Environmental Pollutants

And Cardiovascular Health

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1. Introduction

Heart disease in Canada, as in most developed countries, is the leading cause of death. It accounts for at least 36 per cent of all deaths each year – about 80,000 people across the country.[1] Men and women are almost equally affected. Moreover, about 450,000 Canadians were hospitalized for cardiovascular disease in the year 2000. Similarly, in the United States, heart attack and congestive heart failure are the leading causes of death and strokes are third.[2]

The risk of developing heart disease is attributed to genetics and lifestyle factors, particularly lack of exercise, poor diet, obesity, smoking and exposure to second hand smoke.[3] However, a certain percentage of cardiovascular disease has never been explained by these traditional factors.

As Dr. Aruni Bhatnagar, Professor of Medicine at the University of Louisville in Kentucky, expressed it:

> Several "risk factors" have been associated with the development of CVD [cardiovascular disease], but it is sobering to consider that many patients suffering from heart disease have no established risk, suggesting that quantitatively important determinants of CVD are currently unknown.[4]

In the last ten years, scientists have taken an interest in identifying novel risk factors. As a result of their investigations, evidence has been mounting that environmental substances, particularly air pollutants, contribute to the burden of heart disease in our society. Although considerable attention has been given to the influence of various pollutants on diseases such as cancer and asthma, their effects on cardiovascular disease have not been as well researched or publicized. According to Bhatnagar, the effects of environmental tobacco smoke on the heart have dramatically demonstrated how vulnerable cardiovascular tissues are to environmental pollutants.[5]

The purpose of this report is to review the emerging scientific evidence demonstrating the effects of environmental factors on cardiovascular health, including strokes, and the possible implications for public policy.[6] Birth defects are not considered in this report, although it should be noted that heart defects are the most common form of birth defect and scientists suspect that environmental agents play a role in this too.[7]

2. Overview of Environmental Influences

The relationship between environmental factors and heart disease, which was once considered tenuous, has now been supported by the cumulative weight of many epidemiological and laboratory studies.[8] The term most commonly applied to environmental effects on cardiovascular health is "environmental cardiology". Its importance is being increasingly acknowledged and scientists, including the American Heart Association, continue to raise the level of awareness of environmental risks of heart disease with their colleagues and the general public.

The best documented evidence points to a relationship between air pollution and cardiovascular disease. Particulate matter is considered the greatest villain, but the other major air pollutants -- carbon monoxide, nitrogen oxides, sulphur dioxide, ozone and lead -- have also been identified as contributing to heart disease. In addition, other substances such as arsenic, mercury, solvents and pesticides have been linked with adverse health impacts related to the heart.

Although environmental factors are not featured in the well-established list of major contributors to heart disease, the recent evidence strongly suggests that exposure to environmental pollutants significantly increases the risk of cardiovascular disease, and that cardiovascular disease is part of the overall disease burden of air pollution.

Because of the prevalence of heart disease in our society, even if environmental factors account for only a small percentage of the overall disease, the number of people affected is still large enough to be an important public health concern. In addition, it should be considered that a large number of people are exposed because air pollution is ubiquitous, and people are exposed over their lifetime.

Another important aspect of environmental exposures that affect cardiovascular health is that they may be preventable. Researchers have estimated that chronic exposure to particulate air pollution can result in a substantial loss of life expectancy from cardiovascular disease.[9] A report by the Natural Resources Defense Council in the United States, "Breath-Taking", estimated that there were 64,000 premature deaths from cardiopulmonary disease in the U.S. each year due to particulate air pollution.[10] This represents 6.5 per cent of all cardiopulmonary deaths in the U.S., which total about 986,000 per year.

The inverse is also true -- where air pollutants were reduced, deaths from cardiovascular diseases were also reduced. Canadian researchers have found that "the impact of reductions in sulphate air pollution on quality-adjusted life expectancy is substantial".[11] Therefore, reductions in the environmental factors that cause heart disease may significantly reduce the burden of disease and the costs to the health care system.

The interest in environmental cardiology is particularly pronounced in the United States, where the National Institute of Environmental Health Sciences has invested considerable money for research into the effects of pollutants on heart disease.[12] Researchers in Europe and Canada have also made important contributions to the field of environmental cardiology.

3. Air pollution and Cardiovascular Disease

3.1 Epidemiological Evidence

Extensive epidemiological studies have established a significant link between urban air pollution and mortality in general, and between air pollution and deaths from cardiovascular disease in particular. The majority are short-term "time series" studies that calculate the daily levels of pollutants and the concurrent deaths or hospital emissions. However, they also include long-term studies that identify the risks for heart disease from chronic exposure to air pollution.

Air pollution is a complex mixture of contaminants including carbon monoxide, nitrates, sulphur dioxide, ozone, and particulate matter, as well as heavy metals such as lead and mercury. These pollutants are generated primarily from fossil fuel combustion including vehicle emissions, residential wood burning, coal-fired power generation and emissions from industrial facilities such as cement manufacturing or smelters. As well, erosion of pavement by road traffic and the abrasion of brakes and tires contribute to air pollution.

These air pollutants have been implicated in time series analyses as causes of adverse cardiovascular effects, but the particles, particularly fine particles, are believed to be most damaging to the heart. Coarse particles are those with a diameter of less than 10 microns (PM 10), and fine particles have a diameter of less than 2.5 microns (PM 2.5).[13]

An important step in establishing environmental influences on cardiovascular disease as a serious public health concern was the June 2004 publication of a Scientific Statement by the American Heart Association. In *Circulation*, an expert panel of researchers and physicians representing the American Heart Association reviewed the scientific evidence on Air Pollution and Cardiovascular Disease.[14] The statement acknowledged that a growing body of epidemiological and clinical research has "led to a heightened concern about the deleterious effects of ambient air pollution on health and its relation to heart disease and stroke". [15]

The American Heart Association's Scientific Statement summarized the most compelling evidence of the last ten years, which demonstrated the link between air pollutants and increases in hospitalizations and deaths from cardiovascular disease. Although these studies looked at air pollutants and death from all causes based on death certificates, the studies were able to establish the increased risks of air pollution, and particularly particulate matter, for cardiovascular disease specifically. The authors comment that "the well-established causal associations between active and passive smoking with heart disease and stroke support the plausibility of an adverse effect of PM [particulate matter] on the cardiovascular system".

One of the first large prospective epidemiological studies, which established the link between air pollution and heart disease, was the Six Cities Study, published in 1993 in the *New England Journal of Medicine* by scientists at the University of Harvard.[16] Their study looked at more than 8,000 adults with 14 to 16 years of follow-up and found "statistically significant and robust associations between air pollution and mortality". There was a positive association between ambient urban air pollution, especially fine particulates and sulphates, and increased deaths by cardiopulmonary disease and lung cancer. As the AHA's Scientific Statement pointed out, this study showed that chronic exposure to air pollutants was independently related to cardiovascular mortality, and that "cardiovascular deaths accounted for the largest single category of the increased mortality".[17]

This was followed in 1995 by another major epidemiological study based on data collected by the American Cancer Society as part of the Cancer Prevention II Study. The American Cancer Society study followed half a million people in 150 cities across the United States. C. Arden Pope and the other researchers looking at the data from 1982 to 1989 found that there was a 17 per cent greater risk of death between the city with the highest levels of particulate matter and the city with the lowest.[18] The authors concluded that long-term exposure to combustion-related fine particulate air pollution increased cardiopulmonary and lung cancer mortality.

Another epidemiological study published in 2002 by Pope and his fellow researchers, including Richard Burnett from Health Canada, looked at the same Cancer Prevention II cohort group after16 years and found an overall 6 per cent increase in cardiopulmonary deaths related to fine particulate and sulphur oxide-related pollution.[19] This study also found that there was no "safe" threshold for exposure to particulate matter.[20]

In 2004, Pope's further research of the group showed that fine particulate air pollution was a risk factor for death from cause-specific cardiovascular disease.[21] The results showed that a 10 microgram per cubic metre increase in fine particulate matter was associated with a 12 per cent increase in the risk of cardiovascular causes of death. The authors speculated that mechanisms could include pulmonary and systemic inflammation, accelerated atherosclerosis and altered cardiac autonomic function. They commented that "although smoking is a much larger risk factor for cardiovascular disease mortality, exposure to fine particulate matter imposes additional effects that seem to be at least additive to if not synergistic with smoking".

A follow-up study to the Harvard Six Cities Study, taking eight more years into account, confirmed that there was an increase in overall mortality associated with each 10 microgram/cubic metre increase in fine particulate matter.[22] The study, published in 2006, found that exposure to particulate matter was statistically significantly associated with deaths due to cardiovascular disease, while the association with lung cancer mortality was of borderline significance. With this longer-term follow-up, the researchers were also able to determine that reductions in particulate matter pollution resulted in fewer deaths from cardiovascular and respiratory disease, suggesting that mortality effects may be reversible.

In 2001, a Dutch study by Gerard Hoek and his fellow researchers showed the risks not only of air pollutants in urban settings but the importance of variations within cities.[23] After studying 5,000 people over 8 years, the Dutch researchers showed that a person's exposure to air pollution may vary as much within a city as between cities. In this study, exposure to traffic-related air pollutants was more highly related to mortality than were background levels of air pollution. Living near a major road was most strongly associated with cardiopulmonary mortality.

A time-series study by Hoek's group published in the same year found strong links between air pollution and specific cardiovascular causes of death -- heart failure, arrhythmia, cerebrovascular and thrombocytic causes of death.[24]

More recently, a February 2007 study published in the *New England Journal of Medicine* substantially strengthened the evidence linking fine particulate air pollution and cardiovascular disease. It also expanded the understanding of how fine particulate pollution affects health and who is at risk based on data collected in the Women's Health Initiative observational study.[25]

Investigators from the University of Washington were able to assess the effects of air pollution on the risk of cardiovascular disease by studying 65,893 postmenopausal women aged 50 to 79 who were free of cardiovascular disease at baseline. This excluded cardiovascular risk factors as an explanation for subsequent health impacts. Researchers found that for every increase of 10 micrograms per cubic meter of fine particulate matter, there was a 24 per increase in the risk of a cardiovascular event and a 76 per cent increase in the risk of death from cardiovascular disease. This increase was higher than the estimated risk found in the American Cancer Society study.

Air pollution was also associated with increased risks from stroke and death from stroke. This study looked not only at differences between cities but variations within cities. According to the accompanying editorial in the *New England Journal of Medicine*,

> Their analysis demonstrated a relationship between increased levels of fine particulate pollution and higher rates of death and complications from cardiovascular and cerebrovascular disease, depending not only on which city a person lived in but also on where in that city she lived.[26]

The authors of the editorial, Douglas Dockery and Peter Stone, asked if, on the basis of this and other recent studies, women could be more susceptible to the effects of air pollutants.

In addition to these long-term studies that demonstrate the risks of chronic exposure to air pollution, hundreds of short-term studies across North America and Europe have been published over the last ten years that show the acute effects of air pollution on cardiovascular disease. These short-term studies show an increase in the number of hospital admissions for all cardiovascular causes when pollution levels are high.

They reflect the acute effects of air pollution that most likely affect vulnerable people like the elderly or those with a pre-existing heart condition.

3.2 Canadian Research

The same relationship between air pollution and an increased risk of cardiovascular events has also been demonstrated to occur in Canada. In addition to his contributions to the major epidemiological studies done in the U.S., Richard Burnett of Health Canada, together with Environment Canada researchers, has published several important time-series studies that show the association between various air pollutants and rates of hospitalization and deaths in Canada related to heart disease.

A 1995 study by Burnett and his colleagues, published in the *American Journal of Epidemiology*, looked at admissions to 168 acute care hospitals in Ontario for both respiratory diseases and cardiac diseases.[27] They note that "few studies have focused on hospital admissions for cardiac diseases". The study was conducted over a 6-year period from 1983-1988. In this study, an increase in sulphate levels was associated with an increase in both respiratory and cardiac admissions to hospitals. For every 13 micrograms per cubic metre rise in the levels of sulphates on the day prior to admission, hospital admissions went up *2.8 per cent for cardiac events* and 3.7 per cent for respiratory events. Heart failure was ranked as the highest risk.

In 1997, Burnett and his colleagues in *Epidemiology* looked at the role of ambient air pollution in hospital admissions for congestive heart failure in 10 Canadian cities. The study found that carbon monoxide, of all the air pollutants, showed the strongest and most consistent association with hospitalization rates for congestive heart failure in the elderly.

Another Burnett study published in 1998 of 11 Canadian cities, including Toronto, did not look specifically for cardiovascular effects but showed the impact of ambient urban air pollution on overall daily mortality rates. It covered the period from 1980 to 1991. The pollutants that were measured in the study were carbon monoxide, nitrogen dioxide, sulphur dioxide and ozone. Nitrogen oxide was found to be the most strongly associated with daily mortality, while ozone, sulphur dioxide and carbon monoxide were also significantly associated but not as strongly. The authors concluded that "ambient air pollution generated from the burning of fossil fuels is a risk factor for premature mortality in 11 Canadian cities".

3.3 Effects of Traffic

In efforts to refine the understanding of the contribution of various sources and types of pollutants to heart disease, many studies have looked at proximity to roadways or industrial facilities. Traffic-related studies measure people's proximity to polluted areas

and the level of exposure to air pollutants. These studies have generally shown a significant link between levels of traffic and the risks of heart disease.

An important study published in 2004, looking at the effects of traffic on heart disease, showed that exposure to traffic can trigger heart attacks (myocardial infarction). Researchers analyzing data from southern Germany between February 1999 and July 2001 showed an association between the exposure to traffic and the onset of a myocardial infarction within one hour afterward.[28] The time the subjects spent in cars, on public transportation, or on motorcycles or bicycles was consistently linked with an increase in the risk of myocardial infarction. The use of a car was the most common exposure to traffic.

In January of 2007, researchers from the Harvard School of Public Health found that not only transient exposures but also long term exposures to traffic contributed to the risk of heart attacks. The study looked at more than 5,000 cases of acute myocardial infarction from 1995 to 2003, as part of the Worcester Heart Attack Study, and found that long-term exposure to traffic increased the risks of having an attack.[29] The study observed "a significant increase in AMI [acute myocardial infarction] associated with increasing exposure to traffic within 100 metres of subjects' residence and with living near major roadways".

In July 2007, a German study, published in *Circulation*, of almost 45,00 people in 3 German cities was the first to show that people living near heavy traffic for long periods of time are more likely to get hardening of the arteries which increases their risk of a heart attack.[30] The lead author, epidemiologist Barbara Hoffmann, compared the traffic-related damage to arteries to the damage caused by second hand smoke commenting that "the effect we see here in the study is even larger than that caused by second-hand smoke".[31] She also said that the damage was not limited to people living near freeways but was also present in people living in inner-city homes on heavily travelled streets.

3.4 Air Pollution and Strokes

As well as being a factor in heart attacks, air pollution has been associated with an increase in the risk of strokes, particularly ischemic strokes which are caused by blood clots.

A time series study published in *Stroke*, a journal of the American Heart Association, in 2002 looked at the deaths from acute strokes and the link with air pollution.[32] The study was done in Seoul, Korea, over a 7-year period from January 1991 to December 1997, a city that has experienced a rapid rise in the number of motor vehicles on its streets. Moreover, the proportion of stroke death is higher in Seoul than in most western cities. The researchers found that air pollution was statistically significantly associated with ischemic stroke mortality. The relative risks for the pollutant increases were greater for deaths from ischemic stroke than from hemorrhagic strokes.

A 2005 study, also published in *Stroke*, found that the risk of ischemic stroke was greater on days with relatively high air pollution.[33] In this study, researchers looked at the association between fine particulate matter and hospital admissions for ischemic and hemorrhagic stroke among Medicare beneficiaries over 65 years of age in 9 cities. They found that a transient increase in ambient particles was associated with an increased risk of hospital admissions for ischemic stroke, but not hemorrhagic stroke.

The authors found that, "although the relative increase in risk was small, given the large number of people simultaneously at risk for ischemic stroke and exposed to urban pollution, even a small relative risk may be of significant public health interest".

3.5 Mechanisms

Although scientists have made the link between air pollution and cardiovascular disease, they are still investigating the mechanisms. At least two possible pathways have been suggested.

First, it is believed by many researchers in this field that systemic inflammation is the key to understanding the effects of air pollutants on the heart.[34] The second possible mechanism is the effects of pollutants on autonomic function.

In the *New England Journal of Medicine*, Douglas Dockery and Peter Stone write:

> There is evidence that inhalation of particulate air pollution creates and exacerbates both pulmonary and systemic inflammation and oxidative stress, leading to direct vascular injury, atherosclerosis and autonomic dysfunction. Buildup of atherosclerotic plaque, measured by carotid intima-media thickness, is higher in communities with higher mean PM 2.5 concentrations. Particulate air pollution has been found to lead to rapid and significant increases in fibrinogen, plasma viscosity, platelet activation, and release of endothelins, a family of potent vasoconstrictor molecules.[35]

In laboratory studies, Canadian researchers have made an important contribution to the understanding of how pollutants may affect the heart by demonstrating that repeated exposure to urban air particulates caused a systemic inflammatory response.[36] The American Heart Association Scientific Statement described the Canadian research as providing "experimental evidence to support the hypothesis that the epidemiological data truly reflect the deleterious effects of particulate pollution on the cardiovascular system".[37]

Their studies were carried out on rabbits exposed to particulate matter for four weeks. Exposure to air particulates was associated with progression of the atherosclerotic process in the coronary arteries and aorta, and researchers concluded that "the

progression of atherosclerosis and increased vulnerability to plaque rupture may underlie the relationship between particulate air pollution and excess cardiovascular death".

A July 2007 study by researchers in California, that received widespread media attention, also looked at the possible mechanisms linking cardiovascular disease to air pollution.[38] The researchers exposed human blood cells to a combination of diesel particles and oxidized fats, then extracted the DNA. Mice were also exposed to a high fat diet and exhaust. In both cases, the particles in diesel exhaust in combination with the fats switched on genes that cause inflammation of blood vessels and led to atherosclerosis. Dr. Andre Nel, one of the researchers involved in the study, said that the combination of diesel exhaust with cholesterol "creates a dangerous synergy that wreaks cardiovascular havoc far beyond what's caused by the diesel or cholesterol alone".[39]

4. Metals and Other Pollutants that Affect the Heart

In addition to researching the effects of air pollution on cardiovascular disease, many studies have looked at the possible effects of other pollutants, particularly metals, on the heart. For example, metals such as arsenic are being investigated for their role in the development of atherosclerosis. It has been suggested that certain metals may promote atherosclerosis by increasing oxidative stress or by affecting other cardiovascular risk factors.[40]

4.1 Arsenic

Arsenic exposure has also been implicated as a risk factor for cardiovascular disease. The sources of arsenic to which people are exposed include contaminated drinking water; food, particularly chicken; chromated copper arsenic (CCA) treated wood; and releases from industrial facilities.

Exposure to inorganic arsenic, primarily in drinking water, has been associated with increased mortality from cardiovascular and cerebrovascular disease, hypertension, ischemic heart disease and carotid atherosclerosis.[41] Organic arsenic, which is generally less toxic than inorganic arsenic, is used to treat chickens for parasites and promote growth, and is becoming a concern for human exposure to arsenic.[42]

Arsenic is likely to cause a severe form of peripheral vascular disease, called Blackfoot Disease, which results in gangrene. The strongest evidence for this comes from studies done of people in southwestern Taiwan who were exposed over long periods of time to high levels of arsenic in their drinking water.[43]

A review of the scientific literature related to arsenic exposure and cardiovascular disease published in 2005 in the *American Journal of Epidemiology* commented that:

> The evidence from Taiwan is consistent with a role for high arsenic exposure in atherosclerosis, although the magnitude of the association is uncertain because of the methodologic limitations of the available studies.

The reviewers also found that current epidemiological studies were inadequate for understanding the cardiovascular effects of chronic low-dose exposures, although the possibility that arsenic causes cardiovascular disease is supported by several biologic mechanisms. Because of the exposure of many people to low or moderate arsenic levels, the reviewers concluded that understanding the potential effects of arsenic on cardiovascular risk should be considered important and the need for prospective studies a public health priority.[44]

Because of the possible link between arsenic and cardiovascular disease as well as its potential for causing other serious health effects, concern has also been raised about the level of arsenic exposure to people from eating chicken. Chickens in large commercial operations are treated with products containing arsenic in order to prevent and treat parasites and to promote growth. A 2004 study by scientists at the U.S. Dept. of Agriculture published in *Environmental Health Perspectives* found that chicken consumption is a significant source of arsenic exposure for the general population. [45]

Canadian data was used to calculate levels of organic and inorganic arsenic in chicken. The authors concluded that "higher than previously recognized concentrations of arsenic in chicken combined with increasing chicken consumption may indicate a need to review assumptions regarding overall ingested arsenic intake".

4.2 Lead

Lead, like arsenic, is a metal of concern because of its potential to increase the risk of heart disease. Sources of exposure to lead include drinking water; lead-based paint often found in older homes; batteries; electric and electronic equipment; plastic products; toys; and jewellery.

A recent review in March 2007 of studies of lead exposure and cardiovascular disease in *Environmental Health Perspectives* found a positive association between lead exposure and blood pressure, and confirmation of lead's ability to cause hypertension. The authors found that more than 30 original studies support a positive association between blood lead levels and blood pressure.

The U.S. Environmental Protection Agency's Air Quality Criteria Document for Lead also found that "evaluated as a whole, the earlier blood pressure studies supported a small but significant association between increasing blood lead concentrations and increasing blood pressure in study groups".[46]

Beyond blood pressure and hypertensive effects, lead was also associated with deaths from cardiovascular disease, coronary heart disease and strokes. The authors of the review note, though, that the number of studies for these cardiovascular outcomes is small.

One of the epidemiological studies linking blood lead levels and cardiovascular death is a study by Lustberg and Silbergeld published in 2002. This study used data from the Second National Health and Nutrition Examination Survey (NHANES) in the United States. The authors reported that higher blood lead levels led to increased mortality from cardiovascular causes.[47] People with blood lead levels of 20 to 29 micrograms/decilitre in 1976 to 1980 experienced significantly increased all-cause, circulatory and cardiovascular mortality from 1976 through 1992. These blood lead levels were found in 15 per cent of the U.S. population at the time of the study.

In 2006, an analysis of the third NHANES data found that blood lead levels were associated with an increased risk of death from all causes, cardiovascular disease and cancer.[48] The authors found that although the increased risk was small, it was associated with blood lead levels as low as 5 to 9 micrograms per decilitre.

A subsequent large population-based prospective study in 2006 identified a direct association between higher blood lead levels and increased cardiovascular mortality at substantially lower levels [of lead] than previously reported.[49] The authors concluded that, "despite the marked decrease in blood lead levels over the past 3 decades, environmental lead exposures remain a significant determinant of cardiovascular mortality in the general population, constituting a major public health problem".

Since the March 2007 review, further evidence for an association between the risk of cardiovascular disease and exposure to lead appeared in two reports published in *Environmental Health Perspectives* in August 2007. Both used data from the large U.S. Normative Aging Study centred in Boston, which has followed the health of 2,280 male veterans every 3 to 5 years since 1963.

One report, a prospective study investigating the effects of lead on heart disease, was the first to find that older men with higher blood and bone lead levels were at increased risk for future ischemic heart disease. The researchers followed 837 middle-aged and elderly men over 10 years from September 1999 through December 2001. Although three previous investigations found no evidence of an association between blood lead levels and heart disease, this study measured bone lead levels as well as blood lead levels. Bone lead is considered to be a more accurate assessment of lifetime lead burden than blood lead levels. Those with the highest lead measured in their bones suffered more heart attacks and heart pains than those with lower levels.

The second study, also using data from the Normative Aging Study, found that high stress and high bone lead levels interacted to increase the risk of developing hypertension and high blood pressure in aging men.

4.3 Mercury

Studies have also shown a link between mercury and cardiovascular effects. Sources of mercury include air emissions from the burning of waste and fossil fuels (coal); food, particularly fish; dental amalgams; and some consumer products such as thermometers and batteries.

Mercury from the atmosphere settles in waterways where it is converted to organic and highly toxic methyl mercury by bacteria and taken up by fish. Fish are considered to be one of the most significant sources of mercury exposure for the general population. Many of the studies looking at mercury and cardiovascular effects have included the potential risk of heart disease from eating fish contaminated with high levels of mercury.

The association between methyl mercury and cardiovascular disease was first demonstrated in Finnish studies in 1995. Long-term epidemiological studies examining older men in Finland provide some of the strongest evidence that mercury is a risk factor for the development of cardiovascular disease. In the Kuopio Ischemic Heart Disease Risk Factor study, scientists have been following more than 2000 men between the ages of 42 and 60 without heart disease for several years in order to identify risk factors for heart disease.

One of the first studies of the Finnish men, published in the *New England Journal of Medicine* in 1995, showed that those with high levels of mercury in hair samples had twice the risk of heart attack than men with the lowest hair mercury levels, after adjusting for age and other risk factors.[50] This study was based on 7 years of follow-up. The authors suggested that the "increased risk may be due to the promotion of lipid peroxidation by mercury". Mercury levels in the hair and toenails are both used as markers for the amount of methyl mercury accumulated in the body.

A second study of the Finnish men after an average follow up of 14 years found that "high mercury content in hair is significantly associated with an increased risk of acute coronary events and CVD [cardiovascular disease], CHD [coronary heart disease], and all-cause mortality in men living in eastern Finland".[51] Men who scored in the top 25 per cent for hair mercury content had a 60 per cent increased risk of death from cardiovascular disease compared to men with lower mercury content in their hair. The high levels of mercury in hair were related to the consumption of large quantities of fish, particularly large fish that eat smaller fish and accumulate mercury. The study also showed that men whose hair mercury levels were high had a faster increase in the thickness of the inner walls of their arteries, a measure of atherosclerosis, compared to the other men in the group.[52]

Another study published in the *New England Journal of Medicine* in 2002 of men from eight European countries and Israel found a higher risk of heart disease for men with higher levels of mercury content measured in toenails.[53] In this study the risk of having an acute coronary event was more than twice as high for men in the highest fifth of toenail mercury content compared to men in the lowest fifth. In this study, as in the previous Finnish study, high mercury content attenuated the protective effect of fish for heart disease. The author, Dr. Eliseo Guallar, said that:

> Although it is believed that fish intake may reduce the risk of cardiovascular diseases, current epidemiologic studies of fish intake or fish-oil levels and coronary heart disease in the general population are contradictory. Our findings suggest that mercury found in some fish may counteract the benefits of the omega 3 fatty acids also present in fish.[54]

A study published at the same time in the *New England Journal of Medicine*, however, compared healthy men and men diagnosed with coronary heart disease and found that

mercury exposure was *not* associated with risk of heart disease.[55] This study also used mercury levels in toenails as an indicator.

4.4 Cadmium

There are very few studies that have evaluated cadmium and cardiovascular problems in isolation. Cadmium is often investigated with lead. Although most studies of these metals have focussed on their association with increased blood pressure, there has been work done recently that suggests that exposure to cadmium and other metals may promote atherosclerosis and have an effect on other cardiovascular problems. Exposure to cadmium may be from cigarette smoke; food and, in some instances, drinking water; batteries; or incineration.

In 1993, a study of a cadmium-contaminated region of the Netherlands found a possible influence of long-term low-level cadmium uptake on atherosclerosis.[56] The author identified a significantly higher frequency of atherosclerosis compared to other diseases in the contaminated area, although there was no higher frequency of death for atherosclerosis. He suggested that the influence of long-term low-level cadmium uptake on atherosclerosis required more attention.

More recently, in 2004 scientists used the data from the large National Health and Nutrition Examination Survey (NHANES) to assess the influence of both lead and cadmium on heart disease.[57] The scientists evaluated the relationship between blood lead and cadmium levels and blood pressure in a sample of 2,125 people over 40 years of age. Blood cadmium was used as a biomarker of exposure to cadmium. The study found that blood levels of both cadmium and lead were "strongly associated with an increased prevalence of peripheral arterial disease". The authors commented that these levels were well below current safety standards used by environmental and occupational regulatory agencies.

A second study by the same scientists, published in 2005, strengthened the findings of their first study.[58] Researchers in this study measured a number of metals in urine, and found that urinary cadmium levels were strongly associated with peripheral arterial disease.

4.5 Chemicals Known from Occupational Exposures to Cause Heart Disease

Occupational studies also offer some insight into the risks of certain chemicals for heart disease. Although surprisingly little research has been done on the occupational risks of heart disease, a few specific chemicals including carbon disulfide, nitroglycerin,

halogenated and non-halogenated industrial solvents, arsenic, cobalt and carbon monoxide have been shown to affect the heart.

Pesticides and organic solvents have been shown to cause cardiac arrhythmias and heart attacks. The strongest relationship was between coronary artery disease and carbon disulfide, a solvent used in the rubber industry.[59] Munitions workers in a large cohort study in Virginia were found to have a higher rate of cardiovascular mortality as a result of their exposure to nitroglycerin and dinitrotoluene.[60]

5. Conclusion

Environmental pollutants are beginning to be recognized as a significant risk factor for heart disease. Like other risk factors such as smoking or obesity, pollutants offer an opportunity to prevent disease by reducing their presence in the environment and, consequently, our exposure.

There are regulatory and non-regulatory approaches that could help to reduce environmental risks related to cardiovascular disease.

Regulatory approaches could include strategies such as tightening government standards for water and air pollutants, particularly particulate matter; adopting toxics use reduction legislation that would reduce harmful emissions from industrial facilities through pollution prevention; strengthening limits on fossil fuel emissions, particularly vehicle emissions; and restricting the use of metals such as lead and mercury in consumer products.

Non-regulatory approaches could include improvements in air quality monitoring; the use of the provincial air quality index to warn people at risk when levels of air pollution are high; funding for research into environmental cardiology; the promotion of alternative forms of transportation, particularly in urban areas; and/or public education programs such as the Environmental Protection Agency's advice to "older adults" at risk for heart disease and stroke, entitled "Environmental Hazards Weigh Heavy on the Heart".

Endnotes

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