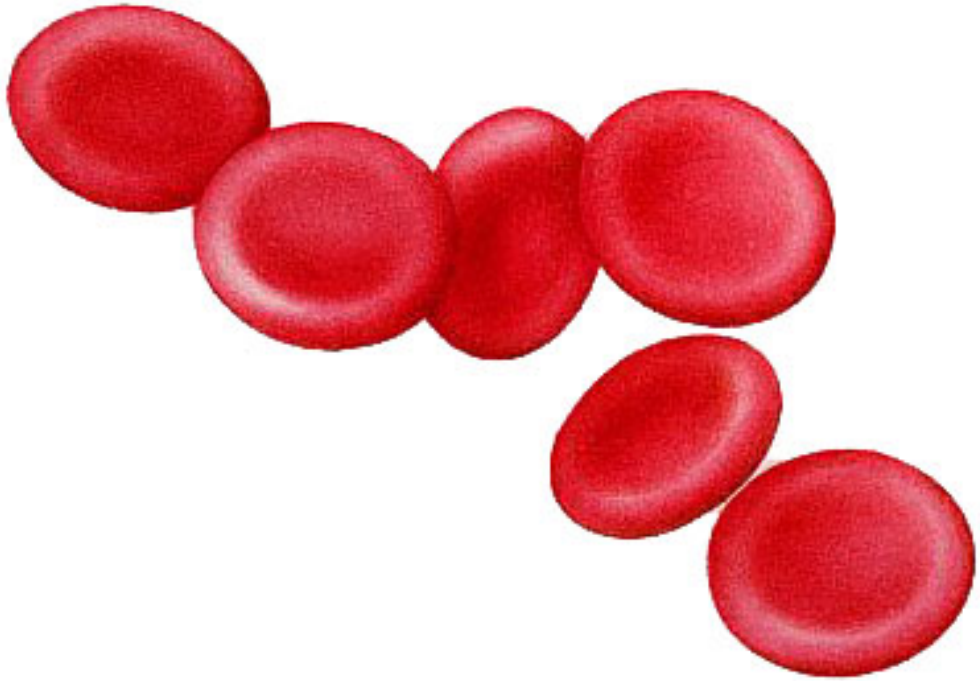


Pernicious Anemia and Vitamin B12 Deficiency Anemia

- Vitamin B12 Deficiency Anemia
  - Due to a lack of Vitamin B12
- Pernicious Anemia
  - Due to a lack of intrinsic factor

Both are megaloblastic, macrocytic anemia and result from the body's inability to properly utilize vitamin B12

Absorption of vitamin B12

- Stomach:
  - Vitamin B12 is freed from protein by gastric acid and enzymes.
  - Vitamin B12 then attaches to salivary R-binder
  - Intrinsic Factor is secreted by parietal cells
- Upper Small Intestine:
  - Pancreatic trypsin destroys R-binder
  - Intrinsic factor binds the vitamin B12, forming a vitamin B12-IF complex

Absorption of Vitamin B12 Cont.

- Ileum
  - With the presence of ionic calcium, B12-IF complex attaches to receptors on the ileal border
  - Vitamin B12 is released and then attaches to holotranscobalamin-II (holo TCII)
  - The TCII-Vitamin B12 complex enters the portal venous blood
  - TCII is recognized by receptors on cell surfaces, and cells receive the vitamin B12

What Exactly **IS** Intrinsic Factor?

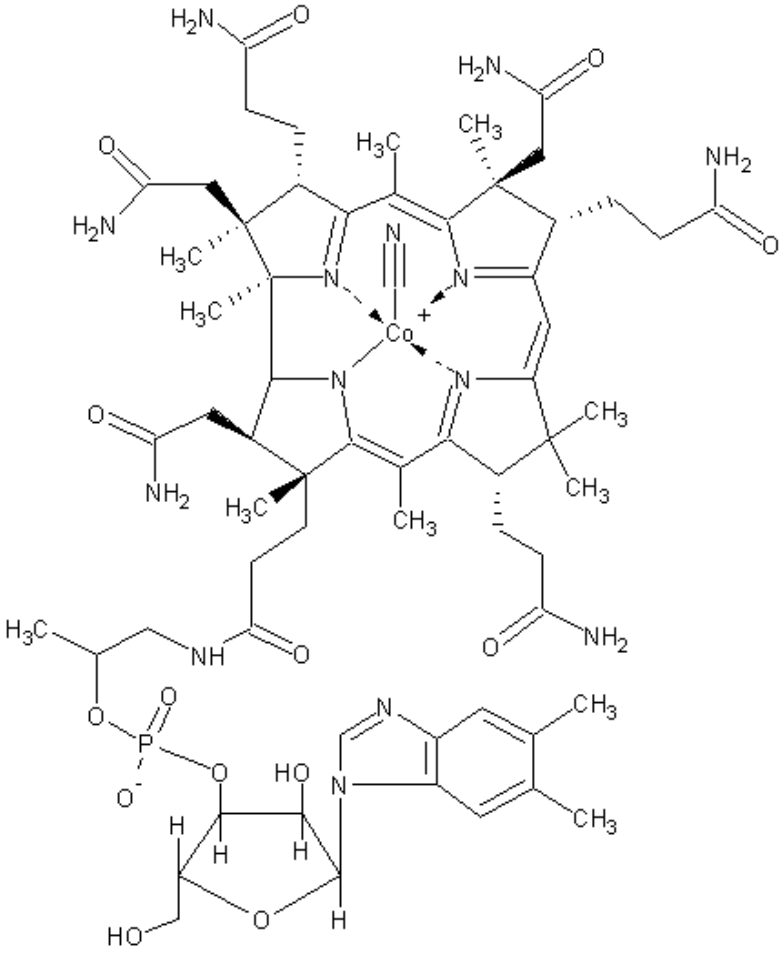
- A glycoprotein in gastric juice
- Secreted by parietal cells
- Necessary to absorb Vitamin B12
  - A carrier protein

Pernicious anemia

- Due to a lack of intrinsic factor
  - Antibodies against intrinsic factor
  - Antibodies against parietal cells in the stomach
  - Inability to produce intrinsic factor

Vitamin B12 Deficiency Anemia Etiology

- B12 is needed for proper development of red blood cells
  - Proliferation during differentiation
- Low vitamin B12 intake
  - Some vegetarians/vegans are at risk
  - We recycle Vitamin B12
- Inability of the body to properly use vitamin B12



ETIOLOGY
CAUSES OF MALABSORPTION OF B12

- Lack of TCII
- Small intestinal disorders affecting the Ileum:
  - Celiac disease, Idiopathic steatorrhea, Tropical sprue, Cancer
- Long-term alcohol or calcium-chelating agent use
- H. pylori infection
  - Parietal cells produce less intrinsic factor

More Causes of Malabsorption

- Drugs
  - Paraaminosalicylic acid (TB, Crohn's disease, Ulcerative Colitis)
  - Colchicine (Gout, anti-inflammatory)
  - Neomycin (Antibiotic)
  - Metformin (Diabetes)
    - Decreases absorption in the ileum by blocking receptors
    - Increased calcium intake can correct this
  - Antiretrovirals (HIV, any retroviral infection)

Signs and Symptoms

- Diarrhea or constipation
- Fatigue
- Light-headedness & shortness of breath with exertion
- Loss of appetite
- Pale skin
- Poor concentration
- Swollen, red tongue, or bleeding gums

Long-term Deficiency Signs &Symptoms

- Nerve Damage
  - Evidenced by:
  - Confusion
  - Depression
  - Loss of balance
  - Numbness/tingling in hands and feet

Signs and Symptoms

Labs

Labs	Normal	B12 Def. Anemia
Mean cell volume	80-96 μm^3	130 (High)
Mean cell Hgb	26-32 pg	34 (High)
Mean cell Hgb content	31.5-36 g/dL	38 (High)
RBC distribution	11.6-16.5%	17.8 (High)
Platelet count	140-440 $x10^3/mm^3$	135 (Low)
Vitamin B12	24.4-100 ng/dL	11 (Low)
MMA (methyl malonic acid)	0.08-0.56 mmol/L	0.75 (High)
White Blood Cells	Varies by type	Normal

Diagnosis

- Measure serum B12 and Folate levels
  - Determine which is low, therefore causing the anemia
  - dU Suppression test- measures how well the de novo pathway is working in DNA synthesis

- Lab Tests that can determine if the problem is a lack of IF
  - Testing for IF antibodies
    - Performed on a patient's serum
  - Schilling Urinary Excretion Test

Schilling Urinary Excretion Test

- Take large doses of B12 to fill stores
- Swallow radioactive B12
- Little vitamin B12 is excreted in the urine, because little to none is absorbed (because of lack of IF)
- Swallow radioactive B12 and IF
- Excretion through urine is almost normal (because of addition of IF)

- If B12 remains unchanged with addition of IF, then patient has a different malabsorption syndrome

Pathophysiology

- Megaloblastic, macrocytic anemia
  - Large, immature red blood cells
- Stages of deficiency:
  - Stage 1: Low holo-TCII value (<40 pg/mL)
  - Stage 2: Low B12 on haptocorrin (B12 storage protein), low B12 on TCII
  - Stage 3: Abnormal erythropoiesis
    - Short term memory loss

PATHOPHYSIOLOGY CONT.

- Stage 4: Clinical damage
  - Includes all symptoms from stages 1 – 3
  - B12 deficiency anemia
  - Macroovalocytic erythrocytes (large and oval shaped)
  - Elevated mean corpuscular volume (average red blood cell volume)
  - Elevated TCII levels
  - Increased homocysteine and methylmalonic acid levels
- B12 <200 pg/mL
  - Leukoencephalopathy (deterioration of white matter in the brain)
  - Psychiatric changes
  - Neuropathy
  - Dementia

PATHOPHYSIOLOGY CONT.

- Affects GI tract, CNS, and PNS
  - Distinguishes from folic acid deficiency anemia
  - Inadequate myelinization of nerves
- Low bone mineral density
- Low vitamin B12 leads to increased homocysteine levels
  - Aggravates heart disease
  - Adverse pregnancy outcomes
- With prolonged deficiency, damage may be irreversible, even with treatment

Treatment

- Injection of 100 mcg vitamin B12
  - Intramuscular or subcutaneous
  - Once per week until improvement is seen, then once a month until remission is retained without injections
- Initial doses should be high when vitamin B12 deficiency is complicated by serious illness (infection, hepatic disease, coma, etc.)

TREATMENT – WHEN MISSING IF

- Very large oral supplements can be used
  - 1,000 mcg/day
  - 1% of vitamin B12 is absorbed through diffusion

MNT

- Increase foods in the diet that are high in vitamin B12
  - Meat (especially beef and pork)
  - Eggs
  - Milk
  - Milk products
- Increase foods high in iron and folate
- High protein will help with liver function and blood regeneration
  - 1.5 g/kg

Recovery

- Hematological improvement
  - High levels of reticulocytes
  - Normal red blood cell production and function
- If B12 deficiency is short-term, all other symptoms will go away
- If B12 deficiency is long-term then negative neurological effects may be permanent

Sports Anemia

Hypochromic Microcycic Transient Anemia

- Increased plasma volume, hemodilution
- Normal erythrocytes
- Does not affect performance
- High risk
  - Athletes beginning rigorous training programs
  - Female, vegetarian athletes who participate in endurance sports, or who are in a growth spurt

Sports Anemia

- MNT
  - Consume iron rich foods to keep hemoglobin at optimal levels for oxygen delivery
  - Consume enough protein
    - 1.2 g/kg for endurance athletes
    - 1.4 g/kg for strength athletes
    - Do not consume more protein than your body can use, as this can compromise your CHO intake, and lead to high fat intake
  - Avoid tea, coffee, antacids, H2-blockers, tetracycline, since these inhibit iron absorption
  - Do not take an iron supplement unless iron deficiency is diagnosed by a doctor

Copper Deficiency Anemia

- Copper is part of a protein called ceruloplasmin
  - Needed to release iron from its storage state
  - Needed for optimal development and function of erythrocytes
  - Low serum iron and hemoglobin result, even if iron stores are adequate
- Amount of copper needed is very small, and therefore you will get enough through an adequate diet
- Those at risk:
  - Infants fed with cow's milk
  - Infants fed with formulas not containing iron
  - Anyone with a malabsorption syndrome
  - Someone on long-term parental nutrition that lacks copper

Vitamin B6 (pyridoxine) responsive Anemia

Sideroblastic Anemia

- Due to a genetic defect that results in malformation of δ - aminoolevulinic acid, which is needed for the complete synthesis of heme.
- Results in
  - Immature erythrocytes that contain iron (sideroblasts)
  - The iron cannot be used for heme synthesis, so it is stored in the cell's mitochondria. The mitochondria cannot function properly.
  - Microcytic, hypochromic RBCs
  - High serum and tissue levels of iron
- Treatment
  - The anemia responds to high doses of vitamin B6 (pyridoxine)
  - 50 – 200 mg are given daily (25 – 100 times the RDA)
  - If the anemia responds, the therapy is continued for life
  - Response to treatment has varries for different people, and none have a full correction of the anemia

Non-nutritional Sickle Cell Anemia

- Affects 1 in 600 African Americans
- Caused by inheritance of hemoglobin S
- Results in defective hemoglobin synthesis
  - Sickle shaped cells
  - Get stuck in capillaries
  - Can't effectively carry oxygen
- Severe abdominal pain from misshapen erythrocytes getting stuck in vessels
- High levels of hemolysis results in impaired renal & liver function, jaundice, gallstones and high levels of iron in the liver
- Those effected have lower vitamin B6 levels, even when intake is the same as those who are unaffected

Sickle Cell Anemia

- Treatment:
  - Management of pain symptoms
  - Keeping body oxygenated
  - Transfusions
- MNT
  - Low iron diet – iron will build up because it is unused
  - Zinc supplementation: increases the oxygen affinity of sickle-shaped erythrocytes. Can also help with other problems seen in people with this disease such as, decreased skeletal growth, muscle mass, and sexual maturation
    - Don't give too much Zinc, because Zinc can compete with copper for absorption

Sickle Cell Anemia

- MNT cont. :
  - Sometimes eat less because of abdominal pain
  - Have higher metabolisms due to chronic inflammation and oxidative stress, need more calories
  - Need lots of folate, because cells are destroyed and new ones are constantly being made
  - Should be on a supplement with 50-150% RDA of folate, zinc, and copper, but NOT iron
  - Need high amounts of fluid (2-3 quarts per day) and low sodium
  - Need high amounts of plant protein, not animal protein because it contains iron
  - Alcohol and ascorbic acid should be avoided, because they increase iron absorption
  - Iron deficiency may be seen in people with Sickle Cell Anemia, because of many transfusions
    - This should be looked at and the diet should be adjusted as necessary