Unexplained (Idiopathic) Cough
ACCP Evidence-Based Clinical Practice Guidelines
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Objective: To review the literature on unexplained cough, previously referred to as idiopathic cough.
Methods: Search of MEDLINE (through May 2004) for studies published in the English language since 1980 on human subjects using the medical subject heading terms “cough,” “unexplained cough,” and “idiopathic cough.” We selected case series and prospective descriptive clinical trials. We also obtained any references from these studies that were pertinent to the topic.
Results: The diagnosis of unexplained (idiopathic) cough should only be considered after a thorough diagnostic and treatment approach for the most common causes of cough has been completed and uncommon causes have been adequately evaluated. Unless this is done, it is likely that many patients with a definable cause of cough will be misdiagnosed as having “unexplained cough.”
Conclusion: The diagnosis of unexplained cough is probably made too often based on an inadequate diagnostic workup or treatment course to determine the specific cause of cough. Nevertheless, there may be a group of patients in whom none of the usual explanations for cough may be present. For this group, the committee unanimously recommends using the diagnostic term unexplained cough, rather than idiopathic cough.

Key words: idiopathic cough; lymphocytic bronchitis; mast cells; unexplained cough

In preparing this section, we searched MEDLINE (through May 2004) for studies published in the English language since 1980 on human subjects using the medical subject heading terms “cough,” “unexplained cough,” and “idiopathic cough.” We selected case series and prospective descriptive clinical trials. We also obtained any references from these studies that were pertinent to the topic.

The conventional definition of a disease or condition being unexplained, previously referred to as idiopathic, is usually that no etiologic explanation can be found after an appropriate and complete diagnostic evaluation. The most difficult aspect of this definition is to define what is, in fact, an “appropriate” or “complete” evaluation. There is a considerable amount of variation among published studies as to the percentage of patients seen with chronic cough in whom no diagnosis can be made. The percentages range from zero in a number of studies1–3 to as high as 33% in one study by Puolijoki and Lahdensuo.4 Based on the information described in the latter article, however, in the majority of the cases labeled as unexplained, a likely diagnosis was actually present.

Common explanations for the inability to accurately diagnose or effectively treat persistent cough in a patient are as follows: failure to empirically treat for upper airway cough syndrome, previously referred to as postnasal drip syndrome, because of the absence of any findings that suggest upper airway cough syndrome; failure to obtain sinus imaging to look for occult sinusitis; lack of performance of bronchoprovocation challenge or an adequate empiric trial for cough-variant asthma; and failure to fully evaluate or aggressively treat patients with gastroesophageal reflux disease, especially when the typical GI symptoms of gastroesophageal reflux disease are lacking. Failure to recognize uncommon or rare causes of cough can also lead to the incorrect diagnosis of unexplained cough. Occult heart failure, interstitial lung disease, neuromuscular disorders, subtle bronchiectasis, suppurative airway disease other than bronchiectasis, thyroiditis, and isolated endobronchial abnormalities are examples of disorders that may be missed.

Therefore, until a thorough diagnostic and treatment approach for the most common causes of cough have been completed and uncommon causes are adequately evaluated, it is likely that many patients will be misdi-
diagnosed as having unexplained cough. In addition, making the distinction between psychogenic or habit cough and unexplained cough can be very challenging. Nevertheless, there may be a group of patients in whom none of the usual explanations for cough may be present and the term unexplained may be appropriate. A limited number of studies have been undertaken that have tried to shed light on this difficult group of patients, but it is important to acknowledge that considerably more work is required to fully understand the etiology and pathogenesis of unexplained cough. A recent case-control study\(^7\) showed that patients with unexplained chronic cough are predominantly female (77%) and are eight times more likely to have an organ-specific autoimmune disease, particularly hypothyroidism. Unexplained cough is associated with airway inflammation. The levels of several tussive mediators, including cysteinyl-leukotrienes, histamine, prostaglandins D\(_2\) and E\(_2\), have been shown to be elevated in induced sputum in patients with unexplained chronic cough compared to healthy control subjects\(^6\). Interestingly, the induced sputum concentration of histamine was increased compared to nonasthmatic chronic coughers, suggesting that this mediator may be particularly important in the genesis of cough in this group.\(^6\) This view is consistent with an earlier bronchoscopy study\(^7\) that reported increased mast cell numbers in BAL fluid. In one study\(^8\) of 19 patients labeled as having unexplained cough after a fairly exhaustive evaluation, evidence for a lymphocytic inflammation was found on bronchoscopy with BAL, but in contrast there was no increase in the lymphocyte numbers in the bronchial wall. In two smaller studies, one reported\(^7\) no bronchoalveolar lymphocytosis, and another\(^9\) found lymphocytic bronchitis in bronchial mucosal biopsy specimens. Therefore, the association between lymphocytic inflammation and unexplained cough is uncertain. These apparent discrepancies probably reflect the diversity of conditions that result in unexplained cough. It is important to remember that it is unknown whether unexplained cough represents a single entity or, as would seem more likely, that it includes many conditions that hitherto have been unknown causes of chronic cough. It is for this reason that the committee prefers using the term unexplained cough rather than idiopathic cough.

The possibility has also been raised that some individuals can simply have a heightened cough reflex in the absence of any discernable disease process. This has been demonstrated on capsaicin cough challenge studies in presumably healthy subjects.\(^10\)

In summary, while truly unexplained cough may exist, it is incumbent on the clinician to make sure that the patient has received a thorough but unsuccessful evaluation (including both appropriate diagnostic and empiric treatment trials, as described in the preceding sections) before applying the term unexplained to the patient’s cough.

### Summary of Recommendation

1. The diagnosis of unexplained (idiopathic) cough is a diagnosis of exclusion. It should not be made until a thorough diagnostic evaluation is performed, specific and appropriate treatment (according to the management protocols that have performed the best in the literature) has been tried and has failed, and uncommon causes have been ruled out. Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

### References