

# Asthma diagnosis: not always simple or straightforward...

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Asthma is a complex and multi-faceted condition, encompassing a variety of phenotypes and endotypes (1,2), and the diagnosis is often not easy in real-world clinical practice due to the lack of a simple 'gold standard' diagnostic test. Textbooks of medicine describe the 'classical' asthma presentation of a patient with intermittent and variable symptoms of wheeze, breathlessness, cough and chest tightness, typically with a diurnal pattern and often with symptoms following exposure to triggers such as exercise, viral infections or aero-allergens. With such a classical history, particularly in a patient with associated risk factors such as a personal or family history of atopy, asthma is very likely. The demonstration of variable or reversible airflow obstruction through basic spirometry and/or serial peak expiratory flow monitoring, and a clinical response to treatment is confirmatory. However, in some patients the history is less typical, and airflow obstruction may be difficult to demonstrate unless the patient is seen when symptomatic or after exposure to a trigger. In patients with a less classical history and non-confirmatory lung function measurements, it may be necessary to resort to more sophisticated diagnostic tests, such as bronchial provocation tests (for example with methacholine or histamine) or to tests of airways inflammation (3). Although guidelines advise clinicians on the criteria that should be met in order to apply a diagnosis of asthma, in the 'real world' of everyday clinical care, diagnostic algorithms may not always be applied rigorously. As a consequence, asthma may be 'missed' in patients with slightly unusual presentations, or indeed may be misdiagnosed in patients with an alternative explanation for their symptoms. The recognition of the pattern of symptoms is pivotal to raising the possibility of asthma in a clinician's mind, but the symptoms of asthma are variable between patients and in a single patient

over time, and sometimes may be unusual. The classical symptoms of breathlessness, wheeze, chest tightness and cough are not specific to asthma but are shared with other diseases; there are a limited number of ways that pathology in the respiratory tract can manifest. Similar symptoms can be produced by other respiratory illnesses (for example infections, malignancies, fibrosis), but also by diseases of other systems, including cardiovascular disease and indeed by psychological illness, where subjective breathing and chest difficulties are common. This raises the possibility that asthma may be over-diagnosed in some and under-diagnosed in others resulting in a failure to prescribe the inhaled corticosteroids and bronchodilator treatments that are so effective in controlling asthma. There is current concern about both over-diagnosis in asthma, with a worry that some patients with non-specific symptoms are labeled as having asthma and commenced on (ineffective) asthma treatment without objective evidence (4), but also, as in the paper from Shen and colleagues on 'chest tightness variant asthma', of under-diagnosis or delayed diagnosis (5).

Shen *et al.* present a case series of 24 patients with chest tightness as their only presenting symptom, who undoubtedly did have asthma, but in whom it took a long time and a specialist assessment before the diagnosis was finally made. The authors propose that 'chest tightness variant asthma' should be recognised as a distinct phenotype of asthma. Although chest tightness is a recognised symptom of asthma, it is usually accompanied by other symptoms, and in isolation may fail to alert clinicians to asthma as the underlying cause. In this study, the patients underwent a rigorous objective assessment of airways dysfunction and inflammation, as well as assessment of atopic and psychological status and detailed testing to rule out alternative diagnoses that could explain the symptoms.

The asthma diagnosis was securely made, and the authors report that asthma treatment was successful when commenced.

This paper presents us with several important messages. Firstly, some patients who do indeed have asthma will not present with classical symptoms, and clinicians need to be aware of this possibility in those with unusual respiratory or chest symptoms, and test appropriately. Secondly, objective confirmation is necessary to make the diagnosis of asthma, particularly in those with unusual symptom patterns. This is likely to require referral to a specialist service, but is vital in a long-term (often life-long) condition like asthma, to allow effective treatment and information to be given and to prevent inappropriate or ineffective treatment (with associated side-effects and expense) and a failure to identify the true driver of symptoms. Thirdly, we need to be aware that all patients are different, and may present and behave in different ways. The same physiological or pathological impairment can result in very different symptoms and subjective experience in different patients. This is clear from the wide discrepancy between patient-reported outcomes, such as symptoms and quality of life on the one hand, and 'objective' measures of disease severity (such as lung function) on the other (6). Shen's paper reports a high level of psychological co-morbidity in these patients with atypical symptoms. There is increasing current interest in the overlap between the asthma and psychological dysfunction (7), with recognition of the effects of psychological and emotional state on the symptoms that a patient perceives. This is not to say that people are 'making up' or 'imagining' their symptoms or that 'it's all in their head', but to recognize the complexity of the interaction between body and brain. Neuro-imaging studies are increasingly revealing to us the 'neural substrate' of breathlessness and symptom perception in chronic lung disease (8), and reveal that the way a patient experiences a given impairment (e.g., bronchoconstriction or airways inflammation) will depend as much on their psychological as on their physical state. Patients with asthma and co-morbid psychological impairment need very careful assessment and appropriate treatments (which will often consist of both pharmacological and psychological-behavioral support) to achieve best results.

Shen *et al.* are to be commended for reporting this interesting group of patients, but wider investigation in other patient groups, particularly in other countries and other linguistic and ethnic groups is needed to confirm that this group is generalizable enough to be described as a new phenotype. The importance of making a correct diagnosis and of recognizing the diversify of asthma is however a universal truth.

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