

# Iron Absorption, Metabolism, testing and Pathologies

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# Why Iron

- Properties of iron
  - $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$  states
  - Redox reactions
  - Free radicals
- Uses of iron
  - Redox reactions (cytochromes)
  - DNA synthesis
  - Oxygen carriers



# Iron Requirements

- Iron is not excreted, but still lost
  - ~1 mg/day
  - Males and post menopausal women must absorb to keep up
  - Menstrual cycle drains 20-40 mg, doubles amount needed
  - Pregnant mothers require much more

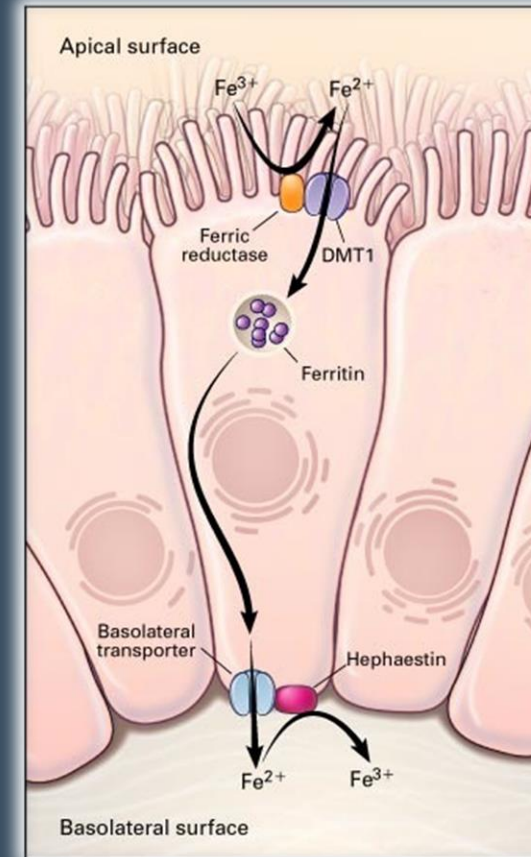


# Dietary Iron

- Inorganic salts
  - $2+/3+$
  - Poor solubility
  - Poor absorption
- Heme iron
  - $2+$
  - Separated from protein
  - Heme absorbed whole
  - Efficient

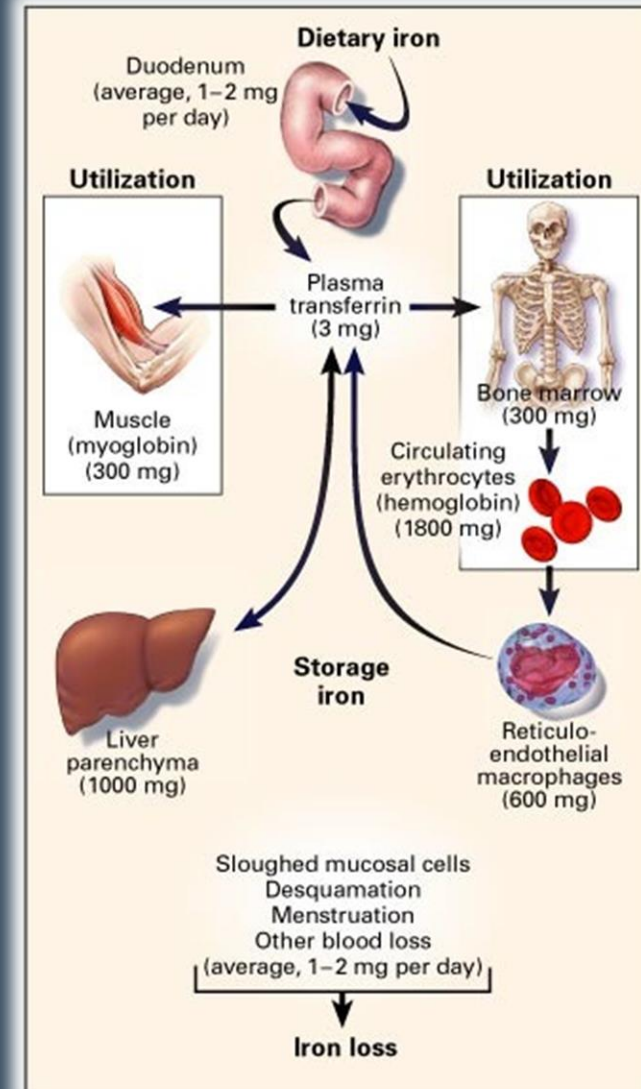
# Iron Absorption

- Must be Fe
- Uses DMT1
- Passes out basolateral transporter
- Oxidized



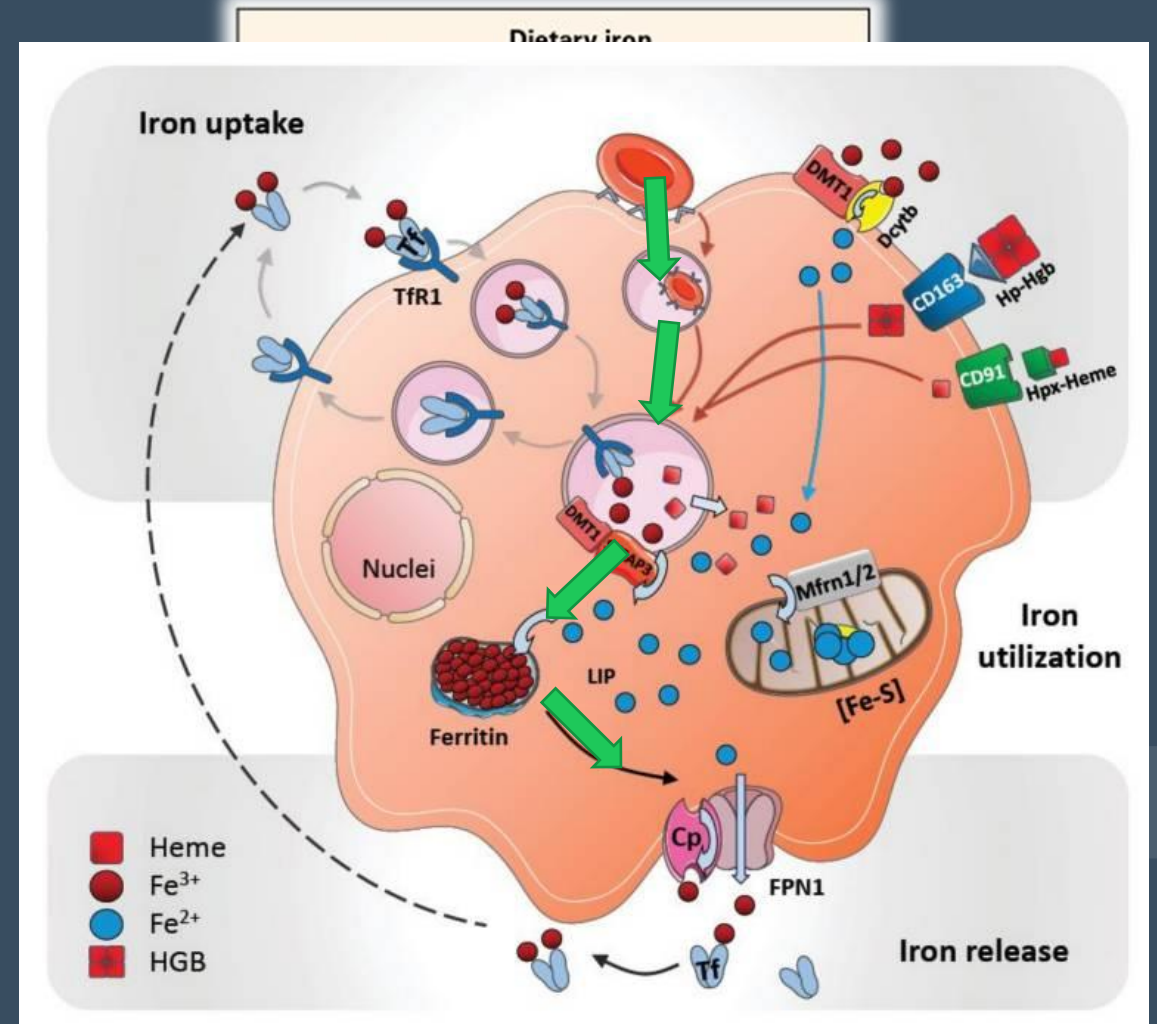
# Iron Distribution

- Iron needed in many places
- RBC production requires 20 mg/day
  - Wait, what?



# Iron Distribution

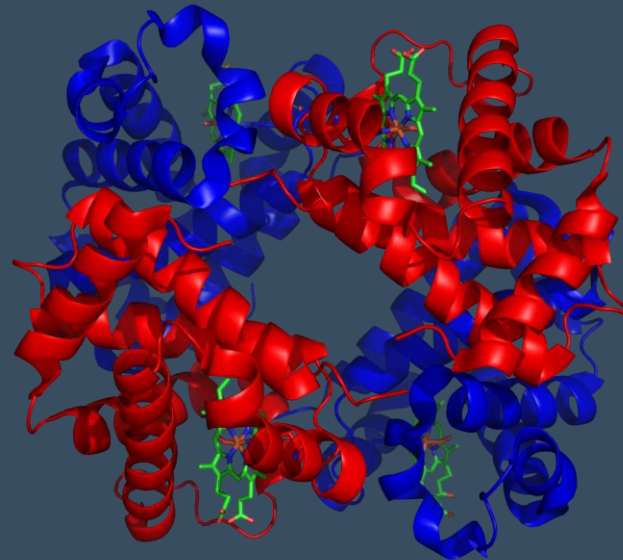
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# Hemoglobin Vocabulary

- Heme: ferrous protoporphyrin with  $\text{Fe}^{2+}$  in the center
- Globin: globular proteins

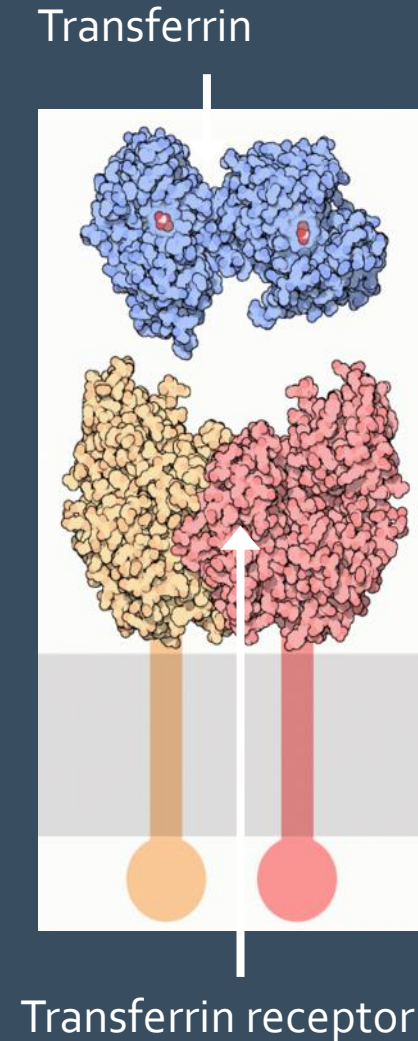
• 4 heme  
+4 globin  
hemoglobin





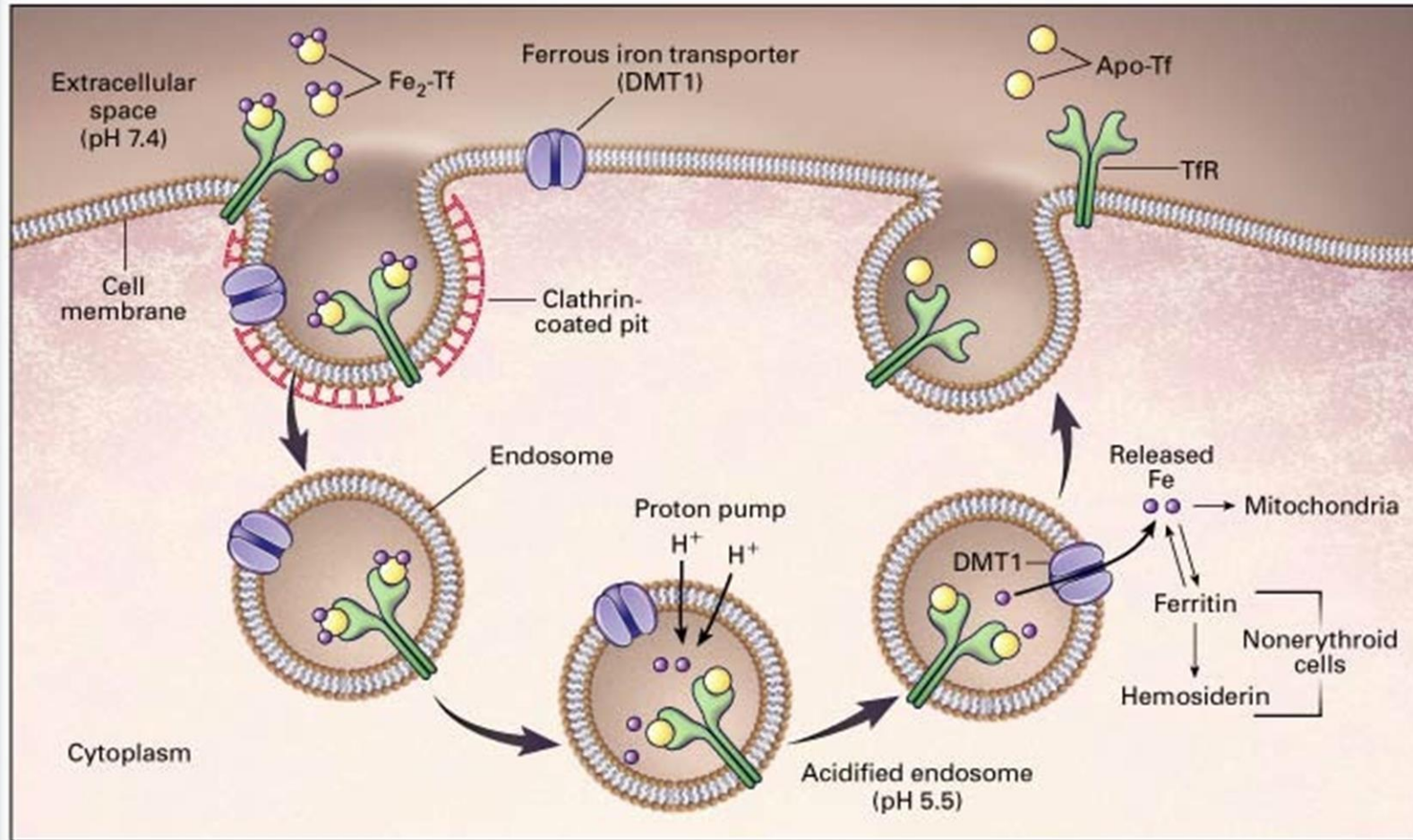
# Iron Transport

- Transferrin
  - 2  $\text{Fe}^{3+}$  per transferrin
  - Receptors on all cells
  - ~20-50% saturated



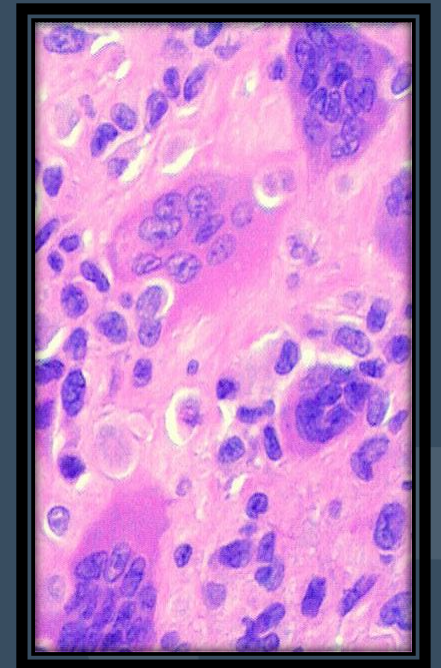
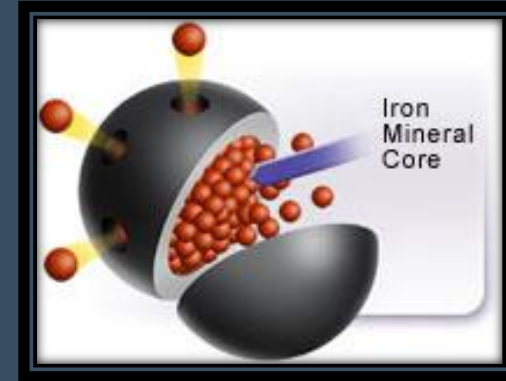
<http://commons.wikimedia.org/wiki/Image:Transferrin.PNG>

# Transferrin Cycle



# Iron Storage

- Ferritin
  - Heavy chain
  - Light chain
  - Ubiquitous, readily mobilized
  - Circulating is in equilibrium with tissue
- Hemosiderin
  - Degraded, Insoluble, Slow



# Iron Testing

- Serum iron
  - Utility?
    - Iron pool turnover
    - Inflow/outflow variation
    - Diurnal Variation



# Iron Assay

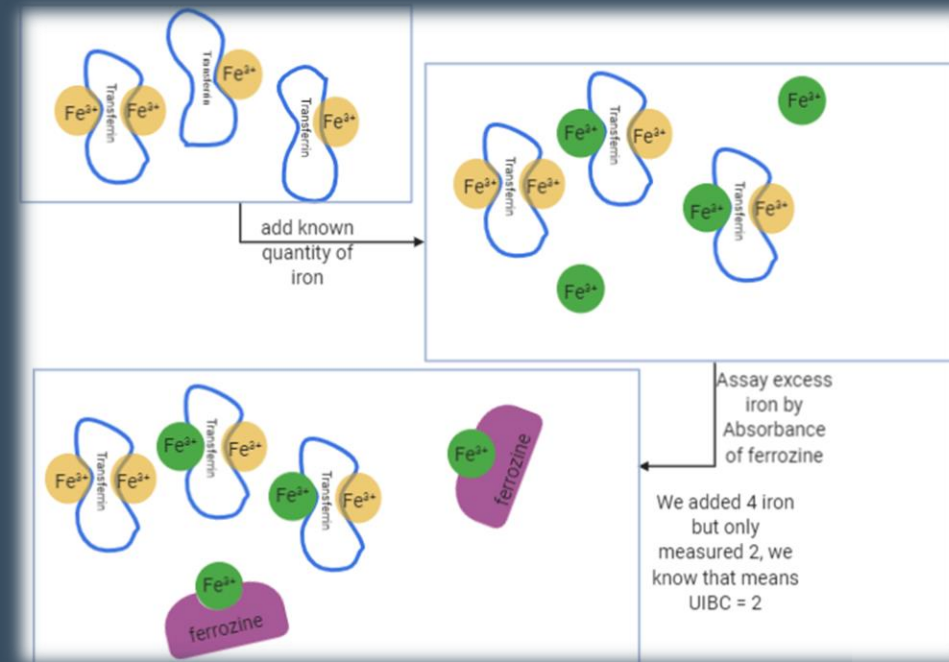
1. Acid pH releases  $\text{Fe}^{3+}$  from transferrin
2. Reducing agent  $\text{Fe}^{3+} \rightarrow \text{Fe}^{2+}$
3.  $\text{Fe}^{2+}$  complexes with ferrozine
4.  $\text{Fe}^{2+}$ -ferrozine absorbs at 562 nm





# Total Iron Binding Capacity

- TIBC
  - Indirectly: transferrin
  - Must measure UIBC (unsaturated iron binding capacity)
  - $TIBC = UIBC + \text{iron}$



# Percent Saturation

- We have measured: UIBC, Iron
  - %saturation = iron/TIBC
    - TIBC = iron + UIBC
    - %Sat = iron / (UIBC + iron)
  - Other methods based on transferrin assay
    - TIBC assay unstable reagents, imprecise

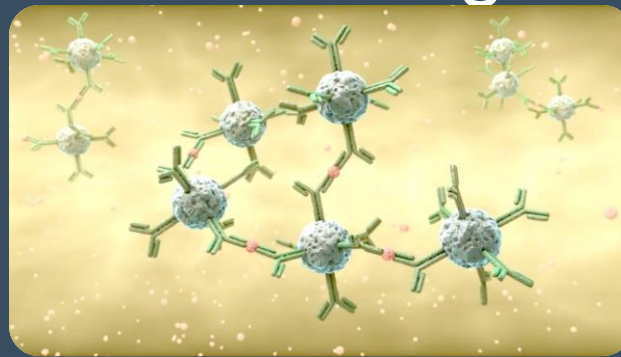
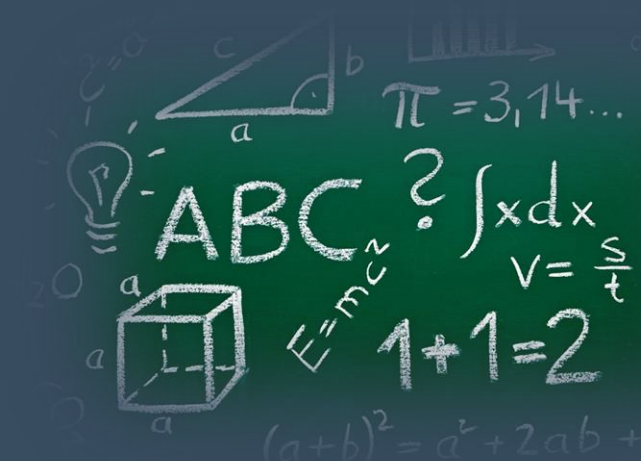
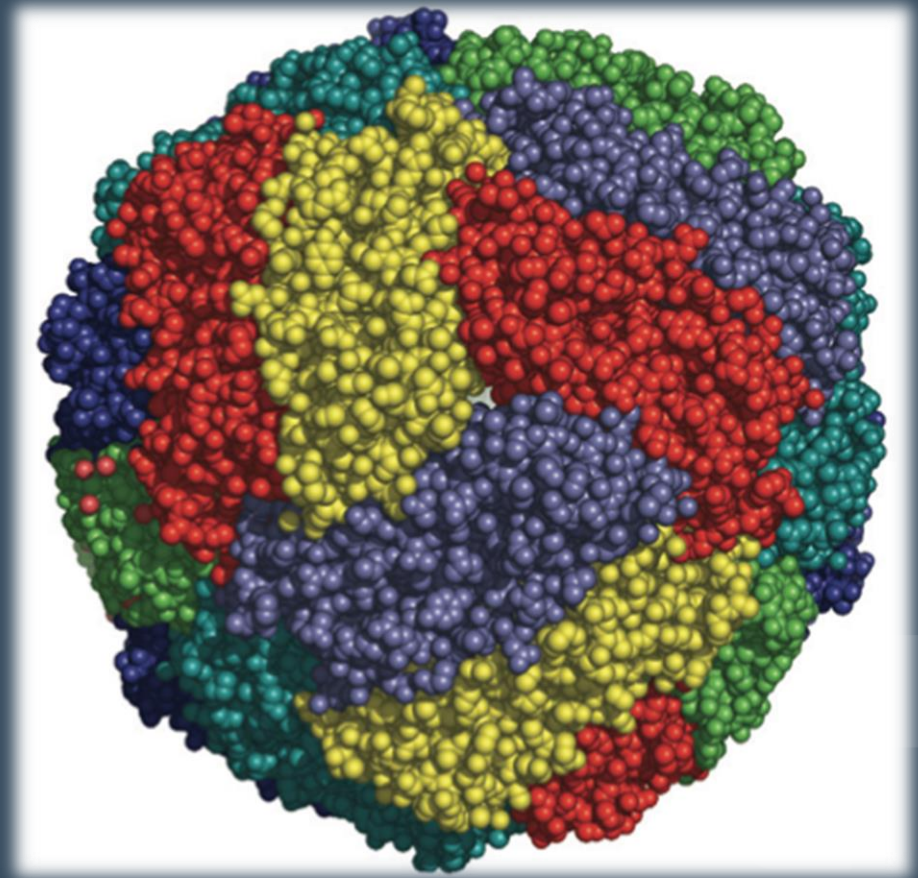


Image:diagnostics.roche.com



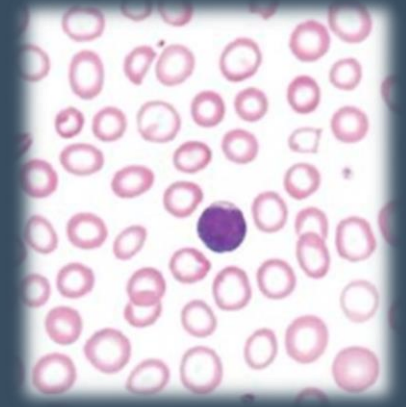
# Ferritin Assay

- Ferritin in low amounts
  - Immunoassays
  - Storage levels





# Pathologies



Images: laboratorytests.org

- Iron Deficiency
  - Insufficient intake
    - Malabsorption
  - Increased output
    - Blood loss
      - ♂ vs ♀
  - Very common
  - Microcytic/Hypochromic anemia

USA in 2016:

- 2.8 million physician office visits
- 526,000 ED admissions

Due to anemia

-According to the CDC's Anemia FastFacts

# Iron Deficiency Progression

## Steps

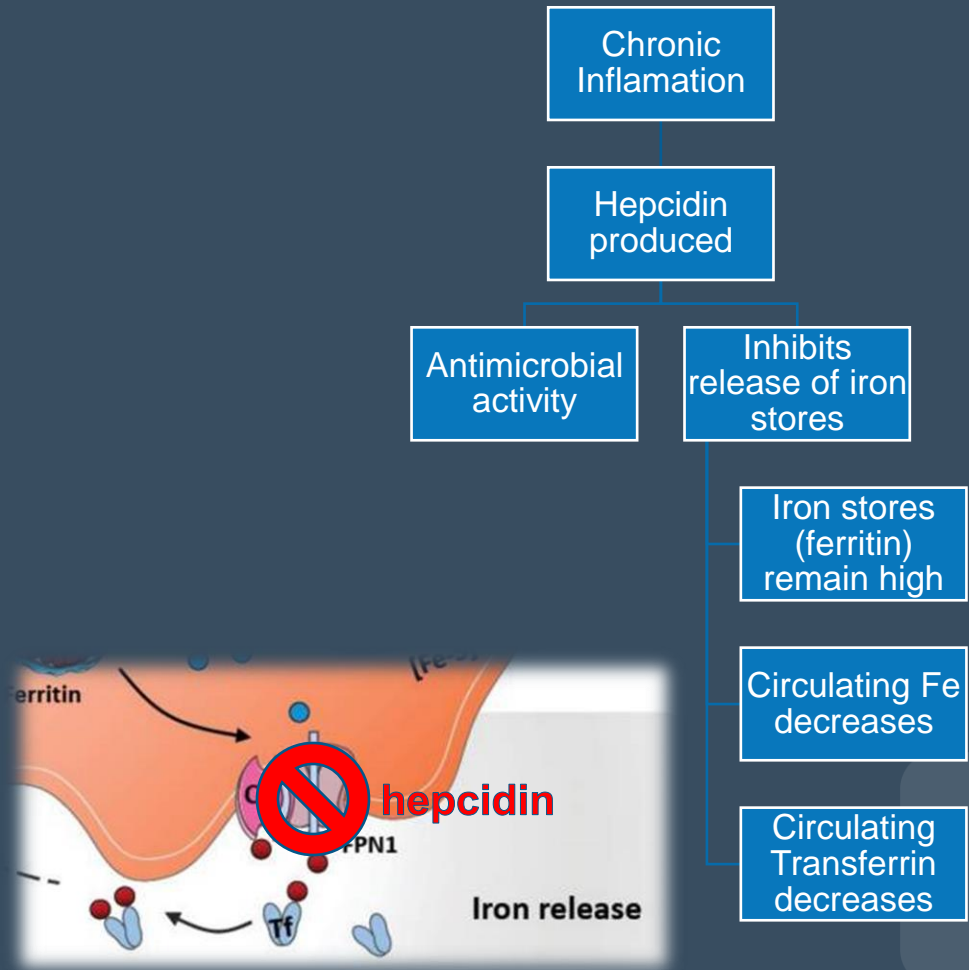
1. Storage iron used up during prolonged negative iron balance
2. Storage is exhausted, transferrin synthesis increases
3. Hgb and RBC synthesis slows, cells that are made are paler and smaller
4. Reticuloendothelial system preserves RBCs, lifespan exceeds 120 days

## Labs

1. RBCs normal, ferritin decreases, other tests normal
2. Transferrin↑ TIBC↑ Iron↓ %Saturation↓ ↓
3. RBC↓ Hgb↓ Hct↓

# Anemia of Chronic Disease

- Results from chronic:
  - Infection
  - Malignancy
  - Rheumatic conditions
- Hepcidin breaks down ferroportins
  - No longer export Fe
- Probably other processes at work



# Hemochromatosis

- Iron Overload
  - Excess absorbed iron
    - Women protected
  - Deposits in liver, pancreas, heart
  - Therapeutic phlebotomy
- May be acquired
  - Ineffective erythropoiesis
  - Chronic liver disease



# Diagnosis Takeaway



**TABLE 18.3 Laboratory Markers of Iron Status in Several Disease States<sup>7</sup>**

Condition	Serum Iron	Transferrin	Ferritin	Percent Saturation	TIBC
Iron deficiency	↓	↑	↓	↓	↑
Iron overdose	↑	↓	↑	↑	↓
Hemochromatosis	↑	Slightly ↓	↑	↑	↓
Malnutrition	↓	↓	↓	Variable	↓
Chronic infection	↓	↓	↑	↓	↓
Acute liver disease	↑	Variable	↑	↑	Variable
Chronic anemia	↓	N or ↓	N or ↑	↓	N or ↓

N, normal; ↓, decreased; ↑, increased.



**Every life deserves world class care.**