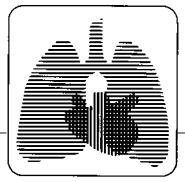

reviews

Chronic Idiopathic Cough*

A Discrete Clinical Entity?

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Study objectives: **Despite the success of specialist cough clinics, there is increasing recognition of a subgroup of chronic coughers in whom a diagnosis cannot be made even after thorough, systematic investigation. We call this condition *chronic idiopathic cough* (CIC). The aim of this study is to compare the clinical characteristics of CIC patients with those of coughers in whom a diagnosis has been established (non-CIC) to see if there is a recognizable clinical pattern that distinguishes CIC from non-CIC.**

Design: **Retrospective analysis of the medical records of chronic cough patients.**

Setting: **The Royal Brompton Hospital Chronic Cough Clinic, London.**

Patients: **One hundred patients with chronic cough referred to the Royal Brompton Hospital Cough Clinic between October 2000 and February 2004.**

Results: **Seventy-one percent of all patients were female. Median age was 57 years (range, 19 to 81 years), with a median duration of symptoms of 48 months (range, 2 to 384 months). The primary diagnoses were CIC (42%), postnasal drip syndromes (22%), gastroesophageal reflux disease (16%), asthma (7%), and others (13%). In CIC patients, the median age at referral, age at onset of cough, and proportion of females did not differ significantly from non-CIC patients. CIC patients had a longer median duration of cough (72 months vs 24 months, $p = 0.002$), were more likely to report an upper respiratory tract infection (URTI) as the initial trigger of their cough (48% vs 24%, $p = 0.0014$), and had a significantly lower cough threshold in response to capsaicin (log concentration of capsaicin required to induce five or more coughs, − 0.009 vs 0.592, $p = 0.032$) than non-CIC patients.**

Conclusions: **Patients with CIC commonly describe a URTI that initiates their cough, which then lasts for many years, and they demonstrate an exquisitely sensitive cough reflex. We believe that CIC may be a distinct clinical entity with an as-yet unidentified underlying pathology.**

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Key words: chronic cough; etiology; idiopathic cough

Abbreviations: C5 = concentration of capsaicin required to induce five coughs; CIC = chronic idiopathic cough; GERD = gastroesophageal reflux disease; URTI = upper respiratory tract infection

Chronic cough is a common yet highly troublesome complaint that is frequently referred to respiratory specialists. A cough is arbitrarily defined as being chronic when it has lasted for > 8 weeks, whereas acute coughing tends to last < 3 weeks. Coughs lasting from 3 to 8 weeks are sometimes referred to as *subacute*.[1] Chronic cough has traditionally been seen as a symptom, the cause of which is often difficult to diagnose and treat. However, with the introduction of specialist cough centers utilizing systematic protocols for investigation and treatment, the underlying diagnoses have been identified in anywhere from 80 to 100% of cases with equally impressive treatment outcomes.[2–8] In all of these centers, the three most common causes of cough have been asthma, gastroesophageal reflux disease (GERD), and postnasal drip syndromes.[9] Our expe-

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rience at The Royal Brompton Hospital Cough Clinic in London has been rather different. The majority (73%) of patients referred to The Royal Brompton Cough Clinic have already been seen and investigated by a respiratory specialist. We are therefore faced with a highly selected population of chronic cough patients whose diagnoses have already eluded specialist investigation. With such extensive exposure to "idiopathic" coughers, we are in the unique position of being able to characterize the syndrome of chronic idiopathic cough (CIC).

Materials and Methods

The medical records of all patients referred to The Royal Brompton Cough Clinic between October 2000 and February 2004 were collected and reviewed. All patients had a cough of at least 8 weeks' duration. Referrals were made by primary care physicians, respiratory specialists, and other hospital specialists. The following information was collected from the medical records: name; date of birth; sex; source of referral; previous investigation by a respiratory specialist; age at onset of cough; duration of symptoms; preceding upper respiratory tract infection (URTI); smoking habits; results of capsaicin challenges (concentration of capsaicin required to induce five coughs [C5]), histamine challenges, and 24-h esophageal pH monitoring; primary, secondary and tertiary diagnoses; and response to treatment.

Investigation and treatment of these patients were based on protocols previously described by Irwin et al.[10] Those patients for whom systematic investigation did not yield a specific diagnosis and in whom trials of specific therapy did not improve their symptoms were given a diagnosis of CIC. The specific treatments that were administered and the minimum duration of treatment given before a diagnosis of CIC was made were as follows: Suspected postnasal drip syndromes were treated with a combination of sedating antihistamine (chlorpheniramine or brompheniramine) and a decongestant (pseudoephedrine) followed by a nasal steroid. Treatment duration was a minimum of 2 months. Suspected GERD was treated with high doses of proton-pump inhibitors followed by the addition of alginates and finally the addition of a prokinetic agent (metoclopramide). Treatment duration was a minimum of 6 months. Suspected asthma was treated in the first instance with a regular inhaled steroid along with a short-acting β_2-agonist as required. If this proved inadequate, treatment was stepped up according to the British Thoracic Society guideline on the treatment of asthma.[11]

The clinical features of patients with CIC were compared with those of patients with other identifiable causes of cough to see if there were any characteristics of CIC patients that distinguished them from other coughers. Statistical analysis of quantitative data (age at referral, age at onset of cough, duration of cough, log C5) was performed using the Mann-Whitney *U* test. Dichotomous data (gender, previous URTI) were analyzed with the χ^2 test. All analyses were performed using statistical software (GraphPad Prism; GraphPad Software; San Diego, CA).

Results

Information was gathered from a total of 100 consecutive new patient referrals between October 2000 and February 2004. Seventy-three of these had been previously seen and investigated for their cough by a respiratory specialist. Seventy-one were female. The median age of the patients at referral was 57 years (range, 19 to 81 years). The median age at the onset of cough was 48.5 years (range, 19 to 76 years). The median duration of symptoms was 48 months (range, 2 to 384 months). Only 3 patients were current smokers, and 45 were ex-smokers, with a mean number of pack-years of 19.3.

A cause for the cough was identified in 58 patients. Fifty of these patients responded successfully to treatment. The other eight patients showed some response to treatment, but the cough still persisted. A cause was not found in 42 patients. These patients were therefore given a diagnosis of CIC. This group consisted of 25 patients in whom all investigation findings were negative and 17 patients in whom investigations suggested a potential cause but specific treatment yielded no sustained benefit. The frequencies of all the primary causes are summarized in Tables 1, 2.

The characteristics of the 42 patients with CIC were compared with those of 58 patients in whom another diagnosis had been made. For the purposes of this analysis, this latter group was described as *non-CIC*. These results are summarized in Table 3 and Figures 1–3. The CIC patients had a median age of 57 years (range, 32 to 81 years). The median age of onset of cough in this group was 46.5 years (range, 27 to 71 years), and 76% were female. The respective values for the non-CIC patients were 58 years (range, 19 to 78 years), 49.5 years (range, 19 to 76 years), and 69%. None of these characteristics were significantly different between the two groups. The median duration of cough in the CIC was group was 72 months (range, 8 to 324 months) compared with 24 months (range, 2 to 384 months) in the non-CIC group ($p = 0.002$). Twenty CIC patients (48%) described the onset of their cough as being triggered by a URTI, compared with 14 patients in the non-CIC group (24%), a difference that was statistically significant ($p = 0.014$). Capsaicin challenge results were available from 25 CIC patients and 20

Table 1—*Primary Diagnoses of Patients With Chronic Cough*

Primary Diagnosis	Patients, No.
CIC	42
Postnasal drip syndromes	22
GERD	16
Other (see Table 2)	13
Asthma	7 (3 cough-variant, 4 classical)
Total	100