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Impact of Effects of Acid Precipitation on Toxicity of Metals

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Acid precipitation may increase human exposure to several potentially toxic metals by increasing metal concentrations in major pathways to man, particularly food and water, and in some instances by enhancing the conversion of metal species to more toxic forms.

Human exposures to methylmercury are almost entirely by way of consumption of fish and seafood. In some countries, intakes by this route may approach the levels that can give rise to adverse health effects for population groups with a high consumption of these food items. A possible increase in methylmercury concentrations in fish from lakes affected by acid precipitation may thus be of concern to selected population groups.

Human exposures to lead reach levels that are near those associated with adverse health effects in certain sensitive segments of the general population in several countries. The possibility exists that increased exposures to lead may be caused by acid precipitation through a mobilization of lead from soils into crops. A route of exposure to lead that may possibly be influenced by acid precipitation is an increased deterioration of surface materials containing lead and a subsequent ingestion by small children. A similar situation with regard to uptake from food exists for cadmium (at least in some countries).

Human metal exposures via drinking water may be increased by acid precipitation. Decreasing pH increases corrosiveness of water enhancing the mobilization of metal salts from soil; metallic compounds may be mobilized from minerals, which may eventually reach drinking water. Also, the dissolution of metals (Pb, Cd, Cu) from piping systems for drinking water by soft acidic waters of high corrosivity may increase metal concentrations in drinking water. Exposures have occasionally reached concentrations which are in the range where adverse health effects may be expected in otherwise healthy persons. Dissolution from piping systems can be prevented by neutralizing the water before distribution.

Increased aluminum concentrations in water is a result mainly of the occurrence of Al in acidified natural waters and the use of Al chemicals in drinking water purification. If such water is used for dialysis in patients with chronic renal failure, it may give rise to cases of dialysis dementia and other disorders. A possible influence on health of persons with normal renal function (e.g., causing Alzheimers disease) is uncertain and requires further investigation.

While all of the mentioned possibilities for increased metal exposures due to acid precipitation do exist, information that allows a quantitative estimation of their importance is almost entirely lacking and more research is needed.

For an evaluation of the impact to human health of increased metal exposures, present knowledge about relationships between dose (or exposure) and the risk for adverse effects are reviewed. It is concluded that improved knowledge would be desirable for several of the metals discussed. Particularly, for an evaluation of possible adverse effects of aluminum in persons with normal renal function, present knowledge is inadequate and more research is needed.

Quantitation of Health Effects in Relation to Exposure

Evaluation of environmental pollution from the public health point of view usually benefits from an analysis in two steps: toxicity evaluation and exposure evaluation.

The toxicity evaluation of possible health effects that can be induced should emphasize adverse health effects that occur at relatively low exposures. Particularly for these effects, detailed knowledge is of importance because such effects are critical in relation to preventive action (*1,2*). These are termed "critical effects." It is desirable to have access to detailed information on the relationship between exposure (or dose) and the incidence of effects in the human population, (i. e.,dose-response relationships) for the critical effects.

The other type of information that is required in order to evaluate an existing pollution situation, from the public health point of view, is information concerning the

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actual human exposure to the pollutant. By combining dose-response data with exposure data the pollution situation in question can be precisely evaluated.

This summary of available evidence on the impact of acid precipitation on the toxicity of metals will adhere to these principles. In several instances uncertainties in dose–response data and exposure data are considerable, thus limiting our possibilities for a precise evaluation. Such uncertainties will be pointed out as a basis suggestion for further research. Possibilities exist for an impact of acid precipitation on the toxicity of several metals. Mercury is probably the metal which has been most studied in relation to this problem and where a reasonable amount of information about dose-response relationships exists and this metal will be discussed first. For other metals treated subsequently (Pb, Cd, Al, etc.), either dose–response data or information about the impact of acid precipitation is available to a lesser extent.

Mercury

General Aspects

Mercury can occur as several chemical species, e.g., metallic mercury, mercuric and mercurous salts, and a number of organometallic mercury compounds. The toxicities of these compounds are quite different. Pulmonary toxicity is the critical effect after short-term inhalation of high concentration of mercury vapor; after long-term inhalation, neurotoxic effects (e.g., neuroasthenia and tremor) and renal effects may occur (*1,3-5*).

In exposures to inorganic mercury salts, renal effects are usually considered as the critical effects. Exposures to organometallic mercury compounds with limited stability in biological systems (e.g., methoxyethylmercuric compounds) can give rise to toxic effects similar to those of inorganic mercuric salts, while compounds with a high stability (e.g. methylmercuric compounds) display entirely different metabolic and kinetic properties. The latter chemical species of mercury gives rise to neurotoxic and fetotoxic effects (*6*).

Exposure to chemical species of mercury other than methylmercury usually does not reach concentrations in exposure media (air, water, food) of the general environment that approach toxic levels, and there are no reports that acidification could mobilize such chemical species to such an extent that toxic concentrations are reached.

The following discussion will focus on the toxicology of methylmercury which has a tendency for bioaccumulation in nature. This tendency is dependent on acidification. In particular, the dose-response relationships for the critical effects of this mercury compound will be dealt with.

Dose–Response Relationships of Methylmercury compounds in Humans

There exists a possibility, discussed in more detail below and by Wood (*7*), that methylmercury concentrations in fish may be increased by acid precipitation. Since human exposures to methylmercury are almost entirely via fish and seafood, any increase in concentration in fish will increase human exposures. Dose–response relationships of methylmercury thus are of interest. Effects that occur at relatively low exposures are of special interest, and in particular effects that are considered to be critical effects. Neurotoxic effects are considered such effects in adults, and neurotoxic fetotoxic effects are of particular interest in relation to exposure of pregnant females.

Although it is true that it has not been possible to collect human evidence concerning these effects under quite as controlled conditions as those possible in laboratory experiments with animals, some (*3*) of the human evidence approaches the criteria that reasonably can be obtained in human studies with regard to definition of dose or exposure and objective registration of adverse health effects.

Dose–Response Relationships for Neurotoxic Effects of Methylmercury in Adult Humans. Methylmercury compounds are absorbed almost completely (90—100%) after ingestion. Methylmercury penetrates the blood-brain barrier as well as the placental barrier. This compound has a relatively long biological half-time and is accumulated at long term exposure. The uptake of methylmercury in the brain varies among animal species and is particularly high in primates. Neurotoxic effects are thus more pronounced in primates than in other animal species (*3*). Through studies in Iraq (*8*) of a number of people who were accidentally exposed to methylmercury through food, information about neurotoxic effects of methyl mercury in humans is available. A detailed retrospective assessment of exposure was made through segmental analysis is mercury concentrations in hair. By the use of blood and hair concentrations of methylmercury and observations of the occurrence of various symptoms such as paresthesia, ataxia, dysarthria, deafness, and—at very high doses—death, it was possible to report on dose–response relationships, i.e., relationships between the maximum tissue concentrations/body burdens reached and the prevalence of symptoms. The hair analysis also made it possible to study the individual biological half-time in each individual. By studying a large number of individuals in this way, it was possible to estimate the interindividual variation in biological half-time in the human population in Iraq (*9*). It was found that the mean value was about 65 days with a variation between 30 and 120 days.

Based on this information on interindividual variation in biological half-time and information on the interindividual variation in critical concentration (critical body burden) for effects (at short-term exposure), the probability for appearance of the critical effect (paresthesia) in the population at long-term exposure can be calculated by a statistical method (*10*). Such dose-response calculations obviously are subject to a certain statistical error, which can be calculated. Also, the dose-response curve is dependent on the choice of statistical distri-

bution for interindividual variation in critical body burden. These uncertainties of the dose-response curve have been computed (*11,12*). Obviously, the uncertainties are largest in the lower part of the dose-response curve, which is, however, also most important for risk assessment in relation to public health. At a daily methylmercury intake of 150 μg in a 70 kg individual, the 90% confidence interval corresponds to a ratio of 3 over and below the mean estimate of 3% (above the background occurrence of paresthesia) if a Weibull distribution is used for estimating. With a log-normal assumption, the estimate will be 0.4% with a confidence interval of a factor of 2. At lower doses, differences are even larger; for example at 30 μg per day (in a 70 kg individual), which corresponds to what has been in Sweden considered an acceptable daily intake, the estimate for the Weibull distribution is 0.32% and with a log-normal distribution 0.00%. The confidence interval of these two estimates do not overlap.

Dose–Response Relationships for Neurotoxic and Fetotoxic Effects in Humans. The fetotoxic effects of methylmercury are probably the best documented example of a metal compound that affects the developmental processes of the central nervous system (*13*). Observations on humans were made during an outbreak of methylmercury poisoning in Minamata, Japan, in the mid 1950s (*14*). The prenatal effects of methylmercury have also been documented in several animal species (*3,13,15*). During a poisoning epidemic in Iraq 1972, detailed dose descriptions of prenatal poisoning cases were made by analysis of hair concentrations of methylmercury in the mothers, as described in the previous section for adult methylmercury poisoning. Marsh et al. (*16*) reported on neurologic examinations of such children in Iraq who had been exposed prenatally to methylmercury. The maximum hair concentrations during pregnancy were also reported. This information has been used to calculate dose–response curves in reports by Clarkson et al. (*17*) and by Berlin (*18*). Clarkson et al. (*17*) arrived at a "threshold" for the lowest exposure giving rise to a small increase in mental retardation in children at a hair level in the mother during pregnancy of 10–20 μg/g. Berlin (*18*) assumed a distribution of interindividual sensitivity according to a logistic distribution and arrived at a curvilinear dose–response relationship.

The statistical uncertainty (95% confidence interval) in this calculated relationship was reported to be considerable (*19*). At the lower end of the confidence interval a concentration in hair as high as 50 μg/g may be associated with a zero risk of mental retardation, the upper confidence limit predicts that concentrations between 10 and 20 μg/g may be associated with a substantial increase above the background.

Mechanism of Damage: Animal and* in Vitro *Studies. While human data—when they are available, as is the case for methylmercury—probably represent the best database for making estimations of the dose–response relationships for methylmercury in humans, animal and *in vitro* studies can provide important insights into mechanisms of damage, which in turn can support or reject assumptions made in the toxicological models used in deriving dose–response relationships. When discussing animal data for methylmercury it should be remembered that there are considerable biological differences, such as binding characteristics in blood and blood clearance rates, placental structure and function, between laboratory rodents and humans which make the former less suitable for making predictions of mechanisms of methylmercury toxicity in humans. It has therefore been necessary to use primates to uncover more subtle but important pathologic changes induced by methylmercury (*3*).

In monkeys the viability of the offspring was compromised at concentrations of mercury in blood above 1000 μg/kg. Similar observations have not been possible to obtain in humans. Pathological changes in the cerebral palsylike syndrome of humans exposed to methylmercury *in utero* indicates the existence of generalized brain hypoplasia but no gross anatomical malformations. High levels of brain mercury have been associated with abnormal neuron migration and deranged organisation of brain centers and layers (*3*).

In laboratory rodents, on the other hand, high doses of methylmercury administered on a sensitive day of organogenesis produced specific gross anatomic malformations (*3*).

Behavioral tests on monkeys (*3*) compatible with mental retardation in the monkeys have demonstrated adverse effects in the offspring of mothers with 500 μg/kg blood level.

Studies in mice have demonstrated an effect of methylmercury on the microtubules of the neurons (*20*). This effect may constitute a plausible explanation for the neuropathological changes observed in human and primate brains with a change in migration pattern of neurons. In these studies on mice, male offspring were shown to be more sensitive than the females. This observation is of interest, since also in humans it has been claimed (*21*) that males are more sensitive than females with regard to development of psychomotor retardation. The studies in mice thus appear to correlate favorably with human evidence; however, further studies on animal species more similar to humans are warranted. *In vitro* studies (*22*) have demonstrated effects on the mitotic spindle which are compatible with an effect on microtubules.

Other Effects of Methylmercury Potentially of Interest in Relation to "Critical Effects" in Humans. There are a few effects of methylmercury exposure that have been observed in animals, and which may be of interest in relation to critical effects in humans. Obviously, the definition of an effect as a "critical effect" is related to existing toxicological evidence, and when new evidence is obtained, it may turn out that an effect can occur at lower exposure levels than previously believed and/or a previously unrecognized adverse health effect is detected and occurs at an exposure level that is lower than those for previously recognized effects.

The effects of methylmercury on viability of offspring may be of interest in relation to critical effects; however, present evidence does not provide sufficient documentation that such effects do occur at lower exposure levels than those giving rise to neurotoxic effect on the fetus when pregnant human mothers are exposed to methylmercury.

Another adverse health effect, first observed by Lee and Dixon (*23*) in methylmercury-exposed rats, is decreased spermatogenesis and abnormal sperm. Recent evidence (*3*) indicates that similar effects can be seen also in male monkeys exposed to methylmercury orally. However, further studies concerning the blood levels and tissue levels of methylmercury associated with the effects on spermatogenesis will be required in the primate model (and if exposed human populations can be found, also in humans) before this effect can be regarded as a critical effect.

Estimation of Possible Impact of Acid Precipitation on Human Exposure to Methylmercury and Possible Influence on Health in Sweden

Exposure levels of methylmercury for the Swedish population were investigated by the Swedish Expert Committee 1971 (*24*). It was concluded that exposure was mainly via fish, particularly freshwater fish. The consumption of fish by the Swedish population varies greatly. Some people are not fish eaters, whereas a few people consume as much as 500 g of freshwater fish per day. Obviously, with concentrations of mercury in freshwater fish (mainly in the form of methylmercury) often above 1 mg/kg, a daily intake of 500 g, i.e., more than 0.5 mg per day, represents a a very real risk of poisoning even for an adult. A few persons with blood mercury levels up to 1μg/g but no cases of poisoning were found among fish consumers. Nevertheless it was considered necessary to regulate intakes in a way to minimize risks of adverse health effects, and in addition to "blacklisting" (i.e., the banning of fishing) of lakes with mercury concentrations in fish exceeding 1 mg/kg, it was recommended that consumption of fish with mercury levels 0.2–1 mg/kg should be limited to once a week. More than 100 lakes, rivers, and coastal water areas were blacklisted in the late 1960s and early 1970s, mainly in areas where mercury-containing effluents from paper pulp mills, emissions (to air and water) of mercury from chloralkali plants, and other industrial activities could be identified. The situation with regard to mercury concentrations in fish has been followed up in these areas, and there has been a slow but clear tendency towards a decrease during the last decade in most of the blacklisted areas (*25*).

The obvious reason for this decrease is that a very ambitious program for abatement of mercury emissions to air and water has been undertaken in Sweden including the banning of the use of phenyl mercury as a slime reducing agent in the paper pulp mills as early as 1967. For some of the water areas which were blacklisted in the 1960s and 1970s mercury levels in fish have dropped to the extent that the ban has been lifted. On the other hand, there has been an addition of a number of lakes without identified mercury sources to the blacklist, so that the number of blacklisted waters is still in the hundreds.

A probable explanation for the increasing levels of mercury in fish in lakes where no local sources can be found is long-range transport of mercury by air and acid precipitation. The ecological processes involved in explaining these phenomena have been discussed in the paper by Wood (*7*).

There are thus large uncertainties concerning the ecological transformation and dispersion models for mercury in the environment. However, an attempt has been made to quantitate the combined influence on mercury concentration in fish by acidification of a lake and mercury deposition originating from a point source. Since the result is dependent on local conditions of the lake, it is not possible to cite any quantitative information that is universally applicable.

Waste incineration has been shown to contribute relatively large emissions of mercury in relation to the heat energy produced and to contribute considerably more to mercury emissions than coal combustion (*19*) in Sweden at present (when coal usage is very low). However, the contribution to acidification is much larger from fossil fuel combustion (including oil combustion).

How does, thus, acid precipitation affect mercury intakes of the Swedish population? Obviously, this is a very difficult question to answer, and it seems impossible to answer it in quantitative terms at present. It may be a reasonable statement (although no solid evidence is available) that the acidification of lakes taking place as a result of acid precipitation has given rise to increased levels of mercury in fish in a large number of Swedish lakes. In a considerable number of these lakes, concentrations above 1 mg/kg have been reached and they have therefore been blacklisted.

Population intakes of methylmercury depend on consumption patterns of fish (and shellfish). These consumption patterns had not been thoroughly investigated in Sweden since the 1960s, when the Expert Committee (*24*) made their evaluation. Thus, there was no information available concerning the influence on consumption patterns of the recommendation to consume fish from lakes no more than once a week. The KHM project (*19*) in their evaluation of the impact of coal combustion on mercury intakes by the population, calculated expected mercury levels in hair of the Swedish population under the assumptions that consumption habits were identical to those found 1968 and that fish from lakes was consumed no more than once a week. These calculations indicated that a major part of the population would have less than 5 ppm in hair and the highest value would be 10 ppm.

In areas where fish consumption from acidified lakes occurs (e.g., along the coast of the gulf of Bothnia), it was considered of interest to investigate exposure levels

in pregnant women (critical population group) by analysis of mercury concentrations in hair. Such an investigation from the National (Swedish) Food Protection Board was presented recently (*26*). Among 29 females who were "high fish consumers," 0.2–2.5 mg/kg was found in the hair samples. Although it is difficult to apply these values directly to the dose-response estimation, e.g., the hair values do not refer to maximum values in the Forhammar study (*19*), it is still evident that only minimal risks of adverse effects on the fetus seem to exist in the Swedish population. Margins of safety are small or nonexistent, however, considering the large uncertainties involved both in the dose-response estimate and the exposure estimate. An increasing exposure that may be a result of increased acidification of lakes should be counteracted as much as possible.

The U.S. Situation

As in other countries, intakes of other chemical forms of mercury, e.g., via drinking water, does not reach levels that are of concern to human health (*27*). The mercury compound that is of major concern for human environmental exposures is methylmercury, and the exposure route is via fish and shellfish.

Methylmercury exposure for the U.S. population is less related to consumption of fish from lakes than in Sweden. The average fish consumption is also lower than in Sweden, and this is one of the reasons why it has not been considered necessary to recommend that fish consumption of certain species of fish be limited to once a week. This means, on the other hand, that theoretically there might exist small groups of individuals with very special consumption habits that might be exposed to relatively large daily doses of methylmercury. On the whole, however, population risks in the U.S. can be regarded as similar to the Swedish situation, and the same evaluation as stated in the foregoing section applies.

Research Needs

Research needs relate to both the exposure evaluation and the dose-response evaluation. Improved information about population exposure to methylmercury can be obtained by collection of additional data on methylmercury levels in various food items and more detailed data on the consumption (particularly of food that have a high concentration of methylmercury, like fish and shellfish). Another, more direct, way of assessing human exposure and accumulation of methylmercury is through biological monitoring. Hair analysis for mercury is of proven value in such assessments and could be used on a larger scale.

When it comes to an estimation of the impact of acid precipitation on methylmercury intakes by humans ecological mobilization and biotransformation processes need to be further studied as discussed in the preceeding section (*7*).

Research of importance for dose-response assessment include enlarged studies of exposed populations for incidence of mental retardation in children in relation to mercury concentration in hair of their mothers during pregnancy. If possible, populations with different selenium intakes should be studied. Exposed males should be studied for abnormalities in spermatogenesis and fertility.

Experiments in animal species with methylmercury metabolism similar to humans (i.e., monkeys) should be performed to investigate mechanisms of fetal damage and dose and tissue levels required for the appearance of such effects. The influence of combination exposures, with selenium compounds should be investigated in such animal models.

Lead

General Aspects

Human lead exposure is also an important consideration in relation to acid precipitation. Like mercury, lead can occur both in inorganic and organometallic forms and human exposures to both form do occur. Since exposures to inorganic lead are much more abundant than exposure to organolead compounds and the former species of lead is the only one which has been related to acid precipitation, organolead compounds will not be further discussed.

There has been an ongoing discussion in the scientific literature concerning what should be regarded as the critical effect of lead exposure in a human population. Increased zinc protoporphyrin (or free erythrocyte protoporphyrin) in red blood cells, decreased conduction velocity of nerves, minimal brain dysfunction with behavioral manifestations in children, and fetotoxic effects have been considered (*1,28,29*). Presently available evidence concerning the neurotoxic effects in children should be considered as the critical effect when exposures to the general population are considered.

Dose–Response Relationships of Lead in Humans

Dose–Response Relationships of Effects of Lead on Hematopoiesis. Dose-response curves for effects of lead on hematopoiesis have been relatively well investigated in humans (*28,30*). A slight decrease in aminolevulinic dehydratase (ALA-D) activity does not have any functional significance for erythropoiesis and cannot be regarded as a critical effect (*1*).

An increased concentration of zinc protoporphyrin in erythrocytes on the other hand is a reflection of an adverse influence. Blood lead levels have been related to the occurrence of abnormal enzymatic activity or various other hematological indicators of adverse influence on hematopoiesis, e.g., zinc protoporphyrin (ZPP) increases in red blood cells. Dose-response relationships are different in children than in adults, and adult females differ from male adults (*30*). Increases in ZPP (FEP) may occur in children and in women in increasing

frequency at PbB values of 15 μg/100 mL and higher.

Neurotoxic Effects of Lead. Evidence relating the occurrence of minimal brain dysfunctions in children to lead exposure from the general environment has been presented (*31–35*). Dose relationships are not as well defined as for effects of lead on hematopoiesis, but it is now widely accepted that such effects may be observed in increasing frequency with blood lead (PbB) values of 30 μg/100 mL and higher. Changes in EEG have been observed at blood lead levels of 15–30 μg/100 mL and higher (*36,37*).

Another neurotoxic effect of lead exposure for which there has been increasing documentation in recent years is a decreased conduction velocity of peripheral nerves. Blood lead levels of 30 μg/100 mL and higher have been associated with such effects both in children (*38*) and adults (*30*).

Other Toxic Effects of Lead. Other effects of lead that may be of interest in relation to a discussion of critical effects for the human population are effects of lead on reproductive function, including fetotoxic effects. Although such effects have been documented both in humans and experimental animals (*39,40*) dose-response relationships are not well known and a quantitative evaluation therefore is difficult.

Another effect that has been investigated recently is the influence of lead exposure on blood pressure (*41*).

The segment of the general population that is most sensitive to lead exposure is small children and pregnant women. Data describing lead concentrations in blood of these population groups thus is of greatest relevance to an assessment of risks. Considerable differences exist among populations in various countries with regard to blood lead levels. These differences among countries are of interest even if the monitoring did not include the most sensitive groups. The variation (from 6 μg/100 mL in Tokyo to 22 μg/100 mL in Mexico as median values in school teachers reported by GEMS (*42*) in all probability also reflects similar differences extending to such sensitive groups.

An extensive pediatric population survey has been reported from the U.S. (*43*) showing that 9% of black children had 30–39 μg/100 mL and 1.7% had more than 40 μg/100 mL. Concentrations found in pediatric populations in Europe are rather less well known, with the exception of a few special and ongoing studies (*44*).

Estimation of Possible Impact of Acid Precipitation on Human Exposure to Lead and Its Health Implications

The Centers for Disease Control of the U.S. Public Health Service recently lowered the definition of an elevated blood lead level in children from 30 to 25 μg/dL. The reasons for this include increasing evidence that low-level lead exposure produces adverse effects on children's behavior and intelligence, the central and peripheral nervous systems of adult workers, heme biosynthesis in children, nucleotide metabolism, and vitamin D metabolism (*45*).

The extent of the impact of acid precipitation on human exposure to lead depends on its influence on various sources of human exposure to lead. Perhaps the most important of these in terms of effects of acid precipitation must be lead content of drinking water and food.

Studies by Sharpe (*46*) indicate that the concentration of lead in soil leachate, an area of high atmospheric lead deposition, is well below the drinking water standard and that there is a higher concentration of lead in water reaching the soil than in the soil leachate.

The relationship between blood lead (PbB) and water lead was found to be closely related statistically. An important finding is that this relationship persists even when lead concentrations in drinking water are below 50 μg/L. They found that the point of a noncontribution of water lead to blood lead is at PbB 5.6 μg/dL.

High intakes of lead from drinking water has been experienced by populations in Scotland following leaching of lead from the plumbing system by acidified drinking water (*47*). In the town of Ayr, maternal blood lead concentrations exceeded 36 μg/100 mL in 10% of examined subjects in 1981 after drinking water levels had reached above 1000 μg/L in some tap samples (in 1980).

Liming of the water raised pH values and lowered blood lead levels so that no examined maternal samples exceeded 25 μg/100 mL. A similar experience of increased lead intakes due to plumbosolvency was experienced in nearby Glasgow a few years earlier (*47*), and this exposure was also greatly diminished by liming of the water. Evidently, with exposures through drinking water giving rise to blood lead levels as high as those cited, adverse effects on health can be expected. Obviously, acidification of natural waters that are used as drinking water is of great concern especially when distribution systems contain lead.

In addition to situations like those described for Glasgow and Ayr, roof catchment systems often contain some parts made of lead-containing materials. In areas where such systems are common, the influence of acid precipitation on lead intakes can be considerable.

An increased exposure of children to lead might occur as a result of acid precipitation if there is an increased corrosion of lead containing materials in the child's environment. An increased weathering rate of lead containing painted surfaces with subsequent increases of ingestion by children is one obvious possibility in environments where such surfaces are common. Some foods and beverages, e.g., wine, contain relatively high concentrations of lead. It may be that acid precipitation can increase exposures by this route through mobilization from lead-contaminated soils.

Research Needs

The impact of acid precipitation on human health is directly related to the extent it increases lead concentration in sources of human exposure. Acidification of drinking water sources significantly increases lead content. Leaded water pipes become particularly hazard-

ous as water pH decreases. Other studies have shown that an increase in soil lead to 1000 μg/g is associated with an increase in blood lead of about 4.2 μg/dL due to increase in soil content of vegetables, so that the contribution of acid precipitation to soil lead may also become a factor. Specific studies might be designed to address this question. Other possibilities for increasing lead exposure from acid precipitation have been cited. A greater amount of information is needed that might be obtained from expanded monitoring activities in areas of acid precipitation. And, finally, the significance of any increased human exposure can only be assessed in terms of available information on effects of lead on biological systems. Research on the minimal levels of lead that will produce such effects must be continued.

Cadmium

General Aspects

Cadmium exposures may give rise to toxicity in several organ systems such as the pulmonary, cardiovascular, hemopoietic, and reproductive as well as the liver and the kidney. The critical effects in long-term low level exposure is usually considered to be a tubular dysfunction of the kidney leading to a low molecular weight proteinuria (*48,49*). Such renal effects develop in humans after decades of exposure and are a result of long-term accumulation of cadmium in renal tubule cells.

There are some effects of cadmium on reproductive processes (e.g., placenta) and the carcinogenicity of cadmium that may be considered in relation to critical effects. However, present evidence is not sufficient to consider them as such for humans (*49*). Exposure of the general population to cadmium is mainly via food, but cigarette smoking is also an important exposure route.

Dose–Response Relationships of Cadmium Compounds in Humans

Because of the long accumulation time of cadmium in the kidney, decades usually being required to induce renal toxicity, direct epidemiological studies of intake levels versus incidence of disease are difficult. However, available evidence obtained through such direct epidemiological studies generally confirm the estimates obtained through the use of calculations based on metabolic models.

The importance of defining as precisely as possible the interindividual variation of the metabolic parameters (gastrointestinal absorption, biological half-time) as well as the variation in critical tissue concentrations for damage has been repeatedly pointed out (*12,48,50*). Uncertainties in these estimates and in estimates of intake levels have been discussed by Piscator (*48*) and will not be repeated here. In keeping with the uncertainties mentioned, it may still be of interest to cite some point estimates obtained by combining data on metabolic variation and variation in critical concentration. In the estimates of Hutton (*51*) based on the data of Kjellström (*52*) as cited and modified by Kjellström (*53*) 5% of a population was estimated to suffer increased β_2-microglobulin excretion in urine (a sensitive indicator of renal tubular dysfunction) at long term intakes of 108 μg (in a 70 kg person). An intake of 242 μg was considered to give rise to the same condition in 20% of the population.

Even if the best possible estimates are used, it should be remembered that the uncertainties in the estimated dose-response curve for cadmium is considerable, certainly much larger than the uncertainties calculated for the dose-response curves for methylmercury.

Exposure Situation for Cadmium and Influence of Acid Precipitation

A summary of available data concerning cadmium intakes from food by the general population has been given by Piscator (*48*). Average intake by this route varies from 13 μg/day (Sweden) to 56 μg/day (some urban areas in Japan). Considering the additional intake from smoking and the variation in intakes in the population, this means that there is a reasonable safety margin for a major proportion of the nonsmoking population in Sweden. Such a safety margin does not exist in some urban areas of Japan (considered not to be contaminated by cadmium). In a few U.S. areas studied (Dallas and Chicago), dietary intakes have been estimated to be in the lower part of the range, similar to Sweden.

It is difficult to assess the role of acid precipitation in relation to cadmium exposures. It has been demonstrated that the pH of soil is of great importance for the uptake of cadmium in crops such as rice or wheat (*54–56*). The cadmium content of tobacco is of concern for smokers. The dominating causes of ongoing acidification of soil is mainly fertilizing methods and agricultural activity itself, while acid precipitation usually contributes only a part of the acidification (*19,57*).

Regardless of the reasons for the acidification of arable soils, however, this process is certainly of importance in effectuating a slow increase of human cadmium intakes. Dry and wet deposition of cadmium on soils from smelting operations, waste incineration, and other industrial activities can contribute to soil cadmium. Some agricultural practices using cadmium-containing phosphates and/or sewage sludge for fertilizing purposes contributes extra cadmium to some soils which subsequently might be mobilized by acidification. Unnecessary addition of cadmium to soils should be limited as far as possible, and agricultural practices could be modified to counteract acidification of soils.

The ongoing acidification of nature may also give rise to a mobilization of cadmium into forage of game animals. Elevated concentrations of cadmium in kidneys and livers of moose in Sweden has thus been found in areas with high acid deposition rates (*58*). Exposure through this route may be of importance for special population groups (i.e., hunters). The monitoring of cadmium concentrations in horses may serve as an indicator

of acidification and Cd contamination of soils (*48*).

The intake of cadmium from drinking water usually is small. For areas where acidified waters occur, mobilization of cadmium from piping materials such as roof catchment systems may occur. This may cause considerable increases in Cd intake. Increased cadmium concentrations have also been found in shallow ground water wells of some acidified areas in Sweden. However, concentrations even in these areas have usually been below 5 μg/L, thus contributing only little to daily intakes.

Research Needs

In most countries, e.g., the United States, present daily oral intake of cadmium (10 - 20 μg) provides a certain margin of safety for a major part of the nonsmoking population. The assessment of risk of renal toxicity (critical effect) is very uncertain, and there is a definite need for further definition of dose-response relationship through improved estimates of interindividual variation in metabolism and improved exposure estimates. Further definition of certain other effects (placental toxicity, carcinogenicity) also is needed.

There are several ongoing processes that tend to increase human oral intakes of cadmium slowly, e.g., increased soil concentrations of cadmium and acidification of soils. These processes may also increase cadmium concentrations in tobacco and subsequently contribute to increased exposures in smokers. The quantitative importance of various soil processes, however, is not well known and needs to be further defined.

As a general rule, however, it might be wise not to spread more cadmium than necessary by any activity, since margins for further increases are small or even nonexistent for special population groups with extra exposures (e.g., smokers, occupationally exposed persons, etc.).

Aluminum

Adverse Health Effects of Aluminum Exposures

Aluminum, the most abundant metal in the earth's crust, has long been considered of low toxicity. Concern has been expressed for the possibility of aluminum toxicity from the use of aluminum cooking utensils and the occurrence of aluminum in a number of medicines as well as in food and drinking water, but these possibilities were dismissed in several comprehensive reviews (*59,60*). In recent years, certain degenerative diseases of the central nervous system have been related to aluminum. Elevated concentrations of aluminum in dialysis fluid in combination with oral intakes of aluminum containing drugs in patients undergoing dialysis because of chronic renal failure are considered to be the causal factor for a high incidence of encephalopathy (dialysis encephalopathy or dialysis dementia) in such patients (*61,62*). The reason for the development of the neurotoxic effects of aluminum in these patients is the lack of excretion of aluminum by the kidneys, normally an efficient process, to eliminate excess aluminum from the body. In patients with chronic renal failure, aluminum accumulates in tissues, causing both encephalopathy and a specific form of metabolic bone disease (osteomalacic dialysis osteodystrophy) and anemia.

The majority of chronic renal failure patients who develop aluminum toxicity are on long-term treatment with either hemo- or peritoneal dialysis; however, some patients with renal disease develop toxicity after treatment with aluminum containing phosphate-binding agents only (*62,63*).

Aluminum in the dialysate is thus the major reason for development of aluminum toxicity in patients with renal failure, and epidemiological studies in the United Kingdom have demonstrated a geographical distribution of osteomalacic dialysis osteodystrophy and dialysis dementia that correlates to the aluminum concentration in tap water used to prepare the dialysate (*64*). The concentration of aluminum in water should be less than 15 μg/L in order to prevent the development of aluminum toxicity in patients on dialysis (*64*). While the role of aluminum in inducing toxicity in patients with impaired renal function is now relatively well documented, the role of aluminum as a toxic agent in other neurological disorders where renal function is normal is less certain.

Aluminum salts are absorbed to a varying degree in the gastrointestinal tract of experimental animals and man; however, detailed knowledge about gastrointestinal absorption rates and mechanisms is lacking. One factor that may be of importance for aluminum uptake is the simultaneous administration of citrate. It has been shown in rats that citrate increased intestinal aluminum uptake with subsequent increases in cerebral and bone aluminum concentrations (*65*). However, considerably more information is needed for an understanding of the conditions under which aluminum can be absorbed from the gastrointestinal tract and accumulated in tissues.

Aluminum salts applied in high concentrations locally to the central nervous system in cats and rabbits has given rise to histological changes similar to those seen in brains of patients with Alzheimer's disease (*66,67*). Increased amounts of aluminum have been reported in brains of individuals dying with Alzheimer's disease compared to nondemented controls (*68*). Attempts to reproduce this finding have produced varying results and remain controversial (*69*).

Accumulation of aluminum in neurons which demonstrate neurofibrillary tangles (a characteristic histological lesion of Alzheimer's disease) was found by means of an electron microprobe (*70*). In the indigenous (Chamorro) population of Guam, renal function is normal, but there is an increased incidence of amyotrophic lateral sclerosis and Parkinson dementia. In brain tissue from such patients an accumulation of aluminum was demonstrated intracellularly in neurofibrillary tangles of the hippocampal region of the brain (*71,72*). Soil and drinking water from areas in which there was a high

incidence of these disorders had high aluminum content and low concentrations of calcium and magnesium. The hypothesis has been advanced that secondary hyperparathyroidism, provoked by the chronic environmental deficiency of calcium and magnesium on Guam, may result in an increased intestinal absorption of aluminum leading to accumulation in the CNS and causing the degenerative CNS disorder (*73*). An observation that may be of importance in relation to the mechanism of aluminum toxicity to the CNS is that aluminum has been reported to affect the permeability of the blood-brain barrier to small peptides (*74*). An alternative interpretation of reported findings is that the aluminum accumulation in brain tissue of patients with Alzheimer's disease is a secondary phenomenon representing a relatively nonspecific "marker" of degenerating neurons. The absence of increased concentrations of aluminum in serum and cerebrospinal fluid is taken to support this view (*75*).

In summary, there is a lack of understanding of aluminum metabolism and toxicity. In particular, conditions which may induce aluminum toxicity to the central nervous system in persons with normal renal function needs to be further defined.

Impact of Acid Precipitation on Human Exposure to Aluminum and its Health Implications

Aluminum concentration in tap water constitutes a considerable problem when using such water for preparation of dialysis fluid, and purification often is necessary in order to prevent aluminum toxicity in patients on dialysis.

In the general population, considerable exposure to aluminum occurs via ingestion of food and drink containing aluminum. Daily aluminum intake is uncertain, with reports ranging from 2 to more than 10 mg/day. Regardless of intake, only a small fraction of ingested aluminum is absorbed by the intestinal tract (*76*). Persons consuming antacid medications may ingest gram amounts of aluminum daily. This may be compared to concentrations of aluminum up to 1.7 mg/L found in drinking water from shallow wells in acidified areas (e.g., in Sweden). considering only total intakes, this does not seem to justify a lot of concern for adverse human health effects from aluminum mobilized by acid precipitation in persons with normal renal function. The possibility certainly exists, however (as mentioned for aluminum given together with citrate), that certain chemical species of aluminum may be taken up much more efficiently from the GI tract and be accumulated differently than other chemical species.

In summary, acid precipitation has a considerable influence in mobilizing aluminum in natural waters. Because of the uncertainties concerning relationships between aluminum exposures and human health effects alluded to in the foregoing section, the possible health inpact of these increases as well as the importance of other sources of human aluminum exposures are difficult to evaluate.

Research Needs

In order to improve our understanding of conditions leading to aluminum toxicity, a spectrum of fundamental studies in humans as well as experimental animals are needed. These studies should define metabolic and kinetic models of various chemical species of aluminum and the influence of other dietary factors on absorption/distribution; define critical tissue/cell concentrations of aluminum that gives rise to toxicity, particularly to the central nervous system; and identify the nature (and biochemical mechanism) of damage.

Another important aspect is to investigate the chemical species of aluminum and the ionic composition of human exposures that are related to acid precipitation.

Epidemiological studies of aluminum concentrations in biological indicator media may be feasible if aluminum species that are particularly easily absorbable are identified in acidified areas.

Other Impacts of Acid Precipitation Potentially of Concern to Human Health

Arsenic and Selenium

Compared to the metals discussed in the foregoing sections of this paper, relatively little attention has been given to a possible impact of acid precipitation on arsenic and selenium in the environment. Health effects of general population exposure to inorganic arsenic via inhalation, food or drinking water have been reviewed (*77*). Critical effects after ingestion of inorganic arsenic are probably the development of skin cancer, although other forms of cancer, neurologic and peripheral vascular disorders may also be considered.

Moderate selenium exposures are considered to be beneficial, and may counteract several adverse effects of exposure to arsenic and toxic metals, at least in animal experiments (*78*). A paper by Mushak (*79*) summarizes available evidence concerning arsenic, selenium, and acidification. Soft, mildly acidic water appears to mobilize arsenic and selenium from plumbing. Elevated arsenic concentration may occur in water from rain water catchment systems in areas with acidic deposition. Acidification of ground waters and aquatic ecosystems (surface waters) that are used as sources of drinking water may also contribute to an increased arsenic exposure by this route. A drinking water survey in the U.S. performed around 1980 indicated a higher occurrence of values above 50 μg/L than a survey performed 10 years earlier. The contribution of acidification to this observation, however, is very uncertain because of considerable differences in study design, analytical methodology etc.

An effect of soil acidification in mobilizing arsenic into

Table 1. Summary of "state of the art" concerning the impact of acid precipitation on metal toxicity.

Metal	Chemical species affected by acid precipitation	Human exposure affected by acid precipitation	Critical effect (or critical organ)	Human DR for critical effect[a]	Research need	
					DR[a]	Exp[b]
Hg	Methyl-Hg	+ ?	Fetal brain	+	+	+ +
Pb	Inorganic Pb	+ ?	Child	+	+	
			CNS[c]			+ +
			FEP[d]	+ +	(+)	
Cd	Inorganic Cd	?	Kidney (adult)	+	+	+ +
Al	?	+ ?	CNS (adult?)	?	+ + +	+ +

[a] DR = dose-response relationship.
[b] Exp = *exposure situation.*
[c] CNS = central nervous system.
[d] FEP = free erythrocyte protoporphyrin increased in erythrocytes.

crops and reducing selenium uptakes has been discussed by Mushak (*79*). Although such an effect is possible, the complex events of biotransformation of arsenic and selenium makes it difficult to predict the magnitude of such an influence. An influence of acidification on the processes of biotransformation may also be of importance.

Asbestos and Copper

Asbestos-cement pipes have been used extensively for larger drinking water pipes, and copper is used particularly in domestic installations. When acidic water of high corrosivity is distributed in such pipes, asbestos fibers may be released and copper dissolved.

Concentrations of copper as high as 20 mg/L may be reached in water standing in pipes overnight. The health impact of high copper concentrations in water is unclear copper being an essential element. Healthy adult individuals appear to tolerate concentrations of 1–2 mg/L without adverse effects, while children with gastrointestinal disorders may tolerate less.

Summarizing Evaluation

The possibility of an impact of acid precipitation on human health via mobilization of environmental metals has attracted considerable interest. In the present paper, available evidence on this question has been summarized and uncertainties have been pointed out both with regard to dose-response estimations and possibilities to estimate the impact of acid precipitation on exposures. Suggestions of needed research have been given. This is briefly summarized in Table 1 for the most important metals. The most urgent research needs are related to dose-response relationships for aluminum where our knowledge is very incomplete. At this time, the relationships between acid precipitation and human exposure to potentially toxic metals are, at best, only partially defined.

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