What are the Human Health Effects of Air Pollution?

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Significant advances in knowledge regarding effects of air pollutants on health in past few years

Public, especially those with respiratory problems, generally aware that adverse respiratory effects result from poor air quality

Conventionally measured pollutants include ground-level ozone, suspended particulate matter, carbon monoxide, nitrogen dioxides, sulfur dioxide and reduced sulfur compounds such as hydrogen sulfide
Introduction

- Air pollutants derive from a variety of sources and are classified according to chemical composition, size and mode of release.
- Distinctions between primary and secondary pollutants and gaseous and particulate pollutants relevant to understanding mechanisms of adverse health effects.
- While primary route of exposure to airborne pollutants is via respiration, air pollutants can extend their effects to organ systems beyond lungs.
Respiratory System – Brief Review

- major function of lungs is gas exchange
- lungs are also the site of some biotransformation
- lungs receive entire cardiac output from right heart via the pulmonary artery
- oxygenated blood leaves the lung via the pulmonary vein
Respiratory System – Brief Review

- Respiratory bronchioles and pulmonary compartment comprise the gas exchange zone.

- As air progresses down the respiratory tract, velocity reduces markedly as cross sectional area increases markedly.

- Gases can penetrate to gas exchange zone; there is differential particulate matter deposition according to particle size.
Respiratory System – Brief Review

- velocity affects suspended particulate deposition as air traverses through the lung
- **coarse particles** (2.5 -10 microns in diameter (including liquid aerosols)) largely deposited in upper airways and unlikely to penetrate into alveoli
- as air passes across airway bifurcations, there is further impaction
- **fine particles** (<2.5 microns in diameter) penetrate into alveoli
- diminished airway velocity corresponds with increased particulate sedimentation
- macrophages scavenge larger particles (0.1-2.5 microns)
- **ultrafine particles** (<0.1 microns) are able to traverse membranes and be absorbed into blood stream and general systemic circulation
Pulmonary macrophage from a coal miner’s lung
The ease with which oxygen and carbon dioxide can pass between air and blood is clear from this electron micrograph of two alveoli (Air) and an adjacent capillary from the lung of a laboratory mouse. Note the thinness of the epithelial cells (EP) that line the alveoli and capillary (except where the nucleus is located). At the closest point, the surface of the red blood cell is only 0.7 µm away from the air in the alveolus.
Possible Mechanisms of Pollutant-Associated Health Effects

1. PM- or- ozone induced pulmonary inflammation (irritation or fibrosis)
2. Free radical and oxidative stress generation by transition metals and organic chemical compounds (e.g. PAH)
3. Covalent modification of key intracellular proteins (e.g. enzymes)
4. Biological compounds, such as endotoxin and glucans, which induce inflammation and innate immune effects
Possible Mechanisms of Pollutant-Associated Health Effects

5. Stimulation of autonomic nervous system activity, which regulates heart rate variability and airway reactivity

6. Adjuvant effects in the immune system (e.g. diesel exhaust particulates and transition metals enhancing responses to common environmental allergens)

7. Procoagulant activity by ultrafine particles after access to the systemic circulation

8. Suppression of normal defense mechanisms (e.g. suppression of alveolar macrophage functions)
Possible Mechanisms of Pollutant-Associated Health Effects

- **Oxidative stress** is defined as a depletion of intracellular glutathione leading to an accumulation of oxidized glutathione.
- Glutathione is a small protein which exists in a reduced state that acts as an antioxidant and protects cells from toxins such as **free radicals** (unprotected electrons).
- When glutathione is not available, an increase in circulating free radicals occurs that in turn increases the propensity for **airway inflammation**, increased susceptibility for infection, and **asthma**.
- Because some people have deficiencies in their enzymes that revert glutathione from the oxidized state to the reduced state, these individuals may be more prone to experience adverse health effects during pollutant exposure compared to persons with normal antioxidant defense.
Particulate matter (PM)
Particulate matter (PM)

- Comprises a complex mixture of dusts generated by mechanical abrasion or through combustion processes
- About two-thirds of PM$_{2.5}$ formed from precursor gases
- These aspects makes investigations more challenging (exposure assessment, size characterization)
- PM can initiate tissue damage and alter defense mechanisms of the body against foreign materials
- Some of the adverse health effects include development of respiratory disease, such as chronic bronchitis, increased risk for respiratory symptoms and declines in lung function
Particulate matter (PM)

- Many studies have shown a consistent relationship between PM10, PM2.5 and mortality as well as hospital admissions and ER visits.
- Some investigations have linked PM to lung cancer.
- Numerous studies linking cardiovascular disease, chronic obstructive lung disease and pneumonia in persons over 65 with exposure to PM$_{10}$.
- Longer term exposure has been associated with increased mortality and lower birth weights; a just published study of Nova Scotia infants has reported no significant relationships between first trimester exposure to PM10, SO2 and ozone after adjusting for birth year.
- The cardiovascular mortality association was highlighted in recent reanalysis of 1952 London smog episode data.
- Causal components of relationship between particulate matter and cardiovascular morbidity and mortality remain to be identified and current studies are unable to define a threshold of no health effects.
- Hence WHO has recommended against establishing a guideline value for PM and suggests instead that risk managers use linear, no threshold health functions for setting air quality targets.
Particulate Matter - UFP

- There is now sufficient reason to believe that ultrafine particles (UFP) are important in morbidity and mortality fractions previously attributed to larger-size fractions.
- Reasons for potential importance include: high pulmonary deposition efficiency, magnitudes higher particle number concentrations than larger particles, ability to carry large amounts of absorbed or condensed toxic air pollutants (oxidant gases, organic compounds, transition metals).
- A study to examine the chemical composition of UFP in southern California noted the trace elements included lead, arsenic, zinc, gold and silver and a range of other transition metals.
- Most of the trace element particles detected in this study were within a range of 0.01-1.0 micron.
Ammonium is a measurable fraction of the fine particle mass across Canada (10-20%).

There is evidence that reductions in ammonia air concentrations will lead to a decrease in fine particle mass, particularly in winter.

- Bob Vet, Meteorological Service of Canada, 2003
Ammonia Released to Air in Canada, 1995

- Agriculture (Livestock): 52%
- Fertilizer Application: 33%
- Light-Duty Gasoline Vehicles: 2%
- Forest Fires: 3%
- Chemicals Industry: 4%
- Other: 6%
Ozone

- Generated almost entirely from precursor gases (NOx)
- Our current understanding of how ozone exerts its adverse health effects has been generated mainly by ozone exposure studies of healthy and asthmatic individuals
- These have consistently demonstrated a decrease in *forced vital capacity* (e.g. ability to blow air out of your lungs) and *forced expiratory volume at 1 second* (FEV1) (a measure of airways constriction) associated with chest discomfort on inspiration and increased nonspecific airway hyperresponsiveness.
- High level exposure in lower lung can result in congestion, hemorrhage and pulmonary edema (rare)
Ozone

- Ozone exposure ranging from 100 to 400 ppb is traditionally accompanied with neutrophilic inflammation in the alveoli as early as one hour after exposure and can persist for up to 24 hours.
- Ozone exposure of less than 500 ppb without exercise typically has no effect on lung function; however, ozone exposure with exercise results in increased breathing frequency, decreased FEV1 and FVC and an increase in airways resistance and symptoms.
- Hence outdoor exercise on days in which air quality is poor should be avoided by susceptible individuals.
Ozone

• Ozone has been significantly associated with mortality, hospital admissions and ER visits, however less consistent mortality results are observed in winter months when ozone levels are lower.

• Links have also been observed between chronic ozone exposure and lung cancer with more significant effects in males.

• Ozone toxicity occurs in a dose dependent fashion with no observable threshold.

• Based on this evidence, the WHO declared it is not possible to assign an air quality guideline but rather that an acceptable risk level would need to be chosen by considering the lower frequency of responders in the population and reduced severity of response at lower levels of exposure.
Sulfur dioxide, nitrogen dioxide and carbon monoxide

- Exposure (5 min) to inhaled SO$_2$ induces rapid onset bronchoconstriction in both healthy (>5 ppm) and asthmatic people (>0.25 ppm) but full recovery occurs within 30 minutes post exposure though for asthmatics this takes longer.
- A recent study found that SO$_2$ exposure was associated with increased hospitalizations for asthma in children but not in adults or individuals with other respiratory conditions.
- Ambient SO$_2$ might contribute to acid aerosol formation and could be important because some studies suggest that asthma symptoms are increased on days with high aerosolized acid levels.
- Exposure to ozone or cold dry air before exposure to SO$_2$ increases bronchial sensitivity to SO$_2$ in asthmatic patients.
Sulfur dioxide, nitrogen dioxide and carbon monoxide

- NO2 is associated with pronounced decreases in pulmonary function and increased rates of respiratory illness though it is difficult to differentiate these effects from ozone related impacts.
- Because NO2 is a precursor to photochemical smog, its major effect on health as an outdoor pollutant is likely through the formation of ozone.
- High NO2 personal exposure the week before the onset of a respiratory viral infection has been linked to increased severity of a resulting asthma exacerbation.
- In challenge studies of healthy subjects and smokers, NO2 exposure induces an inflammatory response in the airways characterized by neutrophil influx and reduced lymphocyte populations.
- Compared with its direct effects on the airways, NO2 might play a more prominent role as a sensitizing agent to inhaled allergen.
- Despite these results, WHO recently concluded that NO2 effects observed in epi studies may be attributable to other pollutants, including particulate matter originating from the same combustion sources.
Sulfur dioxide, nitrogen dioxide and carbon monoxide

- Recent epidemiological studies conducted throughout the world have provided valuable insight into the associations between SO2, NO2 and CO exposure and increases in cardiopulmonary mortality, respiratory and cardiovascular hospital admissions, emergency admissions caused by stroke (NO2) and myocardial infarction (NO2 and CO).
- Such multi-pollutant modeling studies are still in their infancy and more work needs to be done.
Interaction between allergens and pollutants

- Since 1997 studies have focused on automobile-related pollutants and concluded that high vehicle traffic is associated with asthma, cough, and wheeze in children with known allergic sensitization.
- Epi studies investigating the role of allergen-pollutant combinations as triggers of asthmatic attacks have revealed that ozone, NO$_2$, and aeroallergens were independently or interactively related with asthma symptoms and changes in peak flow rates.
- Studies linking asthma admissions with thunderstorms was originally attributed to peak fungal spore counts preceding or during the weather front; more recent investigations have shown a positive association between asthma admissions and higher levels of ozone during these times but failed to show the link with thunderstorms.
Conclusions

• **Important questions:**
  - Does air pollution increase the risk of asthma development?
  - Does air pollution exacerbate asthma or allergic rhinitis?
  - Which air pollutants are most commonly associated with adverse health effects and how can they be reduced or avoided?
  - Are allergic individuals with asthma at greater risk of early death from air pollutants?
Conclusions

- Some answers:
  - Exposure to ground level ozone has been associated with increased risk of asthma development among children in California playing outdoor sports.
  - Ozone can increase airway inflammation and airway responsiveness and also can potentiate the airway response to inhaled allergens.
  - Exposure to nitrogen oxides has been associated with an increase in respiratory infection and wheezing and can increase the effects of inhaled allergen responses.
  - Sulfur dioxide ($SO_2$) in high concentrations with or without exercise is a respiratory irritant, provoking airflow limitations.
  - Particulate matter has been associated with a range of health outcomes; understanding of the impacts of ultrafine particles is only just beginning.
Conclusions

• Despite declines in levels of some air pollutants, recent epidemiological studies continue to demonstrate associations between air pollution and health problems.
• These associations were observed even at low exposure levels measured in Canada and elsewhere.
• Acute exposure-related effects are better understood than chronic disease outcomes.
• Multiple pollutant interactions are just beginning to be investigated.
• Still much that we do not know about the biological mechanisms that cause these health effects.
• Air pollution still remains a significant health risk to Canadians.