ANEMIA OF DISORDERED IRON METABOLISM AND HEME SYNTHESIS

Defect in Heme Synthesis
Defect in Globin Synthesis

FAULTY IRON METABOLISM

- Sideropenic – deficiency of iron for heme synthesis
  - Iron Deficiency Anemia
- Sideroachristic – adequate iron but defective utilization
  - Sideroblastic Anemia
  - Anemia of Chronic Disease

IRON METABOLISM

- Distribution
- Absorption
- Transport
- Storage

DISTRIBUTION

- Total Iron Concentration 40-50 mg
- Hemoglobin = 0.5 mg iron/ml blood
- Transferrin = Transport Protein

ABSORPTION

- Mucosal Cells of Proximal Small Intestine
  - Amount of Iron
  - Bioavailability
  - Iron Balance of Individual

TRANSPORT

- Transferrin – Plasma Transport Protein each gm will bind 1.4 mg of Iron
- TIBC = 250-450 µg iron/dL plasma
- Serum Iron = 65-180 µg/dL male and 50-180 µg/dL female
- Transferrin Receptor = 2.8-8.5 mg/L (Transmembrane Glycoprotein Dimer)

STORAGE

- Liver = Primary iron storage
- Ferritin = Spherical Protein Shell = Stores Iron 20-300 µg/L males and 12-200 µg/L females
- Hemosiderin – Heterogeneous aggregate of protein and iron Reference value 40-60% sideroblasts in BM

REQUIREMENTS

- Daily Requirement for Iron is 1 mg
- Increased Requirements
  - Menstruation
  - Pregnancy
  - Infancy/Children

IRON STUDIES

- Serum Iron
- Total Iron Binding Capacity
- % Saturation
- Ferritin
- Serum Transferrin Receptor

IRON DEFICIENCY ANEMIA CAUSES

- Dietary Deficiency
- Blood Loss
- Hemodialysis
- Malabsorption

IDA Stages

- Stage 1
  - Iron Stores Depleted
  - No Anemia
  - RDW increased, Ferritin Decreased
- Stage 2
  - Microcytes
  - No BM Siderocytes
- Stage 3
  - Microcytic, Hypochromic Anemia

CLINICAL SIGNS OF IDA

- Koilonchia
- Glossitis
- Muscle Dysfunction
- Gastritis
- Pica
- Fatigue and weakness

LABORATORY RESULTS FOR IDA

- Hemoglobin decreased
- MCV decreased
- Iron decreased
- TIBC increased
- % Saturation decreased
- Ferritin decreased
- Transferrin Receptor increased
- Bone Marrow decreased M:E ratio

THERAPY

- Treatment of Cause
- Administer Iron

ANEMIA OF ABNORMAL IRON METABOLISM

- Sideroblastic Anemia
- Anemia of Chronic Disease

SIDEROBLASTIC ANEMIA

- Hereditary
  - Sex-linked defective heme synthesis, abnormal σ-aminolevulinate synthase enzyme
- Acquired
  - Refactory Anemia with ringed sideroblasts
  - Drugs or Toxins
  - Malignancy

LABORATORY FINDINGS IN SIDEROBLASTIC ANEMIA

- Dimorphic
- Increased RDW
- Pappenheimer Bodies
- BM hyperplastic
- Iron Increased
- % Saturation Increased

SIDERBLASTIC ANEMIA THERAPY

- Pyridoxine Therapy
- Eliminating disease or Toxin

ANEMIA OF CHRONIC DISEASE

- Anemia that occurs in patients with chronic infections, chronic inflammatory disorders, or neoplastic disorders
- Cytokines are mediators
  - Inhibit EPO production and erythroid progenitor response
  - Block Iron release from Macrophage
  - Shorten RBC survival

ACD LABORATORY FINDINGS

- Normocytic, normochromic
- RPI <2
- Iron Decreased
- % Saturation normal to decreased
- Ferritin normal or increased
- BM increased M:E ratio

ACD Therapy

- Treat underlying disease

HEMOCHROMATOSIS

- Iron Overload
- Hereditary
  - Recessive
  - HFE Gene
- Secondary
  - Anemias with ineffective erythropoiesis
  - Chronic Liver Disease
  - Transfusions and Iron injections
  - Alcoholism

CLINICAL SYMPTOMS

- Chronic Fatigue
- Arthralgia
- Infertility and Impotence
- Cardiac Disease
- Diabetes
- Cirrhosis
- Hyperpigmented Skin

LABORATORY

- Increased Iron Saturation
- Increased Ferritin

TREATMENT

- Phlebotomy
- Iron Chelators

PORPHYRIAS

- Inherited disorder of porphyrin synthesis
  - Erythopoietic
  - Hepatic
- Defect in enzymes in Heme Synthesis
- Increase in Porphyrin Heme Precursors

CONGENITIAL ERYTHROPOIETIC PORPHYIA

- Autosomal Recessive
- Uroporphyrinogen III Cosynthase
- Normocytic Anemia with Anisocytosis and Poikilocytosis
- Increased Retics
- BM Erythroid Hyperplasia
- Haptoglobin Absent
- Increased Unconjugated Bilirubin, Urinary and Fecal Urobilinogen

ERYTHROPOIETIC PROTOPORPHYRIA

- Autosomal Dominate
- Ferrocheletase

SUMMARY

- Hemoglobin defects
- IDA
- ACA
- SA
- Hemochromatosis
- Porphyrias