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Potential Human Health Effects of Acid Rain: Report of a Workshop.

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This report summarizes the potential impact of the acid precipitation phenomenon on human health. There are two major components to this phenomenon: the predepositional phase, during which there is direct human exposure to acidic substances from ambient air, and the post-depositional phase, in which the deposition of acid materials on water and soil results in the mobilization, transport, and even chemical transformation of toxic metals. Acidification increases bioconversion of mercury to methylmercury, which accumulates in fish, increasing the risk to toxicity in people who eat fish. Increase in water and soil content of lead and cadmium increases human exposure to these metals which become additive to other sources presently under regulatory control. The potential adverse health effects of increased human exposure to aluminum is not known at the present time.

Introduction

This report results from a request by the Committee on Appropriations of the U.S. House of Representatives that the National Institute of Environmental Health Sciences (NIEHS) convene a workshop of scientists with an interest in the area of research on possible health effects associated with acid rain exposure. The workshop was convened by the NIEHS on December 9, 1983, and was attended by both government and nongovernment scientists with expertise in various topics related to the potential health effects of the acid rain phenomenon. The resultant report is largely a review of the current information available on this topic. Specific conclusions are cited at the end of the report.

As background for these considerations, it was determined that the acid rain phenomenon has two components: the predeposition phase, which involves air pollutants, and a postdeposition phase concerning the effects of deposition of acidic substances in water or dry surfaces, including soils and buildings. The effects of the predeposition phase are sometimes referred to as direct or primary, whereas postdeposition effects are not likely to appear immediately and may be regarded as secondary or indirect. This discussion considers the immediate as well as long-term potential impact on human health from both phases of the acid rain phenomenon.

Air Pollution Precursors or Substances Contained in Acid Rain Before Deposition

The primary cause of acid deposition is generally understood to be the oxidation of sulfur, nitrogen, and carbon compounds emitted to the atmosphere from natural and man-made sources. On a global scale, natural sources (e.g., swamps, marshes, lightning) are significant, but in eastern North America an estimated 90 to 95% of precipitation acidity is thought to be related to human activities, largely the combustion of fossil fuels (e.g., power plants, industrial sources, home heating, motor vehicles) and smelting of sulfur containing ores (*1*).

The region of highest acid deposition in North America corresponds closely to the region of heavy industrialization and urbanization along the Ohio River Valley and eastern seaboard, where both anthropogenic emissions and atmospheric loadings of sulfur and nitrogen oxides are also high. These pollutants may be removed directly from the atmosphere as dry or wet acidic deposition or may first undergo atmospheric transformations to sulfuric acid, nitric acid, and several particulate species.

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Photochemical oxidants, such as ozone and hydrogen peroxide, and reactive volatile organic compounds known to play a role in the transformations, are also present in relatively high levels in the same industrialized and urbanized regions.

Thus, the atmospheric precursors to acid deposition involve most of the "traditional" air pollutants; namely, sulfur dioxide, nitrogen oxides, particulate matter, and photochemical oxidants. Deleterious effects have long been attributed to inhalation of high concentrations of these pollutants, and numerous literature reviews and documents have been prepared on their known and potential health effects (*2–9*). The workshop reviewed the contribution of acid deposition to human exposure to these pollutants and the potential health effects of inhaling several specific acid sulfate and nitrate components that are present in elevated concentrations in geographical regions where acid deposition is greatest.

Atmospheric sulfates are derived principally from atmospheric transformations of gaseous sulfur dioxide. The major sulfate species occur as fine (<2.5 μm in size) droplets or solid particles that include various mixtures of hydrogen and ammonium ions ranging in acidity from sulfuric acid to neutral ammonium sulfate. Elevated levels of sulfates occur on a regional scale throughout eastern North America and are highest in the Ohio River Valley. Multi-day events of elevated sulfate concentrations accompanied by high photochemical oxidant levels occur over large-scale regions during the summer months. Elevated sulfate events can also happen in other seasons. Although speciation data are very limited, during such events sulfuric acid equivalent levels may reach 15 to 20 μg^3 or more (*10*).

The more acidic transformation product of nitrogen oxides is nitric acid which at typical ambient humidity and temperature is present as a vapor. Based on limited measurements, ambient concentrations are generally very low, but levels as high as 10 to 20 μg^3 have been observed in the Ohio River Valley (*11*). Particulate nitrate levels (e.g., ammonium nitrate) appear to be low in eastern North America. The highest levels of both nitric acid and nitrate particles occur in western urban areas such as Los Angeles. In southern California, acid fogs have been reported in which nitric acid appears to dominate droplet acidity (*12*).

Nature of Toxic Materials Released Following Deposition

Once deposited, atmospheric acids and acid forming sulfur and nitrogen containing species do not of themselves appear to present a health threat. They may, however, indirectly mobilize toxic materials and add to total human exposure to these materials. To date, the major areas of potential concern include contamination of edible fish by toxic metals, principally mercury, soil leaching in acidified watersheds and corrosion of water and storage distribution systems, leading to elevated levels of toxic elements, chiefly lead, cadmium, and aluminum.

In general, the geographic areas in which such increased exposures might occur are limited to the same regions that appear sensitive to long-term acidification of aquatic ecosystems. This includes large portions of the Northeast, portions of the Appalachian mountains and some of the upper Midwest. Areas that have usual accumulations of metals in sediments or soils and areas which lack drinking water treatment facilities may also be sensitive.

Health Effects of Air Pollutant Precursors to Acid Deposition

General Comments

The health effects of the major pre-deposition pollutants of acid rain, sulfur and nitrogen oxides, have been extensively reviewed by the National Academy of Sciences (*2–4*) and the Environmental Protection Agency (*6,7*). These reports conclude that atmospheric oxides of sulfur and nitrogen can cause human health effects. This report summarizes pertinent information in those documents and describes some of the more recently available data.

Knowledge of the effects of sulfur and nitrogen oxides is derived from three major types of studies —epidemiology, human clinical, and animal toxicology. Epidemiological evidence provides direct information on the responses of humans to actually encountered pollutant conditions, typically consisting of low levels of pollutant mixtures. Both acute and chronic effects can be studied. However, the complexities of human activities result in confounding factors that are not present in chamber studies with man or animals. Human clinical studies involve controlled short-term exposures of volunteers to single or, in a few cases, multiple pollutants. Data can be interpreted directly to human health risk. However, such studies are not designed to cause irreversible effects and, thus, they are very limited. With respect to animal studies, on the other hand, acute and chronic studies are possible, and effects on tissues such as the lung can be studied. Nonetheless, concentrations causing effects in animals cannot yet be directly quantitatively extrapolated to man. Therefore, optimal understanding of the health effects of these pollutants requires integrating information from all three experimental approaches.

Sulfur Oxides

Human Epidemiologic Evidence. There is little information that directly links acid precipitation with effects on human beings. Much of this has been due to the difficulties in measuring the components in the atmosphere. Frequently, the measurement has been of

the water-soluble sulfates without specification as to the type of sulfate present. Evidence from animal studies and limited studies on human beings in chambers do indicate that sulfuric acid for the equivalent amounts of sulfur and of sulfur particle size is more reactive biologically than ammonium sulfate or sodium sulfate. Thus it appears that it is the acidity or the hydrogen ion concentration rather than the sulfate that is the active component. There is a need to develop better methods to analyze air samples for sulfuric acid or nitric acid. Collection requires that the sample be protected from ammonia contamination which would result in measuring lower concentrations of sulfuric acid than was originally present.

There is a certain amount of data, however, that can be used to demonstrate that acid particulate matter may have an effect on human health. The episodes of high pollution in London (*13*), the Meuse Valley (*14*), and Donora, Pennsylvania (*15*), undoubtedly had high acid content in their pollution mix. The concentrations were measured during some of the London episodes (*16,17*); Hemion (*18*) estimated sulfate concentration in the Donora episode. Presumably, similar results would have been obtained in the other event. The persons most effected were the elderly, especially those with cardiovascular diseases, and young children. The concentrations associated with these episodes were high —probably in the range of milligrams per cubic meter. It was not clear which component of this pollution mix was the active agent or whether they worked in conjunction. One hypothesis held that the sulfur dioxide was absorbed into the particles and was then converted to sulfuric acid by the time it was delivered to the lung. Another held that the sulfuric acid could be directly absorbed onto the particles or formed their own aqueous droplet. In addition there may have been synergism between the soot particles and the sulfuric acid droplet.

More recent studies (*19,20*) have used sulfate as a surrogate for sulfuric acid and have presented results that suggest there may be an effect. As with virtually all of these studies, there has been considerable confounding of the effects of one pollutant with other pollutants and it has been virtually impossible to isolate which component was the active one or whether they were acting in concordance.

The Community Health and Environmental Surveillance System (CHESS) studies (*20*), although severely criticized, did draw more attention to the possible effects of acid sulfates. Earlier, Waller and Lawther (*21*) had suggested that sulfuric acid was an active ingredient in the London fogs.

Thus, there is suggestive evidence that sulfates or, more specifically, acidic sulfates can have an effect on health. The evidence from epidemiologic studies is weak due to the confounding factors. Better information as to the effect of sulfuric acid comes from human and animal exposure studies.

In at least one of the on-going Harvard Six Cities epidemiologic studies, efforts are being made to measure sulfuric acid and ammonium sulfates. Thus far only a couple of cities have been monitored. The others will be included later after the initial field testing of the instruments has proven to be satisfactory.

Controlled Chamber Studies with Humans and Experimental Animals. Standard tests of lung mechanics have been used most often as criteria of irritancy potential due to inhaled sulfur oxide aerosols. However, attempts to produce significant changes in respiratory function of resting healthy humans and experimental animals, with the possible exception of the guinea pig, with submicrometer aerosols at concentrations of up to 1 mg/m^3 for up to 1 hr were largely unsuccessful (*22–27*). With exercise, a slight depression in some indices was noted after a 2-hr exposure to 1 mg/m^3 sulfuric acid (*28*). Using bronchial provocation testing following acid sulfate exposures for 16 min at 1 mg/m^3, Utell et al. (*29*) showed a potentiation of human response to carbachol challenge in relation to aerosol acidity, i.e., sulfuric acid > ammonium bisulfate > sodium bisulfate > ammonium sulfate. A few studies have examined responses in people with extrinsic asthma; results are contradictory. Avol et al. (*30*) noted minor changes in pulmonary resistance in two of six asthmatics exposed to 0.075 mg/m^3 (0.3 μm) sulfuric acid for 2 hr. Sackner and Ford (*31*) found no changes in lung mechanics in adult asthmatics exposed to sulfuric acid at 1 mg/m^3 (1.5 μm) for 10 min, while Spektor (*32*) found changes in some indices due to 1-hr exposures to a submicrometer aerosol at the same concentration, and Utell et al. (*29*) noted changes in specific airway conductance after exposure to sulfuric acid at 0.45 or 1 mg/m^3 for 16 min. Most recently, Koenig et al. (*33*) noted significant alteration in lung mechanics of adolescent asthmatics after exposure for 30 min at rest plus 10 min with exercise to 0.1 mg/m^3 sulfuric acid.

Another aspect of lung physiology which has been examined is clearance function, which is involved in lung defense. Decreased ciliary beat frequency was observed in tracheal explants obtained from hamsters exposed for 2–3 hr to submicrometer amounts of sulfuric acid (0.88–1.1 mg/m^3) (*34,35*). Effects upon tracheobronchial mucociliary clearance function in intact animals, which is a more sensitive index than mechanical function, have been reviewed recently by Schlesinger (*36*). Transient clearance rate alterations have been noted in humans and experimental animals following 1-hr exposures to submicrometer amounts of sulfuric acid at 0.095–0.1 mg/m^3 (*25,36,37*). Levels of 1.7 mg/m^3 ammonium sulfate were required for similar responses (*36*) in experimental animals, and no changes have been found for ammonium sulfate at 3–3.6 mg/m^3 for 1–4 hr (*38*).

Transient changes may become long-lasting. Schlesinger et al. (*27*) demonstrated persistently slowed clearance in two of four experimental animals (donkeys) after six individual 1-hr exposures to sulfuric acid at 0.2–1.0 mg/m^3. Subsequently, four animals were ex-

posed 1 hr daily, 5 days/week to sulfuric acid at~ 0.1 mg/m^3. Within the first few weeks of exposure, all four developed erratic clearance rates, while two developed persistently slowed bronchial clearance during the second three months of exposure and during four months of follow-up measurements.

Because persistent clearance alteration is seen in chronic bronchitis, sulfuric acid has been hypothesized as having a role in pathogenesis of bronchitis. Although direct evidence for an association between sulfuric acid and chronic bronchitis is lacking, this hypothesis is strengthened by comparing studies with submicrometer amounts of sulfuric acid and whole fresh cigarette smoke exposures with donkeys and humans (*40*); cigarettes are involved in the etiology of human chronic bronchitis. The effects of both agents on mucociliary clearance are essentially the same in terms of transient acceleration of clearance in low dose exposures, transient slowing following high doses, and alteration in clearance rate persisting for several months following multiple exposures. A recent study by Schlesinger et al. (*41*) adds further support. Rabbits exposed to sulfuric acid at ~0.25–0.5 mg/m for 1 hr/day, 5 days/week, for four weeks demonstrated an increase in secretory cells in the epithelium of small airways, a hallmark of chronic bronchitis. In addition, in some cases, the epithelium was thickened and airway diameters were narrowed.

Clearance from the respiratory airways is mediated by alveolar macrophages, which are also responsible for the lung's bacteriocidal function. Few data exist on effects in this region; and available studies use unrealistically high levels of acid sulfates. Mice exposed to small amounts 80, 150 or 300 mg/m^3 of sulfuric acid for 3 hr showed enhanced mortality due to a subsequently inhaled bacterial aerosol only at the highest concentration, and this was probably due to tissue damage (*42*); no change was noted in the numbers of macrophages in lavage fluid. Macrophages harvested from mice exposed to sulfuric acid from 125 to 154 mg/m^3 from 10–14 days showed decreased interferon titers in their culture fluid (*43*). In the only study of effects upon alveolar clearance in intact animals (*38*), rats exposed for 4 hr (at 39% R.H.) to 3.6 mg/m^3 sulfuric acid exhibited clearance deceleration 2–17 days after exposure, a phase mediated by macrophages.

There are few investigations of the chronic effects of sulfates and these have only been reported with sulfuric acid. Most were conducted at a time before highly sensitive quantitative measurement techniques for lung morphology were available. Interpretation of the studies is made difficult because whole body exposures were used, thereby permitting an uncontrolled neutralization of sulfuric acid within the chamber atmosphere. Therefore, sulfuric acid concentration-response effects cannot be determined with precision.

Guinea pigs were unaffected by a one-year exposure of up to 0.9 mg/m^3 sulfuric acid (*44,45*). Monkeys experienced a transient alteration in pulmonary function during a one and one-half year exposure to submicrometer, but not larger, sulfuric acid at 0.4–0.5 mg/m^3 (*44*). Lung structure was also changed by some of the sulfuric acid concentrations; a typical finding was thickening of the walls of respiratory bronchioles. However, the responses were not consistently relatable to concentration or particle size of sulfuric acid. Lung structure of dogs was not affected by about one and one-half years of exposure to 0.9 mg/m^3 sulfuric acid, although there were some changes in pulmonary function (*46,47*).

Chronic effects of ammonium sulfate are unknown. Recent subchronic studies (exposures of 5 days/week for 4 weeks) have shown that ammonium sulfate is not as innocuous as presumed from acute exposure studies (*48*). A level of 1 mg/m^3 ammonium sulfate caused structural and functional changes in the lungs of rats, and to a lesser degree in guinea pigs. Those animals with laboratory-induced emphysema appeared to be more resistant.

The interaction of sulfuric acid with other particles has been the subject of several studies. Sulfuric acid did not potentiate the effects of ozone, nitrogen dioxide, or sulfur dioxide in normal human subjects exposed acutely (*49*). Guinea pigs exposed to various combinations of sulfuric acid, sulfur dioxide, and fly ash for one year experienced no changes in pulmonary function or structure (*45*). Monkeys exposed for one and one-half years to similar combinations having about 0.9 mg/m^3 sulfuric acid had no alterations in pulmonary function. However, lung structure was altered. Fly ash did not enhance the effects of sulfuric acid.

The most extensive interaction study was conducted with dogs exposed for about five and one-half years to 1.1 mg/m^3 sulfur dioxide plus 0.09 mg/m^3 sulfuric acid and then allowed to remain in unpolluted air for about two and one-half years (*50*). Periodic examinations were made, and some changes in pulmonary functions were noted throughout exposure. The functional losses continued following the termination of exposure. Morphometric measurements of the lungs were made at the two and one-half year post-exposure period (*51*). Several types of changes were observed. The most noteworthy were changes that the authors considered analogous to an incipient stage of human centrolobular emphysema.

The only significant body of data for the interaction of sulfuric acid with gases involves ozone. Generally, the results of these studies are dependent upon the biological system examined and the exposure regimen utilized. Last and Cross (*52*) found synergistic effects of 1 mg/m^3 sulfuric acid and 0.4–0.5 ppm ozone on glycoprotein synthesis (an index of mucus production) in rats. Antagonistic effects on ciliary beating frequency were observed when hamsters were exposed in sequence, first to 0.1 ppm ozone and then to 0.9 mg/m^3 sulfuric acid (*34*). Gardner et al. (*53*) showed additive effects of 0.9 mg/m^3 sulfuric acid and 0.1 ppm ozone for susceptibility to bacterial lung infections of mice exposed in sequence to ozone first.

Nitrogen Oxides

There are virtually no epidemiologic, human clinical, or animal toxicological studies that have examined the effects of nitric acid. Very few data exist concerning response to inhaled particulate nitrogen oxides; those that are available relate most solely to pulmonary mechanics. Dogs exposed to sodium nitrate at 10 mg/m (0.1 μm) for 7.5 min or sheep exposed to 5 mg/m for 4 hr showed no significant change in lung mechanical function (*54*). Similar negative results were obtained in healthy human subjects exposed to sodium nitrate at 1 mg/m for 10 min (*54*) or in healthy and asthmatic adults exposed for 2 hr (with intermittent exercise) to ammonium nitrate at 0.2 mg/m (1.1 μm) (*55*). In a study by Utell et al. (*29*), no significant enhanced effect of a carbachol (bronchoconstrictor) challenge was observed in either a group of normals or asthmatics previously exposed to sodium nitrate at 7 mg/m (0.46 μm) for 16 min; however, two asthmatics did show mild potentiation of the carbachol-induced bronchoconstriction after sodium nitrate exposure. Normal and allergic sheep exposed for 4 hr to 1.6 ppm nitric acid vapor showed no change in pulmonary flow resistance (*56*). With bronchial provocation testing, no significant change in airway reactivity was noted in the normal animals, but mild hyperactivity occurred in allergic sheep within 24 hr after exposure.

Stutts et al. (*57*) found that ammonium nitrate could alter sodium and chloride transport across canine tracheal epithelium. However, the response was ascribed to ammonium ion rather than nitrate ion since sodium nitrate had no effect.

Health Effects That May Occur During the Postdepositional Stage of Acid Rain

General Comments

Several steps are involved in the postdepositional stage of acid rain, so that the potential effects on health resulting from changes occurring during this stage are sometimes referred to as indirect effects. The steps in the postdepositional stage include mobilization of metals from generally fixed sites, such as ores and insoluble deposits, to media that contribute to human exposure, such as water and food, and transformation to more toxic forms (alkylation of mercury to methylmercury). Considerable attention and research have focused on the ecological changes that are involved in the acidic postdeposition stage, including effects on soil systems, vegetation, aquatic chemistry and aquatic biology, particularly the impact on reproduction and growth of fish. These effects are well documented in other major studies, such as the Report of the National Academy of Sciences on Acid Rain Deposition (*1*). It may be argued that effects on soil that influence the ability to grow food crops, effects on crops themselves, and reduction in consumable fish are, in themselves, indirect threats to human health. However, the level of such effects is not sufficient to support such an argument. In fact, no effects on human health have been demonstrated to date to be the result of the sequence of changes that occur during the postdepositional stage of the acid rain phenomenon. The lack of documented effects may reflect that no such effects exist or that interest in the phenomenon of acid rain is recent; few, if any, investigations of possible linkages have been made. In principle, acid rain in the postdeposition stage may influence human exposure to toxic chemicals by two main routes: the accumulation of chemicals in food chains and the contamination of drinking water. Metals are the substances primarily affected, particularly lead, cadmium, mercury, and aluminum.

Mobilization of Metals during the Postdeposition Stage

Williams (*58*) had pointed out that metal ion interactions in biology can be divided into three classes: metal ions in fast exchange; metal ions in intermediary exchange; and metal ions in slow exchange. These changes occur with organic ligands to which metal ions can coordinate. Metal ions in fast exchange are especially important in toxicity considerations. Examples of elements in fast exchange in biology are the alkali metals, sodium and potassium, and the alkali earth metals, calcium and magnesium, as well as the most important hydrogen ion. Solid-state ions of the elements lead, cadmium, and aluminum can be replaced by any of the ions in fast exchange, especially by hydrogen ion, to cause their solubilization in water. This process can make lead, cadmium, and aluminum soluble and available for bioconcentration in food chains and in drinking water sources to which humans are exposed. This must be considered in terms of total exposure to aluminum and aluminum compounds.

In acidic lakes, aluminum is of special concern because it is very abundant in sedimentary rocks (i.e., over 5%). In fact, this element is more abundant than iron in the earth's surface (*59,60*). Acid rain provides the increase in hydrogen ion concentration, which in turn increases the concentrations of soluble aluminum containing chemical species in water. Furthermore, absorption and neurotoxicity of aluminum are enhanced by low dietary calcium and magnesium (*61*). Acidic soils are often deficient in these alkaline earth metals.

The bioaccumulation of mercury occurs in acid lakes by an entirely different mechanism. Inorganic chemistry is introduced as a result of atmospheric deposition. Once present in soils and sediments, such inorganic complexes of mercury are biomethlylated to give the neurotoxins methylmercury and dimethylmercury. Methylmercury is produced in sediments and soils under acidic conditions, whereas dimethylmercury is

produced under alkaline conditions. The details of this mercury cycle are very well understood at the biochemical level. Most of the chemical species of mercury, which are present in acid lakes, have been detected and analyzed by sophisticated analytical techniques. This is not true for the analysis of aluminum-species where the predominant chemical species in acidic waters and in biota are not yet understood.

Mercury

Toxic Effects of Methylmercury in Man. The human toxicology of methylmercury is well described in the literature due to catastrophic poisonings (fish) in Japan in the 1950s and 1960s and to a large poisoning (treated seed) in Iraq in the winter of 1971–72. Studies on a number of cases of industrial poisoning have also contributed substantially to the understanding of the toxic effects of methylmercury on man (*62*), primarily the damaging of the nervous system. The main areas affected are associated with the sensory, visual, and auditory functions and those areas concerned with coordination, especially the cerebellum. The earliest effects are nonspecific symptoms, such as complaints of paresthesia, malaise, and blurred vision. Subsequently, signs appear such as concentric constriction of the visual field, deafness, dysarthria, and ataxia. In the worst cases, the patient may go on to coma and ultimately death. In less severe cases, some degree of recovery occurs in each symptom; this is believed to be a functional recovery that depends on the compensatory function of the central nervous system. The subjective complaint of paresthesia was found to be a permanent symptom with patients exposed in the Japanese outbreak, whereas in the Iraq outbreak, paresthesia in many cases was transient. The reason for the difference is not known.

Dose-effect and dose-response relationships for methylmercury compounds in man have been presented and evaluated previously (*63,62*). The most recent analysis of the Iraq data has been published by Nordberg and Strangert (*64–66*). This analysis took into account not only the individual range of thresholds to such symptoms as paresthesia but also the interindividual variation in whole body biological half-times. These two distributions were combined to give an overall estimate of the risk of paresthesia for a given steady state daily intake of methylmercury. Their calculations indicated that an intake of 50 μg/day in an adult person gives a risk of about 0.3% of the symptom of paresthesia, whereas an intake of 200 μg/day would give a risk of about 8% of symptoms of paresthesia.

The range of individual intakes of methylmercury in the United States is not known. With reference to Table 1, a Pike consumer would need to ingest about three times the average amount to approach a daily intake of 50 μg mercury assuming an average mercury level in Pike of 1 μg Hg/g wet weight. However, these estimates of risk apply only to adults. Observations on both human subjects and experimental animals indicate that the developing central nervous system is more sensitive to damage from methylmercury than the adult nervous

Table 1. Fish and shellfish consumption in the United States (September 1973-August 1974).[a]

	Rank	lb/yr	% of total by weight	Number of actual users (millions)	Mean amount per user, g/day
Total		2957	100.0	197	18.7
Tuna (mainly canned)	1	634	21.4	130	6.1
Unclassified (mainly breaded, including fish sticks)	2	542	18.4	68	10.0
Shrimp	3	301	10.2	45	8.3
Ocean perch[b]	4	149	5.0	19	9.7
Flounder	5	144	4.9	31	8.6
Clams	6	113	3.8	18	7.6
Crabs/lobsters	7	110	3.7	13	10.6
Salmon	8	101	3.4	19	6.7
Oysters/scallops	9	88	3.0	14	7.8
Trout	9	88	3.0	9	12.3
Cod[b]	11	78	2.7	12	8.1
Bass[c]	12	73	2.5	7.6	12.0
Catfish[c]	12	73	2.5	7.5	12.1
Haddock[b]	12	73	2.5	11	8.6
Pollock[b]	15	60	2.0	11	6.8
Herring/smelt					
Sardines	16	54	1.8	10	6.7
Pike[c]	17	35	1.2	2.5	17.4
Halibut[b]	18	32	1.1	5.0	8.0
Snapper	18	32	1.1	4.3	9.3
Whiting	20	25	0.9	3.2	9.7
All other classified		152	5.1		

[a]EPA data.
[b]Mainly imports.
[c]Freshwater.

system. The first indications came from the outbreak of methylmercury poisoning in Minamata, Japan, in the 1950s, when it was found that mothers who were slightly poisoned gave birth to infants with severe cerebral palsy (*67*).

Subsequent studies on animals confirm the increased sensitivity of the fetus. In the Iraq outbreak in 1971–72 cases of severe damage to the central nervous system in infants prenatally exposed were also reported. More recent follow-up studies in Iraq have indicated a milder syndrome at lower exposure levels. In fact, it has been possible to demonstrate a relationship between the maximum hair level in the mothers during pregnancy and the frequency of abnormalities in their infants.

The clinical picture was dose-dependent. In those who were exposed to high maternal blood levels of methylmercury, the picture was of cerebral palsy indistinguishable from that caused by other factors. Microcephaly, hyperreflexia, and gross motor and mental impairment sometimes associated with blindness or deafness was the main pattern (*68*). Milder degrees of the affliction were not easy to diagnose during the first few months of life but they became clear with later times. The cases showed mainly psychomotor impairment and persistence of pathological reflexes. The mildest cases had findings quite similar to the findings in the minimal brain damage syndrome (*68*). The frequency of mental retardation in infants may be correlated with maximum hair levels in the mother. Effects are detectable in prenatally exposed infants with maternal hair levels substantially lower than those associated with the onset of signs in adults.

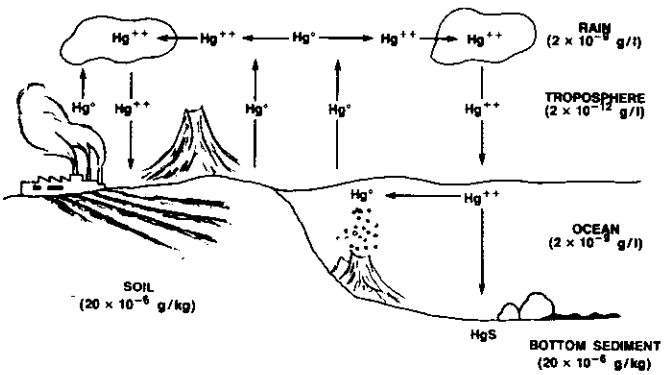

FIGURE 1. A schematic representation of the global cycle of mercury. This scheme is based on reviews by NAS (*100*), Nriagu (*101*), and Lindquist et al. (*69*).

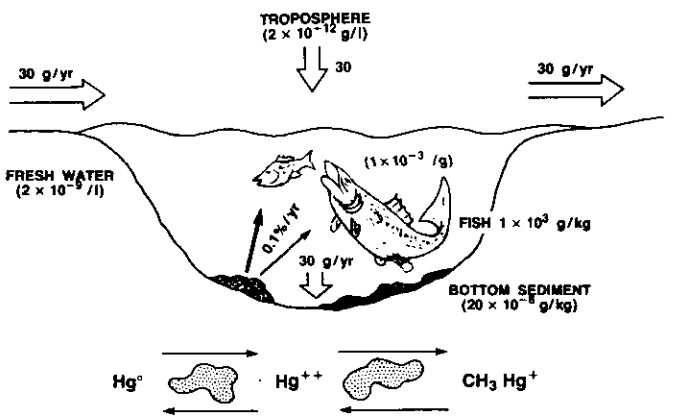

FIGURE 2. A schematic representation of the biomethylation of inorganic mercury and the accumulation of methylmercury in aquatic food chains. The diagram represents a lake surface over 1 km. The open arrows indicate net movement of mercury in grams per year. The other figures give the concentration of mercury in air, water and sediment. The figure is adapted in part from Jernelov et al. (*69*).

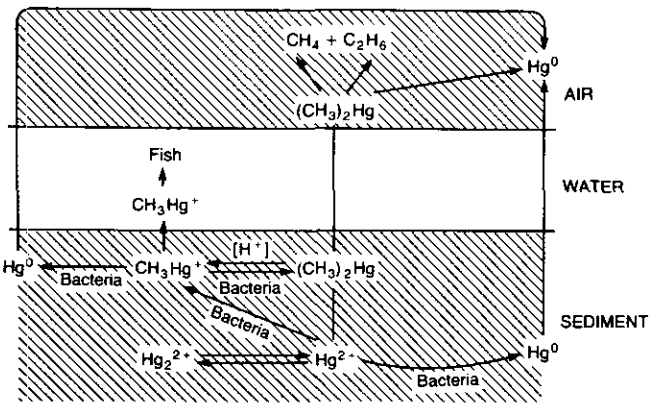

FIGURE 3. A biogeochemical cycle involving bacterial methylation and demethylation of mercury. Adapted from Fig. 3.1 of NAS (*100*).

Role of Acid Precipitation in Mobilization and Transformation of Mercury to Methylmercury. There is mounting evidence that acid precipitation leads to higher levels of methylmercury in edible tissues of freshwater fish (*69*). To appreciate the mechanisms that underly this linkage, it will be useful succinctly to summarize the fate of mercury in the environment. Two cycles are involved: one is global in scope and inorganic in nature; the other cycle is local and biological. The global cycle (Fig. 1) involves the emission of elemental mercury vapor from land and water surface and from anthropogenic sources, especially coal-burning power stations. The anthropogenic contribution (of the order of 3000–5000 tons per year) is probably about 25% of the total emission to the atmosphere. Long distance transport of the elemental vapor occurs in the atmosphere; its residence time is on the order of years. A small fraction of the mercury in the atmosphere is in the water-soluble form. Its precise chemical species is not yet known. This form is returned to the earth's surface in rain water and possibly by dry deposition. Its residence time is of the order of a few days. Bodies of fresh water will receive soluble mercury directly from the atmosphere and indirectly from water run-off from land. A balance study on Swedish lakes indicated the direct and indirect contributions were about equal (Fig. 2). In the water phase, the soluble mercury may be reduced back to metallic mercury and evaporate to the

atmosphere. The remainder attaches to sediment. At this point the biological cycle operates on mercury. Inorganic mercury attached to sediment becomes a substrate for microorganisms that produce mono- and dimethylmercury (Fig. 3). The monomethyl species is avidly accumulated by fish and increases in concentration at higher trophic levels of the aquatic food chain (Fig. 3). Concentrations of methylmercury are highest in the tissue of large predatory fish such as northern pike, lake trout, and bass. The levels of methylmercury present in the water phase are extremely low, probably less than 10^{-11} g/L, whereas the concentration in muscle of northern pike may be as high as 10^{-3} g/kg representing a large bioconcentration factor of one hundred million-fold.

Investigators in Sweden noted unusually high concentrations of mercury in pike in lakes that did not receive any known direct discharge of mercury from anthropogenic sources. Furthermore, the level of methylmercury in fish tissue was statistically correlated with the pH of the water. In the pH range of 5–7, the methylmercury in fish rose as the pH fell. In extremely acidic water, below pH 5, lower mercury levels were seen (Fig. 4). Studies in other countries affected by acid rain, e.g., Norway and Canada, have also noted fish in acidic water tend to have higher methylmercury levels.

Many factors are believed to influence methylmercury levels in fish of which pH is only one. The mechanism of the pH effect is not yet fully understood. Several possible mechanisms have been suggested: acidic precipitation may remove mercury from the atmosphere more effectively than neutral pH. The rate of methylation of inorganic mercury by microorganisms is pH dependent with the maximum rate formation of monomethylmercury occurring at lower than pH 6. The pH influences the species of methylmercury formed by the microorganisms, a higher pH favoring the formation of the insoluble and volatile dimethylmercury which would not be accumulated readily in fish but rather vaporized into the atmosphere (Fig. 3). A reduced pH should favor the presence of a divalent ionic mercury in water, reducing its presence in complexes and chelates, and therefore making mercury more available for methylation reactions. The total biomass in an acidic lake is usually lower than in a neutral lake. Thus, since most of methylmercury is present in the biomass, one would expect its concentration to be necessarily higher in the biomass (including the fish) in the acidic lake.

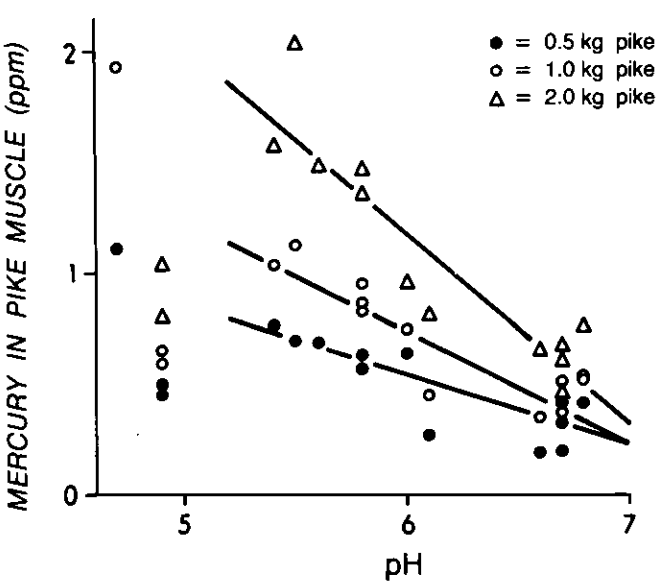

FIGURE 4. The concentrations of total mercury in pike (muscle tissue) as a function of pH. Regression lines were drawn for three groups of fish distinguished by body weight (0.5, 1.0, and 2.0 kg) over the pH range 5 to 7. Adapted from Fig. 3 of KHM, Report No. 192 (*102*).

The consequences of elevated methylmercury levels in freshwater fish may be evaluated from two points of view. First, the current Federal and state guidelines will be enforced, thereby leading to the blacklisting of lakes and rivers having unacceptably high concentrations of mercury in fish. This has occurred in Scandinavia, where there is a Federal action level of 1 μg Hg/g wet weight of fish muscle—the same as the level of the U.S. Food and Drug Administration. The second viewpoint is that human intake of methylmercury will increase. Fish and fish products are the dominant if not only sources of human intake of methylmercury.

The U.S. Department of Commerce (*70*) conducted a survey of over 25,000 individuals representative of the U.S. population with the intention of determining the intake of methylmercury from fish. On a per weight basis, consumption of tuna far exceeds that of other species of fish in the U.S. (Table 1). However, since the actual number of users or consumers of tuna fish is also very high, the amount of tuna consumed per user is not dramatically different than the consumption per user of other species of fish. It is of interest to note that the species with highest consumption per user is northern pike, having a value of 17.4 g/day; species of freshwater fish, catfish, bass, and trout are next highest in per user consumption at about 12 g/day.

Lead. Lead is probably the most ubiquitous toxic metal, and its distribution in the environment, particularly its presence in media that contributes to human exposure, air, water, food, is in large part the result of man's activities. It is clear that the acid rain phenomenon contributes to this problem in a number of ways, but the relative significance of acid rain in a quantitative sense is not yet certain.

Toxicity of Lead. A number of chronic subtle and overt biological effects of lead in humans have been well studied and documented. These include effects on heme biosynthesis and erythropoiesis, central and peripheral nervous system toxicity, kidney effects, derangement of Vitamin D metabolism, and essential trace metal metabolism such as iron, calcium, and zinc. However, it is not possible to quantitate human toxicity risk for lead due to long-term acid precipitation simply because it is not possible to quantitate the potential increase in lead exposure attributable to this factor. But it is possible to

rank the various effects of lead across a gradient of increasing human exposure, as indexed by some biological measure such as blood lead, and, if we are at some time able to identify the contribution of the acid rain phenomenon to increases of lead in the environment, we might then be able to measure the impact of the acid rain phenomenon on the human health effects of lead.

Ranking of health effects of lead must be done with that segment of the U.S. general population at most risk for the adverse effects of lead: preschool children. The threshold for effects of lead occur generally at a lower index of exposure in preschool children than adults (*71,72*). These apparent "thresholds" or lowest observable effect levels are given in Table 2. While basic understanding of some of these effects is still under study, it can be seen that more than one effect may occur at even moderate levels of lead exposure. Furthermore, pediatric population surveys, such as the National Health and Nutrition Evaluation Survey (NHANES II), have shown that there are relatively large numbers of children, particularly those in urban areas, whose blood lead values are at or approaching some of the threshold categories in Table 2 (*73*). For example, NHANES II tabulations show that 45.3% of black children aged 6 months to 5 years have 20–29 μg Pb/dL of blood, 9.2% have 30–39 μg Pb/dL and 1.7% have values higher than 40 μg Pb/dL. It is clear from Table 2 and these percentage distributions that the superimposing of any additional lead exposure factor, such as any due to the acid rain phenomenon, will have a significant impact on these percentages by shifting children to higher exposure categories.

Contributions of Acid Rain to Exposure of Children to Lead. The general population, including pregnant women and children, receives its major exposure to lead through lead content of food and water. In addition, children are further exposed to significant amounts of lead in soil, dust, and paint because of their behavioral relationships to these sources, e.g., hand-to-mouth contamination. Acidification of drinking water increases the solubility of lead in the water. More than half of the U.S. population living in year-round dwelling units receive its drinking water from municipal or private supplies derived from surface and ground water (*74*). Lead may be mobilized from sediments and soils to bodies of water which may serve as sources of drinking water. Davies and Everhart (*75*) have calculated that lead solubility in soft, acidic water can reach potentially toxic levels, ca. 500 μg PbL, while Lazrus and coworkers (*76*) estimated that soft waters could mobilize significant levels of lead in surface runoff in the northeastern U.S. at values of pH which are presently attainable from acid precipitation in this area of the U.S.

Relatively acidic water entering a plumbing system prevents the buildup of a normally protective calcium carbonate plaque in plumbing and permits ongoing dissolution of lead. This problem is most acute in older urban areas of the U.S. such as New England where lead piping itself may be in use (*77*), but will also exist to some degree with copper plumbing having lead solder for sealing of joints (*78*). A sizable data base exists for assessing potential impact of acidic drinking water. Studies of the problem in Glasgow, Scotland, where

Table 2. Lowest observable effect levels in young children for lead.[a]

Lowest observed effect level (lead in blood, μg Pb/dL)	Effect observed	Significance
10	ALA-D inhibited Py-5′-N inhibited	Accumulation of ALA, disturbed heme biosynthesis Disrupted pyrimidine metabolism in red blood cells
15–20	EP elevation	Signals reduced heme formation in tissues and general mitochondrial injury
15–20	EEG disturbances	Indicates central nervous system dysfunction but the significance in terms of performance is presently unclear
15–20	Reduced 1,25-$(OH)_2$ vitamin D synthesis	There is disturbed absorption and availability of calcium for essential metabolic needs
30	Reduced nerve conduction velocities in adults, probably at this level in children	This is an indication of peripheral nervous system dysfunction
40	Reduced hemoglobin Increased urinary ALA Elevated coproporphyrin Cognitive deficits??	These are indices of significant heme biosynthesis impairment Deficits in intelligence and ability to learn at this level of lead are presently being debated
50 and above	Cognitive deficits, renal dysfunction, and overt signs of neurotoxicity	Entering the range of overt toxicity of lead to a number of organ systems

[a]Abbreviations: Pb, lead; ALA-D, aminolevulinic acid dehydratase, Py-5′-N, pyrimidine-5′-nucleotidase; ALA, aminolevulinic acid, EP, erythrocyte protoporphyrin.

levels of lead in drinking water can reach 500 μg PbL because of soft, acidic water and lead plumbing, have shown that these levels of exposure can be toxic (*79,80*).

A further consideration with acid precipitation is the corrosive effect or deterioration or weathering rate of outside surfaces containing paint of high lead content. This weathering process is not restricted to deteriorated housing in inner urban areas of the U.S. but can also occur in rural areas as well. It is known that significant external weathering of painted surfaces over time is an active process (*81,82*), and there is potential for acid precipitation in hastening this process with concomitant transfer to soils and dusts in contact with children, since a common ingredient in high lead paint is basic lead carbonate.

Finally, it must be emphasized that children take in more lead than adults on a unit weight basis, absorb more of the intake, and also retain a higher percentage. Hence, drinking water used in formulae or other food preparation, as well as beverage, would pose a proportionately greater impact on this age group in terms of lead content changes associated with acid precipitation.

Cadmium

Cadmium Toxicity. The major adverse human health effect associated with long-term low level ingestion of cadmium is renal disease (*83*). Although inhalation of cadmium is known to cause lung disease and possibly cancer of the lung, the potential contributions of cadmium to body accumulations are more likely to be by ingestion and not inhalation. Current understanding of cadmium toxicity is that nearly all cadmium ingested over a lifetime is retained; the biological half-time is probably more than 30 years. Accumulation is greatest in renal cortex and it has been learned from exposed human populations and experimental animals that kidney disease may occur when a critical level of cadmium is reached in the kidney cortex. The actual level in the kidney that causes disease and the mechanism or pathogenesis of the disease is still being studied, but much is known. Another factor in the cadmium problem is that there is no acceptable method for removing this metal from the body as there is for most other toxic metals. Therefore, from a public health viewpoint, it is prudent to be particularly concerned about activities that will add to human exposures.

Role of the Acid Precipitation Phenomenon on Human Exposure to Cadmium. Those segments of the U.S. population at increased risk to the adverse effects of cadmium are the elderly, cigarette smokers, and individuals with unusual dietary habits, particularly vegetarians. Cadmium, like lead, is an element which accumulates in the human body. Unlike lead, however, this accumulation is only associated with vital organs such as the kidney and it is thus difficult to forestall adverse effects due to such accumulation by other than a policy of exposure prevention. Cadmium, therefore, epitomizes an agent whose control is of necessity a prospective process; and the impact of long-term acid precipitation needs to be considered in this.

There are at least three routes for long-term impact of acid precipitation on human exposure to cadmium which should be considered. As with lead, relatively acidic water in plumbing systems has the potential to mobilize cadmium from soldered joints of copper plumbing. While the degree of this problem is not that of lead (see above), available data support the notion that it can be a cadmium exposure risk factor. For example, Deane et al. (*84*) reported that 7% of households studied in Seattle had tap water cadmium levels which exceeded the U.S. Public Health Service standard of 10 μgL for cadmium. The Seattle water supply is quite soft. A potentially greater problem may reside in the mobilization of cadmium from crop soils which are dressed with cadmium-containing phosphate fertilizer into various crops because of the long-term impact of acid precipitation on such lands. The crops include not only food categories but other economically important production, particularly tobacco. Tobacco and leafy food vegetables are particularly effective scavengers of soil cadmium under conditions of reduced pH. The amount of land involved is very large and there are presently no regulatory guidelines for the use of cadmium-containing phosphate on such lands (*83*). A third consideration relates to the land application of municipal sewage sludges, which is increasingly being viewed as a disposal option of last resort (*83*). While regulations attending such land spreading include liming to immobilize the cadmium and other toxic elements, the long-term impact of acid precipitation on these control measures can be deleterious. An additional factor is the potential for leaching of cadmium from waste dumps.

Aluminum

Aluminum, the most common metallic element, comprises 5% of the earth's crust. For the most part, aluminum is largely present in insoluble, and thus biologically unavailable, forms. Among the effects of acid rain is the solubilization of significant amounts of aluminum from the soil resulting in increased levels of the element in local lakes and streams. The possible toxic effects of these elevated aluminum levels on fish and vegetation has been the subject of research and there is evidence available that in this setting it can indeed exert a harmful effect on both flora and fauna. In the present state of scientific knowledge, we cannot make any definitive statements as to the potential human health effects of acid rain with respect to aluminum.

Aluminum is not known to be utilized in any natural biologic process and is generally considered to be relatively nontoxic to man. However, within the past several years, aluminum has been implicated in the pathogenesis of several human disorders. Most of these

conditions occur in patients with chronic renal failure. The best characterized is a condition referred to as dialysis encephalopathy or dialysis dementia (*85*). This disorder is characterized by progressive speech disturbance, dementia, and convulsions. The brain tissues, muscle and bone of affected patients show markedly elevated aluminum content. It is generally fatal within six months, although some patients have had clinical improvement following chelation therapy (*86,87*). In general, the aluminum is thought to originate from either dialysis fluid containing excess aluminum or from excess oral intake (*88*). Nondialysis patients with this condition have been found among children with renal failure who were taking oral aluminum hydroxide preparations (*89,90*).

Other aluminum-related problems are seen in patients with chronic renal failure. Osteodystrophy occurs in patients who deposit large amounts of aluminum in their bones (*91,92*). These patients can develop spontaneous fractures and frequently will also have evidence of encephalopathy. One study has shown that the tap water of renal patients with the highest incidence of fractures and encephalopathy had concentrations of calcium and fluorine which were lower and concentrations of aluminum and magnesium which were higher than those in the water of patients without these complications (*93*).

Aluminum has also been considered to play a possible role in the etiology of Alzheimer's Disease. Aluminum salts can induce lesions in the nervous system of the cat and rabbit that are similar, but not identical, to those seen in the brains of Alzheimer's Disease patients (*94,95*). The studies of Crapper and coworkers have shown evidence of increased amounts of aluminum in the brains of individuals dying of Alzheimer's Disease when compared to nondemented controls (*96*). Attempts to reproduce this finding have produced varying results and remain controversial (*97*). Perl and coworkers have evaluated this question on a cellular level, using precise electron probe methods. Their data (*98*) indicate that aluminum accumulation is found in those neurons which demonstrate the presence of neurofibrillary tangles (one of the characteristic microscopic lesions of Alzheimer's Disease).

Similar findings have been reported in neurons containing neurofibrillary tangles in the brains of the Chamorro natives living on the island of Guam (*99*). The Chamorros have been extensively studied over the past 35 years in an effort to explain their remarkable tendency to develop neurofibrillary tangles associated with amyotrophic lateral sclerosis and Parkinsonism with dementia. Extensive data collected on Guam strongly suggests that the unusual tendency towards neurodegenerative disorders is related to local environmental factors and that aluminum accumulates in the brains of affected individuals.

Another recent study demonstrates that aluminum can affect the permeability of the blood-brain barrier to small peptides, a change that may be related to the primary defect responsible for senile dementia (Alzheimer's Syndrome) (*61*).

The present state of knowledge indicates that aluminum in our environment as well as aluminum-containing products constitutes little, if any, risk of acute toxicity to the healthy population. However, those with chronic renal failure, particularly those undergoing renal dialysis, are especially vulnerable to the toxic effects of this element. Whether this risk significantly increases through the liberation of increased amounts of aluminum by the action of acid rain is a debatable question. There is certainly a great deal more aluminum within a single antacid tablet or slice of American cheese than is present in a gallon of stream water coming from an acid rain-washed region. The problem is that one cannot rely purely on a simple parts-per-million concentration of the element. We know very little about the various chemical species in which aluminum exists in nature and their potential bioavailability.

We have even fewer scientific data available with respect to the potential long-term effects of exposure to aluminum in our environment. Although aluminum has now been demonstrated within the damaged nerve cells associated with Alzheimer's Disease, it is still unclear if this phenomenon has etiologic significance. The data from Guam suggests that local environmental factors can play an important role, apparently acting through soil and water supply. Again, details of aluminum speciation on the island are lacking. Factors that allow aluminum to enter the nervous system of one individual and not another are not known. Field data indicate that one of the effects of acid rain is to increase the bioavailability of aluminum to flora and fauna. How high that concept extends up the biologic ladder is unknown. The possibility that it might extend to man is hypothetical, yet is certainly scientifically plausible.

Conclusions

Adverse human health effects, namely acute and chronic respiratory effects, can occur from the predeposition phase of the acid phenomenon due to inhalation of acidic particles and gases. State-of-the-art methodology to evaluate these effects is just now being applied to this question.

The major postdeposition effect of the acid rain phenomenon is to acidify water, increasing solubility and subsequent human exposure to mercury, lead, cadmium, and aluminum. Acidification increases bioconversion of mercury to methylmercury, a highly toxic compound, which accumulates in fish, increasing the risk to toxicity in people who eat fish.

Increase in water and soil content of lead and cadmium increases human exposure to these metals which become additive to other sources presently under regulatory control. The potential adverse health effects of increased human exposure to aluminum is not known at the present time.

Deficiencies in the identification of the contribution of

predeposition of air pollutants and postdeposition mobilization of toxic metals to the recognized potential health effects of the involved toxic substances are due to the fact that scientists have not addressed these specific questions.

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