Lead

Toxicology and assessment in general practice

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BACKGROUND
Despite a consistent fall in the number of reported cases of inorganic lead toxicity, lead remains an important toxicant. While much of the pathology caused by lead is known, much remains to be established regarding its mutagenicity and teratogenicity.

OBJECTIVE
This article briefly outlines aspects of lead toxicity relevant to general practice, and provides an outline for taking a workplace exposure medical history.

DISCUSSION
Recent trends show a continuous decline in the number of lead toxicity cases among workers and nonoccupational cases in adults and children. The protean manifestations of lead toxicity make it difficult for doctors to consider it as a differential diagnosis. A basic understanding of lead toxicology is helpful when assessing its clinical presentation, ordering laboratory tests, advising patients how to avoid workplace exposure, and in understanding why it remains a major concern as a mutagen and teratogen.

Fortunately there has been a steady fall in the incidence of lead toxicity in recent decades. Lead toxicity is a notifiable condition, with laboratories undertaking the notification process.

Nonoccupational toxicity is notifiable at a lower level (0.73 µmol/L) than for occupational cases (2.41 µmol/L), the latter being stipulated by the *National code of practice for the control and safe use of inorganic lead at work*.[1] These levels are the equivalent of 15 µg/dL and 50 µg/dL set by the American National Institute for Occupational Health and Safety.

Annual occupational exposure notifications in Queensland have fallen from 32 in the year 2000 to 12 in 2005, with nonoccupational notifications falling from 54 to 29. Nonoccupational notifications included childhood notifications, which fell from 11 to one in the same period.[2] There has been an increase in the number of specimens tested by laboratories (both from occupational and nonoccupational sources) but a fall in the incidence of lead toxicity, despite well publicised environmental concerns in a few Australian industrial cities.

Recent nonoccupational exposures in Queensland occurred most commonly by exposure to old lead (contained in paint) during demolitions, renovations and maintenance. Occupational exposures occurred most commonly in battery manufacturing, foundry work, and radiator manufacture and repair.[2]

Toxicology

In order to suffer the ill effects of a toxicant, one must be exposed to a sufficient dose, which must in turn be absorbed into the blood. Ingestion and inhalation are both important. Approximately 10–15% of the ingested quantity is absorbed, although this can be higher in the presence of iron deficiency, pregnancy, and fasting.[3,4] For lead to be absorbed by inhalation, the dose must be delivered in a form that is respirable, ie. can be delivered to the alveolus. The particulate size of fume can be as small as 0.1 micron, and almost all of this is absorbed. Lead dust is also respirable as particles may be as small as 0.5–1 microns, well within the range capable of alveolar deposition.[5] It is estimated that approximately 35–40% of inhaled lead dust is actually absorbed into the blood.[3]

Upon absorption, lead binds to erythrocytes, and over a period of weeks is distributed predominantly to bone, liver, kidney, marrow and brain. Over 90% of the body

burden of lead is stored in the compact bone matrix and trabecular bone from which lead may be mobilised.

Lead's primary toxicity is due to its affinity for sulfhydryl groups allowing alteration of protein and enzymatic function. Lead is similar to calcium in its physiochemical properties, accounting for its osseous deposition and its effect within mitochondria where it competitively antagonises the action of calcium. Lead also appears to affect nucleic acids, through mechanisms which are not clear, giving rise to concerns about chromosomal abnormalities.[6]

Lead causes anaemia, both by inhibiting haeme synthesis and accelerating erythrocyte destruction. Enzyme inhibition leads to a range of changes including the accumulation of zinc protoporphyrin (ZPP), which forms the basis of a laboratory test.

Renal toxicity may be reversible with lower exposure, as early pathological changes affect only the proximal tubules. Higher exposure leads to interstitial fibrosis and progressive nephropathy. It is thought that lead affects the renin-angiotensin system, causing hypertension.[3]

There is no active elimination of lead. Elimination occurs through skin desquamation, nail growth, biliary secretion and glomerular filtration.

Points to seek in a workplace history

Details of job tasks undertaken are important in assessing potential lead exposure. For example, in automotive radiator repair, the radiator core is connected to the top and bottom tanks by lead solder, which is also used to repair holes in the radiator. Lead fume is not normally produced by this process as the solder is not hot enough. Soldering is by definition the joining of metals at temperatures of less than 430°C (brazing or welding occurs above this temperature). Lead fume is only produced above 550°C, but may be generated if excessive heat is used during a soldering task (eg. when soldering is performed with an oxyacetylene torch [which should not be permitted]).[5] Exhaust systems should be in operation when lead dust is generated by buffing, rotary brushes or grinding.

Other points to consider in seeking a workplace history include:

- workplace hygiene – cleaning should not be performed in a manner that generates dust (appropriate vacuuming is required)
- kitchen and meal areas – food should not be taken into the workplace. Kitchen and meal rooms should be dust free
- personal hygiene – adequate measures are needed to remove dust before donning nonworkplace clothing
- smoking and nail biting are common sources of ingestion
- overalls should be left at work and not taken home for cleaning. A 'take home' dose may be delivered to family members by lead contaminated clothing.[5]

Larger workplaces tend to have better workplace procedures and compliance with statutory health surveillance. Most cases of toxicity now arise from smaller, poorly managed workplaces.

Biological monitoring of exposed workers must be performed. Legislation in the various states is based on a national standard requiring that employers have a blood lead level test within the first month of employment, after 3 months, and then every 6 months.[2]

The aims of biological monitoring are early detection, minimisation of risk of significant exposure, reduction in overall exposure, and identification of affected workers for exclusion from further lead exposure. It is also a useful source of information when assessing a worker with elevated lead levels.

Clinical presentation

A difficulty with the presentation of lead toxicity is the nonspecific nature of symptoms. These symptoms range from fatigue, concentration difficulties, sleep disturbances, headache, weight loss, nausea and myalgia with mild to moderate toxicity to the classic features of severe toxicity of abdominal cramps, renal disease, encephalopathy, convulsions and peripheral neuropathy. Motor neuropathy leads to the classic lead palsy, affecting the long extensor muscles of the limbs. Lead induced Fanconi syndrome is more likely to occur in children. Unique features include a blue line on the dental margins of the gums and 'saturnine' gout[6,7] (named after the miserable and dull Roman god Saturn, who was reputedly irritable enough to eat his own children).

Lead's adverse effect on neurological development in children is long established. There is recent evidence that, in addition to its other neurological effects, lead causes cognitive abnormalities in adults which are demonstrable on neuropsychological testing.[3]

It is worth noting that the onset of symptoms or signs following lead exposure may be highly variable depending on the intensity of the exposure as well as host factors. For example, a high intensity dose may increase blood level concentration rapidly with the early onset of accompanying symptoms. Levels of 4–5 µmol/L may occur over the course of 1–3 days. With subacute and chronic exposure symptoms may take time to develop. There is also a significant degree of individual variability in susceptibility to overt lead intoxication. The reasons for this are uncertain, but are thought to be associated with specific lead binding proteins made in response to lead exposure.[7]

It should be noted that the toxicity of inorganic lead is very different to that of organic lead (found in some petrochemicals), which causes an organic psychosis.[6]

Laboratory assessment

Elevation of zinc protoporphyrin (ZPP), in addition to serum blood lead levels, may be used as an indicator of lead toxicity. Increases in ZPP lag behind the increase in blood lead level by 2–6 weeks. Therefore, the finding of a normal ZPP with elevated levels suggests acute exposure. Elevation of ZPP may occur with lead levels as low as 1.45 µmol/L. However, the ZPP test is not 90% sensitive until blood lead levels exceed 2.41 µmol/L.[7]

Mutagenicity and teratatogenicity

Lead's reproductive toxicity is well recognised in both males and females. It is associated with sperm abnormalities and miscarriage. Carcinogenesis has been demonstrated in laboratory animals.[3] The International Agency for Research on Cancer has classified

inorganic lead in group 2A, concluding that on current evidence inorganic lead is probably carcinogenic to humans.[8]

The Center for Disease Control has established 0.48 µmol/L as the blood level of concern in children. Because lead crosses the placental barrier readily, fetal blood levels are directly proportional to maternal levels (usually 80% of the maternal level). Thus, the maternal blood level should be no greater than 0.63 µmol/L. Pregnancy and breastfeeding are both indications for workplace exclusion,[1] although lead excretion in breast milk is a less important means of transmission.

It is known that lead can exert toxic effects at levels well below 2.41µmol/L, which is the level at which a male worker must be excluded. For example, sperm morphology abnormalities and abnormal sperm counts have been demonstrated to occur at levels of 1.93 µmol/L. The reproductive effects of paternal levels below 1.9 µmol/L are unknown. This remains a significant issue and further epidemiological research is needed.[7]

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