Folate Deficiency

Folate deficiency occurs due to malabsorption, insufficient dietary intake, impaired metabolism and increased requirements for folate. It results in a macrocytic, megaloblastic anemia similar to Vitamin B12 deficiency; however, unlike Vitamin B12 deficiency it does not result in neurologic symptoms.



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Clinical Features

Macrocytic Anemia

Macaroni Anemone

Macrocytic means “large cell” in Greek and macrocytic anemia refers to RBCs with an MCV>100. To form mature RBCs, RBC precursors divide multiple times, and they get smaller with each division. Without the proper building blocks for DNA, such as adequate levels of folate, the RBC precursors divide fewer times resulting in larger red blood cells.

Megaloblastic Anemia

Mega-blast Anemone

Megaloblastic anemia refers to anemia due to impaired DNA synthesis leading to changes in cell morphology. These changes include large RBCs (macrocytic) and large and hypersegmented neutrophils. Folate deficiency and vitamin B12 deficiency are the most common causes of megaloblastic anemia. In a patient with megaloblastic anemia, vitamin B12 deficiency must be ruled out prior to treating a patient with folate as folate supplementation in a patient with vitamin B12 deficiency can worsen neurologic symptoms.

Etiologies

Malabsorption

Intestinal-mallet

Folate is absorbed in the proximal jejunum and ileum. Damage in these areas, such as transmural inflammation due to Crohn’s Disease, can lead to malabsorption of folate and thus folate deficiency.

Dietary

Nutritional-plate

Inadequate intake of folate, which is primarily found in fresh green leafy vegetables and liver, can lead to folate deficiency. Folate is heat sensitive and thus is lacking in cooked foods.

Tea and Toast

Tea and Toast

The “tea and toast” diet is a diet seen in the elderly where they subsist on food with little nutritious value. This diet is devoid of foods containing folate, such as green leafy vegetables, thus leading to folate deficiency. Body stores of folate can be depleted in 4-5 months.

Alcoholics

Alcoholic-martini

Chronic alcoholics often have poor diets that can result in folate deficiency. Other reasons for folate deficiency in alcoholics include impaired enterohepatic cycling which can lead to malabsorption of folate. Alcoholics can deplete their body stores of folate in 5-10 weeks compared with nonalcoholics who’s stores take 4-5 months to be depleted

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Medication-induced

Pill-bottle

There are many medications that can antagonize the effect of folate and thus lead to folate deficiency.

Methotrexate

Moth-T-Rex-ate

MTX is a folic acid analog that binds and inhibits dihydrofolate reductase, preventing the formation of the biologically active form of folic acid, tetrahydrofolate. This results in a functional folate deficiency as thymidine synthesis does not occur.

Trimethoprim

Tampon

TMP inhibits bacterial dihydrofolate reductase and has been found to exacerbate pre-existing folate deficiency.

Increased Requirement

Up-arrow Mouths

Conditions such as hemolytic anemia and pregnancy that demand a greater amount of folate can result in a relative folate deficiency (folate levels are actually within the normal range).

Hemolytic Anemia

Hemolysing-RBCs from Anemone

In hemolytic anemia the body attempts to compensate for RBC hemolysis by synthesizing new RBCs which require DNA synthesis. This results in a greater requirement for folate and thus a relative folate deficiency.

Pregnancy

Pregnant-woman

There is rapid cell division in pregnancy resulting in a greater requirement for folate and thus a relative folate deficiency.

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