



Education

Éducation

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Lessons in women's health: body image and pulmonary disease

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Women's health refers to a multidisciplinary approach to the screening, diagnosis and management of conditions that have greater or different risks for women than for men or that are more prevalent among women. This approach recognizes that there are both biomedical and psychosocial components to health and that care for women should be based on research that takes into consideration gender differences, includes women as subjects and is designed to answer questions of relevance to women.

The awareness that women's health is much broader than reproductive health has been evolving over the past 10 years.¹ For example, we now recognize that the risk factors, diagnostic tests and therapies for coronary artery disease may be different for women and men,² and we are increasingly aware of the osteoporosis risks related to many therapies. In pulmonary medicine we are only beginning to apply the concepts of women's health, and, not surprisingly, we are finding new and important information about disease etiology, epidemiology and management.

An increasingly recognized determinant of health for women is body image. We are all aware of the increasing incidence of conditions such as anorexia and bulimia. However, body image plays a much broader role in health and, although it is not yet widely recognized, in pulmonary medicine. Smoking and related diseases, pulmonary hypertension secondary to anorexic agents and obstructive sleep apnea are all significant pulmonary conditions in which body image plays a role. These conditions in turn highlight many of the issues and opportunities inherent in developing a women's health focus in pulmonary medicine.

Smoking and related pulmonary diseases

Smoking

As the major preventable cause of lung disease and the most important cause of preventable illness and premature death in Canadians, smoking is a critical public health problem for both men and women.³ For women, however, smoking has very different social and psychological impacts. Initially considered unacceptable for women, smoking became a symbol of freedom and equal opportunity over the course of the 20th century. Women began smoking in significant numbers during World War II, the number of women smokers peaking in the 1960s. Although the prevalence of smoking is now declining among both sexes, the rate of decline has been much slower among women.⁴ This disparity is most alarming among adolescents: the proportion of boys and girls aged 10 to 12 who smoke is the same (4%), but the prevalence of smoking at age 13 and 14 is much higher among girls than boys (15% v. 9%).⁵ Given that most adult smokers began smoking in childhood or adolescence, it is projected that there will be more female than male smokers by the year 2000.⁵

The high prevalence of smoking among women has been attributed to several factors. Girls and young women are currently the primary target of lifestyle advertising, in which the central themes are extreme thinness, fashion and sexualized social encounters. Even as early as the preteen years, girls begin to associate smoking with being thin and socially successful. Young women learn to use smoking to control their weight and to alleviate anxiety and depression. There is increasing evidence that cigarette companies have been reinforcing these associa-



tions in advertising aimed at young women. The substantial revenue derived from cigarette advertising may partly explain the strong correlation between lack of anti-smoking editorial content and the large number of cigarette advertisements in some women's magazines, in which other women's health issues, such as breast cancer, are given ample coverage.⁶

In addition to being more likely than men to begin smoking, women are also less likely to be able to quit.⁷ Although women do not smoke as heavily as men, they report greater physical and emotional dependence on cigarettes. These women have not learned healthy strategies to cope with stress and weight control, and once they reach their 30s and 40s and want to stop smoking, they are much less likely to be able to do so. In order to have an impact on smoking behaviour, physicians and smoking cessation programs must identify and address the motivations and needs of female smokers.⁸

Lung cancer and chronic obstructive pulmonary disease

As might be expected, the increased prevalence of smoking among women has been followed by an increase in smoking-related lung diseases, specifically lung cancer and chronic obstructive pulmonary disease (COPD).

Lung cancer surpassed breast cancer as the number one cause of death from cancer among Canadian women in the early 1990s.³ Between 1950 and 1995 the mortality rate from lung cancer increased by 500% among women in the United States.⁴ Several studies, including a large case-control study in Ontario between 1981 and 1985, have suggested that lung cancer is 2 to 3 times more likely to occur in women smokers than in men smokers.⁹ Although subsequent data conflict as to the magnitude of the effect of gender on the relative risk of smoking-induced lung cancer, it is known that the predominant types of lung cancer are different for women and men.⁴ Adenocarcinoma of the lung is more likely to occur in women, and estrogens may play a causative role. The differences in susceptibility cannot be fully explained by differences in lung size and smoking patterns, and they suggest that fundamental physiologic differences, possibly hormonal, contribute to the development and pathogenesis of lung cancer in women. Data are as yet unclear as to whether the response to cancer treatment differs between men and women.

The increase in the prevalence of lung cancer among women has been mirrored by an increase in the prevalence of COPD. Mortality rates for COPD reflect patterns of smoking initiation 30 to 50 years earlier, and these rates have not declined over the past 20 years. However, a gender analysis of mortality rates has indicated that deaths from COPD may be levelling off among white

men but will continue to increase among women, because smoking among women has not declined to the same extent as it has among men.¹⁰

There is mounting evidence that women may be more susceptible than men to the adverse effects of smoking on lung function. Girls who smoke have a significantly slower growth in forced expiratory volume in the first second (FEV₁) and in mid-expiratory flow rates (FEF₂₅₋₇₅) than girls who do not smoke, a difference not seen in boys who smoke.¹¹ Women smokers experience a greater decline than men in FEV₁ per pack-year (number of packs smoked per day × number of years of smoking). The Lung Health Study¹² reported a significantly higher prevalence of airway hyper-responsiveness in women with mild to moderate COPD than in men with the same stage of disease, in part because of the smaller calibre of women's airways. Increased hyper-responsiveness in COPD is in turn associated with more symptoms and a higher mortality rate. Analysis of long-term home oxygen therapy suggests that women have a better prognosis than men when they start receiving oxygen therapy, regardless of the cause of respiratory failure,¹³ but there is a reluctance among women to begin supplemental oxygen, possibly because they are concerned about their appearance.

Smoking-related pulmonary disease is one of the most rapidly growing areas of preventable disease for women today. Research is increasingly demonstrating gender differences in susceptibility to advertising and initiation of smoking in adolescence, ability to stop smoking, susceptibility to smoking-related diseases, response to treatment and the psychosocial impact of disease. To make an impact on the future burden of respiratory illness, we will require further knowledge in the areas of addiction and body image and the political will to deal with advertising targeted at adolescents.

Primary pulmonary hypertension and anorexic agents

Between 1967 and 1972 a significant increase in the incidence of pulmonary hypertension in Europe was attributed to the appetite depressant aminorex fumarate. Among people taking this drug, the incidence of this condition was estimated at 2 per 1000, and it was 4 times more likely to occur in women than in men. Fifty percent of the women with pulmonary hypertension had been given prescriptions for aminorex despite the fact that they were less than 10% above their ideal body weight! The subsequent mortality rate for the women with hypertension was 50%.

In July 1996 dexfenfluramine, the *d*-isomer of fenfluramine, was approved by the Health Protection Branch of Health Canada as an appetite suppressant for the treat-



ment of obesity, despite reports linking fenfluramine use with pulmonary hypertension. It was believed that this group of drugs was safe because they had a different mechanism of action than aminorex, which is a catechol derivative. Dexfenfluramine acts by increasing serotonin-mediated neurotransmission through serotonin reuptake blockade, enhanced release of endogenous serotonin and activation of serotonin 5-HT₂ receptors. Phentermine, which has been used in combination with fenfluramine as "fen-phen", further increases the effects of serotonin by interfering with its pulmonary clearance. In 1996 more than 18 million prescriptions were written in the US for the fenfluramine-phentermine combination.

In August 1996 an international case-control study indicated that the use of anorexic drugs (mainly derivatives of fenfluramine) was associated with an increased risk of pulmonary hypertension (odds ratio 6.3), and there was a 23-fold increase in the incidence of pulmonary hypertension among those taking the drugs for longer than 3 months.¹⁴ Nevertheless, an editorial published in conjunction with the study findings justified the use of these drugs on the basis that they could theoretically decrease the risks of coexisting diseases associated with morbid obesity.¹⁵ Not until August 1997, when valvular heart disease morphologically similar to that induced by carcinoids and ergotamine was described in more than 30% of women taking the fenfluramine-phentermine combination, was the use of these drugs re-examined.¹⁶ In September 1997 Health Canada issued a public health warning advising consumers of the risks associated with the use of fenfluramine and dexfenfluramine, and the manufacturers agreed to suspend sale of the products in Canada and the US.¹⁷

When the issues of risk-benefit and efficacy-safety are examined, there is little doubt that anorexic drugs have no role in the management of obesity. There is minimal, if any, evidence of efficacy: in one study¹⁸ there was only 10% weight loss in the group taking such drugs (compared with 6% in those receiving placebo) after 48 weeks. Despite the association of morbid obesity with premature death, there is no evidence that short-term weight loss has any beneficial effects on the comorbidities of obesity, such as non-insulin-dependent diabetes mellitus, hypertension and hyperlipidemia. As outlined above, however, there is evidence of a significantly higher risk of pulmonary hypertension and valvular heart disease, particularly in young women, many of whom are only slightly overweight. Monitoring for and diagnosing pulmonary hypertension is difficult at best, and there are only limited treatment options and no cures for this disease, which historically has had a high mortality rate.¹⁹

The use of anorexic drugs is a women's health issue. To date, pulmonary hypertension and valvular heart disease associated with anorexigenics have been described pre-

dominantly in women, which raises important questions about biological and psychosocial risk factors and ethical practice. Do women respond differently to these drugs because of genetic or physiologic factors, or are these drugs being prescribed almost exclusively for women? Was it realistic for the regulatory authorities to believe that these drugs would be used only to treat morbid obesity? Most important, what notion of risk-benefit has allowed women and their physicians to justify the use of potentially lethal drugs to deal with concerns about body image and weight?

Physicians who are approached for appetite suppressants should explain the unacceptable risks involved in using these medications and then work with the individual patient to develop a program that deals realistically with the physiologic and psychosocial issues surrounding weight control for that person.

Obstructive sleep apnea

The lessons of obstructive sleep apnea are somewhat different. They demonstrate how preconceptions about the gender prevalence of a disease can bias physicians' diagnostic suspicions, even in the setting of a major risk factor, such as obesity.

Sleep apnea is associated with significant morbidity and mortality. Recurrent episodes of hypoxemia and sympathetic stress during apneic episodes may result in systemic and pulmonary hypertension, arrhythmias, myocardial ischemia and cardiomyopathy. Disordered sleep produces mental dysfunction and hypersomnolence, which is associated with an increased risk of accidents.

Sleep apnea has traditionally been considered a disease predominantly of men, with a male:female ratio of 8:1 or higher. However, more recent population-based studies^{20,21} have shown that sleep apnea is underdiagnosed in women and that men are affected by the condition only 2 or 3 times as often as women. The prevalence of sleep-disordered breathing is actually about 24% to 26% for men and 9% to 13% for women.²⁰ There is a strong correlation between severe obstructive sleep apnea and excessive weight. Nevertheless, in studies of obese women in eating disorders clinics, 10% to 38% were found to have previously undiagnosed sleep apnea.^{12,22,23}

One possible reason for this gender bias in diagnosis is that the clinical guidelines for evaluating and diagnosing sleep apnea, which were developed almost entirely from clinical observations of and research on men, are not valid for women. However, a recent population study has indicated that women and men report the same symptoms for similar types of sleep apnea.²¹ Women with sleep apnea had no unique symptoms related to fatigue, depression, life satisfaction or perception of health. The sensitivity



and specificity of the classic symptoms — snoring, breathing pauses during sleep and hypersomnolence — were not significantly different, and the positive predictive value of symptoms was similar for men and women.

If clinical indications for sleep apnea evaluation are equally appropriate for women and men, why is there a gender disparity in sleep apnea diagnosis? Why do physicians not screen morbidly obese women for sleep apnea, despite obesity being a well-recognized risk factor? Is it possible that women, particularly obese women, with sleep apnea fail to report their symptoms or to seek medical care? Is there a failure on the part of health care providers to ask about or respond appropriately to women's symptoms because of a preconceived notion about the prevalence of sleep apnea among women? It is critical that primary care physicians and specialists consider the diagnosis of sleep apnea for women who present with any of the classic signs and symptoms of this condition, including obesity, snoring and hypersomnolence, and that these women be referred for appropriate investigation and gender-based management.

Conclusion

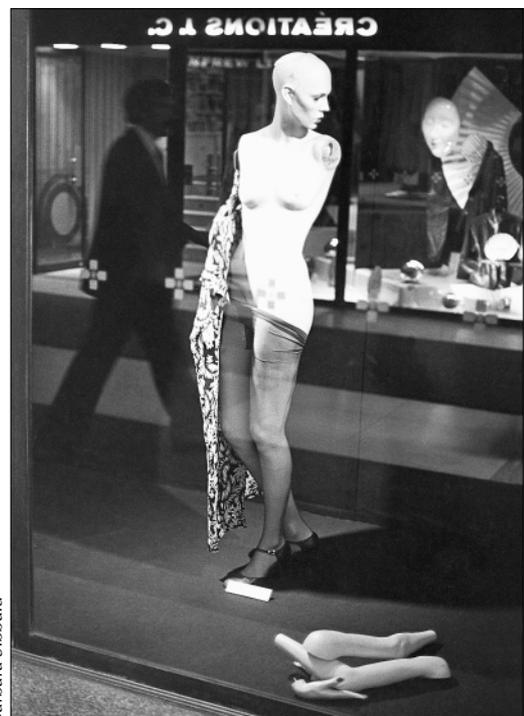
The application of the principles of women's health to pulmonary medicine requires basic, physiologic and epidemiologic research that includes women and explores the impact of gender on disease etiology, pathophysiology and management. In addition, it requires an understanding of and sensitivity to the psychosocial factors that affect the diagnosis, prevalence, impact, management and outcome of disease. Smoking, primary pulmonary hypertension and sleep apnea have been used to illustrate the impact of addressing the biomedical and psychosocial gender issues related to body image. There are issues related to gender and body image in almost every aspect of pulmonary medicine, including asthma, embolic disease, cystic fibrosis, pulmonary fibrosis and transplantation. The questions are limitless, as are the opportunities to have a significant impact on the health of our population.

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