## Overview

### Useful For

Evaluation of central nervous system symptoms, similar to Parkinson disease, in manganese (Mn) miners and processors

Characterization of liver cirrhosis

Therapeutic monitoring in treatment of cirrhosis, parenteral nutrition-related Mn toxicity, and environmental exposure to Mn

### Special Instructions

- Metals Analysis Specimen Collection and Transport

### Method Name

Triple-Quadrupole Inductively Coupled Plasma-Mass Spectrometry (ICP-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Whole blood

### Specimen Required

**Patient Preparation:** High concentrations of gadolinium and iodine are known to interfere with most metal tests. If either gadolinium- or iodine-containing contrast media has been administered, a specimen should not be collected for 96 hours.
**Container/Tube:** Royal blue top (EDTA) Vacutainer plastic trace element blood collection tube
**Specimen Volume:** 0.3 mL
**Collection Instructions:**
1. See Metals Analysis Specimen Collection and Transport for complete instructions.
2. Send whole blood specimen in original tube. **Do not aliquot.**

### Specimen Minimum Volume

0.2 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | OK |

| | |
|---|---|
| Gross lipemia | OK |
| Gross icterus | OK |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole blood | Refrigerated (preferred) | 28 days | |
| | Ambient | 28 days | |
| | Frozen | 28 days | |

## Clinical & Interpretive

### Clinical Information

Manganese (Mn) is a trace essential element with many industrial uses. Mining as well as iron and steel production have been implicated as occupational sources of exposure. It is principally used in steel production to improve hardness, stiffness, and strength. Mn is a normal constituent of air, soil, water, and food. The primary nonoccupational source of exposure is by eating food or Mn-containing nutritional supplements. Vegetarians who consume foods rich in Mn such as grains, beans, and nuts, as well as heavy tea drinkers, may have a higher intake than the average person. People who smoke tobacco or inhale second-hand smoke are also exposed to Mn at higher levels than nonsmokers.

Inhalation is the primary source of entry for Mn but is also partially absorbed (3%-5%) through the gastrointestinal tract. Only very small amounts of Mn are absorbed dermally. Signs of toxicity may appear quickly, and neurological symptoms are rarely reversible. Mn toxicity is generally recognized to progress through 3 stages. Levy describes these stages. "The first stage is a prodrome of malaise, somnolence, apathy, emotional lability, sexual dysfunction, weakness, lethargy, anorexia, and headaches. If there is continued exposure, progression to a second stage may occur, with psychological disturbances, including impaired memory and judgement, anxiety, and sometimes psychotic manifestations such as hallucinations. The third stage consists of progressive bradykinesia, dysarthria, axial and extremity dystonia, paresis, gait disturbances, cogwheel rigidity, intention tremor, impaired coordination, and a mask-like face. Many of those affected may be permanently and completely disabled."(1) Mn is removed from the blood by the liver where it's conjugated with bile and excreted.

The major compartment for circulating Mn is the erythrocytes, bound to hemoglobin, with whole blood concentrations of Mn (in patients with normal levels) being 10 times that of the serum. Mn passes from the blood to the tissues quickly. Concentrations in the liver are highest, with 1 to 1.5 mg Mn/kg (wet weight) in normal individuals. The half-life of Mn in the body is about 40 days, with elimination primarily through the feces. Only small amounts are excreted in the urine.

Elevated levels of whole blood Mn have been reported, with and without central nervous system (CNS) symptoms, in patients with hepatitis B virus-induced liver cirrhosis, in patients on total parenteral nutrition (TPN) with Mn supplementation, and in infants born to mothers who were on TPN. The studies in cirrhotic patients with extrapyramidal symptoms indicate a possible correlation between whole blood Mn and that measured by T1-weighted magnetic resonance in the globus pallidus and midbrain, with whole blood Mn levels being 2-fold or more, higher than normal. Increases in whole blood Mn over time may be indicative of future CNS effects. The data on TPN patients is based on anecdotes or small studies and is highly variable, as is that obtained in infants.(2)

Behcet disease, a form of chronic systemic vasculitis, has been reported to exhibit 4-fold increase in erythrocyte Mn, and it is suggested that increased activity of superoxide dismutase may contribute to the pathogenesis of the disease.

Mn has also been reported as a contaminant in "garage" preparations of the abused drug methcathinone. Continued use of the drug gives rise to CNS toxicity typical of manganism.(3)

For monitoring therapy, whether of environmental exposure, TPN, or cirrhosis, whole blood levels have been shown to correlate well with neuropsychological improvement, although whether the laboratory changes precede the CNS or merely track with them remains unclear. It is recommended that both CNS functional testing and laboratory evaluation be used to monitor therapy of these patients. Long-term monitoring of Behcet disease has not been reported, and it is not known if the Mn levels respond to therapy.

## Reference Values

4.7-18.3 ng/mL

## Interpretation

Whole blood or serum concentrations in combination with brain magnetic resonance imaging scans and neurological assessment may be used to detect excessive exposure. Values between 1 and 2 times the upper limit of normal may be due to differences in hematocrit and normal biological variation and should be interpreted with caution before concluding that hypermanganesemia is contributing to the disease process. Values greater than twice the upper limit of normal correlate with disease. For longitudinal monitoring, sampling no more frequently than the half-life of the element (40 days) should be used.

## Cautions

Whole blood manganese (Mn) concentrations are not responsive to dietary depletion, but measures of serum Mn are potentially useful.

Contamination of the collection site and of the specimen must be avoided. In the case of environmental evaluation, do not collect specimens in the workplace. Failure to use metal-free collection procedures and devices may cause falsely increased results. See Specimen Required and Metals Analysis Specimen Collection and Transport for collection and processing information.

## Clinical Reference

1. Levy BS, Nassetta WJ. Neurologic effects of manganese in humans: A review. Int J Occup Environ Health. 2003;9(2):153-163. doi:10.1179/oeh.2003.9.2.153
2. Choi Y, Park JK, Park NH, et al. Whole blood and red blood cell manganese reflected signal intensities of T1-weighted magnetic resonance images better than plasma manganese in liver cirrhotics. J Occup Health. 2005 Feb;47(1):68-73. doi:10.1539/joh.47.68
3. Sanotsky Y, Lesyk R, Fedoryshyn L, Komnatska I, Matviyenko Y, Fahn S, et al. Manganic encephalopathy due to "Ephedrone" abuse. Mov Disord. 2007;22(9):1337-1343. doi:10.1002/mds.21378
4. Jiang Y, Zheng W, Long L, et al. Brain magnetic resonance imaging and manganese concentrations in red blood cells of smelting workers: search for biomarkers of manganese exposure. Neurotoxicology. 2007;28(1):126-135. doi:10.1016/j.neuro.2006.08.005
5. Guilarte T, Chen M, McGlothan J, et al. Nigrostriatal dopamine system dysfunction and subtle motor deficits in manganese-exposed non-human primates. Exp Neurol. 2006;202(2):381-390. doi:10.1016/j.expneurol.2006.06.015
6. Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, eds: Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier;

2023
7. O'Neal SL, Zheng W. Manganese toxicity upon overexposure: a decade in review. Curr Environ Health Rep. 2015;2(3):315-328. doi:10.1007/s40572-015-0056-x

## Performance

### Method Description
The metal of interest is analyzed by triple-quadrupole inductively coupled plasma mass spectrometry.(Unpublished Mayo method)

### PDF Report
No

### Day(s) Performed
Tuesday

### Report Available
2 to 8 days

### Specimen Retention Time
14 days

### Performing Laboratory Location
Rochester

## Fees & Codes

### Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

### Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information
83785

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| MNB | Manganese, B | 5681-2 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 89120 | Manganese, B | 5681-2 |