THE CLEAN BREATHING INSTITUTE

POLLUTION EFFECTS ON THE UPPER RESPIRATORY TRACT:

SYMPTOMS AND THEIR MANAGEMENT ADVISORY MEETING SUMMARY

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This document provides a summary of an advisory meeting convened by GSK Consumer Healthcare in 2017 entitled 'Pollution Effects on the Upper Respiratory Tract: Symptoms and Their Management'. The advisory meeting invited four international experts to discuss key topics related to air pollution and respiratory health: Christopher Carlsten (the University of British Columbia, Canada), Kian Fan Chung (National Heart & Lung Institute, Imperial College London, UK), Sundeep Santosh Salvi (Chest Research Foundation, India), and Gary W. K. Wong (Department of Pediatrics and School of Public Health, the Chinese University of Hong Kong, Hong Kong). The presentations from experts and associated discussion points are summarised below. For further, in-depth information and for supporting references, please see "The effects of air pollution on the upper respiratory tract: a systematic review".

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THE LINK BETWEEN AIR POLLUTION AND UPPER RESPIRATORY HEALTH

Air pollution consists of a complex mixture of particulate and gaseous components, such as metals, organic chemicals (including volatile organic compounds) and biological materials that surround a carbon core. Particulate matter (PM) can be classified as: coarse PM, with a diameter between 2.5 µm and 10 µm (PM_{10}); fine PM, with a diameter less than 2.5 µm ($PM_{2.5}$); or ultrafine PM, with a diameter less than 0.1 µm. Ultrafine PM is highly dynamic due to its small size, and tends to aggregate with other particles a few hours after generation to form $PM_{2.5}$. Air pollution arises from both natural and man-made sources, including dust, fossil fuel combustion, vehicle emissions, household fuel combustion and photochemical reactions. PM_{10} largely consists of organic materials from natural sources, such as pollen, mould and re-suspended road dust, while combustion processes account for the majority of $PM_{2.5}$ and ultrafine PM.

Although levels and types of air pollution can vary according to geographical location, air pollution is a global problem. In regions such as South Asia and South East Asia, air pollution levels are typically high, whereas in regions such as Europe, North America and Australasia, although levels may still be above World Health Organization standards, they are considerably lower. Globally, air pollution is responsible for approximately 6–7 million deaths per year, and as knowledge of the impact of air pollution increases, levels of air pollution that would formerly have been considered low are now known to have detrimental health effects.

Certain populations are more susceptible to the health effects of air pollution, including children, pregnant women, the elderly, individuals in low socio-economic groups, smokers and those with pre-existing health conditions and allergies. Infants born to women exposed to high levels of air pollutants tend to have a lower birth weight and a higher risk of developing asthma and other respiratory conditions later in life, and may show early marginal markers of ageing even at birth. Elderly patients may be more at risk from the impacts of air pollution due to the presence of pulmonary and cardiovascular co-morbidities, and individuals with genetic vulnerability may also be more susceptible to exposure to air pollution.[1]

Air pollution may have an impact on many body systems and multiple respiratory conditions. How different types of air pollution behave in the airways is important in determining their health effects. For example, the deposition of gaseous components of air pollution in the airways is a function of their solubility, whereas for PM, size is the most important factor. Larger particles (PM_{10}) have a greater impact on the upper airways, and fine ($PM_{2.5}$) and ultrafine particles will more efficiently penetrate to the alveoli, where soluble (and potentially even insoluble) components can then diffuse into the systemic circulation. There are stronger links between exposure to air pollution and diseases of the lower respiratory tract, such as asthma, than those of the upper respiratory tract, such as allergic rhinitis. However, given the growing acceptance of the 'one airway' concept based on links between lower and upper respiratory conditions such as asthma and allergic rhinitis, it is plausible that there may be similarities in the underlying pathology. Exposure to air pollution can result in a range of respiratory and non-respiratory symptoms, which are summarised below (Table 1).

TABLE 1: SIGNS AND SYMPTOMS OF EXPOSURE TO AIR POLLUTION

RESPIRATORY TRACT	OTHER
Throat clearing	Symptoms related to stress hormones (adrenaline, cortisol)
Sore throat	Headache
Rhinitis	Tachycardia
Cough	Raised blood pressure
Sputum production	Itchy or watery eyes
Chest tightness	Metallic taste
Shortness of breath	
Wheeze	
Chest infections (lower respiratory tract infections)	
Increased susceptibility to bacteria and/ or viruses (common cold or flu)	

MECHANISMS UNDERLYING THE EFFECTS OF AIR POLLUTION ON UPPER RESPIRATORY HEALTH

The health effects of air pollution are complex because they are not linked to a single activity or exposure, and are not a single indication or disease but rather a diverse collection of signs and symptoms that may often be related to other conditions. This complexity is in part because air pollution is composed of a range of different components, each one of which may have varying impacts on health. The effects of co-exposure to the multiple components of air pollution are also critical to consider. As a result, a deeper understanding of the impact of different components of air pollution on different populations, including the presence of synergistic interactions between air pollution and other factors, and further knowledge of the dose–response relationship between exposure to air pollution and adverse outcomes, would help to inform the management of air pollution-induced respiratory disease.

Chronic exposure to air pollution has been shown to have an exponential relationship with the development of chronic disease and death, with a steep linear curve starting at lower levels of exposure which ultimately plateaus at the highest exposure levels (Figure 1). Furthermore, a synergistic effect has been observed between air pollution and certain other factors or exposures. Dust mite sensitivity and exposure to air pollution from diesel exhaust particles enhance the prevalence of asthma nearly two-fold compared with either factor alone, and co-exposure to ragweed and diesel exhaust particles (DEP) leads to an increase in immunoglobulin E (IgE) levels versus ragweed exposure alone.[2,3]

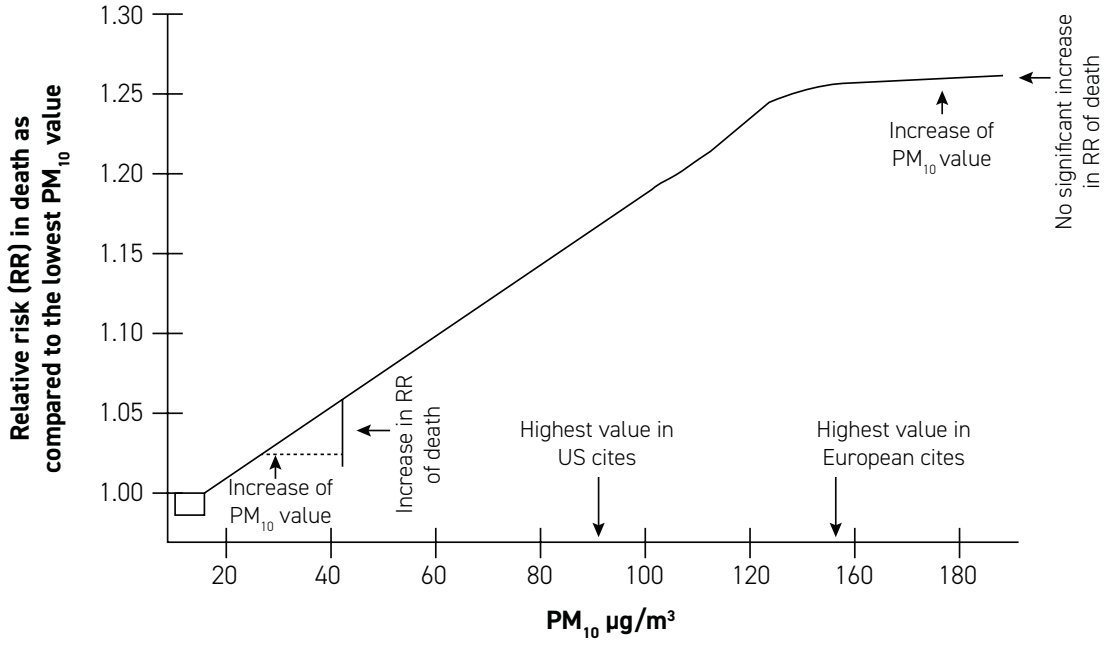

FIGURE 1. RELATIONSHIP BETWEEN AIR POLLUTION LEVELS AND MORTALITY

Adapted by permission from RightsLink Permissions Springer Customer Service Centre GmbH: Springer Nature, European Journal of Epidemiology, The relationship between urban airborne pollution and short-term mortality: Quantitative and qualitative aspects, Izzotti A, Parodi S, Quaglia A et al, Copyright Kluwer Academic Publishers 2000[4]

Several mechanisms have been implicated in the effects of air pollutants, including oxidative stress, alterations in immune function and allergic responses, and changes in nasal cellular structure and function. Specific pathways that have been identified as potentially associated with the effects of air pollution at cellular and molecular levels include the following:[5–7]

- Enhanced T-helper 2 (T_H2) cell response
- Augmented toll-like receptor 4 (TLR4)
- Adjuvant effects of DEP
- Suppressed mucociliary clearance of diesel exhaust particles inducing interleukin-17 (IL-17) pathway
- Mediation via type 2 innate lymphoid cells

Other mechanisms associated with respiratory symptoms include pathways related to neurogenic and transient receptor potential. Exposure to diesel exhaust particles has been shown to trigger release of neuropeptides such as substance P from airway nerve cells, leading to airway hyper-responsiveness, and to trigger cough mediated by transient receptor potential (TRP) channels.[8,9] Emerging pathways such as neural inflammation may also be of interest in managing cough induced by air pollution.

MANAGEMENT AND PREVENTION OF THE EFFECTS OF AIR POLLUTION

Air pollution will always be present due to the ambient level of particulate matter in the air arising from natural events and human activities. The overall goal of interventions should therefore be to prevent or protect against exposure to air pollution or minimise adverse events occurring as a result of exposure, not just to treat the resultant symptoms. Epigenetic changes, primarily DNA demethylation, have been shown to occur after exposure to air pollution, although there is some evidence that these may be reversible.[10] Even in the absence of respiratory symptoms, there is evidence that air pollution can cause cellular damage and a strong inflammatory response can occur in the airway, meaning symptoms should not be the only indicator determining the need to intervene.

In many countries, awareness of the health consequences of exposure to air pollution and how to manage them may be low among community-based healthcare providers. Currently, treatment options are limited and primarily involve reducing personal exposure. The general population can employ lifestyle measures to limit exposure to air pollution, such as staying indoors or limiting outdoor exercise at times of high air pollution, avoiding exercise near busy roads, and cleaning indoor air using air purifiers. Using personal protective equipment such as tight-fitting masks may be helpful, but the evidence for this is mixed and there are potential drawbacks due to the increased resistance to breathing caused by the barrier.

Other options for managing the effects of air pollution include nasal washes that may cleanse the nasal membranes and act to loosen mucus, which facilitates mucociliary transport, a process essential for removing particulate matter from the upper airway. Over-the-counter products such as antihistamines and cough mixtures may provide symptomatic relief. Patients with existing respiratory conditions such as asthma and chronic obstructive pulmonary disease should be treated according to guideline recommendations, and when air pollution is high may wish to stay indoors, limit outdoor exercise or use prophylactic treatments.

Various treatments for symptomatic relief and the management of respiratory symptoms associated with air pollution, such as antioxidants in the form of dietary supplements, have been proposed or are under investigation, and results are awaited with interest.

SUMMARY

The findings of this advisory meeting distilled and clarified the currently available evidence identified in our systematic review of the literature on the health impacts of air pollution, including its effects on the upper respiratory tract, and management strategies currently available for exposure to air pollution.

For more information on the topics described in this summary and for supporting references, please see "The effects of air pollution on the upper respiratory tract: a systematic review".

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