# CORRESPONDENCE

## 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.[1-3] 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[4] and was associated with increased $B_{Mn}$ and $U_{Mn}$ in response to EDTA (2 g intravenously) > 10 μg/day. 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 $U_{Pb}$ provoked by EDTA. The increased lead burden was considered to be the primary indication for DMSA treatment.

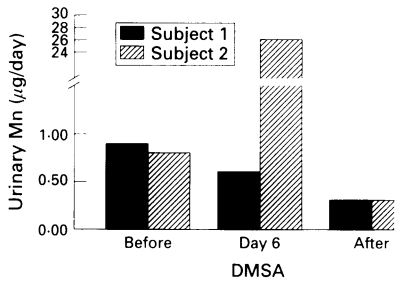


*Figure 1 Urinary manganese (μg/24 h).*

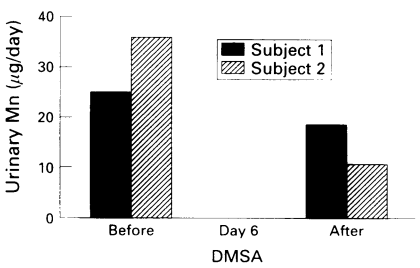


*Figure 2 Urinary manganese (μg/24 h) after 2 g intravenous EDTA.*

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 nmol/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/day, 5·4 nmol/day; Mayo Clinic Laboratory) increased on day 6 only in subject 2 (fig 1).

The $U_{mn}$ response to EDTA (2 g intravenously over 30 min) decreased from 25 μg/day before DMSA to 18·7 μg/day after treatment (455 to 340 nmol/day) in subject 1 and from a mean of 34·5 μg/day (628 nmol/day) before DMSA to 14·8 μg/day (269 nmol/day) six days after treatment in subject 2 (fig 2).

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

There is little information on the response of $U_{Mn}$ to an EDTA challenge. Whitlock *et al*[1] reported $U_{Mn}$ to increase from < 5 μg/l to 100 and 950 μg/l after EDTA (2 g intravenously) was given to two workers with advanced Mn intoxication. Cook *et al*[2] 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*[3] reported that average $U_{Mn}$ increased from < 10 μg/l to approximately 30 μg/l in five workers with Mn intoxication who had unprovoked, 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.

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1 Whitlock CM, Amuso SJ, Bittenbender JB. Chronic neurologic disease in two manganese steel workers. *Am Ind Hyg Assoc J* 1966;27:454–9.
2 Cook DG, Fahn S, Brait KA. Chronic manganese intoxication. *Ann Neurol* 1974;**30**: 59–64.
3 Smyth LT, Ruhf RC, Whitman NE, Dugan T. Clinical manganism and exposure to manganese in the production and processing of ferromanganese alloy. *J Occup Med* 1973; **15**:101–9.
4 Nelson K, Golnick J, Korn T, Angle C. Manganese encephalopathy: utility of early magnetic resonance imaging. *Br J Ind Med* 1993;50:510–3.

# NOTICES

## The 9th International Conference on Occupational Respiratory Diseases 13–16 October 1997. Kyoto, Japan.

The International Labour Office intends to convene this conference to be organised by the Japanese National Organising Committee, in collaboration with the Ministry of Labour of Japan and the Japan Industrial Safety and Health Association (JISHA).

International Pneumoconioses Conferences have been held in Johannesburg (1930), Geneva (1938), Sydney (1950), Bucharest (1971), Caracas (1978), Bochum (1983), Pittsburgh (1988); and Prague (1992). At the 7th and 8th Conferences, it was noted that occupational lung diseases other than pneumoconioses and other respiratory diseases related to exposure in the work environment present an increasing burden on the health of workers in many activities. The title of the next Conference has therefore been modified so as to cover the broad spectrum of work related respiratory diseases.

This 9th Conference on Occupational Respiratory Diseases will provide a forum for the exchange of scientific and technical information on the health effects of air pollutants at the workplace on the respiratory system of exposed workers and on the prevention and control of occupational respiratory diseases.

The main themes will be:

- Epidemiology of occupational respiratory diseases
- Health surveillance of workers exposed to respiratory hazards
- Aetiology, pathogenesis, diagnosis and treatment of occupational respiratory diseases
- Health hazard assessment by environmental and exposure monitoring
- Control measures against health hazards at the workplace
- Respiratory protective equipment
- Information, education, and training on occupational respiratory diseases

Further information from:
The 9th International Conference on Occupational Respiratory Diseases, Secretariat: c/o Japan Industrial Safety and Health Association (JISHA), 5-35-1, Shiba, Minato-ku, Tokyo 108, Japan. Tel 81 3 3452 6841; Fax 81 3 3453 8034.

## NIVA 1996 Calendar—Advanced Courses and Symposia in Occupational Health and Safety

- *Modern principles of air monitoring*
  5–8 February 1996, Sälens Högfjällshotell, Sälen, Sweden
- *Safety research—safety promotion*
  17–22 March 1996, Hotel Hasselbacken, Stockholm, Sweden
- *Bio-aerosol exposures and health problems in relation to waste collection and recycling*
  6–10 May 1996, Hotel Frederiksdal, Lyngby (Copenhagen), Denmark
- *Exposure to biological and chemical agents, and health effects in agriculture*
  6–10 May 1996, Sem Gjestegård, Asker, Norway