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Megaloblastic Anemias

Megaloblastic anemia is caused by either a vitamin B-12 deficiency or a folic acid deficiency that results in impaired DNA synthesis and consequently enlarged red blood cells. These unusually large and structurally abnormal immature red blood cells are called megaloblasts, hence the name of this condition. A common characteristic of megaloblastic anemia is an increase in MCV and a normal MCHC.

Vitamin B-12 Deficiency

Please watch the video [Megaloblastic Anemia Part 1- Vitamin B12 Deficiency Anemia](#)

Vitamin B-12 is essential for DNA synthesis, nuclear maturation, and healthy myelin production for neurons. Vitamin B-12, also known as **cobalamin**, is found in foods of animal origin like meat and dairy products. Because there are so many sources of vitamin B-12, deficiency is fairly rare and is usually only seen in strict vegetarians/vegans.

To fully understand vitamin B-12 deficiency, we must first understand its absorption. Vitamin B-12 is bound to a binding protein when it is ingested and swallowed. In the stomach, pepsin that is produced by the chief cells will digest the binding proteins and release the vitamin B-12. **Haptocorrin** produced by the salivary glands then binds to vitamin B-12 to protect it from the stomach acid. In the duodenum, pancreatic proteases will break down haptocorrin and release the vitamin B-12. Vitamin B-12 will then bind to **intrinsic factor (IF)** which was produced upstream by the parietal cells of the stomach. It then travels to the ileum where the vitamin B-12/IF complex will bind to its receptor called **cubilin**. After binding, the complex is taken into the ileal enterocyte by receptor mediated endocytosis. Once inside the enterocyte, vitamin B-12 will associate with a carrier protein called **transcobalamin II**. This transcobalamin II/vitamin B-12 complex will then be secreted into the blood so vitamin B-12 can be delivered to tissues and organs like the liver and bone marrow.

Vitamin B-12 deficiency comes into play when certain patients lack intrinsic factor. Anemia due to a lack of IF that results in vitamin B-12 deficiency is called pernicious anemia. Someone might lack intrinsic factor because of an autoimmune destruction of parietal cells. Other causes of vitamin B-12 deficiency anemia are ileal resections, neoplasm/cancer in the ileum that interferes with absorption, and a gastrectomy (the patient lacks parietal cells). Vitamin B-12 deficiency anemia manifests itself through a neurological syndrome because of disorganized myelin around neurons. Patients may present with paresthesia (abnormal sensations) in the hands and feet, movement disorders, dementia, and neuropsychiatric changes. Diagnosis of vitamin B-12 deficiency is done by measuring low serum levels of vitamin B-12 and testing for antibodies against parietal cells and intrinsic factor. Treatment of vitamin B-12 deficiency is intramuscular injections of vitamin B-12 and high doses of oral vitamin B-12.

Folic Acid Deficiency

Please watch the video [Megaloblastic Anemia Part 2- Folic Acid Deficiency Anemia](#)

The other type of megaloblastic anemia is caused by folic acid deficiency. Like vitamin B-12, folic acid is used in the synthesis of DNA. Unlike vitamin B-12, folic acid does not require intrinsic factor to be absorbed because it is readily absorbed from the intestine on its own. Folic acid deficiency also doesn't lead to any neurological issues like vitamin B-

12 deficiency. To treat this condition, folic acid supplements are given and the diet is adjusted. Folic acid is found in high amounts in leafy greens, fruits, veggies, cereal, and meats. Causes of folic acid deficiency include:

- Malnutrition or a dietary deficiency that is caused by old age or alcoholism.
- Malabsorption due to celiac disease.
- Some medications, such as anticonvulsants, interfere with the absorption of folic acid.
- Cancer commonly leads to deficiency because cancer cells use a lot of folic acid for cell division.
- Pregnancy increases demand for folate to support the development of the fetus.



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