

# Vitamin B<sub>12</sub> deficiency

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## 1 The incidence of vitamin B<sub>12</sub> deficiency increases with age

The condition affects 5% of adults older than 60 years.<sup>1</sup> Vitamin B<sub>12</sub> (hereafter B<sub>12</sub>) is a cofactor for enzymes involved in DNA synthesis and is necessary for normal bone marrow and central nervous system function.<sup>2</sup> Its absorption in the distal ileum requires intrinsic factor.

## 2 Patients can present with neuropsychiatric findings or hematologic abnormalities

Common symptoms are fatigue and pallor, but features can also include cognitive deficits, subacute combined degeneration of the dorsal and lateral columns of the spinal cord and peripheral neuropathies.<sup>2</sup> Hematologic findings include macrocytic anemia, hypersegmented neutrophils on blood film and pancytopenia.<sup>2</sup> Plasma concentrations of B<sub>12</sub> should be assessed if macrocytosis is identified.

## 3 Diagnosis requires a B<sub>12</sub> plasma concentration less than 148 pmol/L

Marginal deficiency, defined by plasma concentrations of 148–221 pmol/L, is observed in 20% of patients older than 60 years and seldom leads to hematologic abnormalities.<sup>1</sup> Testing for methylmalonic acid and homocysteine levels can be considered in patients with an equivocal plasma concentration of B<sub>12</sub> and symptoms or signs compatible with deficiency.<sup>2</sup>

## 4 Dietary history and medications should be reviewed carefully

Common causes include autoimmune gastritis (which causes pernicious anemia), diets low in animal products, malabsorptive states (e.g., postgastrointestinal surgery), and medications, including metformin, proton pump inhibitors and histamine-2 receptor antagonists.<sup>2,3</sup>

## 5 Patients with documented B<sub>12</sub> deficiency should be treated with supplementation

Daily high-dose (≥ 1000 µg) oral B<sub>12</sub> is as effective as intramuscular supplementation.<sup>4</sup> Concentrations of B<sub>12</sub> can be monitored every 3–6 months while on treatment; hematologic abnormalities should resolve within weeks and neuropsychiatric symptoms within months.<sup>2</sup> Urgent referral can be considered for patients with severe sequelae of deficiency (e.g., pancytopenia, neurologic deficits). If reversible causes are addressed, supplementation can be stopped once B<sub>12</sub> concentrations normalize, whereas patients with irreversible causes often require lifelong treatment. Parenteral B<sub>12</sub> is often prescribed without evidence of deficiency and fails to improve nonspecific complaints, including cognitive dysfunction and fatigue.<sup>5,6</sup> This practice should be discouraged.

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