

Magnesium Guidelines for Use in Adults (2016).

These guidelines relate purely to the correction of acute hyper/hypomagnesaemia. For other indications, please refer to the specific Trust guidelines (e.g. oncology, cardiology, pre-eclampsia, re-feeding syndrome).

Background

Magnesium is an abundant cation in the body and is important for many functions including metabolism, ATPase functions, protein and fatty acid synthesis¹. An average adult will have approximately 1000mmol (24g) of magnesium, 99% of which is stored intracellularly (85% in bone, the rest in muscle and soft tissues). Up to 70% of plasma magnesium exists in the physiologically active (free) ionised form. The rest is protein-bound². Albumin deficiency states may therefore affect extracellular magnesium levels. Serum magnesium may not be an accurate reflection of total body magnesium as only 1% is contained in the extracellular fluid.

HYPOMAGNESAEMIA

Normal Reference range at CHFT is 0.7-1.0 mmol/L. Deficiencies can be subdivided as follows:

- Mild: 0.5-0.7 mmol/L - - - Unlikely to be symptomatic
- Moderate: 0.4-0.49 mmol/L
- Severe: <0.4 mmol/L

Causes of Hypomagnesaemia

There are several possible causes: inadequate magnesium intake, increased gastrointestinal and renal loss, certain drugs or redistribution from extracellular to intracellular space². Extra-renal and renal causes may be distinguished by 24 hour urinary magnesium excretion. <0.5mmol/day indicates a normal renal response, whereas >1.0mmol/day indicates an abnormal renal loss.

Causes of hypomagnesaemia (not exhaustive)¹:

Extra-renal		Renal	
Gastrointestinal	<ul style="list-style-type: none"> • Diarrhoea/steatorrhoea • Alcoholism • IBD • Vomiting • Chronic pancreatitis • Enteral nutrition • Magnesium-free IV infusions • Short bowel syndrome • Gastric suction 	Drugs	<ul style="list-style-type: none"> • Thiazide and loop diuretics • Cisplatin • Aminoglycosides • Amphotericin B • Calcineurin inhibitors e.g.ciclosporin, tacrolimus • Pentamidine • Alcohol • PPIs
Skin	<ul style="list-style-type: none"> • Burns 	Loop of Henle	<ul style="list-style-type: none"> • Hypercalcaemia
Bone	<ul style="list-style-type: none"> • “Hungry bone” syndrome 	Increased tubular flow	<ul style="list-style-type: none"> • Osmotic diuresis • Type I+II DM • Hyperaldosteronism • Volume expansion • Diabetic ketoacidosis
		Tubular dysfunction	<ul style="list-style-type: none"> • Recovery from acute tubular necrosis • Recovery from obstruction
		Congenital renal magnesium wasting	<ul style="list-style-type: none"> • Gitelman syndrome • Familial hypomagnesaemia with hypercalciuria and nephrocalcinosis (FHHNC)

Symptoms of Hypomagnesaemia

Symptoms are not usually manifested unless magnesium levels are less than 0.5mmol/L. Symptomatic depletion is often associated with several other biochemical abnormalities in particular hypokalaemia, hypocalcaemia and metabolic acidosis. Deficiency may be refractory until these are also corrected.

Symptoms of Hypomagnesaemia^{1,2}:

Early symptoms	Severe symptoms
Anorexia	Neuromuscular irritability At levels <0.4mmol/L may develop <ul style="list-style-type: none"> • tetany • seizures • drowsiness • confusion • coma
Nausea	Cardiovascular disturbances <ul style="list-style-type: none"> • arrhythmias
Vomiting	Metabolic disturbances <ul style="list-style-type: none"> • hypokalaemia (in 60% cases) • hypocalcaemia
Lethargy	
Weakness	

Treatment of Hypomagnesaemia

Cause should be investigated and treated if possible.

Magnesium equilibrates slowly within the intracellular compartments therefore slow correction over 3-5 days is recommended. Rapid IV infusion will result in rapid renal excretion as renal reabsorption of magnesium is dependent on plasma levels. If these rise sharply, then this will inhibit renal reabsorption and result in urinary loss of magnesium. Oral magnesium is poorly absorbed, so levels may take several days to rise with oral supplementation.

Standard dose for oral replacement is 24 mmol over 24 hours.

Caution in impaired renal function – magnesium may accumulate in these patients. Reduce dose by 25-50% and monitor carefully. In severe impairment, seek advice from renal team.

Mild-moderate deficiency 0.4-0.69mmol/L

Oral supplementation:	Magnesium aspartate sachets 10mmol 1 sachet up to three times a day
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Severe or symptomatic deficiency <0.4mmol/L

1g Magnesium sulphate = 4mmol Magnesium

Avoid parenteral magnesium in patients with heart block or myocardial damage³.

IV infusion⁴: (preferred method) Peripherally or centrally	<ul style="list-style-type: none"> • Up to 160mmol over 5 days may be required⁵ • Magnesium sulphate 20mmol (5g) in 250-500ml sodium chloride 0.9% over at least 2 hours (4-6 preferably) by peripheral or central route. • Peripheral infusion up to max concentration of 200mg/ml (0.8mmol/ml). • Max rate of administration of 150mg/min (0.6mmol/min).
IV bolus⁴: (urgent correction e.g. seizures, arrhythmias) Large peripheral vein or central line.	<ul style="list-style-type: none"> • 8mmol (2g) in at least 10ml sodium chloride 0.9% over 10-15mins • Max rate 10mg/kg/min • Monitor deep tendon reflexes at 15 mins and continuous ECG⁶
IM⁴: (only if no IV access and po unavailable) Magnesium sulphate 50%	<ul style="list-style-type: none"> • 1mmol/kg (250mg/kg) in divided doses over a 4 hour period. • May be used undiluted or diluted with equal volumes of sodium chloride 0.9% or glucose 5%

*See UCL Injectable medicines Administration Guide⁴

Side-Effects of Hypomagnesaemia:

Hypermagnesaemia, diarrhoea and hypersensitivity are possible. All are more likely in renal impairment.

Diarrhoea is a common side-effect of oral magnesium salts, and may be dose limiting. Administration with or after food may reduce this.

Hypermagnesaemia is unlikely to occur with oral therapy, except in renal impairment. See hypermagnesaemia for symptoms.

HYPERMAGNESAEMIA

Normal Reference range at CHFT is 0.7-1.0 mmol/L.

1.0-2.1 mmol	Typically asymptomatic
2.1-2.9 mmol	Lethargy, drowsiness, flushing, nausea and vomiting, decreased deep tendon reflexes
2.9-5.0 mmol	Somnolence, loss of deep tendon reflexes, hypotension, ECG changes
>5.0 mmol	Complete heart block, cardiac arrest, apnoea, paralysis, coma ¹

Causes of Hypermagnesaemia^{1,7} (not exhaustive)

- Renal impairment or metabolic disorders
- Excessive parenteral or oral supplementation (be aware of magnesium content of antacids and laxatives).
- Magnesium containing enemas and bowel cleansing preparation in renal impairment
- Reduced gastrointestinal transit time
- Damage to gastric epithelium may increase magnesium absorption
- Increased intracellular magnesium release (e.g. tumour lysis syndrome or rhabdomyolysis)
- Lithium toxicity
- Theophylline toxicity
- Acute rhabdomyolysis
- Familial hypocalcaemic hypercalcaemia
- Dialysis with high magnesium dialysate
- Trauma
- Diabetic ketoacidosis

Symptoms of Hypermagnesaemia³

Early Symptoms	Severe symptoms
Lethargy	Drowsiness
Flushing of skin	Loss of deep tendon reflexes
Nausea and vomiting	Hypotension due to peripheral vasodilation
Decreased tendon reflexes	Confusion
Thirst	Slurred speech
	Double vision
	Muscle weakness/paralysis
	Bradycardia/ECG changes
	Complete heart block
	Respiratory depression/Apnoea
	Coma
	Cardiac arrest

Treatment of Hypermagnesaemia⁷

Mild/asymptomatic: 2-4 mmol/L

Stop any magnesium supplements or salts.

Maintain good urine output.

Monitor after 24 hours. In renal impairment may need more intensive monitoring.

Severe/symptomatic: >4 mmol/L

- Stop any magnesium supplement or salts
- Consider 10mL Calcium gluconate 10% by slow IV over at least 5 mins.
- -This will antagonise neuromuscular and cardiovascular effects of magnesium.
- -Caution: renal impairment, hypercalcaemia and conditions related to hypercalcaemia e.g. some malignancies, or history of renal calculi.
IV calcium salts are irritant and can lead to extravasation
calcium salts may enhance cardiac effects of cardiac glycosides (digoxin)
risk of hypercalcaemia greater in those taking thiazide diuretics
- Monitor ECG continuously and check magnesium levels after 4 hours
- May require dialysis if magnesium levels not decreasing sufficiently. Discuss with renal team and biochemistry.
- Monitor other electrolytes and correct.

References:

1. J Wu, A.Carter. Abnormal Laboratory Results-Magnesium: the forgotten electrolyte. Australian Prescriber. Aug 2007: Vol 30; Num 4; p102-5.
2. Hypomagnesaemia. DTB March 2013: Vol 51; Num3; p33-6.
3. How is acute hypomagnesaemia treated in adults? UKMi. From the National Electronic Library for Medicines. www.nelm.nhs.uk. 22nd Dec 2010.
4. UCL Hospitals Injectable Medicines Administration Guide 3rd Edition. Wiley-Blackwell. 2010
5. British National Formulary 72. BMJ Group and Pharmaceutical Press. Sept 2016. www.bnf.org.
6. Low Magnesium. Pocket Electrolyte Guide. East Kent Hospitals University NHS Foundation Trust. April 2013.
7. How is acute hypermagnesaemia treated in adults? UKMi. From the National Electronic Library for Medicines. www.nelm.nhs.uk. 13th Sept 2011.