# Not all wheeze is asthma: time for patients to *exercise* their rights

J H Hull

It is now over a century since Sir William Osler first highlighted the fact that not all breathlessness and wheeze is caused by asthma; with a description that in some, … 'the laryngeal muscle can spasm during periods of stress' and as such act to mimic bronchoconstriction.[1]

Yet despite 100 years of medical progress, when a young individual presents with exertional breathlessness, all too often he or she will get promptly labelled as asthmatic.[2 3] Indeed, we know from studies conducted in both the UK[3] and USA,[4] that when faced with this clinical presentation, primary care physicians have poor access to the most accurate diagnostic tools and a trial of inhaled asthma therapy is often, therefore, employed with 'diagnostic' intent. This is despite the countless number of studies indicating that clinical assessment in this capacity is at best imprecise and at worst no better than a coin toss.[5–7] In other words, in young individuals objective testing is required to determine the cause of their exertional breathlessness.

But work, gathering pace over recent years, is now acting to shine a light on the importance of diagnostic precision in this area.[2 8] It is on this basis we should welcome the study by Johansson *et al*[9] with the aim of evaluating the prevalence of the differential diagnoses for exertional breathlessness in adolescents.

A key condition addressed in this study is exercise-induced laryngeal obstruction (EILO); a phenomenon in which the larynx can transiently narrow *during* intense exercise, typically secondary to an antero-medial 'in-folding' of the supraglottic or arytenoid structures.[2 8] Many will already be familiar with this condition, which, although appears under different guises (eg, exercise-induced vocal cord dysfunction) and has suffered at the hands of a befuddled historical approach to nomenclature,[10] is gaining widespread recognition as a key differential diagnosis for breathlessness in the young. The key mechanism(s) underlying the development of EILO remain to be determined; however, undoubtedly the forces and pressure changes that are manifest across the larynx during intense exercise hyperpnoea play a key role in promoting in-folding of vulnerable laryngeal structures.

Before turning to the study findings, it is worth scrutinising the test procedures employed. Indeed, while the strengths and weaknesses of the protocol employed for laboratory EIB testing will be familiar to many, fewer will be accustomed with the continuous laryngoscopy during exercise (CLE) test.[11] The latter involves placement of a fibreoptic laryngoscope on specialist headgear, in order to allow continuous recorded visualisation of the larynx, throughout an intense exercise bout. This permits a 'real-time' assessment of laryngeal movement and thus delineates any propensity to inappropriate closure.

The CLE test has rapidly become established as the 'gold-standard' means for diagnosing EILO, principally on the basis that EILO is a *peak* exercise phenomenon and rapidly abates on exercise cessation; that is, there is insufficient time to place a scope in the postexercise period. It has now been used in a variety of sport-specific settings[12] and appears to be well tolerated in very young individuals[8]; yet the lack of a robust 'dynamic' system for scoring laryngeal closure, with proven reproducibility, remains an important shortfall.

Regardless of this, using the CLE test, with a widely used scoring system and standard exercise induced bronchoconstriction (EIB) test methodology, the authors report prevalence estimates for EIB and EILO of 19% and 5%, respectively, in this adolescent northern European population.

The authors acknowledge that these figures are somewhat discordant with prior work in the field. Specifically that the EIB estimate is higher than others,[13] yet the EILO estimate is slightly lower.[14] Methodological differences (ie, diagnostic cut-off value for EIB) undoubtedly play a role in this discrepancy; however, the initial inclusion criteria are likely to be relevant; namely 'have you had an attack of shortness of breath that came *following* strenuous activity at any time, in the last 12 months?' This approach may have preferentially enriched the population, in that EILO occurs *during* high-intensity exercise, while EIB is classically considered a *post–exercise* phenomenon. Moreover, it is with some leap of faith that data, obtained from a relatively small subgroup of the total population sampled, can be back-extrapolated, without due consideration for the potentially confounding influence of several biases inherent to this type of approach, for example, responder and selection bias.

One could perhaps, therefore, argue that the greatest utility from the study comes from focusing on the group with exercise-induced breathlessness who completed comprehensive objective testing (n=83). In this group, just under half had evidence of EIB, while EILO was present in one in ten.

These findings are broadly in line with other studies using similar methodology; most notably the work by Nielsen *et al*,[2] who demonstrated a higher case prevalence of EILO of 35%, although in a slightly older cohort of trained athletic individuals. Moreover, the studies align in highlighting the fact that there is a real and distinct overlap between the presence of EIB and EILO, that is, in the current study half of those with evidence of EILO also had EIB. This is important for clinical practice and is likely to be equally applicable in older and certainly less athletic populations, where it is recognised that 'treatment refractory' exertional symptoms in those with asthma may arise from coexistent EILO.[15]

A further important finding from the study[9] is that, despite robust objective testing, nearly half of those with breathlessness were left without a diagnosis. As the authors point out, this is in keeping with prior studies evaluating exertional dyspnoea in the young[2 13] and may be explained by perceptual amplification, de-conditioning or perhaps unrecognised dysfunctional breathing.[16] The key point, however, is that worryingly, yet in keeping with the prior published work in the field, almost half of this group was prescribed inhaler therapy.

So where does this leave the clinician? Clearly, it is of concern to see an ongoing signal to suggest that young individuals with breathlessness continue to be mislabelled and mistreated. The side effect profile and potential deleterious impact of regular β-2 agonist therapy[17] surely underlines the importance of moving forward from a 'suck it and see' approach. In addition, the timely and accurate recognition of EILO facilitates delivery of targeted treatment, including consideration for surgical intervention.[18]

**Correspondence to** Dr James H Hull, Department of Respiratory Medicine, Royal Brompton Hospital, Fulham Road, London SW3 6HP, UK; j.hull@rbht.nhs.uk

Further work is clearly needed to understand the causes of exertional breathlessness in the young and the place and utility of simple less-invasive means for accurate diagnosis. Indeed, there is an uncanny parallel with the arguments made by advocates in favour of simple objective assessment of airway inflammation;[19] perhaps the key message being that we need to accept that more objective testing is needed to facilitate precision.

In this respect, it is encouraging to see work from the IMPRESS Group for the British Thoracic Society (http://www.impressresp.com) and the National Institute of Health and Care Excellence Asthma diagnosis and monitoring guideline development group (https://www.nice.org.uk/Guidance/InDevelopment/GID-CGWAVE0640); acting to place early and accurate diagnosis at the forefront of UK respiratory practice. After all, surely it is high time that patients with exertional breathlessness *exercise* their right to a correct diagnosis and treatment.

**Competing interests** None.

**Provenance and peer review** Commissioned; internally peer reviewed.

**To cite** Hull JH. *Thorax* 2015;**70**:7–8.

Published Online First 14 November 2014

▶ http://dx.doi.org/10.1136/thoraxjnl-2014-205738

*Thorax* 2015;**70**:7–8.
doi:10.1136/thoraxjnl-2014-206096

## REFERENCES

1 Osler W. Hysteria. In: *The principles and practice of medicine*. New York: Appleton, 1902:1087–1100.
2 Nielsen EW, Hull JH, Backer V. High prevalence of exercise-induced laryngeal obstruction in athletes. *Med Sci Sports Exerc* 2013;45:2030–5.
3 Hull JH, Hull PJ, Parsons JP, *et al*. Approach to the diagnosis and management of suspected exercise-induced bronchoconstriction by primary care physicians. *BMC Pulm Med* 2009;9:29.
4 Parsons JP, O'Brien JM, Lucarelli MR, *et al*. Differences in the evaluation and management of exercise-induced bronchospasm between family physicians and pulmonologists. *J Asthma* 2006;43:379–84.
5 Rundell KW, Im J, Mayers LB, *et al*. Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc* 2001;33:208–13.
6 Parsons JP, Hallstrand TS, Mastronarde JG, *et al*. An official American Thoracic Society clinical practice guideline: exercise-induced bronchoconstriction. *Am J Respir Crit Care Med* 2013;187:1016–27.
7 Pratter MR, Abouzgheib W, Akers S, *et al*. An algorithmic approach to chronic dyspnea. *Respir Med* 2011;105:1014–21.
8 Røksund OD, Maat RC, Heimdal JH, *et al*. Exercise induced dyspnea in the young. Larynx as the bottleneck of the airways. *Respir Med* 2009;103:1911–18.
9 Johansson H, Norlander K, Berglund L, *et al*. Prevalence of exercise-induced bronchoconstriction and exercise-induced laryngeal obstruction in a general adolescent population. *Thorax* 2015;70:57–63.
10 Hull JH, Selby J, Sandhu G. 'You say potato, I say potato'—Time for consensus terminology in exercise laryngeal obstruction. *Otolaryngol Head Neck Surg* (in press).
11 Heimdal JH, Roksund OD, Halvorsen T, *et al*. Continuous laryngoscopy exercise test: a method for visualizing laryngeal dysfunction during exercise. *Laryngoscope* 2006;116:52–7.
12 Panchasara B, Nelson C, Niven R, *et al*. Lesson of the month. Rowing Induced laryngeal obstruction—A novel cause of exertional dyspnoea—characterised by direct laryngoscopy. *Thorax* 2015;70:95–7.
13 Abu-Hasan M, Tannous B, Weinberger M. Exercise-induced dyspnea in children and adolescents: if not asthma then what? *Ann Allergy Asthma Immunol* 2005;94:366–71.
14 Christensen PM, Thomsen SF, Rasmussen N, *et al*. Exercise-induced laryngeal obstructions: prevalence and symptoms in the general public. *Eur Arch Otorhinolaryngol* 2011;268:1313–19.
15 Hull JH, Backer V, Ward S, *et al*. S93 Laryngeal obstruction during exercise is prevalent in severe asthma. *Thorax* 2013;68(Suppl 3):A50.
16 Thomas M, McKinley RK, Freeman E, *et al*. The prevalence of dysfunctional breathing in adults in the community with and without asthma. *Prim Care Respir J* 2005;14:78–82.
17 Anderson SD, Caillaud C, Brannan JD. Beta2-agonists and exercise-induced asthma. *Clin Rev Allergy Immunol* 2006;31:163–80.
18 Maat RC, Hilland M, Røksund OD, *et al*. Exercise-induced laryngeal obstruction: natural history and effect of surgical treatment. *Eur Arch Otorhinolaryngol* 2011;268:1485–92.
19 Pavord ID, Gibson PG. Inflammometry: the current state of play. *Thorax* 2012;67:191–2.