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Nutrigenomics
Iron Metabolism and Anemia

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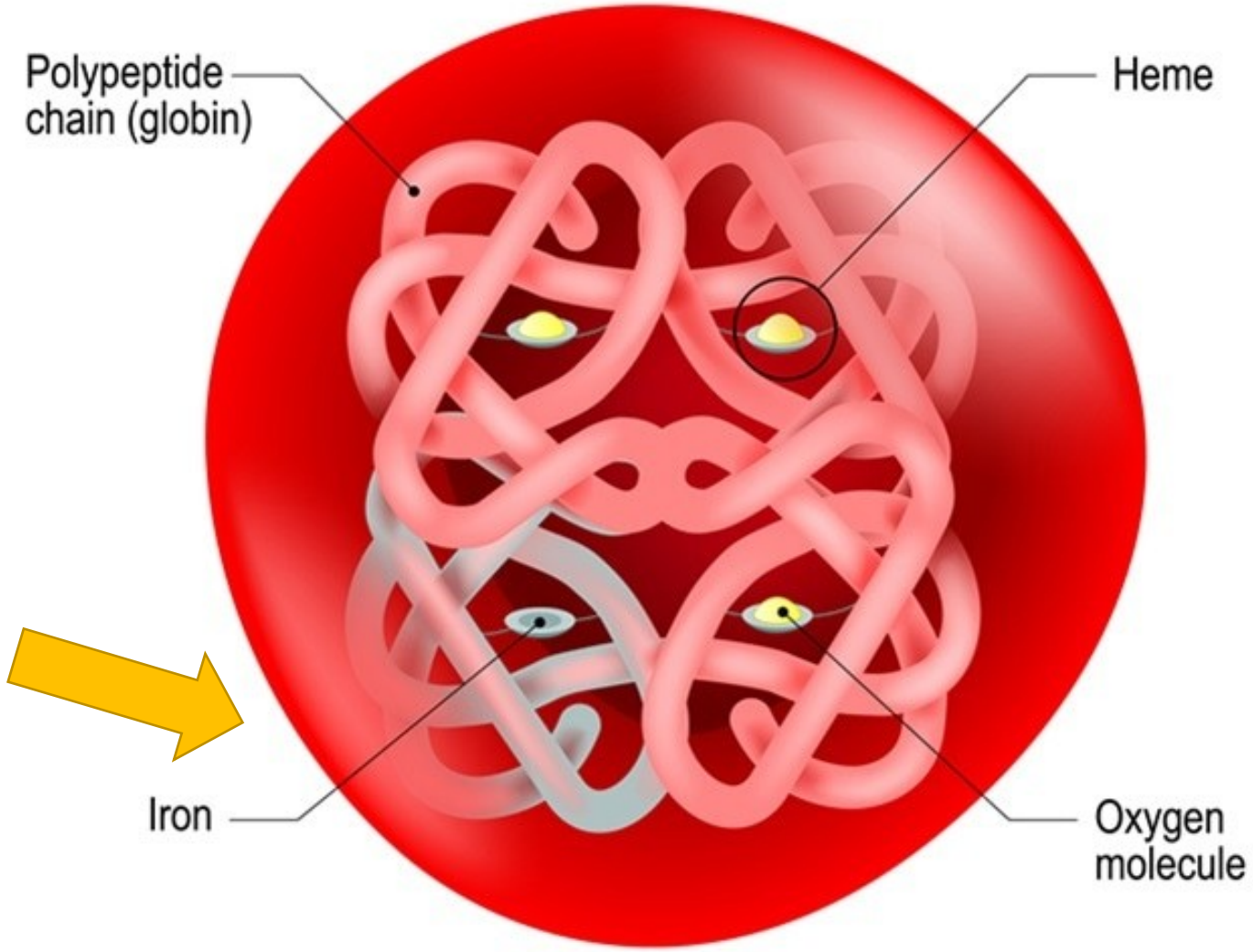
HEMOGLOBIN



Vitamin B6

Iron – Absorption

Iron absorption enhancers:
- Vitamin C
- Fructose
- Sorbitol
- Alcohol

Diet

Duodenum

Transported in the blood

Iron absorption inhibitors:
- Tannins
- Oxalates
- Polyphenols
- Phytates
- Egg & pulse proteins
- Calcium
- Copper
- Manganese

Muscle

Liver

Bone Marrow

Spleen

- Haemoglobin (60%)
- Myoglobin
- Enzymes
- Storage
- Excretion

Absorption =1mg iron per day (about 10%)

In Haemochromatosis, absorption = 2-4mg per day

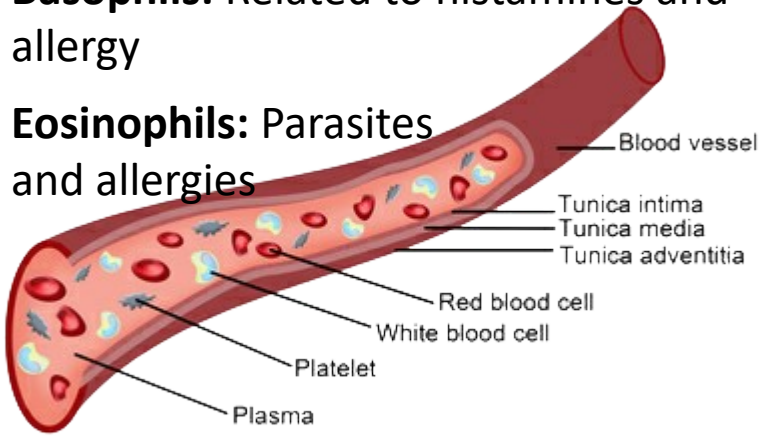
CBC - Complete Blood Count

Anemia Markers

- ✓ **RBC:** Red blood cells - carry oxygen
- ✓ **Hemoglobin:** Transports oxygen and gives the red color to blood
- ✓ **Hematocrit:** Percentage of blood made up of red blood cells
- ✓ **MCV: M**ean **C**orpusclar **V**olume - Red blood cell size, as volume
- ✓ **MCH: M**ean **C**orpuscular **H**emoglobin - the average amount of hemoglobin in red blood cells
- ✓ **MCHC: M**ean **C**orpuscular **H**emoglobin **C**oncentration - the average hemoglobin concentration in red blood cells
- ✓ **RDW:** Variation in the size of the RBC's
- ✓ **Platelets:** Blood cell particles involved with the forming of blood clots

Immune System Markers

- ✓ **WBC:** White blood cells - primary defense against disease
- ✓ **Neutrophils:** Often elevated in bacterial infection
- ✓ **Lymphocytes:** Often elevated in viral infection
- ✓ **Monocytes:** Second line of defense – elevated in recovery stage and chronic infection
- ✓ **Basophils:** Related to histamines and allergy
- ✓ **Eosinophils:** Parasites and allergies

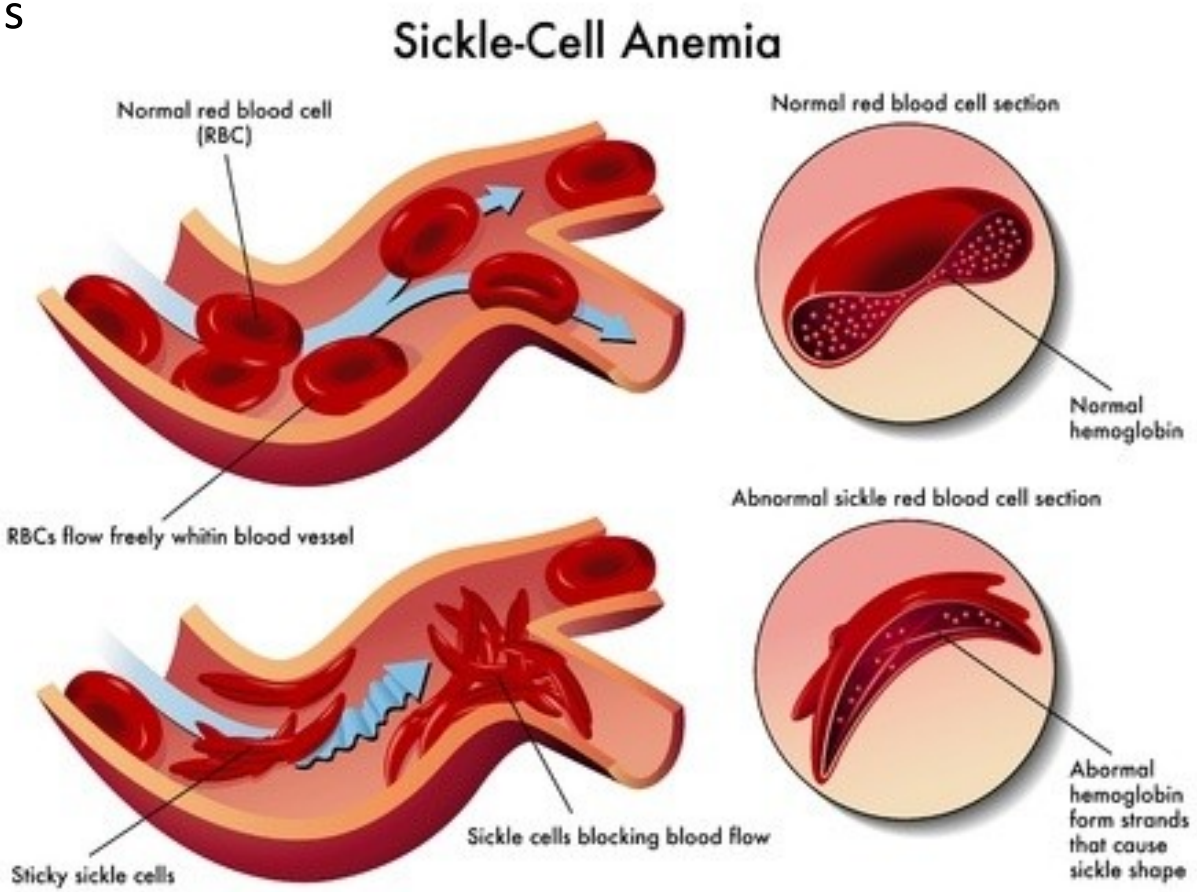


Symptoms of Anemia

- ✓ Fatigue
- ✓ Weakness
- ✓ Headache
- ✓ Shortness of breath after exercise
- ✓ Chest pain
- ✓ Pounding in ears
- ✓ Brittle nails
- ✓ Pallor
- ✓ Palpitations
- ✓ Dizziness
- ✓ Cold hands and feet

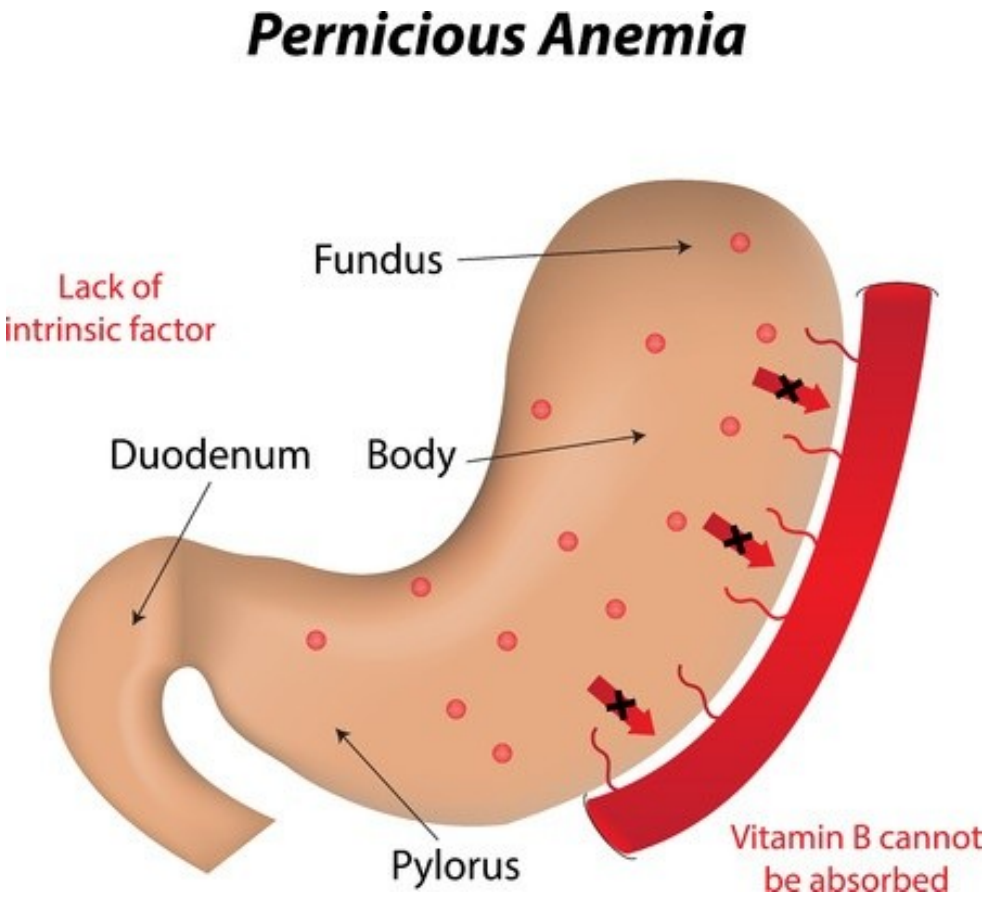
Types of Anemia

- ✓ Iron deficiency
- ✓ B12 deficiency/pernicious
- ✓ Folate deficiency
- ✓ Vitamin B6 deficiency
- ✓ **Serious disease - needs to be evaluated**
- ✓ Chronic disease
- ✓ **Internal bleeding (iron)**
- ✓ Hemolytic anemia
- ✓ Aplastic anemia
- ✓ Protein depletion
- ✓ Liver disease
- ✓ Polycythemia
- ✓ Hemochromatosis



B12 /Folate & Pernicious Anemia

- ✓ Decreased Hemoglobin
- ✓ Decreased Hematocrit
- ✓ Decreased RBC
- ✓ Increased MCV
- ✓ Increased MCH
- ✓ Increased MCHC
- ✓ Normal Iron, Serum (or low if co-existing iron deficiency)
- ✓ Normal TIBC
- ✓ Normal Transferrin
- ✓ Normal Intrinsic Factor Antibody *(+ = Pernicious)



Anemias of Excess

Serious conditions requiring attention from a health care provider

Polycythemia

- ✓ RBC = Increased
- ✓ HCT = Increased
- ✓ HGB = Increased
- ✓ MCV = Normal to Decreased
- ✓ MCH = Normal to Decreased
- ✓ MCHC = Normal to Decreased
- ✓ Serum Iron = Normal to Decreased
- ✓ Total Bilirubin = Increased
- ✓ Alkaline Phosphatase = Elevated
- ✓ Basophils = Increased
- ✓ Total WBC = Increased
- ✓ Uric Acid = Increased

***Slightly elevated RBC in absence of other signs is probably due to dehydration*

Hemochromatosis

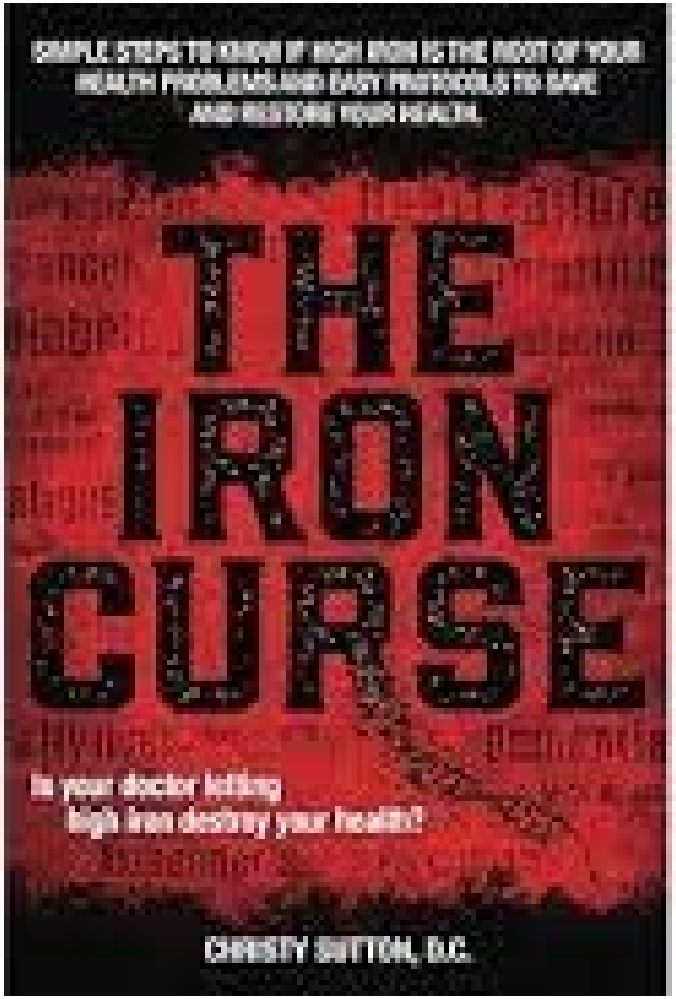
- ✓ RBC = Normal
- ✓ HCT = Normal
- ✓ HGB = Normal
- ✓ MCV = Decreased
- ✓ MCH = Decreased
- ✓ MCHC = Decreased
- ✓ Serum Iron = Increased
- ✓ Iron Saturation = Significantly Increased
- ✓ TIBC = Decreased
- ✓ Ferritin = Significantly
- ✓ Transferrin = Normal or Decreased Slightly
- ✓ SGOT = Normal or Increased

Hemochromatosis

- Absorb more iron from food than they should due to genetic variants.
- The body stores the excess iron in the organs, including the liver, heart, pancreas, skin, pituitary, and thyroid. You also can store iron in your joints and bone marrow

Symptoms of Hemochromatosis

- Joint pain
- Tiredness
- Abdominal pain
- Liver disease
- Diabetes
- Irregular heartbeat
- Bronzed skin color
- Hypothyroidism
- Elevated blood sugar



The Iron Curse, 2023, Dr. Christy Sutton

HFE Genes

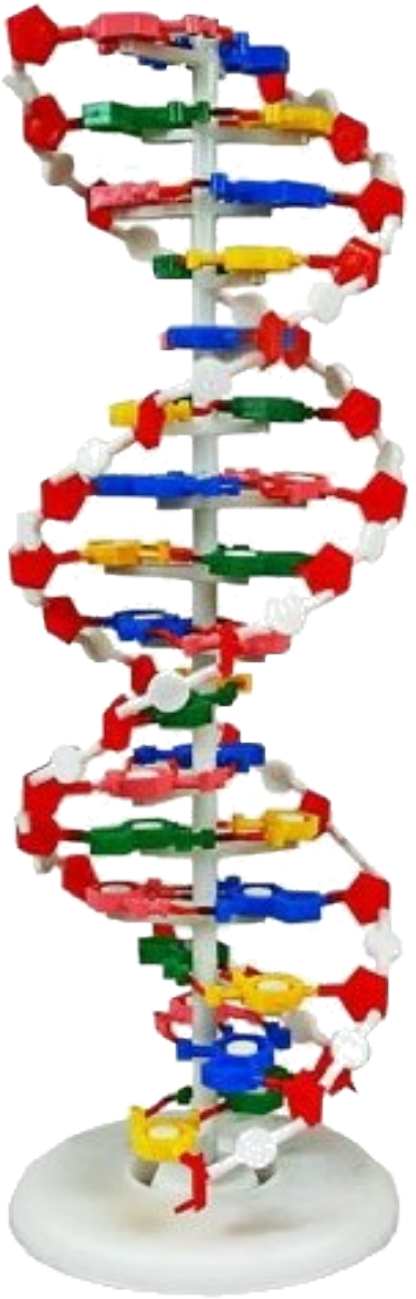
- **HFE C282Y rs1800562**, Risk allele A
  - Most likely SNP to cause high iron
  - Greatly increases iron absorption 40-70% will develop clinical signs of iron overload
- **HFE H63D rs1799945**, Risk allele G
  - Medium risk for symptoms
  - Significant risk if homozygous
- **HFE D65T rs1800732**, Risk allele T
  - Light weight gene for hemochromatosis
  - Slightly increases iron absorption even if homozygous

Iron

Gene	RSID	Risk Allele	Genotype	Phenotype	Page #
HFE C282Y	rs1800562	A	AG	+/-	375-377
HFE H63D	rs1799945	G	CC	-/-	375-377

HFE Gene SNP Combinations Compound Heterozygous Significant Risk

- ✓HFE C82Y and HFE H63D
- ✓HFE C265T and HFE C282Y
- ✓HFE C265T and HFE C282Y



Other SNPs Associated with Iron Excess

- ✓ **HIF1A rs11549465** Pro582Ser, risk allele T
- ✓ **BMP2 rs235756** – affects hepcidin levels,
  - ➢ G/G: lower transferrin
  - ➢ A/G: increased transferrin
  - ➢ A/A: increased ferritin levels in people with HFE variants

Other Genes Related to High Iron

- **BTBD9** rs3923809 risk allele G – higher iron levels
- **TMPRSS6** rs855791 - regulates hepcidin levels
  - G allele: higher iron stores in men with HFE variant
  - A/A: lower iron stores in men
- **SLC40A1** rs11568350 C/C: typical
  - A/C: higher ferritin levels (African American men)
  - A/A: higher ferritin levels (African American men) children less likely to be anemic

Carriers of HFE Variants (Mainly C282Y) Are At A Higher Risk

- ✓ Non-alcoholic fatty liver disease
- ✓ Metabolic syndrome
- ✓ Cardiovascular disease including women with heterozygous variants
- ✓ Slightly higher risk of cancer including breast cancer and liver cancer
- ✓ Alzheimer's disease, including heterozygous carriers
- ✓ Musculoskeletal problems (arthritis symptoms)
- ✓ High blood pressure
- ✓ High uric acid (gout)
- ✓ Lung fibrosis
- ✓ Diabetes
- ✓ Cardiovascular disease in kidney disease patients
- ✓ Increased lead levels

Rare Genetic Mutations Causing Other Forms Of Hemochromatosis - HJV

✓ Hemojuvelin

- Protein made in the liver, heart, and skeletal muscles.
- Plays a role maintaining proper iron levels in the body by controlling the levels of hepcidin.
  - **rs121434375** T allele: HFE2, pathogenic for hemochromatosis type 2A
  - **rs28939076** T allele Hemochromatosis type 4
  - **rs74315325** A allele: Hemochromatosis type 2A
  - **rs74315326** C allele: hemochromatosis type 2A

Iron Deficiency Anemia

- ✓ **TMPRSS6 rs2235321**
  - ➢ Instructions for making a protein called matriptase-2
  - ➢ Affects plasma hepcidin levels, a key hormone in the regulation of iron.
  - ➢ Iron-refractory iron-deficiency anemia - taking iron supplements or eating iron-rich foods will not increase iron levels.
- ✓ **Transferrin Protein G277S**:
  - ➢ Linked with iron deficiency
- ✓ **TF rs3811647:** Transferrin gene
  - ➢ Strongly associated with increased levels of transferrin
  - ➢ Higher total iron-binding capacity (TIBC) and lower transferrin saturation

Sickle Cell Anemia
HBB Gene (Many RSIDs)

- ✓ Encodes a component of hemoglobin which causes hemoglobin molecules to stick together, creating sickle-shaped red blood cells.
- ✓ Often affecting African Americans
- ✓ This can cause serious issues like stroke or eye problems, and the blood cells are destroyed much more rapidly than disc-shaped cells.

Thalassemia
HBA 1 and 2 Genes

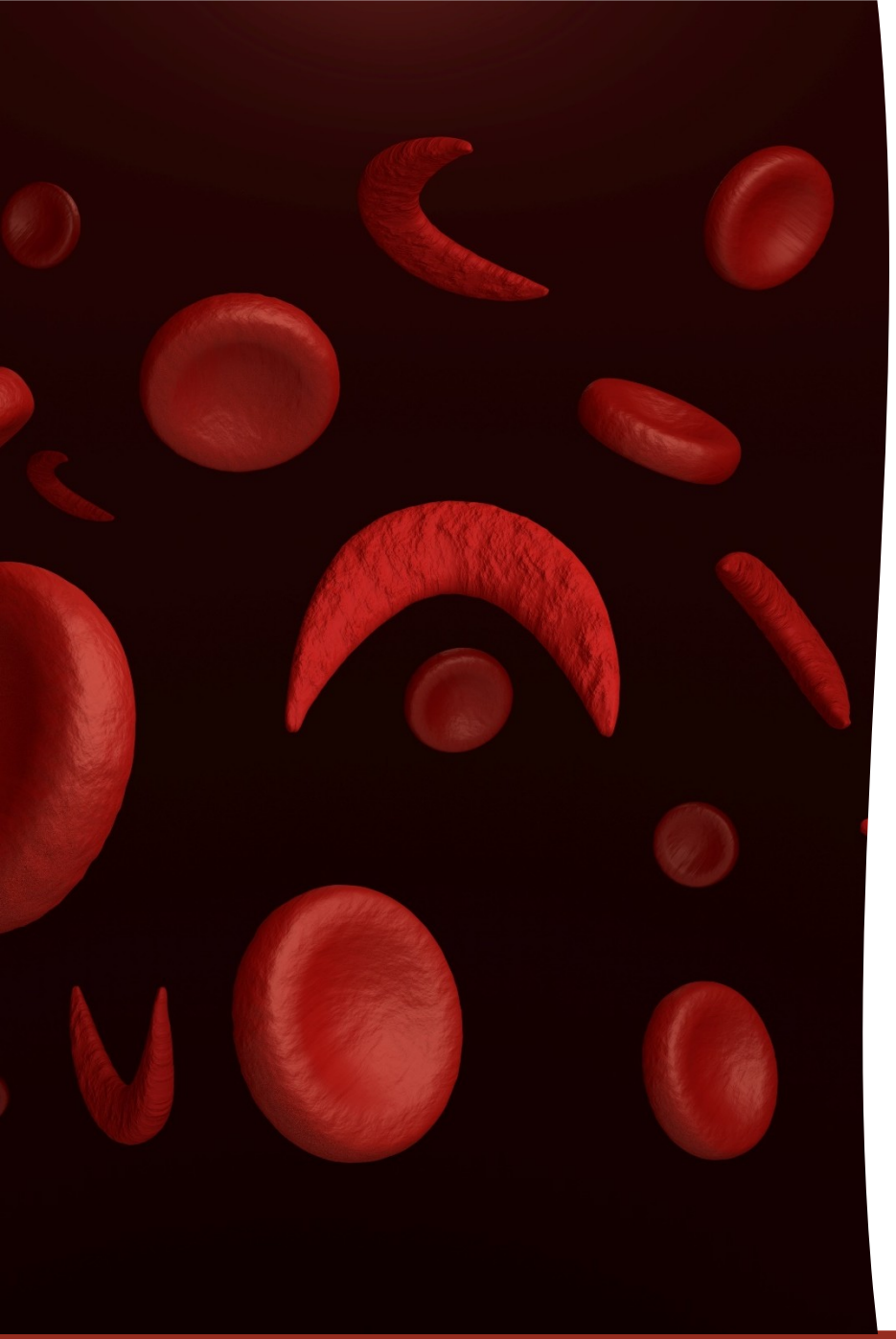
- ✓ Faulty synthesis of hemoglobin that reduces the production of hemoglobin
- ✓ Thalassemia Major – requires blood transfusions
- ✓ Mostly in populations living near the Mediterranean Sea, Africa, the Middle East, and Asia.
- ✓ Certain thalassemia subtypes, like alpha and beta, are diagnosed based on how the hemoglobin protein is changed.
- ✓ Usually diagnosed in early childhood due to signs like slow growth or brittle bones.

Glucose-6-phosphate Dehydrogenase Deficiency (G6PD)

- ✓ Results from a missing enzyme that protects red blood cells from damage.
- ✓ Part of the pentose phosphate pathway and supplies the energy needed to produce NADPH within cells.
- ✓ Can trigger hemolytic anemia

G6PD

- ✓ rs1050828 v98M Risk =T
- ✓ rs5030868 Risk = A
- ✓ rs72554664 Risk = T
- ✓ rs72554665Risk=T
- ✓ Rs5030869 Risk = T
- ✓ rs137852327 Risk = T
- ✓ rs137852327 Risk = T
- ✓ Rs137852330 Risk = A



Summary – Top 5 Genes Related to Impaired Iron Metabolism and Anemia

- ✓ HFE
- ✓ TMPSS
- ✓ HIF1A
- ✓ BMP2
- ✓ MTHFR