Cadmium

March 2002

Introduction

Cadmium is found naturally as cadmium sulfide in greenockite. It is produced commercially as a by-product of the smelting of the sulfide ores of other metals, namely zinc, lead and copper.

Uses

Cadmium is used primarily in the production of nickel-cadmium batteries and for metal plating. Cadmium is used in alloys for soldering, brazing and electrical contacts. Its salts are used in pigments, rubbers, paints, inks etc. and as stabilisers for plastics.

Occupational Exposure

Occupational exposure occurs in processes involving the handling of cadmium metal or its salts, or when thermally generated cadmium fumes occur in the workplace such as in smelting. Welding and thermal cutting of cadmium-plated metal products eg. bolts, is also a potential source of substantial exposure.

The national occupational exposure standard for cadmium and compounds as set by the National Occupational Health and Safety Commission (NOHSC) is a time-weighted average (TWA) of 0.01 mg/m^3 (this value also applies for cadmium oxide fume). NOHSC also classifies cadmium and compounds as probable human carcinogens (Category 2), and as such considers that exposures to these substances in the workplace should be minimised to the lowest practicable levels.[1]

Environmental Exposure

The main source of exposure to cadmium for the general population is dietary. Small amounts of cadmium are present in a wide range of foodstuffs. Results of the 1994 Australian Market Basket Survey (AMBS) conducted by the Australia New Zealand Food Authority indicated that the mean weekly intake for cadmium for all age groups did not exceed 3.5 µg/kg bw (body weight). The Provisional Tolerable Weekly Intake (PTWI)[2] for cadmium is 7 µg/kg bw/week.

Potatoes are a major source of cadmium in the Australian diet; however the results of the 1994 AMBS indicated that the average level of cadmium in raw potatoes was 0.033 ppm which is less than the Maximum Permitted Concentration (MPC) for cadmium in potatoes (0.1 ppm). Offal and molluscs contain higher cadmium concentrations than other foods, but since they are consumed only in small amounts the proportion of cadmium they contribute to the total dietary intake is low.

1. This is achieved by the application of effective engineering control measures, revised workplace practices, and where necessary, complemented by the use of appropriate personal protective equipment.
2. The unit of time for PTWIs (one week) is longer than that used for the acceptable daily intake (ADI). The longer time interval is used because the chronic intake is of greater importance than acute intake for substances that accumulate in the body. Consumption of particular foods may result in a high intake of a contaminant in a single day; however, over a longer period, such as a week, consumption may not be excessive.

Queensland Government
Queensland Health

In a US air sampling study, most samples were less than the limit of detection (10ng/m^3). Exposure from ambient air is not thought to be significant in Australia and if it occurred it would be highly localised about an industrial source. Tobacco smoke contains considerable cadmium, up to 0.1µg per cigarette in the mainstream and 0.4 -0.7 µg per cigarette in the sidestream smoke.

The NHMRC Drinking Water Guidelines (1996) set a Guideline Value of 2 µg/L for cadmium. In natural waters in Australia, cadmium levels are usually below 2 µg/L.

In Australian soils, the background range for cadmium is 0.04 to 2.0 ppm. Fertilised soils have been found to contain 2 to 6 times the cadmium concentration of unfertilised soils, because the use of superphosphate fertiliser has resulted in inadvertent addition of cadmium to the soil in some agricultural areas.

Health Effects

Acute Effects

Absorption of ingested cadmium is poor (about 5%), but up to 50% of inhaled cadmium is absorbed. Cadmium is concentrated in the liver and kidneys in combination with metallothionein, a cadmium-binding protein.

Signs of acute oral toxicity from soluble cadmium salts are effects on the gastrointestinal tract, kidneys and liver. LD_{50} values are in the range of 50-250 mg/kg in rats for the chloride, sulphate and nitrate salts. Persistent vomiting, a choking sensation, abdominal pain and diarrhoea occur after ingestion of cadmium salts.

Following inhalational exposure to cadmium the principal toxic effects are on the lungs. Toxicity is initially characterised by dyspnoea (shortness of breath), cough, and chest tightness, but at levels of exposure sufficient to kill rodents, pulmonary oedema (build-up of fluid in the lungs) may develop within 24 hours of exposure and proliferative interstitial pneumonitis may occur 3 to 10 days following exposure.

Chronic Effects

Cadmium is a cumulative toxicant and the human exposure route of most concern is long-term exposure to elevated levels of cadmium in the diet. In the body, cadmium is primarily bound to metallothionein and these complexes are filtered in the kidney so that cadmium accumulates in the renal cortex. Signs of renal dysfunction are the first indications of chronic cadmium toxicity. Cadmium affects the reabsorption capabilities of the proximal tubules and protein in the urine is the first effect to be detected. Later signs include amino acids and glucose in urine, and decreased ability to concentrate urine. There are also abnormalities in the handling of uric acid, calcium and phosphorus, which can lead to kidney stones and osteomalacia.

It is widely accepted that an accumulation of more than 200µg/g (wet weight) in the renal cortex leads to renal toxicity. Renal cortical levels exceeding 200 µg/g cause tubular damage although the health impact of early kidney damage is difficult to assess. Based on this and with assumptions about absorption and excretion rates, the WHO/FAO Joint Expert Committee on Food Additives and Contaminants set the PTWI for cadmium at 7 µg/kg body weight/ week.

Anaemia has been seen after many years of cadmium exposure, probably due to deficient absorption of iron from the gut. An association between cadmium exposure and hypertension has been the subject of several studies, but the topic remains controversial. Hypertension has been induced by dosing rats, rabbits and dogs with cadmium salts. Overall, the evidence for cardiovascular toxicity resulting from oral exposure to cadmium is suggestive of a slight effect.

The disease "Itai-Itai", which was described in Japan, is characterised by osteomalacia with pain in the back and extremities, difficulty in walking and pseudofractures. It was induced by environmental cadmium exposure primarily in post-menopausal women. Deficiencies in calcium and vitamin D were also important factors. The effects of cadmium on the kidney cause derangement of mineral metabolism, which with nutritional deficiencies, influence the development of symptoms.

Carcinogenicity

Oral doses of cadmium do not increase tumour rates in animals. Injection of cadmium compounds produced local tumours at the site of injection and testicular tumours in rats. The mechanisms proposed are local irritation and impairment of the vascular system of the testes leading to ischaemia.

Carcinogenicity

Oral doses of cadmium do not increase tumour rates in animals. Injection of cadmium compounds produced local tumours at the site of injection and testicular tumours in rats. The mechanisms proposed are local irritation and impairment of the vascular system of the testes leading to ischaemia.

There is little evidence of an association between oral exposure to cadmium and increased cancer rates in humans, but the statistical power of the available studies to detect such an effect was not high. Some epidemiological studies suggest occupational exposure by inhalation to cadmium may cause prostate and lung cancer in man.

The International Agency for Research on Cancer (IARC) has classified cadmium as a probable human carcinogen (Group 2A, limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in animals).

There is not sufficient evidence to evaluate carcinogenic potential by the dermal route. After the most recent evaluation of cadmium by IARC in 1993, it was concluded that "there is no good reason to believe that ingestion of cadmium in such amounts (ie. amounts smaller than those liable to cause nephrotoxicity) would cause any risks to humans, but the possibility they might cause a risk of lung cancer by inhalation can neither be excluded nor affirmed".

There is no clear evidence that cadmium is mutagenic. Many tests have been reported as negative, but there are reports of induced gene mutation and chromosome abnormalities in mammalian cells. The positive results were weak and only seen at high concentrations.

Effects on Reproduction

Cadmium toxicity includes suppression of testicular function. Teratogenic effects in animal studies are thought to be due to cadmium-induced zinc deficiency.

Biological Monitoring

Cadmium can be measured in blood, liver, kidney, hair, faeces and urine. Blood levels of cadmium correlate to recent exposures. Levels in whole blood of persons not occupationally exposed generally range from about 0.0035 to 0.0089 μmol/L for non-smokers and 0.012 to 0.035 μmol/L for smokers. Blood concentrations less than 0.089 μmol/L are considered acceptable in workers with occupational exposure to cadmium. Workers with occupational exposure to cadmium by inhalation may have blood levels up to 0.44 μmol/L.

The levels of cadmium found in liver and kidney cortex, as well as urinary levels, correlate to total body burden, which is the result of chronic exposure. In the general population, the average urinary cadmium level is about 0.00035μmo/mmol creatinine (0.35 μg/g creatinine) in non-smokers and values above 0.002μmol/mmol creatinine (2μg/g creatinine) are rare. In populations with substantial environmental or occupational exposure, values can range up to 0.05 μmol/mmol creatinine (50μg/g creatinine), even among individuals with no signs of renal dysfunction.

Faecal cadmium primarily reflects recently ingested cadmium and is not a good indicator of past exposure. It can be used as a direct indicator of dietary intake because it is so poorly absorbed from the gastrointestinal tract.

Liver and kidney preferentially accumulate cadmium and *in vivo* levels can be measured by neutron activation analysis or in kidney by x-ray fluorescence analysis. Levels in both tissues increase with age. These methods are highly specialised and not suited to general use.

Biomarkers of effects caused by cadmium include measurements of β_2-microglobulin, N-acetyl- β-D-glucosaminidase and metallothionein in urine. The problem with these markers is that they are not specific for cadmium exposure.

Urinary β_2-microglobulin, a low molecular weight protein, has been widely used as a marker of renal tubular dysfunction but it is not a specific marker of cadmium-induced effects. Excretion of urinary β_2-microglobulin rises naturally with age.

Urinary N-acetyl-β-D-glucosaminidase (NAG), a lysosomal enzyme present in high concentration in the proximal tubule, has a better correlation with urinary cadmium levels than does β_2-microglobulin at low cadmium exposure levels (urinary cadmium <10 μg/g creatinine). However, increased urinary NAG activity can result from effects other than nephrotoxicity.

Urinary metallothionein correlates with cadmium concentrations in liver, kidney and urine and relatively strong correlations have been found between metallothionein and cadmium levels in urine in exposed humans. Again, the specificity is questionable and once renal damage becomes pronounced, urinary metallothionein levels increase sharply.

Other markers have been proposed as sensitive indicators of cadmium exposure. These include α_1-microglobulin, trehalase, alanine aminopeptidase. Changes in alkaline phosphatase, γ-glutamyl transferase, urate and phosphate tend to be significant only after other markers of renal damage are clearly elevated.

Regulation

Cadmium compounds are in Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), except cadmium sulphide in preparations containing 2.5% or less of cadmium sulphide for human therapeutic use, which is listed in Schedule 5.

Selected Bibliography

Biological Monitoring of Metals. World Health Organization: Geneva, 1994.

Cadmium in the Human Environment: Toxicity and Carcinogenicity. Ed. Norberg GF, Herber RFM, Alessio L. International Agency for Research on Cancer: Lyon, 1992.

Carson BL, Ellis HV, McCann JL. Toxicology and Biological Monitoring of Metals in Humans. Lewis Publishers Inc, 1986.

Agency for Toxic Substances and Disease Registry. Toxicological Profile for Cadmium. TP-92- 06. 1992.

Joint FAO/WHO Expert committee on Food Additives. Toxicological Evaluation of Certain Food Additives and Contaminants: Cadmium. WHO Food Additive Series 1989: 24, 163-219.

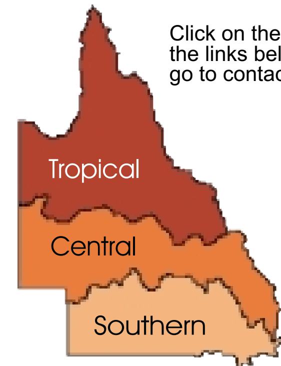
Australia New Zealand Food Authority. The 1994 Australian Market Basket Survey. Australian Government Printing Services (AGPS): Canberra, 1996.

National Occupational Health and Safety Commission. Exposure Standards for Atmospheric Contaminants in the Occupational Environment. AGPS: Canberra, May 1995.

National Health and Medical Research Council/Agriculture and Resource Management Council of Australia and New Zealand. National Water Quality Management Strategy. Australian Drinking Water Guidelines. 1996.

Australian Health Minister's Advisory Council. Standard for the Uniform Scheduling of Drugs and Poisons, No. 12. Effective Date - 21 September 1997. AGPS: Canberra, 1997.

For more information, contact your local public health network



Central Public Health Unit Network servicing Brisbane Northside, Longreach, Redcliffe, Rockhampton, Sunshine Coast, Wide Bay.
For contact details go to
http://www.health.qld.gov.au/phs/cphun/

Southern Public Health Unit Network servicing Brisbane Southside, Darling Downs, Roma, South Coast, South West Queensland, West Moreton
For contact details go to
http://www.health.qld.gov.au/phs/sphun/

Tropical Public Health Unit Network servicing Cairns, Mackay, Mount Isa and Gulf, Townsville
For contact details go to
http://www.health.qld.gov.au/phs/tphun/

For medical advice, contact your doctor, hospital or health clinic.

Published by:
Environmental Health Unit
10th floor, Queensland Health Building
147-163 Charlotte Street,
BRISBANE 4000
GPO Box 48 BRISBANE 4001
Ph: +61 7 3234 0938
Fax: +61 7 3234 1480
http://www.health.qld.gov.au/phs/ehu/

This fact sheet may be reproduced in full, providing the source is acknowledged, but may not be reproduced in part without prior permission of Public Health Services, Queensland Health