Vitamin B12 Injectable

A Preparation from SANUM-Kehlbeck

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Historical background
Vitamin B12, also known as Cobalamine, is a water-soluble vitamin and plays an important part within the organism, especially in erythropoiesis and the formation of nervous tissue.

Vitamin B12 as a substance was not discovered until 1955. A deficiency results in the development of pernicious anæmia (erythropænia with enlargement of the cell volume and elevated hæmoglobin content). This explained why the recommended consumption of cow's liver (rich in Cobalamine) would cure the illness. A few years later, it was shown that B12 could be synthesized by microbes. For the manufacture of the medicine, nowadays Vitamin B12 is either prepared from bacterial cultures as Cyanocobalamine (i.e. vegan) or else from liver extracts in the form of Hydroxycobalamine (i.e. from an animal source).

Biochemistry
Vitamin B12 is a crystalline, red powder, stable in hot conditions, but very photo-sensitive. It consists of one central monovalent Cobalt atom, which is surrounded by four pyrrole rings. We also find this structure in hæme, the substance responsible for the red colour of blood. There are numerous chemical variants of Cobalamine, although only a few are of biological use within the organism. The other forms, the so-called B12 analogues, may even inhibit its effectiveness.

Occurrence
B12 is produced by microorganisms such as algæ, fungi or bacteria. As human beings themselves are incapable of producing Cobalamine, they are reliant on its consumption with food. Various bacteria in the colon produce it, but their role in supplying the human organism is negligible, because its absorption takes place in the terminal part of the ileum, which precedes the colon. It is stored primarily in the liver and musculature.

Most of the higher plant forms contain hardly any Vitamin B12, since it is not required for their metabolism. Small amounts are found in root vegetables and sweet lupins, originating from the smallest microbes in the soil. Thus, eating a certain amount of „dirt" is entirely healthy! Blue algæ synthesize mostly B12 analogues, i.e. forms which are not assimilated by humans. Microbial fermentation of foodstuffs, e.g. the Lactic acid fermentation during the production of sauerkraut, and in the brewing of beer too, is responsible for their Cobalamine content, although the concentrations of it are liable to fluctuate considerably.

Important nutritional sources of Vitamin B12 include (content is shown in µg per 100g of the source substance): wheatgerm (330-700), spinach (145), egg-yolk (160), broccoli (111) and cow's liver (108).

Requirement figures
The amount stored in the body is around 3-5 mg; the vitamin is stored in the form of Adenosylcobalamine, primarily in the liver (60%) and the musculature (30%).

The daily requirement for adults is c. 3 µg; for children, expectant and breastfeeding mothers (Cobalamine is excreted via mother's milk) it is around 4-5 µg.

In the blood, the serum level should be over 250 pg/ml.

Serum levels below 200 pg/ml indicate pernicious anæmia, in which case a Folic acid deficiency frequently also exists.

In funicular myelosis (degenerative changes in the spinal cord owing to Cobalamine deficiency), serum levels below 30 pg/ml are found.

Physiology of Vitamin B12 metabolism
Nutritionally, Cobalamine is bonded with a carrier protein. This bond is broken by Hydrochloric acid and Pepsin in the stomach, after which it is transferred to one of the body's transport proteins. In the duodenum, under the influence of pancreatic enzymes, a further transfer takes place, this time to Intrinsic Factor (IF), which is formed by the parietal cells of the gastric mucosa. This complex becomes absorbed predominantly actively in the terminal ileum, but also passively to a very small extent (1-5%). As only a very small number of receptors is present in the intestines, it is better to consume this vitamin quite frequently in small amounts.

(If extremely large doses of Vitamin B12 are taken orally, some passive assimilation may take place throughout the intestines, even without Intrinsic Factor: if, for instance, 1000µg

of the active substance is taken, then - even with an assimilation of only 1% - the organism will still have 10µg at its disposal. Recent studies have established that even a certain degree of sublingual absorption is possible, which will likewise be independent of IF.)

After this, the vitamin is split up by the Intrinsic Factor and bonds with Transport Cobalamines I or II, so reaching the liver. Here, it is transformed into the two forms which are metabolically active: Methylcobalamine and Adenosylcobalamine. Surplus quantities of the Vitamin B12 are stored in the liver in the form of Adenosylcobalamine, or else are excreted via urine, fæces, bile, sweat and breastmilk.

Tasks of Vitamin B12 in Metabolism

Methylcobalamine is required for the conversion of Homocysteine into Methionine (a high Homocysteine level favours the development of arteriosclerosis), likewise for the synthesis of various amino-acids (Adenine, Guanidine, Thymidine) and thus, for the building up of the body's own protein.

Adenosylcobalamine assumes important enzymatic functions in the Citric Acid cycle, and is therefore involved in the generation of energy and cell-detoxification (e.g. by means of Glutathione).

Numerous processes in the organism depend on an adequate supply of Vitamin B12, in particular:

- Formation of red corpuscles in the bone marrow
- Protein synthesis (production of DNA and RNA, growth)
- Building up the myelin sheath of nerves
- Cellular detoxification
- Metabolism of fatty acids and Folic acid

From this, we can clearly see the extent of Vitamin B12's importance for the metabolism, and in how many ways a deficiency may find expression.

Pathology of Vitamin B12 Metabolism

Cases of under-supply occur mainly in infants and children, since they have hardly any reserves, in expectant and breastfeeding mothers, because of their increased requirement, and also in the elderly, since with increasing age there is decreased absorptive activity in the gut.

If we consider the physiological process of Cobalamine assimilation, then the possible causes of deficiencies will become clear:

- Lack of Hydrochloric acid, Pepsin or Intrinsic Factor production in the stomach in chronic gastritis or following gastric resection
- Pancreatic insufficiency
- Illnesses of the small intestine, e.g. Crohn's disease, cœliac disease, tapeworm infestation
- Inherited or acquired deficiency of Transportcobalamines I and II
- Liver diseases

Insufficient dietary intake is less significant. In most cases, it only shows up years later, since, compared with the daily requirement (c. 3 µg), the reserves (3-5 mg) are sizeable. Even vegans are not bound to suffer a deficiency, so long as they consume enough B12-producing micro-organisms via root vegetables and drinking water.

Further mentionable factors which affect the supply of Vitamin B12 are: alcoholism, nicotine, immune deficiency diseases, medicines (antacids, H2 blockers, oral contraceptives) and chronic diseases. As well as these, very large amounts of roughage and cellulose may inhibit absorption in the small intestine.

Vitamin B12 Deficiency Diseases

- *Neurogenic disorders* from demyelination (insufficient Methionine synthesis from Homocysteine): weakness in arms and legs with prickling and formication, the limbs easily go to sleep. Paræsthesias and polyneuropathies occur, patients exhibit complaints while walking or when lifting objects. Atrophy of the optic nerve may occur, resulting in deterioration of vision.
- *Funicular myelosis* is a degeneration of the lateral and posterior parts of the spinal cord. It is triggered by Vitamin B12 deficiency, because abnormally saturated fatty acids are formed and built into the membrane of nerve cells. This results in focal demyelination in the posterior cords and pyramidal tracts, inter alia in the cervical and thoracic areas of the spinal cord. This disease is favoured by

Nitric oxides, e.g. from cigarette smoke.

- *Pernicious anæmia* originally springs from a lack of Intrinsic Factor and hence on diminished absorption of Cobalamine in the ileum. The red blood cell count is depressed, with the individual erythrocytes becoming enlarged and storing more hæmoglobin (macrocytary, hyperchromic anæmia). Since in most cases too little Hydrochloric acid and Pepsin are being formed in the stomach, this results in disorders of the microbial population of the intestines and, consequently, attacks of diarrhœa. Neurological complaints are likewise possible. Further changes should be mentioned, which show up in laboratory test results: serum Cobalamine level reduced to <100 pg/ml, neutrophile granulocytes suffer a nuclear shift to the right, with elevated excretion of Urobilinogen and Urobilin in the urine. In the elderly, pernicious anæmia often coincides with acute leukæmia.
- *Macrocytic anæmia*, which can generally be triggered by a simultaneous deficiency of Cobalamine and Folic acid.
- *Disordered formation* of erythrocytes, leucocytes and thrombocytes in the bone marrow.
- *Disordered enzymatic activity* in the mitochondria affects the lipid metabolism. Fatty acid production is both increased and abnormal.
- *Non-specific symptoms*, such as reduced performance, loss of appetite, loss of weight, diarrhœa.

Indications for Vitamin B12 Supplementation

In addition to the already-mentioned illnesses, which have their origin in B12 deficiency, many complaints can be influenced positively by doses of this vitamin, e.g.

- *All chronic gastro-intestinal complaints*; following stomach or intestinal resection, lifelong supplementation is necessary
- *Diseases of the pancreas and liver*
- *Parasitoses*, since worms are B12 „robbers“
- *Deficiencies arising from medication*, e.g. contraceptives, antacids, cytostatics, antidepressants, all of which increase the organism's requirement
- *Alcohol and Nicotine abuse*
- *Increased requirement in pregnancy and while breast-feeding*
- *Heart diseases and arteriosclerosis*, since the Homocysteine level can be lowered by Vitamins B6, B12 and Folic acid.
- *Multiple sclerosis*, since frequently the serum levels of Cobalamine are depressed and those of Homocysteine are elevated
- In *asthmatics*, bronchoconstriction can be reduced
- *Diabetes mellitus*, because here, on the one hand, polyneuropathies frequently occur and, on the other hand, a number of oral diabetic medications (biguanidines) prevent B12 absorption
- *Neuro-psychiatric illnesses* of various geneses, e.g. Alzheimer's
- *HIV*: Patients with simultaneous B12 deficiency go on to develop AIDS more quickly.

Dosage and possible Side-effects

In general, an i.m. injection of 1 ampoule (1000µg of Cyanocobalamine) should initially be given twice a week for about 4 weeks. Later, the dosage or interval may be reduced, depending on the illness or symptom picture.

Even though recent investigations may show that Vitamin B12 is partly absorbed orally or – in a higher dosage - intestinally, injection should always be the preferred route, since this represents the most reliable form of uptake.

Since Cobalamine is a water-soluble vitamin, even in high doses, there is no risk of hypervitaminosis. It is possible that regular applications may favour the occurrence of acne.

Size of pack

Vitamin B12 Injectable from SANUM-Kehlbeck is available in packs of 10 or 50 ampoules of 1 ml.

1 ml of injectable contains 1000µg of Cyanocobalamine in aqueous solution.

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