National Environment Protection (Ambient Air Quality) Measure

Report of the Risk Assessment Taskforce

Appendix 4

Health Effects of Criteria Pollutants

CONTENTS

1. INTRODUCTION

Many substances that are known as air pollutants are also known to have health effects at high levels of exposure. This has been documented in case studies of accidental exposure and in high dose toxicology studies in animals. Evidence from periods of very high pollution, such as the London smogs of the 1950s, also show that air pollution can have measurable health effects as demonstrated by increases in hospital admission rates and specific medical conditions.

At lower pollution levels any health effects are more difficult to detect and rely on both toxicology and epidemiological studies which must be carefully designed and executed following appropriate protocols and meeting high academic standards. The results also require appropriate statistical analysis and interpretation in the context of a large amount of pertinent scientific data and information.

Debates amongst researchers and other stakeholders over the health effects of low levels of air pollutants often generate different opinions about the likely health effects from the same evidence.

This appendix documents much of the evidence in the scientific literature which indicates that there are demonstrable associations between commonly occurring air pollutants and health effects. In assessing the risk of health effects in the Australian population, these health studies need to be interpreted in the context of several issues generic to studies of this type. It is the role of a risk assessment protocol as advocated in this report to provide a logical, scientifically valid and transparent process to facilitate appropriate conclusions about risk.

As an example of the variation in opinions, references such as Watson (1997), Vedal, (1997), EM (1997), and Samet (2000) contain examples of the views of various parties debating the health effects of particles.

Key aspects to be considered include:

- exposure data are often the weakest part of an epidemiological study and their accuracy needs to be carefully assessed;
- have the studies been peer-reviewed through publishing in the scientific literature?
- have other influences on the health outcomes been considered? Smoking, extreme temperature events and simultaneous exposure to several pollutants are examples of factors whose effects must be accounted for according to accepted research methodologies;
- if various steps in a study contain uncertainty it is important that each element is treated appropriately in the statistical analysis, to ensure that the total uncertainty is quantified;
- a series of studies showing positive statistical correlation need to be assessed for other factors to establish cause and effect relationship. These include strength of association, consistency across studies, specificity, appropriate temporal relationship, exposure response relationship and biological plausibility; and
- valid negative studies should be given appropriate weight in any assessment and recent research has shown that authors are less likely to submit negative studies for publication (Ricci et al., 1996).

The health effects of the criteria air pollutants have been known for many years. This information has been derived mainly from controlled human exposure and population based epidemiological studies as well as animal toxicological studies. Health effects such as increases in daily mortality, hospital admissions and emergency room attendances (respiratory

and cardiovascular disease) have been associated with exposure to pollutants such as particles, ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Exacerbation of asthma has also been associated with exposure to these pollutants. Elevated levels of blood lead leading to IQ deficits in children have been the most common health effect associated with exposure to lead. There appears to be groups within the population that are sensitive to the effects of air pollution and these include people with existing disease (mainly respiratory and cardiovascular), people with infections such as influenza and pneumonia, asthmatics, the elderly and children.

A brief overview of the health effects of each of the criteria pollutants is presented below.

2. CARBON MONOXIDE

The health effects of carbon monoxide (CO) are associated with the level of carboxyhaemoglobin (COHb) levels in blood. It is generally accepted that maintaining a COHb level below 2.5% will be protective of adverse effects related to exposure to CO. The binding of CO with haemoglobin to form COHb reduces the oxygen carrying capacity of the blood and impairs the release of oxygen from haemoglobin. The toxic effects of CO first become evident in organs and tissues with high oxygen consumption, such as the brain, heart, exercising skeletal muscle and the developing foetus.

The health effects of CO include increases in daily mortality and hospital admissions (mainly cardiovascular disease), increases in angina attacks (patients with ischaemic heart disease), decreases in athletic performance and low birth weights. Many of the early studies showing these effects were conducted on populations exposed to relatively high levels of CO. More recent studies have shown that increases in daily mortality and hospital admissions for cardiovascular disease are observed at levels currently experienced in most cities in Australia and overseas (Linn et al., 2000; Sheppard et al., 1999; Yang et al., 1998; Schwartz 1997; Schwartz 1999; Morris and Naumova 1998; Burnett et al., 1997b; Morris et al., 1995; Burnett et al., 1998; Polniecki et al., 1997). Until recently it was thought that current exposure levels were unlikely to produce serious health outcomes, however the results of these studies brings this into question.

There have been several studies that have shown associations between increases in daily mortality and ambient CO levels. Early studies showed associations between daily mortality and ambient CO levels but at levels much higher that those currently observed in urban areas (UK Department of Health 1998; Bascom et al., 1996). More recent studies have also shown such an association even at the lower levels currently experienced.

A recent study conducted in Santa Clara County, California, has shown an association between CO levels and daily mortality (Fairley, 1999). This study showed highly significant associations between 24-hour average CO levels and mortality. The most significant effect was observed for a 1-day lag. The observed effects were stronger for respiratory and cardiovascular mortality than for all cause mortality. The observed associations lost significance in multi-pollutant models.

In a study by Burnett et al (1998a) an association was found between daily mortality and ambient CO levels in eleven Canadian cities with a 2.5% increase in daily mortality attributable to CO. In multi pollutant models this effect was reduced to 0.9%. The strongest association found in this study was for NO_2 with a 4.1% increase in daily mortality attributable

to NO_2. Associations were also found for SO_2 and O_3. Much of the effect attributable to CO could be explained by SO_2 and NO_2.

In contrast a study conducted in Toronto, Canada (Burnett et al., 1998b) showed that CO was significantly associated with increases in daily mortality. These associations were observed between CO and mortality in all seasons, age and disease groupings analysed. TSP was also associated with increases in daily mortality. In this study it was estimated that ambient CO levels could account for 4.7% of the daily mortality in Toronto while TSP accounted for an additional 1%.

Ambient CO levels have also been associated with increases in daily mortality in Athens (Touloumi et al., 1996). The results of this study, conducted as part of the APHEA project, found a 10% increase in daily mortality for an 8 ppm increase in 8-hour average CO. The strongest effects were observed for same day CO concentrations.

The association between ambient CO levels and increases in hospital admissions is another area that has received considerable attention in recent years. A study by Sheppard et al (1999) has shown an association between hospital admissions for asthma and ambient levels of CO in a non-elderly population in Seattle. Air pollution data for particles (PM_{10}, $PM_{2.5}$ and $PM_{10-2.5}$), O_3, SO_2 and CO were collected for the period 1987-1994. All measures of particles and CO were found to be associated with an increase in hospital admissions for asthma, with the highest risk observed during autumn and spring. An association was also found for O_3 during the summer but no effect was observed for SO_2 for any season. For CO there was a 6% (95% CI: 1.03 – 1.09) increase in hospital admissions per interquartile range of 0.9ppm at a lag of 3 days.

The association between daily hospital admissions and ambient air pollution in Los Angeles has recently been investigated (Linn et al., 2000). In this study CO was consistently associated with cardiovascular admission with a 4% increase per 1 ppm increment in CO levels. Similar associations observed for PM_{10} and NO_2 but the strongest effects were observed for CO. Admissions for respiratory disease were more strongly associated with PM_{10} and NO_2 although significant positive associations were also observed for CO. The mean CO level during the study period was 1.5 ppm.

Yang et al (1998) investigated the effects of ambient CO on hospital admissions for cardiovascular disease in Reno, Nevada for the period 1989-1994. Air pollution levels were low throughout the study period with an average hourly maximum CO level of 3ppm and a maximum of 11ppm. Strong associations were found between ambient hourly maximum levels of CO and hospital admissions for cardiovascular disease and ischaemic heart disease. The association with cardiovascular disease was statistically significant in all age groups and for both males and females. For ischaemic heart disease the association was statistically significant in the elderly (>60 years) and in males. For admissions for cardiovascular disease there was a 1.5% (95% CI: 1.2-1.7%) and ischaemic heart disease 3.5% (95% CI: 2.6-4.5%) increase per 1 ppm increase in maximum hourly CO level. Three statistical methods were used in the analysis and all gave comparable results.

In an earlier study by Schwartz (1997), ambient CO levels were found to be associated with hospital admissions for cardiovascular disease in the elderly (>65 years) in Tuscon, Arizona. An association was also found for PM_{10} but only weak associations were found for O_3, NO_2 and SO_2. Ambient CO levels were low during the study period with a mean hourly maximum level of 3.3 ppm. Levels of PM_{10} were moderately high with an average 24-hour level of 42

$\mu g/m^3$. Both PM_{10} and CO were associated with hospital admissions for cardiovascular disease on the same day with a 2.7% increase in admissions per interquartile range of PM_{10} (23 $\mu g/m^3$) and a 2.8% increase in admissions per interquartile range of CO (1.7 ppm). The regression coefficients obtained from multipollutant models were similar to those from single pollutant models suggesting that the effects of CO and PM_{10} were independent. The findings of this study were similar to those from other studies.

A more recent study by Schwartz (1999) found an association between ambient CO levels and hospital admissions for heart disease in the elderly in 8 US counties. A positive association was also found for PM_{10}. The associations held in both humid and dry locations and were independent of other pollutants and weather. A 2.8% (95% CI: 1.9-3.7%) increase in hospital admissions per interquartile range (1.8 ppm) of CO was observed.

Morris and Naumova (1998) conducted a study to investigate the effects of CO on hospital admissions for congestive heart failure in Chicago. They examined the effects of average maximum one hourly CO level and the impact of temperature on the association with hospital admissions. PM_{10}, SO_2, NO_2 and O_3 were also included in the model. CO was positively associated with hospital admissions for congestive heart failure in both single and multi pollutant models with relative risks associated with the 75th percentile of 1.09 and 1.08 respectively. The effect was temperature dependent with an increase in the relative risk with a decrease in temperature. The maximum effect was observed at temperatures below 4^oC (Relative Risk 1.15), with little effect seen above 24^oC (Relative Risk 1.01). The authors conclude that there is a synergistic effect of cold temperatures and the effect of CO on acute heart failure. The authors propose that this is biologically plausible as both cold temperatures and CO increase the load on the heart that can lead to acute heart failure. These effects are seen at levels below current air quality standards and below levels used in laboratory studies. They suggest that patients with congestive heart failure may form a uniquely susceptible group to the effects of CO and that the threshold for effects in these patients may be below 3% COHb. The results of this study suggest that cold temperatures may reduce this threshold further.

An earlier study in 10 Canadian cities by Burnett et al (1997b) looked at hospital admissions for congestive heart failure and the association with ambient air pollution over an 11 year period. Positive associations were found with CO, NO_2, SO_2, and coefficient of haze. The strongest association was found with CO and was not sensitive to weather or other pollutants. The relative risk for a 1 to 3 ppm increase in CO (25th to 75th percentiles) was 1.065 (95% CI: 1.03-1.10). The effect was strongest for same day exposure. The dose response curves showed a rapid increase in hospital admissions for CO concentrations less than 1 ppm with a slower rate at higher concentrations. There was no obvious threshold observed for the effects of CO. Mean CO levels were 2.3 ppm (1-hour maximum) and 1.6 ppm (8-hour maximum). CO accounted for 90% of the excess hospital admissions attributable to air pollution.

Morris et al (1995) looked at hospital admissions for congestive heart failure and the association with ambient air pollution in 7 US cities. Mean 1-hour maximum CO levels ranged from 1.8 to 5.6 ppm in the cities studied. A strong association was found between hospital admissions for congestive heart failure and CO levels which was independent of season, temperature and other pollutants. The relative risk per 10ppm increase in CO ranged from 1.37 (New York) to 1.71 (Los Angeles). The effects were similar in both single pollutant and multi pollutant models. The maximum effect was observed on the same day. Nitrogen dioxide was also associated with hospital admissions but this association didn't hold in multi

pollutant models. Limiting the analysis to CO concentrations less than 9 ppm had little impact on the effect.

Two studies conducted in Melbourne have shown associations between ambient CO levels and increases in daily mortality and hospital admissions (EPA (Vic), 2000; Geschke, 1999). The EPA study found that for the period 1991 to 1996 ambient CO levels were associated with increases in daily mortality. The effects were strongest in the elderly with existing cardiovascular disease in whole year models and for all cause and respiratory disease during the warm season. In multi-pollutant models the association became non-significant. Maximum average 8-hour CO levels ranged from 0 to 5.7 ppm during the study period. Geschke (1999) found that CO levels were associated with an increase in hospital admissions for cardiovascular disease in Melbourne. The results of this study were similar to the results of recent studies overseas.

2.1 Summary

Exposure to carbon monoxide is associated with a range of health effects including increases in daily mortality and hospital admissions primarily for people with existing cardiovascular disease. The results of epidemiological studies are consistent with the toxicological and clinical studies although effects may be observed at levels lower than expected.

3. NITROGEN DIOXIDE

Exposure to nitrogen dioxide has been associated with increases in daily mortality, increases in hospital admissions and emergency room attendances (respiratory and cardiovascular disease). Exacerbation of asthma, increases in respiratory symptoms and decreases in lung function may also be associated with exposure to NO_2. Asthmatics may be particularly susceptible to the effects of NO_2. Some studies suggest that there is a concentration of NO_2 below which adverse effects are not observed. This concentration, termed the No Observed Adverse Effects Level (NOAEL), is approximately 0.2 ppm (Bascom et al., 1996; WHO, 1999a).

Nitrogen dioxide may also sensitise individuals to the effects of other pollutants. In some controlled human exposure studies, prior exposure to NO_2 increases the response to ozone and sulfur dioxide compared to subjects not exposed to NO_2. Nitrogen dioxide has also been shown to increase the response to allergens. This may be significant for asthmatics. Exposure to NO_2 may impair the host defence mechanisms of the body that leads to an increase in susceptibility to infection. This is thought to be significant in children, as a higher incidence in respiratory infections as children has been associated with the development of chronic respiratory disease in adult life (Bascom et al., 1996; Streeton, 1997). Exposure to NO_2 has also been shown to cause reversible effects on lung function and airway responsiveness. Repetitive exposure in animals can produce changes in lung structure, lung metabolism, and lung defences against bacterial infection.

Nitrogen dioxide appears to contribute both to morbidity and to mortality, especially in susceptible subgroups such as young children, asthmatics, and in those individuals with chronic inflammatory airway disease (chronic bronchitis and related conditions). Nitrogen dioxide appears to exert its effect via an inflammatory reaction on epithelial surfaces in the human lung. This is due to an oxidative reaction on unsaturated fatty acids in cell membranes and in various soluble and structural proteins. This results in the production of inflammatory mediators. Indirect effects arise by the induction of relative impairment of immune defence

mechanisms in the lung. Epidemiological studies suggest that young children are especially susceptible to these effects, resulting in an increase in respiratory infections following disturbances in immune defence mechanisms.

There appears to be separate patterns of responses in susceptible populations to short term acute ambient exposures, in comparison to the responses observed after longer term chronic exposures to mildly increased background concentrations. With acute ambient exposures, immediate effects within one to two days can be demonstrated. These take the form of increased bronchial hyper-responsiveness in asthmatics; and in those with chronic inflammatory lung disease, leading to increased frequency of wheezing, cough, sputum production, with, as a secondary effect, increased frequency of respiratory infections (DoH 1995). On the other hand, longer-term exposure in a chronic indoor environment appears to have more direct effects on the patterns of respiratory infection in young children. Animal toxicological studies suggest that peak concentrations contribute more to the toxicity than does prolonged exposure although the latter is still important.

The most striking feature from the epidemiological studies conducted on the health effects associated with exposure to NO_2 is the inconsistencies with the findings. The mortality studies have indicated that exposure at ambient levels increases daily mortality from respiratory and cardiovascular causes. Effects are seen in all age groups. Many of these studies have been reviewed by UK Department of Health, (1998), Streeton, (1997), WHO, (1997), Bascom et al., (1996).

The results of recent studies have added strength to the possible association between ambient NO_2 exposures and increases in daily mortality. A recent study by Burnett et al (1998) has found an association between 24-hour average NO_2 levels and increases in daily mortality in 11 Canadian cities. Effects were observed for CO, SO_2 and O_3 but these weren't as strong as the NO_2 effect. In single pollutant models a 5.3% increase in all cause mortality was found for an increase in 24-hour average NO_2 levels of 23 ppb. In multi-pollutant models controlling for the effect of the other pollutants the strength of the association with NO_2 was reduced slightly, 4.3% increase in all cause mortality was found for an increase in 24-hour average NO_2 levels of 23 ppb. Daily average NO_2 levels ranged from 14.1 to 27.5 ppb with an average value of 23 ppb.

A meta-analysis from the APHEA studies has shown an association between daily mortality and daily 1-hour maximum NO_2 levels (Touloumi et al, 1997). This analysis was conducted on the results of studies conducted in six cities across Europe. The effect of NO_2 was greatest in cities that had high levels of black smoke. A 1.3% increase in daily mortality was observed for a 40 ppb increase in 1-hour maximum NO_2 levels. The effect of NO_2 was decreased but still significant after controlling for black smoke in multi-pollutant models. The associations observed for NO_2 were consistent across all cities studied. Daily average or 3-5 day average NO_2 levels were also strongly associated with daily mortality, with a 2% increase per 40 ppb increment in NO_2 concentration.

Hospital admissions and emergency room visits for cardiovascular and respiratory causes have also been associated with NO_2 levels in various studies. Poloniecki et al (1997) found an association between hospital admissions for cardiovascular disease in London and ambient NO_2 levels. Daily average NO_2 levels were associated with hospital admissions for acute myocardial infarction (winter only), arrhythmia and combined circulatory disease with a 2.7%, 2.7% and 2.4% increase per 29ppb increment in 24-hour NO_2 respectively. Daily average NO_2 levels ranged from 7.8 to 196 ppb with a median of 34.3 ppb.

Anderson et al (1997) have conducted a meta-analysis of the APHEA studies associating NO_2 exposure to hospital admissions for COPD. Analysis was also conducted for O_3, SO_2, black smoke and TSP. The associations were assessed for all pollutants across all age groups. An association was observed for both 24-hour average and daily 1-hour maximum NO_2 levels. A 1.9% increase in COPD admissions per 24.5 ppb increase in 24-hour NO_2 and 1.3% increase per 24.5 ppb increase in 1-hour maximum NO_2 were observed. The effects were only significant during the warm season. The strongest and most consistent association was found for 8-hour maximum O_3.

A similar meta-analysis on the APHEA results has been conducted by Sunyer et al (1997) for emergency room attendances for asthma. A significant positive association was found between 24-hour average NO_2 levels and emergency room attendances for adult asthma. No seasonal variation was observed. The observed effect was independent of the effect of black smoke. Controlling for black smoke in multi-pollutant models increased the effect of NO_2. A 2.9% increase in emergency room attendances per 24.5 ppb increase in 24-hour NO_2 was observed. 24-hour NO_2 levels ranged from 2.5 to 172 ppb.

Studies in children have found associations between the incidence and duration of respiratory illness and ambient NO_2 levels. An earlier study by Pershagen et al (1995) found an association between ambient NO_2 levels and wheezing bronchitis in children. The effects were stronger in girls than in boys. Wheezing bronchitis is a common cause of hospitalisation in infants and these children run an increased risk of developing asthma. For girls in the highest exposure category, 99th percentile 1-hour NO_2 greater than 34.3 ppb, the relative risk was 2.7. The association was strongest in girls less than 18 months of age. The mean time-weighted NO_2 levels in this study, expressed as 99th percentiles of 1-hour concentrations, ranged from 14.7 to 73.5 ppb.

Epidemiological studies when subjected to meta-analysis do indicate that in children exposed to long term background increases in NO_2 of the order of 14.7 ppb demonstrate an increase in risk of respiratory illness of approximately 20%. This effect is not seen in adults with similar exposures (Streeton, 1997).

Epidemiological studies on lung function response to NO_2 have shown that exposure to ambient levels of NO_2 causes decreases in FEV, FVC and PEF in asthmatic children. Effects in healthy children appear to be minimal. A considerable number of studies have investigated the lung function response to NO_2 in healthy subjects, asthmatics and to a lesser extent, patients with chronic obstructive pulmonary disease (COPD). These results have been quite variable over a wide range of concentrations.

3.1 Australian Studies

Morgan et al (1998a) found a significant positive association between daily average 24-hour NO_2 levels and daily mortality in Sydney. An increase in 24-hour NO_2 levels (lag 1) of 20ppb resulted in an increase of 2.66% (95% CI: 0.04 – 5.35) for all cause mortality. Particles and ozone were also found to be significantly associated with all cause mortality. A study in Brisbane (Simpson et al. 1997) found no associations between NO_2 and daily mortality.

A recent study conducted in Melbourne has shown that NO_2 is associated with increases in daily mortality (Simpson et al., 2000). Significant positive associations were found for both 1-hour and 24-hour maximum NO_2 and increases in all-cause, cardiovascular and respiratory mortality. The effects were strongest for the elderly (>65 years). Strong significant associations were also observed for ozone during the warm months. Controlling for other

pollutants indicated that the association of NO_2 with daily mortality was not independent of ozone but was independent of particles and CO. Mean 24-hour average NO_2 levels during the study period ranged from 1.1 to 33.8 ppb and 1-hour maximum values from 4.5 to 80.5 ppb.

A study conducted in Sydney (Morgan et al, 1998b) found an association between daily maximum 1-hour NO_2 levels and hospital admissions for asthma in children and COPD (chronic obstructive pulmonary disease) and heart disease in the elderly. The strongest effect was observed at zero lag. Effects were also found for particles and O_3 but the effects of NO_2 dominated. Associations were also found for 24-hour average NO_2 levels but these weren't as strong as those observed for the daily 1-hour maximum. A 5.29% increase in admissions for asthma in children was associated with an increase of 29 ppb in 1-hour maximum NO_2 levels. For the elderly a 4.60% and 6.71% increase in admissions for COPD and heart disease respectively were observed for the same increment in NO_2 levels. Daily maximum 1-hour NO_2 levels ranged from 14.7 to 44 ppb (10th to 90th percentiles) with a maximum of 137 ppb. In multi-pollutant models the association between NO_2 and admissions for asthma in children was increased after controlling for the effects of O_3 and particles. The effects of O_3 and particles were unchanged. For admissions for heart disease in the elderly, the association with NO_2 was unchanged but the effects of O_3 and particles decreased. For COPD the associations with both particles and NO_2 were decreased.

A study in Brisbane has also investigated the association between ambient NO_2 levels and hospital admissions for respiratory and cardiovascular disease for the period 1987-1994 (Petroeschevsky et al., 2000). No significant associations were observed in the whole year models, however, significant positive associations were observed in autumn, winter and spring for asthma admissions and admissions for respiratory disease. Associations were also observed for particles, ozone and sulfur dioxide. Daily average NO_2 levels ranged from 0.12 to 4.97 pphm and 1-hour maximum values from 0.35 to 15.58 pphm.

A study conducted in NSW to investigate the effect of emissions from power stations on asthma found no correlation between NO_2 levels and the prevalence of asthma in children (Henry et al., 1991). NO_2 levels in the vicinity of the power station (Lake Munmorah) were considerably higher than those in the control area (Nelson Bay) with yearly average levels of 0.98 ppb and 0.15 ppb at Lake Munmorah and Nelson Bay respectively. Maximum hourly averages were 82.8 ppb and 36.8 ppb at Lake Munmorah and Nelson Bay respectively.

Pilotto 1994 reviewed respiratory symptom diary cards for a cohort of school children in NSW living in homes with gas-appliances or attending gas-heated schools, and compared their scores with those for children not in these conditions. The children were regarded as being exposed to NO_2 if the mean daily-timed NO_2 levels were above 0.04 ppm, and with spike levels of the order of 0.08 ppm or higher compared to background levels of 0.02 ppm or less in non-gas atmospheres. Pilotto observed that there was a significant increase in 'non-zero' symptom scores for colds and/or absenteeism, likewise for sore throats, cough with sputum, and lower respiratory tract infections involving cough and sputum. There was also a suggestion of an increased response effect with increasing spike levels of NO_2 exposure.

3.2 Summary

Exposure to NO_2 has been associated with increases in daily mortality, hospital admissions and emergency room attendances for cardiovascular and respiratory disease, increases in respiratory illness and symptoms and decreases in lung function. The elderly, asthmatics, children and people with existing disease are particularly susceptible to the effects of NO_2.

4. OZONE

Ozone is a highly irritating substance that has significant effects on various parts of the respiratory tract. The health effects associated with exposure to ozone range from minor changes in lung function, irritation of the airways leading to an increase in medication usage, increases in respiratory symptoms such as cough, and chest pain on inspiration through to increases in hospital admissions and emergency room attendances for respiratory and cardiovascular disease. Increases in daily mortality, mainly from cardiovascular and respiratory causes, have also been associated with exposure to ozone.

Subgroups within the population that are susceptible to the effects of ozone include the elderly and asthmatics, however, healthy individuals, including elite athletes, have shown adverse effects on exposure to ozone.

Much of information available on the health effects of ozone has been derived from studies investigating short-term, or acute, effects. Early clinical studies evolved from reports of irritant symptoms and respiratory effects in workers. Workers who were exposed to elevated levels of ozone showed decreases in lung function and chest pain on inspiration. Some of these effects could be reproduced in controlled human exposure studies. These effects have subsequently been shown to occur in the general population. The acute effects of ozone appear to be reversible and there is some evidence that an adaptation process may occur in both animals and humans. The effects of repeated exposures are still unclear.

A number of studies have been published which relate ambient ozone levels to increases in daily mortality (Touloumi et al, 1997; Sartor et al, 1997; Borja-Arburto et al, 1997; Simpson et al, 1997; Loomis et al, 1996). The most consistent associations have been observed for mortality from cardiovascular causes in the elderly. Data on daily mortality and O_3 were obtained for the APHEA cities of Athens, Barcelona, London, Lyon and Paris (Touloumi et al, 1997). As part of a meta-analysis, data were also obtained for Amsterdam, Basel, Geneva and Zurich (which were not originally examined in the APHEA project). Effects for O_3 were found to be greatest in London, where a 25ppb increase in O_3 was associated with an 8.6% increase in risk of death (all causes). A meta-analysis conducted on the results from all cities found a 2.9% (95% CI: 1 – 4.9%) increase in daily mortality associated with a 25ppb increase in daily 1-hour maximum O_3.

In the meta-analysis of the APHEA studies the association was greater for mortality from cardiovascular causes than from respiratory disease. The O_3 association remained significant with the inclusion of other pollutants, although the effect was slightly reduced with the inclusion of black smoke. The authors concluded that the results of the meta-analysis support the hypothesis of a causal relationship between increases in O_3 concentrations and daily mortality. Mean 1-hour O_3 levels in these studies ranged from 7 to 44ppb.

A study from Belgium has also shown an association between ozone has been found increases in daily mortality in the elderly (Sartor et al., 1997). A significant positive association was observed between 24-hour average O_3 levels and daily mortality with the strongest association observed for the daily average O_3 of the previous day. A 12.5% increase in all cause mortality was associated with a 25 ppb increase in daily average ozone concentration. The associations observed in this study were dependent on temperature.

The association between daily mortality and O_3 has been extensively studied in Mexico City (Borja-Arburto et al, 1997; Loomis et al, 1996). In single pollutant models a significant positive association was observed between daily 1-hour maximum O_3 and daily mortality. The effects were greatest for cardiovascular disease in the elderly. The association with cardiovascular disease remained after controlling for TSP although the effect estimate was slightly reduced. The association with cardiovascular disease was dependent on different averaging times with the strongest association observed for 24-hour and 8-hour averages.

The UK Department of Health has recently reviewed the health effects attributed to ozone exposure (UK Department of Health, 1998). Using the data from the APHEA studies it was estimated that 12,500 premature deaths per year could be attributed to O_3 levels in the UK. This estimate was based on the assumption that no threshold exists for the effects of O_3 on daily mortality.

There have been many studies relating an increase in hospital admissions for respiratory and cardiovascular disease with ambient O_3 levels. Extensive reviews of these studies have been conducted (UK Department of Health, 1998; Streeton, 1997; US Environmental Protection Agency, 1996; Bascom et al, 1996). The strongest effect of ozone on admissions is usually observed on a day subsequent to a high level of ozone exposure. These studies do not give an indication of a safe level of exposure.

Recent studies have confirmed the findings of earlier studies. Anderson et al (1997) have conducted a meta-analysis of the APHEA studies associating O_3 exposure to hospital admissions for COPD. Analysis was also conducted for NO_2, SO_2, black smoke and TSP. The associations were assessed for all pollutants across all age groups. The strongest and most consistent association was found for 8-hour maximum O_3. The relative risk per 23.5 ppb increase in 8-hour maximum O_3 was 1.04 (95% CI: 1.02-1.07). The effect was stronger in the warm season. These results are similar to those observed in Canada and the US. Maximum 1-hour O_3 levels were also associated hospital admissions for COPD with a relative risk per 23.5 ppb increase in 1-hour maximum O_3 of 1.029. Median 8-hour maximum and 1-hour maximum O_3 levels in this study ranged from 4.2 to 38.5 ppb and 9.4 to 42.8 ppb respectively.

A similar meta-analysis of the APHEA studies has been conducted for hospital admissions for respiratory disease (Spix et al, 1998). This study looked at two age groups – 15-64 years and over 65 years. The most significant association found was for 8-hour average ozone across both age groups, however the association was stronger in the elderly (over 65 years). The associations were observed for both same day and previous day exposure. For the 15-64 year age group the relative risk per 23.5 ppb increase in 8-hour average O_3 was 1.03 and for the over 65 year age group 1.04. The effects were greatest during the warm season. Using the effect estimates for admissions for respiratory disease obtained from the APHEA studies, the UK Department of Health estimated that 9900 hospital admissions per year could be attributed to ambient O_3 levels in the UK (UK Department of Health, 1998).

A study from Canada has examined the association between hospital admissions for respiratory disease and O_3 in 16 Canadian cities (Burnett et al, 1997a). A significant positive linear association was observed between previous day 1-hour maximum O_3 levels and hospital admissions for respiratory disease. The association remained after controlling for NO_2, SO_2, particles, CO and dew point temperature. No association was observed during winter. A relative risk per 28.2 ppb increase in 1-hour daily maximum O_3 levels of 1.042 was observed. Controlling for CO had no effect on the association but inclusion of a dew point temperature in the model attenuated the effect of O_3 marginally with a relative risk of 1.031 per 28.2 ppb

increase in 1-hour daily maximum O_3 level. The observed effect was similar in the elderly as in the total population. Mean daily maximum 1-hour O_3 levels ranged from 26.3 ppb (winter) to 40.4 ppb (summer).

A study by Korrick et al., (1998) found that low level exposures to ozone was associated with decreases in lung function in healthy adult hikers. The effects were stronger in hikers that had a history of asthma or wheeze with a four-fold greater responsiveness to ozone observed. Average ozone exposures ranged from 21 to 74 ppb. After controlling for confounding variables a 2.6% decline in FEV_1 (95% CI: 0.4-4.7) and a 2.2% decrease in FVC (95% CI: 0.8-3.5) was observed for each 50 ppb increment in mean O_3. Associations were also observed for $PM_{2.5}$ and aerosol acidity.

Recent epidemiological studies have investigated the long term, or chronic, effects associated with exposure to ozone. A study by Beeson et al., (1998) showed an association between long term exposure to ozone and an increase in the incidence of lung cancer in non-smoking males. This study followed a cohort of non-smoking adults over a period of 15 years. The relative risk, RR, per 100 ppb increase in ozone concentration was 3.56. No associations were observed between ozone and the incidence of lung cancer in females. In a similar study, Abbey et al., (1999), a strong association was found between exposure to ozone and lung cancer mortality.

The impact of long term exposure to ozone on lung function has also been investigated (Frischer et al, 1999). This study followed a cohort of children for a period of 3 years in Austria. Exposure to ozone was associated with decreases in the lung function indicators examined, FVC, FEV_1 and MEF_{50}. No associations were found for NO_2, SO_2 or PM_{10}. Annual average ozone levels in this study ranged from 18 to 40.7 ppb.

Gong et al., 1998 and Kunzli et al., 1997 have investigated the effects of long-term O_3 exposure and loss of lung function. The study by Kunzli et al (1997) looked at the association between lifetime ambient O_3 exposure and lung function in college freshman who were lifetime residents in either northern (San Francisco) or southern (Los Angeles) California. Monthly ambient O_3 exposures were based on the lifetime residential history for each subject, which were adjusted for time spent outdoors and time spent in moderate or heavy activity. Two measures of O_3 were used in this study – 8-hour average (10am to 6pm) and hours above 61 ppb. The results of this study showed that for a 20.2 ppb increase in lifetime 8-hour mean O_3 concentration there was a 14% decrease in late forced expiratory flow ($FEF_{0.75}$) and 7.2% decrease in $FEF_{0.25-0.75}$ from the population mean. Lifetime 8-hour average O_3 concentrations ranged from 16 to 75 ppb. The lung function measures used in this study are both small airway flow measures and are considered as early indicators for pathologic changes that might ultimately progress to chronic lung disease. No effects were observed for FVC or FEV_1, which are better indicators of large airway dysfunction.

The relationship between acute O_3 responsiveness and chronic lung function loss has been investigated in a high O_3 community (Gong et al, 1998). The lung function measures used in this study were FVC and FEV_1. The results of this study showed that there was no rapid decline in lung function due to chronic exposure to high levels of O_3 in this cohort. Daily maximum O_3 levels during the study period reached as high as 390 ppb with a maximum annual average of 136 ppb. The authors concluded that no firm conclusions could be drawn from this study and that further work was required to elucidate the chronic effects of O_3 exposure.

4.1 Australian Studies

A study conducted in Brisbane for the period 1987 to 1993 found a significant association between daily all cause mortality and O_3 (Simpson et al, 1997). The significance of the association was not altered by the addition of other pollutants (in the form of high-pollution dummy variables) into the model. A 10ppb increase in average 8-hour O_3 was associated with a 2.4% increased risk of death (all causes). The corresponding increased risk associated with the 1-hour maximum concentration was 1.6%. Although positive associations were also found for cardiovascular and respiratory deaths in the Brisbane study, they were not statistically significant. The results of the Brisbane study also indicated a possible threshold for the effects of O_3 occurring in the highest quintile of data (1-hour maximum O_3, range 31-102ppb, mean 42ppb). Daily maximum 1-hour O_3 concentrations ranged from 2.5 to 101.5ppb with a mean of 24.2ppb. Daily maximum 8-hour O_3 concentrations ranged from 1.7 to 63.4ppb with a mean of 18.1ppb.

The impact of air pollution on hospital admissions has also been investigated in Brisbane (Petroeschevsky et al., 2000). Ozone was consistently associated with admissions for asthma and respiratory disease, with little evidence of a threshold. Control for the effects of other pollutants had little effect on the size of the effect estimate for ozone. Effects were greatest for 8-hour ozone, with a 2.3% increase in admissions for total respiratory admissions per 10ppb in ozone concentration observed. A 9% increase in total asthma admissions was associated with a 10ppb increase in 5-day average 8-hour ozone concentration.

A study conducted in Sydney also found an association between ambient O_3 levels and daily mortality (Morgan et al., 1998a). In the Sydney study a 2.04% increase in all cause mortality was associated with an increase of 30ppb in 1-hour maximum O_3 levels. This association lost significance after controlling for other pollutants in the model. A further study looking at the impacts of air pollution on hospital admissions found a positive, non-significant, association between 1-hour maximum ozone levels and admissions for heart disease in the elderly (Morgan et al., 1998b).

A recent study conducted in Melbourne found a strong association between exposure to ozone and increases in daily mortality (Simpson et al, 2000). The results of the Melbourne study, where a 4.5% increases in all cause mortality was associated with a 25 ppb increase in 1-hour maximum O_3, are consistent with the results of the APHEA study. The association with deaths from respiratory disease was stronger than that for all cause mortality, with an 8.8% increase in daily respiratory mortality per 25ppb increase in same day 1-hour maximum O_3 concentration observed. A similar result was found for all cause mortality in the elderly where an 8.6% increase in mortality was found to be associated with a 25ppb increase in same day 1-hour maximum O_3 concentration.

4.2 Summary

Exposure to ozone has been associated with increases in daily mortality, increases in hospital admissions and emergency room visits (respiratory and cardiovascular disease), decreases in lung function, increases in symptoms of respiratory illness such as cough, phlegm and wheeze, and increases in bronchodilator usage. These effects are observed in sensitive sub-populations although effects on lung function have been observed in the healthy normal population.

5. PARTICLES

Unlike the other criteria pollutants, particles are a broad class of chemically and physically diverse substances. They exist as discrete particles spanning several orders of magnitude in size, 0.005 to 100 μm. They are emitted from a wide range of sources including natural sources such as dusts and pollens. The biological effects of particles are determined by:

- the physical and chemical nature of the particles;
- the physics of deposition and distribution in the respiratory in the respiratory tract; and
- the physiological events that occur in response to the presence of the particle.

The health effects of particles include increases in daily mortality, hospital admissions and emergency room attendances, and exacerbation of respiratory symptoms and asthma. These effects have been found in studies in many parts of the world with differing climates and socioeconomic factors.

The early studies into the health effects of particles were conducted mainly in the USA. These results of these studies were fairly consistent across the US. The dose response relationships derived from these studies are summarised in Table 1.

Table 1: Dose-Response Relationships Derived from US Studies

	Percentage Change in Health Indicator Per 10 μG/M³ Increase in PM_{10}
Daily Mortality (all cause)	1.0
Hospital Admissions	
Respiratory Disease	1.96
COPD	3.26
Pneumonia	1.42
Heart Disease	0.4
Exacerbation of Asthma	3.0

The US studies have been used to make some compelling arguments in support of a causal link between short-term increases in particle pollution and adverse health effects. These studies have been conducted in settings with substantial variability in type and concentrations of co-pollutants and meteorology, with the only consistent factor being the particle concentration. Studies from the eastern US and Canada have had to deal with a mix of summer pollutants which include particles, SO_2 and O_3, as well as acid aerosol. Concentrations of these pollutants are correlated to a greater or lesser extent depending on the setting.

More recent studies conducted in Europe as part of the Air Pollution and Health: A European Approach (APHEA) have shown that although associations are observed between particles and adverse health effects, the results are not as consistent as those observed in the US studies. In general the effect estimates observed in the UK and Europe are lower than those observed in the USA. The reason for this is unclear but may be due to high levels of acid aerosols in the USA, or possibly the use of black smoke in the UK and European studies (UK Department of Health, 1998). The differences observed in the results from the studies in different parts of the world suggest that the dose response relationships determined within a particular country or region may not be readily transferable to other areas.

Recent work conducted in the US as part of the National Morbidity, Mortality and Air Pollution Study (NMMAPS) (Samet et al., 2000) has investigated the association between particles and daily mortality in 20 US cities. The results of this study have shown that there is substantial between location variability in the observed associations and effect estimates. Combining the results of the individual analyses yielded an overall effect estimate for the cities studied of 0.34% per 10 $\mu g/m^3$ in daily PM_{10}. The results of this study also found that the observed associations were more similar for locations close to each other than for cities further away. There is evidence that the association between PM_{10} and mortality in the western US was larger than in the east or south. A similar analysis is currently being undertaken for 90 US cities.

In spite of the large body of literature on the health effects of particles there are still questions regarding the biological mechanisms responsible for the observed effects. Confounding by other pollutants is one issue that is often raised – are particles really the culprit? Which size fraction is important – PM_{10}, $PM_{2.5}$, ultrafine particles or all size fractions – in explaining the observed effects. What role does the composition of the particle play – are crustal particles less damaging than combustion particles – is another question that is often raised.

Attempts to attribute effects to only one pollutant have prompted questions as to whether it is possible to do so. However, the US studies include those performed in settings where there is only minimal concern about the effects of these co-pollutants. For example, the Utah Valley experiences high levels of particles during the winter months that arise mainly from a local steel mill, and very low SO_2 levels. Ozone is only of concern during the summer and therefore does not confound the effects of particles during winter. As the population is predominantly a Mormon community they have a very small proportion, approximately 6%, of the population who smoke.
The studies conducted in this area have looked at increases in daily mortality, hospital admissions, decreases in lung function, increases in respiratory symptoms and increased school absenteeism using a variety of statistical methods. The dose-response relationships derived from these studies are summarised in Table 2.

Table 2: Dose-Response Relationships Derived from Utah Valley Studies

	Percentage Change in Health Indicator Per 10 $\mu G/M^3$ Increase in PM_{10}
Daily Mortality	
All cause	1.5
Respiratory disease	3.7
Cardiovascular disease	1.8
Hospital Admissions	
Respiratory disease	3 to 7.1

As shown in Table 2, the dose-response relationships obtained from the Utah Valley are higher than those obtained from the US as a whole. These findings have provided strong evidence that that there is an independent effect of particles on health.

Recent studies conducted in Helsinki (Ponka et al., 1998), Coachella Valley, California (Ostro et al., 1999) and Phoenix, Arizona (Mar et al., 2000) have indicated that the coarse fraction of

PM_{10}, $PM_{10} - PM_{2.5}$, are associated with increases in daily mortality. These studies have been conducted in areas where the PM_{10} levels are dominated by crustal particles in the coarse fraction of PM_{10}.

There is a considerable amount of research currently underway to investigate the potential mechanisms by which particles may cause adverse health effects. A large amount of this work has been focussed on the effects on the cardiovascular system. Godleski exposed dogs to 100 to 200 $\mu g/m^3$ of fine particles in an exposure chamber for 6 hours per day for 3 days (Godleski et al., 1997). The results of this study showed electrocardiogram changes in the dogs that are risk factors for arrhythmia. Instillation of 250 µg of combustion particles into the lungs of rats produced arrhythmia and deaths (Watkinson et al., 1998). In humans particles have been associated with increases in plasma viscosity (Peters et al., 1997), increased risk of elevated heart rate (Pope et al., 1999) and changes in heart rate variability (Shy et al, 1997; Schwartz et al, 2000).

5.1 Australian Studies

In Australia, the association between daily mortality and air pollution has been investigated in both Sydney and Brisbane (Morgan et al, 1998a; Simpson et al, 1997). Sydney and Brisbane, like most Australian cities, experience very low levels of SO_2 which means that confounding by this pollutant is unlikely. In the Sydney study (Morgan et al., 1998a) nephelometry data, which is an indicator of fine particles, was found to be associated with all cause, respiratory and cardiovascular mortality. The results showed a 2.6% increase in daily mortality was associated with an increase in PM_{10} of approximately 25 $\mu g/m^3$. Daily mortality was also found to be associated with O_3 and NO_2, but when all pollutants were considered in the same model, the effect of particles dominated.

The mortality study conducted in Brisbane (for the period 1987 to 1993) found similar results (Simpson et al, 1997). Significant positive associations were found for daily mortality and fine particles (bsp, measured by nephelometry) and O_3. Maximum 1-hour and 8-hour bsp as well as 1-hour and 8-hour O_3 were associated with total mortality, especially in the summer. The effects of SO_2 and NO_2 on daily mortality were not significant. When all pollutants were considered in the model, O_3 and particles remained significant suggesting that the effects were independent. The associations were more significant for the elderly and for mortality from cardiovascular causes. An increase in fine particle levels corresponding to a 10 $\mu g/m^3$ increase in PM_{10} was associated with an increase in daily mortality of between 1.2 to 1.3%.

A recent study conducted in Melbourne (Simpson et al., 2000) found that ambient particle levels in Melbourne were not significantly associated with daily mortality in whole year models. In contrast however, significant associations were observed with same day 1-hour maximum and 24-hour average bsp in the warm season. These effects were observed for all cause and respiratory mortality in the all ages and 65+ age groups. No significant associations were observed for cardiovascular mortality in either of the age groups examined.

An earlier study conducted in Melbourne investigated the association between asthma attendances at the Emergency Department of the Royal Children's Hospital and nephelometry data from the EPA's air monitoring network (Rennick and Jarman, 1992) during smog days. Peak asthma attendances occurred during the winter months. A statistically significant association was found between asthma attendances and days with high levels of fine particles (reported as API). A lag effect was noted with associations observed up to 2 days after the occurrence of a smog day. Asthma attendances were also associated with API levels up to 2

days prior to the smog day. No association was found between asthma attendances and ozone levels during summer smog periods.

Hospital admissions for COPD and heart disease in Sydney have found to be associated with daily maximum 1 hour fine particle levels as measured by nephelometry (Morgan et al., 1996) for the period 1990-1994. Increases of 3% for COPD and 2.5% for heart disease have been found for an increase in particle levels, PM_{10}, of approximately 25 $\mu g/m^3$.

A study in conducted in Brisbane found significant positive associations between ambient particle levels and hospital admissions for asthma and respiratory disease in summer (Petroeschevsky et al., 2000). These effects were observed in the 15 to 64 age group and for total admissions. After controlling for other pollutants the association observed for the 15-64 age group lost significance.

A further study in Brisbane found that rural dust events impact on asthma severity in Brisbane (Rutherford et al., 1999). This study investigated the effects of dust storms on hospital emergency attendances and PEF and respiratory symptoms as recorded through a diary study. The results indicated that a number of dust events were associated with changes in asthma severity, but general relationships could not be determined.

Corbett et al, (1996) investigated hospital admissions and emergency room attendances for asthma during the NSW bushfires which occurred in 1994. During the 8 day period of the fires, PM_{10} levels were consistently high and peaked at 250 $\mu g/m^3$. No increase was observed in hospital attendances or emergency room attendances during the bushfire period, but this may have been due to the short duration of the event that may not allow for small changes to be detected.

A further study investigating the health effects of particles associated with the bushfires found no association between decreases in peak expiratory flow rates (PEFR) in children (Jalaludin et al., 2000). Children with a history of wheeze were enrolled in a longitudinal study and completed a daily asthma diary. No significant associations were found between mean PM10 and PEFR. The maximum daily PM_{10} level peaked at 210 $\mu g/m^3$.

A large study was conducted in Launceston and the Upper Tamar Valley, Tasmania, during 1992 and 1993 to assess the impact of air pollution in the region on respiratory health (Lyons et al, 1996). Launceston experiences high particle levels during the winter months due to a combination of meteorology and woodsmoke from domestic heating. Hospital admissions data for asthma, bronchitis and COPD were assessed together with two control non-respiratory conditions - appendicitis and myocardial infarction. PM_{10} measurements were collected and averaged over 5 sites in the Launceston area. Hospital admissions for respiratory disease were found to be higher in winter and exhibited a general upward trend between 1991 and 1993. Air pollution levels are also higher during the winter months. Statistical analysis showed no correlation between the hospital admissions data and PM_{10} levels in Launceston. Similar results were found for emergency room attendances. This finding needs to be interpreted carefully due to the small amount of air monitoring data (PM_{10} was collected on an "every-6-day- cycle" for a 3 year period) and the small study population.

A diary study was conducted in Brisbane on behalf of the Asthma Foundation in Queensland, to investigate the association of bioaerosols and air pollution on the incidence of asthma (Simpson et al, 1995). Between 100 and 120 subjects with asthma kept daily diaries of

symptoms, lung function (PEF) and medication use for the period April 1994 to September 1995. Hospital attendance data was also collected during this period. Preliminary results have shown a significant association during the spring between the incidence of asthma severity with elevated levels of particles and pollen. Biomass burning during this period is a major source of respirable particles. No association was found between asthma and particles during the winter months when particle levels are at the lowest levels. Weak, but significant, effects were noted during the autumn period. Particles were measured as PM_{10} and bsp (light scattering coefficient from nephelometry data) and the strongest association between asthma severity and particulate air pollution appeared to be with PM10: bsp was correlated at only one site during 1994. Time series analysis has shown that PM_{10} at both Brisbane South and Ipswich and bsp at Ipswich are associated with decreases in PEF.

Respiratory symptoms in children have been associated with PM_{10} levels in Newcastle and Wollongong in NSW, Australia (Lewis et al., 1998). Statistically significant associations between particle levels and chest colds and night-time cough were observed in children aged between 8 and 10 years. For a 10 $\mu g/m^3$ increment in annual average PM_{10} levels odds ratios of 1.43 for chest colds and 1.34 for night-time cough were observed. There was no significant association observed for SO_2 for any of the health outcomes investigated. Annual average PM_{10} levels ranged between 18.6 and 43.7 $\mu g/m^3$ across the study regions. Excluding the areas with the highest PM_{10} levels increased the odds ratio for chest cold, 2.05 compared with 1.43 for the whole area. The authors concluded that this result suggests that the dose-response curve for PM_{10} and chest colds is curvilinear and much steeper at lower pollution levels.

5.2 Summary

Epidemiological studies show a correlation between exposure to particles and adverse health effects. At this time there is no conclusive evidence regarding the role of particle size in the response. Different sizes may be important for different health outcomes, for example, $PM_{2.5}$ for mortality, PM_{10} for asthma. The evidence of chronic health effects arising from long-term exposure to particles is not clear. The studies showing an effect are currently under review in the US.

At this time the results of toxicological studies are indicating that crustal particles can be as damaging as combustion particles for a given size range. There is no clear evidence of a role for particle composition. The biological mechanisms giving rise to the effects observed in epidemiological studies are still unclear although some information is emerging regarding a possible mechanism for cardiovascular effects.

There is no evidence, based on epidemiological data, that there is a threshold concentration of either PM_{10} or $PM_{2.5}$ below which adverse health effects will not be observed. The differences observed in the results from the studies conducted in different parts of the world suggest that the dose response relationships determined within a particular country or region may not be readily transferable to other areas.

6. SULFUR DIOXIDE

The health effects of SO_2 have been recognised for many years. High SO_2 and particle concentrations have been associated with increased mortality and morbidity in air pollution episodes such as those experienced in London, (1952), Meuse Valley, Belgium, (1930s), and Donora, Pennsylvania. Early analyses of these episodes were unable to separate the effects of individual pollutants.

Most information on the acute effects of SO_2 has arisen from controlled human exposure studies. These studies have involved the exposure of volunteers to SO_2 for periods ranging from a few minutes up to one hour. The results of controlled exposure studies have been reviewed extensively (Bascom et al., 1996; US EPA, 1982, 1986). Acute responses occur within the first few minutes after inhalation. Further exposure does not increase the observed effects. Observed effects include reductions in mean forced expiratory volume over one second (FEV_1), increases in specific airway resistance (sRAW), and symptoms such as wheezing or shortness of breath. These effects are enhanced by exercise. Asthmatics appear to be the most susceptible group to the effects of SO_2. Recent studies have shown that exercising asthmatics are sensitive to brief exposures to SO_2 with bronchospasm occurring at exposures as low as 0.25 ppm SO_2. Such exposures lead to immediate responses and do not appear to cause delayed or prolonged effects.

Recent epidemiological studies have revealed increases in daily mortality from respiratory and cardiovascular causes associated with current ambient SO_2 levels found in various parts of the world. In addition, associations between daily hospital admissions for asthma, chronic obstructive pulmonary disease (COPD) and respiratory disease have also been observed. These effects persist when other pollutants, such as particles, are controlled for. No obvious threshold for the health effects associated with SO_2 has been identified.

Studies into the long-term health effects of SO_2 investigated the associations between ambient levels of SO_2 and prevalence of respiratory symptoms, respiratory illness frequencies or differences in lung function in locations with differing levels of SO_2 and particles (WHO, 1999a). These studies are complicated by the fact that long-term effects are liable to be affected by not only current conditions but by pollution levels and composition that may have differed in earlier years. Cohort studies looking at differences in daily mortality across areas with differing pollution levels have found that the associations are more closely associated with particles than with SO_2. As elevated SO_2 levels are usually associated with elevated particle levels these effects are often difficult to separate.

Some recent studies have shown effects on chronic respiratory symptoms associated with long-term exposure to SO_2. A study in Chile (Sanchez-Cortez, 1997) found that the prevalence of chronic respiratory symptoms was greater in the area with higher annual average SO_2 levels (30% versus 14% for chronic cough and 14.3% versus 6.1% for wheezing). PM_{10} levels were low in both areas. The annual average SO_2 levels were 45.5 ppb versus 24.5 ppb.

Studies of Japanese school children have shown that annual average SO_2 levels are associated with the prevalence of asthmatic symptoms, chest congestion and phlegm (Nitta et al., 1993; Ono et al., 1990; Nakai et al., 1995). Annual average SO_2 levels ranged from 9.4 to 10.8 ppb in urban areas to 4.7 to 8 ppb in background areas.

A study by Chen et al., (1993), found that an annual average SO_2 level of 49 ppb was associated with a lower level of lung function in children aged 10-12. Major decreases were observed in FVC and FEV_1. Similar effects were seen in female adults.

6.1 Australian Studies

Given the low levels of SO_2 in Australian cities, only a limited number of studies have been conducted to investigate the health effects associated with exposure to SO_2. The studies have focussed in areas that are influenced by industry.

A study conducted in New South Wales to investigate the effects of emissions from power stations on asthma found no correlation between SO_2 levels and the prevalence of asthma in children (Henry et al 1991). Sulfur dioxide levels in the vicinity of the power station (Lake Munmorah) were considerably higher than in the control area (Nelson Bay). Yearly average levels of SO_2 were 0.7 and 0.11 ppb at Lake Munmorah and Nelson Bay respectively. Maximum daily averages were 9 and 3.9 ppb at Lake Munmorah and Nelson Bay respectively, with maximum hourly averages of 48.7 and 15.1 ppb.

Another study from New South Wales by Lewis et al (1998) assessed the respiratory health of children aged 8 to 10 living in the Hunter and Illawarra regions in relation to local air pollution. The Hunter and Illawarra regions are influenced by the steel industry in Newcastle and Wollongong. No significant effects were observed for SO_2, but PM_{10} was associated with a significant increase in chest colds (odds ratio, OR 1.43 [1.12 - 1.82]), and night cough (OR 1.34 [1.19 - 1.53]). Sulfur dioxide levels ranged between 1.6 - 9 ppb (mean annual average), and PM_{10} ranged between 18.6 - 58.3 $\mu g/m^3$ (annual average). The results also indicated that passive smoking was significantly associated with chest colds and a history of maternal allergy with all respiratory symptoms, but most strongly with wheeze.

A study conducted in Mt Isa to study the effects of short-term SO_2 peaks on hospital presentations for asthma found no evidence of any positive association (Donoghue and Thomas, 1999). Annual average SO_2 in Mt Isa are less than 7 ppb with peaks as high as 3045 ppb.

Significant positive associations were found for hospital admissions for respiratory and cardiovascular disease and ambient SO_2 levels in Brisbane (Petroeschevsky et al., 2000). Levels of SO_2 in Brisbane are generally low due to the low number of significant point sources in the area. On no occasion over the 8-year study period did SO_2 levels approach current or proposed air quality standards. Despite these low levels, significant positive associations were found for respiratory admissions in the 0-4, 65+ and all ages groups, and for cardiovascular admissions in the 15-64 age group. Effect sizes ranged from an 8% increase in risk of admission (respiratory, all ages) to a 22% increased risk of admission (respiratory, 0-4) per 10 ppb increase in SO_2. Few significant seasonal variations in the impact of SO_2 were observed. 24-hour SO_2 levels ranged from 0 to 35.5 ppb and 1-hour maximum levels from 0 to 66.8 ppb during the study period.

6.2 Summary

Ambient levels of SO_2 have been associated with increases in daily mortality, hospital admissions and emergency room attendances for respiratory and cardiovascular disease and respiratory symptoms and decreases in lung function. These associations have been observed in epidemiological studies in various parts of the world. Due to the high correlation between ambient SO_2 levels and other pollutants, especially particles, it is difficult in this type of study to confidently attribute the observed effects to SO_2 alone. Experimental evidence demonstrates that brief exposures to high levels of SO_2 can cause transient bronchoconstriction and symptoms in some patients with asthma who exercise during the exposure.

7. LEAD

Studies of the health effects of lead exposure have been noted for many years and have been extensively reviewed (WHO 1995; Bascom et al 1996; Needleman and Bellinger 1991). Lead is absorbed after being inhaled or ingested. It can result in a wide range of biological effects depending on the level and duration of exposure. Its toxicity can largely be explained by its interference with different enzyme systems, which it affects in a number of ways. It is for this reason that lead exposure may result in a very wide range of adverse health effects. Effects at the subcellular level, as well as effects on the overall functioning of the body, have been noted and range from inhibition of enzymes to the production of marked morphological changes and death (WHO, 1995).

Absorbed lead is distributed among the soft tissues (blood, liver, kidneys, brain etc) and 'mineralising' systems (teeth and bones). Bones form the major lead storage site in the body, and lead accumulates in the bones over a person's lifetime (WHO, 1995). Because of retention of lead in bone, conditions associated with increased bone catabolism may lead to increased circulating blood lead even when environmental exposures have been reduced or eliminated (Streeton, 1997).

The concentration of lead in whole blood has gained almost universal acceptance as the best available surrogate for cumulative exposure, and surveys of blood lead concentration have come to be regarded as measuring community exposure (Donovan, 1996). The concentration of the lead in blood is usually expressed in micrograms per decilitre (µg/dL).

Foetuses, babies and children (especially those below the age of 4) are considered to be more susceptible to the adverse effects of lead exposure than adults. The reasons for this include their smaller body size (they eat and drink more per unit of body weight than adults so their relative lead intake is increased) and higher rates of gastrointestinal absorption (approximately 50 per cent compared with 10 per cent in adults). A greater prevalence of nutritional deficiencies, such as iron and Vitamin D, which enhance absorption of lead, incompletely developed nervous systems (neurological effects of lead occur at lower thresholds than in adults) and higher rates of and rapid growth (WHO, 1995; Streeton, 1997) also influence the susceptibility of children.
Children up to the age of 4-6 are also considered to be a group at increased risk of exposure due to a range of behavioural characteristics. These include the greater amount of time they spend outdoors, hand to mouth behaviours (such as thumb sucking) and possibly pica. Pica is the compulsive, habitual consumption of non-food items, and where these include dust and paint chips, lead consumption can be significantly increased. Much of the lead poisoning caused by lead based paint has been found to occur because children actively eat paint chips (US EPA, 1986).

Over the past two decades, attention has focused on children as a risk group for central nervous system (CNS) effects, at increasingly lower levels of exposure. As a global measure of CNS-functioning, intelligence quotient (IQ) has received particular attention in such studies. Some analyses have shown that a blood lead increase from 10 µg/dL to 20 µg/dL may be associated with an IQ drop of 1-3 points (Schwartz, 1994; Pocock et al, 1994; WHO, 1995). At blood lead levels greater than 25 µg/dL this relationship may differ (Streeton, 1997).

Existing epidemiological studies do not provide definitive evidence of a threshold (WHO, 1995; Donovan, 1996). Some research suggests that below a blood lead level range of 10-

15µg/dL there is increasing uncertainty attached to identified effects (WHO, 1995). Children subject to such exposures may also show impairment of motor abilities, visual attention and spatial skills, and of their memory for sights or sounds. Greater amounts of blood lead correlate statistically with low levels of educational achievement in reading, spelling and mathematics in some studies (Sciarillo et al, 1992; Needleman et al, 1992). There is some evidence that these effects are persistent and may be irreversible where exposure occurs up to age seven (WHO, 1995).

Lead is foetotoxic. Since the placenta is not an effective biological barrier to lead, pregnant women represent a second group at increased risk because of exposure of the foetus to lead (WHO, 1995). It should be noted that it is not the pregnant women *per se* who are at increased risk, but rather the foetus. Umbilical cord studies involving mother-child pairs have shown a correlation between maternal and foetal blood lead levels (US EPA, 1986). In some studies on pregnant women, blood lead levels above 15 µg/dL have been associated with premature birth and low birthweight babies (Streeton, 1997). The adverse effects of very high lead concentrations in maternal blood on pregnancy outcome are well documented and include sterility, spontaneous abortion and stillbirth. These effects are generally undisputed (Baghurst et al, 1987). The effect of low-level lead exposure on pregnancy outcomes has been reviewed by O'Halloran and Spickett (1992/1993). Preterm delivery, congenital abnormalities, growth stature and birth weight may all be affected by maternal blood lead levels.

Several recent investigations suggest an association between high blood pressure and elevated blood lead levels (Schwartz 1995; Staessen et al 1994; Nowack et al 1992). Lead exposure has also been suggested as being associated with chronic renal disease (Nuyts et al 1991) and nephrotoxicity (Nolan et al 1992).

Based on IQ effects in children the LOAEL and level of concern for lead is 10µg/dL.

7.1 Summary

The adverse health effects of lead exposure are varied. Some recent studies have indicated that adverse health effects may be observed at blood lead levels lower than those previously considered to be safe especially in regard to impairment of neural development, intellectual capacity, leading to behavioural and learning difficulties.

The effects of lead exposure during childhood have been shown to continue into later life with mortality effects in adult life attributed to childhood lead poisoning. Lead exposure has also been associated with increased body mass index and short stature. Preterm delivery, congenital abnormalities, growth stature and birth weight have all been identified as being affected by maternal blood lead levels.

Associations between blood pressure and blood lead levels have also been observed. These effects have been observed in both men and women, and may result in the longer term in increased mortality from stroke and myocardial infarction. There is some evidence that these effects may be explained at least in part by the effects of lead on renal function leading on to nephrotoxicity and renal insufficiency.

In context of air pollution, other non-air sources that contribute to the body burden must be carefully assessed.

8. REFERENCES

Abbey DE, Nishino N, McDonnell WF, Burchette RJ, Knutsen SF, Lawrence Beeson W, Yang JX., (1999) "Long-term inhalable particles and other air pollutants related to mortality in nonsmokers", Am J Respir Crit Care Med., 159(2):373-82.

Abbey, D.E., Burchette, R.J., Knutsen, S.F., McDonnell, W.F., Lebowitz, M.D., and Enright, P.L., 1998, "Long-term Particulate and Other Pollutants and Lung Function in Nonsmokers", *Am. J. Respir. Crit. Care Med.*, 158, 289-298.

Anderson, H.R., Ponce de Leon, A., Bland, J.M., Bower, J.S., and Strachan, D.P., 1996, "Air Pollution and Daily Mortality in London", *Brit. Med. Jour.,* 312, 665-669.

Anderson, H.R., Spix,C., Medina, S., Schouten, J.P., Castellsague, J., Rossi, G., Zmirou, D., Touloumi, G., Wojtyniak, B., Ponka, A., Bacharova, L., Schwartz, J., and Katsouyanni, K., 1997, "Air Pollution and Daily Admissions for Chronic Obstructive Pulmonary Disease in 6 European Cities: Results from the APHEA Project", *Eur. Respir. J.,* 10, 1064-1071.

Bascom, R., Bromberg, P.A., Costa, D.A., Devlin, R., Dockery, D.W., Frampton, M.W., Lambert, W., Samet, J.M., Speizer, F.E., and Utell, M., 1996, "Health Effects of Outdoor Air Pollution: Parts I and II", *Am J Respir Crit Care Med.*, 153, 477-498.

Beeson, W.L., Abbey., D.E., and Knutsen, S.F., (1998), "Long-term Concentrations of Ambient Air Pollutants and Incident Lung Cancer in California Adults: Results from the AHSMOG Study", Environ. Health Perspect., 106(12), 813-823.

Borja-Aburto, Loomis, D., Bangdiwala, S.I., Shy, C.M., and Rascon-Pacheo, R.A., 1997, "Ozone, Suspended Particulates and Daily Mortality in Mexico City", *Am. J Epidemiol.,* 145(3), 258-268.

Burnett, R.T., Cakmak, S and Brook, J.R., 1998, "The Effect of the Urban Ambient Air Pollution Mix on Daily Mortality Rates in 11 Canadian Cities", *Can. J. Public Health,* 89(3), 152-156.

Burnett RT, Cakmak S, Raizenne ME, Stieb D, Vincent R, Krewski D, Brook JR, Philips O, Ozkaynak H., (1998b), "The association between ambient carbon monoxide levels and daily mortality in Toronto, Canada", J Air Waste Manag Assoc. 48(8), 689-700.

Burnett, R.T., Brook, J.R., Yung, W.T., Dales, R.E., and Krewski, D., 1997a, "Association between Ozone and Hospitalisation for Respiratory Diseases in 16 Canadian Cities", *Environ. Research,* 76, 24-31.

Burnett, R.T., Dales, R.E., Brook, J.R., Razienne, M.E., and Krewski, D., 1997b, "Association between Ambient Carbon Monoxide levels and Hospitalisations for Congestive Heart Failure in the elderly in 10 Canadian Cities", *Epidemiol.,* 8, 162-167.

Burnett, R.T., Cakmak, S., Brook, J.R., and Krewski, D., 1997c, "The Role of Particulate Size and Chemistry in the Association between Summertime Ambient Air Pollution and Hospitalisation for Cardiorespiratory Diseases", *Environ. Health Perspect.,* 105, 614-620.

Delfino, R.J., Murphy-Moulton, A.M., and Becklake, M.R., 1998, "Emergency Room Visits for Respiratory Illnesses among the Elderly in Montreal: Association with Low Level Ozone Exposure", *Environ. Research,* 76, 67-77.

Delfino, R.J., Murphy-Moulton, A.M., Burnett, R.T., Brook, J.R., and Becklake, M.R., 1997, "Effects of Air Pollution on Emergency Room Visits for respiratory Illnesses in Montreal, Quebec", *Am. J. Respir. Crit. Care Med.,* 155, 568-576.

Dockery, D.W., and Pope, C.A., 1994, "Acute Respiratory Effects of Particulate Air Pollution", *Ann. Rev. Public Health,* 15, 107-132.

Dockery, D.W., Pope, C.A., Xu, X., Spengler, J.D., Ware, J.H., Fay, M.A., Ferris, B.G., and Speizer, F.E., 1993, "An Association Between Air Pollution and Mortality in Six U.S. Cities", *N. Engl. J. Med.*, 329,1753-1759.

EPA (Victoria), (2000), "Melbourne Mortality Study: Effects of Ambient Air Pollution on Daily Mortality in Melbourne 1991-1996", EPA Publication 709.

Euler, G.L., Abbey, D.E., Magie, A.R., and Hoddkin, J.E., 1987, "Chronic Obstructive Pulmonary Disease Symptom Effects of Long-Term Cumulative Exposure to Ambient Levels of Total Suspended Particulates and Sulphur Dioxide in California Seventh-Day Adventist Residents", *Arch. Environ. Health.,* 42(4), 213-224.

Fairley, D., (1999), "Daily mortality and air pollution in Santa Clara County, California: 1989-1996", Environ Health Perspect., 107(8), 637-41.

Frischer, T., Studnicka, M., Gartner, C., Tauber, E., Horak, F., Veiter, A., Spengler, J., Kuhr, J., and Urbanek, R., (1999), "Lung Function Growth and Ambient Ozone", Am. J. Respir. Crit. Care Med., 160, 390-396.

Fryer, A.D., and Jacoby, D.B., 1993, "Effect of Inflammatory Cell Mediators on M_2 Muscarinic Receptors in the Lungs", *Life Sci.,* 52, 529-536.

Godleski, JJ., Lovett, EG., Siouta, C., Killingsworth, CR., Krishnamurthi, GG., Hatch V., Wolfson, M., Ferguson, ST., Koutrakis, P., Verrier, RL., (1997), "Impact of Inhaled Concentrated Ambient Air Particles on Canine Electrocardiograph Patterns", Proceedings 13th Health Effects Institute Annual Conference, HEI., Cambridge Massachusetts, USA.

Godleski, J.J., Hatch, V., Hauser, R., Christiani, D., Gasula, G., and Sioutas, C., 1995, "Ultrafine Particles in Lung Macrophages of Healthy People", *Am. J. Respir. Crit. Care Med.,* 151, A264.

Gong, H., Lachenbruch, P., Harber, P., and Linn, W., 1995, "Comparative Short-term Health Responses to Sulfur Dioxide Exposures and Other Common Stresses in a Panel of Asthmatics", *Toxicol. Ind. Health,* 11, 467-487.

Gong, H., Simmons, M.S., Linn, W.S., McDonnell, W.F., and Westerdahl, D., 1998, "Relationship between Acute Ozone Responsiveness and Chronic Loss of Lung Function in Residents of a High Ozone Community", *Arch. Environ. Health.,* 53(5), 313-319.

Horstman, D., Roger, L., Kehrl, H., and Hazucha, M., 1986, "Airway Sensitivity of Asthmatics to Sulphur Dioxide", *Toxicol. Ind. Health,* 2, 289-98.

Jalaludin B., Smith, M., O'Toole, B., and Leeder, S., (2000), "Acute Effects of Bushfires on Peak Expiratory Flow Rates in Children with Wheeze: a Time Series Analysis", Aust. N.Z. J. Public Health., 24(2), 174-7.

Katsouyanni, K., Touloumi, G., Spix, C., Schwartz, J., Balducci, F., Medina, S., Rossi, G., Wojtyniak, B., Sunyer, J., Bacharova, L., Schouten, J.P., Ponka, A., and Anderson, H.R., 1997, "Short-term Effects of Ambient Sulphur Dioxide and Particulate Matter on Mortality in 12 European Cities: Results from Time Series Data from the APHEA Project", *Brit. Med. J*, 314(7095), 1658-63.

Korrick, S.A., Neas, L.M., Dockery, D.W., Gold, D.R, Allen, G.A., Hill, L.B., Kimball, K.D., Rosner, B.A., and Speizer, F.E., 1998, "Effects of Ozone and Other Pollutants on the Pulmonary Function of Adult Hikers", *Environ. Health Perspect.,* 106(2), 93-99.

Kunzli, N., Lurmann, F., Segal, M., Ngo, L., Balmes, J., and Tager, I.B., 1997, "Association between Lifetime Ambient Ozone Exposure and Pulmonary Function in College Freshmen – Results of a Pilot Study", *Environ. Research,* 72, 8-23.

Lee, J.T., Shin, D., and Chung, Y., 1999, "Air Pollution and Daily Mortality in Seoul and Ulsan, Korea", *Environ. Health Perspect.,* 107(2), 149-154.

Lewis, P.R., Hensley, M.J., Wlodarczyk, J., Toneguzzi, R.C., Westley-Wise, V.J., Dunn, T., and Calvert, D., 1998, " Outdoor Air Pollution and Children's Respiratory Symptoms in the Steel Cities of New South Wales", *Med. J. Aust.,* 169, 459-463.

Linn, W.S., Szlachic, Y., Gong, H., Kinney, P.L., and Berhane K.T., (2000), "Air Pollution and Daily Hospital Admission in Metropolitan Los Angeles", *Environ. Health Perspect.,* 108(5), p427-434.

Loomis, D.P., Borja-Aburto, V.H., Bangdiwala, S.I., Shy, C.M., 1996, *"Ozone Exposure and Daily Mortality in Mexico City: A Time-Series Analysis",* Health Effects Institute Research Report No. 75, Cambridge, MA.

Lyons, L., et al., (1996), *Air Pollution, Environmental Health and Respiratory Diseases, Launceston and Upper Tamar Region, 1991-1994,* Northern Region Working Party, Launceston, Tasmania.

Morgan, G., Corbett, S., Wlodarczyk, J. and Lewis, P., 1998a, "Air Pollution and Daily Mortality in Sydney, Australia, 1989 to 1993", *Am. J. Public Health,* 88(5), 759-64.

Morgan, G., Corbett, S., and Wlodarczyk, J., 1998b, "Air Pollution and Hospital Admissions in Sydney, Australia, 1990 to 1994", *Am. J. Public Health,* 88(12), 1761-1766.

Morris, R.D., and Naumova, E.N., 1998, "Carbon Monoxide and Hospital Admissions for Congestive Heart Failure: Evidence of an Increased Effect at Low Temperatures", *Environ. Health Perspect.,* 106(10), 649-653.

Morris, R.D., Naumova, E.N., and Munasinghe, R.L., 1995, "Ambient Air Pollution and Hospitalisation for Congestive Heart Failure among Elderly People in Seven Large US Cities", *Am. J. Public Health,* 85, 1361-1365.

Needleman HL, Bellinger D, 1991. "The Health Effects of Low Level Exposure to Lead", Ann. Rev. Pub. Health; 12: 111 - 40.

Nolan CV, Shaikh ZA, 1992. "Lead Nephrotoxicity and Associated Disorders: Biochemical Mechanisms", Toxicol; 73: 127 - 46.

Nowack R, Wiecek A, Ritz E, 1992. "Lead and Hypertension", In: Berlyne GM ed, "*The Kidney Today: Selected Topics in Renal Science."* Contrib. Nephrol., Karger, Basel; 100: 25-34.

Nuyts GD, Daelemans RA, Jorens PhG, Elseviers MM, Van de Vyver FL, De Broe ME, 1991. "Does Lead Play a Role in the Development of Chronic Renal Disease?", Nephrol. Dial. Transplant; 6: 307 - 15.

O'Halloran K, Spickett JT, 1992/1993. "The Interaction of Lead Exposure and Pregnancy", Asia-Pacific J. Publ. Health; 6(2): 35 - 9.

Orberdorster, G., Ferin, J., Gelein, R.M., Solderholm, S.C., and Finklestein, J., 1992, "Role of the Alveolar Macrophage in Lung Injury; Studies with Ultrafine Particles", *Environ. Health Perspect.,* 97, 193-197.

Orberdorster, G., Ferin, J., and Lehnert, B.E., 1994, "Correlation Between Particle Size, *in vivo* Particle Persistence and Lung Injury", *Environ. Health Perspect.,* 102, Suppl. 5., 173-179.

Orberdorster, G., Gelein, R.M., Ferin, J., and Weiss, B., 1995, "Association of Particulate Air Pollution and Acute Mortality: Involvement of Ultrafine Particles?", *Inhal. Toxicol.,* 7, 111-124.

Ostro BD, Hurley S, Lipsett MJ., (1999), "Air pollution and daily mortality in the Coachella Valley, California: a study of PM10 dominated by coarse particles", Environ Res, 81(3): 231-8.

Pershagen, G., Rylander, E., Norberg, S., Eriksson, M., and Nordvall, S.L., 1995, "Air Pollution Involving Nitrogen Dioxide Exposure and Wheezing Bronchitis in Children", *Int. J. Epidemiol.,* 24(6), 1147-1153.

Peters, A., Doring, A., Wichmann, HE., and Koenig, W., (1997), "Increased Plasma Viscosity During an Air Pollution Episode: A Link to Mortality?", Lancet., 349, 1582-1587.

Petroeschevsky, A., Simpson, R.W., Thalib, L., and Rutherford, S., (2000), "Associations between Outdoor Air Pollution and Hospital Admissions in Brisbane, Australia", Arch. Environ. Health, accepted for publication.

Poloniecki, J.D., Atkinson, R.W., Ponce de Leon, A., and Anderson, H.R., 1997, "Daily Time Series for Cardiovascular Hospital Admissions and Previous Day's Air Pollution in London, UK", *Occup. Environ. Med.,* 54, 535-540.

Ponce de Leon, A., Anderson, H.R., Bland, J.M., Strachan, D.P., and Bower, J., 1996, "Effects of Air Pollution on Daily Hospital Admissions for Respiratory Disease in London between 1987-88 and 1991-92", *J. Epidemiol. Commun. Health,* 50(suppl. 1), S63-S70.

Ponka, A., Savela, M., and Virtanen, M., 1998, "Mortality and Air Pollution in Helsinki", *Arch. Environ. Health,* 53(4), 281-286.

Pope, CA., Dockery, DW., Kanner, RE., Villegas, GM., and Schwartz, J., (1999), "Oxygen Stauration, Pulse Rate and Particulate Air Pollution: A Daily Time Series Panel Study", Am. J. Crit. Care. Med., 159, 365-372.

Pope, C.A., Thun, M.J., Namboodiri, M.M, Dockery, D.W., Evans, J.S., Speizer, F.E., and Heath, C.W., 1995, "Particulate Air Pollution As A Predictor Of Mortality In A Prospective Study Of US Adults", *Am. J. Respir. Crit. Care Med.,* 151, 669-674.

Rennick, G.J., and Jarman, F.C., (1992), "Are Children with Asthma Affected by Smog?", Med. J. Aust., 156, 837-841.

Ritz, B, and Yu, F., 1999, " The Effect of Ambient Carbon Monoxide on Low Birth Weight among Children Born in Southern California between 1989 and 1993", *Environ. Health Perspect.,* 107(1), 17-25.

Romieu, I., Meneses, F., Ruiz, S., Sienra, J.J., Huerta, J., White, M.C., and Etzel, R.A., 1996, "Effects of Air Pollution on the Respiratory Health of Asthmatic Children Living in Mexico City", *Am. J. Respir. Crit. Care Med.,* 154, 300-307.

Rutherford, S., Clark, E., McTainsh, G., Simpson, R., and Mitchell, C., (1999), "Characteristics of Rural Dust Events shown to impact on Asthma Severity in Brisbane, Australia", Int. J. Biometeorol., 42(4), 217-25.

Samet., J., Dominici, F., Zeger, S.L., Schwartz, J., and Dockery, D., (2000), "National Morbidity, Mortality and Air Pollution Study; Part 1: Methods and Methodologic Issues", Health Effects Institute Report No. 94, USA.

Sartor, F., Demuth, C., Snacken, R., and Walckiers, D., 1997, "Mortality in the Elderly and Ambient Ozone Concentration during the Hot Summer, 1994, in Belgium", *Environ. Research,* 72, 109-117.

Schwartz J, 1994. "Societal Benefits of Reducing Lead Exposure", Environ. Res; 66: 105 - 24.

Schwartz J, 1995. "Lead, Blood Pressure and Cardiovascular Disease in Men", Arch. Environ. Health; 50(1): 31 - 7.

Schwartz, J., 1997, "Air Pollution and Hospital Admissions for Cardiovascular Disease in Tucson", *Epidemiol.,* 8, 371-377.

Schwartz, J., 1999, "Air Pollution and Hospital Admissions for Heart Disease in Eight US Counties", *Epidemiol.,* 10, 17-22.

Schwartz, J., Dockery, D.W., and Neas, L.M., 1996, "Is Daily Mortality Associated Specifically with Fine Particles?", *J. Air Waste Manage. Assoc.,* 46, 927-939.

Sheppard, L., Levy, D., Norris, G., Larson, T.V., and Koenig, J.Q., 1999, "Effects of Ambient Pollution on Nonelderly Asthma Hospital Admissions in Seattle, Washington, 1987-1994", *Epidemiol.,* 10, 23-30.

Shy, CM., Creason, J., Williams, R., Liao, D., Hazucha, M., Devlin, R., and Zweidinger, R.., (1997), "Physiological Response in the Elderly Exposed to Ambient Particle Air Pollution", Proceedings 13th Health Effects Institute Annual Conference, HEI., Cambridge Massachusetts, USA.

Simpson, R.W., Denison, L., Petroeschevsky, A, Thalib, L., and Williams, G., (2000), "Effects of Ambient Particle Pollution on Daily Mortality in Melbourne 1991-1996", Int. J. Expos. Anal. Environ. Epidemiol., submitted for publication.

Simpson, R.W., Williams, G., Petroeschevsky, A., Morgan, G., and Rutherford, S., 1997, "Associations between Outdoor Air Pollution and Daily Mortality in Brisbane, Australia", *Arch. Environ. Health.,* 52(6), 442-454.

Simpson, R., Mitchell, C., Williams, G., Rutherford, S., and Owen, J., (1995), "The Relationship Between Outdoor Airborne Bioaerosols and the Incidence of Asthma in Brisbane", Report to The Asthma Foundation of Queensland.

Spix, C., Anderson, H.R., Schwartz, J., Vigotti, M.A., LeTertre, A., Vonk, J.M., Touloumi, G., Balducci, F., Piekarski, T., Bacaharova, L., Tobias, A., Ponka, A., and Katsouyanni, K., 1998, "Short-term Effects of Air Pollution on Hospital Admissions of Respiratory Diseases in Europe: A Quantitative Summary of APHEA Study Results. Air Pollution and Health: a European Approach", *Arch. Environ. Health.,* 53(1), 54-64.

Staessen JA, Bulpitt CJ, Fagard R, Lauwerys RR, Roels H, Thijs L, Amery A, 1994. "Hypertension Caused by Low-Level Lead Exposure: Myth or Fact?", J. Cardiovas. Risk., 1, 87-97.

Streeton, J.A., 1997, "*A Review of Existing Health Data on Six Air Pollutants",* Report to the National Environment Protection Council", Australia.

Sunyer, J., Spix, C., Quenel, P., Ponce de Leon, A., Ponka, A., T. Barumandzadeh, Touloumi, G., Bacharova, L., Wojtyniak, B., Vonk, J., Bisanti, L., Schwartz, J., and Katsouyanni, K., 1997, "Urban Air Pollution and Emergency Admissions for Asthma in Four European Cities: the APHEA Project", *Thorax,* 52, 760-765.

Touloumi, G., Katsouyanni, K., Zmirou, D., Schwartz, J., Spix, C., Ponce de Leon, A., Tobias, A., Quennel, P., Rabczenko, D., Bacharova, L., Bisanti, L., Vonk, J.M., and Ponka, A., 1997, "Short-term effects of Ambient Oxidant Exposure on Mortality: A Combined Analysis within the APHEA Project", *Am. J. Epidemiol.,* 146(2), 177-185.

Touloumi G, Samoli E, Katsouyanni K., (1996), "Daily mortality and "winter type" air pollution in Athens, Greece--a time series analysis within the APHEA project", J Epidemiol Community Health. 50, Suppl 1:s47-51.

UK Department of Environment, 1994, "*Carbon Monoxide",* Expert Panel on Air Quality Standards, HMSO, London.

UK Department of Health, 1993, "*Oxides of Nitrogen",* Advisory Group on the Medical Aspects of Air Pollution Episodes, Third Report, HMSO, London.

UK Department of Health, 1998, "*Quantification of the Effects of Air Pollution in Health in the United Kingdom",* Committee on the Medical Effects of Air Pollutants, The Stationary Office, London.

US Environmental Protection Agency, 1986, "*Review of the National Ambient Air Quality Standards for Sulfur Oxides: Updated Assessment of Scientific and Technical Information",* Office of Air Quality Planning and Standards Staff Paper, Research Triangle Park, NC., Environmental Criteria and Assessment Office.

US Environmental Protection Agency, 1992, "*Review of National Ambient Air Quality Standards for Carbon Monoxide: Assessment of Scientific and Technical Information",* Office of Air Quality

Planning and Standards Staff Paper, Research Triangle Park, NC., Environmental Criteria and Assessment Office.

US Environmental Protection Agency, 1996, "*Review of the National Ambient Air Quality Standards for Nitrogen Dioxide: Policy Assessment of Scientific and Technical Information*", Office of Air Quality Planning and Standards Staff Paper, Research Triangle Park, NC., Environmental Criteria and Assessment Office.

US Environmental Protection Agency, 1996a, "*Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information*", Office of Air Quality Planning and Standards Staff Paper, Research Triangle Park, NC., Environmental Criteria and Assessment Office, EPA-452/R-96-013.

US Environmental Protection Agency, 1996b, "*Air Quality Criteria for Ozone and Related Photochemical Oxidants, Vol. 1-III*", Office of Air Quality Planning and Standards, Research Triangle Park, NC., Environmental Criteria and Assessment Office, EPA/600/P-93/004a-cF.

US Environmental Protection Agency, 1996c, "*Air Quality Criteria for Particulate Matter, Vol. 1-III*", Office of Air Quality Planning and Standards, Research Triangle Park, NC., Environmental Criteria and Assessment Office, EPA/600/P-95/001a-cF.

Vedal, S., 1997, "Ambient Particles and Health: Lines that Divide", *J. Air & Waste Manage. Assoc.*, 47, 551-581.

Verhoeff, A.P., Hoek, G., Schwartz, J, et al, 1996, "Air Pollution and Daily Mortality in Amsterdam", *Epidemiology*, 7, 225-230.

Walters, S., Griffiths, R.K., and Ayres, J.G., 1994, "Temporal Association between Hospital Admissions for Asthma in Birmingham and Ambient Levels of Sulfur Dioxide and Smoke", *Thorax*, 49, 133-140.

Watkinson, W.P., Campen, M.J., and Costa, D.L., (1998), "Cardiac Arrythmia Induction after Exposure to Residual Oily Fly Ash Particles in a Rodent Model of Pulmonary Hypertension", Toxicol. Sci., 41, 209-216.

World Health Organisation, (1999) "Guidelines for Air Quality", WHO Geneva, (http://www.who.int/).

World Health Organisation, 1987, "*Air Quality Guidelines for Europe*", WHO Regional Publications, European Series No. 23, Copenhagen.

Yang, W., Jennison, B., Omaye, S.T., 1998, "Cardiovascular Disease Hospitalisation and Ambient Levels of Carbon Monoxide", *J. Toxicol. Environ. Health*, 55, 185-196.

Zmirou, D., Schwartz, J., Saez, M., Zanobetti, A., Wojtyniak, B., Touloumi, G., Spix, C., Ponce de Leon, A., Le Moullec, Y., Bacharova, L., Schouten, J., Ponka, A., and Katsouyanni, K., 1998, "Time-Series Analysis of Air Pollution and Cause Specific Mortality", *Epidemiol.*, 9, 495-503.