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Estimating the prevalence of clinical manganism using a cascaded screening process in a South African manganese smelter

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ABSTRACT

Objectives: A diagnostic algorithm for clinical manganism was developed to screen all employees at a South African manganese smelter.
Methods: The study design was for all 754 smelter employees in 2006/7 to be screened by an occupational health nurse using nine questions and nine brief neurological examination procedures. More than one symptom, any neurological sign, or blood manganese exceeding 40 μg/l triggered referral for neurological examination by an Occupational Medical Practioner (OMP). Abnormal findings by the OMP triggered referral to a movement disorders specialist neurologist and to a neuropsychologist. Features of parkinsonism and a clinical picture consistent with the scientific literature were used to diagnose manganism.
Results: Total manganese dust was mostly within (<5 mg/m^3) or near (<9 mg/m^3) the South African Occupational Exposure Limit, with one outlier near 20 mg/m^3. Occupational Health Service problems and uncertainty about the nature of manganism before the full diagnostic algorithm was developed, resulted in 10 referrals who were certified as manganism cases by the state compensation authorities. They were only assessed in the early stages of this screening programme, and never examined by the above specialists. Of 744 employees screened with the full diagnostic algorithm, the nurse referred 152 (20.3%) and the OMP 27 (3.5%) of all those screened respectively. No definite manganism cases were diagnosed, while one (0.13%) employee was found to have possible manganism and another had an indeterminate neurological diagnosis. A sensitivity analysis assuming that all 10 compensated cases were either normal, or alternatively had definite manganism, yielded a prevalence range for definite manganism from 0% to 1.3%.
Conclusion: Acknowledging possible downward bias when excluding the 10 employees who did not receive the full workup, the true prevalence of definite manganism was likely to be either zero or close to zero.

1. Introduction

This paper focuses entirely on the clinical manifestations of manganese neurotoxicity or manganism which was first reported by Couper in 1837 (Couper, 1837). Subsequently occupational (Greenhouse, 1971; Huang et al., 1998, 1989, 1993; Rodier, 1955; Rosenstock et al., 1971; Schuler et al., 1957; Smyth et al., 1973; Tanaka and Lieben, 1969), and more recently non-occupational (Burkhard et al., 2003; Fell et al., 1996; Selikhova et al., 2008; Stepens et al., 2008) cases have been reported. The latter include patients in chronic hepatic failure (Burkhard et al., 2003) and those reporting intravenous drug abuse with methcathinone (Selikhova et al., 2008; Stepens et al., 2008). Early reports comprised mostly occupational cases, some case series and mass screenings of industrial populations (Tanaka and Lieben, 1969) at risk. There have been few occupational epidemiologic studies examining overt clinical manganism (Huang et al., 1989) using modern diagnostic methods. Most modern studies examine subclinical endpoints such as various neuropsychological tests and neurometric tests (Bast-Pettersen et al., 2004; Ellingsen et al., 2008; Myers et al., 2003a, 2003b).

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The definition of clinical manganism in the literature is not very clear and more recent articles tend to echo previously reported descriptions (Calne et al., 1994; Cersosimo and Koller, 2006; Couper, 1837; Olanow, 2004; Ostiguy et al., 2006; Rodier, 1955; Sadek et al., 2003; Schuler et al., 1957; Selikhova et al., 2008; Smyth et al., 1973; Stepens et al., 2008; Tanaka and Lieben, 1969). Ostiguy (Ostiguy et al., 2006) reported on Canadian attempts to adopt a systematic approach to the diagnosis of manganism. Broadly conceived, the clinical picture is some combination of parkinsonism and neuropsychiatric abnormalities. The American Conference of Governmental Industrial Hygienists (ACGIH) (ACGIH, 1996) in 2001 and the UK Institute for Environmental Health (IEH) (Levy et al., 2003) in 2003 conducted comprehensive reviews of manganese neurotoxicity in the context of setting occupational exposure limits. When compared with other occupational diseases like silicosis or dermatoses it is notable that, other than very recently among welders, there have been relatively few occupational manganism cases (fewer than 500) reported since Couper's report some 172 years ago, with about 12 cases reported since the 1980s (Huang et al., 1989). Such cases arise typically from settings with very high exposures, way in excess of 5 mg/m^3 total or inhalable dust. The ACGIH Threshold Limit Value (TLV) is the airborne concentration of manganese (Mn) under which it is believed that nearly all workers may be repeatedly exposed day-after-day without adverse effects. From 1982 to 1995 this was 5 mg/m^3 and the IEH (Levy et al., 2003) reported no clinical cases with exposures below 5 mg/m^3.

More recently there has been a substantial increase in clinical manganism compensation claims by welders in the USA and other developed countries (Ostiguy et al., 2006). Racette (Racette et al., 2006), using modern diagnostic criteria (e.g. the United Parkinson's Disease Rating Scale Part III (UPDRSIII)) (Goetz et al., 2007, 2008), found prevalences of parkinsonism between 6% and 13% in 2081 such medico-legal referrals. The large number of medico-legal referrals in welders is unexpected given the rarity of clinical manganism reports from those occupationally exposed to manganese in industry more generally. Most studies of welders have looked at subclinical endpoints. There have also been recent clinical and neuropathological reviews of manganism in relation to Idiopathic Parkinson's Disease (IPD) by Olanow (2004) and Jankovic (2005).

The background to our current study was television media exposure in early 2005 of a group of former ferroalloy smelter workers with purported manganism. In response, the study smelter management decided to design and implement a medical surveillance system to assess whether or not clinical manganism was present at its works.

2. Methods

A cross-sectional cascaded screening process took place in 2006/7 during the course of which all smelter employees were screened. Of 754 employees, 744 were fully, and 10 partially, screened. There were three levels of screening. An occupational health nurse applied nine questions and nine brief neurological examination procedures (Table 1) at the first level of screening, referring those with two or more symptoms, or one or more neurological signs, or blood manganese (MnB) above 40 μg/l.

The OMP at the smelter conducted a full neurological examination at the second level of screening, referring any neurological abnormalities to the third level of screening involving a neurological examination by a movement disorders subspecialist neurologist together with a specialized neuropsychological evaluation. The duration of specialist level examinations, which was assisted by isi-Zulu interpreters, varied between 1 and 3 h.

The diagnostic approach of the specialist neurological examination was based on the presence of two or more cardinal signs of parkinsonism, these being bradykinesia, tremor, rigidity, and postural instability/gait abnormality.

The UPDRSIII assessment (Goetz et al., 2007, 2008) (range 0–108) was conducted on all subjects to provide a baseline for comparison in anticipation of a longitudinal surveillance programme. Two self-report questionnaires (shared with the neuropsychologists) were administered. The questionnaires were specifically designed for this study and focused on signs and

Table 1
Level 1 screening instrument.

Items	Questions	Answers
Questionnaire: do you experience any of the following:		
1. Mood	Do you often feel irritated without any particular reason?	Yes/no
2. Memory	Do you find it difficult to remember things?	Yes/no
3. Concentration	Do you often have problems concentrating?	Yes/no
5. Tremor	Have you noticed a tremor (shaking) of your hands since the last time you were examined here in the clinic?	Yes/no
6. Coordination	Do you find it difficult buttoning and unbuttoning your clothes?	Yes/no
7. Gait	Do you feel that the way you walk has changed? If yes, in what way?	Yes/no
8. Muscle pain	Do you get cramps in your muscles? Do you get painful muscles without an explanation (for example without playing sport or working extra hard). Both parts must be answered positively for yes	Yes/no
9. Dysphagia	Have you noticed any changes when you swallow food or drink? If yes, describe the changes	Yes/no

Items	Signs	Answers
Examination: are any abnormalities present?		
1. Facies	Immobile or inexpressive	Abnormal/normal/unsure
2. Toe-heel walking	unbalanced	
3. Sharp turn	Unbalanced and reduced arm swing	
4. Squatting	Unbalanced going down or rising	
5. Hand tremor	postural	
6. Muscle tone	rigidity	
7. Finger-nose test	Difficulty with coordination and touching nose	
8. Dysdiadochokinesis	Incoordination with rapid pronation/supination	
9. Drawing a spiral	Irregular drawings	
Biological exposure monitoring:		
Blood Mn	Value in relation to normal scale (0.3–12 μg/l). Refer if above 40 mg/l	Date