BMJ Best Practice

Assessment of magnesium deficiency

Straight to the point of care

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Summary

Magnesium deficiency is a state of decreased total body magnesium content. The human body contains 21-28 g of magnesium, the majority of which is localised in bone (>53%) and non-muscular tissue (approximately 19%). Hypomagnesaemia (low serum magnesium concentration) is generally defined as serum magnesium <0.75 mmol/L (<1.5 mEq/L).[1]

Serum magnesium level is a poor indicator of the total magnesium content and availability in the body, because only 1% of magnesium is found in the extracellular fluid. There is no simple, rapid, and accurate laboratory test to determine total body magnesium status in humans.[2]

Determination of urinary magnesium level provides an indirect assessment of whole body magnesium content, especially when the urinary value is compared with the serum level.[3]

Magnesium deficiency is usually detected because of the resultant hypomagnesaemia. However, it may also be revealed by the development of clinical symptoms, or associated hypokalaemia or hypocalcaemia.

- Calcium competes with magnesium for uptake in the loop of Henle, and an increase in the filtered calcium load can impair magnesium reabsorption. Hypomagnesaemia, in turn, leads to parathyroid hormone (PTH) resistance and a decrease in PTH secretion, both of which lead to hypocalcaemia.
- Hypokalaemia is commonly seen in patients with hypomagnesaemia, partly because the associated underlying disorders can produce both these disturbances. However, there is also evidence that hypomagnesaemia can lead to increased renal potassium wasting.

Patients with abnormalities of magnesium homoeostasis typically fall into one of three groups:

- Patients with magnesium deficiency (low total body magnesium content) and a resultant hypomagnesaemia (low serum magnesium concentration)
- Patients with hypomagnesaemia (low serum magnesium concentration) in the absence of magnesium deficiency (i.e., a normal total body magnesium content)
- Patients with magnesium deficiency (low total body magnesium content) but no evidence of hypomagnesaemia (i.e., a normal serum magnesium concentration).

Magnesium homoeostasis

About 60% of magnesium in the serum is free, whereas approximately 33% is bound to proteins, and <7% is bound to citrate, bicarbonate, ATP, and phosphate.[4]

Magnesium status is regulated by the intestines, which control absorption; the kidneys, which control excretion; and bone, which is the major storage site. Absorption and excretion are mediated by the selective magnesium channel TRPM6, whereas magnesium uptake and release from tissues outside the intestines and kidneys is controlled by TRPM7, which has an approximately 60% homology to TRPM6.[5][6]

- Absorption: magnesium absorption is a saturable process that occurs throughout the small and large intestines, with most of the absorption taking place in the colon. The average daily intake of magnesium is approximately 320 mg in men, and 240 mg in women; approximately two-thirds of this amount is eliminated with the faeces, while one third is absorbed and passed into the circulation.[7] Magnesium regulates the expression of TRPM6; a sustained fall in magnesium level results in increased expression, and increased magnesium absorption.[8] [9]

- Excretion and reabsorption: the major site of reabsorption is the loop of Henle, although additional reabsorption takes place in the distal convoluted tubule.[10] Approximately 2400 mg/day of magnesium passes through the kidneys, <5% of which is eventually excreted. Because magnesium regulates the expression of TRPM6, a sustained fall in magnesium level results in increased magnesium reabsorption.[8]
- Although there is no direct hormonal control of magnesium absorption, excretion, and reabsorption, TRPM6 expression appears to be under oestrogen modulation.

There is normally very little exchange between intracellular and extracellular magnesium. In the acute phase of a fall in magnesium content, intestinal absorption and renal reabsorption both increase. Hormones such as glucagon, catecholamines, and PTH can mobilise magnesium from bone and other tissues.[11] Magnesium, in turn, exhibits negative feedback on catecholamine release. Conversely, hormones such as insulin, antidiuretic hormone (ADH), and thyroid hormone promote magnesium uptake and storage.[11]

Cellular functions of magnesium

Magnesium is a predominantly intracellular ion and is distributed between the nucleus, endoplasmic or sarcoplasmic reticulum, mitochondria, and cytoplasm.[12] Approximately 200 enzymes involved in cellular metabolism and the cell cycle require magnesium as a co-factor, including adenyl cyclase and ATPases. Magnesium is also an important co-factor for potassium and calcium channels, and therefore plays a role in regulating action potentials in cardiac and neural tissues, as well as calcium signalling in a wide range of tissues.[13]

Recommended dietary allowance for magnesium

The recommended dietary allowance for magnesium varies according to age and sex as follows:[1]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	30 mg*	30 mg*		
7-12 months	75 mg*	75 mg*		
1-3 years	80 mg	80 mg		
4-8 years	130 mg	130 mg		
9-13 years	240 mg	240 mg		
14-18 years	410 mg	360 mg	400 mg	360 mg
19-30 years	400 mg	310 mg	350 mg	310 mg
31-50 years	420 mg	320 mg	360 mg	320 mg
51+ years	420 mg	320 mg		

*Adequate Intake (AI)

Recommended Dietary Allowances (RDAs) for Magnesium

Table used with permission from the U.S. Department of Health and Human Services, National Institutes of Health. Original source for figures: Institute of Medicine (IOM). Food and Nutrition Board. Dietary reference intakes: calcium, phosphorus, magnesium, vitamin D and fluoride. Washington, DC: National Academy Press, 1997.

Aetiology

Magnesium deficiency can be caused by decreased magnesium intake from the diet, decreased magnesium absorption, or increased renal magnesium excretion (renal magnesium wasting). Deficiency may result in an associated hypomagnesaemia, which depends on the severity of the magnesium loss and the effectiveness of the compensatory homoeostatic responses. Hypomagnesaemia without magnesium deficiency can be caused by modest acute magnesium losses that deplete circulating magnesium, or by redistribution of extracellular magnesium to the intracellular compartment.

Nutritional

Dietary magnesium deficiency

- Dietary deficiency is the most common cause. Dietary sources of magnesium include green vegetables, fruits, fish, fresh meat, and cereals.[14] Magnesium dietary intake in the US has been decreasing, most likely due to the increasing use of processed foods and fertilisers.[15]
- Diabetic patients with poor magnesium intake are prone to hypomagnesaemia.

Malnutrition

- Magnesium deficiency can also occur in generalised malnutrition, especially in patients with alcoholism, or those with decreased food intake in the prolonged postoperative state.

Toxic/iatrogenic

Drug-induced[16] [17]

- Medications can induce renal magnesium wasting. Thiazide diuretics inhibit the sodium-chloride co-transporter, decreasing the voltage gradient that drives magnesium reabsorption. Other diuretics increase magnesium loss by increasing tubular flow.
- Proton pump inhibitors (PPIs) reduce intestinal magnesium absorption through TRPM6 and produce renal magnesium wasting by an unknown mechanism.[18] [19] The incidence of severe hypomagnesaemia associated with PPI use is increasing. The US FDA has issued a warning about this iatrogenic complication. Serum magnesium level should be carefully monitored in patients taking a PPI in conjunction with anti-arrhythmic drugs.[20]
- Digitalis increases intracellular sodium and calcium levels, with a resultant displacement and loss of magnesium.
- Ciclosporin (cyclosporine) and cisplatin impair renal reabsorption, and promote renal excretion of magnesium.[21] [22]
- Cetuximab inhibits the extracellular growth factor receptor (EGFR), which controls magnesium channels.[21]
- Antibiotics such as aminoglycosides, gentamicin, and tobramycin inhibit renal reabsorption in the loop of Henle.
- Insulin causes increased intracellular uptake of magnesium, and can therefore produce hypomagnesaemia.[17]

Alcohol misuse[17] [23]

- Magnesium deficiency is due partly to alcohol-induced osmotic diuresis, leading to renal magnesium wasting, and partly to associated malnutrition.

Other causes

- Laxative abuse increases the production and loss of gastrointestinal (GI) secretions, which contain large amounts of magnesium.[17] Volume expansion due to intavenous fluids impairs passive magnesium transport, leading to renal magnesium wasting.[24]

Gastrointestinal

Secretory diarrhoea

- Upper GI secretions contain 0.5 mmol/L (1 mEq/L) magnesium, and lower GI secretions contain 7.5 mmol/L (15 mEq/L) magnesium. Any condition that significantly increases GI secretions can produce excessive magnesium loss. Common examples include gastroenteritis (due to any cause), inflammatory bowel disease, GI cancers, and Whipple's disease.[24] [25]

Malabsorption syndromes

- Magnesium absorption occurs in the ileum; it can be decreased by malabsorption syndromes such as coeliac disease, or by short gut syndrome produced by extensive bowel resection or radiation enteritis.[24]

Pancreatitis

- The aetiology of magnesium loss is multifactorial. Acute pancreatitis causes hypomagnesaemia by increasing magnesium and calcium deposition into areas of fat necrosis. In chronic pancreatitis, patients may develop a malabsorption syndrome, leading to magnesium deficiency.[26] In addition, some magnesium loss may occur due to increased magnesium level in pancreatic secretions.

Cirrhosis[27]

- In the liver, cirrhosis produces volume expansion, which impairs passive magnesium transport, leading to renal and faecal magnesium wasting.

Endocrine

Diabetic ketoacidosis

- Osmotic diuresis, which occurs in diabetic ketoacidosis, leads to renal magnesium wasting.
- Insulin therapy given to treat diabetic ketoacidosis also produces hypomagnesaemia, by causing a shift of magnesium into the intracellular compartment.[17] [24]

Hyperaldosteronism[28]

- Elevated aldosterone level increases sodium retention by the kidneys, leading to an expansion of intravascular volume. This, in turn, impairs passive magnesium transport, leading to renal magnesium wasting.

Hypoparathyroidism

- Decreased parathyroid hormone (PTH) level leads to decreased mobilisation of magnesium from bone, producing hypomagnesaemia, as well as to renal magnesium wasting, which results in magnesium deficiency. Hypomagnesaemia, in turn, can cause PTH resistance and decreased PTH secretion.[29]

Hyperthyroidism[30]

- Increased thyroid hormone level produces renal magnesium wasting, leading to magnesium deficiency and hypomagnesaemia. The hypomagnesaemia is exacerbated by concurrent stimulation of magnesium uptake into cells.

Hungry bone syndrome[24]

- Hyperparathyroidism and hyperthyroidism produce an increase in bone turnover. When PTH or thyroid hormone levels are rapidly normalised following a parathyroidectomy or a thyroidectomy, osteoclast activity normalises faster than osteoblast activity. This leads to a net uptake of calcium, phosphate, and magnesium into bone, which can cause severe hypomagnesaemia and hypocalcaemia.

Renal

Recovery phase of acute tubular necrosis[24]

- Acute tubular necrosis is caused by ischaemic or nephrotoxic injury to renal tubular epithelial cells, which results in cell death or detachment from the basement membrane.
- The pathogenesis has three stages. The initiation phase involves an acute decrease in glomerular filtration, produced by worsening injury. The maintenance phase is a period of established renal injury associated with renal failure. During the recovery phase, the injury is repaired and renal function recovers; the diuresis that occurs during this phase can produce magnesium wasting.

Renal tubular acidosis

- Includes a range of disorders in which the excretion of fixed acid (in distal disease) or the reabsorption of filtered bicarbonate (in proximal disease) is impaired, to a degree disproportionate to any existing impairment of glomerular filtration rate. The acid retention or bicarbonate loss results in the development of hyperchloraemic metabolic acidosis.
- Magnesium wasting occurs because of increased renal flow, loss of the voltage gradient that drives magnesium re-uptake, or direct toxic damage to the kidney.

Post-obstructive diuresis

- Patients with obstructive uropathy develop diuresis once the obstruction is relieved, as a physiological response to volume expansion, and local accumulation of solutes in the obstructed kidney. The condition can cause magnesium wasting. The diuresis typically resolves once homoeostasis is achieved, but may progress to a pathological form.

Primary renal magnesium wasting

- Encompasses a range of genetic conditions in which there is a loss of function of magnesium channels, their regulatory receptors, or the transporters that generate the voltage gradient to drive magnesium reabsorption. These conditions may be caused by mutations in TRPM6, claudins, renal

Na/K-ATPase, thiazide-sensitive sodium-chloride co-transporter (Gitelman's syndrome and Bartter's syndrome), or the calcium sensing receptor.[5] [31] [32] [33] [34] [35][36]

Obstetric

Pregnancy

- Produces an expansion in plasma volume and an increase in magnesium demand, which can lead to hypomagnesaemia if magnesium intake is not increased. Hypomagnesaemia is associated with premature labour.[37]

Pre-eclampsia

- Patients with pre-eclampsia and eclampsia have lower serum magnesium levels than normal pregnant patients.[38] [39] It is not known whether hypomagnesaemia is a cause or a consequence of this condition.

Urgent considerations

(See Differentials for more details)

Hypomagnesaemia

Generally defined as serum magnesium <0.75 mmol/L (<1.5 mEq/L).

Severe magnesium deficiency

Patients with severe magnesium depletion (<0.5 mmol/L [<1 mEq/L]) are symptomatic.[40] Symptoms include hallucinations, seizures, muscle spasms, swallowing difficulty or inability (spasms of oesophageal muscles), and irregular heart beats. The condition can be life-threatening due to recurring seizures or irregular heart beats that can progress towards arrhythmias, extrasystoles, torsades de pointes, ventricular tachycardia, or ventricular fibrillation.

Intravenous magnesium replacement is indicated if the serum magnesium is <0.5 mmol/L (<1 mEq/L), or if the patient is symptomatic.[40] Local protocols should be consulted and followed. Higher infusion rates may be required in emergencies (e.g., seizures). The underlying cause should also be treated.

Mild magnesium deficiency

Patients with mild magnesium depletion (serum magnesium 1-1.5 mEq/L) are usually asymptomatic and can be managed with oral magnesium replacement.[40] Local dosing recommendations may vary and should be followed.

Cardiac arrhythmias

Magnesium depletion produces characteristic changes in the ECG. Modest depletion causes widening of the QRS complex, with resultant prolongation of the QT interval, and peaking of T waves. If the depletion worsens, the QRS complex continues to widen, prolongation of the PR interval occurs, and the T wave is diminished.[41] Ventricular arrhythmias result, usually in patients with concurrent ischaemic heart disease; these include ventricular extrasystolic beats, ventricular tachycardia (particularly torsades de pointes), and ventricular fibrillation. It is not clear whether these arrhythmias are due to hypomagnesaemia, associated hypokalaemia, or both.

Patients with ECG changes require oral magnesium replacement. Patients with arrhythmias require intravenous magnesium sulfate. Local protocols for adult dosing may vary and should be consulted. Specialist advice should be sought for dosing in children. Patients with a sustained ventricular tachycardia that does not respond to initial therapy require cardioversion. Defibrillation is required in cases of ventricular fibrillation, in accordance with advanced life support algorithms. See Sustained ventricular tachycardias and Cardiac arrest .

Prolonged QT intervals are often observed in severe hypomagnesaemia. Prolonged QT intervals due to inherited channelopathies can be complicated or aggravated by underlying hypomagnesaemia, especially if severe.[42] Restoration of proper serum magnesium level by oral supplementation for mild hypomagnesaemia or with intravenous magnesium for severe hypomagnesaemia is recommended to attenuate incidence of prolonged QT intervals and prevent occurrence of torsades de pointes.

Eclampsia

Eclampsia is characterised by the occurrence of seizures in a patient with pre-eclampsia in the absence of any other identified cause. Eclampsia is treated with intravenous magnesium sulfate.[14] Local protocols may vary and should be consulted. Any woman who presents with seizures in pregnancy requires immediate treatment, even if the diagnosis is not yet established. The diagnosis is confirmed by the presence of hypertension and proteinuria, and exclusion of other causes of seizures. See Pre-eclampsia (Management) .

Diabetic ketoacidosis

An acute and potentially fatal metabolic complication of diabetes mellitus caused by absolute insulin deficiency. Symptoms usually develop rapidly over one day or less, and include polyuria, polydipsia, weakness, weight loss, nausea, vomiting, and occasionally abdominal pain. Signs of volume depletion, Kussmaul's respiration, and acetone breath are also present. Ketoacidosis is often precipitated by suboptimal insulin therapy or an acute medical illness in people with known diabetes, but is also a common first presentation of type 1 diabetes mellitus. Treatment involves immediate fluid replacement and intravenous insulin.[43] Potassium, phosphate, magnesium, and bicarbonate may also be required, depending on the degree of electrolyte and acid-base disturbance that is present. See Diabetic ketoacidosis (Management) .

Metabolic alkalosis

Some causes of hypomagnesaemia, such as renal disease, chronic diuretic use, or hyperaldosteronism, may produce a concomitant severe metabolic alkalosis (arterial pH >7.6). Rapid reduction of arterial pH can be achieved by controlled hypoventilation, sedation, and mechanical ventilation. Volume depletion should be corrected with normal saline, and associated electrolyte abnormalities should be corrected. If normal saline is contraindicated (due to volume overload or severe renal failure), hydrogen chloride (HCl) or ammonium chloride can be used to correct the alkalosis. However, these treatments carry a high risk of complications (haemolysis and tissue necrosis with HCl, and ammonia toxicity with ammonium chloride). If a diuretic is suspected as the cause, the dose should be reduced, or the drug discontinued. Hyperaldosteronism requires treatment with spironolactone and/or resection of the aldosterone-secreting tumour.

Refractory hypocalcaemia

Hypocalcaemia in the presence of hypomagnesaemia will not resolve unless the magnesium level is normalised. Appropriate magnesium supplementation should be given. Normomagnesaemic magnesium deficiency should always be considered as a cause of refractory hypocalcaemia; a therapeutic trial of magnesium supplementation improves calcium level in this condition.

Refractory hypokalaemia

Hypokalaemia in the presence of hypomagnesaemia will not resolve unless the magnesium level is normalised. Appropriate magnesium supplementation should be given. Normomagnesaemic magnesium deficiency should always be considered as a cause of refractory hypokalaemia; a therapeutic trial of magnesium supplementation improves potassium levels in this condition.

Approach

Magnesium deficiency is a state of decreased total body magnesium content. Only 1% of the total body magnesium is located in the extracellular fluid; hence, the serum magnesium level is a poor indicator of total body magnesium content and availability. A serum magnesium <0.75 mmol/L (<1.5 mEq/L) is termed hypomagnesaemia.[1]

Patients with abnormalities of magnesium homoeostasis typically fall into one of three groups:

- Patients with magnesium deficiency (low total body magnesium content) and a resultant hypomagnesaemia (low serum magnesium concentration)
- Patients with hypomagnesaemia (low serum magnesium concentration) in the absence of magnesium deficiency (i.e., a normal total body magnesium content)
- Patients with magnesium deficiency (low total body magnesium content) but no evidence of hypomagnesaemia (i.e., a normal serum magnesium concentration).

Magnesium deficiency should be suspected in patients with a relevant chronic disease causing abnormalities in magnesium homoeostasis, symptoms of magnesium deficiency, or persistent associated electrolyte abnormalities such as hypocalcaemia or hypokalaemia.[4] [44] However, often it may only be detected following a blood test.

Clinical features of magnesium deficiency and/or hypomagnesaemia

Most patients with mild magnesium deficiency and/or hypomagnesaemia are asymptomatic. Although symptoms tend to appear once the serum magnesium falls below 0.5 mmol/L (1 mEq/L), there is no direct correlation between serum magnesium and the severity of the symptoms.

The symptoms are non-specific and include:

- Neuromuscular irritability similar to that produced by hypocalcaemia, manifesting with extensor plantar reflexes, positive Trusseau's and Chvostek's signs, and, in severe cases, tetany; hypoparathyroidism should be considered if these signs are present
- Cardiovascular features such as rapid heartbeats and an increased blood pressure, tachycardia, and/or ventricular arrhythmias[14]
- CNS symptoms of vertigo, ataxia, depression, and seizure activity.

Elucidating the cause

Malnutrition

- General inspection may reveal signs of generalised malnutrition, including loss of subcutaneous fat, apathy and lethargy, pallor, depigmentation, enlarged abdomen, winged scapula, flaky skin, and bipedal oedema. Food deprivation, a malabsorption syndrome, neglect, an eating disorder with consumption of a diet low in magnesium, or decreased food intake due to a prolonged postoperative course should be considered.
- Signs of specific vitamin and mineral deficiencies may also be noted, and suggest reduced intake or a malabsorption syndrome.

- Increased prominence of superficial cutaneous vasculature, peripheral neuropathy, alterations in normal dentition, and halitosis suggest alcohol abuse.
- Magnesium malabsorption should be considered if there is a history suggestive of coeliac disease or short gut syndrome. Both conditions may also present with symptoms and signs of associated vitamin deficiencies or chronic diarrhoea. A skin rash consistent with dermatitis herpetiformis suggests coeliac disease. A history of extensive bowel resection, abdominal radiation injury, or gastroschisis suggests short gut syndrome.

Pregnancy

- Should prompt suspicion as the cause of magnesium deficiency, due to increased magnesium demand and volume status. Pre-eclampsia should also be considered and excluded. Seizures in a pregnant woman should prompt suspicion of eclampsia.

Volume depletion

- Diarrhoea results in gastrointestinal magnesium loss. Causes to consider include gastroenteritis, inflammatory bowel disease, and Whipple's disease. Tenesmus should prompt suspicion of inflammatory bowel disease. A travel history should be obtained to assess traveller's diarrhoea. A history of laxative abuse should be sought.
- Abdominal tenderness with distension may indicate gastroenteritis or laxative abuse. Tenderness without distension may indicate inflammatory bowel disease or pancreatitis (which typically produces epigastric tenderness). Patients with acute pancreatitis have a history of epigastric pain, fever, tachycardia with a prior history of cholelithiasis, or high alcohol intake. Patients with chronic pancreatitis usually have a history of alcohol abuse, with epigastric abdominal pain radiating to the back, steatorrhoea, malnutrition, and associated diabetes mellitus.
- Acute-onset polyuria, polydipsia, weakness, weight loss, nausea, vomiting, or abdominal pain should prompt suspicion of diabetic ketoacidosis. A history of an associated acute medical illness or suboptimal insulin therapy may also be present.
- Most patients with renal disease do not have symptoms related to magnesium abnormalities. However, patients in the recovery phase of acute tubular necrosis develop diuresis that may lead to magnesium deficiency and/or hypomagnesaemia. A history of hypotension, fluid depletion, or exposure to nephrotoxic agents may be present. There may be a history of renal tubular acidosis, or of recent relief of an obstructive uropathy, leading to post-obstructive diuresis.

Signs of hypervolaemia

- These include jugular venous distension and peripheral oedema, and may indicate hyperaldosteronism, cirrhosis, or obstructive uropathy.
- Hypervolaemia, polyuria, and polydipsia in association with paraesthesia, headache, and muscular weakness may indicate hyperaldosteronism.
- Jaundice, ascites, hepatomegaly, or small liver suggest liver disease. The patient may have a known history of cirrhosis.
- There may be a history of excessive administration of intravenous fluids.

Weight loss

- A history of increased appetite, weight loss, heat intolerance, and hair loss should prompt suspicion of hyperthyroidism. Examination may reveal a fine tremor, goitre, and exophthalmos.

- If the patient has had a recent parathyroidectomy for hyperparathyroidism, or a thyroidectomy for hyperthyroidism, hungry bone syndrome should be considered. Hungry bone syndrome is usually asymptomatic, but may present with bone pain.

Primary renal magnesium wasting is rare, but should be suspected if there is a positive family history with symptoms of polyuria, polydipsia, and/or volume depletion. Associated growth retardation with severe cramps involving the arms and legs should prompt suspicion of Gitelman's syndrome. Associated growth and developmental delay, with or without sensorineural deafness, should prompt suspicion of Bartter's syndrome.

Initial investigations

Serum magnesium

- Assessment of serum magnesium level can be routinely conducted in medical clinical laboratories.[45] However, there is no simple, rapid, and accurate laboratory test to determine total body magnesium status in humans.[2] Hypomagnesaemia is generally defined as a serum magnesium <0.75 mmol/L (<1.5 mEq/L).[1]
- A low serum magnesium level may be due to underlying magnesium deficiency, magnesium redistribution, or modest acute losses that deplete circulating magnesium, without affecting magnesium stores. A normal serum magnesium level does not exclude magnesium deficiency.
- Intracellular magnesium determination: assessment of total and free intracellular magnesium contents can be useful to determine the possibility of tissue magnesium deficiency, and should be considered. As the determination is labourious and time-consuming, and prone to possible misinterpretation depending on the procedure used, this type of determination is not commonly performed as it requires specialised lab settings.

Serum calcium, potassium, and sodium

- Abnormalities in magnesium homoeostasis may co-exist with other electrolyte abnormalities. Magnesium deficiency and hypomagnesaemia should be considered as causes of hypocalcaemia or refractory hypokalaemia.
- Symptoms of hypomagnesaemia and hypocalcaemia are similar, and the two abnormalities may co-exist. Calcium competes with magnesium for uptake in the loop of Henle, and an increase in the filtered calcium load can impair magnesium reabsorption. Hypomagnesaemia, in turn, leads to parathyroid hormone (PTH) resistance and a decrease in PTH secretion, both of which result in hypocalcaemia.
- Hypokalaemia is commonly seen in patients with hypomagnesaemia, partly because the associated underlying disorders can produce both these disturbances. However, there is also evidence that hypomagnesaemia can lead to increased renal potassium wasting.
- Hypernatraemia may be present if hyperaldosteronism is the cause. Increased aldosterone level increases sodium retention by the kidneys. This leads to an expansion of intravascular volume, which impairs passive magnesium transport, resulting in renal magnesium wasting.

Urinary magnesium

- Indicated to identify renal magnesium wasting or as a test for magnesium deficiency in patients with a normal serum magnesium.
- Magnesium depletion in patients with a normal serum magnesium should be considered in patients with unexplained hypocalcaemia or hypokalaemia and a history consistent with magnesium loss.[41] The best test to diagnose this syndrome is not, as yet, clear.

- Decreased 24-hour urinary magnesium excretion, or decreased excretion following an infused magnesium load, may indicate extrarenal magnesium losses. However, these parameters are not specific.[45]

Therapeutic trial of magnesium supplementation

- This should be considered in patients with unexplained or refractory hypocalcaemia or hypokalaemia.[41] Magnesium supplementation may produce resolution of hypokalaemia or hypocalcaemia.[41]

ECG

- All patients require an ECG to search for characteristic changes associated with hypomagnesaemia. These include widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, and prolonged PR interval.[41] A sinus tachycardia, ventricular extrasystolic beats, or ventricular tachycardias (especially torsades de pointes) may also be detected.

Subsequent investigations and identification of cause

The following procedures may point to possible diagnoses.

- A trial of discontinuation of causative medications may produce resolution of symptoms and hypomagnesaemia.
- A diagnostic interview may help identify alcohol dependence. The alcohol level (breath and blood) may be elevated.
- Stool culture and examination is required if clinical features suggest infective diarrhoea due to a non-viral cause. The underlying organism may be detected in bacterial infection, and parasites or ova may be detected in parasitic infections.
- Serum urea and creatinine may be elevated in patients with renal disease. A urea:creatinine ratio of ≥10, with a fractional excretion of sodium and chloride >2%, suggests acute tubular necrosis (ATN). Urinalysis for sediment reveals tubular epithelial cells, epithelial cell casts, or muddy brown casts in ATN.
- Urinalysis should be performed in pregnant patients. Proteinuria >300 mg per 24 hours (suggested by 1+ proteinuria on dipstick), in association with hypertension, is diagnostic of pre-eclampsia.
- Patients with suspected diabetic ketoacidosis require measurement of serum sodium, potassium, magnesium, calcium, and glucose. Serum magnesium, sodium, and calcium are decreased. Serum potassium is elevated, but the total body potassium is usually depleted. Plasma glucose is elevated, and urine ketones are positive. ABG reveals a metabolic acidosis, with a pH ranging from 7 to 7.3 and a bicarbonate level ranging from 10 to 15 mmol/L (10 to 15 mEq/L).
- Serum iron or vitamins A, B1, B2, B6, B12, C, D, and E may be decreased in malabsorption syndromes. An elevated INR suggests vitamin K deficiency. An immunoglobulin A-tissue transglutaminase (IgA-tTG) test should be performed if coeliac disease is suspected. A small bowel biopsy can be performed if the results of this test are equivocal. Colonoscopy and oesophagogastroduodenoscopy should be performed to define intestinal anatomy, length, and health of remaining bowel in patients with short gut syndrome.
- Elevation of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) with an ALT:AST ratio ≥1 indicates hepatocellular damage in patients with cirrhosis. Alkaline phosphatase and gamma-GT are elevated in cirrhotic patients with cholestasis. Abdominal ultrasound can be considered to assess liver damage and portal circulation. A liver biopsy may also be helpful.

- Serum amylase and lipase are elevated in acute pancreatitis. Use serum lipase testing in preference to serum amylase.[46] Serum lipase and amylase have similar sensitivity and specificity, but lipase levels remain elevated for longer (up to 14 days after symptom onset vs. 5 days for amylase), providing a higher likelihood of picking up the diagnosis in patients with a delayed presentation.[47]
- Abdominal computed tomographic (CT) scan can be performed if chronic pancreatitis is suspected, and reveals characteristic signs. Direct pancreatic function tests can be considered, and show decreased function in chronic pancreatitis.
- Elevated erythrocyte sedimentation rate may indicate inflammatory bowel disease. Stool testing for faecal occult blood is often positive, and faecal leukocytes are also present. Colonoscopy should be considered, and reveals the characteristic abnormalities and distribution pattern of the underlying cause.

Tests for the rarer causes are only performed if clinical features suggest the diagnosis. These include the following procedures.

- Upper gastrointestinal endoscopy, with or without small bowel biopsy, should be considered to diagnose Whipple's disease.
- An elevated serum aldosterone level indicates hyperaldosteronism. Low serum renin activity indicates primary disease, whereas increased activity indicates secondary disease. CT or magnetic resonance imaging (MRI) of adrenal glands may detect a macroadenoma.
- A decreased or undetectable PTH level in the presence of hypocalcaemia indicates hypoparathyroidism. Vitamin D level should be considered if the alternative diagnosis of vitamin D deficiency is suspected.
- A decreased thyroid-stimulating hormone (TSH) level with elevated serum free T4 indicates hyperthyroidism. Radioactive iodine intake should also be performed; it is elevated in Graves' disease, normal in toxic multinodular goitre, and decreased in acute or subacute thyroiditis. Positive TSH-receptor antibodies are diagnostic of Graves' disease, but are rarely required for diagnosis.
- Decreased serum phosphate, in combination with low magnesium and calcium levels, may indicate hungry bone syndrome. Bone biopsy reveals extensive bone remineralisation.
- Decreased serum bicarbonate with increased serum chloride suggests renal tubular acidosis (RTA). The serum potassium is decreased in proximal and classic distal RTA, but increased in hyperkalaemic distal RTA.
- Genetic testing reveals the underlying causative mutations of primary renal magnesium wasting.

Differentials overview

Common
Malnutrition
Isolated dietary magnesium deficiency
Drug-induced
Alcohol misuse
Laxative abuse
Crohn's disease
Gastroenteritis
Ulcerative colitis
Coeliac disease
Short gut syndrome
Diabetic ketoacidosis
Uncommon
Excess of intravenous fluids
Acute pancreatitis
Chronic pancreatitis
Whipple's disease
Cirrhosis
Hyperaldosteronism
Hypoparathyroidism
Hyperthyroidism
Hungry bone syndrome

Uncommon
Recovery phase of acute tubular necrosis
Renal tubular acidosis
Post-obstructive diuresis
Primary renal magnesium wasting
Pre-eclampsia
Pregnancy

Differentials

Common

◊ Malnutrition

History	Exam	1st Test	Other tests
protein calorie deprivation, malabsorption syndrome; neglect, history of an eating disorder	loss of subcutaneous fat, apathy and lethargy, pallor, depigmentation, enlarged abdomen, winged scapula, flaky skin, bipedal oedema	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**serum calcium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

◊ Isolated dietary magnesium deficiency

History	Exam	1st Test	Other tests
consumption of diet low in magnesium, decreased food intake in prolonged postoperative state	usually normal	»**serum magnesium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

◊ Drug-induced

History	Exam	1st Test	Other tests
use of known causative medications including thiazide diuretics, loop diuretics, proton pump inhibitors, digitalis, ciclosporin (cyclosporine), cisplatin, cetuximab, aminoglycosides, gentamicin, tobramycin, and insulin	normal	»**trial of discontinuation of causative medication:** resolution of hypomagnesaemia and symptoms »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** normal or increased

Common

◊ Alcohol misuse

History	Exam	1st Test	Other tests
history of chronic alcohol intake, CAGE questionnaire score >2	increased prominence of superficial cutaneous vasculature, peripheral neuropathy, alterations in normal dentition, and halitosis; possible signs of liver disease: hepatomegaly or small liver, jaundice, ascites	»**serum magnesium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**diagnostic interview:** diagnosis of alcohol dependence »**alcohol level (breath and blood):** elevated »**24-hour urinary magnesium:** elevated

◊ Laxative abuse

History	Exam	1st Test	Other tests
history of laxative abuse; loose stools, possible colicky abdominal pain, dizziness; history of eating disorder	abdominal distension and tenderness, lethargy; signs of volume depletion: decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** decreased

◊ Crohn's disease

History	Exam	1st Test	Other tests
abdominal pain, fever, weight loss; diarrhoea with or without blood; large volume of watery diarrhoea suggests small bowel involvement; frequent small bowel movements with tenesmus suggest colonic involvement	mild disease: normal; severe disease: signs of volume depletion (decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure), abdominal tenderness, perianal fistulas, perirectal abscess; extraintestinal manifestations affecting joints, eye, mucous membranes, and skin	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**erythrocyte sedimentation rate:** elevated »**CRP:** increased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval »**CT or MR enterography:** skip lesions, bowel wall	»**colonoscopy:** normal rectum, small discrete aphthous ulcer, serpiginous and linear ulcers, skip lesions (normal mucosa and areas of erythema), isolated terminal ileum involvement »**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

Common

◊ Crohn's disease

History	Exam	1st Test	Other tests
		thickening, surrounding inflammation, abscess, and fistulae	

◊ Gastroenteritis

History	Exam	1st Test	Other tests
diarrhoea with or without blood, nausea, vomiting, tenesmus and lower quadrant pain in lower gastrointestinal (GI) infection; periumbilical pain in upper GI infection; history of travel	fever, abdominal distension and tenderness, lethargy; signs of volume depletion: decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**stool culture and examination:** identification of causative organism in bacterial infection; parasites or ova seen in parasitic infection Only indicated if bacterial or parasitic infections are suspected. »**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

◊ Ulcerative colitis

History	Exam	1st Test	Other tests
bloody diarrhoea, rectal bleeding, abdominal pain, fever	mild disease: normal; severe disease: signs of volume depletion (decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure), abdominal tenderness; extraintestinal manifestations affecting joints, eye, mucous membranes, and skin	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**erythrocyte sedimentation rate:** normal or elevated »**CRP:** increased »**colonoscopy:** variable degree of inflamed mucosa »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or	»**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

Common

◊ Ulcerative colitis

History	Exam	1st Test	Other tests
		diminished T waves, prolonged PR interval	

◊ Coeliac disease

History	Exam	1st Test	Other tests
positive family history; unexplained gastrointestinal symptoms, chronic diarrhoea, unexplained iron deficiency anaemia or vitamin deficiency	skin rash consistent with dermatitis herpetiformis, signs of vitamin and mineral deficiencies	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**FBC:** microcytic anaemia due to iron deficiency »**immunoglobulin A-tissue transglutaminase (IgA-tTG) test:** positive »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**small bowel biopsy:** intraepithelial lymphocytes, villous atrophy, and crypt hyperplasia »**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

◊ Short gut syndrome

History	Exam	1st Test	Other tests
history of small bowel resection, colectomy, extensive abdominal radiation injury, or gastroschisis; fatigue, weight loss, diarrhoea	peripheral or pre-sacral oedema, signs of vitamin and mineral deficiencies; signs of volume depletion: decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**serum calcium:** normal or decreased »**vitamins A, B1, B2, B6, B12, C, D, and E:** decreased »**INR:** elevated in vitamin K deficiency »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or	»**oesophagogastroduodenoscopy and colonoscopy:** defines intestinal anatomy, length, and health of remaining bowel; excludes other pathologies »**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

Common

◊ Short gut syndrome

History	Exam	1st Test	Other tests
		diminished T waves, prolonged PR interval	

Diabetic ketoacidosis

History	Exam	1st Test	Other tests
acute-onset polyuria, polydipsia, weakness, weight loss, nausea, vomiting and occasionally abdominal pain; history of suboptimal insulin therapy or acute medical illness in a known diabetic patient	Kussmaul's respiration, acetone breath; signs of volume depletion: decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure	»**serum magnesium:** decreased »**serum potassium:** elevated »**serum sodium:** decreased »**serum calcium:** decreased »**plasma glucose:** elevated »**urine ketones:** positive »**ABG:** pH varies from 7 to 7.3; bicarbonate ranges from 10 to 15 mmol/L (10 to 15 mEq/L) »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**blood urine or sputum cultures:** positive in the presence of infection »**24-hour urinary magnesium:** increased

Uncommon

◊ Excess of intravenous fluids

History	Exam	1st Test	Other tests
history of intravenous fluid administration	normal	»**serum magnesium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or	»**24-hour urinary magnesium:** normal or increased

Uncommon

◊ Excess of intravenous fluids

History	Exam	1st Test	Other tests
		diminished T waves, prolonged PR interval	

Acute pancreatitis

History	Exam	1st Test	Other tests
epigastric pain, nausea, vomiting, prior history of cholelithiasis or high alcohol intake	epigastric tenderness, fever, and tachycardia	»**serum lipase or amylase:** elevated (three times the upper limit of normal) Use serum lipase testing in preference to serum amylase.[46] Serum lipase and amylase have similar sensitivity and specificity, but lipase levels remain elevated for longer (up to 14 days after symptom onset vs. 5 days for amylase), providing a higher likelihood of picking up the diagnosis in patients with a delayed presentation.[47] »**AST/ALT:** high; predicts gallstone disease as aetiology in 95% of cases »**FBC:** high WBC »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased »**abdominal ultrasound:** may see ascites, gallstones, dilated common bile duct, and enlarged pancreas Abdominal imaging is not needed for diagnosis in most patients. However, once a diagnosis of acute pancreatitis has been made, trans-abdominal ultrasound is required to rule out gallstones as the aetiology.[46] »**CT scan of abdomen with oral and intravenous contrast:** may show pancreatic inflammation, peri-pancreatic stranding, calcifications, or fluid collections; confirms or excludes gallstones Abdominal imaging is not needed for diagnosis in most patients. Necrosis generally takes around

Uncommon

Acute pancreatitis

History	Exam	1st Test	Other tests
			5 days to develop, so an early CT scan cannot be used to assess disease severity. American College of Gastroenterology (ACG) guidelines recommend CT or MRI after 48 hours in patients who do not improve or whose symptoms worsen.[46] Other guidelines recommend a delay of 72 to 96 hours after symptom onset before contrast-enhanced CT or MRI to assess for necrosis.[48] [49] »**MRI/magnetic resonance cholangiopancreatography (MRCP):** findings may include stones, tumours, diffuse or segmental enlargement of the pancreas with irregular contour and obliteration of the peri-pancreatic fat, necrosis, or pseudocysts ACG guidelines recommend CT or MRI after 48 hours in patients who do not improve or whose symptoms worsen.[46] Other guidelines recommend a delay of 72 to 96 hours after symptom onset before

Uncommon

Acute pancreatitis

History	Exam	1st Test	Other tests
			contrast-enhanced CT or MRI to assess for necrosis.[48] [49] MRI employing MRCP has the advantage of not requiring intravenous contrast or radiation, although intravenous gadolinium enhances images compared with non-contrast MRI. In addition, MRCP allows better visualisation of common bile duct stones and the pancreatic duct compared with CT. It can more readily distinguish solid from cystic in dealing with peri-pancreatic collections.[50]

◊ Chronic pancreatitis

History	Exam	1st Test	Other tests
history of alcohol abuse, nausea, vomiting epigastric abdominal pain radiating to the back, steatorrhoea, malnutrition, diabetes mellitus	weight loss, jaundice	»**abdominal CT scan:** pancreatic calcifications, focal or diffuse enlargement of the pancreas, ductal dilatation, and/or vascular complications in chronic pancreatitis »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or	»**direct pancreatic function tests:** decreased function in chronic pancreatitis »**24-hour urinary magnesium:** decreased »**urinary excretion of infused magnesium load:** decreased

Uncommon

◊ Chronic pancreatitis

History	Exam	1st Test	Other tests
		diminished T waves, prolonged PR interval	

Whipple's disease

History	Exam	1st Test	Other tests
middle age, white ethnicity, male sex; weight loss, arthralgia, diarrhoea, fever; possible steatorrhoea, oedema, fatigue, lethargy	skin darkening, neurological signs	»**serum magnesium:** normal or decreased »**serum potassium:** normal or decreased »**erythrocyte sedimentation rate:** elevated »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval »**upper gastrointestinal endoscopy:** duodenal mucosa may appear macroscopically pale yellow, microscopically with clumsy and dilated villi and ecstatic lymph vessels	»**24-hour urinary magnesium:** decreased

Cirrhosis

History	Exam	1st Test	Other tests
history of alcohol misuse, intravenous drug use, unprotected sexual intercourse, obesity, blood transfusion, known hepatitis infection; fatigue, weakness, weight loss, or pruritus	oedema, jaundice, ascites, collateral circulation, hepatosplenomegaly, leukonychia, palmar erythema, spider angiomata, telangiectasia, jaundiced sclera, hepatic fetor, altered mental status	»**serum magnesium:** normal or decreased »**erythrocyte sedimentation rate:** elevated »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** decreased

Uncommon

Cirrhosis

History	Exam	1st Test	Other tests
		»**serum ALT and AST:** elevated with ALT:AST ratio ≥1 if hepatocellular damage; normal in cholestasis »**serum alkaline phosphatase and gamma-GT:** elevated in cholestasis	

◊ Hyperaldosteronism

History	Exam	1st Test	Other tests
muscular weakness, paraesthesia, headache, polyuria, polydipsia	elevated blood pressure; signs of hypervolaemia, including increased jugular venous distension, peripheral oedema, or ascites	»**serum magnesium:** normal or decreased »**serum potassium:** decreased »**serum aldosterone:** high »**serum renin activity:** low in primary; high in secondary »**ABG:** may show metabolic alkalosis »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**CT or MRI of adrenal glands:** normal, or may reveal typical hypodense unilateral macroadenoma (>1 cm) »**24-hour urinary magnesium:** increased

◊ Hypoparathyroidism

History	Exam	1st Test	Other tests
muscle twitches, cramps or spasms, confusion, depression, gait disturbances; history of parathyroid or thyroid surgery	positive Trousseau's and Chvostek's signs, seizures; developmental delay, short stature, cataracts; presence of surgical scar on the neck	»**serum magnesium:** decreased »**PTH level:** decreased or undetectable »**serum calcium:** decreased »**serum potassium:** decreased	»**24-hour urinary magnesium:** increased

Uncommon

◊ Hypoparathyroidism

History	Exam	1st Test	Other tests
		»**ABG:** demonstrates metabolic alkalosis »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	

◊ Hyperthyroidism

History	Exam	1st Test	Other tests
history of autoimmune disease; increased appetite, weight loss, heat intolerance, hair loss	fine tremor, goitre, exophthalmos; tachycardia, hypertension	»**serum magnesium:** normal or decreased »**thyroid-stimulating hormone (TSH):** decreased »**serum free T4:** elevated »**serum potassium:** low »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**radioactive iodine intake:** elevated in Graves' disease; normal in toxic multinodular goitre; decreased in acute or subacute thyroiditis »**TSH receptor antibodies:** positive in Graves' disease »**24-hour urinary magnesium:** normal or decreased

◊ Hungry bone syndrome

History	Exam	1st Test	Other tests
recent parathyroidectomy for hyperparathyroidism, or thyroidectomy for hyperthyroidism; usually asymptomatic; may present with severe bone pain	may be normal, or show positive Trousseau's and Chvostek's signs	»**serum magnesium:** decreased »**serum phosphate:** decreased »**serum calcium:** decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**bone biopsy:** extensive bone remineralisation »**24-hour urinary magnesium:** increased

Uncommon

◊ Recovery phase of acute tubular necrosis

History	Exam	1st Test	Other tests
usually asymptomatic; history of hypotension, fluid depletion, or exposure to nephrotoxic agents	usually normal	»**serum magnesium:** normal or decreased »**serum urea:** elevated »**serum creatinine:** elevated »**urea:creatinine ratio:** ≥10 suggests diagnosis »**fractional excretion of sodium and chloride:** >2% »**urinalysis for sediment:** tubular epithelial cells, epithelial cell casts, or muddy brown casts support acute tubular necrosis »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**ABG:** metabolic acidosis »**24-hour urinary magnesium:** elevated

◊ Renal tubular acidosis

History	Exam	1st Test	Other tests
usually asymptomatic; history of urinary tract obstruction, diabetes mellitus, primary biliary cirrhosis, nephrocalcinosis, nephrolithiasis, or use of known causative medications or toxins	usually normal	»**serum magnesium:** normal or decreased »**serum bicarbonate:** decreased »**serum chloride:** elevated »**serum potassium:** decreased in proximal and classic distal renal tubular acidosis (RTA); elevated in hyperkalaemic distal RTA »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or	»**abdominal x-ray:** nephrocalcinosis »**arterial blood pH:** decreased »**24-hour urinary magnesium:** elevated

Uncommon

◊ Renal tubular acidosis

History	Exam	1st Test	Other tests
		diminished T waves, prolonged PR interval	

◊ Post-obstructive diuresis

History	Exam	1st Test	Other tests
prior history of urolithiasis, benign prostatic hyperplasia, prostate cancer or bladder cancer	signs of fluid overload, diuresis as much as 200 mL/hour	»**serum magnesium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** elevated

◊ Primary renal magnesium wasting

History	Exam	1st Test	Other tests
positive family history; polyuria, polydipsia; Gitelman's syndrome: cramps (which may be severe, and usually involving arms and legs), severe fatigue	signs of volume depletion (decreased skin turgor, dry mucous membranes, reduced jugular venous pressure, decreased blood pressure); Bartter's syndrome: growth and developmental delay, possible hypotension and/or sensorineural deafness; Gitelman's syndrome: growth retardation, tetany	»**urinary chloride:** high (>10 mmol/L [>20 mEq/L]) »**urinary calcium:** high in Bartter's syndrome, low in Gitelman's syndrome »**serum potassium:** low »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	»**24-hour urinary magnesium:** elevated »**genetic testing:** identification of causative mutation

Pre-eclampsia

History	Exam	1st Test	Other tests
>20 weeks gestation; history of chronic hypertension; headache, seizures; visual disturbance	gravid uterus; elevated blood pressure; possible epigastric tenderness	»**serum magnesium:** normal or elevated »**urinalysis:** proteinuria: >300 mg per 24 hours (suggested by 1+	

Uncommon

Pre-eclampsia

History	Exam	1st Test	Other tests
		proteinuria on dipstick); >5 g in 24 hours is consistent with severe pre-eclampsia »**FBC:** elevated WBC and Hb »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	

◊ Pregnancy

History	Exam	1st Test	Other tests
may be in third trimester	gravid uterus	»**serum magnesium:** normal or decreased »**ECG:** normal, or widening of the QRS complex, prolonged QT interval, peaked or diminished T waves, prolonged PR interval	

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Images

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	30 mg*	30 mg*		
7-12 months	75 mg*	75 mg*		
1-3 years	80 mg	80 mg		
4-8 years	130 mg	130 mg		
9-13 years	240 mg	240 mg		
14-18 years	410 mg	360 mg	400 mg	360 mg
19-30 years	400 mg	310 mg	350 mg	310 mg
31-50 years	420 mg	320 mg	360 mg	320 mg
51+ years	420 mg	320 mg		

*Adequate Intake (AI)

Figure 1: Recommended Dietary Allowances (RDAs) for Magnesium

Table used with permission from the U.S. Department of Health and Human Services, National Institutes of Health. Original source for figures: Institute of Medicine (IOM). Food and Nutrition Board. Dietary reference intakes: calcium, phosphorus, magnesium, vitamin D and fluoride. Washington, DC: National Academy Press, 1997.

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This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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