From the authors:

We thank R.D. Turner and G.H. Bothamley for their supportive comments concerning our task force report on chronic cough [1]. There is much to agree with in their remarks. But perhaps we would differ with respect to their emphasis and reliance on clinical measurement as the cornerstone of diagnosis and management. Understanding a patient's illness requires a careful synthesis of history, examination, and finally, specific investigations. Dependence on a single strand or even several strands decreases the physician's perception of the true nature of the illness.

The analogy of cough hypersensitivity syndrome with chronic obstructive pulmonary disease (COPD) was deliberately chosen. COPD is an invented and artificial paradigm, which nonetheless is useful in conveying information. No one thinks COPD is a single disease. R.D. Turner and G.H. Bothamley would have us believe that because a physiological measurement (forced expiratory volume in 1 s (FEV_1)) is useful in assessing the patient with airflow obstruction, it defines the illness. All experienced clinicians will have seen patients with gross emphysema but with a well preserved FEV_1, who do not fit into their COPD box. Similarly, chronic pain is now widely considered a disease in its own right (with its own International Classification of Diseases code). In this syndrome a fair degree of progress has been made in our understanding despite the lack of a specific tool to "measure" clinical pain.

In chronic cough great efforts have been made, many by the authors of the task force report, to enumerate the dreadful suffering of patients with this disorder. Three basic modalities have been explored. First, cough challenge which was initially used in 1954 and although refined has not entered routine clinical practice since it does not differentiate health from disease with sufficient discrimination (an optimist would say we have yet to find the right challenge). However, challenges are clearly of use in phenotyping patients [2], assessing tussive mechanisms and clarifying target engagement for therapies directed at specific channels. Secondly, various subjective measures for assessing quality of life and cough-related symptoms have been developed. Finally, most progress has been made in the area of cough counting, where with modern technology reproducible measures of the acoustic signature of cough can now be made over prolonged periods. However, none of these measures express the whole syndrome of chronic cough, but rather describe the different facets as in a three circle Venn diagram [3]. A patient with double incontinence through coughing or life-threatening cough syncope may have an unbearable quality of life and yet only have occasional paroxysms of coughing. These three metrics, even if perfected, will only give an incomplete portrait of the complex clinical picture.

Our correspondents are correct in suggesting that there is much future work to be carried out on cough hypersensitivity syndrome. However, the accusation that little or no progress has been made is surely incorrect. The developments enumerated above have allowed clinical trials to be undertaken with rigorously defined end-points, which are at last showing promise of therapeutic success [4–6]. The purpose of the task force report was not to chronicle these developments. It was rather to highlight the value of seeing cough as an overarching clinical syndrome due to an afferent neuronal hypersensitivity, a view that was endorsed by the overwhelming majority of key opinion leaders surveyed. Just as COPD has helped us to understand and promulgate the management of patients with smoking-related airflow obstruction, cough hypersensitivity syndrome can aid the understanding of patients with chronic cough. It is not merely a symptom.

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Cough hypersensitivity syndrome can aid the understanding of patients with chronic cough. It is not merely a symptom http://ow.ly/JXCaN

Alyn H. Morice[1], Eva Millqvist[2], Maria G. Belvisi[3], Kristina Bieksiene[4], Surinder S. Birring[5], Kian Fan Chung[6], Roberto W. Dal Negro[7], Peter Dicpinigaitis[8], Ahmad Kantar[9], Lorcan P. McGarvey[10], Adalberto Pacheco[11], Raimundas Sakalauskas[4] and Jaclyn A. Smith[12]

[1]Centre for Cardiovascular and Metabolic Research, Respiratory Medicine, Hull York Medical School, University of Hull, Cottingham, UK. [2]Dept of Internal Medicine/Respiratory Medicine and Allergology, University of Gothenburg, Gothenburg, Sweden. [3]Respiratory Pharmacology Group, Pharmacology and Toxicology Section, National Heart and Lung Institute, Imperial College London, London, UK. [4]Dept of Pulmonology and Immunology, Lithuanian University of Health Science, Kaunas, Lithuania. [5]Division of Asthma, Allergy and Lung Biology, King's College London, London, UK. [6]National Heart and Lung Institute, Imperial College London and Biomedical Research Unit, Royal Brompton and Harefield NHS Trust, London, UK. [7]Centro Nazionale Studi di Farmacoeconomia e Farmacoepidemiologua Respiratoria CESFAR, Verona, Italy. [8]Einstein Division/Montefiore Medical Center, Albert Einstein College of Medicine, New York, NY, USA. [9]Paediatric Cough and Asthma Centre, Istituti Ospedalieri Bergamaschi, Bergamo, Italy. [10]Centre for Infection and Immunity, Queen's University Belfast, Belfast, UK. [11]Chronic Cough Unit, Pneumology Service, Hospital Ramón y Cajal, Madrid, Spain. [12]Centre for Respiratory and Allergy, University of Manchester, University Hospital of South Manchester, Manchester, UK.

Correspondence: Alyn H. Morice, Centre for Cardiovascular and Metabolic Research, Respiratory Medicine, Hull York Medical School, University of Hull, Castle Hill Hospital, Castle Road, Cottingham, East Yorkshire, HU16 5JQ, UK.
E-mail-a.h.morice@hull.ac.uk

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Screening for latent tuberculosis before tumour necrosis factor antagonist therapy

To the Editor:

We read with great interest the recent letter by Woodfield *et al.* [1]. The authors report a retrospective study evaluating the use of either an interferon-γ release assay (IGRA) result or a chest radiograph, alone, as a screening approach for identifying patients with latent tuberculosis (TB) infection (LTBI) before initiating tumour necrosis factor (TNF)-α antagonist therapy. In this study, 353 IGRA-negative patients were commenced on TNF-α antagonists for a variety of inflammatory conditions without further LTBI assessment; one patient subsequently developed active TB.

This approach differs from our practice, we currently advocate a "triple testing" approach in all patients referred for LTBI screening with a combination of risk stratification according to the British Thoracic Society (BTS) guidelines [2], tuberculin skin test (TST) and IGRA (T-Spot.*TB*: Oxford Immunotec, Oxford, UK) to aim for maximum sensitivity. We have previously published an evaluation of this approach in 137 patients receiving immunosuppression and found that 111 (81.0%) were IGRA negative [3]. Of these, a total of 41 patients had either TST positive and/or were classified as high risk according to the BTS algorithm [3]. Therefore, use of the "IGRA alone" screening method, as advocated by Woodfield *et al.* [1], would have resulted in a sizeable reduction (62%) in the total number of patients receiving chemoprophylaxis in our cohort.

A significant advantage of IGRAs is an improved specificity, but a reduced sensitivity in the context of immunosuppression is well recognised, particularly in those with HIV infection [4]. There are also descriptions of patients who have developed active TB despite a negative IGRA [5]. In addition, discrepancies have been illustrated between the two commercially available IGRAs [6].

Studies have shown that even in patients with prior bacillus Calmette–Guérin vaccine (BCG), a TST may add a further yield of those with possible LTBI [7]. Importantly, treatment on the basis of a positive TST and/or chest radiograph reduced the risk of TB reactivation in a high-risk population by 74%, with low rates of isoniazid-induced hepatotoxicity [8].

In the data, detailed by Woodfield *et al.* [1], a further 41 patients in the IGRA-negative group, with available demographic data, could have been offered chemoprophylaxis on the basis of risk stratification. The authors note this would be associated with additional resource costs. Use of the IGRA-alone screening approach in their cohort led to one patient developing active TB. The authors do not disclose the ethnicity of this case or elaborate on prior immunosuppressant therapy used, but do comment that the patient would have otherwise been treated based on risk stratification.