Calcium

Calcium intake can be assessed by taking a dietary history and comparing intake against national recommended values *(195)*. As the optimal dose for mitigating the effect of lead exposure is unknown, the guideline development group decided to refer to recommended daily intake values. It is recognized that calcium requirements may be different in different dietary cultures; therefore, national guidelines should be used when possible *(195)*. When determining a dosage for a pregnant or lactating woman, health-care providers should consider the woman's calcium intake from other sources, such as medications (e.g. antacids) *(211)*.

While the evidence supported use of calcium supplements, calcium intake can also be improved by increasing the amount of calcium-rich foods in the diet, use of fortified foods or traditional supplements such as dried fish. As calcium supplements may be manufactured from natural sources such as animal bone, they may be contaminated with lead, and care should be taken in sourcing products *(214, 215)*.

Vitamin D is important for calcium absorption and homeostasis; therefore, it is also necessary to maintain an adequate vitamin D intake. In the case of pregnant women, WHO does not recommend routine vitamin D supplementation, and women should be advised that sunlight is the most important source of vitamin D *(216)*. If vitamin D deficiency is suspected, vitamin D supplements may be given at the current recommended nutrient intake of 200 IU (5 µg) per day *(216)*.

In children, it is suggested that dietary calcium intake be re-assessed after 3 months. If it is still inadequate and the blood lead concentration remains elevated, consideration should be given to a further period of supplementation. If necessary, the source of lead exposure should be investigated further.

In pregnant women, calcium should be given for the duration of pregnancy and consideration given to extending supplementation into lactation.

Iron

Iron deficiency can be determined by estimating the serum ferritin concentration and a marker of inflammation (e.g. C-reactive protein or a1-acid glycoprotein) *(217)*. If serum ferritin cannot be measured, evaluation of anaemia is a non-specific marker of iron deficiency. Note that anaemia may also be a feature of lead toxicity.

The optimal dose and duration of iron supplementation for mitigating the effects of lead exposure are unknown; therefore, reference should be made to WHO guidance for treating iron deficiency *(196, 197)*, which recommends a minimum treatment duration of 3 months, after which the iron status should be re-assessed to evaluate continuation *(197)*. In malaria-endemic areas, iron supplementation may be harmful to children who do not have regular access to malaria surveillance and treatment services *(196)*. Children with malaria may, however, be more susceptible to the neurotoxic effects of lead when they are exposed to high levels *(111)*. These two considerations should be taken into account when deciding on iron supplementation.

Inclusion of vitamin C will improve iron absorption from the diet and from iron supplements *(195)*.

7.3 Chelation therapy in individuals exposed to lead

7.3.1 Introduction

Chelating agents are pharmaceuticals that, by physicochemical means, bind to lead and other trace elements and facilitate their excretion from the body *(218)*. The aim of chelation therapy is to facilitate renal excretion, thereby decreasing the lead body burden and, potentially, resolving toxic effects and improving clinical outcomes by decreasing the availability of lead for binding at its sites of action. Four chelating agents were reviewed: dimercaprol, penicillamine, sodium calcium edetate and succimer *(10–13)*. In evaluating the efficacy of chelation therapy, the following critical and important outcomes were considered:

Critical outcomes

- blood lead concentration;
- neurological (cognitive, neurobehavioural and neuromotor) effects of lead poisoning measured in standardized, validated tests;
- mortality;
- symptoms and signs of lead poisoning, e.g. abdominal colic and encephalopathy; and
- long-term health outcomes that may be affected by lead exposure, such as cardiovascular and renal effects.

Important outcomes

- urinary excretion of lead,
- mobilization of lead from bone and
- adverse events associated with chelation therapy.

In view of the importance of preventing the harmful effects of lead in children without overt lead poisoning, studies in children with blood lead concentrations < 45 µg/dL were analysed separately for the outcomes for which data were available.

The evidence review found very few randomized or non-randomized controlled studies, and most of the data found were from retrospective or prospective case series. The latter studies did not include control for the confounding effect of removal from lead exposure, which is an essential aspect of management. This made it difficult to differentiate the impacts of chelation and of removal from exposure on the studied outcomes. The certainty of the evidence for most outcomes was therefore very low.

The only blinded, randomized, placebo-controlled trial of chelation was the treatment of lead-exposed children (TLC) Trial, conducted with children with blood lead concentrations < 45 µg/dL treated with succimer.