

Medical geology

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Mother nature is a polluter

In June 1991 the volcano Pinatubo had an eruption. Over just two days the volcano ejected about 10 billion tons of magma and 20 million tons of sulphur dioxide, and the resulting aerosols influenced the global climate for at least three years. This event alone introduced 2 million tons of zinc, 1 million tons of copper and 5,500 tons of cadmium into the surface environment. The millions of tons of ash pumped into the atmosphere spread over thousands of square kilometres, probably containing all the elements in the Periodic System. In addition to the elements known to be essential to life, such as hydrogen, carbon, nitrogen, oxygen, sodium, potassium, calcium, mag-

nesium, iron, copper, zinc, phosphorus, sulphur and iodine, volcanoes also redistribute those elements which under certain conditions are regarded as harmful, such as arsenic, beryllium, cadmium, mercury, lead, radon and uranium plus the remaining elements, some of which have still undetermined biological effects. Similar volcanic events have occurred every few years throughout geological history (Figure 1). From the standpoint of natural releases of metals to the environment, it is important to realize that there are on an average 60 volcanoes erupting on the surface of the earth at any given time. The total flux of metals from these eruptions is significant. Submarine volcanism is even more significant than that at continental margins. It has been conservatively estimated that there are at least 3,000 vent fields on the mid-ocean ridges.

The planet earth is thus the ultimate source of all metals. Metals are ubiquitous in the lithosphere, where they are inhomogeneously distributed and occur in different chemical forms. Ore deposits are merely natural concentrations which are commercially exploitable. While such anomalous accumulations are the focus of mineral exploration the background concentrations of metals which occur in common rocks, sediments and soils are of greater significance to the total



FIGURE 1 Volcanic eruption at Krafla, Iceland 1980.

metal loading in the environment. Indeed, all known elements are present at some level of concentration throughout the natural environment. They are present in minerals, vegetables and animals, and their beneficial and harmful effects have been present since evolution began.

An understanding of the nature and magnitude of these geological sources is a prerequisite for developing approaches in assessing the risk posed by metals in the environment. It is important to be able to distinguish between natural and anthropogenic contributions to metal loadings. In addition, a knowledge of natural processes is fundamental in understanding the fate of those metals which are released as a result of human activity. Keep in mind that Mother Nature is indeed a polluter.

Natural prerequisites for life

Geology creates the natural prerequisites for life. The crust of the earth has been evolving constantly since the planet formed some 4.5 billion years ago. The crust and uppermost mantle comprise rigid plates which move relative to one another, driven by the dissipation of heat from the earth's interior. New crust is created at the boundaries of these plates. Metals and other elements continuously enter the hydrosphere, atmosphere and biosphere from the lithosphere as a result of these geological processes. There are many such pro-

cesses but it is sufficient to consider two broad categories: Those which bring metals to the surface from deep in the earth and secondly, those which redistribute metals in the surficial environment.

The first process results in an *inhomogenous* distribution of metals in rocks. Concentrations of metals can range over orders of magnitude among different types of rocks. Accordingly, concentrations of elements such as nickel and chromium are much higher in basalts than in granites whereas the reverse is true for lead. In sediments, the so called heavy metals tend to be concentrated in the fractions with the finest grain size and the highest content of organic matter. Thus, black shales tend to be enriched in these elements (Table 1).

The second process that redistributes metals in the surficial environment is weathering. Many weathering processes occur in a time frame that makes them relevant in the environmental context. Weathering refers to the breakdown of rocks and may involve physical, chemical and biological processes. Physical processes ultimately reduce massive rock to particle sizes that are readily eroded by surface water and wind. Soils form through the interaction of weathered rock and organic material. Chemical processes change the mineralogical form in which the metal occurs and can mobilize metals to dissolve in water and as

TABLE 1 Average abundance of some elements in the earth's crust and rocks (all values in parts per million, ppm)

Element	Earth's crust	Ultrabasic	Basalt	Granite	Shale	Limestone
As	1.8	1	2	1.5	15	2.5
Cd	0.2	-	0.2	0.2	0.2	0.1
Co	25	150	50	1	20	4
Cr	100	2000	200	4	100	10
Cu	55	10	100	10	50	15
Pb	12.5	0.1	15	20	20	8
Se	0.05	-	0.05	0.05	0.6	0.08
U	2.7	0.001	0.6	4.8	4	2
W	1.5	0.5	1	2	2	0.5
Zn	70	50	100	40	100	25

such react with organisms. Biological processes comprise activities of flora and fauna. Weathering plays a critical role in the transfer of metals from the bedrock to the other environmental compartments.

Elements are both necessary and toxic

Paracelsus (1493 – 1541) defined the basic law of toxicology “All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy.” This relation between the dose and effect for any substance is shown by the curve starting at zero (green line) in Figure 2. Increase of the amount/concentration (on the horizontal axis) causes increasing negative biological effects (on the vertical axis), which may lead to inhibition of biological functions, eventually to death. Evidently, decreasing concentrations of *non-essential* elements/substances are beneficial. The situation for *essential* elements is different. Negative biological effects increase both

for increasing and decreasing concentrations, illustrated by the red curve in Figure 2. That may lead to inhibition of life functions in both cases. Thus, too much or too little, both are equally harmful.

All elements are present in nature itself. Most of them are essential, i.e., indispensable wheels in the fantastic watch of life. But which are those elements essential for humans and animals? Major elements essential for human and animal life are for example calcium, chlorine, magnesium, phosphorus, potassium, sodium and sulphur. Essential trace elements in low concentrations for human and animal life are for example chromium, cobalt, copper, fluorine, iodine, iron, manganese, molybdenum, selenium and zinc. However, elements with probably no recognized biological role are called non-essential elements, often with harmful properties, e.g. cadmium, arsenic, mercury and lead.

Several elements are frequently involved in environmental toxicity problems, for example

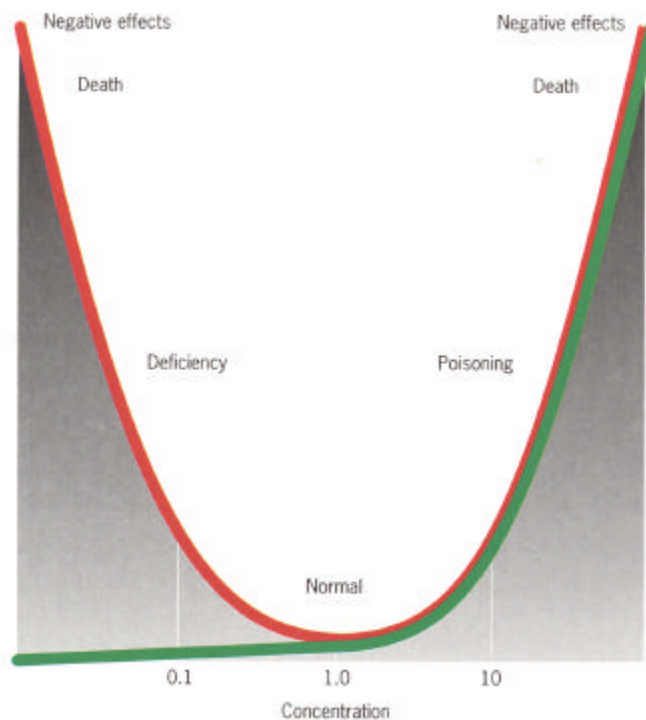


FIGURE 2 Dose-effect curve showing the relationship between concentrations and biological effects of essential (red) and of non-essential (green) elements.

TABLE 2 Diseases associated with deficiency and toxicity of a given element

Element	Deficiency	Toxicity
Iron	Anaemia	Haemochromatosis
Copper	Anaemia	Chronic copper poisoning
	"Sway back"	Wilson, Bedlington disease
Zinc	Dwarf growth	Metallic fever
	Retarded development of gonads	Diarrhoea
	Akrodermatitis enteropathica	
Cobalt	Anaemia	Heart failure
	"White liver disease"	Polycythaemia
Magnesium	Dysfunction of gonads	Ataxia
	Convulsions	
	Malformations of the skeleton	
	Urolithiasis	
Chromium	Disturbances in the glucose metabolism	Kidney damage (Nephritis)
Selenium	Liver necrosis	"Alkali disease"
		Muscular dystrophy "Blind staggers"
		("White muscle disease")

arsenic, boron, chromium, copper, fluorine, molybdenum, nickel and zinc. Although it is not possible to quantify the hazards and deleterious effects associated with the trace elements in common use, some elements clearly present a more serious problem than others, for example lead, mercury and cadmium, which are in a class by themselves and have received attention from scientists.

Are all elements bioavailable?

Before governments commit scarce resources to clean up or protect the environment from man-made contamination, it would seem prudent to determine how much "contamination" merely reflects the pre-existing natural background. Naturally occurring elements can have detrimental effects on health when ingested in increasing quantities. Metals have always existed and will forever exist, but we cannot avoid the fact that human beings and animals are influenced by

metals in the environment. Human activities of all kinds have redistributed metals from sites where they are fairly harmless to places where they affect humans and animals negatively. This is especially serious since acid rain and acidification mobilizes metals, e.g. mercury, zinc, aluminium and manganese, making them easily available and thus enabling them to be taken up in the nutritional chain. Another consequence of acidification is that negatively charged essential trace elements, such as selenium and molybdenum, become less available to living organisms.

The total metal content in an environmental medium, e.g. soil, is an unreliable guide to hazard identification, as different metals can have different and variable bioavailability. Common environmental assessment assumes that the total content of a metal is bioavailable and able to be absorbed. Evidence indicates however that many of the metals in soil are in highly insoluble form and are not taken up by plants.

TABLE 3

Parameters that influence metal bioavailability, applied to various media (e.g. water, soil and sediment)

pH
 Eh (Oxidation/reduction redox potential)
 Hardness
 Alkalinity
 Ionic strength
 Organic carbon
 Temperature
 Inorganic ligands (e.g. F⁻, Cl⁻)
 Inorganic oxides of Fe, Mn, Al and Si
 (in sediments only)
 Sulphides
 Chelating agents (e.g. humic substances,
 organic compounds)
 Concentrations of other metal ions
 Methylating agents
 Cation and anion exchange capacity

The bioavailability, transport and toxicity of metals depends not only on the physical and chemical forms in which the metal is present but also on local factors in the environment (Table 3). For example, pH is an important determining factor in the bioavailability of metals in soil. The bioavailability and mobility of metals such as zinc, lead and cadmium is greatest under acidic conditions, while increased pH reduces bioavailability. The type of soil, such as clay and sand content, and its physical properties also affect the migration of metals through soils. The organisms present in soils likewise affect metal solubility, transport and bioavailability. The toxicity of metals is also dependent on certain parameters such as chemical form, molecular, atomic and ionic species, ligands, buffer capacity and ionic exchange capacity, for example organic compounds of mercury and lead are much more toxic than inorganic forms. The state of oxidation may also affect the degree of toxicity; chromium, for example, is more toxic in the hexavalent than in the trivalent state.

Elements interact with each other

Interactions are common in nature and occur in the food chain (Figure 3). They might be fairly simple or more intricate. Interaction may depend on interactive parameters as well, such as coupled equilibria and enzymatic interactions, sometimes rather intricate and difficult to understand.

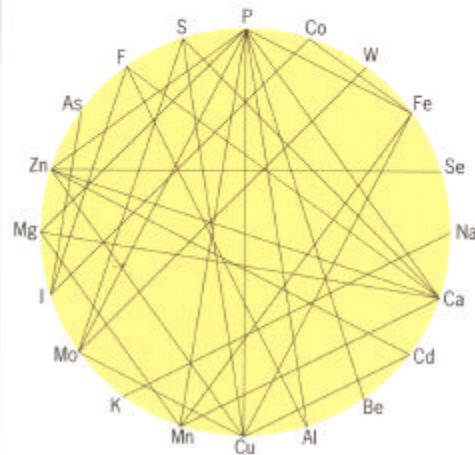


FIGURE 3 Interaction of elements

Not only copper

In Norway and Sweden, hazardous copper levels have seldom been found in pasture plants. In spite of this, copper poisoning in sheep frequently occurs. Thus faulty conclusions may easily be drawn if only copper levels in the feed or soil are determined and evaluated. In this case, low molybdenum levels may result in the Cu:Mo ratio being too high, with chronic copper poisoning as a result. The increased intake of molybdenum causing deficiency increases the need for additional copper in the diet of sheep and cattle to prevent occurrence of copper deficiency.

Metal uptake by plants depends on many factors of which the bioavailability in soil is one. It is influenced mainly by the geological background, but depends on other parameters too, e.g. pH (Table 3). A change of the ratio between copper, molybdenum and sulphur in plants will influence

Some copper-containing enzymes are part of the anti-oxidative defence of the body, e.g. Cu- and Zn-containing superoxide dismutase. Cell respiration depends on cytochrome oxidase, another copper-containing enzyme. Crosslinked collagen and elastin are essential for the strength and elasticity of the body, the crosslinking being performed by another copper-containing enzyme, lysyl oxidase. This enzyme is also essential for the synthesis of the connective tissue of bone. Other copper-containing enzymes take part in the synthesis of signal substances for the nervous system. In copper deficiency, iron is not incorporated into the hemoglobin of red blood cells, causing anaemia. Copper is necessary for the immune system and for the synthesis of proteins and enzymes, e.g. the synthesis of at least two selenium-containing enzymes is copper-dependent.

the copper metabolism in ruminants, which is quite different from that of monogastric animal species. Copper uptake from food in ruminants is controlled by interaction between copper, molybdenum and sulphur in the rumen by intricate processes. Sulphate is reduced to sulphide which substitutes oxygen atoms of the negatively charged molybdate anion and results in thiomolybdates with high affinity for copper. Thus copper is inactivated and is withdrawn from the metabolism. High concentration of molybdenum in relation to copper decreases the amount of copper available for metabolism, leading eventually to copper deficiency. On the other hand, low amounts of molybdenum increase copper uptake and result in accumulation of copper. In fact, the ratio between copper and molybdenum is decisive for copper uptake. High molybdenum concentration in the food, and consequently in the rumen, results in high concentration of thiomolybdates. These compounds not only remove copper from the metabolism, but a fraction of them are distributed in the whole organism where they may react with copper containing biomolecules. The hepatic cop-

per pool will decrease. This phenomenon has been used for therapeutic purposes in preventing outbreaks of chronic copper poisoning in sheep. Unfortunately, once thiomolybdates are in the body they find their way to essential copper-containing enzymes, the enzymatic activity of which is inhibited, with consequences fatal to ruminants.

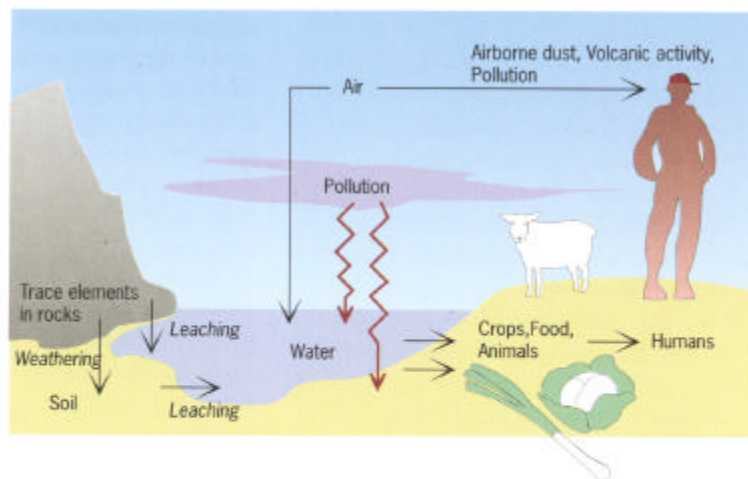
Other examples of interactions

Plants growing in high-phosphorus soils (including those enriched with fertilizers) are frequently deficient in zinc. This can be a particular problem because phosphorus is a major ingredient in fertilizer. Uptake of high levels of zinc by plants may limit the extent to which plants can take up cadmium; thus the application of zinc to cadmium-rich soils could be helpful in controlling a potentially harmful accumulation of high cadmium concentrations in food crops. Sulphur may "compete with" selenium during uptake in plants, but experimental results are inconsistent: applying sulphur-containing fertilizers to low-selenium soils has depressed the levels of selenium in plants even further, but on the other hand efforts to prevent accumulation of high selenium levels in plants growing on selenium-rich soils by applying sulphur have not worked well.

In animals, metabolic processes involving magnesium, potassium, and calcium have been shown to be interrelated, and evidence indicates that the same is true in humans and animals. Thus a deficiency in one element may disturb the balance of others. Copper is essential to the proper metabolism of iron and molybdenum may also affect iron metabolism by biochemical interaction with copper in ruminants. Plant fiber may inhibit the absorption of zinc in the human digestive tract. Zinc and cadmium may compete in humans as well as in plants, hence increased zinc consumption may afford some protection against cadmium. Selenium may protect against the harmful effects of most mercury compounds.

Selenium is also a strong antagonist to arsenic and vice versa. Therefore the absence of effects from arsenic exposure could be due to adequate or excessive uptake of selenium in the organism.

FIGURE 4
**Pathways by which
 trace elements enter
 the body**



What is Medical Geology?

Why is geology important for our health? We have discussed the environment as the entire web of geological and biological interactions in the relationship between life and the planet earth. Environmental problems, challenges and issues are widespread. Both essential and non-essential elements in bedrock or soils may under certain circumstances become a direct threat to human and animal health; and may be the underlying cause of both deficiency and toxicity. Figure 4 demonstrates the pathways by which trace elements enter the body.

As long as medical science has existed it has been known that certain human illnesses are related to geographical areas. The Greek physician Hippocrates mentioned such examples more than 2400 years ago. Knowledge on specific animal diseases also originated long ago. Even in Chinese medical texts of the third century BC such relationships are found. However, most such observations were lost because they were not written down. As science grew, many of the previously unknown relations of causes between geology and health eventually began to be understood and a new scientific field evolved: *Medical Geology*.

Medical Geology (or Geomedicine) is defined as the science dealing with the influence of geological environmental factors on health problems in man and animals. This is a complicated subject, and interdisciplinary contributions from essen-

tially different scientific fields are required when these problems are to be solved.

There is a paradox in studies in Medical Geology. Industrialized countries should be well suited for such activities because of good public health records and detailed geological information. However, citizens of these countries are nowadays rarely dependent on locally grown food and in many cases not even on local drinking water. In addition, municipal drinking water is often treated. Therefore, the most suitable areas for this research are in the developing countries.

Radon, too, is a consequence of geological activities. Important parts of the bedrock have elevated uranium contents. These include for example alum shales and certain granites and pegmatites. Radon derived from natural radioactive sources has in recent years also been acknowledged as a public-health problem. The number of radon-related cases of lung cancer is increasing, thus establishing radon as the major radiation problem with respect to health in several countries. Building traditions, such as the use of light concrete based on uranium-rich alum shale, and a reduction in circulating air to improve heating economy have in many cases aggravated the problem. More recently, interest has focussed on radon in domestic water as a potential radiation protection problem. Previous risk assessments have focussed on radon emanating from the domestic use of water as an additional source of

radon in indoor air. Recent studies suggest that intake of radon-rich water should be considered a risk as such, especially for critical groups such as infants. The radon content of water is coupled directly to local geological conditions.

How does geology affect our health?

Too much selenium...

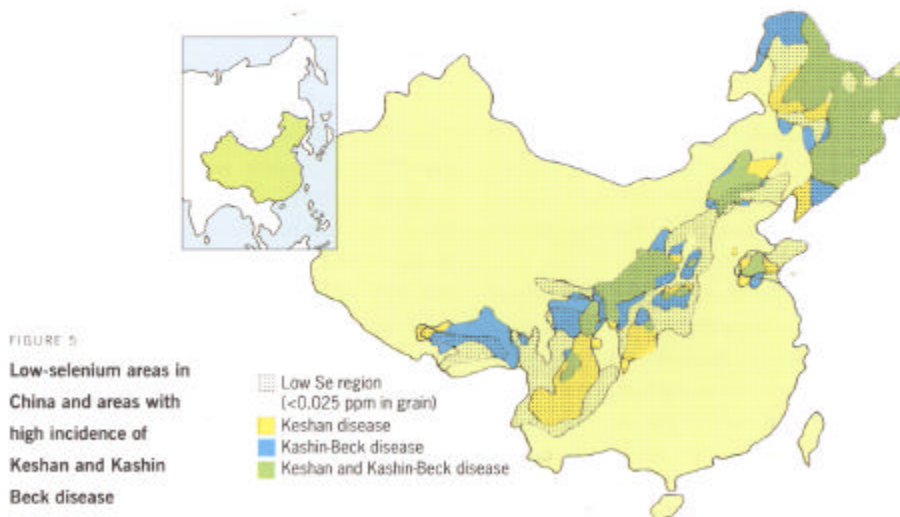
Marco Polo gave us one of the oldest documentations of medical geology. He left Venice together with his father and uncle in 1271 to travel to China. In 1275 they arrived at the summer residence of Kublai Khan. Marco Polo reported that he could only use local horses in the mountainous areas of China because his imported European horses died. They did not avoid poisonous plants, and he also described the symptoms of toxicity. He did not know that his reports would be considered as descriptions of diseases of geomedical origin. However, we now know that the areas he described have high natural contents of selenium, and the symptoms of the disease were those of selenium toxicity.

Another example of selenium poisoning can be found in the USA. In the San Joaquin Valley in California, drainage water from irrigated farmland was until some years ago directed into the Kesterson Wildlife Refuge. In 1983 strange malformations and deaths of wildfowl were observed

and traced to high concentrations of selenium in the drainage waters and adjacent wetland soils. This posed a threat to human health as well. Two-thirds of all bird embryos were found dead. Fish, insects and microorganisms were also affected. The selenium came from long-weathered seleniferous pyrite in rocks of the Coast Range mountains. The farming in the San Joaquin Valley is intensive and requires irrigation. The groundwater contains selenium, though not in great amounts, and for irrigation it is pumped up from aquifers situated under a clay layer. Because of the impermeable clay horizon the irrigation water cannot be transported away naturally, therefore the water is transported away in canals leading to the Kesterson reservoir which is supplied with increasing contents of selenium. Thus human activity, by a redistribution of natural selenium contents, has eventually caused poisoning of a whole ecosystem. In 1986 drainage water was diverted away from the Kesterson ponds.

... and too little selenium

But other diseases are caused by the lack of selenium. A new type of disease was recorded in the northeast of China at the beginning of this century. In the winter of 1935 it became prevalent in Keshan County and was later called the Keshan disease (Figure 5). It appeared in a large area from southwestern to northeastern China. It was a



heart-muscle disease. In the 1960s scientists suspected that the disease was of geological origin and in the 1970s the probable solution was found. The disease was always located in low-selenium areas which geographically form a low-selenium belt. The use of selenium in prevention and treatment of the disease was a great success. This was how the direct association of selenium with human health was first identified. The Keshan disease was obviously caused by very low concentrations of selenium in bedrock, soils and natural waters.

One other example in China is the Kashin-Beck disease (KBD) (Figure 5). The KBD has long been known. Initial symptoms of KBD are joint swelling, pain, and general illness. It affects children. Skeletal remains indicate that it goes back to at least the 16th century. KBD was first described by a Russian surveyor, Kashin. Kashin and his group worked in the area east of Lake Baikal and were assigned to a Cossack brigade on the Urov river. The Russian administrative authorities were terrified by crippling skeletal deformations in the Cossack villages and moved several populations to other locations along the river. KBD is mainly limited to a southwest – northeast belt of China and was later found to be fairly common in China and has been studied for more than 40 years. KBD occurs almost exclusively in the farming population, though cases are occasionally seen in families that obtain their food from endemic areas. The size of the affected population is not known, but estimates are about one to three million in China. Research and public-health efforts have focused on two main causal mechanisms. First, the toxic effects caused by mycotoxins produced in stored maize. Second, the role of low natural contents of selenium. The probable cause of KBD is selenium deficiency caused by low natural contents of selenium in bedrock.

Selenium has the characteristics of essential elements. Selenium-accumulating plants may cause *poisoning* of plant-eating animals, whereas deficiency may result in lesions leading to death both of humans and of animals. During the 1950s great efforts were made in Sweden to control muscle degeneration and mulberry heart disease in swine (muscle and heart lesions) causing economic loss



FIGURE 6 White muscle disease (muscle degeneration) in sheep

for the farmers. The cause of the damage was shown to be selenium *deficiency*, often together with deficiency of vitamin E. Selenium is an important essential element and is important for the activity of the enzyme glutathion-peroxidase (GSH.Px) protecting the organism against oxidative damage. Other selenium-containing enzymes and proteins were also found in animals.

Scandinavia is poor in selenium because of the geological conditions, and the selenium content of plants is generally low. Therefore selenium enrichment of fodder has been permitted by law since the beginning of the 1980s. The deficiency symptoms in swine have since then disappeared, but signs of selenium deficiency still appear in cattle, sheep and horses, because selenium content in pasture is not satisfactory (Figure 6). Animals in hard physical training or hard work need increased amounts of selenium and vitamin E. Half of Sweden has been mapped for selenium availability by the moose. In spite of great regional differences the moose seems not to suffer from selenium deficiency. Perhaps wild animals have adapted to low natural selenium concentrations in plants and the deficiency is compensated by enzymes with the same function but without selenium (e.g. not selenium dependent glutathion-peroxidases).

Widespread arsenic poisoning

When the first water bubbled from wells sunk deep into the soils of West Bengal in India a generation ago, locals called it the devil's water.

Historically the villagers have used surface water, but with new tube wells tapping water from more than 150 metres below ground they can now grow three or four crops. But those talking about devil's water soon changed their minds as the water irrigated rice crops all year round and brought new prosperity to their villages. However, the water contained high levels of arsenic and for hundreds of thousand of villagers the improved harvest turned out bitter. More than 400 villages have been affected across West Bengal and the world's largest arsenic poisoning so far has left more than 600,000 people disfigured and facing an early death.

Studies beneath the villages have revealed a series of layers of sedimentary rocks containing arsenic, mostly in seams of iron pyrite which contaminated many wells. Overpumping has also lowered the water table in many rocks. As the water table has fallen, the arsenic-bearing sulphide rocks dried out, and oxygen penetrated the rocks, oxidizing the sulphur minerals. This has freed the arsenic to be dissolved in the groundwater and washed into the wells. Today more than 700 wells supply water that contains more than $10 \mu\text{g}$ of arsenic/l, the maximum limit set by the WHO. Average arsenic levels are between 20 and

70 times the WHO maximum with individual wells up to 200 times the limit. Arsenic in groundwater above the WHO maximum permissible limit has been found in six districts in West Bengal with a population of 30 million.

International incidents of arsenic contamination in groundwater and the consequent state of health of people have been widely reported from other places as well (Figure 7). The arsenic contamination incident in the well-water of Taiwan (1961 – 85) caused an illness called black-foot disease. The population of the endemic area was about 100,000. Similar problems were reported from Antofagasta in Chile where almost 100,000 people out of a total population of the city of 130,000 were drinking water with elevated arsenic content between 1959 and 1979. Chronic arsenic poisoning is also reported in some parts of Region Lagunera, Mexico. The arsenic concentration in groundwater was $400 \mu\text{g}/\text{l}$. Similar incidents were reported in 1955 from Argentina. Many other incidents are also reported from many parts of the world.

Zinc and diabetes

Environmental factors may possibly contribute to the aetiology of diabetes mellitus type 1 among



FIGURE 7 Examples of arsenic contamination

children. Childhood-onset diabetes is almost exclusively of the autoimmune insulin-dependent type (type1). Genetic prerequisites are clearly not sufficient causes of the disease. Studies from incidence registers from homogeneous countries in Scandinavia have shown a significant intra-country geographical variability in insulin-dependent diabetes mellitus incidence rates which cannot be explained by a slight south-north gradient only. A case control study has been designed comparing cases and controls as to estimates of zinc, obtained in biogeochemical samples from areas of residence. A high concentration of zinc in water was associated with a significant decrease in risk of disease. This could provide evidence that a low groundwater content of zinc is associated with later development of childhood-onset diabetes.

Sickness country in Australia

Some areas in Australia are regarded as holy places by the aborigines. One of these areas, the "sickness country" in the Kakadu region, is an area which will make people sick if they go there. Hence such areas are regarded by aborigines as taboo and should not be entered. Geochemical researchers have found this area interesting and therefore geochemical surveys have been conducted there since 1980.

The bedrock in the region consists of granites and volcanic rocks. These rock types contain elevated amounts of certain elements. A large part of the sickness country is found to coincide with a region containing localized areas with unusually high natural levels of thorium, uranium, arsenic, mercury, fluorine and radon in groundwater and drinking water. The aborigines had also used ochre as a pigment in painting, containing extremely high contents of uranium, lead, arsenic and mercury. The reason why these areas are sacred is thus the serious health effects caused by natural contents of these elements. The natural levels of concentration in the land and water systems thus constitute a health hazard as recognized by local people.

Cobalt and copper in animals

Health disturbances in sheep and cattle are a



FIGURE 8 Lamb with clinical signs of cobalt deficiency, with excessive lacrimation.

result of mineral deficiencies attributable to the geological background. Sheep suffer badly from cobalt deficiency in many parts of the world (Europe, New Zealand, Australia). Because of the poor health of sheep on the island of Gotland in the Baltic Sea, numerous studies were performed to find the reason of an illness affecting sheep and lambs. Chemical analysis of liver revealed a severe cobalt deficiency. The situation became even more serious when it was detected that cobalt deficiency was accompanied by copper deficiency (Figure 8). The geological background of Gotland is of sedimentary origin and poor in cobalt and other metals. The geological background in the east and south-east part of Sweden too, exhibits the same conditions to some extent. Thus farmers must take steps to prevent mineral-deficiency diseases in cattle and sheep,

Despite the nutrient-poor geological background both copper deficiency and copper toxicity appear in sheep on nearby farms. For metabolic reasons sheep accumulate copper in their liver. The sheep are sensitive to the balance between copper, molybdenum and arsenic in their feed which is critical for their wellbeing. Once hepatic copper concentration reaches a certain level, any stress can start an irreversible biological process, and the acute stage of chronic copper poisoning and hemolytic crisis caused by rupture of red blood cells resulting from the oxidative effect of a high uptake of copper is in most cases fatal. No doubt sheep are extremely sensitive to copper toxicity, but they are also sensitive to copper



FIGURE 9 Ataxy in lamb caused by copper deficiency (swayback lamb).

deficiency (Figure 9). In fact, cattle are even more sensitive to copper deficiency than to copper toxicity.

Fluorine and iodine, deficiency and excess

It was already known at the beginning of the 20th century that high contents of fluorine could cause fluorosis. The natural concentration of fluorine in drinking water is normally 0.1 – 1 mg/l. In many places all around the world, for example India, China and Africa, the concentration might go as high as 40 mg/l, which leads to severe fluorosis. The picture is rather complicated, however, because there are also antagonistic effects. Molybdenum and selenium can reduce the effects of high contents of fluorine. Fluorine is an essential element with a recommended daily intake of 1.5 – 4.0 mg. Health problems may arise from deficiency (caries) or excess (dental mottling and skeletal fluorosis). Unlike other essential elements for which food is the principal source to the extent of about 80%, the principal source of fluorine is water. Fluorine in surface and ground waters is derived from the following natural sources: leach-

ing of rocks, dissolution of fluorine from volcanic gases, springs and marine aerosols. After the eruptions of the volcano Hekla on Iceland in 1693, 1766 and 1845, detailed descriptions of fluorosis were reported and acute poisoning was described. Since World War II Hekla has had eruptions in 1947, 1970 and 1980 and a number of analyses of fluorine have been performed. The volcano delivered huge amounts of fluorine and concentrations of 4300 mg/kg in grass have been found.

The connection between geology-water-food-chain diseases can also clearly be shown for iodine. In ancient China, Greece and Egypt, and among the Incas, people were affected by goitre, but they were treated with seaweed which is rich in iodine. Goitre is still a serious disease in many places all around the world. In all these places the content of iodine is very low in drinking water because of low concentrations of iodine in bedrock. More than a billion people, mostly living in the developing countries, are at risk in respect of Iodine Deficiency Disorders (IDD). Goitre, which is the enlargement of the thyroid gland, is the best-known form of IDD. One form of IDD is cretinism. A cretin is physically and mentally retarded and deaf-mute. China has 425 million people who are at a risk in regard to IDD. They constitute 40% of the world's population in that category.

The need for other major elements

The inverse relationship between cardiovascular disease and water hardness (Calcium and Magnesium) in connection with geology was first reported in USA in 1956 and from Japan in 1957. Observers found a close positive correlation of death rates from apoplexy with the acidity of river water. In Canada and USA several other studies on water hardness in relation to cerebrovascular and ischaemic heart disease (IHD) were performed. A significant inverse relationship was found between water hardness and total cardiovascular mortality. A higher sudden-death rate in soft-water areas compared with hard-water areas was also reported. For many years the regional variations in cardiovascular disease in Great Britain have also aroused considerable interest.

In the "WHO myocardial infarction registry network" all cases of myocardial infarction were registered in a standardized way in 15 WHO countries in Europe. Higher rates of IHD were found in towns served by soft water than in towns with hard water. Research has also been carried out in Sweden. It has shown that water hardness (Ca + Mg and other minor constituents) and the sulphate and bicarbonate concentrations of the drinking water were inversely related to IHD and to stroke mortality. The variation in the drinking-water composition in these areas reflects the geological variation in the region.

Magnesium is a major element, the lack of which can also give rise to deficiency disorders. Magnesium deficiency occurs in ruminants, especially cattle, and is manifested by acute convulsions – hypomagnesemic tetany – and occurs in its typical form in animals which have been turned out to graze after winter-housing ("grass tetany"). The occurrence of hypomagnesemic tetany in grazing animals may be associated with the use of fertilizers. Application of potassium at high rates reduces the availability of magnesium.

Calcium and phosphorus are of particular significance with regard to deficiency diseases in animals. Among other functions, these two elements are important in bone mineralization, together with vitamin D and satisfactory copper supplementation. In addition to the two individual elements, a correct ratio between the two is extremely important. Too high a level of phosphorus may induce a secondary calcium deficiency.

A deficiency of phosphorus is a condition which also is most likely to cause a problem under natural grazing conditions. It is widespread in many countries and shows a distinct geographical distribution that is dependent on the phosphorus content of the soil. Deficiency disorders are most common in grazing animals during the dry season. Phosphorus deficiency can be prevented by providing rock phosphates or bone meal. The addition of phosphate to drinking water has also been employed. The topdressing of pasture with superphosphate is an adequate method of correcting a phosphorus deficiency and also has the advantage of increasing the bulk and quality of the pasture.

Mapping for environmental and medical reasons

The natural contents of elements are of the utmost importance for our wellbeing, both excessive and deficient contents. But how can we determine the distribution of metals and other elements in our environment? Two techniques from Sweden will be described for the innovative monitoring of metals in the environment by the use of aquatic mosses and the roots of aquatic higher plants, a technique developed at the Geological Survey of Sweden, and organ tissues of the moose (*Alces alces* L.), a wild ruminant used for monitoring by the National Veterinary Institute in Sweden since early 1980.

Aquatic roots and mosses as environmental monitors

The distribution of metals on both a regional and a national scale can be compiled by geochemical mapping based on the systematic sampling and analysis of rocks, soils, stream sediments, lake sediments, surface waters and vegetation.

The Geological Survey of Sweden started a monitoring/mapping programme in 1980. A new biogeochemical method is used which reflects the metal concentrations in stream water, whereby metal concentrations are determined in aquatic mosses and roots of aquatic higher plants. These are barrier-free with respect to trace-metal uptake and reflect the metal concentrations in stream water. They respond closely to chemical variations in background levels related to different bedrock types in addition to effects of pollution. Aerial parts of many plant species, however, do not generally respond to increasing metal concentrations in the growth medium because of physiological barriers between the roots and the above-ground parts of plants. In addition, aerial parts may be contaminated by deposition of particles from air. The biogeochemical samples render integrated time-related information on the metal contents in the water for a period of some years and also provide information on the time-related *bioavailable* metal contents in aquatic plants. Another great advantage of using biogeochemical samples instead of water samples is that the bio-

geochemical samples provide integrated information on the metal contents in the water for a period of some years. Water samples suffer from seasonal and annual variations, depending on precipitation for example.

The mapping programme now covers about 60% of the land area of Sweden (35,000 sample points), where about 75% of the population of Sweden lives. As an example, the cadmium contents in southern Sweden can be shown. The contents are enhanced in the most southerly-counties of Sweden and along the west coast. The latter distribution is derived mainly from transboundary atmospheric transport and deposition of anthropogenic origin. The contents of Cd in the southernmost part, however, are much higher. This region is a densely populated farming area from which growing crops are distributed to the rest of Sweden. Samples of autumn wheat have been taken in this region showing that samples had an average of 73 µg Cd/kg d.w. (dry weight), with several areas exceeding 100 µg Cd/kg d.w. By comparison, an area in central Sweden yielded on analysis only 29 µg Cd/kg d.w. on average in autumn wheat. In the affected region, drinking water from many wells shows an almost identical distribution of high cadmium concentrations as depicted in the biogeochemical map. For drinking water, the WHO has set a limit of 5 µg Cd/l. By comparison, the wells within the region with a high cadmium burden have average levels of about 400 µg Cd/l.

Several factors may interact with each other and contribute to the high cadmium concentrations found in this region, for example deposition of airborne cadmium as well as acid rain from Eastern, Western and Central Europe. Cadmium may also originate from local sources, for example, from phosphate fertilizers used in agriculture. However, recent studies have shown that the high contents of cadmium are probably derived from the sedimentary bedrock (sandstones with disseminated Cd). Therefore we have a reason to believe that the findings indicate a clear connection between geology, acidification and possible health effects caused by cadmium.

*The moose (*Alces alces* L.) as an environmental monitor*

A separate chapter of this book discusses cadmium, a non-essential metal, and its negative biological effects in humans. However, other organisms/animals are also affected by cadmium. Wild animals eat what is afforded by nature. Animals browsing in extensive areas and eating various kind of plants may become natural monitors for bio-available cadmium. The animals act as sample collectors – “vacuum cleaners” – in more or less limited natural regions. Metals taken up by plants, according to their bio-availability, from the underlying geological background become integrated by browsing in the animal body.

The cadmium uptake by animals has been studied in a great variety of wild animals. The moose (*Alces alces* L.) was found to be a good monitor of the bio-availability of cadmium. The moose, a large wild ruminant, is found in most parts of Sweden. It is relatively stationary and its range of seasonal migration seldom exceeds 50 – 60 km. Its age is easy to determine which is important to know, since cadmium accumulation in organs (liver and especially in kidneys) is age-dependent. Organ tissues for investigation can be obtained through co-operation with hunters' organizations during regular hunting seasons in the autumn.

From more than 4,300 moose, samples of liver and kidneys, and also of the left mandible for age determination, were collected in the whole of Sweden during the hunting seasons in 1981 and 1982. The cadmium burden of the moose was calculated after analysis by expressing it on a standardized basis as the *average yearly cadmium uptake by the moose kidney*. Using this model, the cadmium burdens in the 25 investigated regions were calculated. The map according to Figure 10 shows these burdens in 25 regions of 23 counties of Sweden. The highest cadmium burden was found in the southern and south-western parts of Sweden, which is attributable to metal mobilization by acid rain.

The moose is a good monitor for detecting the presence of cadmium in nature and for demonstrating the distribution of acidification and the

effect of acid rain on cadmium mobilization. In addition, changes in nature are detectable when the investigation is repeated and compared the results with earlier measurements. Thus the moose is a reliable alarm clock. Monitoring by moose is not limited to cadmium. By analyzing moose organs concentrations of other essential and non-essential elements were also determined.

Two complementing methods

The biogeochemical technique and the animal monitoring technique using moose as a monitor for mapping the bioavailability of elements in the environment complement each other, however, on different levels in the food chain. The results obtained by using roots of aquatic plants and aquatic mosses and those obtained by using organ tissues from the moose collected during the same period of time appear to be remarkably similar, in spite of the higher trophic level of the latter. The two methods elucidate the usefulness of the techniques in monitoring and detecting metal burdens of regions on toxic levels as well as deficiency of essential elements. Geochemical monitoring provides a useful time-dependent catalogue of baseline data showing the integrated natural and anthropogenic distribution of chemical elements. Such information contributes to and facilitates interpretation of biological data and has predictive value in biological contexts. In addition, the moose is a reliable monitor for detecting rapid changes in the environment related to basic data collected in 1982.

We are now disturbing the natural circulation

The composition of the natural environment is very important for our health, and the distribution, mobilization and interaction of elements is a very delicate matter. Unfortunately we are now disturbing the natural equilibrium and circulation. One of the most serious environmental problems is the acidification of soil and water. The other is liming in industrialized countries with the intention of restoring nature to the time before acidification. Not only is environment affected but there is also a potential threat to the health of

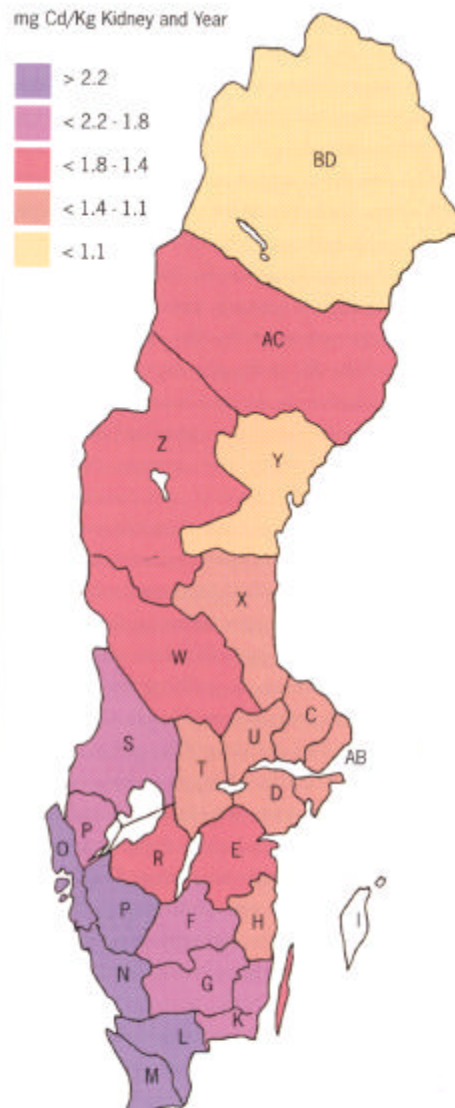


FIGURE 10 Cadmium burden in Sweden with the moose as monitor. Average renal cadmium uptake per year.

humans. These effects of acidification can be of two kinds: direct effects of inhalation of acid particles formed by discharge of sulphur oxides and nitrogen oxides and indirect effects of increased exposure to several toxic metals. Sulphur dioxide and nitrogen oxides are the chief causes of soil and water becoming acidified. Sulphur com-

pounds are responsible for about two-thirds of the acidification of rain, and nitrogen compounds for the rest. Sulphur in gaseous form, sulphur dioxide (SO₂), is mainly formed by combustion of oil and coal. The largest single source of nitrogen-oxide emissions is road traffic.

Airborne pollution can thus affect the environment both directly and indirectly. Sulphur dioxide and nitrogen-oxide gases in high concentrations can cause damage to trees and lichens, lakes and wetlands; they can affect people's health and corrode structural materials, such as steel. These direct effects are often greatest in the vicinity of the emission sources. Sulphur dioxide and nitrogen oxides can, however, also form sulphuric acid and nitric acid which may be transported by transboundary pollution. Thus soil and water can become acidified far away from the sources of emission.

As mentioned earlier, elements in bedrock are released and redistributed by weathering. Aerial deposition of sulphuric and nitric oxides however, may influence weathering of bedrock and soils. The concentration of metals in upper soil layers may change as a result of mobilization and the metals become more available via plants to grazing animals. Elements that are easily mobilized are calcium, magnesium, manganese, aluminium, nickel, zinc and cadmium, and to a lesser extent mercury, lead and copper. When the buffering capacity of the soil is insufficient, acid rain may cause trace-element imbalance in plants and via plants in herbivorous animals. Certain essential trace elements, such as selenium and molybdenum, become less soluble in acidic environment and their availability to plants decreases. Changes in the uptake via plants may result in changed metal concentrations as well as imbalance between metal concentrations in organ tissues, with severe consequences for grazing animals. Liming is used against acidification, but recent investigations indicate that, by changing the pH, it can have negative health effects in plants and wild ruminants as the mobility of certain negatively charged naturally occurring elements is altered.

One other consequence of acidification is its effect on nutrients in soils. Phosphorus, for exam-

ple, is an important nutrient for plants. When pH decreases, for example with increasing acidification, the phosphates which are necessary for plants become less available.

Nature can resist acidification ... to a certain extent

The extent of acidification depends on the resistance that soil and water offer to it. In some areas, acidification has reached the stage where flora and fauna are affected, whereas other areas appear to be completely uninfluenced. Naturally, this depends on the variability of deposition of acidic substances, but this is not the entire explanation. Another and perhaps just as important factor is the soil's ability to tolerate acidic deposits.

The geochemical status of the soil has a strong influence on its buffer capacity. During its passage through the soil, the rainwater is exposed to a number of chemical processes. Among these processes, there are various buffering systems that depend on the mineral composition of the soil and are of great importance for the neutralisation of acidic rainwater. Acidic rainwater in combination with deficient or absent neutralising capacity, may lead to undesirable consequences for the ecosystems. If the soil contains lime, then a carbonate buffering system takes over and acidic water is efficiently neutralised. A critical situation arises when the pH value in the ground falls below 4.5, which implies that the ground's reserve of exchangeable, beneficial base cations is temporarily depleted. Such situations may easily arise if the content of easily weathered minerals in the ground is low. In such a situation, another buffering system is activated, whereby otherwise slowly soluble aluminium compounds are dissolved, i.e., aluminium is mobilized. This process is rapid and effective and thus high concentrations of aluminium may suddenly appear in the groundwater. In addition, the decrease in pH may lead to mobilisation of other metals (e.g., cadmium). Many parts of the world are risk areas since the bedrock is commonly dominated by rocks with low contents of easily weathered material. The relative response of ecosystems to acidic deposition is determined by a combination of land cover, soil

buffering and climate. Geology plays a very important role in this effect.

Health effects of acidification

Acidification can influence human health by two main pathways: a deleterious effect on drinking-water quality in the form of metal contamination and an altered intake of certain elements caused by increased trace-element content in fish, shellfish, game or crops. Both of these pathways are very closely bound up with geological conditions (Figure 11).

Cadmium becomes more mobile...

It is not likely that acid groundwater will in itself be harmful to humans. But where the water is highly acidic, metals such as aluminium and cadmium may appear at increased concentrations, since they are released from the soil when the pH is below 5. Cadmium is the most mobile of the common heavy metals. Since it is one of the elements to which people in the industrialized world have already been exposed in dangerously high concentrations, alertness is required to the danger of levels rising in the groundwater. Cadmium is an element that leaves the body very slowly. In several countries, the amount of cadmium in soil that is available to plants is rising. This is due

in part to acidification, but in the case of farmland more to its presence in fertilizers. The levels in many plants, including farm crops, have consequently increased. The uptake by plants increases still further when the groundwater becomes acidified. At the same time people who are already ingesting dangerous amounts of cadmium, for instance by smoking, will be at severe risk if more cadmium gets into the drinking water. Acidification of drinking-water supplies can constitute a risk to human health through the leaching of toxic compounds from watersheds and sediments into groundwater or surface water sources.

Bio-availability of cadmium and other elements depends on several parameters. Deposition of atmospheric particulate matter from highly industrialised countries also contributes to the amount of cadmium in the soil. For uptake by plants, the mobility of the metal, which is pH-dependent, is important. At low (acid) pH, cadmium is easily mobilized as a positively charged cation. The pH decrease in soil during acidification depends on the type and amount of acidifying compounds and the buffering capacity of the soil; the pH of lakes and wetlands indicates the extent of acidification. In acidified regions the mobility of cadmium increases, along with its uptake via plants by plant-eating animals.

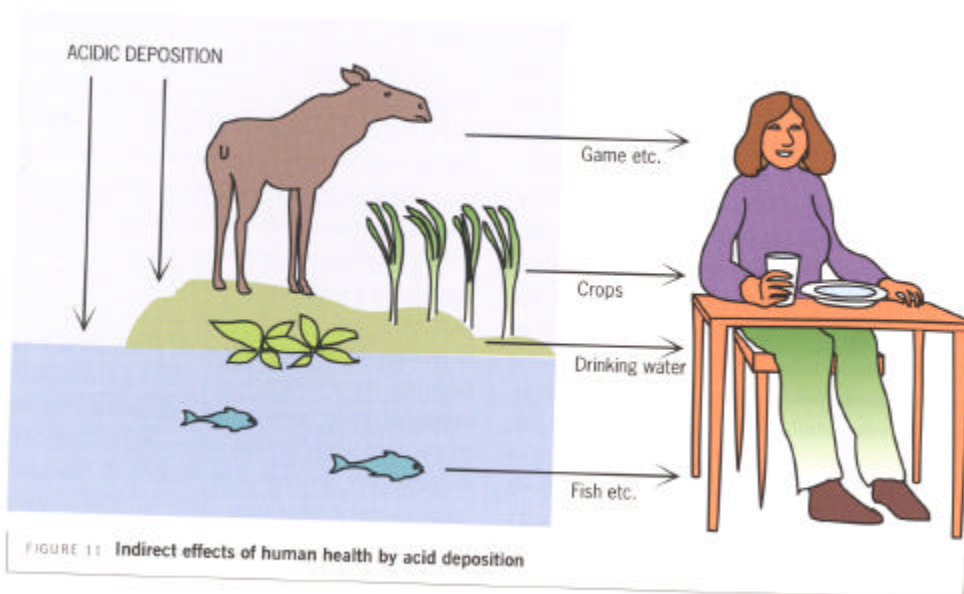


FIGURE 11 Indirect effects of human health by acid deposition

...but so do other metals

Aluminium is a common metal in the earth's crust. Normally it is tightly bound to minerals, but acidification and increased weathering make it markedly more soluble. The aluminium contents in acidified areas have shown a tenfold increase. Aluminium in water is chiefly a problem for kidney patients. In dialysis, when aluminium is present in water, it enters the blood stream directly without first having passed the body's normal protective barriers, which may cause skeleton and brain injuries. Lately it has come to light that even individuals who are not suffering from kidney trouble may be endangered by taking in aluminium. It has also been noticed that high contents of mobilized aluminium can cause problems in lakes, because fish may be affected by it, to the point of death.

Lead is also liberated by acidified water. In ancient Rome lead poisoning was a problem because of the usage of lead in water pipes. In Great Britain, where it is also commonly used for water-pipes, it is said that about five million people are using drinking water in which the levels of lead are in excess of those recommended by the European Union. Lead is liable to harm the nervous system, especially in children (hyperactivity). In the long term, the increased circulation of metals poses a distinct threat to health. A long time may elapse, too, before the effects become apparent.

Copper is also a metal of which water pipes are most commonly made in many countries. When the groundwater becomes more corrosive, the copper is dissolved.

A decrease of pH and alkalinity in lakes and streams can lead to an enhanced mobilization of metals. The possible result is increased trace-element concentration in water plants and plankton used as food by fish, shellfish and game. There is also evidence that a pH decrease leads to enhanced mercury accumulation in fish, constituting a health threat to fish-consumers. Pregnant women and their unborn children may represent a special group at risk. The mobilization of trace elements by acidification can result in an increased trace-element concentration in crops, plants and grazing animals thus becoming a risk to consumers.

Among animals there is a general characteristic that the contents of rubidium in various organs increase strongly with the acidity in the ground. This also occurs in plants and mushrooms. An increased rubidium/potassium ratio characterizes all living levels in the strongly acidified ecosystem because the concentration of potassium is fairly constant in every type of living material.

The highly toxic methylmercury is fat-soluble and has a tendency towards bioaccumulation in nature, and the increased mobility is dependent on acidification. There is evidence that acid rain leads to higher levels of methylmercury in edible tissues of freshwater fish. In many studies, a correlation between the mercury content in fish and pH has been demonstrated. In lakes with low pH values the mercury content in fish is generally higher than in less acid lakes. When a lake is acidified, changes occur in the turnover of compounds and in the biotic structure of the ecosystem of the lake that indirectly affects the flow and turnover of mercury.

The moose disease

Human beings are the last link in the food chain, but it is evident that earlier links in the chain are also influenced by geochemistry. The earlier the link, the more effects of geology. At higher levels in the food chain, in browsing animals, the dependence on geology is apparent.

However, the sensitivity of animals to deficiency or toxicity varies between different species and races. As mentioned, cattle are most sensitive to copper deficiency. Another example of extreme sensitivity has been noticed in Sweden during the last decade. During the second half of the 1980s a disease not observed earlier was reported in the moose population in the south-west of Sweden. The disease was called "Älvsborg disease", as the highest frequency of the disease is reported from the south part of Älvsborg county. The region is strongly affected by acid rain, and fields and pastures have been limed since the 1970s. To counteract the negative effects of acidification of lakes and wetlands, liming was intensified during the second half of the 1980s, simultaneously with the outbreak of the disease.

The multi-faceted clinical signs and lesions in this moose disease resulted in much speculation concerning the cause. After more than 10 years the disease is still limited to one geographic region and has not spread to other counties, apart from a few cases reported from the whole country of natural reasons-copper deficiency is always present in any moose population (see below). However, the theory of a possible microbiological cause (virus) in the absence of any outbreak of epizooty receives only very slight attention today.

Chemical investigations of moose organs, liver and kidneys, collected in connection with the regular moose hunt in the affected region, have shown that the hepatic copper concentration decreased by 50%, and cadmium by about 30% during a period of ten years. During the same time, molybdenum concentration increased between 22 and 40% in this "healthy" moose population in comparison with values in 1982, which was before the outbreak of the disease. The increase of molybdenum is significant, although the different values in 1988, 1992 and 1994 are probably due to climatic variations.

Understanding of the disease is facilitated when the multi-faceted clinical signs and necropsy findings are compared with those of molybdenum-caused secondary copper deficiency in cattle and to some extent in sheep. Most of the clinical signs

Most clinical signs and organ lesions include diarrhoea, anorexia, emaciation, loss of hair colour, loss of hair, neurological signs, apathy, motor disturbances, hind-limb lameness, sudden heart failure and osteoporosis. Findings from necropsy included mucosal oedema, an oedematous appearance of organs, mucosal lesions of the upper alimentary tract, including the mouth and tongue, vesicles and also ulcerative and multiple erosions of the alimentary-tract, neuropathy, neuronal degeneration, and uni- or bilateral corneal opacity, often with pronounced oedema. The findings in the affected moose are consistent in principle with the observations in conditioned copper deficiency caused by molybdenosis in cattle and sheep.

and organ lesions can be explained by the harmful effects of deficiency in, or decreased activity of, copper-containing enzymes.

Concentration decrease of cadmium, concomitant with increase of molybdenum was found in liver and kidneys in the investigations. As cadmium is a cation and molybdate an anion, consequently, this indicates according to the basic laws of physical chemistry, a pH increase in the moose's environment. Thus the cause of the moose disease appears to be severe copper deficiency and molybdenosis. This occurs because of elevated amounts of molybdenum in the moose diet, changing the ratio between copper and molybdenum therein. *It is noteworthy that the occurrence of the disease in the mid-1980s coincided with increased liming activities against the effects of acidification in this region.*

We must listen to nature

We have now seen that all living organisms, humans and animals, are built up of major, minor and trace elements, given by nature and supplied by geology. The presence of these gifts in nature is unevenly distributed. Occurrence of elements varies locally. Sometimes it is too much, sometimes too little, which is equally harmful. We have also disturbed the natural circulation. However, it is our duty and privilege to study, learn and provide ourselves with knowledge about natural prerequisites, e.g. the geological background and the bioavailability of elements which are essential for healthy life. By using monitoring techniques like analysing roots of aqueous plants or moose organs we have the instruments to make use of and display the secrets of nature.

We just have to listen and nature gives us advice!

OLLE SELINUS

OLLE SELINUS is a PhD in geology and worked during the 1960s and 1970s on mineral exploration with a mining company and at the Geological Survey of Sweden. Beginning in the 1980s he has carried out work and research mainly in environmental geochemistry and geostatistical methods, including medical geology. He is the organizer of several international conferences in this field and an editor of publications, and has published some 40 papers. He is presently at the *Geological Survey of Sweden* working on research and international affairs. Olle Selinus is also an officer of the *international environmental geology commission COGEOENVIRONMENT* and the chairman of its international working group on Medical Geology.

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Environmental medicine



Editor: Lennart Möller

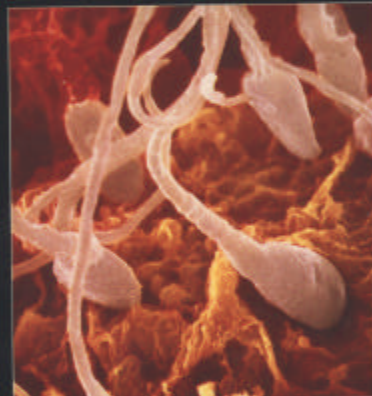
Environmental Medicine deals with environmental risk factors and human health. This is related to all of us since we are all exposed to air to breathe, water to drink, food and beverages. The risk factors can be of many different kinds like radioactivity, chemicals or ultra-violet radiation from the sun. Many of the risk factors could be avoided or reduced with the knowledge that they exist and what the risk situations are.



In this book you will find a number of scientists and physicians who are involved in research and human health care. They want to transfer their knowledge to students, decision makers and people interested in these matters which is the reason why the book is in a form of popularized science with many illustrations and photographs.

The 18 chapters deal with the process of cancer, genetics, air pollution, atmospheric chemistry, UV-radiation, allergens, algae toxins, water and soil contamination of mutagens and metals, the Chernobyl accident, radon, acidification, metal toxicity, organic chlorinated hydrocarbons, endocrine disruptors, food mutagens, mycotoxins, acute poisoning and risk perception.

The authors are from Karolinska Institutet (the Medical University of Stockholm) in Sweden, MIT and Harvard Medical School in Boston, US Environmental Protection Agency, US National Cancer Institute and University of California. Further, Huddinge University Hospital, The Agricultural University, National Veterinary Institute, The Geological Survey and Lund University of Sweden are represented, together with The South African Medical Research Council and Carleton University of Canada.



One author, professor M.J. Molina from MIT, received the Nobel Prize 1995 for his and his colleagues' research in atmospheric chemistry.



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