Dimercaptosuccinic acid (DMSA): negligible effect on manganese in urine and blood

Editor—Chelation treatment of chronic manganese (Mn) intoxication is problematic because of the limited effect on Mn in blood (B_Mn) and urine (U_Mn), the inconsistent association of B_Mn and U_Mn with intoxication, and most relevantly because neurotoxicity persists after clearance of Mn from the brain and lung. Calcium disodium versenate (EDTA) has a significant effect on U_Mn but a minimal effect on clinical symptoms. In the absence of information on the response to oral dimercaptosuccinic acid (DMSA), the response of B_Mn and U_Mn to DMSA treatment was tested in two men with occupational exposures to Mn.

Subject number 1 was a 49 year old machine operator with 19 years exposure to Mn dust and fumes from the ambient air of a shop for the cutting, gouging, and welding with 18% Mn alloy rods, and reassembly of railway track connectors (frogs) of 11%-15% Mn alloy steel. His exposure ended one month before the DMSA treatment began. His pattern of cognitive and autonomic dysfunction was similar to that of his coworkers that included an index case of manganese poisoning and was associated with increased B_Mn and U_Mn in response to EDTA (2 g intravenously) > 10 μg/dl. Informed consent was given for DMSA treatment.

Subject number 2 was a 56 year old iron worker with 30 years experience of welding, cutting, and brazing mild steel (1%-2% Mn alloy) that included recently three months work on overhead equipment in a lead smelter. He had a cognitive and autonomic dysfunction profile similar to that of the Mn workers and increased U_Mn and U_Mn provoked by EDTA. The increased lead burden was considered to be the primary indication for DMSA treatment.

Both men were treated orally with 1 g/m²/day of DMSA (25 mg/kg/day; three doses/day) for seven days followed by 0.67 g/m²/day (15 mg/kg/day; two doses/day) for 14 days with appropriate monitoring.

The B_Mn (reference range 0.4-0.85 ng/ml, 7.2-15.5 mmol/l; Mayo Clinic Laboratory) before, on day 6, and at six days after treatment was unchanged in both subjects (1.1-1.1; 0.7 ng/ml in subject 1; 0.8-1.1; 0.9 ng/ml in subject 2). The U_Mn (reference range < 0.3 μg/dl, 5.4 nmol/dl; Mayo Clinic Laboratory) increased on day 6 only in subject 1 (fig 1).

The U_Mn response to EDTA (2 g intravenously over 30 min) decreased from 25 μg/dl before DMSA to 18.7 μg/dl after treatment (455 to 340 nmol/day) in subject 1 and from a mean of 34.5 μg/dl (628 mmol/day) before DMSA to 14.8 μg/dl (269 nmol/day) six days after treatment in subject 2 (fig 2).

No subjective benefits were reported; adverse effects were limited to complaints dysuria in subject 1. In subject 2, who had also been exposed to lead, the U_Pb provoked by DMSA decreased from 228 μg/dl (1100 nmol/day) before DMSA to 68 μg/dl (328 nmol/day) after treatment.

There is little information on the response of U_Mn to an EDTA challenge. Whitlock et al reported U_Mn to increase from < 5 μg/l to 100 and 950 μg/l after EDTA (2 g intra- venously) was given to two workers with advanced Mn intoxication. Cook et al reported U_Mn to increase from 1–2 μg/l to 7–44 μg/l on day 1 of EDTA (1 g/day) in five Mn process workers; in two control subjects, U_Mn increased from 1–3 μg/l to 10–23 μg/l. Smyth et al reported that average U_Mn, increased from < 10 μg/l to approximately 30 μg/l in five workers with Mn intoxication who had unproven, spot U_Mn, < 6 μg/l. Information defining the U_Mn response to DMSA in controls and Mn workers is not available.

Although DMSA might provide an oral challenge test of chelatable Mn, the negligible responses of B_Mn and U_Mn do not encourage trials of DMSA in Mn poisoning.