Manganese

Atomic number 25
Atomic weight 54.94

Collection

Serum/Plasma	2 mL	Plastic container. Trace element tube
Blood	2 mL	Plastic container. Trace element tube EDTA anticoagulant
Urine	20 mL	Sterile Universal

Whole blood is preferred to serum/plasma. As manganese is present in stainless steel needles it is necessary to collect a blood sample for manganese after blood has been drawn for other analyses at the same time, otherwise the first 5ml of blood should be discarded. Alternatively, a plastic cannula or patent line in the patient should be used.

Reference ranges

			Reference
Serum/plasma	nmol/L	11-42	1,2
Blood	nmol/L	80-260	3-6
Urine	nmol/L	2-24	1
	nmol/L	<8.5	10,11
	nmol/24 h	2-22	2
	nmol/mmol creatinine	Less than 4	7
	µmol/mol creatinine	1.3 95th percentile	11

Age	Serum/plasma
0-6 months	8.7-68.8
0-12 months	10.7-66.3
1-2 years	Less than 61.1
2-4 years	8.1-42.1
4-6 years	3.3-49.3
6-10 years	5.2-40.8
10-14 years	7.6-36.4
14-18 years	7.8-27.8

Pregnancy, Neonates	Blood
10-20 weeks	43-257
25 weeks	52-291
34 weeks	94-366
Neonates; 3-4 days old	318-1157

Notes

Age related ranges for serum are from Reference 8, a study of 137 healthy children attending pre-op assessment (orthopaedic, tonsillectomy) clinics in Germany. The age stratified subgroups contain small numbers of subjects.

Age related ranges for blood are from Reference 9 a study of 19 women in Australia with samples collected at the times shown.

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Clinical

Manganese is an essential trace element that is present in enzymes involved in carbohydrate, nitrogen, oxygen radical, glycosaminoglycan and cholesterol metabolism (1). Manganese superoxide dismutase (MnSOD) is the principal SOD antioxidant in human mitochondria and catalyses the conversion of the superoxide anion to hydrogen peroxide (2).

The recommended daily allowance for Mn has not been established but adequate intake levels have been derived by observation of apparently healthy individuals (3).

	Oral/Enteral (mg/day)	Parenteral (mg/day)
Adults >19 years	M 2.3 / F 1.8	0.06 – 0.1 (all adults)
Pregnant	2.0	
Lactating	2.6	
0-6 months	0.003	1 µg/kg/day (max 50 µg/day) (all children)
7-12 months	0.6	
1-3 years	1.2	
4-8 years	1.5	
9-13 years	M 1.9 / F 1.6	
14-18 years	M 2.2 / F 1.6	

Rich sources of manganese include whole grains, nuts, vegetables and black tea. It is present in some health supplements marketed to promote bone, joint and connective tissue health. Oral manganese is poorly absorbed with less than 5% of the manganese present in a meal being absorbed. Manganese and ferrous (Fe2+) iron are both absorbed in the GI tract by the DMT-1 pathway. Manganese absorption is increased during iron deficiency which can lead to increased whole blood manganese concentrations (4,5). Manganese homeostasis is thought to be maintained by regulation of absorption and biliary excretion.

Deficiency

Patients on long term total parenteral nutrition (TPN) require manganese either as a supplement or as a contaminant PN fluids however manganese deficiency in this patient group is not thought to be a problem. Dietary manganese deficiency in experimental animals resulted in impaired insulin production, lipoprotein metabolism, anti-oxidant defence mechanisms and perturbations in growth factor metabolism. Deficiency during early animal development has produced severe skeletal abnormalities and irreversible ataxia (7). In humans, experiments using manganese deficient diets have demonstrated mildly abnormal glucose tolerance in young women (8) and a fleeting dermatitis with reduced cholesterol concentrations in male subjects (9). An epidemiological study linked low blood manganese levels with Perthes' disease in children in Liverpool, UK (10). Low whole blood manganese has also been associated with epilepsy although patients whose epilepsy was caused by trauma have shown significantly higher blood manganese concentrations (11). Epileptic syndromes have also been reported in cases of manganese intoxication (12).

Toxicity

The body is protected against manganese toxicity primarily by low absorption and/or rapid presystemic elimination of manganese by the liver. Manganese intoxication resulting in a neurotoxic syndrome often referred to as manganism may occur from industrial exposure to the metal or as a complication of TPN particularly in patients with hepatobiliary disease.

Manganese neurotoxicity in industrial workers was first described in 1837 in Scottish workers exposed to high levels of dust while grinding manganese oxide (13). The symptoms of muscle weakness, tremor, bent posture, whispered speech and excess salivation were later recognised as being similar to those found in Parkinson's disease. Manganese intoxication may also produce behavioural problems including nervousness, hallucinations, memory loss, cognitive problems, bizarre behaviour and flight of ideas (14,15). Occupational exposure today occurs mainly in mining, alloy production, processing, ferro-manganese operations, welding and work with agrochemicals. The psychiatric and extrapyramidal motor dysfunction associated with manganese toxicity result from focal injury to the basal ganglia and are irreversible. Manganese toxicity should be considered in the differential diagnosis of Parkinson's disease in occupationally exposed subjects.

Parenteral nutrition bypasses the homeostatic mechanisms regulating manganese absorption and therefore patients on TPN are at risk of accumulating manganese particularly if cholestasis present. Neurological extrapyramidal symptoms and alterations of the basal ganglia signal intensity on brain magnetic resonance images (MRI) have been reported in patients receiving TPN (16). This is particularly the case when patients have cholestasis and/or small bowel resection (17). Many studies have related these neurological symptoms to high blood manganese levels and manganese deposition in the basal ganglia. Removal of manganese supplementation from patients receiving TPN has been shown to improve neurological symptoms related to manganese (18). It is currently recommended that parenteral manganese should be reduced or withheld where there is significant cholestasis, elevated blood manganese concentrations, or symptoms/signs of manganese toxicity (3).

A genetic predisposition to manganese accumulation in the liver and basal ganglia has been described. This treatable condition is due to mutation of the human manganese transporter SLC30A10 (19).

Pregnancy/Neonate

Whole blood manganese concentrations have been shown to increase throughout pregnancy. Concentrations are high in the neonate and decline rapidly in the first few weeks of life (20).

Laboratory Indices

NICE and ASPEN recommend measuring whole blood manganese in patients on long term TPN (3,21). There is debate as to whether whole blood or serum is best for assessing manganese status. Plasma manganese is more prone to contamination than whole blood due to the low concentrations. Blood

samples may be contaminated if taken via a stainless steel needle and ideally a plastic cannula should be used or the first few millilitres of blood discarded. Blood collection tubes that are not certified trace-element free may contain significant quantities of manganese. Urine manganese may be useful in the investigation of subjects with occupational exposure.

Clinical indications for testing:

1. Occupational exposure
2. Patients receiving long term TPN (>3 months)
3. Unexplained neurological disorders particularly if Parkinsonium features are present.

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