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Biomarkers of manganese intoxication

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Abstract
Manganese (Mn), upon absorption, is primarily sequestered in tissue and intracellular compartments. For this reason, blood Mn concentration does not always accurately reflect Mn concentration in the targeted tissue, particularly in the brain. The discrepancy between Mn concentrations in tissue or intracellular components means that blood Mn is a poor biomarker of Mn exposure or toxicity under many conditions and that other biomarkers must be established. For group comparisons of active workers, blood Mn has some utility for distinguishing exposed from unexposed subjects, although the large variability in mean values renders it insensitive for discriminating one individual from the rest of the study population. Mn exposure is known to alter iron (Fe) homeostasis. The Mn/Fe ratio (MIR) in plasma or erythrocytes reflects not only steady-state concentrations of Mn or Fe in tested individuals, but also a biological response (altered Fe homeostasis) to Mn exposure. Recent human studies support the potential value for using MIR to distinguish individuals with Mn exposure. Additionally, magnetic resonance imaging (MRI), in combination with noninvasive assessment of γ-aminobutyric acid (GABA) by magnetic resonance spectroscopy (MRS), provides convincing evidence of Mn exposure, even without clinical symptoms of Mn intoxication. For subjects with long-term, low-dose Mn exposure or for those exposed in the past but not the present, neither blood Mnn or MRI provides a confident distinction for Mn exposure or intoxication. While plasma or erythrocyte MIR is more likely a sensitive measure, the cut-off values for MIR among the general population need to be further tested and established. Considering the large accumulation of Mn in bone, developing an X-ray fluorescence spectroscopy or neutron-based spectroscopy method may create yet another novel non-invasive tool for assessing Mn exposure and toxicity.

Keywords: Manganese, Biomarker, Iron, Mn/Fe ratio or MIR, GABA, Magnetic resonance imaging or MRI, Magnetic resonance spectroscopy or MRS, Positron emission tomography or PET, Oxidative stress