

For the Primer, visit [doi:10.1038/nrdp.2017.40](https://doi.org/10.1038/nrdp.2017.40)

➔ Vitamin B<sub>12</sub> (B12) — also known as cobalamin — has an important role as a cofactor in many cellular processes, including DNA synthesis and methylation, and mitochondrial metabolism. Deficiency is associated with various symptoms, of which the haematological (mainly anaemia) and neurological (such as sensory and motor disturbances, ataxia and psychiatric disorders) manifestations are the most characteristic.

## MECHANISMS

! Autoimmune destruction of parietal cells and the consequent absence of intrinsic factor causes the classic manifestation of B12 deficiency — pernicious anaemia

## PREVENTION

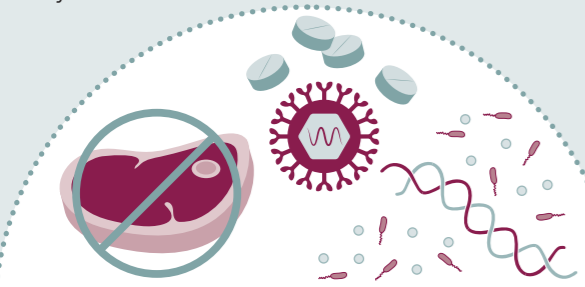
B12 deficiency is an emerging public health concern, especially in developing countries and in populations at risk. In addition, correction of B12 levels

can lower increased homocysteine levels in populations receiving folic-acid-fortified products or in individuals using folic acid

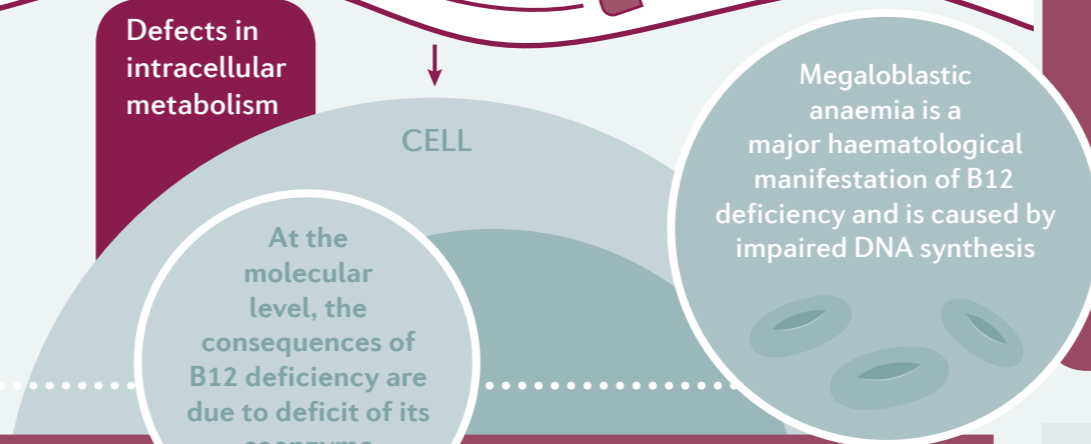
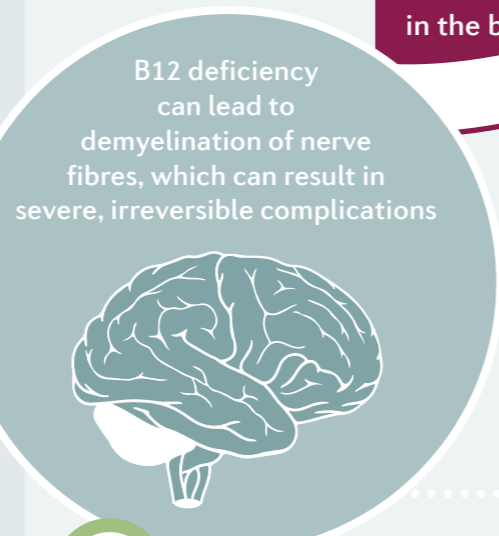
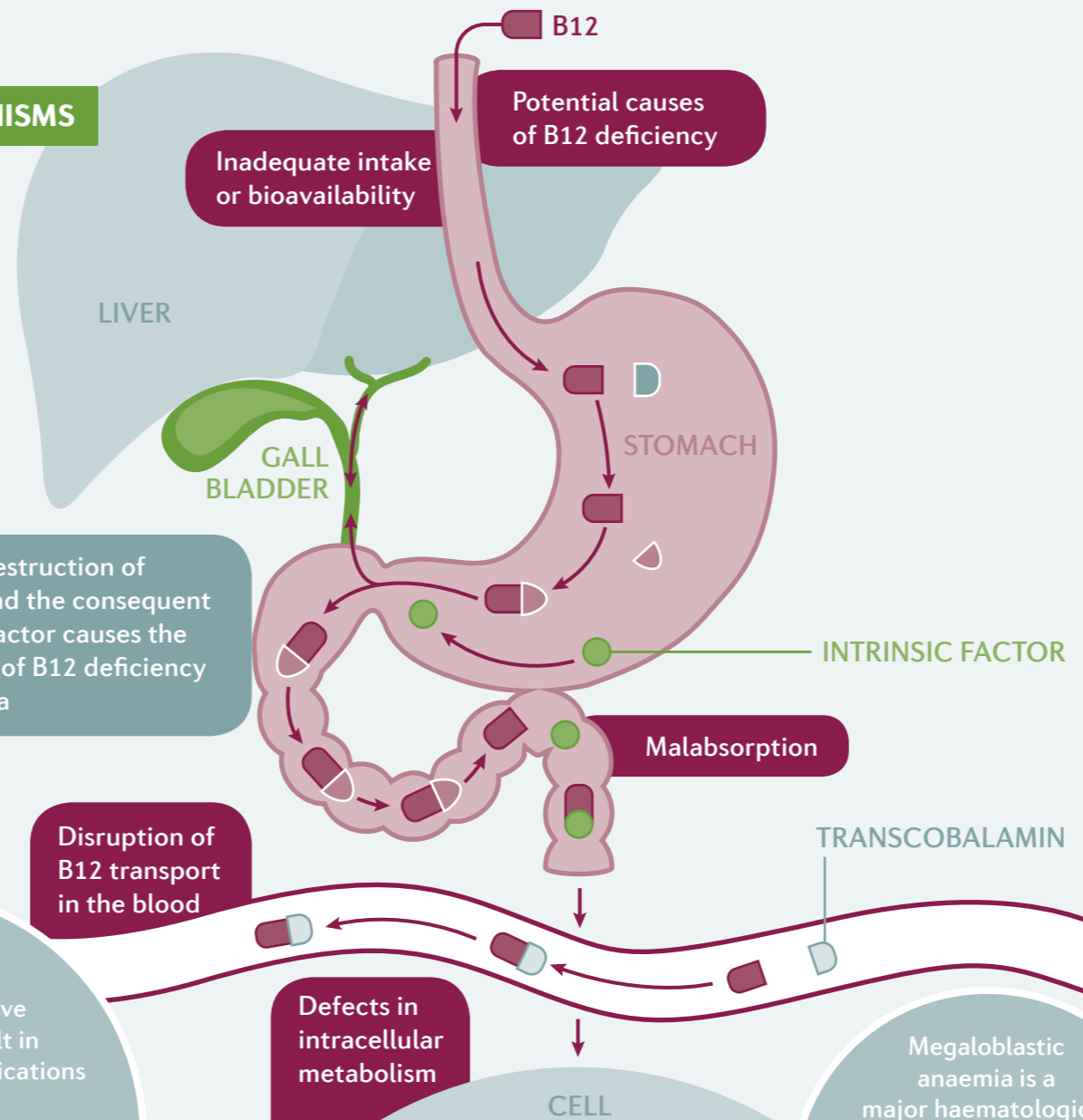
supplements. Low B12 levels and increased homocysteine levels have been associated with cognitive impairment in elderly individuals.

## EPIDEMIOLOGY

Clinical B12 deficiency associated with either severe anaemia or neurological manifestations or both is uncommon (1–2% of individuals >60 years of age), but subclinical deficiency affects 3–26% of the general population in the United States, depending on the biomarker cut-off levels used. Prevalence is much higher in South America, Asia and Africa. Demand and availability of B12 varies throughout life, making specific subpopulations vulnerable to deficiency, especially infants, children, women who are pregnant or breastfeeding and elderly individuals.

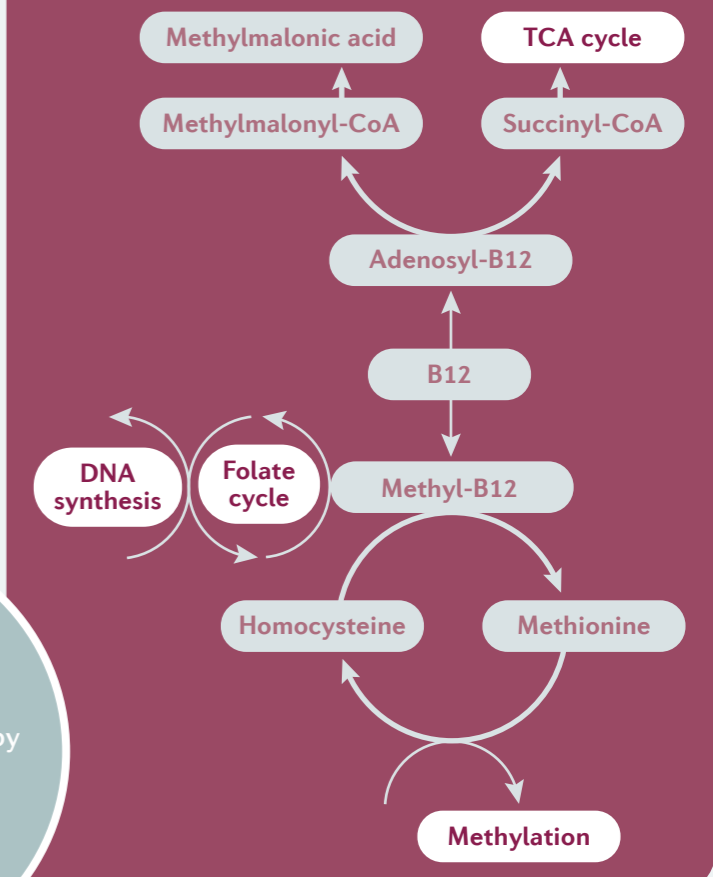


! Risk factors for developing B12 deficiency are failure of the intrinsic factor–B12 absorption pathway, inadequate intake of B12-containing foods (mainly meat), genetic factors, gastrointestinal infection or surgery, long-term use of drugs (such as gastric H<sup>+</sup>/K<sup>+</sup> inhibitors or histamine H<sub>2</sub> receptor antagonists) and concomitant illnesses such as HIV infection and tuberculosis.



## DIAGNOSIS

As the clinical presentation of B12 is so varied, a combination of blood biomarkers is often used for diagnosis, despite limitations. These markers include low total B12 levels and transcobalamin-bound B12 levels (that is, the active form of B12), and increased homocysteine and methylmalonic acid levels. However, the exact cut-off levels to classify normal, subclinical or clinical B12 deficiency are not firmly established.



## MANAGEMENT Rx

Depending on the underlying cause, B12 repletion generally involves oral (if the cause is inadequate intake) or parenteral (if the cause involves malabsorption) B12 administration. After a high initial load, the dose is usually reduced.