ANEMIA

- **Anemia**: a deficiency in the size/number of RBC or the amount of hemoglobin they contain that limits the exchange of oxygen and carbon dioxide between the blood and the tissue cells.

- **Classification based on:**
  - size: macrocytic, normocytic, microcytic
  - Hemoglobin content: hypochromic, normochromic, hyperchromic
ANEMIA

• **Nutritional causes of anemia**
  - nutritional deficit
    - iron, folate, and vitamin $B_{12}$

• **Treatment**
  - Treat the underlying disease first
  - Treat anemia
NUTRITIONAL ANEMIAS

- Populations of Concern:
  - Hospitalized patients
  - Pregnant women
  - Young children
  - Elderly
  - Blood loss
IRON DEFICIENCY ANEMIA
OVERVIEW OF IRON

• Essential Nutrient

• Human Stores
  • Functional Iron
    • Hemoglobin, Myoglobin, Enzymes
  • Storage Iron
    • Ferritin, Hemosiderin, Transferrin
# RECOMMENDED INTAKE

## Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals, Minerals

Food and Nutrition Board, Institute of Medicine, National Academies

<table>
<thead>
<tr>
<th>Life/Stage Group</th>
<th>Calcium (mg/d)</th>
<th>Chromium (µg/d)</th>
<th>Copper (µg/d)</th>
<th>Fluoride (mg/d)</th>
<th>Iodine (µg/d)</th>
<th>Iron (mg/d)</th>
<th>Magnesium (mg/d)</th>
<th>Manganese (mg/d)</th>
<th>Molybdenum (mg/d)</th>
<th>Phosphorus (mg/d)</th>
<th>Selenium (µg/d)</th>
<th>Zinc (mg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6 mo</td>
<td>210*</td>
<td>0.2*</td>
<td>200*</td>
<td>0.01*</td>
<td>110*</td>
<td>0.27*</td>
<td>30*</td>
<td>0.003*</td>
<td>2*</td>
<td>100*</td>
<td>15*</td>
<td>2*</td>
</tr>
<tr>
<td>7-12 mo</td>
<td>270*</td>
<td>5.5*</td>
<td>220*</td>
<td>0.5*</td>
<td>130*</td>
<td></td>
<td>75*</td>
<td>0.8*</td>
<td>3*</td>
<td>275*</td>
<td>20*</td>
<td>3*</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 yr</td>
<td>500*</td>
<td>11*</td>
<td>340*</td>
<td>0.7*</td>
<td>90</td>
<td>7</td>
<td>80</td>
<td>1.2*</td>
<td>17</td>
<td>460</td>
<td>20</td>
<td>3*</td>
</tr>
<tr>
<td>4-8 yr</td>
<td>800*</td>
<td>15*</td>
<td>440*</td>
<td>1*</td>
<td>90</td>
<td>10</td>
<td>130</td>
<td>1.5*</td>
<td>22</td>
<td>500</td>
<td>30</td>
<td>5*</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-13 yr</td>
<td>1300*</td>
<td>25*</td>
<td>700*</td>
<td>2*</td>
<td>120</td>
<td>8</td>
<td>240</td>
<td>1.9*</td>
<td>34</td>
<td>1250</td>
<td>40</td>
<td>8*</td>
</tr>
<tr>
<td>14-18 yr</td>
<td>1300*</td>
<td>35*</td>
<td>890*</td>
<td>3*</td>
<td>150</td>
<td>11</td>
<td>410</td>
<td>2.2*</td>
<td>43</td>
<td>1250</td>
<td>55</td>
<td>11*</td>
</tr>
<tr>
<td>19-30 yr</td>
<td>1000*</td>
<td>35*</td>
<td>900*</td>
<td>4*</td>
<td>150</td>
<td>8</td>
<td>400</td>
<td>2.3*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>11*</td>
</tr>
<tr>
<td>31-50 yr</td>
<td>1000*</td>
<td>35*</td>
<td>900*</td>
<td>4*</td>
<td>150</td>
<td>8</td>
<td>420</td>
<td>2.3*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>11*</td>
</tr>
<tr>
<td>51-70 yr</td>
<td>1200*</td>
<td>30*</td>
<td>900*</td>
<td>4*</td>
<td>150</td>
<td>8</td>
<td>420</td>
<td>2.3*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>11*</td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>1200*</td>
<td>30*</td>
<td>900*</td>
<td>4*</td>
<td>150</td>
<td>8</td>
<td>420</td>
<td>2.3*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>11*</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-13 yr</td>
<td>1300*</td>
<td>21*</td>
<td>700*</td>
<td>2*</td>
<td>120</td>
<td>8</td>
<td>240</td>
<td>1.6*</td>
<td>34</td>
<td>1250</td>
<td>40</td>
<td>8*</td>
</tr>
<tr>
<td>14-18 yr</td>
<td>1300*</td>
<td>24*</td>
<td>890*</td>
<td>3*</td>
<td>150</td>
<td>15</td>
<td>360</td>
<td>1.6*</td>
<td>43</td>
<td>1250</td>
<td>55</td>
<td>9*</td>
</tr>
<tr>
<td>19-30 yr</td>
<td>1000*</td>
<td>25*</td>
<td>900*</td>
<td>3*</td>
<td>150</td>
<td>18</td>
<td>310</td>
<td>1.8*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>8*</td>
</tr>
<tr>
<td>31-50 yr</td>
<td>1000*</td>
<td>25*</td>
<td>900*</td>
<td>3*</td>
<td>150</td>
<td>18</td>
<td>320</td>
<td>1.8*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>8*</td>
</tr>
<tr>
<td>51-70 yr</td>
<td>1200*</td>
<td>20*</td>
<td>900*</td>
<td>3*</td>
<td>150</td>
<td>8</td>
<td>320</td>
<td>1.8*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>8*</td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>1200*</td>
<td>20*</td>
<td>900*</td>
<td>3*</td>
<td>150</td>
<td>8</td>
<td>320</td>
<td>1.8*</td>
<td>45</td>
<td>700</td>
<td>55</td>
<td>8*</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤18 yr</td>
<td>1300*</td>
<td>29*</td>
<td>1000*</td>
<td>3*</td>
<td>220</td>
<td>27</td>
<td>400</td>
<td>2.0*</td>
<td>50</td>
<td>1250</td>
<td>60</td>
<td>13*</td>
</tr>
<tr>
<td>19-30 yr</td>
<td>1000*</td>
<td>30*</td>
<td>1000*</td>
<td>3*</td>
<td>220</td>
<td>27</td>
<td>350</td>
<td>2.0*</td>
<td>50</td>
<td>700</td>
<td>60</td>
<td>11*</td>
</tr>
<tr>
<td>31-50 yr</td>
<td>1000*</td>
<td>30*</td>
<td>1000*</td>
<td>3*</td>
<td>220</td>
<td>27</td>
<td>360</td>
<td>2.0*</td>
<td>50</td>
<td>700</td>
<td>60</td>
<td>11*</td>
</tr>
<tr>
<td>Lactation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤18 yr</td>
<td>1300*</td>
<td>44*</td>
<td>1300*</td>
<td>3*</td>
<td>290</td>
<td>10</td>
<td>360</td>
<td>2.6*</td>
<td>50</td>
<td>1250</td>
<td>70</td>
<td>14*</td>
</tr>
<tr>
<td>19-30 yr</td>
<td>1000*</td>
<td>45*</td>
<td>1300*</td>
<td>3*</td>
<td>290</td>
<td>9</td>
<td>310</td>
<td>2.6*</td>
<td>50</td>
<td>700</td>
<td>70</td>
<td>12*</td>
</tr>
<tr>
<td>31-50 yr</td>
<td>1000*</td>
<td>45*</td>
<td>1300*</td>
<td>3*</td>
<td>290</td>
<td>9</td>
<td>320</td>
<td>2.6*</td>
<td>50</td>
<td>700</td>
<td>70</td>
<td>12*</td>
</tr>
</tbody>
</table>

HUMAN STORES

- Men
  - ~3.6 g TBI
- Women
  - ~2.4 g TBI
IRON ABSORPTION

- Heme
  - About 15% absorbed
  - Food sources: liver, beef
  - MFP – Meat Fish and Poultry Factor

- Non-heme
  - 3-8 % absorbed
  - Food sources: dried fruits, green leafy vegetables, fortified cereals
SITE OF ABSORPTION

- **Stomach**
  - Alcohol (20% of total)

- **Small Intestine**
  - Calcium, magnesium, iron
  - Glucose
  - Water-soluble vitamins
  - Alcohol (80% of total)
  - Sodium, potassium
  - Water-soluble vitamins
  - Fat-soluble vitamins
  - Amino acids
  - Fats
  - Vitamin B-12
  - Bile
**ABSORPTION**

**A** Heme iron is transported across brush border and enters the same pool as non-heme iron. Dietary non-heme iron (Fe^{3+}) must be reduced for transport across the brush border.

**B** Some iron is used or stored within the enterocyte in ferritin and lost when the intestinal mucosa is sloughed.

**C** Ferroportin aids in export of iron out of the intestinal cell for incorporation into serum transferrin.
# FACTORS OF ABSORPTION

<table>
<thead>
<tr>
<th>Increase Absorption</th>
<th>Decrease Absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric acid</td>
<td>Phytic acid (in fiber)</td>
</tr>
<tr>
<td>Heme iron in food</td>
<td>Oxalic acid in leafy vegetables</td>
</tr>
<tr>
<td>High body demand for red blood cells (blood loss, high altitude, physical training, pregnancy)</td>
<td>Polyphenols in tea, coffee, red wine, and other foods</td>
</tr>
<tr>
<td>Low body stores of iron</td>
<td>Full body stores of iron</td>
</tr>
<tr>
<td>Meat protein factor (MPF)</td>
<td>Excessive intakes of other minerals (Zn, Mn)*</td>
</tr>
<tr>
<td>Vitamin C intakes</td>
<td>Reduced gastric acid output</td>
</tr>
<tr>
<td>Calcium-containing supplements and antacids (small effect in the long run)</td>
<td></td>
</tr>
</tbody>
</table>

*Especially when taken as supplements
FUNCTIONS

- Hemoglobin:
  - Transport of Oxygen
- Myoglobin
  - Storage of Oxygen
- Enzymes
  - Energy Metabolism
- New Cell Growth
PREVALENCE/INCIDENCE

• Most common nutritional deficiency

• Iron Deficiency
  • 9-11% of adolescent girls and women in US
  • ≈ 20% of adults over 65 years old

• Iron Deficiency Anemia
  • 2-5% of adolescent girls and women in US
    • Greater in Developing Countries
ETIOLOGY

- Inadequate absorption
- Inadequate use of intestines
- Defects in release from stores
- Inadequate utilization
- Increased blood loss or excretion
- Increased requirement
ETIOLOGY

• Inadequate Intake
  • Recommended Intake:
    • 18 mg/day - Women
    • 8 mg/day - Men
  • Poor Diet, Vegetarians

• Malabsorption
  • Gastric Disorders
  • Drug Interference
ETIOLOGY

• Increased Iron Requirements
  • Periods of Growth
    • Pregnancy, Lactation, Infancy, Adolescents
      • 27mg/day - Pregnant Women

• Increased Excretion
  • Menses in Females
  • Gastrointestinal Bleeding
    • Ulcers, GERD
ETIOLOGY

• Defective Release of Iron
  • Chronic Inflammation
    • Hospitalized Patient
STAGE I & II

• Stage I
  • Moderate Depletion of Iron Stores
    • No Dysfunction

• Stage II
  • Severe Depletion of iron stores
    • No Dysfunction
STAGE III & IV

• Stage III
  • Inadequate Iron in the Body
    • Dysfunction & No Anemia

• Stage IV
  • Inadequate Iron in the Body
    • Dysfunction & Anemia
SIGNS AND SYMPTOMS

Normal RBCs

Microcytic Hypochromic RBCs
SIGNS AND SYMPTOMS

- Inadequate muscle function
- Pallor of Skin
- Growth Abnormalities
- Epithelial Disorders
- Compromised Immune System
SEVERE SIGNS & SYMPTOMS

- Glossitis
- Angular Stomatitis
- Dysphagia
- Koilonychia

- Untreated Anemia
  - Cardiovascular Problems
    - Leads to Cardiac Failure
DIAGNOSTIC TESTS

- Measurement of:
  - Ferritin Levels
    - Serum, Bone Marrow
  - Transferrin Level
    - Serum, STfR
  - Iron Levels
    - Serum & TIBC
  - Protoporphyrin
### Diagnosis of Iron Metabolism

<table>
<thead>
<tr>
<th>Stage</th>
<th>Positive Balance</th>
<th>Normal</th>
<th>Depletion</th>
<th>Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Iron overload</td>
<td>4+</td>
<td>3+</td>
<td>2-3+</td>
</tr>
<tr>
<td>Stage II</td>
<td>Positive iron balance</td>
<td>300</td>
<td>300</td>
<td>330 ± 30</td>
</tr>
<tr>
<td>Stage I Early negative iron balance</td>
<td>Normal</td>
<td>100 ± 60</td>
<td>&lt;25</td>
<td>20</td>
</tr>
<tr>
<td>Stage II Iron depletion</td>
<td>Normal</td>
<td>5-10</td>
<td>10-15</td>
<td>10-15</td>
</tr>
<tr>
<td>Stage III Damaged metabolism: iron-deficient erythropoiesis</td>
<td>Normal</td>
<td>115</td>
<td>115</td>
<td>&lt;60</td>
</tr>
<tr>
<td>Stage IV Clinical damage: iron-deficiency anemia</td>
<td>Normal</td>
<td>40-60</td>
<td>40-60</td>
<td>40-60</td>
</tr>
<tr>
<td></td>
<td>Microcytosis/hypochromic</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

#### Iron Stores
- RE marrow Fe: $<300$ µg/100ml
- Plasma ferritin (µg/L): $>300$
- Iron absorption (%): $>15$
- Plasma iron (µg/100ml): $>175$
- Transferrin saturation (%): $>60$

#### Circulating Iron
- Sideroblasts (%): 40-60
- RBC protoporphyrin: 30
- Erythrocytes: Normal
- Serum transferrin receptors: Normal

#### Erythron Iron
- Ferritin-iron (haloferritin) (ng/ml): Very high

---

* IRON EXCESS*

---

* IRON INSUFFICIENCY*

---

* NEGATIVE BALANCE*
CBC

- **RBC**: count of the actual number of red blood cells per volume of blood.
- **HGB**: measures the amount of oxygen-carrying protein in the blood.
- **HCT**: measures the percentage of red blood cells in a given volume of whole blood.
- **MCV**: a measurement of the average size of your RBCs.
- **MCH**: a calculation of the average amount of oxygen-carrying hemoglobin inside a red blood cell.
- **MCHC**: a calculation of the average concentration of hemoglobin inside a red cell.
- **RDW**: a calculation of the variation in the size of your RBCs.
- **ZPP**: Identifies a disruption in the formation of heme.
PREVALENCE AND INCIDENCE

- CDHS 2005 data
  - 47% women anemic
    - 35% mild
    - 10% moderate
    - 1% severe
  - High parity, little/no education, pregnant, living in poor households
  - Anemia is higher among rural than urban women

Figure 4.6: Trends in anemia status among women age 15-49

source: CDHS 2005
IRON DEFICIENCY ANEMIA IN PREGNANT WOMEN

- Affect growth and development of the fetus

- Helminths
  - “feed on blood and cause further bleeding by releasing anticoagulant compounds”.

- Antihelminthic drugs
HELMINTHS AFFECT YOUNG CHILDREN
IRON DEFICIENCY AND YOUNG CHILDREN

- Low income families

- NHANES III survey
  - approximately 10% of children ranging from one to two years of age, are in iron deficient
MNT

- Ferrous
  - 50 to 200 mg

- Ferritin
FOODS REDUCING IRON ABSORPTION

• Interfering agents:
  • Carbonates, oxalates, phosphates, phytates, tannins

• Examples:
  • Unleavened breads
  • Unrefined cereals
  • Soybeans
  • Tea, coffee
IRON ABSORPTION

• Best
  • Empty stomach

• Side Effects
  • nausea, epigastric discomfort/distention, heartburn, diarrhea, constipation
  • Counteract: Take supplements with meals

• Ascorbic acid
FOLATE DEFICIENCY ANEMIA
FOLATE

• an essential water soluble vitamin
• found in green leafy vegetables

• DRI
  • All adults: 400 micrograms DFE*/day (RDA)
  • Pregnant women: 600 micrograms DFE*/day (RDA)
  • Lactating women: 500 micrograms DFE*/day (RDA)

*DFE: dietary folate equivalent
  DFE = micrograms food folate
  + (1.7 x micrograms synthetic folate)
FOLIC ACID
FOLATE (FOLIC ACID)

- **Folate**
  - Has 3-10 glutamates
  - Found naturally in food

- **Folic acid**
  - Has only one glutamate
  - The most stable form of folate
  - Used for supplementation and fortification.
FOLATE METABOLISM

Fig. 47-4. Schematic for the absorption of folic acid. MG is the monoglutamate form. THF is the coenzyme, tetrahydrofolate.

Folate can accept four hydrogens to become tetrahydrofolic acid (THFA), the active coenzyme form.

THFA accepts and donates single carbon groups during DNA synthesis.
FOLATE METABOLISM (CONT.)

5-CH₃-THF-G₁

Methionine

CH₃

Homocysteine

Vitamin B₁₂ required

THF-G₁ (active form)

Many reactions

THF-G₂-7

Many reactions
FUNCTION OF FOLATE

- Folate works as a cofactor of many metabolism pathways in human body
  - homocysteine metabolism
  - thymine synthesis
  - serine synthesis
  - histidine catabolism
- thymine synthesis is required for normal DNA synthesis that is important for cell division and growth
Folate’s Absorption and Activation

In foods, folate naturally occurs as polyglutamate. (Folate occurs as monoglutamate in fortified foods and supplements.)

In the intestine, digestion breaks glutamates off and adds a methyl group. Folate is absorbed and delivered to cells.

In the cells, folate is trapped in its inactive form.

To activate folate, vitamin $B_{12}$ removes and keeps the methyl group, which activates vitamin $B_{12}$.

Both the folate coenzyme and the vitamin $B_{12}$ coenzyme are now active and available for DNA synthesis.
ERYTHROCYTE SYNTHESIS IN BONE MARROW

Stem Cell

Normal

Cell division times

Hb 20%

Hb 33%

Low Fe

Hb 20%

Hb 33%
ERYTHROCYTE SYNTHESIS IN BONE MARROW

Normal: Stem Cell → Cell division times → Hb 20% → Hb 33%

Low Folate: Stem Cell → Cell division times → Hb 20% → Hb 33%

Hb: Hemoglobin
NORMAL VS MACROCYTIC CELLS

http://www.umm.edu/imagepages/1218.htm

http://www.kosmix.com/topic/macrocytic_anemia/Images
MACROCYTOSIS

http://meds.queensu.ca/medicine/deptmed/hemonc/anemia/macroc.htm
CAUSATIONS

1. Inadequate ingestion
   Poor diet

2. Inadequate absorption
   Celiac disease, Jejunal disease, and short-bowel syndrome
   Drugs (anticonvulsants, metformin, sulfasalazine, etc.)
   Alcohol

3. Inadequate use (metabolic block)
   Folic acid antagonists (methotrexate, triamterene)
   Alcohol
   Vitamin B<sub>12</sub> deficiency (Methylfolate Trap)
CAUSATIONS

4. Increased requirement
   Pregnancy, lactation, infancy
   Malignant tissue, increased hemotopoiesis
   Drugs

5. Increased excretion
   Liver disease, kidney disease, exfoliative dermatitis
   Vitamin B12 deficiency

6. Increased destruction
   Oxidants in diet
DEPLETION STAGES

Stage 1 – Early negative folate balance (serum folate level < 3ng/ml). Liver folate and red blood cell folate are not significantly affected.

Stage 2 – Folate depletion (red blood cell folate < 160ng/ml). Liver folate is slightly decreased.
DEFICIENCY STAGES

Stage 3 – Damaged metabolism (folate deficiency erythropoiesis). Defective DNA synthesis.

Stage 4 – Clinical damage (folate deficiency anemia). Macroovalocytic red blood cells, an elevated mean corpuscular volume, and serum hemoglobin < 12 g/dl.
* Dietary excess of folate reduces zinc absorption.
† Designates the degree of hypersegmentation of neutrophils.
SEQUENCE OF EVENTS

- Low Serum Folate
- Hypersegmentation
- High Urine FIGLU
- Low RBC Folate
- Macroovalocytosis
- Megaloblastic Marrow
- Anemia
DIAGNOSIS

• Serum folic acid level
• Red blood cell folate
• Serum vitamin B12
• Vitamin B12 bound to TCII
Radioimmunoassay (RIA) or enzyme immunoassay (EIA) are common.
- Normal serum folate: 5-25ng/ml
- Folate deficiency anemia: <3ng/ml

May increase in pernicious anemia
- Due to the lack of vitamin B12, folic acid is not normally metabolized

May increased by recent massive blood transfusion

Decreased for a short-term by alcohol intake
RED BLOOD CELL FOLATE

• Thought as an indicator of long term folate status
  • Folate deficiency anemia: < 140-160ng/ml

• Less sensitive to short term dietary intake

• A superior measurement of folate tissue stores

• Decreased in vitamin B12 deficiency
# FOLATE VS. VITAMIN B12 DEFICIENCY (DIAGNOSIS)

<table>
<thead>
<tr>
<th></th>
<th>Folate deficiency</th>
<th>Vitamin B$_{12}$ deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Folate</td>
<td>Low</td>
<td>Could be high</td>
</tr>
<tr>
<td>Red Blood Cell Folate</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Serum Vitamin B$_{12}$</td>
<td>Normal</td>
<td>Low</td>
</tr>
<tr>
<td>Vitamin B$_{12}$ bound to TCII</td>
<td>Normal</td>
<td>Low</td>
</tr>
</tbody>
</table>
SIGNS AND SYMPTOMS

- Decrease the number of erythrocytes, leukocyte, and platelets.
- GI symptoms
  - Glossitis, fissures, diarrhea, inflammation of the pharynx or esophagus, ulceration of the stomach and intestine
- Nerve damages
  - Irritability, forgetfulness, hostile/paranoid behavior
- Others
  - Weakness/tiredness, dyspnea, anorexia/weight loss, syncope, headache, palpitation.
COMPLICATIONS

• Pregnancy women: Neural Tube Defect (NTD), prematurity of fetus
• Children: growth retardation
• Female: delay the onset of menstruation
# FOLATE VS. VITAMIN B12 DEFICIENCY
## (SIGNS AND SYMPTOMS)

<table>
<thead>
<tr>
<th></th>
<th>Folate Deficiency Anemia</th>
<th>Vitamin B12 Deficiency Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megaloblastic Macrocytic erythrocytes</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Occurrences (after a deficient diet)</td>
<td>After 2-4 months</td>
<td>After several years</td>
</tr>
<tr>
<td>GI Symptoms</td>
<td>Diarrhea</td>
<td>Constipation</td>
</tr>
<tr>
<td>Nerve Damage</td>
<td>Mild</td>
<td>Severe (Myelin damage)</td>
</tr>
<tr>
<td>NTD</td>
<td>+</td>
<td>-/?</td>
</tr>
</tbody>
</table>
• 1 mg folate, every day for 2 or 3 weeks

• Adjusted to 500 to 1000 mcg of folic acid daily
  • to prevent the depletion of the regained stores.

• Complications
  • Example: alcoholism, suppresses hematopoiesis
  • 2nd dose range: 500 to 1000 mcg
    • adequately compensate for the complication.
MNT - FOODS

• First: corrected through medication

• Second: patient encouraged to eat foods that are high in folate:
  • Turkey, black beans, yogurt, milk, fresh oranges, broccoli, wheat germ, fortified cereals
  • at least one fresh, uncooked fruit or vegetable or to drink a glass of fruit juice daily
VITAMIN $\text{B}_{12}$

PERNICIOUS ANEMIA
VITAMIN B12

- **Functions**
  - DNA synthesis
  - Regenerates Folate
  - Nerve cell maintenance
  - Cell metabolism

- **Food Sources**
  - Animal products, dairy products
  - Fortified cereal, soy, meat substitutes, and yeast
B₁₂ is consumed tightly bound to dietary protein
In the stomach pepsin hydrolyzes the protein and R-binder protein binds forming a complex
Travels to small intestine where trypsin releases B₁₂ allowing Intrinsic Factor (IF) to bind
The IF-B₁₂ complex with the aid of Ca is absorbed by brush border of the ileum
In blood stream, Transcobalamin carries B₁₂ to the cell receptors.
NECESSARY COMPONENTS

- **R-binder protein** – secreted in saliva and other gastric intestinal secretions
- **Parietal Cells** – secrete gastric acid and IF
- **Intrinsic Factor** – Glycoprotein necessary for B12 absorption
- **Brush border of Ileum** – main site of B12 absorption
- **Transcobalamin** – (TCII) transport protein for B12
PERNICIOUS ANEMIA

- Characterized by megaloblastic macrocytic anemia caused by deficiency of vitamin B12, secondary to lack of Intrinsic Factor
- Can be masked by folate deficiency anemia
- If not corrected damage to nervous system can be permanent
Normal blood cells in the bloodstream. The size, shape, and color of the red blood cells show that they are normal. Mature red blood cells have lost their nuclei.

Megaloblastic blood cells seen here in the bone marrow are arrested at an immature stage of development. They still have their nuclei and are slightly larger than normal red blood cells.
RDA

- Adults – 2.4 micrograms
- Pregnant – 2.6 micrograms
- Lactating – 2.8 micrograms
ETIOLOGY

- Malabsorption
- Autoimmunity
- Lack of B12 in the diet
MALABSORPTION

• Mouth – lack of secretions limit the production of R-binding protein
• Stomach
  • Parietal cells – lack of or damage due to genetics, disease, or surgeries limit production of IF
  • Atrophic Gastritis– major concern in elderly- shrinking of stomach muscles also decreases production of IF.
• Small Intestine
  • Pancreas – pancreatitis or other diseases that disrupt the function of the pancreas to produce trypsin and bicarbonate
  • Ileum – major site of B12 absorption – diseases such as crohn’s, celiac disease, enteritis, or gastric resections limit body’s absorption of B12
AUTOIMMUNITY

• Anti-IF antibodies
  • Type I – blocks IF from binding to B12
  • Type II – binds to IF preventing B12 from binding

• Anti-parietal cell antibodies
  • 90% of patients with pernicious anemia have anti-parietal cell antibodies and over half of those also have anti-IF antibodies.
DIET

- Very rare and happens after many years due to the long term B₁₂ storage ability
- People of concern
  - Vegans
  - Elderly
  - Chronic alcoholics
  - Religious Groups
THE ELDERLY

- 30% of people over the age of 50 have Atrophic Gastritis
- Decreases gastric acid secretion resulting in an impaired ability to release $B_{12}$ bound to dietary protein and decreased production of IF.
- Lower gastric acid also results in overgrowth of bacterial flora which use $B_{12}$ for their use.
COURSE OF THE CONDITION

• **Stage 1** – Negative Vitamin B12 balance
  • Low B12 levels resulting in low transcobalamin levels

• **Stage 2** – Depletion
  • Without transcobalamin, any B12 present in the body cannot be transported to the cells

• **Stage 3** – Metabolism Damage
  • Damaged RBC synthesis, lower TIBC, low folate levels

• **Stage 4** – Clinical Damage
  • Anemia, increased homocysteine levels, nervous system damage
SIGNS AND SYMPTOMS

- Megaloblastic Macrocytic Anemia
  - Large immature RBC
- Yellow skin, glossitis, fatigue
SIGNS AND SYMPTOMS

• Megaloblastic Madness
  • Numbness, tingling, memory loss, hallucinations, loss of motor control, poor perception of balance
  • Later stage of the condition
  • May be permanent if not treated
DIAGNOSIS

• Blood indices – if macrocytic anemia proceede to the following
  • B12 serum and excretion levels
  • Test for antibodies
  • Schillings test
SERUM/EXCRETION LEVELS

- Blood sample tests for serum B12 levels.
  - Indicator of recently digested B12
  - Low levels indicate Pernicious Anemia
- Urine Analysis
  - Measures the byproduct of B12 metabolism: methylmalonic acid
  - Better indicator of long term B12 levels
  - High levels indicate Pernicious Anemia
ANTIBODIES

• Radioimmunoassays are much a easier and cheaper diagnostic procedure
• Test for anti-parietal and anti-IF antibodies
• Distinguishes if malabsorption is caused by lack of IF or due to an intestinal problem
• **Stage I** – Patient is given radioactive B12 and urinary B12 levels are measured
• **Stage II** – Patient is given radioactive B12 and IF and urinary B12 levels are measured
  • If urinary B12 levels are higher than Stage I, the patient is lacking IF
  • If urinary B12 levels are the same as in Stage I, the patient the malabsorption is due to intestinal problems.
MNT

- intramuscular or subcutaneous injection
- Reduces symptoms of decreased appetite, decreased alertness
• intake of foods high in iron and folate

• chicken, hamburger, salmon, yogurt, and fortified breakfast cereals
VITAMIN B12 ABSORPTION

• increased intake of calcium has been shown to reverse vitamin B$_{12}$ malabsorption
CASE STUDY

Client name:  Sarah Henley
DOB:  10/7
Age:  31
Sex:  Female
Education:  High school diploma
Occupation:  Stay-at-home mother
Hours of work:  NA
Household members:  Sons ages 12 months and 3 years, husband age 35—all in good health
Ethnic background:  Caucasian
 Religious affiliation:  None
Referring physician:  Frieda Bowman, MD
**Nutrition Hx:**

*General:* Patient states that appetite is good right now. She suffered a lot of morning sickness during her first trimester but is better now.

**Usual dietary intake:**
- **AM:** Coffee, cold cereal, occasionally toast
- **Lunch:** Sandwich or soup
- **Dinner:** Casserole such as Hamburger Helper, hot dogs, soup; sometimes she cooks a full meal with meat and vegetables. Her husband works nights so she doesn’t always cook except on his days off.

**24-hr recall (PTA):**
- **AM:** 2 c Frosted Flakes, ½ c whole milk, black coffee
- **Lunch:** Hot dog on bun, ½ c macaroni and cheese
- **Dinner:** 3 oz Salisbury steak, 1 c green beans, 1 roll, 1 c black coffee
ASSESSMENT

- Pt noticed small amount of bleeding after fall.
- Sx: Abdominal Pain, SOB, fatigue (pt claimed this was due to her 2 small children), pale.
- Pregnant – second trimester.
- Smoker
- Describes herself as picky eater.
- Taking a prenatal vitamin – does not take them everyday due to side effects (nauseous)
- Ht 5’5”
- Prepregnancy: Wt 135 #  BMI 22.4 = Normal
- Pregnant: Wt 145#  gained 15-18 lbs previous pregnancies
<table>
<thead>
<tr>
<th>Test</th>
<th>Normal Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.6-5</td>
<td>g/dL</td>
</tr>
<tr>
<td>Total protein</td>
<td>6-8</td>
<td>g/dL</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>19-43</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Transferrin</td>
<td>200-400</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Sodium</td>
<td>135-155</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5-5.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>98-108</td>
<td>mmol/L</td>
</tr>
<tr>
<td>PO4</td>
<td>2.5-4.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.6-2.6</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Osmolality</td>
<td>275-295</td>
<td>mmol/kg H2O</td>
</tr>
<tr>
<td>Total CO2</td>
<td>24-30</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>70-120</td>
<td>mg/dL</td>
</tr>
<tr>
<td>BUN</td>
<td>8-26</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6-1.3</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Uric acid</td>
<td>2.6-6 (women)</td>
<td>mg/dL</td>
</tr>
<tr>
<td></td>
<td>3.5-7.2 (men)</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.7-10.2</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>0.2-1.3</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Ammonia (NH3)</td>
<td>9-33</td>
<td>μmol/L</td>
</tr>
<tr>
<td>SGPT (ALT)</td>
<td>10-60</td>
<td>U/L</td>
</tr>
<tr>
<td>SGOT (AST)</td>
<td>5-40</td>
<td>U/L</td>
</tr>
<tr>
<td>Alk phos</td>
<td>98-251</td>
<td>U/L</td>
</tr>
<tr>
<td>CPK</td>
<td>26-140 (women)</td>
<td>U/L</td>
</tr>
<tr>
<td></td>
<td>38-174 (men)</td>
<td>U/L</td>
</tr>
<tr>
<td>LDH</td>
<td>313-618</td>
<td>U/L</td>
</tr>
<tr>
<td>CHOL</td>
<td>140-199</td>
<td>mg/dL</td>
</tr>
<tr>
<td>HDL-C</td>
<td>40-85 (women)</td>
<td>mg/dL</td>
</tr>
<tr>
<td></td>
<td>37-70 (men)</td>
<td>mg/dL</td>
</tr>
<tr>
<td>VLDL</td>
<td>&lt; 130</td>
<td>mg/dL</td>
</tr>
<tr>
<td>LDL</td>
<td>125</td>
<td>mg/dL</td>
</tr>
<tr>
<td>LDL/HDL ratio</td>
<td>2.27</td>
<td></td>
</tr>
<tr>
<td>Apo A</td>
<td>101-199 (women)</td>
<td>mg/dL</td>
</tr>
<tr>
<td></td>
<td>94-178 (men)</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Apo B</td>
<td>60-126 (women)</td>
<td>mg/dL</td>
</tr>
<tr>
<td></td>
<td>63-133 (men)</td>
<td>mg/dL</td>
</tr>
<tr>
<td>TG</td>
<td>35-160</td>
<td>mg/dL</td>
</tr>
<tr>
<td>T4</td>
<td>5.4-11.5</td>
<td>μg/dL</td>
</tr>
<tr>
<td>T3</td>
<td>80-200</td>
<td>ng/dL</td>
</tr>
<tr>
<td>HbA1c</td>
<td>4.8-7.8</td>
<td>%</td>
</tr>
</tbody>
</table>
CBC

- **RBC**: count of the actual number of red blood cells per volume of blood.
- **HGB**: measures the amount of oxygen-carrying protein in the blood.
- **HCT**: measures the percentage of red blood cells in a given volume of whole blood.
- **MCV**: a measurement of the average size of your RBCs.
- **MCH**: a calculation of the average amount of oxygen-carrying hemoglobin inside a red blood cell.
- **MCHC**: a calculation of the average concentration of hemoglobin inside a red cell.
- **RDW**: a calculation of the variation in the size of your RBCs.
- **ZPP**: Identifies a disruption in the formation of heme.
**HEMATOLOGY**

**DAY:** 1  
**DATE:** 1/17  
**TIME:**  
**LOCATION:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>4.3-10</td>
<td>7.2</td>
</tr>
<tr>
<td>RBC</td>
<td>4-5 (women)</td>
<td>3.8 L</td>
</tr>
<tr>
<td></td>
<td>4.5-5.5 (men)</td>
<td></td>
</tr>
<tr>
<td>HGB</td>
<td>12-16 (women)</td>
<td>9.1 L</td>
</tr>
<tr>
<td></td>
<td>13.5-17.5 (men)</td>
<td></td>
</tr>
<tr>
<td>HCT</td>
<td>37-47 (women)</td>
<td>33 L</td>
</tr>
<tr>
<td></td>
<td>40-54 (men)</td>
<td></td>
</tr>
<tr>
<td>MCV</td>
<td>84-96</td>
<td>72 L</td>
</tr>
<tr>
<td>RETIC</td>
<td>0.8-2.8</td>
<td>0.2 L</td>
</tr>
<tr>
<td>MCH</td>
<td>27-31</td>
<td>23 L</td>
</tr>
<tr>
<td>MCHC</td>
<td>31.5-36</td>
<td>28 L</td>
</tr>
<tr>
<td>RDW</td>
<td>11.6-16.5</td>
<td>22 L</td>
</tr>
<tr>
<td>Plt Ct</td>
<td>140-440</td>
<td>282</td>
</tr>
<tr>
<td>Diff TYPE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% GRANS</td>
<td>34.6-79.2</td>
<td>36.2</td>
</tr>
<tr>
<td>% LYM</td>
<td>19.6-52.7</td>
<td>41.3</td>
</tr>
<tr>
<td>SEGs</td>
<td>50-62</td>
<td>52</td>
</tr>
<tr>
<td>BANDS</td>
<td>3-6</td>
<td>4</td>
</tr>
<tr>
<td>LYMPHS</td>
<td>25-40</td>
<td>31</td>
</tr>
<tr>
<td>MONOS</td>
<td>3-7</td>
<td>3</td>
</tr>
<tr>
<td>EOS</td>
<td>0-3</td>
<td></td>
</tr>
<tr>
<td>TIBC</td>
<td>65-165 (women)</td>
<td>172 H</td>
</tr>
<tr>
<td></td>
<td>75-175 (men)</td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td>18-160 (women)</td>
<td>10 L</td>
</tr>
<tr>
<td></td>
<td>18-270 (men)</td>
<td></td>
</tr>
<tr>
<td>ZPP</td>
<td>30-80</td>
<td>18 L</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>100-700</td>
<td>250</td>
</tr>
<tr>
<td>Folate</td>
<td>2-20</td>
<td>2</td>
</tr>
<tr>
<td>Total T cells</td>
<td>812-2318</td>
<td>250</td>
</tr>
<tr>
<td>T-helper cells</td>
<td>589-1505</td>
<td>250</td>
</tr>
<tr>
<td>T-suppressor cells</td>
<td>325-997</td>
<td>12</td>
</tr>
</tbody>
</table>
**HEMATOLOGY**

**DAY:** 1  
**DATE:** 1/17  
**LOCATION:**

<table>
<thead>
<tr>
<th><strong>NORMAL</strong></th>
<th><strong>UNITS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC</strong></td>
<td>4-3-10</td>
</tr>
<tr>
<td><strong>RBC</strong></td>
<td>4-5 (women)</td>
</tr>
<tr>
<td></td>
<td>4.5-5.5 (men)</td>
</tr>
<tr>
<td><strong>HGB</strong></td>
<td>12-16 (women)</td>
</tr>
<tr>
<td></td>
<td>13.5-17.5 (men)</td>
</tr>
<tr>
<td><strong>HCT</strong></td>
<td>37-47 (women)</td>
</tr>
<tr>
<td></td>
<td>40-54 (men)</td>
</tr>
<tr>
<td><strong>MCV</strong></td>
<td>84-96</td>
</tr>
<tr>
<td><strong>RETIC</strong></td>
<td>0.8-2.8</td>
</tr>
<tr>
<td><strong>MCH</strong></td>
<td>27-31</td>
</tr>
<tr>
<td><strong>MCHC</strong></td>
<td>31.5-36</td>
</tr>
<tr>
<td><strong>RDW</strong></td>
<td>11.6-16.5</td>
</tr>
<tr>
<td><strong>Plt Ct</strong></td>
<td>140-440</td>
</tr>
</tbody>
</table>

| **DIFF TYPE**       |           |       |
|---------------------|-----------|
| **% GRANS**         | 34.6-79.2 | 36.2 | %        |
| **% LYM**           | 19.6-52.7 | 41.3 | %        |
| **SEGs**            | 50-62 | 52 | %        |
| **BANDS**           | 3-6 | 4 | %        |
| **LYMPHS**          | 25-40 | 31 | %        |
| **MONOS**           | 3-7 | 3 | %        |
| **EOS**             | 0-3 | 0 | %        |
| **TIBC**            | 65-165 (women) | 172 H | µg/dL |
|                     | 75-175 (men) |          |
| **Ferritin**        | 18-160 (women) | 10 L | µg/dL |
|                     | 18-270 (men) |          |
| **ZPP**             | 30-80 | 18 L | µmol/L   |
| **Vitamin B₁₂**     | 100-700 | 250 | pg/mL    |
| **Folate**          | 2-20 | 2 | ng/mL    |
| **Total T cells**   | 812-2318 | 2 | mm³      |
| **T-helper cells**  | 589-1505 | 2 | mm³      |
| **T-suppressor cells** | 325-997 | 2 | mm³      |
| **PT**              | 11-13 | 12 | sec      |
DIAGNOSIS

• PES:
  • Inadequate Iron intake required for the increased demands of pregnancy related to iron deficiency anemia as evidenced by hemoglobin, hematocrit, TIBC, and serum iron.
INTERVENTION

• Nutrition Education – educate patient on relationship of heme and non-heme iron sources.
• Discuss dietary sources that increase and decrease iron absorption.
• Educate her on the importance of prenatal vitamins and identify ways to decrease side effects.
• Identify dietary sources of heme iron

• Goal: Pt will be able to verbalize food sources high in iron and identify ways to increase iron absorption as well as manage the side effects of her prenatal vitamins.
MONITOR & EVALUATION

• Will follow up in one month to assess understanding and implementation of the nutrition education received.
• Will also assess bio labs to confirm dietary changes are in effect.