Vitamin B12 (Cobalamin) Mechanism and Deficiency

Vitamin B12, also called cobalamin, is a water-soluble vitamin with an essential role in the normal functioning of the nervous system and proper formation of blood cells. Vitamin B12 is found in foods that come from animals and is stored largely in the liver. It is involved in cellular functions in every cell of the body including roles in DNA synthesis, fatty acid synthesis and energy production. Vitamin B12 dependent enzymes including methylmalonyl Coenzyme A mutase, which converts methylmalonyl CoA to succinyl CoA and methionine synthase, which converts homocysteine to methionine. A vitamin B12 deficiency will hinder these reactions. Inability to convert homocysteine to methionine causes poor DNA synthesis and can cause macrocytic megaloblastic anemia with hypersegmented neutrophils. This can also be seen in a folate deficiency, which is also necessary to complete this reaction. However, a vitamin B12 deficiency will uniquely cause defects to the nervous system because elevated levels of methylmalonic acid can cause abnormal fatty acids to be incorporated into myelin, resulting in demyelination. This often causes damages to specific neuron tracts including the posterior columns, lateral corticospinal tract, and spinocerebellar tracts.



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Mechanism

Cobalamin
Cobra-man

Vitamin B??, also known as cobalamin, is a water-soluble vitamin featuring a central cobalt ion within a corrin ring structure. It plays a pivotal role as a cofactor in enzymatic reactions crucial for DNA synthesis, myelin formation, and the metabolism of fatty acids and amino acids. Vitamin B12 is also called cobalamin, which is derived from English terms to mean “cobalt vitamin”.

Large reserve pool in the liver
Holding up Liver

Vitamin B12 is found in foods that come from animals and is stored largely in the liver, where it creates a substantial reserve for extended periods without animal-based foods.

Homocysteine to methionine
Home-O-Sistine to Methyl-thimble

Methionine synthase is a vitamin B12-dependent enzyme. This enzyme converts homocysteine to methionine, which plays a key role in DNA synthesis.

Methylmalonyl CoA to succinyl CoA
Methyl-melon Coin-A purse to Sucker Coin-A

Methylmalonyl Coenzyme A mutase is a vitamin B12-dependent enzyme. This enzyme converts methylmalonyl CoA to succinyl CoA.

Deficiency Signs and Symptoms

Macrocytic Megaloblastic Anemia
Macaroni Megablast Anemone

Because vitamin B12 plays an essential role in DNA synthesis, a vitamin B12 deficiency can cause abnormalities in blood cells, which have rapid turnover and are significantly affected by poor DNA synthesis. Therefore, a vitamin B12 deficiency can manifest as a macrocytic, megaloblastic anemia, indicating immature red blood cells.

Hypersegmented Neutrophils
Segway with (neutrophil) Nude-trojan

Because vitamin B12 plays an essential role in DNA synthesis, a vitamin B12 deficiency can cause abnormalities in blood cells, which have rapid turnover and are significantly affected by poor DNA synthesis. Therefore, a vitamin B12 deficiency can manifest as hypersegmented neutrophils, indicating immature neutrophils.

Neurologic defects
Neuron paddles

A vitamin B12 deficiency can be distinguished from a folate deficiency by the presence of neurologic symptoms resulting from damage to the spinal cord.

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Posterior column

Post-terrier

The posterior column (also known as the dorsal column–medial lemniscus pathway) is a white matter sensory tract located on the dorsomedial side of the spinal cord. It comprises two bundles: The fasciculus gracilis (medial) carrying information from the lower limbs, And the fasciculus cuneatus (lateral) carrying signals from the upper body. In vitamin?B?? deficiency, impaired myelin synthesis leads to demyelination, especially in the central fibers of the posterior columns, typically in the cervical and upper thoracic spinal levels. The accumulation of methylmalonic acid disrupts lipid metabolism, further compromising myelin integrity. Clinically, damage results in loss of vibration sense, proprioception, and impaired two-point discrimination.

Lateral corticospinal tract

Ladders on Corticospinal Tract

The lateral corticospinal tract is a major descending motor pathway originating in the primary motor cortex, responsible for voluntary control of contralateral limb muscles. Vitamin B?? (cobalamin) is a water-soluble vitamin essential for myelin synthesis and neurological function. Deficiency in vitamin B?? can lead to subacute combined degeneration (SCD) of the spinal cord, affecting both the dorsal columns and lateral corticospinal tracts.

Spinocerebellar tract

Silver-cerebellum-bell

This is a set of fibers that begins in the spinal cord and terminates in the ipsilateral cerebellum where it conveys information about limb and joint position. This tract is especially important for fine movement and damage to this tract can cause ataxia. This tract is commonly affected in vitamin B12 deficiency due to demyelination caused by buildup of methylmalonic acid.

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