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Manganese and Its Compounds

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NATURAL OCCURRENCES AND CHEMICAL PROPERTIES

The chemical symbol for manganese is Mn; its atomic weight is 54.94, specific gravity is 7.2, and melting point is 1260° C.[65] The chemical behavior of manganese is similar to that of iron, and they are often associated in their natural occurrence. The valences of manganese are commonly 2, 4, or 7, but can also be 1, 3, or 6. Manganese is divalent in the most stable salts.

Manganese does not occur naturally as the metal but is widely distributed in the earth's crust and is the twelfth most abundant element. Deposits of manganese ore of high concentration are found in African countries (Gabon, Ghana, Morocco, South Africa, and Zaire), Australia, Brazil, China, India, and the former Soviet Union (Georgia and Ukraine).[36] Since the United States has deposits of only lower-grade ore, it depends on the imported ores for almost all of its manganese supply.[36] The ocean floor also contains vast deposits of manganese oxide nodules. However, commercial exploitation of ocean deposits has been hampered by various economic as well as political, if not technologic, reasons.[9,36] Pyrolusite, a mineral form of MnO_2, is one of the more common and commercially important ores. Other manganese ores include braunite, hausmannite, manganite, and psilomelane.[55] The Bureau of Mines classifies manganese ores by their manganese content; manganese ore (35% or more), ferruginous manganese ore (10% to 35%), and manganiferous ore (5% to 35%). More detailed descriptions of mining and industrial uses of manganese ore are found elsewhere.[36,55]

INDUSTRIAL USES AND EXPOSURES

Manganese ores are mined in both open pits and underground, and mining methods vary from primitive to modern. In particular, the job of drilling with pneumatic drills has been one of the most significant sources of manganese exposure and poisoning.[60,66,76] The ores are washed, separated from the rock, crushed, and, in some cases, roasted, sintered, and nodulized before shipment.[55] After arrival at the port of importing countries, the ores are crushed to a smaller size, ground, and bagged for further industrial uses. The grinding and bagging processes have also been responsible for many cases of manganese poisoning.[12,18,20]

Manganese is essential to the production of steel and is also an ingredient in making important alloys with aluminum, copper, magnesium, and cast iron. Because of its ability to provide strength and hardness to metals, more than 80% of the manganese used in the United States is for the production of steel and various alloys.[36,37] Standard high-carbon ferromanganese contains 78% to 82% manganese, and silicon/manganese contains 65% to 68% manganese. Poisoning has occurred among workers making such alloys,[35,69] among workers crushing and screening ferromanganese,[69] and among workers performing arc-welding or arc-burning of steel that contained 11% to 14% manganese.[71,74] A crane operator who worked over the furnaces which melted steel and manganese ore was also affected.[62]

In the chemical industries, manganese dioxide ores are used in the production of hydroquinone, potassium permanganate, and manganese sulfate. Manganese sulfate is added to fertilizers to provide this trace element to the soil. Manganous oxide (MnO) is added to animal and poultry feed.[55] The common dry-cell battery uses manganese dioxide, and cases of manganese poisoning have occurred in its manufacturing.[23]

Chemicals containing manganese are used in the ceramics industries to color glass and to make face brick and other ceramic products. Welding rods and fluxes contain manganese. Manganese dioxide and other manganese compounds are used in the manufacture of dyes, paint, varnish, dryers, and pharmaceuticals.[55] Maneb, a fungicide containing an organic manganese compound (manganese ethylene bisdithiocarbamate), was reported to have caused manganese poisoning among agricultural workers who applied it.[28] Methylcyclopentadienyl manganese tricarbonyl (MMT) is added to fuel oil as a smoke inhibitor and to leaded gasoline as an antiknock additive to reduce the amount of tetraethyl lead in gasoline.[25]

In 1989, the United States imported 0.64 million short tons of manganese ore and 0.48 million short tons of ferromanganese.[37] Metallurgic applications accounted for most manganese consumption, with about 90% used in steelmaking. The number of U.S. workers potentially exposed to manganese and its compounds was estimated to be from 68,000 to 185,000.[53] The world production of manganese ore in 1989 was 26.5 million short tons.[37] This suggests that a large number of workers are exposed to various forms of manganese worldwide.

BIOLOGIC EFFECTS[14,55,70,75]

Physiologic Role

Manganese is an essential mineral for humans and animals. It is necessary for normal bone formation and for the synthesis of chondroitin sulfate. Manganese is required for optimal melanocyte function and for the metabolism of catecholamines in the brain.[16] Although manganese deficiency has been reported to cause sterility, neonatal death, and skeletal deformities in the newborn of various animal species, similar effects of manganese deficiency have not been reported in humans.

The daily intake of manganese in human diets varies considerably but averages from 3 to 7 mg. It has been estimated that a normal 70-kg man has a total of 12 to 20 mg of manganese in his body.[55] In rats, manganese is widely distributed in the body but tends to concentrate in the mitochondria.[45] Among nonexposed human adults, the usual range of manganese concentrations is 0.8 to 1.6 μg/100 ml blood,[10] and 0.11 to 2.67 μg/L urine (geometric mean: 0.56 μg/L).[72]

In animal feeding studies, rats tolerated high concentrations of dietary manganese; their growth rate was unaffected by concentrations as high as 2000 parts per million (ppm). Dietary supplements of 820 ppm had no detectable effects on the growth or appetite of calves, but at 2460 ppm, they showed decrease in both food intake and body-weight gains.[55]

Route of Entry and Absorption

Inhalation of dust or fume is the major route of entry in occupational manganese poisoning, although oral entry can occur from drinking water contaminated with manganese,[38] or under poor conditions of industrial or personal hygiene.[18] Tricarbonyls of manganese can be absorbed through the skin.[27]

When radioactive manganese (as $MnCl_2$) was orally administered to rats, only about 4% of the radioactivity was absorbed.[29] After injection, radioactive manganese disappeared rapidly from the bloodstream, and 10% to 30% of the dose was accumulated in the liver. From there, manganese was excreted almost totally in the bile into the intestinal tract to be eliminated in the feces, and very little manganese was excreted in the urine.[29] In humans, 30% of injected radioactive manganese was eliminated via a fast pathway with a half-life of 4 days, while the remaining 70% took a slow pathway with an average half-life of 39 days.[43]

INDUSTRIAL MANGANESE POISONING

The primary target organs of manganese toxicity are the brain and the lungs. The toxicity to the brain is manifested as a chronic disorder of the central nervous system resembling Parkinsonism. Toxicity to the lungs is manifested as increased susceptibility to bronchitis or, in more serious cases, manganic pneumonia. The term *manganism* or *manganese poisoning* usually refers to the chronic neurologic disorder caused by inhalation of dusts containing manganese.

Since 1837, when Couper[18] first reported manganism among men who ground the black oxide of Mn, numerous cases have been reported from various corners of the world, even in recent years.* Many more cases are suspected to be occurring but go unrecognized or unreported.[71]

*References 13, 23, 30, 32, 35, 61, and 62.

Pathophysiology

The symptoms and signs of manganism resemble those of Parkinsonism and are consistent with the lesions observed in the extrapyramidal tract of the brain. Marked morphologic changes and degeneration of neurons occur in the basal ganglia and the gray matter of the midbrain, affecting the pallidum, putamen, and caudate nucleus;[5,11] while in Parkinsonism, the lesions are seen in the substantia nigra, locus ceruleus, and dorsal nucleus of the vagus nerve.[2] Therefore, clinical manifestations of these disorders are not identical. Manganese was thought to affect the dopaminergic components of the extrapyramidal system in a manner similar to Parkinsonism.[50] However, manganism is said to be more akin to dystonia than to Parkinsonism,[7] and a pathophysiologic mechanism different from that of Parkinsonism has been proposed in recent years. According to the new theory, manganese neurotoxicity results from the enhanced autoxidation of dopamine by a higher-valency Mn^{3+} ion with increased generation of cytotoxic free radicals.[19,58] It has been further suggested that the pathology of manganese neurotoxicity may be dependent on the ease with which simple Mn^{3+} complexes are formed in the brain and the efficiency with which they destroy catecholamines.[4]

Clinical Manifestations

The onset of manganism is insidious and appears after months or years of manganese exposure. In one case series, the latent period ranged from 1 month to 10 years, the median lying between 1 to 2 years.[60] There are reports that workers developed major symptoms several years after the cessation of manganese exposure.[13]

The disease is roughly divided into two stages: the early stage is characterized by subjective symptoms reflecting emotional instability and irritability; the advanced stage is characterized by the manifestation of neurologic signs. (Rodier used a three-stage classification of prodromal, intermediate, and established.[60]) Clinical features reported by previous investigators are summarized below.*

In the early stage, the affected worker develops or complains of apathy, asthenia, lassitude, insomnia or somnolence, and slowed movements. He or she may show a form of aggressiveness and mental excitement, termed *manganese psychosis*. Many patients report decreased libido or impotence[41,60] (or difficulty maintaining an erection[51]) which may be preceded by a short period of increased libido. Other symptoms include muscle pains and cramps, lumbar pain, headache, giddiness, clumsy movement, difficulty in speech and gait, increased salivation, profuse sweating, and paresthesia. The duration of this stage is estimated to last from one to several months, but is often difficult to determine due to the insidious progression of the disease. The development and course of disease probably depend on the degree of exposure as well as the individual susceptibility.[12,23] Thereafter, the condition slowly progresses to the next stage unless the worker is removed from the exposure.

The advanced stage is characterized by various neurologic abnormalities similar to those of Parkinsonism. Difficulties in coordinating movements, which was previously felt only by the patient, now may become noticeable to observers. This may be the first time that the patient is brought to the physician's attention, and specific questions may have to be asked to elicit symptoms of

*References 12, 13, 20, 48, 60, and 66.

the previous stage. Monotonous or slurred speech, and diminished facial expression (masklike face) are noted.

The gait is disturbed by propulsion, and walking backward or making quick turns become almost impossible. When pushed by the examiner, the patient is unable to balance himself to maintain the standing position. In advanced manganism, walking becomes slower, spastic, and labored, presenting a peculiar high-stepped gait called *Hehnetritt* (cock walk).[20] On passive flexion of the extremities, muscle rigidity produces a cogwheel resistance. Impulsive laughter or spasmodic weeping may also be observed.

Fine tremors of the fingers and extended tongue, as well as gross rhythmic movements of arms and legs, may be observed. Handwriting becomes shaky and micrographic. Adiadochokinesia is evident in many cases, which is thought to be due to poor muscle control rather than to loss of proprioception.

Other less frequently reported symptoms and signs are dysphagia, nystagmus, and torticollis. Changes in superficial and deep sensation were reported.[66] Visual sense is well preserved, although a few cases of diplopia and abnormal convergence have been reported.[66] Some patients complained of dysuria and urinary incontinence.[71]

Some investigators do not consider manganism a form of Parkinsonism. They maintain that the former is predominantly a dystonic disease characterized by a postural instability of complementary muscle groups.[8] Others noted that the tremor in manganism is frequently an intention tremor, while in Parkinsonism it is the classical resting tremor.[39] As alluded to in the pathophysiology section, these differences may be explained by the difference in the location of pathologic lesions in the brainstem.[8]

Based on a questionnaire survey, it was reported that manganese-exposed workers were found to have fathered a significantly fewer number of children during their period of exposure compared to the nonexposed.[41] The airborne concentration of manganese dusts ranged from 0.07 to 8.61 mg/m^3 (geometric mean: 0.94 mg/m^3). Although a reproductive interference could occur at any stage of the fertility process, the reduced libido of male workers due to manganese was suspected to account for some of the lowered fecundity of their spouses. (However, no data on neurologic inquiry including questions on libido were reported.)

Diagnosis of Manganism

Careful review of the occupational history is most important. Diagnostic problems arise when the physician does not suspect an occupational origin for the worker's complaints or is not familiar with the toxic effects of manganese. Many worker/patients may not necessarily be aware of the toxicity of materials to which they are exposed. The word *manganese* is frequently confused with the word *magnesium*.[71] Early diagnosis is often made difficult due to the insidious onset and progress of the disease. Because of manganese-induced apathy, the patient may not voluntarily seek medical help. Symptoms may be mistaken as unrelated to work exposure by fellow workers, the worker's family, or even by health care providers. If an occupational cause is suspected, the physician should not hesitate to obtain necessary information by contacting the employer (with patient's consent) or the appropriate federal or state agency. If manganism is suspected, a consultation with a neurologist may be in order.

It has been reported that for early detection of manganism, psychomotor tests (such as simple reaction time, audioverbal short-term memory capacity, eye–hand coordination, diadochokinesia, finger tapping, and digit span) are more sensitive than the standardized neurologic examination.[61,73] However, low specificity of these tests in general would make the interpretation of individual results difficult.

The usefulness of manganese assay in blood or urine for diagnosis of manganism has been unsettled,[23,35] probably due to the lack of reasonable relationship among the exposure to manganese, biologic manganese levels, and the severity of clinical findings.[13,15,21,61,71] This uncertainty is likely the result of the fairly rapid turnover of absorbed manganese in contrast to the slow progression of the disease.[7]

When analyzed by flameless atomic absorption (FAA) spectrophotometry, manganese concentrations above the range of 5 to 10 μg/100 ml blood or above 5 to 10 μg/L urine were considered to be indicative of increased manganese exposure.[10,72] An elevated blood manganese level may not by itself necessarily establish the diagnosis of manganism, but it should call for a closer examination of the exposure and worker's health status. More recently, however, it was reported that a threshold of 1 μg/100 ml blood existed for the eye–hand coordination test.[61] When compared to the previous report of 0.8 to 1.6 μg/100 ml blood among nonexposed adults,[10] the latter finding is intriguing and would call for further investigation. Elevated manganese concentrations in the scalp hair and pubic hair (by neutron activation method) were reported among ferromanganese workers who developed manganism.[32] Although analysis of the hair for manganese may be useful to document the past exposure, its value as a periodic monitoring tool is questionable. Likewise, since the urinary manganese concentrations correlated with atmospheric manganese levels only on a group basis,[71] it is perhaps of little value for diagnostic purpose, although comparison of manganese excretion in the urine samples of prechelation and postchelation was suggested as a diagnostic aid.[74]

Differential diagnosis of manganism should rule out Parkinsonism of nonoccupational origin (absence of exposure and higher age; idiopathic Parkinsonism is rare in persons under age 45), Wilson's disease (presence of hepatic involvement and Kayser-Fleischer ring), multiple sclerosis (presence of visual and other sensory disturbances, nystagmus, and history of temporary remissions), and neurosyphilis.

In countries where exposure to high concentrations of manganese (at about or above 5 mg/m^3 air) has been more or less under control, there is still a concern as to what the health effects of long-term, low-level exposures (at about or below 1 to 3 mg/m^3) to manganese might be. Since manganese is an essential mineral for animals and humans, and since our normal diet contains anywhere from 3 to 7 mg of manganese,[55] there has been a general notion that a low degree of manganese exposure would not be harmful. However, it has been recently reported that workers exposed to low concentrations of manganese exhibited significantly increased frequencies of some symptoms such as reduced libido and increased tiredness.[51] The exposed workers also showed impaired performances in such psychomotor tests as reaction time, diadochokinesia, P-300 latency time (event-related auditory evoked potential), finger tapping and digit span,[73] or elevated olfactory threshold.[51] Since there were no gross neurologic or psychiatric abnormalities, such results were interpreted as early latent or subclinical signs of manganism. If that were the case, there seems to be a need to reconcile the discrepancy between the normal dietary intake of manganese (which is supposedly necessary for the normal body functions) and potentially toxic effects of low degree industrial manganese exposure. Whether the discrepancy is due to the difference in the route of entry and absorption (oral–intestinal vs. respiratory–hematogenous), in the chemical state of manganese (manganese in food-

stuffs vs. manganese dusts and fumes), or due to some other factors must be further investigated.

Prognosis and Treatment of Manganism

If manganese poisoning is detected in its early stage and the worker is removed from exposure promptly, the neurologic abnormalities will disappear without specific treatment.[20] Spontaneous recovery may take 1 to 3 months. It is believed that in such cases the brain cells were not permanently damaged and that the body's natural clearance mechanism was sufficient in removing excess manganese. To accelerate the elimination, some have advocated chelation therapy using calcium disodium ethylenediamine tetraacetic acid ($CaNa_2EDTA$).[40,59] For patients in the advanced stage of the poisoning, the effectiveness of removal from exposure and $CaNa_2EDTA$ therapy has been insignificant,[32] only temporary,[13] or variable,[59,74] probably depending on whether irreversible damage to the brain cells has occurred.[60,74] Barbeau[7] argued that chelating agents were of no value in treatment of workers with established manganism who had been taken out of exposure, since there was no longer a manganese overload.

Once established, manganism is an intractable and permanently disabling occupational disease for which currently there is no complete cure. Although there is no immediate threat to life, the quality of the patient's life is significantly impaired as in the case of Parkinsonism.

In Parkinsonism, brain cells are depleted of the catecholamine neurotransmitters and of melanin.[17] Based on this information, levodopa (3,4-dihydroxyphenylalanine), the precursor of the neurotransmitters, was administered to Parkinsonism patients to produce clinical improvement.[47] Since a similar depletion of the neurotransmitters was also observed in manganism, and because of the clinical similarities of idiopathic Parkinsonism and manganism, levodopa was tried on manganism patients with some success.[50,62] Others reported that combination of levodopa and carbidopa was effective.[32]

However, the effectiveness of levodopa for treatment of manganism has been inconsistent and controversial. It has been suggested that the pathophysiology of these diseases appears different.[13,30] Based on in vitro and animal experiments, Parenti et al.[57,58] observed that the decreased availability or autoxidation of dopamine attenuated the neurotoxicity of manganese, suggesting that manganese increases toxic products originating from dopamine catabolism. Thus, the previous notion that manganism can be a clinical model for Parkinsonism has been seriously challenged,[7] and administration of drugs such as levodopa may be harmful if used for treatment of manganism.[57] Rather, it has been proposed that administration of an antioxidant such as vitamin E may be effective to counter the effect of manganese to reduce dopamine.[58]

Recently, Shuqin et al.[68] reported that two patients with chronic manganism were successfully treated with sodium paraaminosalicylic acid (Na-PAS) to show a marked improvement in long-standing symptoms. Since the number of cases was small and the pharmacologic rationale for its effectiveness has not been clarified at this time, additional studies on this drug are needed to confirm its effectiveness.

Manganic Bronchitis and Pneumonia

In addition to the neurologic effects, manganese is known to cause respiratory effects. In 1921, Brezina reported five pneumonia deaths among 10 workers exposed to manganese in an Italian pyrolusite industry.[55] In 1939, Elstad[22] reported an epidemic of lobar pneumonia in the town of Sauda, Norway. A plant near the town smelted ferromanganese containing 80% manganese and silicon/manganese. During the year with heavy pollution, lobar pneumonia accounted for 32% of all deaths in the town, almost nine times the rate for the country. In the manufacture of potassium permanganate, the incidence of pneumonia among the workers exposed to the dusts of manganese oxides was 36 times higher than that of the unexposed.[42] In a more recent study, the manganese-exposed group in a plant producing manganese oxide and salts had a significantly higher prevalence of cough in the cold season, dyspnea during exercise, and recent episodes of acute bronchitis than the control group.[61]

Based on the results of animal experiments in which animals were exposed to pathogens with or without manganese oxide, it has been postulated that manganese may potentiate infectious processes in the lungs.[1,44]

ORGANIC MANGANESE COMPOUNDS

Although there are a variety of organic manganese compounds, only two are discussed here because of their potential for exposure to workers.

Methylcyclopentadienyl manganese tricarbonyl (MMT)

MMT is a dark-orange liquid with a herbaceous odor, low volatility (vapor pressure of 9.3 mm Hg at 100° C), and high thermal stability (a boiling point of 232° C at 1 atmospheric pressure and a closed-cup flash point of 96° C) but is subject to rapid photochemical decomposition.[26] Manganese comprises about 25% of the molecular weight.

MMT has been added to fuel oil as a smoke inhibitor or combustion improver. As an antiknocking agent, it is added to all unleaded gasoline in Canada at a rate of up to 0.063 g (as manganese) per gallon. In the United States, MMT is allowed to be added to only regular leaded gasoline, partially substituting tetraethyl lead.[25]

Following oral or intravenous administration of ^{54}Mn-tagged MMT to rats, most of the radioactivity was excreted in the urine and feces in the first few days.[52] This route of excretion is contrasted to that of inorganic manganese which is excreted very little by way of the urine. The toxicity of MMT varied among the species of animal, rats being more susceptible than others (LD_{50}: 58 mg/kg).[31] Reactions of exposed animals included excitation, tremors, convulsions, and bloody diarrhea. Gross pathologic changes were observed in the lungs, liver, kidneys, and spleen.[31]

MMT can be absorbed through the skin[3] but is not strongly irritating to the skin or eyes. Therefore, workers should be cautioned not to depend on irritation as a warning sign of skin exposure. In an incident of accidental spill reported by a manufacturer of MMT, six workers were dermally exposed to MMT for up to 30 minutes.[27] The symptoms, which appeared 5 minutes to an hour after exposure, included headache, nausea, dyspnea, chest tightness, paresthesia, and abdominal distress. Most of the symptoms subsided in several hours. In another episode, two workers kept working with MMT-soaked clothing for up to 1.5 hours. Their urinary manganese levels were 46 and 137 μg/L on the same day, and dropped to 2.9 and 3.4 μg/L, respectively, a few weeks later. These incidents point to the importance of avoiding skin contact with MMT. If such spills occur, contaminated clothing should be removed promptly and the skin washed thoroughly. Exposed workers should be followed by medical evaluations.

Manganese Ethylene Bis Dithiocarbamate (Mn-EBDC; Maneb)

Maneb is one of several EBDCs which are used to protect a wide variety of fruit and vegetable crops as well as ornamental plants and turf against fungal pathogens.[24] Ethylene thiourea (ETU) is a common contaminant, metabolite, and degradation product of these EBDCs. Maneb is a water-soluble, yellowish powder (or crystals) which is mixed into formulations at various concentrations. Based on animal experiments, it is reported to have carcinogenic, mutagenic, and teratogenic potentials.[65] Brazilian farm workers who had been exposed to maneb for more than 6 months were found to have a higher prevalence of signs and symptoms suggestive of manganism such as headache, nervousness, memory complaints, sleepiness, and "plastic" rigidity of the muscles with cog-wheel phenomenon.[28] The U.S. Environmental Protection Agency (EPA) conducted a thorough review of the use, toxicity, and effects to humans and the environment of EBDCs.[24] Based on this review, it was proposed that the sale, mixing, and application of maneb and other EBDCs be permitted under strictly controlled conditions which are to be specified on the label.

PREVENTION PROGRAM

Even if effective drugs may become available in the future, the prevention of manganese poisoning must be accomplished through the control of exposure by programs of industrial hygiene, worker education, and medical monitoring.[33,63,75] Only their principles are presented in this chapter. For the purpose of compliance with federal regulations which delineate hierarchical program requirement, readers in the United States are advised to consult the specific documents published by the governmental agencies related to this subject.[54,56] Also, it is very important to note that the cloud of manganese metal dust is explosive.[70]

Medical Program

As recommended by various authors,[60,64,75] the baseline health status of workers should be established by a preplacement medical examination, and subsequent examinations should be given at periodic intervals to monitor any changes in health status. These intervals may vary from 1 to 12 months, depending on the type and degree of exposure. The program should include review of symptoms and signs and blood-manganese analysis performed by a dependable laboratory. If a worker is found to have some of the symptoms and signs of manganism, or if the blood-manganese concentration is above the reported normal range, he or she must be evaluated further and, if indicated, removed from the exposure to be followed up by repeated examinations. However, Barbeau[7] stated that once the worker was taken out of exposure, determination of the blood-manganese level would be of little value, since manganese overload was present only during exposure and blood-manganese levels were not in parallel to the presence of extrapyramidal symptoms.

As discussed earlier, various neurobehavioral and psychomotor tests have been reported, particularly for the purpose of detecting the early signs of manganism.[6,34,51,61,73] However, their usefulness as part of routine health monitoring program for Mn exposed workers remains to be established.

It has been reported that individual susceptibility to manganese varies considerably among workers under similar exposure conditions.[12,23] The exact nature of this phenomenon has not been fully elucidated. Nutritional deficiency, in particular, iron deficiency anemia, has been suggested as a factor.[49,67] Since iron and manganese atoms are chemically similar, it has been postulated that manganese may be more readily absorbed in an iron-deficient state.[43,46] Although this hypothesis has not been tested epidemiologically among workers exposed to manganese, it may be prudent to add a hemoglobin determination to the medical program for workers exposed to manganese.[64]

The medical program should also include screening of the workers for pulmonary insufficiency and counseling for smoking cessation, in view of the known respiratory effects of manganese exposure.[64]

RECOMMENDED EXPOSURE LIMITS

There has been a wide range of manganese concentrations in the air to which workers in various countries are permitted to be exposed.[33] In the United States, the federal permissible exposure limit (PEL)[56] for manganese dust and compounds (as manganese) is a ceiling value of 5 mg/m^3 air. Some investigators questioned the adequacy of protection afforded by this level and recommend stricter exposure control.[1] For manganese fumes and manganese tetroxide, the federal limit is 1 mg/m^3 for an 8-hour time-weighted average (TWA), and 0.1 mg/m^3 TWA for MMT. In 1992, the American Conference of Governmental Industrial Hygienists (ACGIH) published a notice of intended changes to lower the threshold limit value (TLV) of elemental manganese and inorganic manganese compounds (as manganese) to 0.2 mg/m^3 TWA from the current 5 mg/m^3 for manganese dust and compounds, and 1 mg/m^3 TWA and 3 mg/m^3 short-term exposure limit (STEL) for manganese fumes. MMT has a TLV of 0.2 mg/m^3 (as manganese) with a notation for skin absorption.[3]

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