

# Global Alliance against Chronic Respiratory Diseases symposium on air pollution: overview and highlights

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## Abstract

A 1-day symposium before the annual meeting of the Global Alliance against Chronic Respiratory Diseases, gathered authorities and researchers from around the world to discuss the impact of air pollution on human and planetary health. Air quality is a high priority for Global Alliance against Chronic Respiratory Diseases and China, the host country. This article presents a summary, commentary, and amplification of the 17 presentations. Air pollution is closely linked with global warming and harms most body systems even at levels below international standards. Information about the genetic, cellular, and metabolic effects of exposure to air pollution is important for better understanding of individual responses and even potential therapeutic mediation. Reducing air pollution at its source leads to prompt and important benefits and should be the first priority for political and public action.

**Keywords:** Air pollution; Global Alliance against Chronic Respiratory Diseases; Symposium; World Health Organization

## Introduction

On October 25, 2019, the Global Alliance against Chronic Respiratory Diseases (GARD), an alliance of the World Health Organization,<sup>[1]</sup> held a 1-day symposium on air pollution, the day before the annual GARD meeting, which was held in Beijing 2019, 13 years after GARD's first meeting also held in Beijing. The topic and location were timely because China has significant air pollution problems and, in recent years, the government has developed transforming policies to reduce air pollution. The conference was organized by Dr. Chen Wang and his associates at the Chinese Academy of Medical Sciences and Peking Union Medical College and the World Health Organization. Nineteen authorities from around the world have presented the different aspects of air pollution. This report touches on highlights of the meeting, contains additional explanations and supporting literature, and proposes directions to mitigate the impact of air pollution. Selected topics covered are listed with their speakers. Some of the presentations have a full article in this issue of the Chinese Medical Journal and are referenced for more details.

## Health Impact of Air Pollution in Europe (Giovanni Viegi)

The air quality in Europe has greatly improved in recent years, but air pollution still largely exceeds World Health Organization (WHO) guidelines, which are more stringent than European Union (EU) standards. The European

Environmental Agency's "Air Quality in Europe - 2019 Report" stated that in 2017, the WHO air quality guidelines for particulate matter (PM) were exceeded in 51% of the reporting stations and in all reporting countries, except Finland, Estonia, and Ireland.<sup>[2]</sup> The WHO air quality guideline for ozone (O<sub>3</sub>) was exceeded in 95% of all reporting stations. Although concentrations of nitrogen dioxide (NO<sub>2</sub>) continue to decrease, 10% of the reporting stations recorded concentrations above the WHO air quality guideline.<sup>[2]</sup> The level of PM less than or equal to 2.5 μm in diameter (PM<sub>2.5</sub>) was the greatest in Northern Italy and Poland, although hot spots were also reported in Greece, Turkey, and Romania.<sup>[2]</sup>

Air pollution in the 41 countries of Europe was associated with more than 400,000 premature deaths in 2016; these were largely attributable to PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>.<sup>[2]</sup> Although meeting WHO guidelines would save many lives, levels below these standards were also associated with excess deaths. See article by Viegi *et al*.<sup>[3]</sup> in this issue of the Chinese Medical Journal.

## Impact of Air Pollution on Asthma and Rhinitis (Jean Bousquet)

The evidence that air pollution increases the incidence and exacerbations of asthma and rhinitis is overwhelming. A significant portion of childhood asthma is attributable to outdoor air pollution and these cases can be prevented.<sup>[4,5]</sup>

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A European study showed that if the WHO air quality recommendations were met for levels for NO<sub>2</sub>, PM<sub>2.5</sub>, and black carbon, it is estimated that 23%, 33% and 15%, respectively, of incident asthma cases would be prevented.<sup>[4]</sup> Allergens and air pollution have synergistic effects; for example, O<sub>3</sub> has a greater effect during the grass season.

POLLAR (Impact of air POLLution on sleep, Asthma and Rhinitis) is a European Innovation Institute for Technology and Health project that monitors symptoms in persons with asthma as well as atmospheric pollutants and pollens and warns the asthmatic of unfavorable atmospheric conditions.<sup>[6]</sup> Air quality alerts reduce the use of asthma medications. See article by Sofiev *et al*<sup>[7]</sup> in this issue of the Chinese Medical Journal.

### Air Pollution and Exacerbations of Chronic Obstructive Pulmonary Disease (Pi-Xin Ran)

The association between air pollution and chronic obstructive pulmonary disease (COPD) has been noted at least since the London smog of 1952.<sup>[8]</sup> In that fog, the greater effects on persons with chronic bronchitis and emphysema were attributed to sulfuric acid in the air,<sup>[8]</sup> but now at least five different pollutants (sulfur dioxide [SO<sub>2</sub>], NO<sub>2</sub>, PM<sub>10</sub>, PM<sub>2.5</sub>, and O<sub>3</sub>) are known to increase the risk for hospitalization for persons with COPD. With the improved air quality in Guangdong Province between 2013 and 2017, it appears that decreases in PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub> benefited persons with COPD most. The relationship between outdoor air quality and COPD exacerbations is well known. Another study examined the relationship between indoor air quality and COPD exacerbations in Taiwan, China. Both indoor and outdoor air quality affected hospitalizations for COPD, with PM<sub>10</sub>, PM<sub>2.5</sub>, and O<sub>3</sub> having the greatest effect.<sup>[9,10]</sup>

### Air Pollution, Climate Change, and Allergic Respiratory Diseases (Cun-Rui Huang)

Climate change and air pollution act separately and together to worsen asthma and allergic lung diseases. Both pollutants and allergens directly increase the risk for an asthma attack. Warmer climate and hotter temperature are associated with more O<sub>3</sub>, NO<sub>2</sub>, PM, heat waves, dust storms, wild fires, air stagnation, and other conditions. Climate change causes a migration of plants, animals, and humans, exposing people to new allergens. Increasing carbon dioxide (CO<sub>2</sub>) and temperature increase aeroallergens. Thunderstorms can concentrate fine-particle pollens and trigger asthma attacks in susceptible persons. Temperature variation both within the same day<sup>[11]</sup> and on neighboring days<sup>[12]</sup> increases asthma exacerbations. Persons with chronic lung disease are more susceptible to heat waves.<sup>[13]</sup> Flooding promotes mold growth, and mycotic products are associated with asthma.<sup>[14]</sup> See article by Deng *et al*<sup>[15]</sup> in this issue of the Chinese Medical Journal.

### Air Pollution Mechanisms, Systemic Effects, and Benefits of Its Reduction (Dean Schraufnagel)

Systemic inflammation is the most well-studied mechanism of how air pollution harms health: the pollutants induce an

inflammatory response in the lung, and migratory cells, cytokines, and other mediators spread through the body to involve inflammatory processes in essentially all organs.<sup>[16]</sup> Particle size is the major determinant of which part of the lung the inflammation occurs, with the greatest particle deposition at the level of the terminal bronchiole.<sup>[17]</sup> Fine (PM<sub>2.5</sub>) and ultrafine (PM<sub>0.1</sub>) particles can gain access to the alveoli. PM<sub>0.1</sub> crosses cellular membranes and readily translocates via the blood stream and lymphatics to most cells of the body. PM<sub>0.1</sub> can gain access to the brain by ascending the olfactory nerves. The greater penetration of cells may be part of the reason why finer PMs are more toxic than larger ones.<sup>[18]</sup> Another way PM causes lung disease is by overwhelming the clearance mechanisms, namely, the mucociliary escalator, alveolar macrophages, and lymphatics. This results in local accumulations of soot that can become permanent and cause local fibrosis and scarring.<sup>[17]</sup>

Controlling pollution at its source results in prompt benefits. Reducing traffic and factory emissions during the Beijing and Atlanta Olympics – for only a few weeks – resulted in halving asthma medical visits and reducing cardiovascular mortality.<sup>[5,19]</sup> National and supranational programs that have reduced air pollution have saved hundreds of thousands of lives and trillions of dollars.<sup>[5]</sup>

### Environmental Pollution and Altered Lung Function (Wei-Hong Chen)

Cohort studies in Wuhan (a city with high air pollution) and Zhuhai (a city with low air pollution), of persons followed since 2011 and using personal monitors of PM<sub>2.5</sub>, measures of polycyclic aromatic hydrocarbon (PAH) metabolites, lung function, and mediators of exposure and inflammation, found high PM<sub>2.5</sub> levels were associated with spirometric lung function decline. Short-term (1–7 days) exposure to PM<sub>2.5</sub> was associated with a drop in forced vital capacity and forced expiratory volume in 1 s (FEV<sub>1</sub>). Long-term measurements (6 years) showed greater decline in FEV<sub>1</sub>/forced vital capacity in those with persistent high PM<sub>2.5</sub> exposure.

PAH metabolite levels were associated with a decrease in spirometric lung functions and the effects were more pronounced in smokers. Exposure to PM<sub>2.5</sub>-bound PAHs was related to lung function reduction and was mediated by oxidative damage and inflammatory response. These studies show that an interaction of pollution factors affects lung function decline and that epigenetic factors induced by pollutants are also important. Finding which genes become activated and which metabolite levels change on exposure to air pollution could help determine who will be affected, how air pollution will affect individuals and which sources of pollution are most deleterious. See article by Cao *et al*<sup>[20]</sup> in this issue of the Chinese Medical Journal.

### Short-term Cardiopulmonary Effects of Indoor PM in Patients with COPD (Fu-Rong Deng)

In most places, people spend more than 80% of their time indoors, which highlights the importance of indoor air. PM<sub>2.5</sub> can enter houses through windows, doors, and the

ventilation systems or originate indoors from cooking, smoking, and other activities. Using a detailed series of investigations in patients with COPD and their spouses (as controls), Dr. Deng reported that exposure to indoor-originating PM<sub>2.5</sub> was more strongly associated with decreased cardiopulmonary function compared with outdoor-originating PM<sub>2.5</sub> in patients with COPD. In the heating season, exposure to indoor-originating PM<sub>2.5</sub> was associated with a decrease of FEV<sub>1</sub>. Exposure to outdoor PM<sub>2.5</sub> was more related to an increase of diastolic blood pressure in healthy elderly adults. Higher body mass index had an additive effect with air pollution in decreasing heart rate variability and increasing cardiovascular risk for the persons with COPD. Decreased heart rate variability had a greater lag time in patients with COPD than controls. Smaller-size PM had larger effects on both the heart (heart rate and heart rate variability) and lungs (spirometric measures), and indices of inflammation. Seven urinary markers changed with the oxidative stress that air pollution caused and were often associated with energy generation. Identification and study of these markers should help to better understand the mechanisms of harm caused by air pollution and the potential to intervene.

#### **Taurine Ameliorates PM<sub>0.1</sub>-Induced Emphysema by Affecting Mitochondrial Function (Rui Chen)**

On high pollution days, people may feel its effects and be aware of it, but the long-term effects of lower concentrations of air pollution are generally not appreciated by exposed individuals, and the long-term health effects are less clear. Almost nothing is known about therapies that might reduce the effects of pollution. A recent study showed that metformin prevented PM-induced generation of specific mitochondrial reactive oxygen species that are necessary to open calcium release-activated channels and produce interleukin-6, which in turn accelerate arterial thrombosis.<sup>[21]</sup> PM<sub>0.1</sub> is a toxic pollutant commonly found in diesel exhaust that causes mitochondrial dysfunction. The PAH, 1-nitropyrene, is a major component of diesel exhaust. After working out its pathogenic mechanisms, Dr. Chen reported that taurine ameliorated PM-induced emphysema in mice by inhibiting oxidative stress and autophagy in the lung.

#### **Air Pollution and Cardiopulmonary Disease (Tang-Chun Wu)**

People spend most of their time indoors and 60% of that is in their home. Reducing indoor air pollution at its source is a priority. In rural China, solid fuel used for cooking and heating is associated with higher risk of cardiovascular, respiratory, and all-cause mortality.<sup>[22]</sup> Similar findings have also been found in urban areas.<sup>[23]</sup> The risks can be lowered by switching to clean fuels and using better ventilation in both urban and rural residencies.<sup>[22,23]</sup>

PAH exposure has been imputed as a major human toxin in air pollution, especially in association with the PM<sub>0.1</sub> and PM<sub>2.5</sub> of diesel exhaust<sup>[18]</sup> and coal fires. PAHs cause DNA damage and increased frequency of micronuclei. Micronuclei are chromosomal fragments not incorporated into daughter nuclei of dividing cells. They are frequently

found in cancer cells and are considered a marker of genotoxicity. PAH exposure alters regulating microRNA, which may be a mechanism of its toxicity.<sup>[24]</sup> PM<sub>0.1</sub> often has attached PAH and toxic heavy metals, and this combination appears to make the air pollution much more toxic.<sup>[25]</sup> Another mechanism of PAH-induced toxicity is by methylating cytosine-phosphoguanine islands (CpG) of DNA. CpG are CG-rich DNA segments that are often associated with DNA maintenance and regulation of DNA function. Methylating, and thus silencing them, occurs with naphthalene exposure. Naphthalene is a carcinogenic PAH. PAH may also be involved with accelerated aging by the methylation process.<sup>[26]</sup>

#### **Effects of Air Pollution on the Elderly (Song Tang)**

Air pollution affects the elderly more than healthy young people. The early results of a trial of personal monitoring for PM<sub>2.5</sub> in healthy elderly individuals that sought biomarkers using “omics” technology to understand the body’s response to PM<sub>2.5</sub>, found several responsive biomarkers and underlying mechanisms associated with PM<sub>2.5</sub> exposure. The preliminary results show that PM<sub>2.5</sub> has a metabolic profile in both urine and serum and is associated with electrocardiographic changes (decreased QRS interval/heart rate).

#### **COPD Hospitalization Expenditure due to Respiratory Tract Infections and COPD in China (Shao-Wei Wu)**

Chinese national PM<sub>2.5</sub> levels and hospital expenditure data for 117 cities from 2013 to 2017 were accessed. Although the ambient PM<sub>2.5</sub> levels during this time decreased, PM<sub>2.5</sub> air pollution was associated with increased hospital stays and expenditures, with the strongest relationship for lower respiratory tract infections and COPD. Financial data, such as this, are important in convincing politicians and policy makers about the monetary value of clean air.

#### **Lung Cancer Risk Assessment in Hong Kong, China (Lap-ah Tse)**

Lung cancer, the leading cancer killer in the world, is linked to air pollution. The change in prevalence of cancer subtypes away from squamous and toward adenocarcinoma may reflect the larger influence of the environment, as squamous cell carcinoma has a stronger association with smoking.<sup>[27]</sup> Recently, many countries have developed screening programs using chest computed tomography, but these programs are expensive and can lead to valueless procedures with complications. Therefore, several algorithms have been developed to increase the yield and reduce the costs of screening programs. Dr. Tse reported a screening algorithm developed in Hong Kong, China that took air pollution into account in assessing risk for lung cancer. The algorithm predicted cancers better than other available models without that component. The score also improved with gender and cell type. Dr. Tse also noted that indoor pollutants in developed countries, including exposure to radon, second-hand smoke, frying, mosquito coil burning, and incense burning, may be important.



### Action for Clean Air in Cote d'Ivoire (Isabella Annesi-Maesano)

Air pollution is a significant problem in Africa with about 700,000 deaths in 2012.<sup>[28]</sup> However, there is little data and no monitoring. Africa has a burgeoning population and urbanization with which comes large energy demands and utilization. Major causes of its air pollution are traffic, waste burning, and domestic fires. PM<sub>2.5</sub> is the major pollutant, as most gaseous pollutant levels are still within the WHO guidelines. During the summer (rainy season), smoke from fires in Central Africa contributes to pollution in West Africa. Traffic and landfill burning produce most air pollution during the dry season while domestic fires produce the most during the rainy season because the burning of wet wood is incomplete.

Cote d'Ivoire sets up policies to reduce air pollution by reducing emissions associated with domestic burning, reducing sulfur content in fuels, and working with Sahelian countries to reduce land degradation to decrease the spread of airborne dust. It is also improving socioeconomic data, encouraging research on emission factors, improving measurements of pollutants and supporting capacity building. The hope is that determining which policies are most important will improve health with less cost.

### Personal Intervention (Hai-Dong Kan)

Some of the worst pollution in the world has been in China and Northern India, but in last 7 years, there has been a significant reduction in air pollution in China.<sup>[29]</sup> China had an estimated 1,946,000 deaths associated with long-term exposure to outdoor PM<sub>2.5</sub>. Deaths primarily resulted from ischemic heart disease, stroke, COPD, and lower respiratory tract infections.<sup>[30]</sup>

Although most air purifier studies have been done in low-pollution countries, they may be more useful in the high-pollution setting. Air purifiers have undergone at least six controlled, randomized, cross-over studies. Purifiers result in decreased PM and allergens and are associated with lower levels of inflammatory markers, hormones (such as cortisol, epinephrine, and norepinephrine), insulin resistance, markers of oxidative stress, and, in some studies, blood pressure.<sup>[31]</sup> However, they have not been shown to improve lung function and heart rate variability.<sup>[32]</sup> Their effect on blood pressure has been mixed.<sup>[32]</sup>

Respirators (face masks) may reduce inflammatory markers and blood pressure and increase heart rate variability<sup>[33]</sup> but do not affect lung function, and may make people feel stressed. An impairment to the benefit may also be that their use is not standardized and that the respirators do not effectively exclude all pollutants, such as PM<sub>0.1</sub>.<sup>[5]</sup>

### Clean Air Actions and Plans for China (Xiao-Ming Shi)

China is making a concerted and coordinated government effort to reduce air pollution. Since 2013, China has established 1436 monitoring sites in 338 cities to release hourly data on SO<sub>2</sub>, NO<sub>2</sub>, carbon monoxide (CO), PM<sub>10</sub>,

PM<sub>2.5</sub> and an air quality index. As of 2018, the percentage of the monitoring sites which did not attain the Chinese air quality standards was: PM<sub>2.5</sub> 56.2%, PM<sub>10</sub> 43.2%, O<sub>3</sub> 34.6%, SO<sub>2</sub> <0.1%, NO<sub>2</sub> 15.4%, and CO 0.3%. PM dominates the air pollution problem in China. All of the major pollutants have improved since 2013.

The 2013 action plan called for reducing emissions especially in the energy intensive and polluting industries, promoting public transportation, increasing the supply of clean energy, creating new mechanisms and incentives, and upgrading standards and law enforcement. Goals include the elimination of coal-fired boilers and old, highly polluting cars and industries. They will promote clean and energy-saving processes and industries, with increased monitoring, upgrading standards and laws, and establishing accountability for local governments. Health vision 2030 initiatives seek better health for all with air quality being a major part of it and adopting the health indicators of high-income countries. China is also stimulating research on air pollution and health.<sup>[34]</sup>

### Air Pollution Effect Reduction: Planetary Health Approach (Josep Antó)

What is good for our planet is good for human health, and what is bad for our planet is bad for humans. Climate warming is now proceeding at its fastest rate in the last 66 million years. The energy and transportation sectors account for 84% of the United States' emissions of the radiatively important gases and the majority of the emissions causing air pollution.<sup>[5]</sup> Microplastic particles are ubiquitous. Their health impact is yet unknown, but it is known that they will last for many future generations. Products that have advanced health standards in the past, now present as health hazards. Fertilizers impact the nitrogen cycle. Herbicides, insecticides, and antibiotics have a negative effect on many species on our planet.

Dr. Antó recommended that we adopt a planetary health approach at the highest governing levels by health authorities, health organizations, and health professional societies and embed planetary health into the core of our health education programs from universities to society. We need to transform current health and health care policies and practices to make them planetary regenerative.

### Political Action for Clean Air, Vilnius Declaration (Arunas Valiulis)

The essential ingredient in improving air quality is political will. A meeting in Vilnius in 2018 was a regional initiative that sought to highlight the goal of reducing air pollution and improving health that involved legislators and policy makers.<sup>[35]</sup> Regional meetings that involve policy-makers are important to shore up political will and consolidate plans and actions arising from major global meetings and directives.

Additional important activities include national and supranational standardization, multi-sectoral involvement, expansion of new technology, personalized approaches, encouragement of self-management, and

shared decision-making. Expansion of health standards, pollution control, and health-related policies beyond national borders can add to the health of all, although there must be sensitivity to individual societies. There should be a healthy balance between global and local initiatives; too global can be seen as too foreign or far from local needs and benefits; too local may not bring in the greater benefits of supranational programs. Achievable goals are a strong stimulus for cooperation and adherence. Guidelines that are contradicted by other opinions and recommendations lead to confusion and lack of follow-through. Guidelines should be evidence-based, but there must be acknowledgement of their limitations as well as benefits.

Global health is benefiting from the adoption of new methods of electronic and mobile medicine. Use of mobile technology can guide both the practice of medicine by health-care provider and self-management by individual patients. Teaching and public awareness programs must be ongoing to attain desired goals.

### Conclusion

Air pollution is an enormous global problem that gravely impacts our health and longevity. It usually impairs organ function without the affected person or the medical provider knowing it. Air pollution below global guidelines still contributes to illness and death.

Air pollution hits the vulnerable harder, contributing to death by heart attacks, stroke, and lung disease, and by making other chronic diseases worse. Air pollution affects the lung both chronically and acutely causing a decrease in vital capacity and its components in healthy individuals as well as those with asthma or COPD. In asthma, it is more than additive when combined with allergens.

We live indoors; indoor air quality is evermore important, but often has been neglected. Smoky homes account for more than 4 million deaths per year.<sup>[36]</sup> and must be a high priority for action. Protection with effective ventilation, air purifiers and personal respirators may help, but need more evidence, and is patchwork compared to stopping or reducing the air pollution at its source.

The causes of air pollution and climate change greatly overlap, and the two are synergistic in their harm to health. Climate change causes weather aberrations, which increase pollutants and their effects. Global warming promotes migration, which increases contact to new vectors of disease.

We have raised awareness to the problem. Now we must act. Meetings like this one fortify our resolve. We need to learn more about how air pollution harms health and the mediator studies may greatly improve our understanding and potentially lead to personal interventions to reduce that harm. Even more importantly, we must create political will and public demand for life-saving clean air. Stopping air pollution at its source has prompt and important benefits. “Prompt” means days to weeks and “benefits” mean halving asthma attacks and saving lives.

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### Conflicts of interest

None.

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