



EDITORIAL

Chronic cough: a rational approach to investigation and management

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Chronic cough is a common problem: community surveys suggest a prevalence of recurrent cough of up to 40% and persistent cough of up to 10% [1–3]. Approximately 10% of new patients seen in respiratory clinics are referred with an isolated chronic cough [4]. Most patients referred for a specialist opinion are nonsmokers with normal findings on basic screening investigations, such as chest radiograph, serial peak expiratory flow measurements and spirometry. Females account for 60–70%, and many report a long-standing cough, which started at around the time of the menopause [5]. The current evaluation of chronic cough is based on the “anatomic, diagnostic” protocol originally described by IRWIN *et al.* [6] >20 yrs ago. This investigation protocol is based on the view that most cases of nonasthmatic chronic cough are caused by rhinosinusitis and/or gastro-oesophageal reflux [6, 7]. The investigation protocol remains largely based on expert opinion, and there is a lack of evidence from randomised, double-blind, placebo-controlled trials supporting central tenants of the anatomic, diagnostic protocol [8, 9]. Nevertheless, there are multiple reports of the successful management of cohorts of patients with chronic cough using variants of the anatomic, diagnostic approach to investigation, and the protocol has largely stood the test of time [10]. Despite this, many clinicians view chronic cough as a difficult clinical problem [11]. Amongst the most significant problems is the difficulty in knowing how far to take investigations in patients who commonly report a long-standing cough, which, although distressing, is not obviously progressive.

The anatomic, diagnostic approach to the investigation of chronic cough has spawned a number of variants varying in their reliance on investigations. These approaches to investigation range from a “test and treat” strategy [12] to empirical treatment trials based on a best guess of the underlying cause of the cough [13]. The former approach often leads to an exhaustive and expensive number of investigations, which, in any one patient, could include: spirometry; peak expiratory flow monitoring; a methacholine inhalation test; induced sputum analysis; endoscopic examination of the upper and lower airways and upper gastrointestinal tract; computerised tomography (CT) of the thorax and sinuses; and oesophageal manometry and pH monitoring. Abnormalities of some of these tests are common in patients with airway disease of any kind [13–16]; other tests, such as bronchoscopy and chest CT

scanning, have a very low yield in the absence of suggestive symptoms or chest radiographic changes [12, 13, 17]. Furthermore, with the exception of sputum eosinophilia and a positive response to corticosteroid treatment [4, 18], there is limited evidence that abnormalities detected by these investigations are predictive of the success of a treatment [9, 19].

Recognising the limitations of the test and treat approach to investigation of chronic cough, KASTELIK *et al.* [13] have reported a probability-based algorithm for the investigation and management of chronic cough in this issue of the *European Respiratory Journal*. The investigation algorithm is similar to that recently recommended by the ERS Task Force on the diagnosis and management of chronic cough [20], and the results go some way towards validating this approach. Important elements of the algorithm include a careful clinical assessment, and targeted investigations and treatment trials based on clinical suspicion. The results were impressive: 93% of patients reported substantial improvement or complete resolution of their cough; 26% were managed without recourse to special investigation; and there was a strong suspicion that treatment success was achieved more rapidly, and at a lower cost, than it would have been with other cough investigation algorithms.

Another notable feature of the study by KASTELIK *et al.* [13] was that the presence of regular sputum production and chest radiograph abnormalities were both predictive of an intrapulmonary pathology. Bronchiectasis, which was largely diagnosed after a chest CT scan, was a common diagnosis. Earlier case series have not reported such a high incidence of bronchiectasis [6, 7], perhaps because high-resolution thoracic CT scanning was not an established part of the investigation algorithm. The series reported by KASTELIK *et al.* [13] also differs from earlier studies in that only 52% of patients were thought to have what had hitherto been thought to be the most common causes of isolated chronic cough: asthma, rhinitis and gastro-oesophageal reflux. Other recent case series have come to a similar conclusion [4, 19]. One potential explanation is the overdiagnosis of rhinitis in earlier studies, perhaps because a response to nonselective antihistamines was wrongly assumed to reflect a specific effect on rhinitis-associated cough when, in fact, it was due to the broad antitussive effect of these agents [21, 22]. The difference could also reflect different referral practices. Many series have not included patients with chest radiograph abnormalities, and the prevalence of cough-variant asthma, eosinophilic bronchitis, rhinitis-associated cough and gastro-oesophageal-associated cough is likely to depend on the extent to which treatment trials are instigated before referral.

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Whatever the explanation, the clear implication of these studies is that there is now more to isolated chronic cough than asthma, rhinitis and gastro-oesophageal reflux.

The prospect for identifying a treatable cause of chronic cough was poor in patients who had no symptoms suggesting a pulmonary or extrapulmonary cause for their cough, and had normal investigations, with only a third reporting improvement in response to empirical treatment trials. There is increasing recognition amongst clinicians with an interest in cough that an important minority of patients have no obvious cause for their cough [4, 19, 23, 24]. Recent research has identified some potential explanations for otherwise unexplained chronic cough. A case control study has highlighted an association with organ-specific autoimmune disease, particularly thyroid disease [23], and there is evidence of a low-grade lymphocytic airway and alveolar inflammation [5, 24], with an abnormal release of protussive mediators in the airway [25], in some patients with unexplained chronic cough. Familial chronic cough has been described in a family with hereditary sensory neuropathy type 1 [26], and cough has also been linked to Holmes-Adie syndrome with autonomic dysfunction [27], suggesting a wider association with neurological diseases. Chronic enlargement of the tonsils [28] and external or middle ear disease [20] are other potential causes of otherwise unexplained cough; they are important conditions to consider, since the cough is treatable.

The many clinicians who find isolated chronic cough difficult will view the investigation algorithm proposed by KASTELIK *et al.* [13] as a rational and feasible approach to the investigation of a common clinical problem. One result of its widespread adoption might be an increase in the proportion of patients with unexplained chronic cough seen in clinics that provide a specialist cough service. Clinicians providing such a service will need to be aware of less common causes; they may find that they need to develop a more intensive approach to assessment, which incorporates objective markers of cough severity to validate the presence of cough and assess its response to treatment.

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