibitor (omeprazole, esomeprazole, lanzoprazole) and conservative measures such as weight reduction, a high-protein low-fat diet, elevation of the head of the bed while sleeping, and avoidance of coffee, tea, chocolate, mints, alcohol, and tobacco may resolve cough in a majority of patients. Antireflux surgery is usually reserved for patients with proven GERD who do not respond to maximal medical treatment. The definitive diagnosis of chronic cough due to GERD is made when cough ceases with specific GERD therapy.

CONCLUSIONS

The pathogenic triad of chronic cough: Postnasal Drip Syndrome, Asthma, and Gastroesophageal Reflux Disease (GERD), single or in combination are the vast majority etiology of chronic cough in nonsmoker adult with normal chest X-ray. The clinical investigations, which should be performed, are spirometry pre-post bronchodilator and bronchoprovocation testing for asthma; plain sinus radiograph and or computed tomographic imaging of the sinus for PNDS due to sinusitis; gastrointestinal investigation 24 hours oesophageal pH monitoring and upper gastrointestinal endoscopy for GERD. Themedical treatment of PNDS is antihistamine-decongestant, steroid intranasal, antibiotic; the medical treatment of asthma is inhaled b2-agonist and inhaled anti-inflammatory agents; and the medical treatment of GERD is proton pump inhibitor.

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