Chronic Cough With a History of Excessive Sputum Production*

The Spectrum and Frequency of Causes, Key Components of the Diagnostic Evaluation, and Outcome of Specific Therapy

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Study objective: To determine (1) the spectrum and frequency of causes of chronic cough with a history of excessive sputum production (CCS) and (2) the response of these causes to specific therapy.

Study design: Prospective study utilizing the anatomic diagnostic protocol originally developed to diagnose chronic cough.

Patients: Seventy-one immunocompetent adults who complained of expectoration of greater than 30 mL of sputum per day.

Location: University hospital pulmonary outpatient clinic.

Results: Patients were seen an average of 4.2 times over 4.6 months before a specific diagnosis was made. The cause of CCS was determined in 97%. It was due to one cause in 38%, 2 in 36%, and three in 26%. Postnasal drip syndrome (PNDS) was a cause 40% of the time, asthma 24%, gastroesophageal reflux disease (GERD) 15%, bronchitis 11%, bronchiectasis 4%, left ventricular failure 3%, and miscellaneous causes 3%. Among patients with a normal chest radiograph who were nonsmokers and not taking an angiotensin converting enzyme inhibitor, CCS was due to PNDS, or asthma, or GERD, or all three in 100% of cases. Chest radiograph, methacholine inhalational challenge, 24-h esophageal pH monitoring, bronchoscopy, and spirometry with bronchodilator each had a sensitivity and negative predictive value of 100%. Chest radiograph and barium swallow had positive predictive values of only 38% and 30%, respectively.

Conclusions: (1) The anatomic diagnostic protocol for cough is also valid for CCS; (2) the major causes of chronic excessive sputum production and chronic cough are so similar that CCS should be considered a form of chronic cough; (3) the evaluation of CCS is more complicated and takes longer than the evaluation of chronic cough; (4) the major strength of the laboratory diagnostic protocol is that it reliably rules out conditions; (5) the outcome of specific therapy is almost always successful; and (6) the term “bronchorrhea” can be misleading if it is applied to excessive sputum production before a specific diagnosis of its source is made since the most common cause of excessive sputum that is expectorated (PNDS) is a disorder of the upper respiratory tract. Therefore, nonspecific therapies theoretically aimed at reducing mucus production in the lower respiratory tract are not likely to be helpful. (CHEST 1994; 108:991-97)

ACEI=angiotensin converting enzyme inhibitor; CCS=chronic cough with a history of excessive sputum production; GERD=gastroesophageal reflux disease; LVF=left ventricular failure; MIC=methacholine inhalational challenge; PNDS=postnasal drip syndrome

Key words: bronchorrhea; cough; sputum

Among the six major respiratory symptoms (cough, dyspnea, chest pain, hemoptysis, expectoration, and wheeze), the least is known about the complaint of chronic excessive production of sputum. Although a fairly substantial body of literature exists on the physical/chemical characteristics of respiratory secretions, there is minimal knowledge of what conditions cause excessive chronic sputum production most frequently and how well they respond to therapy.1-5

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Although patients may present to a physician with a complaint of excessive sputum production, sputum must be expectorated with a cough. Therefore, we reasoned that cough and sputum production are related in either a cause and effect manner or they have common etiologies, and the evaluation of excessive sputum production could be conducted in the same fashion as the evaluation of chronic cough. Since 1981, an anatomic diagnostic protocol has been found to be extremely useful in the evaluation of chronic cough.6

The same protocol with minor modifications has been validated for use on adults in a tertiary care setting, on children in a tertiary care setting, and on adults in a community hospital setting.7-9

To our knowledge, no study has used the anatomic diagnostic protocol or any other systematic approach for the evaluation of chronic cough with a history of...
excessive sputum production (CCS). Therefore, the only information regarding the etiology of CCS comes from case reports. These mention bronchiectasis and chronic bronchitis most often as the cause of excessive sputum production. It seemed to us that the emphasis on these two entities may be misleading. The prevalence of bronchiectasis has been dramatically reduced since the introduction of antibiotics. Therefore, its importance among the causes of excessive sputum production may be less than has been previously thought. In addition, although chronic bronchitis is common among smokers, many of those people attribute their symptoms to “smoker’s cough” and do not seek medical attention. This accounts for the relatively low incidence of chronic bronchitis in two recent series of adult patients with chronic cough. Lastly, reports that focus on treatment of excessive sputum production either describe treatment of chronic bronchitis or bronchiectasis, or describe nonspecific methods to reduce sputum production regardless of the cause.

We believed that a study that evaluated the clinical aspects of CCS was important to undertake for the following reasons: (1) to determine the spectrum and frequency of causes of CCS; (2) to determine whether using an anatomic diagnostic protocol designed to detect abnormalities that affect the afferent limb of the cough reflex is appropriate for the evaluation of CCS; (3) to describe the similarities and differences between the syndromes of CCS and chronic cough; (4) to determine which diagnostic studies are most useful in the evaluation of CCS; and (5) to determine whether specific therapy directed at the cause or the presumed operant pathophysiologic mechanism is effective in treating CCS or whether more effective nonspecific therapies need to be developed.

We used the anatomic diagnostic protocol to prospectively evaluate an unselected group of consecutive patients who presented to our pulmonary subspecialty clinic with a complaint of cough productive of excessive sputum.

**Materials and Methods**

From February 23, 1988 to March 2, 1992, 97 consecutive and unselected, immunocompetent patients with CCS defined as cough with production of greater than 30 mL of sputum per day for at least 3 weeks, were seen by one of us (R.S.L) in our pulmonary outpatient clinic. Of these, 26 failed to return for follow-up and were eliminated from analysis. The remaining 71 patients made up our study group. Seventy-three percent were referred by another physician; 27% were self-referred. The entrance criterion of a duration of 3 weeks was part of our 1981 and 1990 studies of chronic cough. It was included again in an attempt to eliminate patients who had transient cough and sputum production associated with the common cold. The entrance criterion of more than 30 mL sputum volume produced was chosen on the basis of studies by Miller et al and Ashcroft. No attempt was made to measure sputum volume to verify its quantity since our goal was to measure our success in evaluating and treating a symptom.

**Diagnostic Protocol**

The diagnostic protocol used contained only minor refinements from that previously published.

First, in all patients, a history and physical examination were performed, concentrating on anatomic locations of the afferent limb of the cough reflex, and a chest radiograph was obtained.

Second, in current tobacco smokers or patients taking an angiotensin-converting enzyme inhibitor (ACEI) drug, no additional studies were ordered until the response to cessation of smoking or discontinuation of the drug therapy for 4 weeks was assessed.

Third, depending on the results of the initial, routine evaluations and elimination of irritants, some, none, or all of the following studies were obtained: sinus radiographs and allergy evaluation; spirometry before and after bronchodilator or methacholine inhalational challenge (MIC); barium swallow or 24-h esophageal pH monitoring or both; expectorated sputum for microbiologic study or cytologic study or both; fiberoptic bronchoscopy; and noninvasive studies or invasive cardiac studies or both. (1) If history, results of physical examination, and chest radiographs did not suggest a cause, the first additional study ordered was pulmonary function testing. (2) If history or physical examination results or both suggested a postnasal drip syndrome (PNDS), sinus radiographs and an allergy evaluation were routinely obtained. (3) If history, physical examination results, chest radiographs, and pulmonary function testing did not suggest a cause, tests to evaluate gastrointestinal reflux disease (GERD) were ordered even in the absence of upper gastrointestinal symptoms typical of GERD. If results of barium swallow tests were normal (ie, barium was not refluxed to midesophagus or higher), 24-h esophageal pH monitoring was performed.

Fourth, when chest radiograph and clinical findings did not suggest the cause of CCS, sputum studies, bronchoscopy, cardiac studies, or all three were ordered only as a last resort.

Fifth, the cause of CCS was determined by observing which specific therapy eliminated CCS as a complaint. Specific therapy was defined as therapy specifically directed at the presumed operant pathophysiologic mechanism or etiology of CCS. If the evaluation suggested more than one possible cause, therapies were initiated in the same sequence that the abnormalities were discovered. Since cough can be simultaneously caused by more than one condition, therapy that appeared to be partially successful was continued and other treatment sequentially added to it.

Pulmonary function studies consisted of spirometry before and after the inhalation of albuterol or methacholine. Our equipment and techniques for performing these tests have been previously reported. A positive response to methacholine consistent with symptomatic asthma was defined as a decrease in FEV1 from the post saline solution baseline of 20% or greater after the inhalation of 10 μmol or less of methacholine. The cumulative provocative dose was reported as the PD20. GERD was evaluated by barium esophagography or 24-h esophageal pH monitoring or both. Our technique for prolonged esophageal pH monitoring has also been reported previously.

**Pretreatment Diagnostic Criteria**

Prospective criteria were established for the presumptive diagnoses of PNDS, asthma, GERD, chronic bronchitis, and bronchiectasis as the cause of CCS.

PNDS was considered when (1) patients described the sensation of having something drip down into their throats, nasal discharge, or the need to clear their throats frequently, or (2) physical examination of the nasopharynx and oropharynx revealed mucoid or mucopurulent secretions or a cobblestone appearance of the mucosa. Patients with PNDS were considered to have sinusal when

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sinus radiographs demonstrated (1) >6 mm of mucosal thickening, (2) air-fluid levels, or (3) opacification of any sinus and also when cough was associated with nasal congestion and a purulent discharge was seen on examination of the nasal cavities or posterior oropharynx in the absence of an abnormal radiograph.

Asthma was considered when (1) patients complained of episodic wheezing, shortness of breath plus cough, and were heard to wheeze, or (2) reversible airflow obstruction was demonstrated by pulmonary function testing (FEV1 increased at least 15% from baseline and approached normal after albuterol even in the absence of wheeze), or (3) MIC was positive in the presence of normal routine spirometry and absence of wheeze. The diagnosis of asthma was not made in any patient who had experienced an obvious respiratory tract infection within 2 months prior to examination and in whom sputum production was transient and self-limited.

GERD was considered when (1) patients complained of heartburn or sour taste in their mouths more frequently than every 3 weeks, or (2) barium esophagography demonstrated reflux of barium to the mid esophagus or higher, esophagoscopy with biopsy specimen showed esophagitis, or 24-h esophageal pH monitoring was abnormal in the absence of upper gastrointestinal complaints.

Chronic bronchitis was considered when patients met the criteria set forth by the British Medical Research Council.25 When pulmonary function tests were performed in these patients for other clinical reasons (ie, coexisting dyspnea), they must have failed to demonstrate reversibility when pulmonary function studies revealed airflow obstruction (FEV1 remained reduced after increasing no more than 14% from baseline after the inhalation of albuterol).

Bronchiectasis was considered when chest radiographs demonstrated increase in size or loss of definition of the markings in specific segmental areas of the lung; crowded markings and atelectasis; cystic spaces; honeycombing; signs of compensatory hyperinflation; or when purulent appearing sputum was expectorated.17

Posttreatment Diagnostic Criteria

The final diagnosis of the cause of CCS required fulfillment of pretreatment criteria plus having sputum production disappear with specific therapy.

Specific therapy for PNDS depended on the etiology; the etiology was diagnosed by clinical criteria and sinus radiographs.26,27,28 Allergic, perennial nonallergic, postinfectious, environmental irritant, and vasomotor rhinitis were treated initially with oral dexibrompheniramine maleate and d-isophedrine for 3 weeks followed by intranasal beclomethasone dipropionate if there was a favorable response. The newer relatively nonsedating histamine type 1 (H1) antagonists were not used routinely because of their inferior results in nonhistamine-mediated postnasal drip syndromes.26 Whenever possible, the allergic or irritating precipitating factor was eliminated. Vasomotor rhinitis that failed to respond to the above measures was treated with intranasal ipratropium bromide. Sinusitis was treated with a combination of antibiotic and dexibrompheniramine maleate plus d-isophedrine for at least 3 weeks plus a decongestant nasal spray (oxymetazoline hydrochloride) for 5 days. Asthma was treated with an initial regimen of inhaled β2-agonist bronchodilators with or without corticosteroids. Long-term maintenance therapy included inhaled corticosteroids. When therapy with metered-dose inhalers delivered with a spacer device was observed to provoke coughing due to airway irritation by a constituent of the aerosol, oral β2-agonist therapy was used. GERD was treated with a regimen that consisted of the following: (1) a high-protein, low-fat (45 g), antireflux diet; (2) a protonic agent or histamine type 2 (H2) blocker or both; (3) head of bed elevation; (4) eating three meals a day without snacking; and (5) not eating or drinking except for taking medicines for 2 to 3 h prior to lying down. Chronic bronchitis was treated with removal of the environmental irritant. Bronchiectasis was treated with β2-agonists, theophylline, antibiotics, and chest physiotherapy with postural drainage when necessary. Left ventricular failure (LVF) was treated with diuresis, afterload reduction, antianginal medications, digoxin, and in one instance with peritoneal dialysis. Bronchogenic carcinoma was treated with resectional lung surgery; cystic fibrosis with antibiotics, chest physiotherapy and postural drainage, and bronchodilators; and aspiration due to pharyngeal dysfunction with speech therapy. If more than one disorder was implicated as the cause of CCS, the effect of therapy on the most clinically prominent condition was evaluated before adding treatment for the other. No patient received nonspecific, symptomatic therapy as long as specific therapy was available. The success rate of specific therapy was assessed during follow-up clinic visits or by telephone when patients lived out of state and country. Therapy was deemed successful when patients no longer complained of CCS because it had markedly improved, was controlled with treatment, or disappeared.

Statistical Analysis

Probability statistics were used to describe the testing characteristics of individual components of the diagnostic protocol in terms of sensitivity, specificity, positive predictive value, and negative predictive value as they applied to CCS.23 A test was deemed a true positive or false positive on the basis of the response to specific therapy. If specific therapy was successful, it was determined to be a true positive result. Differences between groups were compared with Student's t test and χ2 analysis. The 0.05 level of significance (type I error rate) was used throughout.

RESULTS

Spectrum and Frequency of the Causes of Chronic Cough With a History of Excessive Sputum Production

Our study group consisted of 39 men and 32 women with an average age of 58±17 years (range, 18 to 86 years). They had complained of cough productive of more than 30 mL of phlegm per day for an average of 69±95 months (range, 1 to 480 months). Using posttreatment diagnostic criteria, the cause of CCS was determined in 69 of 71 (97%) patients. The only patients who failed to respond to treatment adequately were (1) a woman who met pretreatment diagnostic criteria for PNDS and GERD, had an initial favorable response to therapy, but then had a rapid relapse with no further response; and (2) a woman who met pretreatment criteria for PNDS, asthma, and GERD but had a maximum 50% reduction in sputum production with a near immediate relapse to baseline.

In the 71 patients, 131 causes of CCS were identified. Their spectrum and frequency are shown in Figure 1. As shown in Figure 2, CCS was due to multiple causes in 62% of patients.

PNDS was the single most common cause of CCS; it represented 40% (52/131) of all causes of CCS identified. PNDS was most often due to sinusitis (31/52 cases), although cases of perennial nonallergic rhinitis (4), allergic rhinitis (1), postinfectious rhinitis (1), vasomotor rhinitis (1), and drug-induced rhinitis (1) were also identified. In 13 patients, the cause of postnasal drip could not be defined more specifically. Asthma was the second most common cause of CCS; it repre-
sented 24% (31/131) of all causes of CCS. In 6.5% of asthmatics, CCS was the sole presenting manifestation. MIC was singularly useful in making the diagnosis of asthma in these patients.

GERD was the third most common cause of CCS, accounting for 15% (20/131) of the diagnoses made. In 10% of patients with GERD, cough was the sole presenting manifestation. Twenty-four-hour esophageal monitoring was singularly useful in making the diagnosis of GERD.

Acute and chronic bronchitis taken together were the fourth most common cause of CCS, occurring with a frequency of 11% (15/131) of all causes. All cases of chronic bronchitis were due to the inhalation of tobacco smoke.

Bronchiectasis was the fifth most common cause of CCS, accounting for 4% (5/131) of all diagnoses. LVF was the cause in 3% (4/131). The miscellaneous group included one case each of bronchogenic carcinoma, cystic fibrosis, idiopathic vocal cord ulceration, and aspiration due to pharyngeal dysfunction.

Overall, CCS was due to PNDS, asthma, GERD, and/or bronchitis 90% of the time. In 43 patients (62%), more than one cause of CCS was found to exist. The most common etiologic combinations were

**Usefulness of the Diagnostic Protocol**

The testing characteristics of various laboratory components of our diagnostic protocol are shown in Table 1. All laboratory tests had sensitivities and negative predictive values >92%, and only sinus radiograph and barium swallow showed values of less than 100% for these parameters. On the basis of a specific therapy failing to eliminate CCS as a complaint and subsequently determining the cause, the following tests were determined to be falsely positive in predicting that the abnormality found was the cause of CCS:

### Table 1—Testing Characteristics of CCS Protocol*

<table>
<thead>
<tr>
<th>Test</th>
<th>n</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Positive Predictive Value, %</th>
<th>Negative Predictive Value, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray</td>
<td>67</td>
<td>100</td>
<td>54</td>
<td>38</td>
<td>100</td>
</tr>
<tr>
<td>Sinus x-ray</td>
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<td>97</td>
<td>75</td>
<td>81</td>
<td>95</td>
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<tr>
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<td>100</td>
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<td>82</td>
<td>100</td>
</tr>
<tr>
<td>BaS</td>
<td>44</td>
<td>92</td>
<td>42</td>
<td>30</td>
<td>93</td>
</tr>
<tr>
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</tr>
<tr>
<td>Bronch</td>
<td>12</td>
<td>100</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Spiro p+p</td>
<td>26</td>
<td>100</td>
<td>14</td>
<td>76</td>
<td>100</td>
</tr>
</tbody>
</table>

*BaS=barium esophagogram; esoph pH=24-h esophageal pH probe monitoring; bronch=fiberoptic bronchoscopy; spiro p+p=spirometry before and after inhaled albuterol.
sinus radiographs, 12%; chest radiographs, 36%; barium swallow, 41%; spirometry before and after bronchodilator, 23%; MIC, 13%; 24-h esophageal pH monitoring, 9%; and fiberoptic bronchoscopy, 33%. The relative usefulness (true positive result) of various components of the diagnostic protocol in determining the cause of CCS is shown in Figure 3.

**Outcome of Specific Therapy**

Specific therapy was successful in eliminating CCS as a complaint in 69 of 71 (97%) of patients. None of these patients were given nonspecific antitussive therapy. On average, patients were seen 4.2 times in clinic over an average of 4.6 months before a specific diagnosis was made and successful specific therapy prescribed.

CCS due to bronchiectasis and miscellaneous causes took, on average, more visits to the physician to respond to specific therapy than when it was due to all other causes (4.5±0.7 and 4.7±4.6 visits, respectively). PNDS, asthma, GERD, and bronchitis each required 3.3 visits on average before sputum production was eliminated with therapy.

**DISCUSSION**

Human respiratory mucus is a mixture composed of approximately 95% water, 1% protein, 0.9% carbohydrate, and 0.8% lipid. The constituents of mucus are produced by a variety of cells in the lining of the respiratory tract, including goblet cells, submucosal gland cells, plasma cells, Clara cells, and alveolar type II pneumocytes. The normal volume of mucus produced by the lower respiratory tract in humans has been estimated to range from 10 to 100 mL/d. Mucus is also produced in the upper respiratory tract, but the volume produced in that location is even more difficult to estimate. The primary function of normal mucus is to serve as a transport medium for removal of respiratory debris, such as dead cells and their products as well as inhaled particles. Since mucus is generally swallowed and inactivated by the acidic medium of the stomach, expectoration of sputum implies that the normal mechanisms for mucus clearance are either overwhelmed or malfunctioning. While healthy individuals produce respiratory tract mucus, it is not normal for them to expectorate it. To do so signifies the presence of a disease process that can be transient as in the common cold, or chronic as in asthma, chronic bronchitis, or bronchiectasis. Expectorated sputum is usually a combination of upper and lower respiratory tract mucus mixed with saliva, tissue fluid transudate containing enzymes, fibrinogen, and immunoglobulins, as well as bacteria, dead respiratory lining cells, and a variety of inflammatory cells such as neutrophils or eosinophils.

Different volumes of daily sputum ranging from 26 to 500 mL have been used to explain the meaning of “excessive.” We decided on a volume of 30 mL/d because of studies by Miller et al. and Ashcroft that showed that healthy subjects and most patients with chronic bronchitis expectorated less than this volume. In addition, from our own clinical experience, we believed that 30 mL was an easily estimated volume (two tablespoons or one shotglass) and a quantity that seemed to separate patients who complained of “excessive” sputum production from those who did not. It is important to note that sputum volumes in this study were reported by our patients and not measured. Based on the results of this study, several conclusions about CCS can be made.

First, the anatomic diagnostic protocol previously utilized for the complaint of chronic cough is also valid for the evaluation of chronic excessive mucous production. By systematically evaluating conditions that may affect the afferent limb of the cough reflex, we were able to determine the causes of CCS and prescribe therapy that was successful in 97% of our patients. The diagnostic and therapeutic success rates achieved in this study of CCS are similar to those reported by ourselves and others using the anatomic, diagnostic protocol in the evaluation of chronic cough.

Second, we have discovered many similarities between patients who primarily complain of chronic mucus production and those who complain of chronic cough. For example, the most common causes of CCS and chronic cough are the same. PNDS, asthma, GERD, and bronchitis were the most common causes, accounting for 90% of causes of CCS in this study and 91% of causes of chronic cough in our 1981 and 1990 studies. Among nonsmoking patients with a normal chest radiograph who were not taking an ACEI, either PNDS, or asthma, or GERD, or all three accounted for 100% of causes of CCS in the current study and 100%
of causes of chronic cough in the 1990 study. These similarities are so striking that we now consider the chronic excessive expectoration of mucus to be a variant of chronic cough.

Third, as in the evaluation of chronic cough, the major strength of the laboratory diagnostic protocol in evaluating CCS is that it reliably rules out conditions. Chest radiograph, MIC, fiberoptic bronchoscopy, and prolonged esophageal pH monitoring each have sensitivities and negative predictive values of 100%. However, MIC has a positive predictive value of 82% and a specificity of 71%. These results are consistent with previous reports.7,24 Similarly, barium swallow and chest radiograph, with positive predictive values of 30 and 38%, frequently detect abnormalities that are not related to the cause of the patient’s CCS.

We did not analyze the accuracy of spirometry in diagnosing asthma. In our most recent prospective study of chronic cough, only 4 of the 32 patients diagnosed as having asthma had reversible airflow obstruction at baseline. The remainder required MIC to document bronchial hyperresponsiveness.7 This shows that spirometry with or without bronchodilator is not the study of choice in the diagnosis of cough variant asthma and is unlikely to be the most appropriate study in the diagnosis of CCS due to asthma. However, we did analyze the usefulness of spirometry with bronchodilator to supplement the clinical diagnosis of chronic bronchitis. We found that spirometry with bronchodilator has a 100% sensitivity and negative predictive value when it is used for this indication. In other words, all patients in this study whose cough was found to be due to chronic bronchitis had associated irreversible airflow obstruction.

Based on all of these results, it can be said that a negative test result, for all intents and purposes, rules out the entity that it was intended to detect. We believe that in evaluating CCS, as in chronic cough, a positive test result must be confirmed by a favorable response to specific therapy to be considered diagnostic; objective tests may detect abnormalities that are unrelated to the excess production of sputum. These abnormalities must be addressed independently as indicated.

Fourth, there were differences in comparison to what we know about the evaluation of chronic cough. The evaluation of CCS appears to be more difficult. On average, patients were seen 4.2 times over 126 days before a specific diagnosis was made and successful specific therapy had been prescribed. This was different than our recent experience with chronic cough, where on average patients were seen in clinic 3.5 times over 96 days to reach the same results. In addition, patients with CCS were more likely than patients with chronic cough to have multiple causes for their symptoms. Thirty-six percent of patients with CCS were found to have two causes and 26% had three causes.

In comparison, only 23% of patients with chronic cough were found to have two causes, and only 3% had three causes. Because we administer specific therapy in a sequential manner, the larger number of patients with multiple causes may be the reason why it took longer to arrive at a final diagnosis and prescribe treatment.

Fifth, although the spectrum of the most common causes of CCS and chronic cough is the same, there are differences in the frequency of causes. GERD, which is the third most common cause of both CCS and chronic cough, constitutes only 15% of cases of CCS in comparison to 21% of cases of cough. Bronchitis, which is the fourth most common cause of both entities, represents 11% of causes of CCS but only 5% of causes of chronic cough. In addition, LVF is an unexpectedly important cause of CCS, making up 3% of all causes found. Only one case of chronic cough due to LVF was found in the 1990 study. Based on the medical literature, the relative infrequency with which bronchiectasis was found to be the cause of excessive sputum production in this study was another important finding. This confirms our original suspicion that bronchiectasis is now only a common cause of excess sputum production among patients with predisposing medical conditions. Among the conditions that have been associated with bronchiectasis are bronchial obstructions, inadequately treated pneumonia, abnormalities of ciliary function, cystic fibrosis, allergic bronchopulmonary aspergillosis, various immune deficiencies, $\alpha_1$-antiprotease deficiency, defects of bronchial anatomy, chronic sarcoidosis, toxic inhalations, neoplasms, yellow nail syndrome, and tuberculosis.10

Among the many other causes of excessive sputum production that have been described but were not seen in our study are the following: endobronchial tuberculosis,23 bronchoalveolar carcinoma,25 long-term sulfur oxide exposure,26 lymphatic obstruction with chyloptysis,27 fungal infection,28 metastatic carcinoma,29 and acute quadriplegia.30 With the exception of endobronchial tuberculosis and bronchial inflammation secondary to sulfur oxide exposure, usually one would consider the presence of these entities only when the chest radiograph is abnormal. Contrary to the prevailing belief, chronic excessive sputum production is associated with a normal chest radiograph in most cases. In our patients, PNDS, asthma, GERD, and bronchitis accounted for 90% of the causes of excessive sputum production that we found. Patients with these entities usually present with a normal chest radiograph, although occasionally aspiration associated with GERD may produce an abnormal result of the study.

Sixth, we have shown that excessive mucus that is expectorated can originate from the upper respiratory tract. Since mucus comes from the upper respiratory tract in PNDS, and PNDS is the most common cause
of CCS, nonspecific therapies aimed at reducing mucus production in the lower respiratory tract are unlikely to be successful. Since specific therapy for CCS appears to be extremely successful and some causes of expectation are associated with potentially life-threatening diseases, we believe that an aggressive attempt at making a specific diagnosis and initiating specific therapy is warranted. In addition, the term bronchorrhea can be a misnomer when applied before a specific diagnosis is made, since that word implies that excessive sputum originates from the lower respiratory tract.

In conclusion, we believe that the anatomic diagnostic protocol used for evaluating chronic cough is valid for the evaluation of CCS. The most common causes of CCS and chronic cough are the same—PNDS, asthma, GERD, and bronchitis. Bronchiectasis is a common cause of excess sputum production only among patients with certain disease states, primarily those involving reduced pulmonary defenses against infection. The major strength of the laboratory diagnostic protocol in the evaluation of CCS is in ruling out entities. The evaluation of CCS appears to be more difficult than the evaluation of chronic cough, requiring more time and visits to the physician than with chronic cough. In addition, patients with CCS were more likely than patients with chronic cough to have multiple causes for their symptoms. Specific therapy for chronic excessive sputum production is very effective and therefore should be pursued whenever possible.

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