Cadmium exposure and occupational health

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Cadmium (Cd) is a naturally occurring heavy metal that usually complexes with other elements, such as zinc, lead and chloride.[1, 2] It is a toxic environmental and occupational pollutant.[1, 3, 4] In the early 20th century, itai-itai disease (referred to as ouch-ouch disease due to the pain in bones and joints), the most severe form of chronic Cd poisoning, occurred in Japan due to both environmental pollution and occupational exposure.[3]

Most commonly, occupational exposure to Cd occurs during battery recycling, fabrication of nickel-cadmium batteries, manufacturing of Cd-containing paint pigment, lead smelting, galvanising of steel, and in nuclear power plants. Cadmium is also used as an anti-corrosive agent and a stabiliser in plastics,[1] and phosphate fertilisers contain large concentrations of Cd.[2]

In humans, occupational exposure occurs mainly from inhalation, particularly during welding and soldering.[1] Exposure from ingestion comes from the consumption of contaminated water and foods such as high fibre-containing foods, shellfish, organ meats and leafy vegetables. Dermal absorption is negligible.[1,2]

Cigarette smoking is also a significant source of Cd exposure. The lung can absorb up to 60% of Cd present in tobacco smoke. Smokers can have up to five times the blood levels of Cd present in non-smokers.[2] Smokers of 20 cigarettes a day absorb approximately 0.5-2.0 ug Cd.[5]

Absorption of Cd in the lung alveoli from inhaled Cd-containing respirable dust and fumes is dependent on particle size and solubility. Approximately 10-50% of inhaled Cd-containing dust is absorbed. Following ingestion, 5-10% of Cd is absorbed. Several factors influence Cd absorption, e.g. age, composition of the ingested contaminant, and zinc and calcium deficiencies which potentiate the absorption of Cd. Interestingly, iron deficiency also enhances Cd absorption in the gut. At low iron levels, the expression of the metal ion transporter (DCT-1) is stimulated, facilitating Cd uptake. Generally, urinary Cd levels in women and children may be higher than in men as iron deficiency tends to be more prevalent in these groups.[1,2,5,6]

The distribution of absorbed Cd is independent on the route of absorption and is distributed to other tissues from the liver, bound to proteins – primarily metallothionein (MT) – and less frequently, albumin.[5] Absorbed Cd accumulates in the liver and kidney and induces synthesis of MT.[3] Cd complexes with MT and is transported to the renal cortex – the major site of Cd deposition. The kidney is the preferred organ for uptake of Cd, given this receptor-mediated uptake by MT. The Cd-MT complex is filtered through the glomerulus and reabsorbed in the proximal tubules of the kidney.[3]

The MT from the CD-MT complex is degraded in the lysosomes of the renal tubule, releasing the free Cd into the tubules, while the MT becomes available again to rebind further absorbed Cd. This is a cyclical process, ensuring that Cd remains in a minimally toxic state.[2,5] When the concentration of Cd in the renal cortex exceeds the MT availability, renal tubular damage occurs. The free Cd generates reactive oxygen species within the renal cortex, causing cell death and tubular necrosis. The earliest manifestation of this is tubular dysfunction that results in the loss of low molecular weight proteins (tubular proteinuria), such as beta-2-microglobulin, in the urine. The tubular dysfunction results in conditions such as Fanconi's syndrome.[1, 2, 5]

Cd is a cumulative toxin, the kidney being the main organ of long-term Cd accumulation, with a half-life of approximately 10-20 years.[3, 7] After long-term low-level exposure, half the body burden of Cd is localised in the kidney and liver.[7] Some authors state that the primary organ of accumulation of Cd depends on the duration of exposure. Short-term exposure results in accumulation in the liver.[3] The other target organ affected by long-term exposure to Cd is the skeleton, as manifested by osteoporosis and osteomalacia.[2,5,7] This is a result of the disruption of Vitamin D metabolism in the kidney as well as renal loss of calcium and phosphorous from renal tubular dysfunction.[2,3] Other clinical manifestations of chronic Cd exposure include olfactory dysfunction, cardiovascular disease, hypertension, and male infertility.[1,2]

Cd is classified as a suspected human carcinogen. The International Agency for Research on Cancer (IARC) has classified Cd and its compounds as a Group1 human carcinogen implicated in lung cancer. The National Toxicology Program in 2000 has also classified Cd and its compounds as a human carcinogen.[8] Recently, further epidemiological studies have
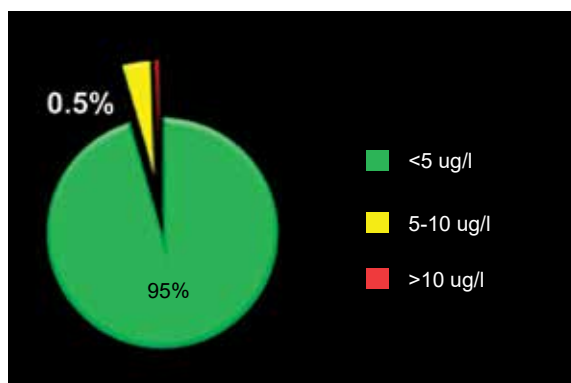
Figure 1. Blood cadmium exposure levels, Ampath industrial clients 2015-2018
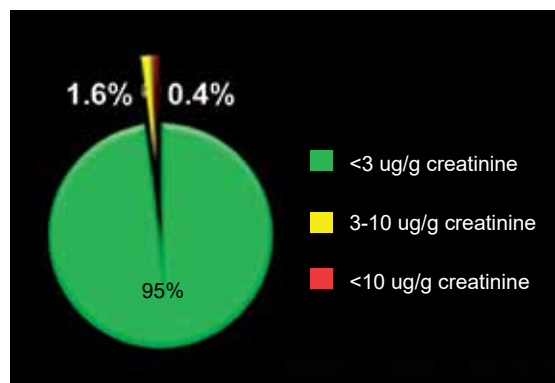
Figure 2. Urine cadmium exposure levels, Ampath industrial clients 2015-2018

shown a link between Cd exposure and prostate, breast and pancreatic cancers.[8,9]

Several molecular and cellular mechanisms act synergistically to induce carcinogenesis from long-term chronic Cd exposure. In general, the main pathogenesis is from mutagenic oxidative stress, epigenetic changes, and dysregulation in cellular proliferation.[5,6]

As excretion of Cd is very slow (excreted mainly in the urine but also in faeces, hair and nails), Cd concentrations increase with age.[5,7] The biological exposure-monitoring of Cd uses two biological samples for Cd level estimation, i.e. blood and urine, both influenced by current exposure and body burden.[7] The half-life of Cd in blood is approximately 75-128 days, most likely reflecting deposition in target organs.[1] Further, in moderately exposed individuals, blood Cd reflects recent exposure (a few months).[1,7] Urine Cd levels are influenced by the intensity of exposure and whether renal damage is present or not:

1. In new exposures there is a time lag before one can correlate urine Cd levels with exposure.
2. At low exposure levels, urine Cd levels reflect body burden.
3. At high exposure levels and without renal damage, urine Cd is influenced by body burden and also correlates with renal concentrations of Cd1.[7]

Several occupational organisations have suggested different biological exposure indices (BEIs) and action levels. At Ampath, the BEI of 10 ug/g creatinine is used as per the Occupational Health and Safety Act (Act No. 85 of 1993). The World Health Organization (WHO) and OSHA (Occupational Safety and Health Administration of the United States) suggest that control measures should be taken when levels exceed 5 ug/g creatinine. OSHA suggests an action level of 3 ug/g creatinine. Epidemiological studies relating BEIs and biological effect suggest that biological evidence of renal tubular dysfunction increases in individuals whose urine Cd exceeds 10 ug/g creatinine.[7]

In figures 1 and 2, the distribution of urine Cd and blood Cd levels are represented for Ampath's industrial clients. These results reflect that occupational exposure to Cd is consistent with recommended guidelines. In view of this, it will be interesting to investigate the degree of renal dysfunction as assessed by urine beta-2-microglobulin levels, at the different cut points of urine Cd concentrations.

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