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THE ROLE OF VITAMIN B12 IN THE DIET – IMPACT ON THE BODY. A LITERATURE REVIEW

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ABSTRACT

Vitamin B12 is a key chemical compound for human health, involved in processes such as homocysteine methylation, DNA synthesis, and mitochondrial function. We present current knowledge on the causes and clinical significance of hypervitaminosis B12 and discuss cobalamin deficiency and excess in selected risk groups: pregnant women, vegetarians and vegans, athletes, and the elderly.

Aim of the study: The aim of the study is to assess the impact of vitamin B12 on the functioning of the human body. The analysis focuses on the role of vitamin B12 in the proper functioning of the nervous, hematopoietic, and cardiovascular systems. Furthermore, the study determines the effects of vitamin B12 deficiency and excess in the diet.

Material and methods: A literature review was conducted from the PubMed and Google Scholar databases. Key phrases as "vitamin B12", "cobalamin", "vitamin B12 deficiency" and "excess vitamin B12" were used.

Results and conclusions: Vitamin B12 plays a crucial role in the proper functioning of the human body, influencing the nervous, hematopoietic, and cardiovascular systems. Symptoms such as fatigue, anemia, and impaired concentration have been observed among individuals with vitamin B12 deficiency. The analysis revealed a significant correlation between vitamin B12 supplementation and bodily function. Therefore, it can be concluded that adequate levels of vitamin B12 in the diet are crucial for maintaining health.

KEYWORDS

Vitamin B12, Cobalamin, Vitamin B12 Deficiency, Excess Vitamin B12

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Introduction

Vitamin B12 (cobalamin) is a water-soluble organic compound belonging to the B group of vitamins [1].

Vitamin B12, produced by bacteria in the large intestine, cannot be utilised by the body because its synthesis occurs below the section of the digestive tract responsible for its absorption. Therefore, humans obtain cobalamin exclusively from food and supplements. The highest amounts of vitamin B12 are found in animal products such as liver, kidneys, ruminant meat, seafood, dairy products and eggs. Small concentrations can also be found in some fermented vegetables, such as fermented soybeans [1].

One of its most important functions is to participate in the methylation of homocysteine, leading to the formation of methionine, which is the main source of methyl groups used for the methylation of DNA, RNA, and proteins that form steroid hormone receptors [2].

Characteristics of Vitamin B12

The size of a cobalamin molecule is up to 1,500 Da in size, and its complete synthesis requires up to 25 distinct stages, which can be aerobic or anaerobic and involve high energy expenditure. Vitamin B12 synthesis is carried out by microorganisms of the Eubacteria and Archaea genera, while other organisms that use cobalamin must obtain it from other sources, such as food, and modify it. At present, approximately 20 human genes are known to be responsible for the proper utilisation of dietary vitamin B12 by the body [3].

Vitamin B12 usually occurs in a form bound to proteins. The protein necessary for its activation is pepsin, whose precursor, pepsinogen, is produced by the parietal cells of the stomach and then activated by hydrochloric acid or pepsin [3].

After consuming foods containing vitamin B12 and digesting them, it is bound by haptocorrin. Haptocorrin is a protein found in saliva and stomach contents [4] and acts as a defence mechanism for vitamin B12, protecting it from destruction [3].

Upon reaching the duodenum, the vitamin B12 complex with TCL-1 is broken down by proteolytic enzymes. The released cobalamin then binds to intrinsic factor (IF), which allows it to be absorbed in the terminal ileum. The B12-IF complex is taken up by cells via endocytosis after prior recognition by the cubam receptor. In subsequent stages, the intrinsic factor is broken down, vitamin B12 is separated from it and enters the circulation, where it binds to transcobalamin 2 (TCL-2) or haptocorrin [3].

Cells utilise vitamin B12 bound to transcobalamin 2 (TCL-2) much more efficiently because the receptor responsible for recognising this complex (TCL2-R) is present in virtually all tissues, enabling its uptake by endocytosis. Furthermore, the level of TCL2-R expression is higher in cells with a high demand for cobalamin and lower in cells with lower metabolic activity, so that vitamin B12 is primarily delivered where it is needed. In contrast, the cobalamin-haptocorrin complex remains largely unavailable to cells [3].

The Function of Vitamin B12 in Mitochondria

Vitamin B12 (cobalamin) plays a key role in mitochondria as a coenzyme for two enzymes: methylmalonyl-CoA mutase and methionine synthase. Its main function in mitochondria is to catalyse the conversion of L-methylmalonyl-CoA to succinyl-CoA, which is an important step in the citric acid cycle (TCA) and cellular energy production [5-6]. Vitamin B12 deficiency leads to the accumulation of methylmalonate, disturbances in ATP production and mitochondrial dysfunction, which can manifest itself in neurological and haematological symptoms, among others [3] [7].

In addition, vitamin B12 influences mitochondrial biogenesis and dynamics (mitochondrial fusion and fission), indirectly regulating these processes through methylation pathways and the availability of S-adenosylmethionine (SAM), a key methyl group donor [8-9]. It has been shown that B12 deficiency can lead to epigenetic changes, oxidative stress and mitochondrial dysfunction, which is particularly important in the context of neurodegenerative diseases [7] [10].

Vitamin B12 Deficiency

Of all water-soluble vitamins, vitamin B12 has the lowest daily requirement. [11]

The metabolism of vitamin B12 is a complex process. It acts as a cofactor in the mitochondrial reaction - the conversion of methylmalonyl-CoA to succinyl-CoA and in the cytosolic reaction – the conversion of homocysteine to methionine. As a result of disturbances in these reactions, vitamin B12 metabolites may accumulate, which can adversely affect the functioning of various systems, such as the hematopoietic and nervous systems. [11]

Vitamin B12 deficiency is present in all age groups, but it is most common in people with malabsorption disorders, the elderly, and people with restricted meat diets. [11] The prevalence of vitamin B12 deficiency increases in predisposed groups. [13] Among the elderly, those with multiple comorbidities and those living in nursing homes are most at risk for vitamin B12 deficiency. [16]

Vitamin B12 deficiency can result from many causes, including impaired absorption in the gastrointestinal tract due to gastrointestinal diseases, Crohn’s disease, celiac disease, and gastrectomy; insufficient intake due to a diet low in animal products; and impaired intracellular transport of vitamin B12. [22] Age is an important risk factor for vitamin B12 deficiency, as indicated by data from the US and the UK. In people under 60, vitamin deficiency affects approximately 6%, while in those over 60, it reaches 20%. In addition, other risk factors for vitamin B12 deficiency include long-term use of medications that reduce stomach acidity, such as H2 Blockers or proton pump inhibitors. [23] Another cause may be an autoimmune issue associated with pernicious anemia and iatrogenic causes, such as long-term use of metformin. [24] Usually, the most severe forms of deficiency are associated with malabsorption. [28][29][30]

Vitamin B12 deficiency leads to increased homocysteine levels due to reduced methionine synthase activity, and additionally increases methylmalonate (MMA) levels resulting from reduced methylmalonyl-CoA mutase activity. [24][25][29]

Impaired absorption and problems related to the transport of vitamin B12 can lead to a gradual depletion of its reserves, resulting in symptoms. [29] Symptoms of vitamin deficiency include neurological and hematological symptoms. These include sensory disturbances, cognitive impairment, ataxia, thrombocytopenia, macrocytosis, megaloblastic anemia, and leukopenia. [24][30] Macrocytosis, which is a symptom of vitamin B12 deficiency, results from impaired DNA synthesis in erythroblasts. [25] Often, the presence of atypical symptoms can delay the correct diagnosis. [28]

Population screening of people without risk factors for the disease is not recommended. The first step in diagnosing vitamin B12 deficiency is to assess blood count and serum vitamin B12 levels. [12] Measuring

vitamin B12 levels is not sufficient for diagnosis; it is only one of the starting points. [17] A crucial step in diagnosing a deficiency is determining its cause. [11] A complementary test is the measurement of methylmalonate levels. [12] Additionally, holotranscobalamin and homocysteine levels are assessed. [22][15] There is no ideal method for diagnosing vitamin B12 deficiency; it is necessary to combine the interpretation of the results with risk factors and symptoms. [14][15] Early diagnosis and treatment of deficiency is crucial, as prolonged vitamin B12 deficiency can result in permanent neurological damage. [17] An important aspect of vitamin B12 deficiency symptoms is that the deficiency can be present even in the absence of anemia, resulting in a slower diagnosis. [15]

Preventing vitamin B12 deficiency involves consuming a well-balanced diet rich in animal products. [11] Prevention also includes daily oral intake of vitamin B12 by people who have undergone bariatric surgery. Furthermore, another method of prevention is monitoring patients taking proton pump inhibitors. [12]

Treatment of vitamin B12 deficiency involves replenishing the deficiency through oral or intramuscular supplementation. [11] If the vitamin B12 deficiency is severe, intramuscular therapy is recommended, as it acts more quickly and effectively. [12] Treatment of vitamin B12 deficiency also depends on its cause. If the cause of the deficiency is an inadequate diet, oral supplementation is used to address the issue. However, if the cause is malabsorption, intramuscular supplementation is used. [13]

Cause	Example	Mechanism	Refc.
Autoimmune	Addison-Biermer disease	Presence of antibodies against Castle's instrinsic factor and parietal cells	[13][17]
Diet	Vegetarian diet, vegan diet	Deficiency of animal sources of vitamin B12	[15][18][19]
Malabsorption disorders	Celiac disease, Crohn's disease, gastrectomy	Castle'a intrinsic factor deficiency, hydrochloric acid deficiency	[13][16]
Medications	Long-term metformin therapy, H2 Blockers, proton pump inhibitors	Inhibition of vitamin B12 absoption in the intestine	[13][15][19]
Congenital defects in cobalamin metabolism	Transcobalamin II deficiency	Impaired conversion of vitamin B12 to active forms	[13]
Impaired intestinal flora	Parasitic infections, SIBO	Impaired absorption of vitamin B12, increased consumption of vitamin B12 by intestinal flora	[13][16]
Pancreatic diseases	Exocrine pancreatic insufficiency	Impaired binding of vitamin B12 to Castle's intrinsic factor due to lack of proteases	[14][18]
Increased demand	Hyperthyroidism, pregnancy	Increased vitamin B12 metabolism	[14][18]
Other	Kidney disease, liver disease, alcohol	Decreased vitamin B12 metabolism and storage	[13][19]

The Role of Vitamin B12 in The Body

Nervous System

Vitamin B12 is involved in many key processes within the nervous system. It acts as a cofactor in two biochemical pathways. One of these is the conversion of homocysteine to methionine, which allows the formation of S-adenosylmethionine (SAM), a protein involved in the methylation of RNA, DNA, phospholipids, and myelin proteins. This protein acts as a methyl group donor. Disruption of the methylation cycle can lead to demyelination. In addition, vitamin B12 is a cofactor in the conversion of methylmalonyl-CoA to succinyl-CoA. Disruption of this reaction can result in damage to axons and myelin due to the accumulation of fatty acid derivatives and MMA. [20]

Vitamin B12 deficiency can lead to damage to the lateral and posterior columns of the spinal cord, as well as sensory polyneuropathy due to MMA accumulation and reduced methylation efficiency. [20]

In a systematic review by A.R. Mathew et al., the authors emphasize that abnormal vitamin B12 metabolism in the nervous system may lead to changes in ribosomal gene expression, resulting in epigenetic remodeling of the brain. [21]

The study shows an increased risk of neurodegeneration in the nervous system associated with vitamin B12 deficiency. This is associated with the possible anti-inflammatory effect of vitamin B12. [22]

Vitamin B12 deficiency promotes the development of depression, cognitive impairment, and neuropsychiatric symptoms. The development of the following symptoms may result from impaired methylation mechanisms, which are associated with increased levels of homocysteine and MMA. [20]

Research suggests that a vitamin B12 deficiency, accompanied by excessive folic acid, may have an additional adverse effect on the nervous system, which is associated with cognitive impairment and the onset of neurological symptoms. [23]

Hematopoietic System

Disruption of the role of vitamin B12 as a cofactor in biochemical pathways leads to impaired DNA synthesis and disruption of cell nucleus maturation, resulting in ineffective erythropoiesis and megaloblastic anemia. [24]

Normal vitamin B12 levels are essential for the proper functioning of the hematopoietic system. A deficiency of this vitamin can lead to megaloblastic anemia, macrocytosis, pancytopenia, and hypersegmentation of neutrophils. Often, the bone marrow can mimic the course of cancers such as leukemia. [25]

In addition, symptoms of vitamin B12 deficiency in the hematopoietic system may include leukopenia or neutropenia, which can result in an increased incidence of infections, as well as thrombocytopenia, associated with an increased tendency to bleed. [24]

Cardiovascular System

According to research, vitamin B12 deficiency and an imbalance between vitamin B12 and folic acid may be risk factors for cardiovascular disease. Vitamin B12 deficiency leads to the accumulation of homocysteine in the plasma, resulting in increased blood clotting, enhanced platelet adhesion, vascular dysfunction, damage to vascular endothelial cells, and heightened inflammation. [26-30]

The study by A. Mohan et al. demonstrated that combining folic acid supplementation with vitamin B12 enhances vascular endothelial function and reduces inflammation. [27]

According to the authors of studies from 2015 and 2023, a 5 μmol/L increase in homocysteine levels above normal is associated with a 20% increase in cardiovascular risk. [26][27]

Vitamin B12 deficiency can lead to a decrease in HDL-C and an increase in LDL-C levels, which is associated with an increased risk of visceral obesity. [28] In addition, increasing vitamin B12 intake may be associated with lower LDL-C and triglyceride levels, which contribute to a lower risk of developing metabolic syndrome. [30]

The authors of the JAMA Network Open analysis suggest that both low and high levels of vitamin B12 may have adverse effects, as both are associated with an increased risk of cardiovascular disease. [29]

Vitamin B12 and Covid-19

Vitamin B12 may have a beneficial effect on the immune system, which is associated with supporting COVID-19 therapy. [31] A study conducted on patients with COVID-19 showed that the use of vitamin B12 reduced the expression of inflammatory genes, resulting in decreased inflammation. [32] COVID-19 patients experience a strong inflammatory response characterized by a cytokine storm, as well as a disturbance in the metabolism of sulfur amino acids such as homocysteine, in which vitamin B12 plays a crucial role as a cofactor. [32] An additional effect of vitamin B12 may be the suppression of pro-inflammatory genes in leukocytes, which may also reduce inflammation. [32] Furthermore, vitamin B12 may contribute to reducing oxidative stress by increasing glutathione production and enhancing the sulfur amino acid pathway. [33]

Excess Vitamin B12

Elevated vitamin B12 levels are of little significance in clinical practice, but they are a significant metabolic anomaly whose pathological significance appears to be underdiagnosed. Traditionally, doctors have focused mainly on the consequences of its deficiency, but recent studies suggest that its excess may indicate the existence of serious diseases such as renal failure, chronic liver disease, solid tumors, or hematological cancers. [34]

The most common cause of elevated vitamin B12 levels is excessive supplementation of this vitamin, but this phenomenon does not only apply to people taking cobalamin preparations. Higher concentrations can also be observed in patients who do not supplement vitamin B12, which also increases the clinical significance in interpreting this indicator.[35,45] After recent supplementation of this vitamin, an increase in its concentration in the body is expected and usually has no toxicological significance, as high B12 intake is not considered harmful. Extremely high values have sometimes been reported, which were thought to be associated with the formation of antibodies against transcobalamin, the protein responsible for transporting cobalamin. The immunoglobulin-transcobalamin-B12 complex is very often observed in the first weeks after cobalamin administration, but it cannot penetrate cells and has no documented clinical consequences. [45]

Excess vitamin B12, if persistent, should be considered a potentially significant marker of serious diseases and is a reason for systematic differential diagnosis of parenchymal organ pathology, liver and kidney dysfunction, and hematological diseases. [34] The B12 x CRP index, which is available in laboratory tests, is important for prognostic assessment and warrants particular attention. The correlation with short-term mortality in patients with advanced cancer and values above 40,000 may indicate its potential usefulness as a prognostic biomarker that can be used in oncology. [34]

Causes of elevated vitamin B12 levels in the absence of supplementation. [35]

Hepatic	Alcoholic liver disease Cirrhosis of the liver Acute hepatitis
Renal	Kidney failure
Hematological	Chronic myeloid leukemia Acute leukemia Polycythemia vera Myelofibrosis
Solid tumors	Hepatocellular carcinoma Liver metastases Breast cancer Colorectal cancer
Interfering antibodies	Macro-vitamin B12

The Importance of Vitamin B12 in Different Groups

Pregnant Women

Vitamin B12 is a micronutrient that is essential for the body to function properly. Deficiencies of this vitamin and other micronutrients are also currently found in developing countries, mainly affecting women of childbearing age, adolescents, children, and older people who are in difficult economic situations. [36] The main role of vitamin B12 is to participate in metabolism and the development of the nervous system, particularly in the process of myelination and the formation of cognitive functions. A deficiency of this vitamin can lead to permanent neurological development disorders in children and immune, vascular, and inflammatory disorders in adults. [36][38]

In the third week of pregnancy, the development of the central nervous system begins, which continues throughout early childhood. Both the processes of myelination and synaptogenesis, which occur particularly intensively from the third trimester onwards, depend on adequate levels of vitamin B12, which influences the development of memory and attention. [36] There is a correlation between the mother's nutritional status and the concentration of vitamin B12 in the child, which indicates that infants of mothers who follow a vegan or vegetarian diet, especially if they do not supplement B12, are at risk of deficiency from birth or in the first months of life. An increased risk can be observed in women who have been pregnant multiple times. [36][38]

Many severe cases of vitamin B12 deficiency symptoms in infants have been described in the literature, such as hypotonia, feeding difficulties, tremors, lethargy, psychomotor regression, hyperactivity, and, in extreme cases, coma. Imaging studies often reveal brain structure atrophy. One recent case involved a 9-month-

old girl with hypotonia, and psychomotor regression caused by vitamin B12 deficiency. [36] Children of mothers who do not provide their bodies with adequate amounts of micronutrients may also have iron and zinc deficiencies, but this does not fully explain the neurodevelopmental disorders that result from vitamin B12 deficiency. [36]

In low-income countries, vitamin B12 deficiency is becoming a significant problem, especially among pregnant women, infants, and preschool children. There is a correlation between vitamin B12 levels in mothers and their children, which is why nutritional interventions during pregnancy are emphasized. In this context, food fortification, especially flour, can play an important role, in line with the recommendations of the Food Fortification Initiative and the WHO. By fortifying flour with folic acid and vitamin B12, it is also possible to prevent the potential consequences of excessive folic acid intake combined with vitamin B12 deficiency. [36]

Proper fetal development requires adequate levels of folic acid and vitamin B12, which participate in the one-carbon cycle. Deficiencies in these nutrients may increase the risk of neural tube defects, stillbirths, premature birth, miscarriage, fetal growth restriction, cognitive impairment, and low birth weight. Nevertheless, the role of vitamin B12 supplementation during pregnancy is still underestimated, especially in developing countries where deficiency is common. [37] In addition, an imbalance between vitamin B12 and folic acid may have an adverse effect on the course of pregnancy through placental mechanisms. [37]

Vegetarians and Vegans

Vitamin B12 is an essential nutrient, and its synthesis occurs in microorganisms. Plant products, unless fortified, are not a reliable source of this vitamin. It can be noted that some plant products, such as seaweed, contain cobalamin, but this presence is due to contamination with microorganisms that produce vitamin B12. It is worth noting that the bioavailability of this component in such products is unstable, variable, and insufficiently confirmed, which limits their use as nutritional sources. [36][38]

Diets based exclusively on plant products, especially without supplementation, are significantly associated with an increased risk of deficiencies, particularly of micronutrients such as calcium, iodine, iron, selenium, and vitamin B12, which is found in negligible amounts in plant-based foods. Systematic observations show that people who base their diet on vegan products without supplementation have the lowest intake and the most frequent cobalamin deficiency, while the incidence of deficiency also remains significant among vegetarians. This risk is particularly high in people who have been on a plant-based diet since early childhood and in vegetarians who switch to a vegan diet when their vitamin B12 levels are already low. [38][39][40]

Chronically low vitamin B12 intake leads to physiological deficiency and increases the risk of health complications, including neurological, neuropsychiatric, and hematological disorders. Available data suggest that vitamin B12 deficiency may contribute to bone metabolism disorders and lead to an increased risk of fractures, most likely because of accelerated bone turnover and coexisting nutritional deficiencies observed in people following a plant-based diet. [38] Low vitamin B12 levels are a risk factor for neuropsychiatric disorders, and selected studies suggest adverse associations between mental health and vegetarian and vegan diets. [38]

Despite numerous descriptions of the risks associated with plant-based diets, their popularity is growing rapidly due to health, ethical, and environmental considerations. According to epidemiological data, vegetarians have lower mortality rates from ischemic heart disease and a significantly more favorable metabolic profile, which includes lower BMI, lower cholesterol and glucose levels, and lower blood pressure compared to people on a mixed diet. [39][41] The vegan population has a lower incidence of obesity and favorable values for selected cardiovascular disease risk indicators.[41] In the absence of adequate supplementation and food fortification, particularly in the context of vitamin B12, whose deficiency is the most documented health problem associated with vegan diets, these benefits may be significantly reduced. [36][38][41]

Athletes

Vitamin B12 is an important coenzyme involved in the synthesis of DNA and neurotransmitter serotonin. Maintaining normal levels of vitamin B12 may have a potential effect on the regulation of anxiety responses by modulating serotonin production, which translates into improved psychomotor skills that require precision, such as shooting performance. [42] Clinical studies have confirmed the importance of vitamin B12 in the functioning of the central nervous system. In a cross-sectional study involving 100 patients with amnesia and mild cognitive impairment (MCI), individuals with low and high but still normal vitamin B12 concentrations

were compared. Memory functions were assessed using the Auditory Verbal Learning Test. The results showed that participants with low vitamin B12 levels, as well as those with normal but low levels, had deficits in learning, overall memory performance, and recognition. This finding was associated with reduced microstructural integrity of the hippocampus, which may indicate the neurobiological sensitivity of this area to near-optimal vitamin B12 supply. [42]

Cobalamin is essential for maintaining normal cognitive function, as it supports effective information processing and concentration. This is particularly important in the context of sports activities, as optimal cognitive functioning is a prerequisite for quickly acquiring new technical skills, maintaining attention during prolonged exertion, and responding appropriately to environmental stimuli. [42]

It has also been shown that adequate concentrations of vitamin B12 and vitamin D promote proper iron metabolism, which may reduce the risk of iron deficiency anemia. [43] Folic acid and vitamin B12 play a significant role in erythropoiesis by participating in DNA synthesis in erythrocyte precursor cells. Insufficient supply of these nutrients in athletes can result in the development of megaloblastic anemia, which manifests itself in easy fatigue, reduced exercise capacity, and weakness, all of which affect athletic performance. [44]

Elderly People

Vitamin B12 deficiency is a significant problem in the elderly population, as it is associated with the development of cognitive impairment, dementia, and megaloblastic anemia. The spectrum of symptoms is broad and may include both their absence and the occurrence of rather nonspecific, but also severe, possibly irreversible neurological disorders if left untreated. [45][46]. Vitamin B12 deficiency remains poorly understood despite its high prevalence. The diagnosis of this vitamin deficiency is often made incidentally during routine laboratory tests. [45]

In older people, cobalamin deficiency is influenced by many factors, including both reduced supply and impaired absorption. Poor eating habits can lead to insufficient intake of this vitamin, as can difficulties in chewing and swallowing, limited access to food, or the deliberate exclusion of animal products, for example for economic reasons, due to a vegetarian diet, or for cultural reasons. [45] Even with adequate intake, reduced bioavailability of vitamin B12 may result from disorders of the gastrointestinal tract. The aging process can lead to pathophysiological changes, including reduced secretion of stomach acid, pancreatic enzymes, and proteases, which disrupts the process of separating vitamin B12 from dietary proteins and reduces its absorption. Cobalamin from supplements, which is not bound to protein, is less susceptible to these processes. [45] A particularly significant cause of malabsorption is pernicious anemia, which results from autoimmune damage to the parietal cells of the stomach and a deficiency of intrinsic factor. Chronic Helicobacter pylori infection causes atrophic gastritis, which results in parietal cell dysfunction and secondary vitamin B12 deficiency. [45]

Older people often take long-term medications that interfere with the absorption of cobalamin, which is a significant factor in its deficiency. Metformin reduces the absorption of vitamin B12, with the risk increasing with the duration of use and the dose. Proton pump inhibitors and H2 receptor antagonists have a similar effect, inhibiting the release of vitamin B12 from dietary proteins by suppressing gastric acid secretion. The use of these drugs for more than 12 months significantly increases the risk of vitamin B12 deficiency. Cholestyramine, colchicine, aminoglycosides, and nitrous oxide can also interfere with cobalamin absorption. [45]

Vitamin B12 plays a key role in maintaining the proper functioning of the central nervous system. Its deficiency is a potentially reversible cause of dementia. Decreased vitamin levels are associated with progressive cognitive decline and mental disorders such as mania, suicidal behavior, psychosis, and agitation. [46] Symptoms of mental disorders may also occur at cobalamin concentrations that are within the lower range of normal, which shows the limited diagnostic value of serum levels alone. [36][46]

In order to prevent irreversible neurological damage, deficiency must be detected early and substitution therapy initiated promptly. The first-line treatment for older people is usually intramuscular administration of vitamin B12, as this bypasses absorption disorders in the gastrointestinal tract. Recent studies suggest that high-dose oral vitamin B12 supplementation may be equally effective. In many patients, such therapy is prescribed for life, especially when the causes of the deficiency are irreversible. [45]

Summary

Vitamin B12 is essential for DNA synthesis and proper function of the nervous, haematopoietic, and mitochondrial systems. Its metabolism relies on gastrointestinal absorption and transcobalamin transport. Both deficiency and excess of B12 have significant clinical implications.

Vitamin B12 deficiency is common in the elderly, patients with malabsorption disorders, those on a plant-based diet, and patients taking metformin or PPIs. It leads to DNA synthesis disorders, megaloblastic anaemia, neuropathy, demyelination, cognitive impairment and increased homocysteine levels, increasing cardiovascular risk. Diagnosis requires assessment of MMA, homocysteine and holotranscobalamin, and treatment consists of oral or intramuscular supplementation.

Excess vitamin B12, although often resulting from supplementation, can also occur without it and then be a marker of serious diseases such as haematological cancers, solid tumours, kidney failure or liver disease. The B12 × CRP ratio has potential prognostic value in oncology.

The clinical significance of vitamin B12 is particularly important in pregnant women, where its deficiency increases the risk of neural tube defects and neurodevelopmental disorders; in vegans and vegetarians, who almost always develop a deficiency without supplementation; in athletes, in whom low concentrations impair cognitive function and performance; and in older people, in whom deficiency often leads to reversible cognitive impairment.

In summary, adequate vitamin B12 levels are fundamental to health, and both deficiency and excess require careful interpretation and proper diagnosis and supplementation.

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