Is asthma overdiagnosed?

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Martin Luther likened human reason to a drunken man on horseback, alternately falling off to the left and then to the right.1 The same is true of diagnosing asthma; undoubtedly in the past it was underdiagnosed, but have we gone too far in the opposite direction? The evidence is that we have; for example, in an Australian paper, in which more than 100 children with chronic cough were investigated intensively, including with bronchoscopy (which we do not recommend as a routine diagnostic test!), half were given a diagnosis of asthma prior to investigation; the number actually thought to have asthma had dwindled to 5% at the end of testing.2 Although cough-variant asthma exists, it is overdiagnosed; isolated cough in the community is rarely, if even, due to asthma,3 and even in a tertiary centre, atopic children with cough only infrequently have eosinophilic inflammation.4 Key to diagnosing asthma correctly is being confident in making that most difficult diagnosis of all, normal child; and this requires detailed knowledge of the range of symptoms with upper respiratory infections in the normal child.5

Overdiagnosis of asthma clearly matters. The fiscal cost of asthma medications is not trivial. Inhaled corticosteroids (ICS), when properly used, drastically reduce short-acting β2 agonists via an appropriate device and measure the acute response to a short-acting β2 agonist (SABA).4 There will be none if peak flow is normal, but a simple exercise challenge test could be considered, although with the realisation that such field tests may lack specificity.12 Home peak flow meters are notoriously underused by children in the long term, but a two-week trial should be practical.13 It is totally legitimate for the child to have access to SABAs via an appropriate device during this period, and this provides an opportunity to see if there is fluctuation in peak flow either spontaneously or with SABA. Such testing is known to be specific but lacks sensitivity; the harder the paediatrician tries to demonstrate variable airflow obstruction, and the more this is not seen, the less likely is a diagnosis of asthma.

Thus far physiology has been addressed, but what about airway inflammation? ICS are an excellent treatment for eosinophilic airway inflammation, but if this is not present, should they be prescribed? Where does FeNO fit into the picture, if the measurement is available? First, atopy without asthma causes an elevation of FeNO;14 it is not an asthma diagnostic test. Knowledge of whether the child is atopic is useful; if a school-age child is not atopic, eosinophilic airway inflammation is unlikely, but not impossible. However, FeNO is not needed to diagnose atopy; skin prick tests to common aeroallergens are more than sufficient. Second, in ICS-naive patients with asthma, FeNO correlates with airway eosinophilia.15 Hence if FeNO is available and normal, this means a diagnosis of asthma characterised by eosinophilic airway inflammation, and therefore being ICS-responsive, is unlikely. If FeNO is elevated, then ICS-responsive asthma may be present, but this is not certain.

An alternative surrogate for eosinophilic airway inflammation is peripheral blood eosinophilia.16 Careful interpretation is needed; blood eosinophilia may be driven by extrapulmonary atopic disease such as eczema, but a normal blood eosinophilia is another pointer that airway eosinophilia is unlikely.17

Blind therapeutic trials are another trap for the unwary. We suggest they should only be carried out when objective measurements cannot be made, and then too in a very focused manner. There is no evidence base, but we suggest a trial period of a moderate dose of ICS (eg, 200 μg beclometasone equivalent twice daily) for no more than 6 weeks, at the end of which, irrespective of the clinical state, treatment is stopped. If there has been no response, and (a big if!) if treatment has really been given, the diagnosis of asthma with eosinophilic inflammation can be discarded. If symptoms have disappeared and only if they subsequently reappear
and again respond to ICS should a diagnosis of asthma be made, and ICS treatment titrated to the lowest effective dose. This staged trial avoids the paediatrician mistaking spontaneous improvement for therapeutic benefit.  

A further safeguard is to consider the diagnosis of asthma as dynamic—many children outgrow their symptoms, and many professors frequently get things wrong. No matter who has made the diagnosis, always consider whether it was actually correct in the first place, or whether it is still relevant. Asthma therapy should not be escalated heedlessly if there is no response—for most children, the plateau of the ICS dose-response curve is as low as 100 μg fluticasone twice daily.  

Oliver Cromwell’s advice is still apposite: ‘I beseech you, in the bowels of Christ, think it possible that you may be mistaken’.  

The present proposals by NICE are welcome in principle, but there are still many gaps which we should not tolerate. We need to move the diagnostic process forward in a number of ways. First, we need to bring objective testing into the preschool years; off-line FeNO, multiple breath washouts and even induced sputum can all be performed, and surely should be performed, in non-straightforward airway disease in this age group. Second, we should be more objective about therapeutic trials; they should be placebo-controlled, cross-over, of N of 1 trials, during which neither the paediatrician nor the family know whether the patient is being treated. If we can obtain placebo inhalers for randomised-controlled trials and for Respiratory Nurses to demonstrate inhaler technique, why not for therapeutic trials? Electronic monitoring of adherence and peak flow measurements is surely the 21st century gold standard, and adherence monitoring should move beyond whether the device has been activated to measuring whether someone has actually inhaled adequately from the device. Finally, we need to go beyond umbrella labels for airway diseases such as asthma, and move to phenotyping childhood airway diseases in terms of parameters such as fixed and variable airflow obstructions, presence or otherwise, and nature of, airway inflammation, and whether there is chronic infection. The aim is not to split and phenotype for the sake of it, but to identify treatable characteristics and treat them appropriately.  

But that is another story.

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REFERENCES

1 Martin Luther. Werke 1883;54:111.


8 https://www.replondon.ac.uk/projects/national-review-asthma-deaths

9 http://www.nice.org.uk/guidance/gid-cgw26040/resources/asthma-diagnosis-and-monitoring-draft-nice-guideline2


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