COPD and lung cancer have come a long way...baby

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COPD and Lung Cancer Have Come a Long Way . . . Baby

A famous tobacco advertisement from the 1970s made the claim that women were biologically superior to men:

We make Virginia Slims especially for women because they are biologically superior to men . . . . Women have two “X” chromosomes in their sex cells while men have only one “X” chromosome and a “Y” chromosome, which some experts consider to be the inferior chromosome . . . . In view of these and other facts, the makers of Virginia Slims feel it highly inappropriate that women continue to use the fat stubby cigarettes designed for mere men. Virginia Slims. Slimmer than the fat cigarettes men smoke . . . . You’ve come a long way, baby. (1)

Duplication of the X chromosome has obvious genetic advantages, but does this translate into resistance to the respiratory health effects of tobacco use, such as chronic obstructive pulmonary disease (COPD) and lung cancer? This duplication results in a variety of hormonal and enzymatic outcomes that, ultimately, make women and men different but also, potentially, confers sex-related differences in susceptibility to disease.

In recent years, COPD has become an “equal opportunity” disease with more women developing COPD and suffering COPD-related morbidity and mortality in high-income countries around the world (2–5). The increasing prevalence of COPD among women in high-income countries is due, in large part, to the historic increase in smoking among women in these populations. In low- and moderate-income countries, COPD prevalence remains lower in women compared with men and the risk factors for disease may also vary, with exposure to indoor air pollutants, poor diet, and poverty being more important than they are in high-income countries (6, 7).

In a similar way, lung cancer has also become a disease affecting an increasing number of women (8). Since the mid 1980s in the United States, more women have died annually of lung cancer than from breast cancer (9). By 1999, 4.6% of deaths among men and 5.1% of deaths among women were from COPD and 5.0% of deaths among women and 7.6% of deaths among men were from lung cancer (9). By 1999, 4.6% of deaths among men and 5.1% of deaths among women were from COPD and 5.0% of deaths among women and 7.6% of deaths among men were from lung cancer (9).

The link between COPD and lung cancer has been well established in several different cohorts, although the reasons for this association remain unclear (10–12). A number of the sex-related differences in susceptibility to COPD and lung cancer in women have been described in the development of COPD and lung cancer and in the metabolism of tobacco smoke constituents. The authors acknowledge

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that this is an area of research with a great deal of uncertainty. Women have a lower risk of cardiovascular mortality during early adulthood (14), compared with men, so one explanation for increased susceptibility might be a cohort effect—that is, the pool of people at risk for developing cardiovascular and respiratory disease changes over time because a larger proportion of men die of cardiovascular disease at a young age. This lower risk of cardiovascular mortality in women is most likely related to hormonal and sex differences that, ironically, may be the exact same factors that the authors point to as increasing the risk of developing COPD and asthma.

Ben Zaken-Cohen and coworkers (13) show that certain cytochrome P450 (CYP) enzymes, CYP1A1, CYP1A2, and CYP3A4 (Table 1) have increased expression in women and suggest that these differences may lead to sex-related differences in susceptibility to tobacco smoke (and presumably other smoke) toxins. Table 1 in their article also shows, however, that we do not know whether the other enzymes in the cytochrome P450 family are up- or down-regulated in women. Does up-regulation (or down-regulation) of these enzymes lead to the development of lung cancer? This is unknown but certainly an area where a great deal more research is needed and welcome.

Does impaired lung function in women lead to a differentially higher risk of lung cancer than that seen in men? Figure 1 in Ben Zaken-Cohen and colleagues’ article (13) demonstrates that when one compares women with men, the loss of lung function is more important as a risk factor for lung cancer in women. Interestingly, though, in the studies from which these data were derived (10, 15), men were significantly more likely to develop lung cancer than women. Thus, an alternative explanation for the pattern seen in Figure 1, is that, among men and women with the best lung function (quintile 5), women are actually less likely to develop lung cancer than men and that this benefit is extinguished when lung function is lost.

While COPD and lung cancer in women have come a long way in the past 35 years, we still have a long way to go to understand how men and women differ in their risk for exposures to tobacco smoke and other factors in the development of these diseases. Ben Zaken-Cohen and colleagues provide some provocative and investigable reasons for sex differences in the development of COPD and lung cancer and the relationship between these two important and lethal diseases (13). Whether women are more or less likely to develop these diseases remains an open question, but developing a better understanding of how sex and hormonal differences influence disease development and progression can hopefully lead to improved interventions and outcomes for our patients.

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References

Can a Deep Breath Blow Away the Fog Surrounding Airway Hyperresponsiveness?

The most consistent diagnostic feature of asthma is the presence of airway hyperresponsiveness (AHR). Therefore, understanding the mechanisms underlying AHR seems essential for the development of interventions to control or cure asthma. Despite enormous research effort, we still do not fully understand why the asthmatic airways respond to much lower concentrations of provoking agents than do normal airways. We do know, however, that the lung volume at which we breathe and the presence of deep inspirations (DI’s) have the capacity to markedly modulate these airway responses and exhibit different effects on individuals with and without asthma. Therefore, it seems reasonable to propose that an understanding of mechanisms underpinning the DI responses may shed light on the nature of AHR itself.

During bronchial challenge, DI causes bronchodilatation in individuals without asthma (1), whereas this effect is less marked or absent in patients with asthma (2). In spontaneous asthma

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