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The weight of obesity on lung health

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Obesity has reached alarming levels with approximately one third of the adult U.S. population now obese and projected to rise to over 50% by the year 2030 [1,2]. It is startling to realize that only a minority of the U.S. population are of normal weight. This epidemic is not at all unique to the United States; it is a global epidemic that is changing the nature of human health and disease [3]. The articles in this Special Issue of PPT focus on some of the major ways that obesity is affecting lung health. The reports highlight important new findings pertaining to the effects of obesity on lung physiology and pathology; they show how obesity is transforming the presentation of common lung diseases. Understanding the effects of obesity is now essential for anyone in the field of lung health. Furthermore, although there exists a substantial body of work detailing the cardiovascular and endocrinological effects of obesity and the metabolic syndrome, comparably little is known in the fields of pulmonary and critical care.

That obesity produces major changes in lung physiology has been known for many years. How this relates to diseases such as asthma, is just beginning to be understood. The contribution by Mahadev et al. [4] highlights changes in respiratory physiology that occur with obesity and how this may lead to symptoms of asthma. Obesity increases the occurrence of expiratory flow limitation during tidal breathing in response to bronchoconstriction in both asthmatics and non-asthmatic controls. This is clearly associated with symptoms of breathlessness. Expiratory flow limitation during tidal breathing is one mechanism that could contribute to the development of severe asthmatic symptoms in the setting of obesity; this has major implications for our approach to the treatment of such patients.

Mediators produced by adipose tissue, adipokines, play an important role in physiological processes in the lung tissue, and also fundamentally alter both innate and adaptive immune responses. Vernooij et al. [5] review the pleiotropic effects of leptin on such diverse processes as lung development and function, and innate and adaptive immune responses, and the potential importance of this to a number of human diseases [5]. In separate articles, Konter et al. [6] and Medoff [7] review the effects of adiponectin on the alveolar-capillary membrane and the pulmonary vasculature and inflammation. Studies of the effects of adipokines in the lung are going to be an important area of investigation in the coming years.

Obesity is characterized by a number of metabolic derangements, which include abnormalities of cholesterol metabolism. Disorders of cholesterol metabolism are likely to have broad effects on innate and adaptive immunity, which in turn have important implications for many lung diseases as outlined in the paper by Gowdy and Fessler [8]. One such disease is acute lung injury. Obesity is a risk factor for acute lung injury as outlined in the paper by Konter et al. [6]. It also appears to alter the course of ALI, through apparently anti-inflammatory effects [9]. One possible mechanism for this finding is through the effects of hypercholesterolemia. Palvinskya et al. [10] show how chronic hypercholesterolemia impairs neutrophil functional responses and that these defects may be in part due to protracted signaling responses to low density lipoprotein and its oxidized forms. Thus, hypercholesterolemia may be an important factor altering the course of acute lung injury and immune responses in the lung [10].

Respiratory infections are fundamentally altered by the presence of obesity. This was highlighted by the 2009 H1N1 pandemic in which obese individuals were at high risk of severe disease. The paper by Mancuso reviews some of the recent work on obesity and both viral and bacterial pneumonia [11]. In particular, Dr. Mancuso reviews how leptin and adiponectin may be involved in both the pulmonary innate and adaptive immune response, and how the absence of or resistance to these adipokines may alter host defense and thus the susceptibility to pulmonary infections. Understanding how obesity may affect response to immunizations and common pulmonary infectious diseases is going to be critical if we are to develop a rational approach to treating patients with pulmonary infections in the coming years.

The link between obesity and asthma has been recognized for at least the last decade, and there has been important progress made in understanding the link between these diseases which is addressed in papers in this issue. The publication by Williams et al. [12] demonstrates that airway reactivity in obese mice is eliminated in mice deficient in tumor necrosis factor-receptor 2, and this appears to be associated with increased levels of interleukin 17A in bronchoalveolar lavage fluid, implicating these pathways in the development of asthma in obesity. The publication by Sideleva et al. reviews the epidemiological links between obesity and asthma, and discusses the importance of the recently recognized phenotypes of asthma in obesity. These new insights are likely to drive a critical paradigm shift in our understanding of asthma in obesity, which will move forward our understanding and approach to these patients [13].

Recent studies do suggest that obesity is a risk factor for pulmonary hypertension, and work described by Medoff in this issue show that adiponectin may be a key factor involved in the pathogenesis of pulmonary hypertension in obesity [7]. Adiponectin levels decrease in the setting of obesity, and this may be important as adiponectin can reduce vascular remodeling in response to environmental insults such as inflammation and hypoxia. Interestingly, a role for circulating adiponectin as a protector of the alveolar-capillary membrane as well is suggested by Konter et al. in their review on obesity and acute lung injury in this issue [6]. Understanding the link between obesity and pulmonary vasculopathy should be an important research priority in the coming years.

Obesity is a multi-faceted disease process, often both characterized and driven by physical inactivity. The publication by Stevenson & Yew-Booth provides insights into the potential importance of this in lung disease [14]. The authors review data suggesting that exercise and aerobic capacity are important predictors of outcome in many diseases, particularly in chronic obstructive pulmonary disease. Their provocative hypothesis that low aerobic capacity increases a smoker's risk for developing chronic obstructive pulmonary disease appears to be borne out by recent animal modeling studies. Thus, understanding how physical inactivity may predispose to the development of lung disease is likely to be an important field of investigation as our population becomes increasingly obese, older and sedentary.

Obesity is profoundly altering human physiology and pathology: it is changing the nature of both health and disease throughout the world. Common diseases are being profoundly altered by obesity both in their incidence and behavior. Drugs designed to work in lean individuals, on diseases that we understand in the setting of the lean state, are unlikely to work the same way in obesity. If we are to understand disease in the 21st century, we need to concentrate our research efforts on understanding the 'new normal' these demographic trends portend.

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The PRG is a non-profit organization that was formed in the 1960s and now serves the research and medical community by organizing yearly symposia on topics related to pulmonary function, disease and treatment. The overall goal of the PRG is to provide a forum for the dissemination and open discussion of research in the pulmonary area, in particular novel therapeutic strategies, compounds and biologics for the treatment of respiratory diseases. Information on becoming a member of the PRG and future PRG meeting topics is available at the website: www.pulmonaryresearch.org.

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