Review Article

Lead exposure, interactions and toxicity: food for thought

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The recognition that nutritional status plays a role in altering susceptibility to lead absorption and toxicity has triggered the development of this review. There has been a significant increase worldwide in awareness and concern about the effects of lead on human health and the environment over the last two decades. Both occupational and environmental exposures to lead remain a serious problem in many developing and industrialising countries, as well as in some developed countries. Port Pirie (South Australia) has the world's largest lead smelter and the surrounding population continues to be exposed to environmental lead. The increased awareness of the detrimental impacts of 100 years of smelting at Port Pirie led in 1984 to the development of the Lead Implementation Program, run by the Environmental Health Centre (EHC), Department of Human Services (DHS). The major focus of the program is to reduce household lead exposure for pregnant women and children below the age of five years. Despite intervention efforts by all stakeholders in Port Pirie, 55% of children less than 4 years old have blood lead levels above the National Health and Medical Research Council (NH&MRC) goal of 10µg/dl. The Port Pirie Lead Implementation Program includes components on nutrition education aimed at reducing lead absorption and toxicity. However, nutritional intake and nutritional status of Port Pirie residents, in particular children under five years, has not been evaluated. This review focuses on nutrition as a component of intervention in lead toxicity and it discusses the nutritional concerns in relation to lead exposure. Fortunately most food patterns that reduce susceptibility to lead toxicity are consistent with recommendations for a healthy diet. The relationship between nutritional status and lead uptake and toxicity is most clearly established for irregular food intake (i.e. periods of fasting), marginal calcium ingestion and (subtle) iron deficiency.

Key Words: lead, toxicity, nutrition, interactions, Port Pirie, Australia

Introduction

Over the last two decades there has been a significant increase worldwide in awareness and concern about the effects of lead on human health and the environment.[1] Lead is the most abundant of the heavy metals in the Earth's crust and has become widely distributed and mobilized in the environment. The pre-industrial or natural blood lead level in humans is estimated to have been about 0.016 µg/dl, 50-200 times lower than the lowest reported levels of the southern and northern hemispheres (0.78 µg/dl and 3.20 µg/dl respectively).[2] In developed countries, where considerable efforts have been made to control lead (e.g. conversion to unleaded petrol and phasing out of lead based paints), vast reservoirs of the metal remain in the soil, dust and house paint, and these sources will continue to affect populations for many years.[2] Lead continues to be a significant public health problem in developing countries, where there are considerable variations in the sources and pathways of exposure. Awareness of the public health impact of exposure is growing, but relatively few of these countries have introduced policies and regulations for significantly combating the problem. Exposure to lead from lead mining, smelting, battery factories, leaded petrol and cottage industries is a significant environmental hazard in developing countries.[2]

In China, childhood lead poisoning may be widespread as a result of rapid industrialization and the use of leaded petrol.[2] In India, direct testing for blood lead was carried out randomly on 2031 children and adults in five cities with high population densities where leaded petrol had contributed to environmental lead levels. Approximately 51% had levels >10 µg/dl and 13 % had values >20 µg/dl.[2] The level of exposure to lead is, however, falling in some developing countries because of the reduced use of lead in petrol. In Thailand, for example, leaded petrol was phased out during the period 1984-96 and was associated with a marked decline in atmospheric lead levels in Bangkok.[2]

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Lead is a non-biodegradable, toxic metal. It remains in the soil indefinitely. Point sources such as non-ferrous smelters have a potential to remain as major sources of lead emissions.[1] Non-ferrous (lead, zinc, copper) smelters are located worldwide, usually in rural and remote locations. In many locations, populations have grown around the smelter due to employment. As a result, the risk of exposure to lead (Pb), arsenic (As), cadmium (Cd), mercury (Hg), copper (Cu) and sulphur dioxide (SO_2) from smelting operations is increased.[3,4]

There are few visible biophysical health effects of relatively low levels of lead exposure and in many cases, visible symptoms only occur at very high levels. Invisibility in many cases reduces residents' concern about lead contamination and their use of coping strategies, including health interventions.[5] Children are generally acknowledged to be among the groups at greatest risk from environmental lead exposure. Scientific research in Australia and overseas has overwhelmingly concluded that exposure to even low doses of lead can result in serious and irreversible health and behavioural problems, especially in young children.[1,2] Even low lead levels can have a detrimental effect on intellectual development. The epidemiologic evidence of the link between low-level lead exposure early in life and later deficits in intellectual and school performance is strong.[6] There is no evidence for a threshold below which lead has no adverse effects.[6,7] The precautionary principle when applied to lead exposure means that any reduction in exposure is beneficial to health.[6] Moderate lead exposure during early childhood can lead to further consequences during late childhood, pregnancy, lactation, and even late in life, and that bone lead stores can serve as a significant internal source of lead exposure throughout life.[8] Because of the persistence of lead in various environmental sources and its long skeletal half life, approximately 20 years or more for cortical bone, skeletal lead concentrations increase inevitably with age.[9] Biochemical and functional changes have been demonstrated in the heme biosynthetic pathway and in the renal, cardiovascular, endocrine, immune and nervous systems. Low level lead exposure has been associated with elevated blood pressure, renal dysfunction, and anaemia in adults.[10]

The role of nutritional status in altering susceptibility to lead toxicity has long been recognized. Several nutritional factors interact with lead in intestinal absorption, in mobilization and distribution of lead between osseous and non-osseous tissues, and in retention and excretion of lead in the body.[10-12] Dietary elements may lead to decreased absorption of ingested lead either by competing with lead for attachment to an intestinal transport protein (e.g calcium), by formation of an insoluble complex (e.g phosphorus), or by adsorption of the lead ion (e.g fibre). Dietary factors also may alter the function of an intestinal transport protein important in the absorption of lead. Finally, some dietary factors might moderate or increase the toxicity of ingested lead. Lead, for example, appears more neurotoxic to animals that are iron deficient. Fortunately most food patterns that reduce susceptibility to lead toxicity are consistent with the recommendations for a healthy diet. The public health dilemma is not how should these diets be chosen, but how to foster these food patterns.[13]

The relationship between nutritional status and lead uptake and toxicity is most clearly established for irregular food intake (i.e. periods of fasting), marginal calcium ingestion and (subtle) iron deficiency.

Other nutrients that influence lead uptake and susceptibility to lead effects are: zinc, high fat intake, vitamin D, phosphorus, various vitamins (e.g. ascorbic acid, E, niacin, B6, B12), selenium, and protein. Lead and zinc interactions are not as well defined as those between lead and calcium, and between lead and iron. Data regarding the influence of dietary fat on lead absorption and toxicity are limited to a few studies with experimental animals.[13]

Background

Port Pirie houses the world's largest lead smelter (~230,000 T/year).[3,14] The surrounding population continues to be exposed to environmental lead. Detailed chemical characterization of fugitive emissions from the smelter revealed that the blast furnace fume was significantly elevated in lead, cadmium and arsenic.[3] Exposures to fugitive material from the smelter therefore not only poses a risk in terms of lead, but also possibly for cadmium and arsenic.[3]

The Department of Human Services (DHS) established the Environmental Health Centre (EHC) in Port Pirie in 1984.[15] The major focus of the Lead Implementation Program has been to reduce household lead exposure for pregnant women and children below the age of five years. The Centre investigates the ongoing pathways of lead exposure, provides community education on minimizing exposure and monitors exposure by providing free routine blood lead testing for pregnant women and young children. Several strategies have been implemented from 1984 to 1994 such as: measurement of blood lead in 0-4 year olds and in pregnant women with compliance levels greater than 90%, personal exposure evaluation, environmental monitoring including testing and analysis of dusts, soils, paints and rainwater samples, abatement of approximately 2200 domestic residences, demolition of properties unsuitable for abatement, treatment of institutions frequented by young children, soil stabilization and general city greening, footpath sealing, family support and counselling and community education.

In July 1994, a new program commenced with the goal of further reducing children's lead exposure towards the revised NH&MRC action guidelines "to achieve for all Australians a blood lead level below 10 µg/dl".[15] Despite intervention efforts by all stakeholders in Port Pirie, 55% of children less than 4 years old had blood lead levels above the National Health and Medical Research Council (NH&MRC) goal of 10µg/dl in 2001.[14] This is of concern in view of recent international findings that report adverse effects of lead at levels as low as 5µg/dl.[16] The Port Pirie Lead Implementation Program includes components on nutrition education aimed at reducing lead absorption and toxicity. However, nutritional intake and nutritional status of Port Pirie residents, in particular children under five years, has not been evaluated. In a study done by Baghurst *et al.,* between May 1979 and

May 1982 the relationship between blood lead concentrations of pregnant women and various factors including dietary factors were reported.[17] No studies have been done more recently into nutritional intake and nutritional status of pregnant women. Evaluation and improvement of the nutritional intake of children under five years and pregnant women is recommended and may assist in further reduction of blood lead levels.

There is a large body of evidence that shows the interactions between lead and various nutrients. However, it was beyond the scope of this review to study the interactions between lead, cadmium and arsenic. A brief literature review shows that cadmium interacts with the metabolism of zinc, iron, calcium and copper. Arsenic uptake and toxicity may be influenced by phosphate, selenium, a low protein diet and dietary antioxidants (e.g. vitamin A).[18] Most of these nutrients have been mentioned to influence lead absorption and toxicity; hence a healthy eating pattern may also have a positive influence on cadmium and arsenic toxicity.

The relationship between nutritional status, lead absorption and lead toxicity

Irregular food intake

Overall patterns and frequency of food intake influence the absorption of lead from the gastrointestinal tract. Lead ingested during fasting is absorbed at a much higher rate than lead ingested with a regular food intake.[11-13,19] This phenomenon occurs because food contains a large number of lead chelators (phytates and fibers) and inorganic anions (phosphates) that precipitate lead out of solution.[20] For example, Mahaffey reported the findings by Rabinowitz *et al*., showing that among adult male subjects, lead ingested without food was 35 % absorbed whereas trace amounts of lead ingested with food were 8.2 % absorbed.[12] There are no data available for children as to whether fasting does or does not increase lead absorption. It is likely that this result in adults can be extrapolated to children. It may be that children have increased lead absorption following even shorter fasting times than adults because of more rapid gastric emptying times. The fasting and non-fasting retention of lead is likely to be even more important in children because of more rapid gastric emptying times.[13] Optimal meal timing in lead exposed infants and toddlers should include breakfast on rising and regular meals and snacks throughout the course of the day.

Calcium

Extensive data indicate that dietary calcium intake and nutritional status of calcium influence susceptibility to lead toxicity.[9-11,13,20] Lead and calcium interactions are probably the most studied nutritional factors affecting lead toxicity, both clinically and experimentally. Diets low in calcium increase lead absorption and toxicity.[12,21,22] Calcium inhibits the absorption of lead in mammals by binding to and displacing lead from common mucosal carriers in the intestinal tract. The effect of this dietary factor is probably short-lived, because it must be present with the lead as it passes through the absorptive areas of the intestinal tract.[20] The toxic effects of lead are related to blood lead concentrations and in turn to soft tissue concentrations. Low dietary calcium increases the concentration of lead in critical organs. More recently, Goyer reported the findings by Bogden *et al.,* showing an inverse relationship between brain lead and dietary calcium, confirming that nutritional deficiency of calcium not only elevates blood lead concentrations but also increases lead in the critical organs for toxicity in infants and young children.[23] Calcium concentrations of the blood as well as calcium intake have been inversely related to blood lead levels in both normal and lead-burdened children. Calcium deficiency mobilizes lead from the bone and distributes it to blood and soft tissue.[24] Lead-induced impairment of hematopoiesis and changes in renal histology were much greater on the low-calcium diets. It is still not clear to what extent the rise in non-osseous tissue lead concentrations reflect greater absorption of lead from the gastrointestinal tract, reduced bone formation or mobilization of lead as skeletal mineral is resorbed.[13] Lead can be remobilised from the bone during conditions of high calcium demand, such as pregnancy, lactation, menopause, and osteoporosis. Administration of calcium may displace lead from non-osseous tissue to bone, thereby reducing neurotoxic effects. Studies on the effect of a dietary excess of calcium on lead toxicity indicate that a small decrease in lead absorption and blood concentration can be achieved; however, this effect is not as dramatic as the effect of calcium insufficiency on lead uptake and retention.[18] Therefore the achievement of adequate rather than excessive dietary calcium seems to be more useful in combating lead intoxication.

Mahaffey *et al.*, reviewed the relationship between blood lead concentrations and dietary calcium intake in 3000 children examined as part of the second National Health and Nutrition Examination Survey (NHANES 2). A significant and independent inverse association was observed between dietary calcium intake, estimated from dietary recall data, and blood lead concentrations.[25] The importance of adequate dietary calcium in the prevention of childhood lead toxicity is now well accepted and children at risk are provided calcium supplements in state and city lead-prevention programs in the United States. The Centre for Disease Control guideline for the prevention of childhood lead poisoning recommends adequate dietary calcium (and iron) as measures to prevent lead toxicity.[23]

An increase in dietary calcium may have some potential drawbacks. Calcium is known to decrease iron and zinc absorption so it will be important to include adequate amounts of these key nutrients in the diet, especially since it may also reduce gastrointestinal absorption of lead. Another concern is that an increase in dietary calcium may enhance hypercalciuria and promote the development of kidney stones. Intakes consistently above 2000 mg/day may be detrimental and are not recommended.[9]

Iron deficiency

Iron deficiency as well as inadequate dietary intake of iron may increase absorption, tissue concentrations of lead and thus susceptibility to lead toxicity at the cellular level. Iron prevents the accumulation of body burden of

lead rather than stimulating excretion of lead.[26] Iron deficiency has been shown in experimental animals to increase lead absorption from the intestinal tract, but attempts to demonstrate this relationship in humans have not been consistent. Some investigators find increased lead absorption in at least half of the iron deficient subjects, while other groups report no change from normal subjects.[12,23] Because lead and iron compete for critical binding sites, iron deficiency results in increased vulnerability to lead toxicity, and the presence of lead can exacerbate iron deficiency.[11] Unlike calcium deficiency, iron deficiency in rats appeared not to result in a redistribution of lead to non-osseous tissues.

Iron deficiency and lead poisoning frequently coexist, and both negatively effect neurocognitive development. Evidence suggests that the toxic effects of lead are enhanced in the iron-deficient state.[20] The relationship between iron deficiency and the impaired cognitive and behavioural development seen in children with excess lead exposure is complex in that iron deficiency in itself may impair early mental development.[23] The severity of iron deficiency or lead exposure, as well as the timing of these conditions, can be expected to greatly influence the extent of the cognitive deficit. Iron deficiency is recognized world wide as one of the most prevalent nutritional problems. An inadequate amount of iron in the diet is the most common cause of anaemia in U.S. children, although there are other causes not related to nutrition.[27] Both iron deficiency and lead poisoning disproportionately affect children younger than 5 years and those of lower socio-economic status.[28] Iron deficiency is most prevalent during the first 2 years of life when the infant brain is still developing. Severe iron deficiency anaemia during this period may cause permanent neurologic damage.[27] In contrast to the admittedly limited understanding of the interaction of lead and iron in cognitive deficits, the effect of lead and iron on the heme biosynthetic pathways have been well characterised biochemically.[12, 13]

Iron deficiency should be considered in any child with an elevated blood lead level.[20] All children with elevated blood lead (>20 µg/dl; in Australia the NH&MRC recommendations are >15 µg/dl) should be evaluated for iron deficiency. Elevated erythrocyte protoporphyrin (>35 µg/dl) is a good indicator of iron deficiency in children older than 12 months of age with blood lead <20 µg/dl.[20] Alternatively, other measures of iron status, such as serum ferritin or transferrin saturation, could be obtained to assess iron status. Low ferritin is a highly sensitive and specific indicator of iron deficiency with or without anaemia. If ferritin levels are depleted, later signs of iron deficiency may develop, including low hematocrit, haemoglobin, and mean corpuscular volume (iron deficiency – ferritin cut off value ≤ 12ng/ml). Children with low ferritin levels, regardless of the level of environmental contamination, have higher lead levels than those with normal ferritin levels. In a study done by Bradman *et al*., the iron deficient children averaged 1-2 µg/dl higher blood lead than children with adequate iron status, with as high as 3 µg/dl difference for children in the most contaminated environments.[29] These results suggest that inadequate iron status may amplify the effect of lead contamination in the environment by increasing absorption and possibly retention of lead in the body and/ or increasing hand to mouth or pica behaviour and thus lead ingestion (literature reports show low iron levels can lead to pica which may include soil consumption). This finding is consistent with several studies that have reported higher proportions of children with elevated blood lead among those with low iron levels. Yip and Dallmann found that the correlation of iron deficiency and blood lead was strongest among the youngest children (1-2 years), weaker in older children, and not significant in adults.[29]

Most studies of Port Pirie residents did not investigate iron status. Data is lacking for South Australia and Port Pirie in particular on the prevalence of iron deficiency anaemia in the very young child. Health of rural Australians compares poorly relative to city dwellers, therefore it is expected that iron deficiency is likely to be higher in Port Pirie than the rest of the population. In Australia population screening has been done on populations at risk. In the Aboriginal population in the Northern Territory, about 47-56% of the 0 – 5 year olds were found to have anaemia (defined by finger prick haemoglobin of less than 110 g/L). In Sydney school children iron deficiency occurred in 2.8 % with 1.1% being anaemic.

The outcome of iron deficiency may be two fold – it may compound the lead exposure problem (it may increase absorption, tissue concentrations of lead) and it leads to impairment of neurocognitive development. One could postulate that iron-deficiency compounds the problem of lead toxicity.

Because iron deficiency has independent effects on cognitive functioning in children that are similar to those of lead poisoning, there should be important prophylactic benefits for children's health and development if organized intensive iron deficiency screening, nutritional counselling, and supplementation were implemented in areas where children are at high risk of both conditions.[29] It would appear prudent to ensure a diet meeting the recommended daily intake for iron. The role of iron supplementation in the prevention of lead poisoning, however, remains a controversial issue. The effect of iron status and iron supplementation on radio labelled lead retention in humans is controversial. Given the knowledge that iron deficiency is a common nutritional problem in the same children who are at risk of lead toxicity, it is general practice in the United States to supplement these children with iron as well as calcium. Children may require iron supplements if their eating patterns do not provide enough iron in food.

Zinc

Lead and zinc interactions are not as well defined as those between lead and calcium, and between lead and iron. It has been shown experimentally that lead increases zinc excretion and that zinc deficiency enhances lead absorption.[23] Zinc deficiency is known to increase tissue lead levels in animals exposed to equal doses of lead. Further, zinc at the cellular level protects some enzymes required for heme synthesis against the effects of lead.[26] Zinc influences both tissue accumulation of lead and

susceptibility to lead toxicity.[18] Studies show that as dietary zinc increases, lead absorption and its subsequent toxicity decrease, indicating that zinc exerts its effect on lead in the gastrointestinal tract. It would appear prudent to ensure a diet meeting the recommended daily intake for zinc.[26]

Total fat intake

Although the influence of dietary fat level as a determinant of the fraction of lead absorbed has provoked a number of inquiries, data on this topic are limited to a few studies with experimental animals.[13] Mahaffey reported the findings by Barltrop and Khoo that lead absorption is dependent upon the quantity and type of dietary fat. By comparison with the degree of documentation of the effects of other nutrients (e.g. calcium and iron), the role of dietary fat remains poorly established.[13] Another study by Barltrop and Khoo have demonstrated in rats that high fat diets facilitate lead absorption and increase tissue lead concentrations.[26] Reducing the dietary fat level to nearly zero did not reduce lead concentrations in tissues. It is very difficult to translate this data to humans on a quantitative basis because rats normally consume a diet much lower in fat than humans.[26] A study by Bell and Spickett showed that rats receiving 11.5 % and 20% of energy as fat had similar levels of tissue lead, increasing the fat level to 40% and 60% of energy resulted in significant increases in tissue lead concentrations. The groups receiving 60% of energy as fat had more than twice the level of lead in femur, kidney, liver and brain compared to the control rats fed 11.5 % energy as fat, even though they ingested the same amounts of lead.[30]

Adequate amounts of fat are essential to health. Fat in foods not only supplies energy and essential fatty acids but it is also a vehicle for fat soluble vitamins (vitamin A,D,E and K). The World Health Organization (WHO) recommends that women of reproductive age should consume at least 20% of their energy needs as fat and dietary fat should supply at least 30% - 40% energy in children up to 2 years.

For 2-5 year olds the 1995 version of the NH&MRC's *Australian dietary guidelines for children and adolescents* recommended 35% - 40% of energy from fat, but the more recent draft version of these guidelines has revised this to 30% energy. Low fat diets are not suitable for young children. For older children, a diet low in fat, in particular saturated fat, is appropriate.[31]

The National Nutrition Survey which was conducted in 1995 in conjunction with the 1995 National Health Survey was the first truly national dietary survey conducted in Australia since 1944 and provides detailed intake data for individuals aged two years and over. The 1995 National Nutrition survey showed that the contribution of total fat remained constant at about 33% energy for children in all age groups.[32]

Vitamin D

Lead affects the activity of 1,25 vitamin D hydroxylase at extremely low concentrations and through this mechanism can have profound effects on bone metabolism and growth.[11] Rosen *et al*., have observed that lead burdened children have reduced ability to form the active metabolite of vitamin D, even though their dietary intake of vitamin D was normal, as shown by serum levels of 25-hydroxycholecalciferol.[26] Epidemiological studies have consistently found that lower dietary intake of vitamin D and lower serum vitamin D levels were associated with higher blood lead levels in children. Vitamin D may be involved in increased intestinal absorption of lead.[10,18] When calcium levels are low, serum levels of the vitamin D hormone, 1,25 –dihydroxy-vitamin D, are elevated to stimulate intestinal absorption of calcium and synthesis of calbindin-D, a calcium-binding protein.[18] Vitamin D may primarily modify bone metabolism (while vitamin C and iron may act primarily to modify excretion of lead from the chelatable bone pool or that bound in red blood cells, and thus are most closely related to blood lead, rather than bone lead).[10]

Phosphorus

Lead uptake occurs at the same site as phosphate. Low dietary phosphate has been shown to enhance lead retention in rats, increasing lead uptake by a factor of nearly three. Small studies of radio labelled lead absorption in human adults confirm findings of animal studies. Phosphorus inhibits lead absorption probably through binding of lead in the small intestine to form an insoluble complex. The effect of this dietary factor is probably short-lived, because it must be present with the lead as it passes through the absorptive areas of the intestinal tract.[20] Western-type diets are usually quite high in phosphorus so that no special attention is required to maintain an adequate intake of this nutrient.[26] Calcium reduced lead absorption more than equal weights of phosphorus. Calcium and phosphorus together reduced absorption considerably more than either calcium or phosphorus alone.[20]

Ascorbic acid

Some animal studies suggest that orally administered ascorbic acid may chelate lead and decrease the risk of the toxic effects of lead. However, results from several small studies in humans have yielded inconclusive evidence of a beneficial effect of ascorbic acid on lead toxicity. Ascorbic acid level was inversely related to blood lead level among adults and youths enrolled in the third National Health and Nutrition Examination Survey (NHANES 3). Each 10 mg increment in dietary ascorbic acid intake was associated with a 3.5% decrease in the prevalence of elevated blood lead level. This result indicates that serum ascorbic acid level is an important independent correlate of blood lead level among Americans. To the authors' knowledge, this report is the first population-based study to establish such an association. If a causal relationship is confirmed, higher intakes of ascorbic acid may have public health implications for the prevention of lead toxicity.[33] A study done by Cheng *et al*., suggests that lower dietary intake of vitamin C enhances the absorption and retention of lead in the body.[10] Vitamin D may primarily modify bone metabolism, while vitamin C and iron may act primarily to modify excretion of lead from the chelatable bone pool or

that bound in red blood cells, and thus are most closely related to blood lead rather than bone lead.[10]

Selenium

Animal experiments have demonstrated that selenium can partly reduce toxic effects of lead, such as nephrotoxicity and neurotoxicity.[34] The impact of selenium on blood-lead absorption is not widely studied.

Vitamin E

Vitamin E deficiency greatly increased the susceptibility of rats to lead toxicity, particularly increasing red blood cell fragility and severity of lead-induced anaemia. In humans, vitamin E deficiency is not considered prevalent in the paediatric population. However, very few dietary surveys have attempted to establish vitamin E status in children, so that complete clinical evaluation of this interaction cannot be made at this time.[26]

Protein

Studies with experimental animals have shown that low or high protein diets increase the severity of effects of lead exposure. Some amino acids facilitate lead absorption which might explain the increased effects of lead that occur when a high protein diet is fed.[26]

Niacin, B6 and B12

In the production of the haemoglobin molecule, the human body produces a series of chemical intermediaries or building blocks. The presence of lead adversely effects the production of haemoglobin at some of these intermediaries, but the administration of niacin can help prevent lead from doing this. Two other vitamins, B6 and B12 also protect the haemoglobin assembly line from lead.

Lead mobilization during pregnancy

Mobilization of long-term stores of lead from the maternal skeleton may be a major determinant in transfer of lead from mother to infant during pregnancy and lactation. Studies from several countries including Australia, Sweden, France, and Mexico in women with lead exposure ranging from low to high generally support the concept that blood lead increases during pregnancy. Based on isotopic studies, Gulson *et al*., estimated that approximately 31% (range: 13-65%) of the rise in blood lead concentrations during pregnancy was from skeletal stores of lead. Lead in endogenous sources, especially the maternal skeleton, can be mobilized during pregnancy and even more so during the post-pregnancy period. Ratios of breast milk lead levels to maternal blood lead concentrations approximated those of plasma. Where maternal blood lead levels are significantly elevated, lead in breast milk rises proportionately. Increased mobilization of skeletal lead is consistent with increased bone resorption, and may be associated with an inadequate calcium intake. Calcium supplementation may be an important means of limiting fetal exposure to lead.[35] As the women's age increased, there was a steeper increase in blood lead as pregnancy progressed through the last trimester. The lower the maternal calcium intake the more likely the maternal skeleton becomes an important source of calcium, and thus lead, for the fetus. The findings of Hertz-Picciotto *et al*., suggest that relatively high intakes of calcium (>2000 mg/day; the upper level for calcium is 2500 mg/day for all adults) may be needed to obtain the maximum blunting of the rise in blood lead during pregnancy.[36] Fetal lead exposure can come from the maternal stores (skeletal) and/or maternal environment and diet. Lead readily crosses the placenta.[37] Because of concern that maternal blood lead concentrations be maintained as low as possible during pregnancy, this remobilisation of lead from bone has substantial public health interest. In a study done by Baghurst *et al*., between May 1979 and May 1982 for example a low socio-economic status and low dietary intake of calcium were factors that were associated with a higher blood lead concentration.[17] With regard to dietary calcium, the total daily calcium intake as estimated from a dietary questionnaire was high (1010 mg/day). The mean blood lead concentration among approximately 13% of the women who reported an intake of less than 500mg calcium per day was 1.2 µg/dl higher than that of women who consumed larger amounts. Lower blood lead concentrations were observed in women who took iron and folic acid to supplement their diet.[17]

Nutritional status surveys

Mahaffey and Michaelson summarized three national nutritional status surveys for infants and young children. Iron deficiency was the most prevalent nutritional problem in children under 2 years of age, particularly those from low-income groups. Other common nutritional deficiencies in low-income groups included zinc, vitamins A and C, and calcium.[11]

The 1997 US dietary reference intakes (DRIs) for calcium are 800-1300 mg/day for the various age and gender subgroups above 3 years of age. Dietary intakes of calcium for most Americans fall well below the DRIs. Both animal and human studies suggest that current intakes of calcium are not high enough to achieve maximum beneficial effect on lead absorption and toxicity. A recent study of more than 20.000 adults showed that despite attempts to promote increased consumption of dairy foods, the calcium intake of the US population decreased by 5.1% between 1987 and 1992. Thus, the US population is unlikely to achieve intakes that approach the 1997 DRIs without food fortification.[9]

In Australia population screening has been done on populations at risk. In the Aboriginal population in the Northern Territory, about 47-56% of the 0 – 5 year olds were found to have anaemia (defined by finger prick haemoglobin of less than 110 g/L). In Sydney school children iron deficiency occurred in 2.8 % with 1.1% being anaemic.

The National Nutrition Survey which was conducted in 1995 in conjunction with the 1995 National Health Survey and provides detailed intake data for individuals aged two years and over. Below follows an overview of the intake data for specific nutrients mentioned to influence absorption and toxicity of lead, particularly focusing on the group below 5 years of age:

- Australians' mean nutrient intake from food and beverages was very close to, or exceeded the RDIs for most vitamins and minerals in all age groups.
- The exception was calcium for females in most age groups except those aged 2-3 years. Less than 75% of males and less than 50% of females had a calcium intake which exceeded the RDI.
- The contribution of total fat to energy intake remained constant at about 33% for children in all age groups.
- Approximately 30% of 2-3 year olds ate seven or more times per day, and this proportion decreased with age. Over 90% of children usually ate breakfast five or more times per week.
- Macronutrients: young children aged 2-3 years generally had the lowest median intake.
- Protein contributed about 14% for children under 15 years.
- Two to three year olds had the highest intakes of calcium and pro-vitamin A per 1,000 kJ of energy, because of their high intake of milk and milk products.
- Ninety percent of Australians in most age by sex groups exceeded the RDI for protein, thiamin, niacin equivalents and vitamin C. For phosphorous, riboflavin and potassium, more than 75% of Australians of most ages exceeded the RDI.
- Zinc - intakes were less than the RDI for most people except young children.

In summary the 1995 National Nutrition Survey intake data show that:

- calcium intake for females in most age groups, except those aged 2-3 years, are below the RDIs;
- the National Nutrition Survey summary did not reveal results on iron intake for the group below 5 years of age;
- ninety percent of children usually ate breakfast five or more times per week;
- total fat intake generally meets the RDIs;[32]
- nutrient intake data for particular subgroups of the population such as the lower socio-economic groups do not appear in the survey results. Particular subgroups, such as low income groups and Aboriginal and Torres Strait Islander people are at higher risk of a poor nutritional status and iron-deficiency.

The Australian Bureau of Statistics developed Socio-economic Indexes for Areas (SEIFA) from the 1996 Population Census data. The SEIFA summarize a large number of socio-economic variables into a single measure that can be used to rank areas on a broad socio-economic scale. Relatively disadvantaged areas have a low SEIFA. The index was designed to have an average across all Australia of 1,000. The Index of Relative Disadvantage for the Mid North region was 932, below the South Australian figure of 984. The index of Relative Disadvantage for Port Pirie city was 881. In 1998, 9,164 or 76.32% of people in the postcode area of 5540 (Port Pirie) were recipient of a pension or benefit.

Role of nutrient supplements in lead toxicity

Studies on the effect of a dietary excess of calcium on lead toxicity indicate that a small decrease in lead absorption and blood concentration can be achieved; however, this effect is not as dramatic as the effect of calcium insufficiency on lead uptake and retention. An adequate rather than excessive dietary calcium intake seems to be more useful in combating lead toxicity.[18]

It would appear prudent to ensure a diet meeting the recommended daily intake for iron. The role of iron supplementation in the prevention of lead poisoning, however, remains a controversial issue.[19] Children may require iron supplements if their eating patterns do not provide enough iron in food.

Conclusions

An adequate intake of the nutrients as mentioned in this review, is highly recommended as a component of intervention in lead toxicity. The nutritional advice is consistent with the healthy eating guidelines.

Iron deficiency is recognized world wide as one of the most prevalent nutritional problems.[27] Both iron deficiency and lead poisoning disproportionately affect children younger than 5 years and those of lower socio-economic status. Calcium intake for females in most age groups, except those aged 2-3 years, in the 1995 National Nutrition Survey were below the RDIs.

Low income populations are at greatest risk of marginal nutritional status which increases their susceptibility to lead toxicity. Since Port Pirie is regarded as a relatively disadvantaged area, one could expect the population to be more nutritionally deprived and therefore more susceptible to lead poisoning. Nutritional intake and nutritional status of Port Pirie residents, in particular children under five years, has not been evaluated. Further research into the nutritional intake and nutritional status (in particular calcium and iron) of Port Pirie residents, most vulnerable to lead toxicity such as children under 5 years of age and pregnant women, is recommended.

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