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Asthma and Chronic Obstructive Pulmonary Disease: Are They the Same or Are They Distinct Diseases?

To the Editor:

The recent Pro/Con editorial debate between Kraft and Barnes (1–4) on whether asthma and chronic obstructive pulmonary disease (COPD) are the same or distinctly different diseases was very stimulating. The major thrust of both the authors was on clinical, physiologic, and pathologic similarities and differences. If the issue was not resolved, it is perhaps due to the inadequacies in our present state of knowledge. There is enough available literature on these two diseases that can be cited either way and agreeing to disagree is perhaps the best way to conclude the debate.

Some similarities can be expected as the lungs in airway diseases can respond clinically and physiologically in only a limited manner. Recently, we reported that the use of the test of reversibility of airways obstruction for separating the two has limited value (5). The pharmacologic treatment may appear to be superficially similar, but this is because it is largely symptomatic or suppressive. Statistically speaking, the chances of a patient having both diseases are also fairly high. For a 10% prevalence of each, 1% of the population would have both diseases.

However, there are vital differences between the two diseases that were ignored by both the authors. First, the natural histories of asthma and COPD are quite different. Pulmonary artery hypertension leading to right heart failure is extremely common during the later stages in COPD. This course is extremely rare in asthma, so much so that it merits reporting (6). The second difference lies in the ventilatory response during acute exacerbations. Hyperventilation and acute respiratory alkalosis are the rule in acute severe asthma, except in later stages. These findings are uncommon in acute exacerbations of COPD where hypercapneic respiratory failure with acute respiratory acidosis is the rule. Failure of ventilation is also evident in chronic COPD. Type II respiratory failure requiring long-term oxygen therapy is common in terminal stages in COPD, but almost never seen in asthma. These acute and chronic events suggest that patients with COPD may have a blunted ventilatory drive. Unfortunately, very little work has been done in this field in COPD and asthma.

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Beyond the Dutch Hypothesis

To the Editor:

In their recent Pro/Con editorial debate, Kraft and Barnes agree that the Dutch hypothesis considers asthma and chronic obstructive pulmonary disease (COPD) as a single entity whose pathogenesis involves environmental and host factors (1–4). Barnes acknowledges that some patients exhibit features of both asthma and COPD, but states it is likely that they occur concurrently rather than as the continuum posited by the Dutch hypothesis. Concurrence of unrelated diseases should be random, but this is not the case for asthma and COPD. Of 2,926 subjects in a population-based cohort, 7.3% had asthma, 4.3% had asthma and COPD, and 11.1% had COPD (5). Concurrence predicts a prevalence of 0.8% (7.3% $\times$ 11.1%), but the actual prevalence was more than five times higher, and in fact 37% of all patients with asthma had concomitant COPD.

Further evidence undermining the concept of concurrence derives from a 20-yr prospective study finding that *asthma* was the strongest risk factor for subsequent COPD (hazard ratio [HR] =12.5; attributable risk [AR] =18.5%); *tobacco smoking* had an HR of 2.9 for current smoking and an AR of 6.7% for ever-smoking (6). Primary care clinicians who practice long enough report patients with acute bronchitis that morphs into chronic asthma that then develops into severe COPD (7).

Kraft correctly notes that atopy and airway hyperresponsiveness are the two cardinal host characteristics emphasized by the Dutch hypothesis. However, epidemiologic evidence now strongly suggests that atopy plays a minor role in asthma (8). Barnes asserts that the Dutch hypothesis predicts that the susceptibility genes should be the same and that environmental factors determine the difference in clinical presentation. I suggest the opposite possibility, that a common environmental factor is responsible for a large proportion of asthma and COPD, and that disease phenotype (including not having disease) is determined by host genetic factors.

Consider an analogy with a set of known chlamydial disease entities: acute cervicitis, endometritis, salpingitis, and tubal infertility. Taken separately, each of these four entities has a unique clinical presentation and histopathology, yet the same infectious organism causes them all. Not all women with acute cervicitis will develop tubal pathology and infertility; other women with asymptomatic infections will develop infertility. Why? Probably because of different genetic response(s) to infection (9).

As Adlai Stevenson once said when put in a difficult political position, "I agree with everything you said that was correct, and disagree with everything you said that was incorrect." I suggest that we do the same with the Dutch hypothesis, and move to the next level of understanding.

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From the Authors:

With regard to our recent Pro/Con editorial debate (1–4), we agree with Prof. Chhabra that the ventilatory response in chronic obstructive pulmonary disease (COPD) differs from that in severe asthma, but whether these differences are due to a reduction in ventilatory drive in COPD is not conclusive. The causes of hypercapnia in COPD are multifactorial and include increased physiologic dead space due to $\dot{V}/\dot{Q}$ mismatching, higher resistive and elastic load of the respiratory muscles due to dynamic hyperinflation, and reduced gas exchange because of emphysema (5, 6). Although decreased ventilatory drive is not usually associated with asthma, a subset of patients with asthma exhibit a reduced ventilatory drive due to the inability to achieve full neural activation of the diaphragm with voluntary efforts (7).

In response to Dr. Hahn, we disagree about the role of atopy, as many studies have demonstrated a strong relationship between atopy and asthma (8), but this does not mean that other factors, such as infection, are not important. In COPD, bacterial load and serotype contribute to the decline in lung function (9). In asthma, several studies have shown that viral and bacterial infections can influence the presentation, severity, and persistence of asthma (10, 11). We agree that the genetic response to infection is critical and requires further investigation.

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