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
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

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