FOCUS REVIEW

The effects of outdoor air pollution on chronic illnesses

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Chronic diseases, especially cancer, cardiovascular disease, and respiratory diseases, are the leading causes of morbidity and mortality worldwide. In Canada alone, chronic diseases account for 87% of total disability and 89% of all deaths (1). It is estimated that half of the Canadian population live currently with a chronic illness and more than 90% of them have these three diseases (1). Chronic diseases develop typically over long periods of time and have multiple risk factors. The major causes of cardiovascular disease include high cholesterol, high blood pressure, and obesity (2-6). For lung cancer and respiratory disease, tobacco smoking and exposure to toxic chemicals are important risk factors (7-15). More recently, ambient air pollution has been implicated in increasing the incidence and mortality from lung cancer and from cardio-pulmonary diseases (16-19).

Present-day urban air pollution comprises hundreds of substances, including sulphur dioxide, ozone, nitrogen oxide, nitrogen dioxide, carbon monoxide, carbon dioxide, particulate matter, rubber dust, polycyclic aromatic hydrocarbons, and many different volatile organic compounds. Particles are a heterogeneous mixture of solid and liquid droplets with wide distributions of size and mass. Coarse particles, greater than 2.5 μm in median aerodynamic diameter, derive from a variety of sources including windblown dust and grinding operations; fine particles are primarily from the combustion of fossil fuels (20). Common constituents of particulates include elemental and organic carbon, sulphates, nitrates, pollen, microbial contaminants, and metals (20). Fine particles can react with sulphur dioxide and oxides of nitrogen in the atmosphere to form strong acids, such as sulphuric acid, nitric acid, hydrochloric acid, and acid aerosols (20). In addition, urban air also contains benzene and 1,3-butadiene that are considered carcinogenic (21).

The health impact of outdoor air pollution became apparent during the smog episodes in London, England, (Figure 1) in the 1950s and in some other places. In London, the lethal fog, which occurred because a temperature inversion trapped heavy combustion-related emissions of particles and SO2 (traffic and coal-fired heating), resulted in approximately 3,000 more deaths than normal during the first three weeks of the smog event (Figure 2) (22). During five days of a smog episode in Donora, Pennsylvania, a small town of 14,000 residents, 20 people died and over 7,000 were hospitalized (23). These episodes demonstrated conclusively that the confluence of adverse weather conditions and extremely high levels of pollution from ambient particles and sulphur dioxide can cause immediate and dramatic increases in mortality (24;25).

In the subsequent decades, especially in economically developed countries, changes in fuels (e.g., low sulphur fuels), improved combustion technology, and regulations (e.g., the clean air acts in the UK, USA, and Canada) have led to significant reductions in the levels of ambient air pollution (Figure 3). Unfortunately, the situation in some other less developed countries is not encouraging. For example, Delhi, India, is subjected frequently to high levels of total suspended particulates, with an annual mean concentration well exceeding 600 μg/m3 (26). In many other parts of the world, such as Mexico City and Beijing (Figure 3), similarly high levels of total suspended particles are observed frequently (27;28). In contrast, the maximum annual

Figure 1: The London smog episode of 1952. A photograph during the day.

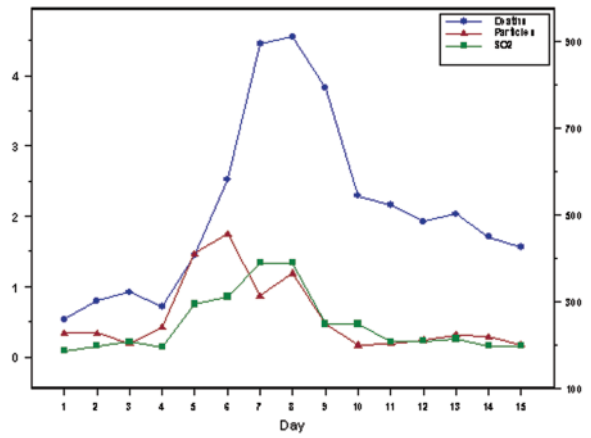

Figure 2: The association between total suspended particles, sulphur dioxide, and nonaccidental deaths during 15 days in the London smog episode of 1952. The right hand vertical axis shows the number of deaths per day and the left hand axis represents concentrations of the two pollutants, on a relative scale.

level of total suspended particles in Windsor, Ontario, one of the most polluted cities in Canada, is usually below 120 µg/m3 (29).

THE EVIDENCE

Over the past 25 years, considerable epidemiological research has been conducted to investigate acute and chronic effects on health as a result of exposure to ambient air pollution. The bulk of this work has been focused on health effects from short-term (i.e., day to day) fluctuations in ambient levels of pollution. Associations have been found between exposures occurring on the day of the event or the preceding days and daily non-accidental mortality, cardio-respiratory deaths, hospitalizations, and emergency room visits (30-50). There is also evidence that certain subgroups of the population are at higher risk. The conclusion is clear: short-term elevations of ambient air pollution cause a variety of acute health events, especially in certain subgroups of the population, such as the elderly, children, and those who are impaired physiologically (e.g., congestive heart failure, diabetes, and cardiovascular disease) (47;51). In contrast, the effects of air pollution on chronic diseases have not been studied as extensively. This is due to the difficulty of assembling large cohorts, following subjects through a long enough period of time, and the difficulty in measuring personal exposures to ambient air pollution.

We have recently completed a structured review of the association between long-term exposure to ambient air pollution and the risks in adults of nonaccidental mortality and the incidence and mortality from cancer and cardiovascular and respiratory diseases (52). A total of 17 cohort studies and 20 case-control studies, published between 1950 and 2007, of the long-term effects of air pollution were identified. We abstracted characteristics of their design and synthesized the quantitative findings in tabular and graphical form. We estimated "summary" relative risks for exposure to certain frequently measured specific pollutants by combining statistically the estimates from the different studies. We also assessed whether there were large variations in the estimates of relative risk between studies (referred to as "heterogeneity").

Our analysis of the published studies showed a 6% increase in non-accidental mortality for every increase of 10 µg/m3 of fine particles, independent of age, gender, and geographic region. This was derived from a log-linear exposure-response pattern; that is, mortality increased exponentially with increasing concentrations of fine particles.

This result can be translated to an estimate of an additional risk in nonaccidental mortality of 1.8% for residents of Windsor, Ontario (annual mean concentration of fine particles: 13 µg/m3) (53), a 16% increase in risk for residents of Mexico City (annual mean of fine particles: 35 µg/m3) (54;55), and a 96.6% increase in risk for residents of Delhi, India (annual mean of fine particles: 126 µg/m3) (26) as compared with those who were exposed to 10 µg/m3 of fine particles (World Health Organization recommended long-term guideline value for fine particles) (56).

We also found that long-term exposure to fine particles was associated log-linearly with an increased risk of mortality from lung cancer (range: 15%-21% per a 10 µg/m3 increase) and overall cardiovascular mortality (range: 12%-14% per a 10 µg/m3 increase) (Figure 4). In addition, we found living close to highways or major urban roads appears to be associated with elevated risks of these three health outcomes. For the other pollutants and health outcomes, data were not sufficient to draw any meaningful conclusions. (57-62)

At first glance, the magnitudes of these associations are smaller than those of some other risk factors, such as smoking. For example, smoking 1 to 14 cigarettes each day was associated with a six-fold increase in risk of dying from lung cancer (63) and a two-fold increase in fatal coronary heart disease (64;65). It is impossible to compare these relative risks directly as the metrics of exposure are different. Because population exposures to air pollution are virtually ubiquitous, there is a very large impact on chronic illness due to exposure to ambient pollution.

NUMBER OF PERSONS AFFECTED BY AIR POLLUTION

Using the pooled estimates of relative risks from our analysis, we estimated that exposure to fine particles at the current ambient level in Canada would lead to

Figure 3: Photographs of air pollution in Montreal and Beijing. Panel A: a "clean" day in Montreal, August 27, 2002, mean concentration of fine particles 3 µg/m3. Panel B: a "dirty" day in Montreal, August 14, 2002, mean concentration of fine particles 37 µg/m3. Panel C: a "clean" day, in Beijing, mean concentration of respirable particles 3 µg/m3; Panel D: a "dirty" day, in Beijing, mean concentration of respirable particles 254 µg/m3

approximately 5,000 deaths each year nationwide (66). Among these deaths, 1,100 deaths would be from lung cancer and 2,700 deaths would be from cardiovascular diseases. In fact, it has been reported that for Austria, France, and Switzerland combined, 40,000 deaths per year are likely to be attributable to outdoor air pollution (67). Chronic health effects from exposure to urban air pollution have thus been estimated to account for almost 60% of the total environmentally-related health effects, exceeding the effects from other environmental risk factors, such as environmental tobacco smoking and lead contamination in drinking water (68).

BIOLOGICAL MECHANISMS

The mechanisms by which air pollution influences the risk of cardiovascular disease are still under investigation. Most of the research in the past 15 years has been focused on the effects of particulates despite the evidence of associations for other pollutants, especially for acute effects. In any event, several potential pathophysiological pathways for the effects of particles have been suggested (18;69). First, repeated inhalation of ambient particulates may result in low-to-moderate-grade pulmonary oxidative stress and inflammation (70-73), which subsequently triggers systemic inflammatory responses with a cascade of reactions: production and mobilization of proinflammatory leukocytes and platelets into the circulation (74;75); increase in circulating inflammatory mediators, such as interleukins (IL)-6 (76;77); and stimulation of the production of acute phase proteins, such as C-reactive protein and fibrinogen (70). This induced systemic inflammatory response may in turn lead to increasing blood coagulability, accelerating atherosclerosis progression, and ultimately precipitating or aggravating cardiovascular events (78-80). This possible biological mechanism, proposed by Seaton et al. (79) and van Eeden et al. (80), has been supported by accumulated epidemiological evidence (67;81) that exposure to ambient fine particles is positively associated with development of atherosclerosis. Second, it has been hypothesized that sustained inflammation of the lung may also exacerbate pre-existing lung diseases such as chronic obstructive pulmonary disease, which further contributes to cardiovascular risk (82). A third hypothesized pathophysiological pathway suggests that ultrafine particles and soluble components of fine particles may cross the pulmonary epithelium into the circulation, thus conferring a direct effect on the cardiovascular system by altering cardiac autonomic function: perhaps contributing to the instability of a vascular plaque or initiate cardiac arrhythmias (18;69). There is evidence that decreases in resting heart rate, an

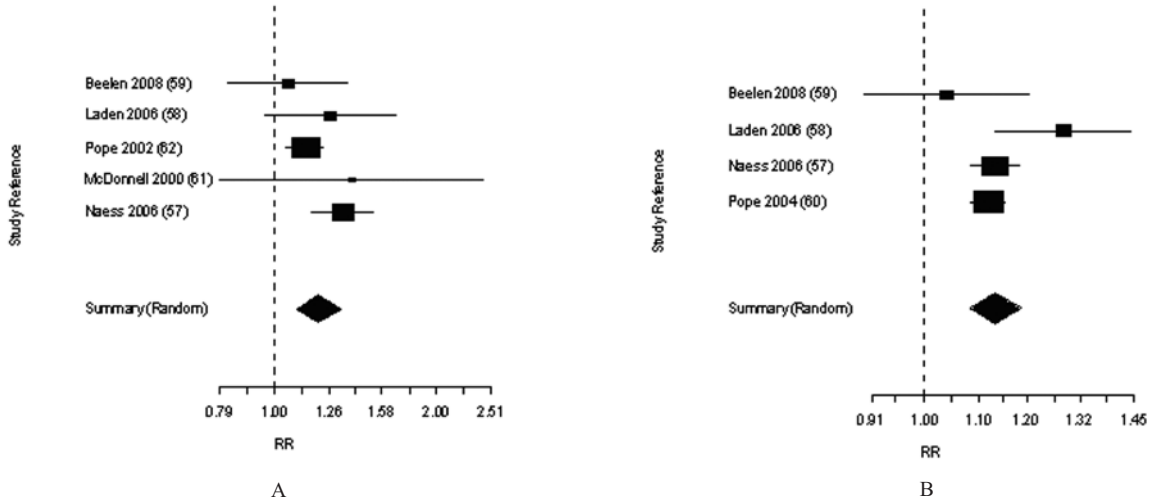

Figure 4: Meta-analysis of epidemiological studies (1950-2007) of the association between long-term exposure to fine particles and mortality from lung cancer (A) and of the association between long-term exposure to fine particles and overall cardiovascular mortality (B). [For each study (shown by last name of first author, year of publication, and reference number), the rectangular box represents the size of study population, the center of the box denotes the point estimate of the relative risk, and the horizontal bar indicates 95%CI of the relative risk. The diamond symbol depicts the summary estimate of the relative risks using a random effects modeling. RR denotes relative risk]

indicator of cardiac autonomic function, are associated with increased risk of cardiovascular morbidity and mortality in the elderly and those with heart disease (83;84). This latter pathway may explain both the acute and the long-term cardiovascular effects of particulate pollution.

In contrast, it appears that the gaseous pollutants may not play a great role in carcinogenesis because they are not mutagenic. Although urban air also contains volatile organic compounds (e.g., benzene) and polycyclic aromatic hydrocarbons (e.g., benzo[a]pyrene) that are both mutagenic and carcinogenic (21), most of these compounds have not been investigated in population-based epidemiological studies. The biological mechanisms underlying the association between fine particles and lung cancer have not been elucidated. It is hypothesized that lung cancer develops through a series of progressive pathological changes occurring in the respiratory epithelium as a result of direct genotoxicity effects of particulate air pollution (85;86). Some studies have suggested that urban air pollution, in particular polycyclic aromatic hydrocarbons, may cause cancer mediated through the formation of DNA adducts (87-90). Polycyclic aromatic hydrocarbons can adhere to fine particles (91). Indeed, it was found that more than 90% of the particulate phase of polycyclic aromatic hydrocarbons are associated physically with particulates under 3.3 μm (92).

CONCLUSIONS

Air pollution does not recognize national boundaries and it may be transported over distances of thousands miles (20). Even at its current level, air pollution threatens the health of entire populations. Air pollution is a growing, global problem. Yet approaches to controlling air pollution have not been up to the task. The overall evidence from the past and present epidemiological studies strongly supports tighter standards for air pollution, especially particulate pollutants, in Canada and in other countries.

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