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Review

# Nutritional aspects of manganese homeostasis

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**Abstract**

Manganese (Mn) is an essential mineral. It is present in virtually all diets at low concentrations. The principal route of intake for Mn is via food consumption, but in occupational cohorts, inhalation exposure may also occur (this subject will not be dealt with in this review). Humans maintain stable tissue levels of Mn. This is achieved via tight homeostatic control of both absorption and excretion. Nevertheless, it is well established that exposure to high oral, parenteral or ambient air concentrations of Mn can result in elevations in tissue Mn levels. Excessive Mn accumulation in the central nervous system (CNS) is an established clinical entity, referred to as manganism. It resembles idiopathic Parkinson's disease (IPD) in its clinical features, resulting in adverse neurological effects both in laboratory animals and humans. This review focuses on an area that to date has received little consideration, namely the potential exposure of parenterally fed neonates to exceedingly high Mn concentrations in parenteral nutrition solutions, potentially increasing their risk for Mn-induced adverse health sequelae. The review will consider (1) the essentiality of Mn; (2) the concentration ranges, means and variation of Mn in various foods and infant formulas; (3) the absorption, distribution, and elimination of Mn after oral exposure and (4) the factors that raise a theoretical concern that neonates receiving total parenteral nutrition (TPN) are exposed to excessive dietary Mn.


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*Abbreviations:* CNS, central nervous system; DMT-1, divalent metal transporter 1; EAR, estimated average requirement; ESAADI, estimated safe and adequate dietary intake; IPD, idiopathic Parkinson's disease; Mn-SOD, Mn superoxide dismutase; NAS, National Academy of Sciences; NIEHS, National Institute of Environmental Health and Safety; NRC, National Research Council; RDA, recommended dietary allowance; ROS, reactive oxygen species; TPN, total parenteral nutrition; Tf, transferrin

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## 1. The essentiality of manganese

Manganese (Mn) is an essential trace metal that is found in all tissues and is required for normal amino acid, lipid, protein, and carbohydrate metabolism. Mn-dependent enzyme families include oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases. Manganese metalloenzymes include arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase, and Mn superoxide dismutase (Mn-SOD). Mn is involved in the function of numerous organ systems. It is needed for normal immune function, regulation of blood sugar and cellular energy, reproduction, digestion, bone growth, and it aids in defense mechanisms against free radicals. Mn in concert with vitamin K supports blood clotting and hemostasis.

No formal recommended dietary allowance (RDA) for Mn has been established, but the US National Research Council (NRC) has established an estimated safe and adequate dietary intake (ESADDI) of 2–5 mg/day for adults (Greger, 1998). Factors that influence the daily Mn requirement have been recently reviewed (National Academy of Sciences, 2001), and some of these factors will be detailed below in Section 2. The National Academy of Sciences (2001) has established an adequate intake (AI) for Mn. AI is defined as a nutrient consumption value that is experimentally derived or is an approximation of an observed mean nutrient intake for a group of apparently healthy individuals. An AI is established when there is not sufficient scientific evidence to calculate an estimated average requirement (EAR). The EAR is the daily intake value that is estimated to meet the nutritional requirement, as defined by a specific indicator of adequacy, in one-half of the apparently healthy individuals in a life stage or gender group. The AI replaces the ESADDI. The Mn AI for adult men and women is 2.3 and 1.8 mg/day, respectively (National Academy of