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**Megaloblastic Anemia**

Megaloblastic anemia is characterized by RBCs that are larger than normal. There also aren’t enough of them.When RBCs aren’t produced properly, it results in megaloblastic anemia. Because the blood cells are too large, they may not be able to exit the bone marrow to enter the bloodstream and deliver oxygen.

**Causes of megaloblastic anemia**

The two most common causes of megaloblastic anemia are deficiencies of vitamin B12 and folate.These two nutrients are necessary for producing healthy RBCs. When subject don’t get enough of them, it affects the makeup of the RBCs. This leads to cells that don’t divide and reproduce the way they should.

**Vitamin B12 deficiency**

Vitamin B12 is a nutrient found in foods and drinks such as:

\*lamb liver, beef, and other types of meat \*sardines, tuna, and other types of fish

\*eggs\*milk \*fortified nutritional yeast

Some people can’t absorb enough vitamin B12 from their diet, leading to megaloblastic anemia. Megaloblastic anemia caused by vitamin B12 deficiency is known as vitamin B12 deficiency anemia.One rare type of vitamin B12 deficiency anemia is pernicious anemia.

**Pernicious anemia** is an autoimmune condition and is due to the lack of a protein in the stomach called intrinsic factor. Without intrinsic factor, vitamin B12 can’t be absorbed, regardless of how much is consumed.

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It’s possible to develop vitamin B12 deficiency anemia because there simply isn’t enough vitamin B12 in the diet. Since B12 isn’t naturally found in any plant-based products, vitamin B12 deficiency is common in people following a vegetarian or vegan diet.

The subject can also develop vitamin B12 deficiency anemia if he take medications that deplete vitamin B12, such as proton pump inhibitors and metformin (Fortamet, Glumetza). Having certain types of surgery, including bariatric surgery, can also result in an inability to absorb vitamin B12.

**Symptoms of megaloblastic anemia**

The most common symptom of megaloblastic anemia is \*fatigue.Symptoms can vary from person to person. Other common symptoms include:

\*shortness of breath \*muscle weakness\*skin that is paler than usual

\*glossitis, or a swollen tongue \*a smooth or tender tongue

\*loss of appetite or weight loss \*diarrhea

\*nausea\*fast heart rate \*tingling in the hands and feet

\*numbness in the hands and feet

**Symptoms of vitamin B12 deficiency**

A vitamin B12 deficiency can lead to disruption in the nervous system and the circulatory system.Vitamin B12 deficiencies can lead to megaloblastic anemia, a condition where the bone marrow produces large abnormally shaped red blood cells that do not function properly.

Psychological conditions such as dementia, paranoia, depression, and behavioral changes can result from a vitamin B12 deficiency. Neurological damage sometimes cannot be reversed.

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Vitamin B12 deficiency can cause the following symptoms:

\*tiredness or fatigue \*weakness \*constipation

\*loss of appetite \*weight loss\*numbness and tingling in the hands and feet

\*balance problems \*confusion \*poor memory \*soreness of the mouth or tongue

**Dietary vitamin B12 deficiency** usually results from inadequate absorption, but deficiency can develop in vegans who do not take vitamin supplements. Deficiency causes megaloblastic anemia, damage to the white matter of the spinal cord and brain, and peripheral neuropathy. Diagnosis is usually made by measuring serum vitamin B12 levels. The Schilling test helps determine etiology. Treatment consists of oral or parenteral vitamin B12. Folate (folic acid) should not be used instead of vitamin B12 because folate may alleviate the anemia but allow neurologic deficits to progress.

Cobalamin is a general term for compounds with biologic vitamin B12 activity. These compounds are involved in nucleic acid metabolism, methyl transfer, and myelin synthesis and repair. They are necessary for the formation of normal red blood cells and normal neural function (see table Sources, Functions, and Effects of Vitamins).

Dietary sources of vitamin B12 include meats (especially beef, pork, and organ meats [eg, liver]), poultry, eggs, fortified cereals, milk and milk products, and seafood such as clams, oysters, mackerel, and salmon. Food-bound vitamin B12 is released in the stomach’s acid environment and is bound to R protein (haptocorrin). Pancreatic enzymes cleave this B12 complex (B12-R protein) in the small intestine. After cleavage, intrinsic factor, secreted by parietal cells in the gastric mucosa, binds with vitamin B12. Intrinsic factor is required for absorption of vitamin B12, which takes place in the terminal ileum.

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Vitamin B12 in plasma is bound to transcobalamins I and II. Transcobalamin II is responsible for delivering vitamin B12 to tissues. The liver stores large amounts of vitamin B12. Enterohepatic reabsorption helps retain vitamin B12. Liver vitamin B12 stores can normally sustain physiologic needs for 3 to 5 years if B12 intake stops (eg, in people who become vegans) and for months to 1 year if enterohepatic reabsorption capacity is absent.

**Etiology of Vitamin B12 Deficiency**

Vitamin B12 deficiency can result from:

\*Inadequate intake

\*Inadequate absorption

\*Decreased utilization

\*Use of certain drugs

Inadequate vitamin B12 intake is possible in vegans but is otherwise unlikely. Breastfed babies of vegan mothers may develop vitamin B12 deficiency by age 4 to 6 months because in these babies, liver stores (which are normally extensive in other babies) are limited and their rapid growth rate results in high demand.

Inadequate vitamin B12 absorption is the most common cause of deficiency In the elderly, inadequate absorption most commonly results from decreased acid secretion. In such cases, crystalline vitamin B12 (such as that available in vitamin supplements) can be absorbed, but food-bound vitamin B12 is not liberated and absorbed normally.

Inadequate absorption may occur in blind loop syndrome (with overgrowth of bacteria) or fish tapeworm infestation; in these cases, bacteria or parasites use ingested vitamin B12 so that less is available for absorption.Vitamin B12 absorption may be inadequate if ileal absorptive sites are destroyed by

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inflammatory bowel disease or are surgically removed .Less common causes of inadequate vitamin B12 absorption include chronic pancreatitis, gastric or bariatric surgery, malabsorption syndromes, AIDS, use of certain drugs (eg, antacids, metformin), repeated exposure to nitrous oxide, and a genetic disorder causing malabsorption in the ileum (Imerslund-Graesbeck syndrome).

Less commonly, decreased utilization of vitamin B12 or use of certain drugs causes vitamin B12 deficiency.

Pernicious anemia is often used synonymously with vitamin B12 deficiency. However, pernicious anemia specifically refers to anemia resulting from vitamin B12 deficiency caused by an autoimmune metaplastic atrophic gastritis with loss of intrinsic factor. Patients with classic pernicious anemia, most commonly younger adults, are at increased risk of stomach and other gastrointestinal cancers.

**Diagnosis of Vitamin B12 Deficiency**

Complete blood count (CBC) and vitamin B12 and folate levels

Sometimes methylmalonic acid levels or Schilling test

Diagnosis of vitamin B12 deficiency is based on CBC and vitamin B12 and folate levels. CBC usually detects megaloblastic anemia. A vitamin B12 level < 200 pg/mL (< 145 pmol/L) indicates vitamin B12 deficiency. The folate level is measured because vitamin B12 deficiency must be differentiated from folate deficiency as a cause of megaloblastic anemia; folate supplementation can mask vitamin B12 deficiency and may alleviate megaloblastic anemia but allow the neurologic deficits to progress or even accelerate.When clinical judgment suggests vitamin B12 deficiency but the vitamin B12 level is low-normal (200 to 350 pg/mL [145 to 260 pmol/L]) or hematologic indexes are normal, other tests can be done. They include measuring the following

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Serum methylmalonic acid (MMA) levels: An elevated MMA level supports vitamin B12 deficiency but may be due to renal failure. MMA levels can also be used to monitor the response to treatment. MMA levels remain normal in folate deficiency.Homocysteine levels: Levels may be elevated with either vitamin B12 or folate deficiency.Less commonly, holotranscobalamin II (transcobalamin II–B12 complex) content: When holotranscobalamin II is < 40 pg/mL (< 30 pmol/L), vitamin B12 is deficient.

After vitamin B12 deficiency is diagnosed, additional tests (eg, Schilling test) may be indicated for younger adults but usually not for the elderly. Unless dietary vitamin B12 is obviously inadequate, serum gastrin levels or autoantibodies to intrinsic factor may be measured; sensitivity and specificity of these tests may be poor.

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