Chronic cough: symptom, sign or disease?

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Heritability can be added to the characteristics of chronic cough, making it a disease in its own right https://bit.ly/3ykD6gB

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The *Oxford English Dictionary* defines a symptom as "A (bodily or mental) phenomenon, circumstance, or change of condition arising from and accompanying a disease or affection, and constituting an indication or evidence of it; a characteristic sign of some particular disease." However, over the years, clinicians have differentiated symptoms from signs; so the definition continues "a subjective indication, perceptible to the patient, as opposed to an objective one or sign". So, is chronic cough a symptom or a sign?

Until recently we had to rely on the patient's recollection of the symptom of chronic cough but with the advent of electronic cough recorders, initially of short duration but now increasingly with continuous 24/7 cough monitoring [1, 2], we have not only patient-reported outcomes (PROs) (symptoms) but also objective measurements (signs). Thus, chronic cough has become both a symptom and a sign. Unfortunately, there is a relatively poor correlation between short-term cough counting and PROs due to the day-to-day variability in coughing, which may amount to 39% (unpublished data). For reliable data on the patient's lived experience, for the present, we should put greater reliance on what the patient tells us.

The real question from the definition above is what is the accompanying disease or affection? In the 1980s, the triad of asthma, postnasal drip and gastro-oesophageal reflux disease were popularised as the accompanying diseases [3]. However, the majority of patients either did not fit into these diagnostic boxes (unexplained chronic cough) or were refractory to standard medical therapy (refractory chronic cough). At present, there is a myriad of different labels attached to these patients who also suffer from accompanying symptoms such as throat clearing, dysphonia and exquisite sensitivity to external triggers. A paradigm shift was proposed in the European Respiratory Society (ERS) chronic cough guidelines [4], which recognised that chronic cough itself constituted a disease with different phenotypes. The ERS NEUROCOUGH clinical research collaboration [5] is working towards a redefinition of chronic cough into primary and secondary, thus simplifying the present chaotic nomenclature.

In the clinic, the key to diagnosis is a careful clinical history. One part of the history is that of the ailments suffered by relatives. Because chronic cough is poorly recognised as a disease, often, a family history of asthma or COPD is reported. The follow-up question should be, yes but do they have a bad cough? In this issue of *ERJ Open Research*, Emilsson *et al.* [6] explore the heritability of cough using data from the RHINESSA Generation Study, which asked detailed questions of 7155 parents and 8176 of their offspring. Subjects from northern Europe, Spain and Australia were studied over a decade from the turn of the century. After correcting for confounding factors, of parents who reported a dry chronic cough, 7% of their offspring were similarly affected. For productive cough, it was even higher at 14%. There was no statistical crossover between the groups. The authors conclude that chronic cough, be it productive or nonproductive, is a heritable trait independent of a diagnosis of asthma.

What makes a disease? A unique clinical profile, unique demographics (predominantly middle-aged women) and, to that we can now add, heritability. More will be revealed in future with the recent reports of

the high prevalence of mutation in the *RFC1* gene, which causes the neurological condition CANVAS (cerebellar ataxia, neuropathy and vestibular areflexia syndrome) [7], in patients attending cough clinics. There is much more to learn about chronic cough but we now know it is a symptom, a sign and a disease in its own right.

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