

Transformational thinking about asthma



Although asthma has been recognised for thousands of years, the disorder was widely misunderstood until the 20th century.¹ The first widely accepted disease definition was released only 30 years ago.² Although this definition continues to be cited, most clinicians do not actually measure airway inflammation and hyper-responsiveness when they examine a patient with asthma. Yet most patients, clinicians, and researchers claim to recognise “asthma” when they see it—and surveillance programmes continue to document enormous morbidity and costs worldwide.^{3,4}

The *Lancet* Clinical Commission, *After asthma: redefining airways diseases*, by Ian Pavord and colleagues⁵ provides a vision of “where we are and where we need to go”.⁵ The Commission challenges mainstream thinking about asthma. Most importantly, the Commission shows that the current physiology-based classification system for airways diseases is outdated because it largely ignores the diverse mechanisms that underlie the different types of asthma. Although this idea is slowly gaining acceptance, at least among asthma researchers,⁶ Pavord and colleagues conclude that future advances require improved clarity about the meaning of commonly used terms. Specifically, they recommend that the term “asthma” be used solely as a descriptive label for a collection of symptoms, with no assumptions about pathophysiology. They also recommend that asthma and other airways diseases should be deconstructed into measurable components (eg, using biomarkers) that will help clinicians identify patients who are at increased risk of specific outcomes and who might benefit more from specific treatments (eg, inhaled corticosteroids). These are, of course, central tenets of precision medicine.⁷

How will this new approach be implemented in diverse health-care settings? The Commission highlights the importance of teaching patients and clinicians about the emerging types of asthma and need for increased testing. However, the Commission does not provide these distinct audiences with short, easily understood messages that are accurate and reasonably complete. Such “soundbites” would be useful for any future educational campaigns.

As a “pragmatic solution” to the challenge of using inhaled corticosteroids in a more targeted and efficient

manner, the Commission recommends increased use of an as-required combination of low-dose inhaled corticosteroids and rapid-onset β 2-agonist inhalers as the “default” reliever option. This major change in asthma management seems reasonable, especially among patients with eosinophilic airway inflammation, as does the Commission’s recommendation that the approach “will need to be tested formally in appropriate health-care settings” before widespread implementation. Support for this bold recommendation is based largely on a belief that, on average, more patients will be helped by the new approach than by current practice.^{8,9} Nonetheless this public health approach should be balanced with consideration of more precise, individually tailored treatments.

The Commission next discusses the implications of asthma heterogeneity for our understanding of asthma pathogenesis across the lifecycle. Pavord and colleagues wisely caution against over-reliance on the reductionist approach used by many researchers today, and call for increased emphasis on systems biology approaches that may reveal how multiple mechanisms interact and change over time. The complementary use of these two scientific approaches will accelerate progress in asthma research.

The Commission calls for a greater focus on primary prevention or cure of asthma than on the management of established asthma. Unfortunately, like medication adherence, these tasks are easier said than done. While

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some risk factors (and mechanisms) may contribute to several types of asthma, others will be more (or less) important for specific asthmas. Large observational studies, with markedly improved asthma phenotyping, are needed to develop better asthma risk scores and to provide the foundation for primary prevention and cure.

The Commission proposes zero tolerance for “asthma attacks” and improved treatment of patients with “severe” asthma. Although both goals are commendable, the terminology seems problematic. Most asthma exacerbations develop over several days¹⁰ and, for that reason, differ from a heart or brain attack. In my clinical experience in the USA, many patients receiving emergency asthma treatment will, on direct questioning, deny that they are having an “asthma attack” because they have felt ill for days. Rather than teaching patients to think of their asthma as worsening suddenly, clinicians should probably emphasise the gradual worsening of most exacerbations, which highlights an underutilised opportunity for intervention. Regarding “severe” asthma, this popular term includes a mix of patients with severe persistent asthma and patients with a severe exacerbation (eg, intermittent asthma with one asthma-related hospitalisation). We probably should move away from terminology that encompasses such seemingly different types of asthma.

Lastly, Pavord and colleagues call for better clinical, epidemiological, and basic science research. They recommend improved characterisation of the type(s) of asthma in every future study and that we challenge the assumption that asthmas across the world are the same. Their goal is to “move away from observational studies towards intervention studies.” However, research into the emerging types of asthma, and their development across the lifecycle, will require observational studies—not randomised trials. High-quality observational studies will continue to inform the design and implementation of randomised trials, which tend to be highly focused and resource intensive. Moreover, newer types of observational studies enable causal inferences.¹¹

Thus, both observational and interventional studies are needed for future progress.

Pavord and colleagues have written an extraordinary report that proposes a “revolution in thinking about asthma” and possibly other airways diseases. With a few exceptions, the new model in this *Lancet* Commission does start to make the existing asthma model look obsolete, and this justifies their forceful call for action. This provocative Commission is certain to spark discussions that will provide a mixture of heat and light. I am optimistic, however, that the authors’ transformational thinking will benefit our diverse patients and their different asthmas.

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I have received personal fees for asthma-related consultation from AstraZeneca, GlaxoSmithKline, Novartis, Regeneron, and Teva.

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