Review

Lead, the ugly trace element: occurrence, effects, screening and treatment

K.A. Essa[1]

Introduction

Environmental problems such as air, water, the work environment and their control have received a considerable amount of interest and publicity. We have come to realize that this is a very complex area, and while many advances have been made in recent years, much is yet to be learned about pollution. The importance of environmental protection and conservation measures has been increasingly recognized in the past three decades. It is now generally accepted that environmental protection will not be sustainable without developmental controls. Thus, environmental protection and development are two sides of the same coin. Wise management of the environment requires an ability to forecast, monitor, measure and analyse environmental trends and assess the capabilities of air, land and water at different levels to detect environmental trace elements.

Interest in the role of trace elements in biological processes has resulted in many studies in recent years. The influence of trace elements on various clinical disorders in humans and animals is currently considered of great importance. This has led to awareness that trace element deficiency and/or excess occurs in many diseases that affect physical and mental health. The biological mechanisms involved are often difficult to identify, and questions remain unanswered as to the correct concentration of trace elements in the body that are conducive to a healthy existence. The number of elements classified as essential for health has increased as a result of scientific research. A deficiency of essential elements can be caused by poor diet or physical malfunction, and such a deficiency can cause pathological disorders. For many elements, there is a normal range of concentration necessary to maintain a healthy state.

Lead awareness

Recent years have seen increasing awareness and global concern over the quality of the environment and the potential dangers associated with lack of environmental and hazardous chemical management. Chemicals as an example of toxic trace elements, enter the environment in a number of ways. These include release during production, from industrial effluents, direct applications, disposal and transportation accidents and a wide variety of patterns of use. The movement of these anthropogenic materials through the environment can result in

[1]*Faculty of Science, El-Gabal El-Gharbi University, Zentan, Libyan Arab Jamahiriya.*
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deleterious effects upon ecosystems and human populations, in some cases far removed from the points of release. The contaminant migration is often dictated by the routes of environmental distribution and chemical partitioning properties.

Understanding chemical characterization requires some degree of laboratory testing of environmental samples to obtain data that can be used in risk assessment, risk management and risk remediation. This article addresses salient issues for consideration to illustrate that environmental contaminant characterization of trace elements can indicate their apparent and hazardous effects. Among these trace elements is lead.

The toxic effects of long-term exposure to lead have been known for a long time. Lead poisoning is recognized as a public health problem because its environmental sources are widespread. There are many sources of lead exposure, but lead-based paint is the most common high-dose source for pre-school children, who become poisoned by ingesting paint chips or contaminated dust or soil. A thumbnail-sized paint chip may contain 50–150 μg of lead, and ingestion of a few chips a day is a toxic dose. This problem continues even though exterior and interior lead-based paint for residential use has been banned. Childhood lead poisoning has also resulted from exposure to lead-contaminated dust during renovation or remodeling of older homes. Lead poisoning is not a problem that is limited to families in the lower socioeconomic brackets. For example, infants who are fed home-reconstituted baby formulas have suffered lead poisoning from the local water used in the formula. The other main source of environmental lead is tetraalkyl-lead found in petrol. This has been significantly reduced in many countries with the advent of lead-free petrol [*1*]. The effect that this will have on the exposure to lead of the general population will be determined by monitoring. The lead added to petrol is only one of many sources of lead and contributes only 20%–30% of the total blood lead [*2,3*].

Less common now, but of possible significance in the past, is the infiltration of lead into drinking water from lead pipes used in plumbing systems. Lead is no longer used in drinking water systems. A somewhat more likely source, however, is pottery utensils. Lead salts have been common constituents of some glazes used since antiquity to decorate pottery and, while apparently inert, some lead may be leached out under acidic conditions, particularly if the glaze is improperly fired. One theory for the decline of the Roman Empire suggests that much of the population was impaired by chronic lead poisoning as a result of wine stored in lead-glazed vessels. Other sources of lead in the human environment have been lead arsenate and lead acetate used as insecticides.

Lead in the body

Lead is a very heavy metal without any known function in the human body. It is absorbed slowly and incompletely from the gastrointestinal tract and can also be absorbed from the respiratory tract after inhalation. The distribution of lead in the body is primarily in two pools: in the blood and soft tissues, and in bones. In the blood, nearly all circulating inorganic lead is associated with the erythrocytes. Following absorption, lead is distributed in soft tissues with the highest concentration in the kidneys. Over a period of time, the lead is redistributed and accumulated in bone, teeth and hair, with a small quantity of inorganic lead becoming deposited in the brain. Since

the rate at which lead is excreted is very slow, it tends to accumulate in the body. Lead is excreted mainly by the kidneys [*4*].

Blood lead concentration provides the best index of recent exposure to this element and has been used for the biological monitoring of populations exposed to environmental lead in many countries. Once absorbed, lead is distributed to blood, soft tissues and bones. It is the lead in blood and soft tissues that causes symptoms of lead poisoning. Chronic exposure results in hypermineralization of bone, which is evident radiographically. Severity of blood intoxication is not directly related to lead concentration in blood and soft tissues. Doubling of the body burden of lead only increases blood lead concentration by a few micrograms per decilitre.

Lead is known to interfere with various steps of the biosynthetic pathway of haeme biosynthesis and consequently causes many haematological disorders. The most evident haematological disorder is anaemia from reduced haeme synthesis. Since nutritional iron deficiency is common among children from lower socioeconomic levels who are also at risk of lead poisoning, childhood anaemia is frequently caused by both nutritional iron deficiency and lead poisoning. Anaemia caused by lead poisoning alone is quite rare. Signs and symptoms of lead poisoning may include malaise, anorexia, abdominal pain, vomiting, lethargy, colic, constipation, irritability and apathy. Manifestations of lead poisoning include effects on the haematopoietic, renal and central nervous systems. Lead encephalopathy is characterized by a sudden onset of cerebral oedema, coma, convulsions and death. Sequelae may include mental retardation, seizure disorders, behavioural abnormalities and occasional blindness, aphasia and hemiparesis. Neurological damage, especially in children, is often irreversible and acute neurological toxicity may develop without previous symptoms. Therefore, it is important to detect and treat lead poisoning before symptoms become obvious.

The limits between normal lead levels and excessive exposure are ill defined. Because the symptoms of lead poisoning are variable and lead encephalopathy so catastrophic, many clinicians have questioned whether low lead levels may produce subtle forms of brain injury. Some studies have suggested, in fact, that asymptomatic lead poisoning may cause significant and permanent impairment of the nervous system. At present, there is no evidence that blood lead concentrations below 25 µg/dL result in any impairment.

Lead analysis

The blood lead concentration is the most reliable indication of exposure. Recently, new approaches to obtain reliable quantitative blood lead data have been explored. These approaches have resulted in many state-of-the-art measurement techniques. For the management of lead in exposed persons, the most important parameter is the blood lead level, since many countries define maximum permissible threshold levels of lead in the blood. Analytical methods with high precision and accuracy are required to determine these thresholds.

There are two methods well suited for testing lead levels that can be compared: graphite furnace atomic absorption spectrometry evaluation against control samples with known lead contents; and anodic stripping voltammetry directly applied in diluted blood, which is evaluated against a calibration solution. The first procedure has on average, depending on the number of subsamples and firings per sample, an imprecision rate of about 2.5%–5%, the

second procedure one of 5%. Samples throughout are comparable at the same imprecision rate. Accuracy of both procedures, checked by mass spectrometric isotope dilution analysis and differential pulse anodic stripping voltammetry after complete digestion, has been found to be quite satisfactory.

Accuracy and precision in determination of low concentrations of lead, however, requires meticulous attention to detail. The ubiquity of lead in the environment requires that specimens be collected with care to avoid contamination.

The routine method of determination of lead in whole blood by electrothermal atomization from a L'vov platform and atomic absorption spectrometry has significantly improved in the past two decades. The use of the above techniques and an integrated absorbance signal has facilitated the determination of lead in whole blood and erythrocytes with reference to standard calibration plots [*5,6*].

The sample preparation is simple. The whole blood dilution is performed with a diluent containing a mixture of ammonia solution, ammonium dihydrogen phosphate and ethylenediaminetetraacetic acid–ammonium salt. The addition of detergents such as triton C-100 in the presence of ammonia solution results in complete lysis of red cells and the production of a clear homogeneous solution that would give an acceptable work calibration range for the method and complete lysis [*7*].

An automated graphite-probe atomizer has been used recently for the direct analysis of diluted urine samples for the determination of lead by electrothermal atomic absorption spectrometry. The method has been applied successfully in reference materials, quality control urines and patients samples. However, this application often causes more difficulties than the analysis of whole blood, because of the lower levels of lead present in urine and the variability in matrix interfence from sample to sample [*8*].

Generally, blood lead concentration is expressed in μg/dL or by SI units in μmol/L. The conversion between the two units is μg/dL × 0.04826 = μmol/L.

Treatment of lead poisoning is by chelation therapy using calcium disodium ethylenediaminetetraacetate ($CaNa_2EDTA$) and D-penicillamine [not approved by the Food and Drug Administration (FDA), but in the United States of America it is used in some centres]. Succimer (meso-2,3-dimercaptosuccinic acid) was approved by the FDA in 1991.

Symptomatic patients, or those with blood lead higher than 45 μg/dL should be treated with chelation therapy immediately. Asymptomatic patients with initial concentrations between 25 μg/dL and 45 μg/dL are given the $CaNa_2EDTA$ challenge test to assess the burden of lead. The ratios of lead excreted in urine per dose of $CaNa_2EDTA$ are calculated. An 8-hour challenge test is considered positive if the ratio is higher than 0.6. Children with blood lead concentration of 25–45 μg/dL and a positive challenge test should undergo a 5-day course of chelation. Chelation treatment may be repeated if blood lead remains or rebounds to 50 μg/dL or higher.

Conclusions

Lead is a very dangerous element since the rate of excretion from the body is clearly slow, and it tends to deposit finally in the brain. The environmental sources of lead are widespread. Consequently, it is important to prevent lead spreading, and to detect its traces before its effects become serious.

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