

Chronic cough

Three most common causes

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ABSTRACT

OBJECTIVE To describe an approach to diagnosis and treatment of patients with chronic cough.

QUALITY OF EVIDENCE MEDLINE was searched for reports of studies conducted between 1970 and 2000 on chronic cough and its epidemiology, natural history, diagnosis, and therapy. Articles were further selected based on clinical relevance and design. Most articles reviewed were epidemiologic cohort and case studies and reviews.

MAIN MESSAGE Chronic cough, a common ailment among adults, is often a diagnostic challenge. Most cases of chronic cough are associated with postnasal drip syndrome (PNDS), asthma, gastroesophageal reflux disease (GERD), or some combination of these. Initial investigations should include chest radiography to rule out more ominous causes of chronic cough. Examinations and trials of treatment can diagnose PNDS, asthma, and GERD. Combination treatments are often necessary for managing chronic cough.

CONCLUSION The most common causes of chronic cough are PNDS, asthma, GERD, or some combination of these. A systematic approach to diagnosis and treatment is effective for most cases of chronic cough.

RÉSUMÉ

OBJECTIF Décrire une méthode de diagnostic et de traitement de la toux chronique.

QUALITÉ DES DONNÉES Toutes les études portant sur la toux chronique, son épidémiologie, son évolution naturelle, son diagnostic et son traitement ont été recensées dans MEDLINE entre 1970 et 2000. Une sélection a ensuite été effectuée en fonction de l'intérêt clinique de ces études et de leur type. La plupart des articles retenus étaient des études de cas et des études de cohorte de type épidémiologique ainsi que des articles de revue.

PRINCIPAL MESSAGE La toux chronique est fréquente chez l'adulte et son diagnostic est souvent difficile. La plupart des cas sont attribuables au syndrome d'écoulement postnasal (SEPN), à l'asthme, au reflux gastro-œsophagien (RGO) ou à une combinaison de ces affections. L'investigation initiale devrait comporter une radiographie des poumons afin d'éliminer les causes plus graves de toux chronique. Les cas de SEPN, d'asthme et de RGO peuvent être identifiés à l'aide d'examen et d'essais thérapeutiques. Une combinaison de traitements est souvent nécessaire pour venir à bout de la toux chronique.

CONCLUSION Les causes les plus fréquentes de toux chronique sont le SEPN, l'asthme et le RGO. Dans la majorité des cas, un diagnostic et un traitement adéquats sont possibles grâce à une approche systématique du problème.

This article has been peer reviewed.

Cet article a fait l'objet d'une évaluation externe.

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Chronic cough has been reported to be the fifth most common complaint seen by primary care physicians.¹ The definition of chronic cough is controversial; it has been characterized as a cough lasting more than 3 weeks.² Recently, Irwin and Madison³ proposed that the period be increased to 8 weeks. The duration of the cough is an important diagnostic feature. This article uses the definition of chronic cough as cough lasting more than 8 weeks.

The exact prevalence of chronic cough in Canada has not been well studied but is estimated at 1% based on an American health survey.⁴ Other epidemiologic studies have shown the prevalence of chronic cough to be higher in urban populations exposed to car exhaust and industrial pollution,⁵ in school-age children,⁶ and in elderly people.⁷

Chronic cough can cause complications in respiratory, cardiovascular, central nervous system, gastrointestinal, genitourinary, and musculoskeletal systems. Hence, chronic cough is a multisystemic health concern for many patients seen by family physicians. This paper focuses on management of the most common causes of chronic cough in adults: postnasal drip syndrome (PNDS), asthma, and gastroesophageal reflux disease (GERD).

Quality of evidence

MEDLINE was searched for articles related to diagnosis and treatment of chronic cough, using the key words chronic cough, postnasal drip syndrome, asthma, cough variant asthma, and gastroesophageal reflux disease. The search was limited to human investigations completed between 1970 and 2000, written in English and conducted on both sexes. Bibliographies from these articles were screened for additional references. A total of 33 articles were used in this review; most were cohort and case studies and review articles. Few randomized control studies were found.

Importance of chronic cough

Cough, an important respiratory defense mechanism, is responsible for clearing excessive secretions, fluids, or foreign material from the airway.^{2,8} Despite its protective role, excessive coughing can cause multisystem problems. Common complications, such as anxiety, fatigue, insomnia, myalgia, dysphonia,

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perspiring, and urinary incontinence,^{2,9} often force patients to seek medical help. Other difficulties, including heightened self-consciousness and changes in lifestyle, are also frequent consequences of chronic cough.¹⁰ The severe effects on health and the possibility of more serious causes of cough warrant spending time to arrive at an accurate diagnosis and treatment plan.

Differential diagnosis

Chronic cough can have many causes (**Table 1**). Almost all chronic coughs, however, can be attributed to PNDS, asthma, GERD, or some combination of these in immunocompetent, non-smoking patients who have normal results of chest radiographs and do not take angiotensin-converting enzyme (ACE) inhibitors.² These three common clinical conditions should be considered first during diagnostic evaluation. Often, a careful history and physical examination can suggest, but are not sufficient to diagnose, the cause of chronic cough. For example, classic findings on history and physical examination associated with PNDS, asthma, and GERD can be unreliable because there are silent forms of these diseases.¹¹⁻¹³ The features and timing of chronic cough are also of little diagnostic value.¹⁴ Additional investigations and responses to trials of empiric therapy based on the most likely etiology are essential (**Figure 1**).

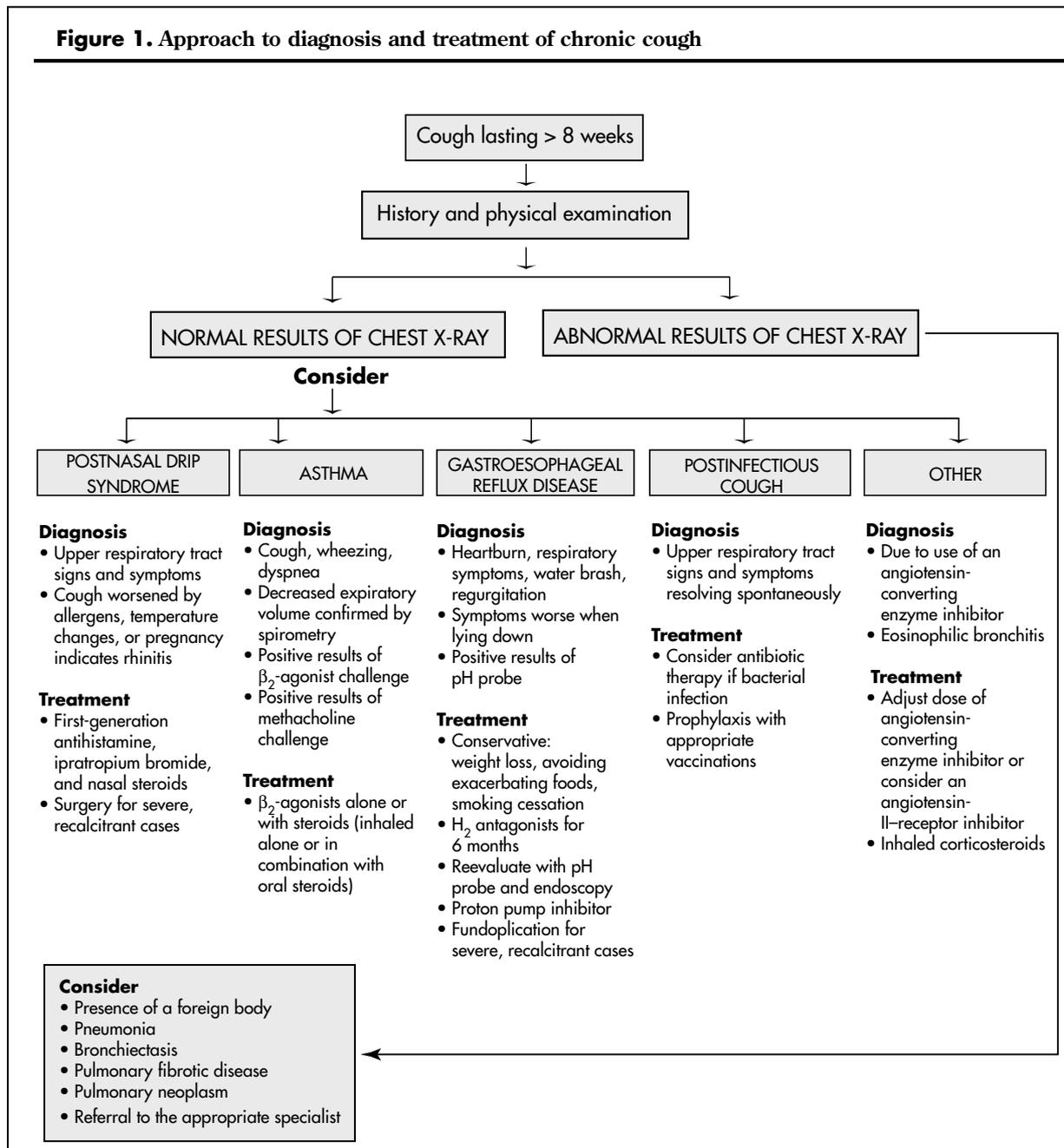
Initial investigations should include a chest radiograph, which can detect many of the more ominous diseases mentioned in **Table 1**. Evidence of these diseases

Table 1. Differential diagnosis of chronic cough

SYSTEM AFFECTED	CAUSES
Upper respiratory tract	Allergic or vasomotor rhinitis, postnasal drip syndrome,* postinfectious cough,* sinusitis
Lower respiratory tract	Abscess, allergic inflammation, aspiration, asthma,* bronchiectasis, bronchitis, chronic obstructive pulmonary disease, cystic fibrosis, drugs (ie, angiotensin-converting enzyme inhibitors), eosinophilic bronchitis, interstitial lung disease, pertussis, primary or metastatic lung tumours, sarcoidosis, tuberculosis
Cardiovascular system	Left ventricular failure, mitral stenosis
Gastrointestinal system	Gastroesophageal reflux disease*
Central nervous system (psychological response)	Habit cough, psychogenic cough

*Most common causes of chronic cough.

Figure 1. Approach to diagnosis and treatment of chronic cough



should prompt appropriate referral and treatment. When results of chest radiographs are normal or unchanged from those of radiographs taken for previous unrelated diseases in immunocompetent patients, PNDS, asthma, GERD, or some combination of these is highly probable.² Additional investigations, including a methacholine challenge test, sinus radiography, and an esophageal pH probe, might be necessary.

Often, a positive response to empiric therapy for a suspected cause of chronic cough is essential

for confirming its diagnosis. Optimizing therapy by adding treatments for concomitant causes of chronic cough might be required for some patients. Repeated failure of therapy or combination therapy should prompt referral to an appropriate specialist.

Postnasal drip syndrome

Postnasal drip syndrome is the most common cause of chronic cough. It most often occurs after viral upper respiratory tract infections, such as those

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Chronic cough

caused by respiratory syncytial or parainfluenza viruses and sometimes by *Chlamydia pneumoniae* (TWAR strain), *Mycoplasma pneumoniae*, or *Bordetella pertussis*.^{2,15} Other causes of PNDS include perennial rhinitis; rhinitis as a consequence of seasonal allergens, irritants, drugs, and vasomotor responses; and chronic sinusitis.² Whatever the cause, chronic inflammation augments nasal and sinus secretions that continuously stimulate the cough reflex.

Diagnosis of PNDS is based on a combination of historic, physical, and radiologic findings, and responses to treatment. The most common complaint of those with PNDS is a sensation of tickling or a constant drip in the back of the throat.² Throat clearing, nasal congestion, rhinorrhea, and hoarseness are other symptoms of PNDS; some of those with PNDS have no symptoms.³ Exacerbation of symptoms after exposure to allergens, irritants, or drugs suggests rhinitis as the cause of PNDS. Onset of watery rhinorrhea with changes in temperature implies vasomotor rhinitis. Radiographs of sinuses showing air-fluid levels, opacifications, or mucosal thickening (>6 mm) are diagnostic of chronic sinusitis.²

A positive response to therapy is essential for determining that PNDS is the cause of chronic cough. Treatment for postinfectious, perennial, and vasomotor rhinitis includes a first-generation antihistamine, such as dexbrompheniramine, in combination with a pseudoephedrine decongestant.^{11,16,17} The cough, if caused by PNDS, usually improves within a few days to 2 weeks after therapy begins. Poor improvement suggests that an inappropriate antihistamine was used or that there are other concomitant causes of chronic cough. The efficacy of first-generation antihistamines in treating PNDS is attributed to their anticholinergic properties, which make them effective against nonhistamine-mediated causes of PNDS. Insomnia, anxiety, tachycardia, palpitations, hypertension, diminished micturition, increased intraocular pressure, dry eyes, and a dry mouth are all potential side effects. Ipratropium bromide is useful for treating perennial and vasomotor rhinitis.^{2,3}

Managing allergic rhinitis should begin with allergen testing to identify environmental exposures and indicate exposures to be avoided. Newer nonsedating antihistamines, such as loratadine, are effective.³ Steroids, sodium cromoglycate, or intranasal antihistamines (eg, azelastine) are also successful treatments for allergic rhinitis.²

Treatment of chronic sinusitis includes a combination of antibiotic, anti-inflammatory, and

decongestant therapy.^{2,3,11,16,17} A 3-week course of antibiotic therapy is needed to treat the most common microbes responsible for sinusitis (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Staphylococcus aureus*). In addition, dexbrompheniramine and pseudoephedrine should be used for 3 weeks, followed by nasal steroids, which can be used for up to 3 months. Surgery should be considered for recalcitrant chronic sinusitis.²

Asthma

Chronic cough is often caused by asthma. Its usual clinical manifestations include some combination of cough, wheezing, dyspnea, and chest tightness. In up to 57% of asthma cases, however, cough is the only presenting symptom¹⁸ (cough variant asthma). Given the high prevalence of asthma in patients of all ages, asthma should always be entertained as a cause of chronic cough.

Along with the symptoms noted above, airway hyperresponsiveness¹⁹ and reversible airflow obstruction²⁰ can establish a diagnosis of asthma. Degree of obstruction is most accurately assessed by spirometry, which measures forced expiratory volume in 1 second (FEV₁). In asthma patients, at least a 12% reversibility of baseline airflow obstruction occurs spontaneously or in response to therapy.^{20,21} Because reversible airflow obstruction is uncommon in patients with cough variant asthma, their airway hyperresponsiveness must be measured. A methacholine challenge test has a positive predictive value up to 88% and negative predictive value of 100%.^{2,3,11} While negative results of a methacholine test rule out cough variant asthma, positive results only suggest it. A definitive diagnosis can be made when the cough resolves after a trial of therapy.

Conventional asthma treatment reduces both airway hyperresponsiveness and chronic cough in most patients with cough variant asthma.^{2,3} Canadian consensus guidelines for asthma include use of β -agonists to relieve symptoms immediately and inhaled corticosteroids (with or without oral corticosteroids, depending on severity) to control inflammation.²¹ β -Agonists give patients only transitory relief from chronic cough.²² Most patients' chronic coughs are relieved completely in 6 to 8 weeks^{2,3} with β -agonists plus either inhaled corticosteroids²³ or a combination of inhaled and oral corticosteroids.²⁴ Steroid therapy can be discontinued once the cough stops.^{2,3} Sometimes cough recurs, especially with exposure to precipitating respiratory irritants or allergens.

Gastroesophageal reflux disease

Gastroesophageal reflux disease is a common cause of chronic cough. Most people have some retrograde motion of acidic stomach contents into the esophagus,^{25,26} but GERD is diagnosed when this reflux produces symptoms or when complications arise. Transient loss of tone in the lower esophageal sphincter is the probable mechanism.^{27,28} Coughing induced by GERD can exacerbate loss of tone in the lower esophageal sphincter and perpetuate the cycle of more reflux, irritation, inflammation, and coughing.²⁷⁻²⁹

The clinical presentation of GERD varies; in up to 75% of cases the sole presenting symptom is chronic cough.² In adults with microaspiration, symptoms of heartburn, regurgitation, sour taste, dysphonia, hoarseness, and throat pain precede development of the cough.^{2,30-2} Macroaspiration sufferers often experience wheezing, dyspnea, hemoptysis, chest pain, nocturnal fevers, and night sweats.^{2,31} Macroaspiration can also be heralded by dysphagia, heartburn, water brash, and regurgitation, all of which are worse when patients are lying down.² Another mechanism of GERD-induced chronic cough includes exacerbations of a vagally mediated distal esophageal-tracheobronchial reflex. When this happens, low pH in the distal esophagus can induce a persistent cough and symptoms of asthma even without aspiration.²

Management of GERD involves a trial of antireflux therapy. Preventive measures include weight reduction, smoking cessation, and a diet low in acidic foods or foods that reduce the tone of the lower esophageal sphincter. A combination of a proton pump inhibitor and a prokinetic agent relieves GERD-induced cough in most cases,^{2,3} although full recovery might not be evident for as long as 6 months.^{11,33} Failure of therapy to reduce a suspected GERD-induced cough should prompt more aggressive antireflux therapy for a longer period even if other symptoms of GERD have improved. For recalcitrant cases, a pH probe can be used to assess the efficacy of treatment or to evaluate the need for fundoplication.^{2,3} Physicians should also consider treating other potential causes of chronic cough that could exacerbate the reflux-cough cycle.

Conclusion

Chronic cough is a common complaint with an extensive differential diagnosis, although most cases are caused by PNDS, asthma, GERD, or some combination of these. Although cough is a protective respiratory clearance reflex, for many adults it is a

Editor's key points

- Chronic cough, a common condition in adults, can present a diagnostic challenge, although family physicians can readily identify the usual causes.
- The most common causes are postnasal drip syndrome, asthma, and gastroesophageal reflux disease, or a combination of these.
- Chest x-ray examination should be done first to rule out more ominous causes of cough, followed by an empirical trial of therapy directed at the most likely cause based on history and examination. Improvement in the cough confirms the diagnosis.

Points de repère du rédacteur

- Le diagnostic de la toux chronique fréquemment observée chez l'adulte peut être un problème pour le médecin de famille, même s'il est généralement apte à en identifier les causes habituelles.
- Les causes les plus fréquentes sont le syndrome d'écoulement postnasal, l'asthme, le reflux gastro-oesophagien ou une combinaison de ces affections.
- Une radiographie pulmonaire doit être faite pour éliminer les causes de toux les plus graves, après quoi on procède à un essai thérapeutique empirique selon la cause la plus probable suggérée par l'anamnèse et l'examen du patient. Une réponse favorable confirme le diagnostic.

severe and prolonged health complaint. A systematic approach to diagnosis of chronic cough can reduce much of its morbidity for most of those who suffer from it. ✦

Competing interests

None declared

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