

## Editorial

# Air Pollution and Lung Function Loss: The Importance of Metabolic Syndrome

Zhang L<sup>1,2</sup>, Crowley G<sup>1</sup>, Haider SH<sup>1</sup>, Zedan M<sup>1</sup>,  
Kwon S<sup>1</sup> and Nolan A<sup>1,3,4\*</sup>

<sup>1</sup>Department of Medicine, Division of Pulmonary, Critical Care and Sleep Medicine, New York University, USA

<sup>2</sup>Department of Respiratory Medicine, PLA, Army General Hospital, China

<sup>3</sup>Department of Environmental Medicine, New York University, USA

<sup>4</sup>Bureau of Health Services and Office of Medical Affairs, Fire Department of New York, USA

\*Corresponding author: Anna Nolan, Division of Pulmonary, Critical Care and Sleep, NYU School of Medicine, New Bellevue, 7N Room 24462 1st Avenue, New York, NY 10016, USA

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## Air pollution: an international issue

A multinational study spanning over 20 years showed that approximately 5.5 million deaths were attributed to air pollution [1]. Even brief ambient Particulate Matter (PM) exposure significantly decreases FEV<sub>1</sub> [2-6]. Development of airway injury following PM exposure is a major health concern worldwide and is associated with an increased risk for hospital admission due to respiratory and vascular diseases [7]. Furthermore, a reduction of pollutants has the potential to save five million lives per year [8]. Both diseases place tremendous burden on the world's health resources. The costs and challenges of remedying the pollution burden may have a more profound effect on developing countries. As a pulmonologist in Beijing, pollution has always been a significant contributor to the disease burden of my patients. My experience in the Division of Pulmonary and Critical Care at New York University has raised my awareness about the relevance of air pollution and associated diseases. This brief overview will serve to highlight the challenges faced in dealing with this international issue of pollution and Metabolic Syndrome (MetSyn) which are both significant contributors to loss of lung function.

## Air pollution in China

In 2010, approximately 1.2 million deaths may have been secondary to the negative health effects of ambient PM exposure. These deaths represent a 33% increase when compared to data published in 1990 [9]. In 2013, Beijing had a "haze event;" some estimates indicate PM<sub>2.5</sub> levels reached a monthly average above 170 µg/m<sup>3</sup>, peaking at 677 µg/m<sup>3</sup>. This haze event may have been responsible for an estimated 690 deaths, 5470 hospitalizations for respiratory illness, and an increase in hospitalizations for cardiovascular disease [10]. In my hometown of Beijing, the pollution remains severe. These high levels of PM originate from a number of sources; the burning of fossil fuels and biomass are significant contributors [11]. PM<sub>2.5</sub> includes products of combustion and is considered on a mass basis to be more toxic due to

its hazardous components which stay airborne longer and can more readily reach the lung [12,13]. Epidemiologic studies have associated PM<sub>2.5</sub> pollution with adverse health effects, linking PM<sub>2.5</sub> exposure to the development of vascular and pulmonary diseases [14-23].

## PM exposure causes systemic inflammation and chronic lung disease

Airflow obstruction from PM and smoke exposure is a heterogeneous process. PM exposure causes systemic inflammation, endothelial dysfunction, and subsequent end-organ damage [24-26]. The development of obstructive airways disease from PM induced inflammation is poorly understood [27]. In addition to the aforementioned short term effects of PM exposure, long-term exposure also impairs lung function [17,28-31]. A 3.4% change in forced vital capacity per 10 µg/m<sup>3</sup> change in concentration of PM<sub>10</sub> has been reported [28]. The group that I am working with has focused on the exposure that occurred after the destruction of the World Trade Center (WTC) complex on 9/11/2001. Similarly, many firefighters, rescue workers, and lower Manhattan residents who were exposed to WTC-PM and other toxins also experience a loss of lung function [32,33]. However, we know there to be heterogeneity in the development of lung disease even after a high intensity exposure; therefore, we and other investigators have tried to identify other cofactors such as MetSyn that contribute to disease development.

MetSyn, the collection of risk factors including hypertension, dyslipidemia, insulin resistance, and abdominal obesity, is a key cofactor that, according to 2012 estimates, affects at least 34% of Americans [34-36]. Previous cross-sectional studies have suggested associations between impaired lung function and MetSyn [37-41]. Longitudinal assessment showed that lower baseline FEV<sub>1</sub> was an independent predictor of development of MetSyn [42]. In New York City 2014, the average value of PM<sub>2.5</sub> was 8.48 µg/m<sup>3</sup> and the PM<sub>10</sub> 24-hour maximum concentration was 46.25 µg/m<sup>3</sup>. While these levels are well below what is found in my native city of Beijing, there may still be room for improvement. Nearly half of COPD patients exhibit MetSyn [43]. In air pollution studies, long-term PM exposure and coexisting MetSyn increase systemic inflammation [34]. In the WTC exposed FDNY cohort, dyslipidemia (defined as an elevated triglycerides and low high-density lipoprotein) was significantly predictive of developing a FEV<sub>1</sub> less than the lower limit of normal [24]. The systemic inflammatory effects of lipids and subsequent end-organ effects are of great interest. In light of these findings, our work has focused on the effects of lipids and inflammation in the development of PM-induced lung injury.

The Chinese economy has undergone significant growth in recent years. The lifestyle and dietary choices of the Chinese population have similarly undergone changes that have led to the estimated prevalence of obesity in the Chinese adult population to be 30% [44]. Childhood obesity (BMI ≥ 95<sup>th</sup> percentile) is rising in China (from

1.2% to 10% for boys age 7-18 and from 1.1% to 5.2% for girls age 7-18 between 1985 and 2000, in Beijing) [45,46]. Unhealthy eating habits, however, are not the only factors contributing to the rise in obesity. As discussed in more detail in previous sections of this paper, PM exposure has been linked to a number of adverse health effects [14-23]. Recently, ambient levels of Beijing PM have been shown to induce systemic inflammation and metabolic dysfunction in an exposed rat population, resulting in significantly increased body weight (when compared to a population exposed to filtered air) [44]. If these findings are found to be generalizable to the human population, it would indicate ambient Beijing PM has led to metabolic dysfunction in the people of Beijing. The adverse effects from this exposure coupled with an increase in unhealthy lifestyle choices of a city-dwelling population would be a probable explanation of the high prevalence of MetSyn in China which has been cited to be as high as 21.3%, with urban populations being more likely to exhibit MetSyn (compared to rural populations, OR=1.27) [47].

Metabolic biomarkers of obstructive airway disease not only have prognostic utility, they can direct future research into mechanisms producing airflow obstruction and fuel future work into their downstream effects. Multiple biomarkers have been identified and studied in clinical trials [48]. Our studies have focused on the well-phenotyped World Trade Center (WTC)-exposed Fire Department of New York (FDNY) cohort. In this population, we have observed classic lipid and non-lipid vascular risk factors predict abnormal lung function in the WTC-PM exposed cohort [24,49-51]. This data fits into a larger set of studies demonstrating an increased risk of patients with dyslipidemia for developing COPD due to air pollution and smoking [52]. The mechanism of bioactive lipid induced pulmonary inflammation is poorly understood but is an area of significant interest [53,54]. Biologically active lipid metabolites may identify plausible pathways of disease that could be pharmacological targets. Given the high prevalence of metabolic syndrome in my home country of China and throughout the world, establishing a mechanistic link between lipid mediators of MetSyn and lung injury is crucially important. The adverse impact on quality of life and sizable cost of WTC-lung disease are both public health concerns. Validating metabolic contributors of PM associated lung disease in the Chinese population is necessary. Future work will focus on the metabolomics of these PM exposed populations. Finally, if metabolic biomarkers are validated predictors of PM associated lung disease, then targeted behavioral dietary modification may mitigate disease severity and improve their health and well-being.

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