

CHERYL KOVALSKI, DO FACOI
NO DISCLOSURES

ACOI BOARD REVIEW 2019

ANEMIA

- ▶ Hemoglobin <13 grams or
- ▶ Hematocrit<39%

ANEMIA

MCV

RETICULOCYTE COUNT

Corrected retic ct = hematocrit/45 x retic %

(45 considered normal hematocrit)

>2%: blood loss or hemolysis

<2%: hypoproliferative process

ANEMIA

- ▶ MICROCYTIC
- ▶ Obtain and interpret iron studies
- ▶ Serum iron
- ▶ Total iron binding capacity (TIBC)
- ▶ Transferrin saturation
- ▶ Ferritin-correlates with total iron stores
- ▶ can be normal or increased if co-existent inflammation

IRON DEFICIENCY

- ▶ Most common nutritional problem in the world
- ▶ Absorbed in small bowel, enhanced by gastric acid
- ▶ Absorption inhibited by inflammation, phytates (bran) & tannins (tea)

CAUSES OF IRON DEFICIENCY

- ▶ Blood loss – most common etiology
- ▶ Decreased intake
- ▶ Increased utilization-EPO therapy, chronic hemolysis
- ▶ Malabsorption – gastrectomy, sprue

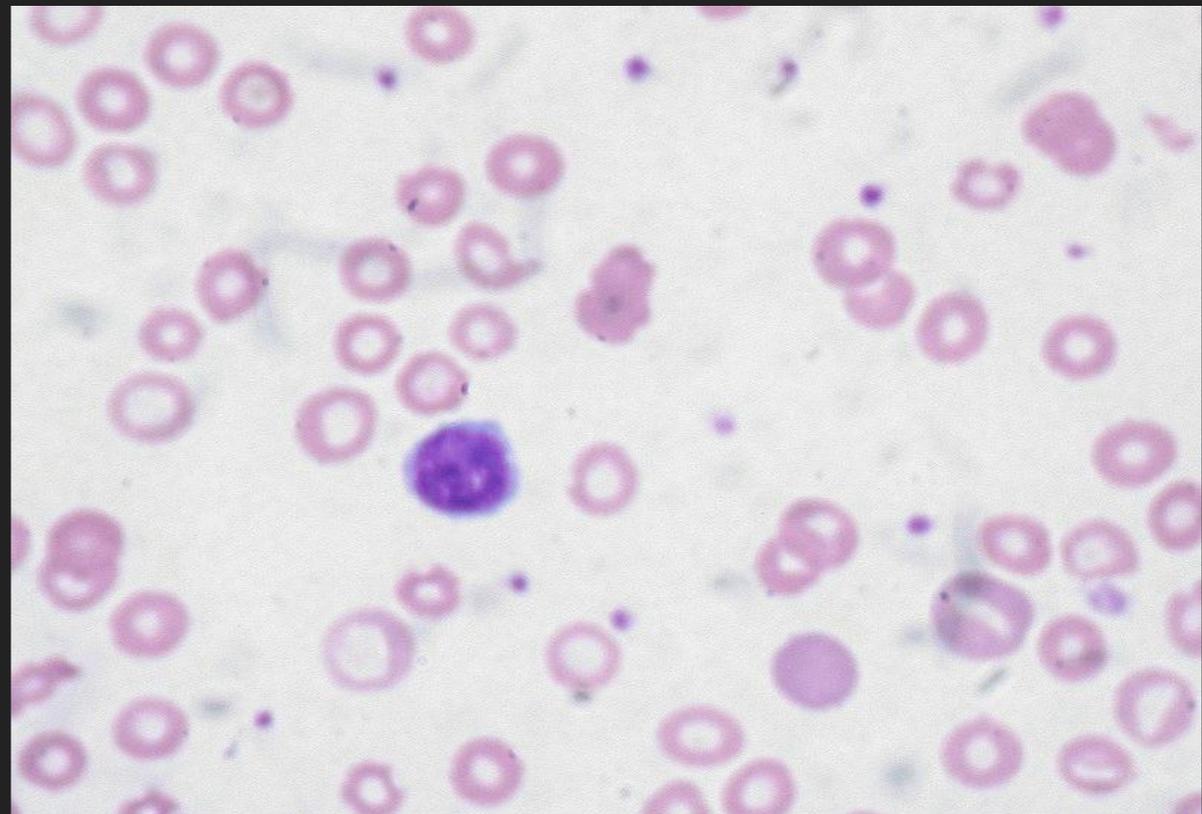
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CLINICAL MANIFESTATIONS OF IRON DEFICIENCY

- ▶ Impaired psychomotor development
- ▶ Fatigue, Irritability
- ▶ PICA
- ▶ Koilonychia, Glossitis, Angular stomatitis
- ▶ Dysphagia

IRON DEFICIENCY LAB FINDINGS

- ▶ Low serum iron, increased TIBC
- ▶ % sat <20



MANAGEMENT OF IRON DEFICIENCY

- ▶ MUST LOOK FOR SOURCE OF BLEED: ie: GI, GU, Regular blood donor
- ▶ Replacement:
 1. Oral: Ferrous sulfate 325 mg TID until serum iron, % sat, and ferritin mid-range normal, 6-12 months
 2. IV

SIDEROBLASTIC ANEMIAS

Diverse group of disorders of RBC production characterized by:

1. Defect involving incorporation of iron into heme molecule
2. Ringed sideroblasts in bone marrow

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CLASSIFICATION OF SIDEROBLASTIC ANEMIA

- ▶ ACQUIRED IDIOPATHIC –one of the MDS categories
- ▶ REVERSIBLE – alcohol, INH, chloramphenicol
- ▶ LEAD POISONING – autonomic & motor neuropathy, abdominal pain

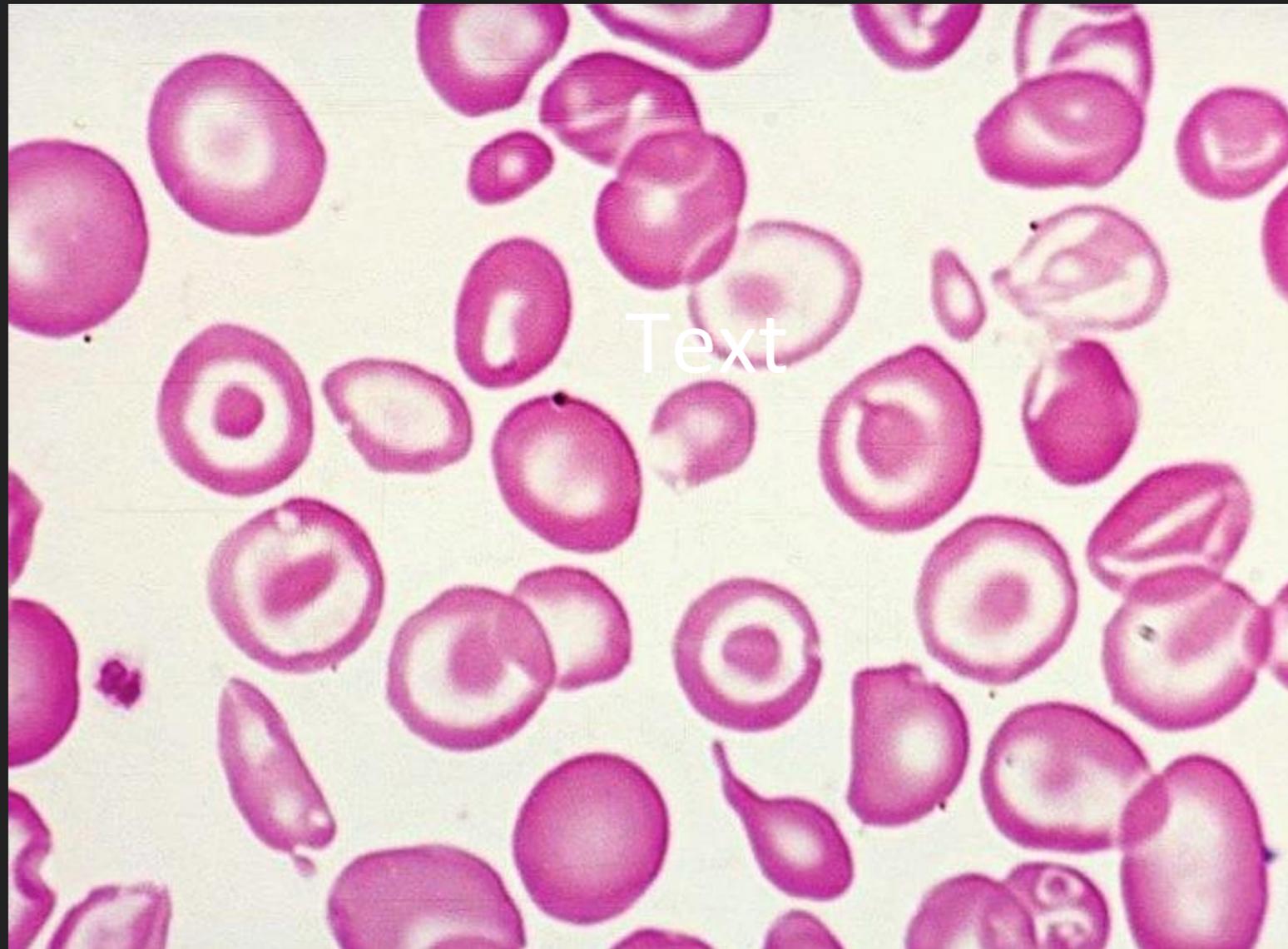
THERAPY OF SIDEROBLASTIC ANEMIA

- ▶ SUPPORTIVE
- ▶ PYRIDOXINE
- ▶ ALLO BMT
- ▶ EPO

THALASSEMIA

- ▶ Perhaps man's most common genetic disorder
- ▶ Beta Thal – decreased synthesis of beta globin chain mostly caused by point mutations, resulting in relative excess of alpha globin chains, dx-Hg electrophoresis
- ▶ Alpha Thal – decreased synthesis of alpha globin chains mostly caused by gene deletion resulting in relative excess of beta globin chains, dx-Alpha thal gene probe

THALASSEMIA



CLINICAL CLASSIFICATION OF B-THALASSEMIA

- ▶ B-Thalassemia trait (B-thalassemia minor): uncomplicated heterozygous B-Thal. Microcytosis, hypochromia +/- mild anemia, elevated hemoglobin A2 >3.5%.
- ▶ B-Thalassemia intermedia: many different genotypes, microcytic anemia-may need transfusion, high Hg F
- ▶ B-Thalassemia major (Cooley's anemia): homozygous or compound heterozygous B-thal; transfusion dependent, bone disease, pulmonary hypertension, iron overload
- ▶ genotype-phenotype correlations often difficult to make: 100s of mutations, frequent interactions, role of other modifying genes and environment

BETA THALASSEMIA: COMPLICATIONS

If transfusion dependent, best if managed in thalassemia center

- ▶ Pulmonary hypertension
- ▶ Thromboembolism
- ▶ Heart Disease
- ▶ Endocrinopathies
- ▶ Bone Disease
- ▶ Liver Disease
- ▶ Growth Retardation/Skeletal changes



ALPHA THALASSEMIA

- ▶ Silent carrier: heterozygous α^+ thal; 3 of 4 alpha genes present and functional; +/- mild microcytic anemia
- ▶ Trait: 2 of 4 alpha genes present and functional; +/- mild microcytic anemia; Hb Barts (gamma 4) in 2-10% newborns
- ▶ Hemoglobin H Disease: genotype α^{-}/α^{-} ; 20-40% Hb Barts in newborns; 5-40% Hg H(Beta 4) in adults; hemolysis of varying degrees, microcytosis, splenomegaly ineffective erythrocytosis, iron overload
- ▶ Hemoglobin Bart's Hydrops Fetalis: Homozygous alpha 0 (α^{-}/α^{-}); no functional alpha globulin genes: Hb Barts, eclampsia in mother, stillbirth, erythroblastosis in infant

THALASSEMIA

BIGGEST MISTAKE:

Treated with iron without benefit of iron studies

NORMOCHROMIC NORMOCYTIC ANEMIA

ANEMIA OF CHRONIC DISEASE

Hypoproliferative anemia

- ▶ Decreased red cell survival
- ▶ Impaired EPO production
- ▶ Impaired marrow response to EPO
- ▶ Impaired mobilization of iron
- ▶ Inflammatory response to underlying disorder

ANEMIA OF CHRONIC DISEASE

- ▶ Chronic nonhematologic conditions:

Infectious

Malignant

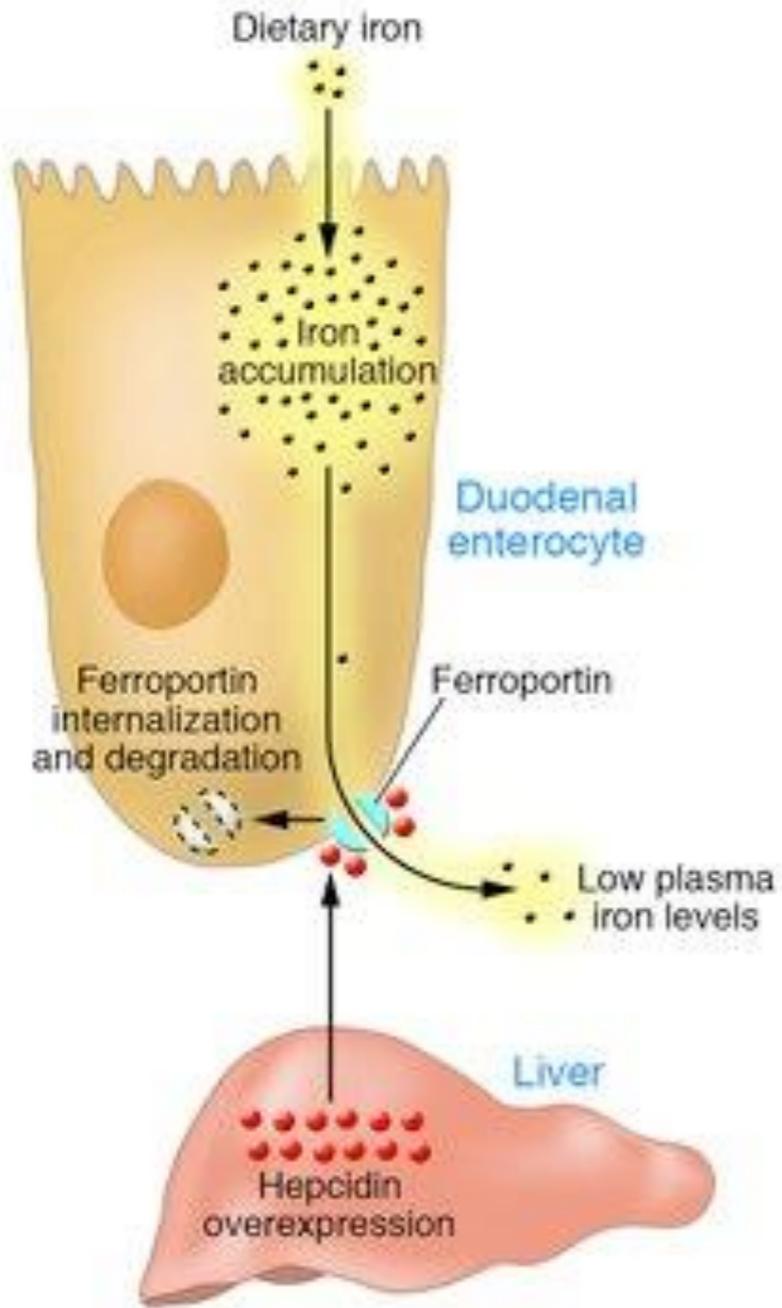
Inflammatory

Traumatic

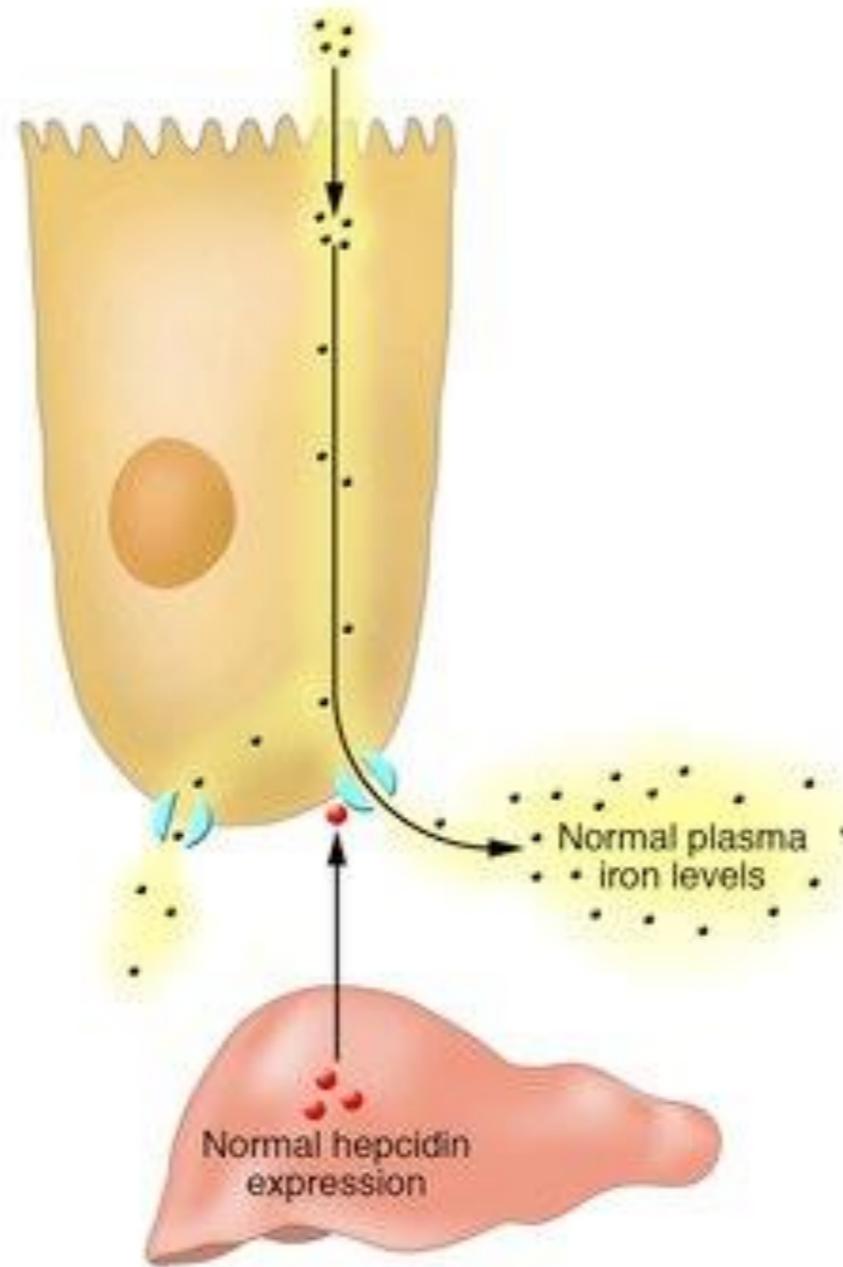
ANEMIA OF CHRONIC DISEASE: DIAGNOSIS

- ▶ Exclude other etiologies of anemia
- ▶ Confirm hypoproliferative anemia
- ▶ Low serum iron despite increased iron stores in bone marrow & macrophages

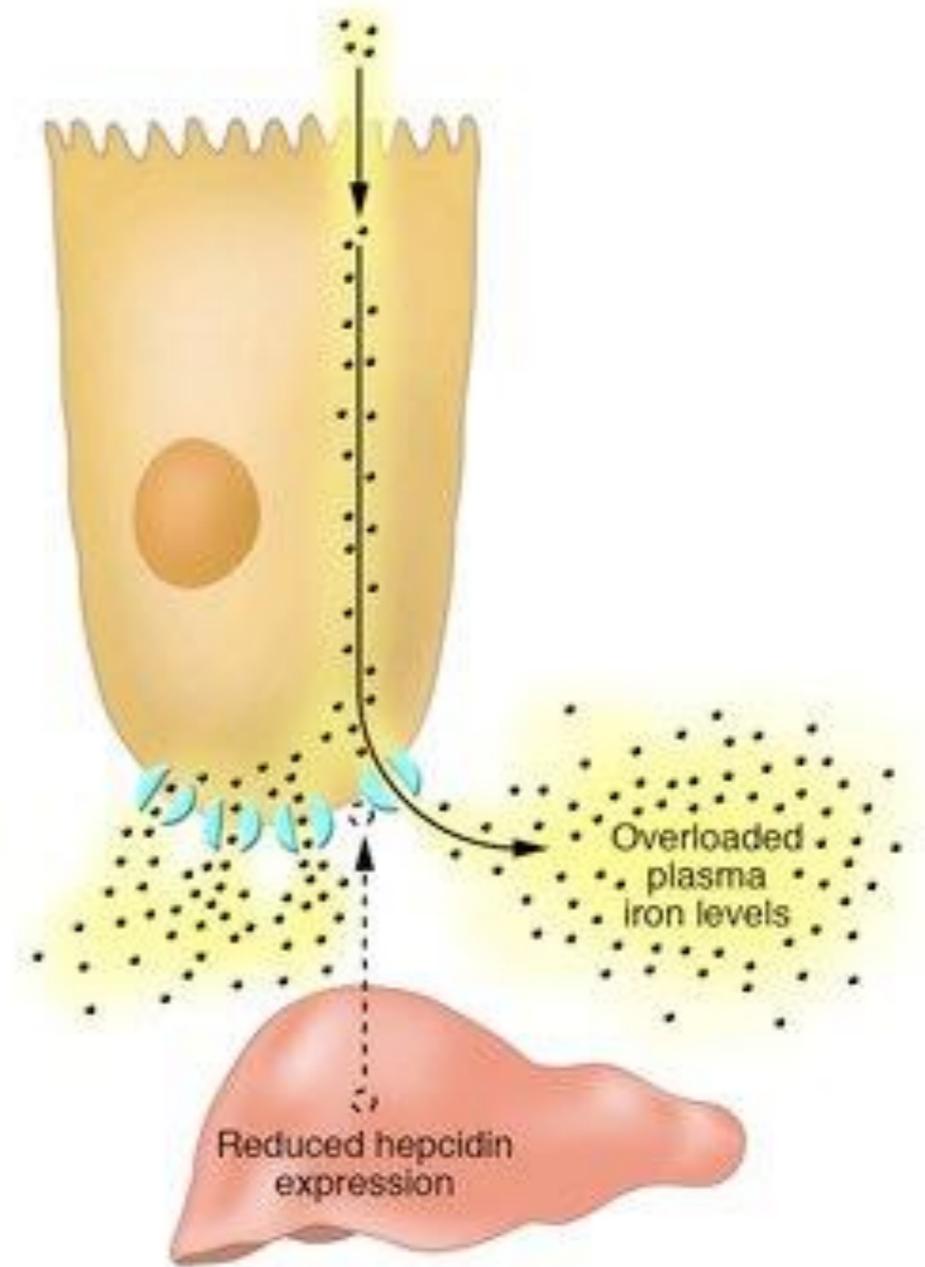
A Anemia of chronic disease



B Normal



C Hemochromatosis (iron overload)



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ANEMIA OF CHRONIC DISEASE: THERAPY

- ▶ Most are self-limiting and need no specific treatment
- ▶ Treat the underlying disorder
- ▶ Correct any coexistent deficiency
- ▶ Selected patients may benefit from EPO

MACROCYTIC ANEMIA

- ▶ Characterized by abnormal nuclear maturation of red cell precursors
- ▶ B12 Deficiency: consider if <300
- ▶ Folic Acid Deficiency
- ▶ Chemotherapy
- ▶ MDS
- ▶ Monoclonal protein

B12 ABSORPTION

- ▶ STOMACH: Acid, pepsin
 - Parietal cells
 - Intrinsic factor
- ▶ DUODENUM
- ▶ TERMINAL ILEUM

CAUSES OF B12 DEFICIENCY

- ▶ Dietary lack
- ▶ Inadequate proteolysis of B12
 - H2 Blockers, PPIs
- ▶ Deficiency of intrinsic factor
 - Gastrectomy, H2 Blockers
 - Pernicious Anemia
- ▶ Associated autoimmune disorders: hypothyroidism , Hashimoto's, vitiligo, diabetes, Addison's disease

CAUSES OF B12 DEFICIENCY

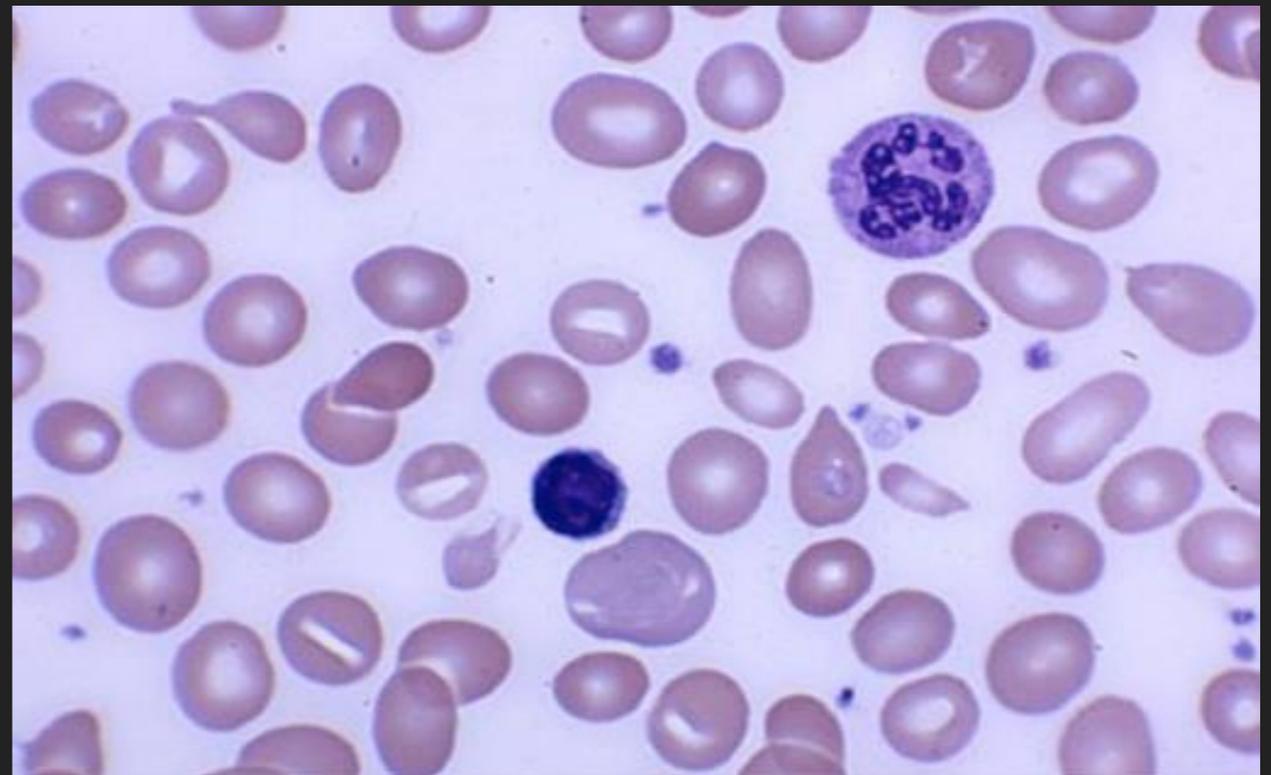
- ▶ Metformin
- ▶ Infections: HIV, H. pylori
- ▶ Blind loop
- ▶ Diphylobothrium latum
- ▶ Intestinal malabsorption
- ▶ Congenital disorders
- ▶ Nitrous Oxide inhalation
- ▶ Pancreatic insufficiency

SYMPTOMS OF B12 DEFICIENCY

- ▶ Brain and cranial nerves-dementia, personality changes, psychiatric disorders, disturbances in taste & smell, optic nerve abnormalities
- ▶ Peripheral neuropathy-paresthesias, sensory disturbances, diminished vibration and position senseAutonomic dysfunction
- ▶ Myelopathy affecting:
 - posterior columns: acroparesthesias, sensory disturbances, incoordination, ataxia, diminished vibration, position
 - lateral columns: weakness, spasticity

DIAGNOSIS

- ▶ Neuropsych symptoms can predate hematological changes.
- ▶ Serum B12 level is standard diagnostic test but may not accurately reflect tissue levels
- ▶ Hyperlobated WBCs



B 12 DEFICIENCY

- ▶ Methylmalonic acid and homocysteine levels elevated
- ▶ Antibody testing to diagnose PA:
 - anti-parietal cell ab
 - anti-intrinsic factor ab

TREATMENT

- ▶ Oral- becoming the replacement mode of choice; includes sublingual
- ▶ IM or SQ
- ▶ Nasal, expensive
- ▶ Prophylactic for gastric or ileal resection

CAUSES OF FOLATE DEFICIENCY

- ▶ Dietary deficiency, can evolve in months
- ▶ Increased requirements
- ▶ Intestinal malabsorption
- ▶ Drugs that interfere with folate metabolism

DIAGNOSIS OF FOLATE DEFICIENCY

▶SERUM FOLATE

- May normalize after 1 meal
- May be low normal with true folate deficiency

▶RBC FOLATE

- Normal or borderline in 60% pregnant pts
and 30% alcoholics with true folate deficiency

▶
▶
▶

TREATMENT

- ▶ Folic acid 1 mg po daily is usually adequate
 - Maintenance Rx: depends on underlying disorder
 - Prophylactic Rx: Pregnancy, prematurity, hemolysis, dialysis

HEMOLYTIC ANEMIA

PREMATURE DESTRUCTION OF RBC'S

Occurs by 2 different mechanisms

- ▶ Extra vascular hemolysis: RBCs prematurely removed from circulation by liver or spleen
- ▶ Intravascular hemolysis: RBCs lyse in the circulation

HEMOLYTIC ANEMIA

2 MAIN CAUSES

- ▶ Intrinsic RBC defects (inherited)
- ▶ Extra-corpuscular causes (acquired)

HEMOLYTIC ANEMIA

HEREDITARY HEMOLYTIC DISORDERS

- ▶ RBC Enzyme Defects
- ▶ RBC Membrane Defects
- ▶ Hemoglobinopathies
- ▶ Thalassemias

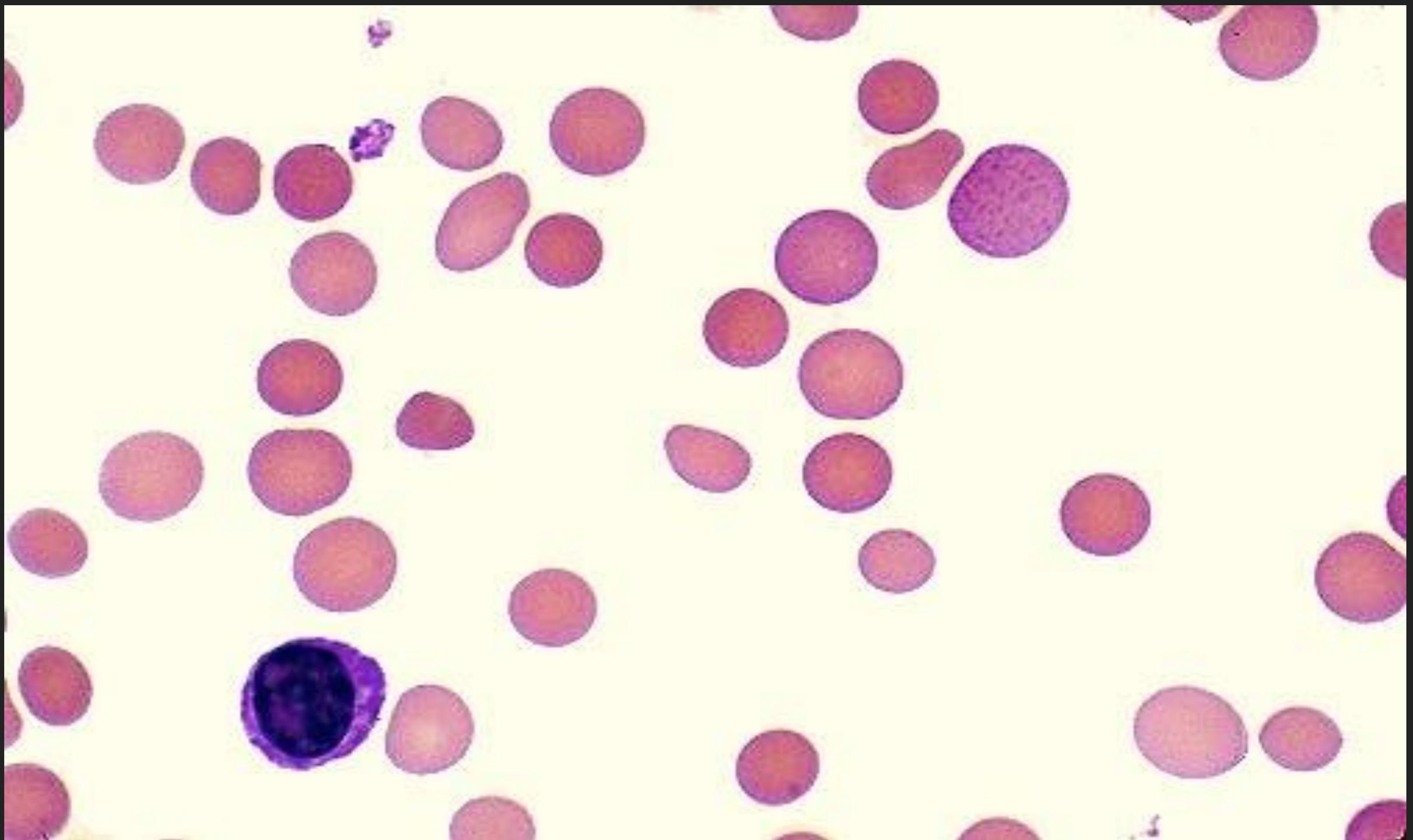
HEMOLYTIC ANEMIAS

- ▶ ACQUIRED HEMOLYTIC DISORDERS
- ▶ Immune Hemolytic Anemias
- ▶ Splenomegaly
- ▶ Microangiopathic Hemolytic Anemia
- ▶ PNH
- ▶ Direct toxic effect (malaria, clostridia)
- ▶ Spur Cell Anemia

DIAGNOSIS OF HEMOLYTIC ANEMIA

- ▶ Corrected Retic ct $>2\%$
- ▶ Elevated indirect bilirubin
- ▶ Elevated LDH
- ▶ Haptoglobin low or absent
- ▶ Urine hemosiderin: present in intravascular hemolysis only
- ▶ Urine hemoglobin: present in severe intravascular hemolysis-urine dipstick positive for blood but no RBCs seen on micro

AUTOIMMUNE HEMOLYTIC ANEMIA



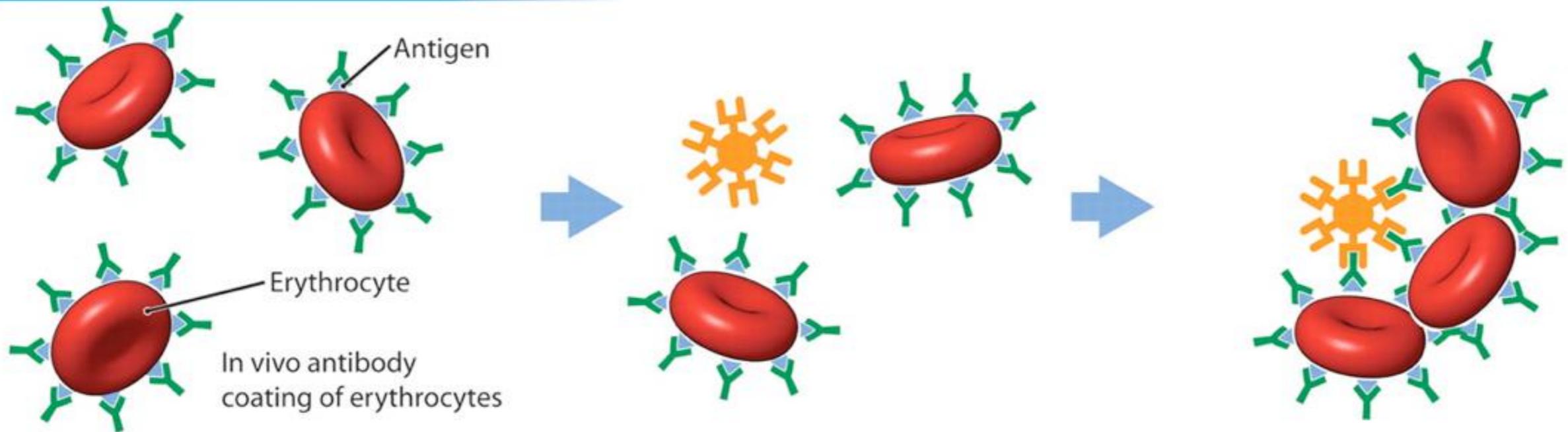
DIAGNOSIS: DIRECT ANTIGLOBULIN TEST-COOMBS

- ▶ Useful in diagnosing immune hemolytic anemia where there is antibody coating a patients red blood cells
- ▶ Done by mixing patients erythrocytes with antihuman globulin containing antibody to IgG and C3
- ▶ Test positive if agglutination occurs

INDIRECT ANTIGLOBULIN TEST (INDIRECT COOMBS)

- ▶ Useful to detect antibodies present in patient's serum
- ▶ Helpful in detecting alloantibodies induced by prior transfusion or by fetal transfer to mother

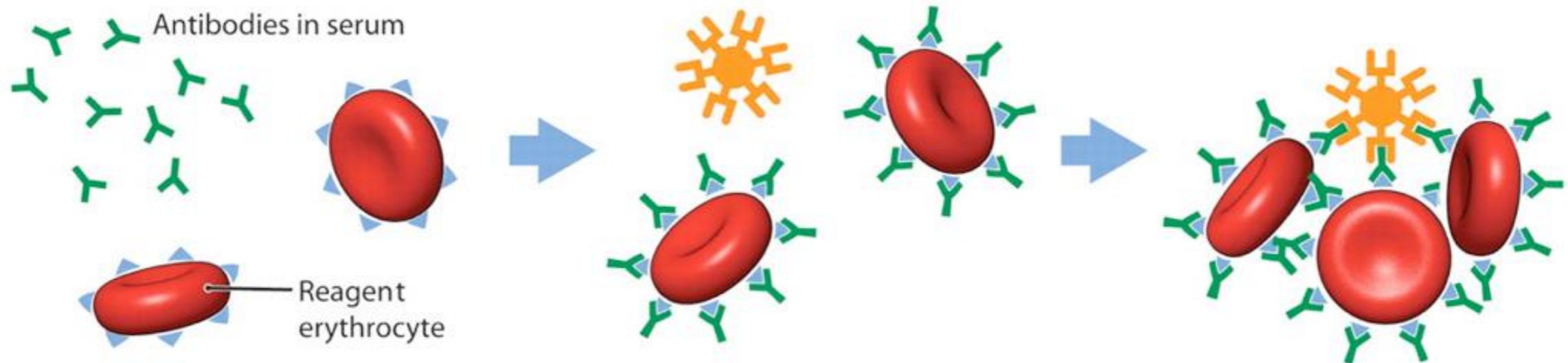
Direct Antiglobulin Test



Anti-IgG AHG reagent added after erythrocytes are washed

AHG reagent causes IgG-coated erythrocytes to agglutinate

Indirect Antiglobulin Test



IMMUNE HEMOLYTIC ANEMIA

- ▶ 40-50% Idiopathic
- ▶ Induced by binding of antibody &/or complement to RBC membrane
- ▶ Caused by autoantibody directed against patients own RBCs or acquired alloantibody directed against transfused RBCs
- ▶ Coombs is only test that provides definitive evidence of immune hemolysis.

IMMUNE HEMOLYTIC ANEMIA

Warm-antibody Autoimmune Hemolytic Anemia

- ▶ Autoantibodies optimally reactive at 37C
- ▶ IgG present on RBC surface
- ▶ May also have C3
- ▶ Most cases idiopathic
- ▶ Can be a complication of underlying disease

IMMUNE HEMOLYTIC ANEMIA

Warm Antibody Related Diseases

- ▶ Chronic lymphocytic leukemia
- ▶ Collagen vascular diseases
- ▶ Ulcerative colitis
- ▶ Congenital immunodeficiency

TREATMENT OF WARM-REACTIVE AIHA

- ▶ Prednisone 1 mg/kg/d
- ▶ Folic acid
- ▶ Splenectomy if refractory to prednisone
- ▶ Immunosuppressive drugs
- ▶ IVIg, Rituximab
- ▶ TRANSFUSE LEAST INCOMPATIBLE BLOOD

IMMUNE HEMOLYTIC ANEMIA

▶ COLD ANTIBODY

-Cold Agglutinin disease

idiopathic

chronic lymphocytic leukemia

mycoplasma infection

infectious mononucleosis

-Paroxysmal Cold Hemoglobinuria

TREATMENT OF COLD ANTIBODY AIHA

- ▶ Avoid cold exposure
- ▶ Folic acid therapy
- ▶ Treatment of underlying disorder
- ▶ Immunosuppressive agents
- ▶ Splenectomy of little value
- ▶ Rituximab
- ▶ Plasmapheresis

TREATMENT OF COLD ANTIBODY AIHA

- ▶ Transfusions of packed red blood cells:
- ▶ Compatibility testing should be done at 37°C
- ▶ Transfuse warm blood recommended

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

- ▶ Acquired clonal stem cell disorder-in which a mutation of PIG-A gene causes defective production of GPI Anchor Protein
- ▶ Only a portion of RBCs affected
- ▶ Defective platelets & WBCS
- ▶ Increased sensitivity of RBCS to complement mediated hemolysis

PNH: CLINICAL PRESENTATION

- ▶ May remain undiagnosed for a long period of time
- ▶ History of unexplained, chronic hemolysis, hemoglobinuria, pancytopenia & thrombotic events
- ▶ Intravascular hemolysis
- ▶ Absent haptoglobin, increased LDH, hemoglobinuria, & hemosiderinuria

PNH: CLINICAL PRESENTATION

- ▶ Can be found in the setting of another specified bone marrow disorder:

Aplastic Anemia

Refractory Anemia-MDS

- ▶ Can be subclinical (no hemolysis)

PNH: DIAGNOSIS

Flow cytometry using antibodies directed against GPI-AP

(glucosyl phosphatidylinositol-anchored proteins)

PNH: TREATMENT

- ▶ Folic acid
- ▶ Corticosteroids
- ▶ RBC Transfusions
- ▶ Iron (can precipitate hemolysis)
- ▶ Anticoagulation with warfarin
- ▶ Eculizumab (Solaris)
- ▶ Stem cell transplant

NONIMMUNE HEMOLYTIC ANEMIA

Inherited nonimmune hemolytic anemia

RBC membrane disorders:

Hereditary spherocytosis

Hereditary elliptocytosis

Hereditary stomatocytosis

G6PD deficiency

HEREDITARY SPHEROCYTOSIS

- ▶ Molecular defect in one or more of the proteins in the red blood cell cytoskeleton causing the cell to contract into a sphere shape. It has a high osmotic fragility and more prone to physical degradation.
- ▶ Osmotic fragility test

HEREDITARY SPHEROCYTOSIS

- ▶ Mild to severe hemolytic anemia
- ▶ Spherocytes on peripheral smear
- ▶ Increased osmotic fragility
- ▶ Negative direct antiglobulin test
- ▶ Aplastic crisis with viral infection
- ▶ Splenectomy is treatment of choice in severe cases

HEREDITARY SPHEROCYTOCYTOSIS



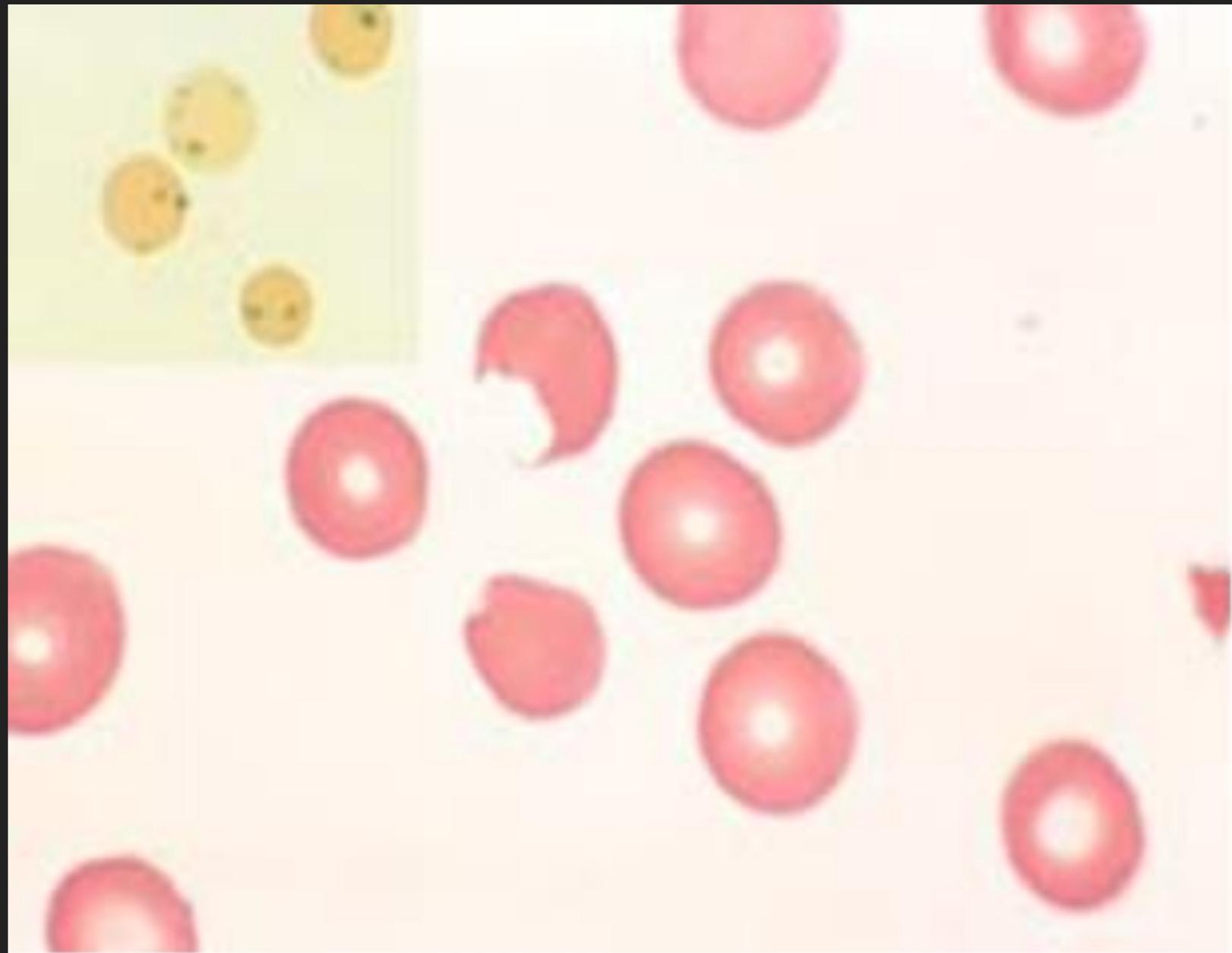
G6PD DEFICIENCY

- ▶ Most common enzyme deficiency worldwide.
- ▶ Different gene mutations cause different levels of enzyme deficiency and disease manifestations G6PD helps protect hemoglobin from oxidation upon exposure to a drug or toxin that results in the generation of free radicals
- ▶ Drugs associated with hemolysis: primaquine, sulfa, dapsona, nitrofurantoin
- ▶ Fava beans will cause acute hemolysis shortly after ingestion

G6PD DEFICIENCY

- ▶ Acute hemolysis lasts 2-4 days, self-limiting, rarely requiring transfusion
- ▶ Infections and diabetic ketoacidosis can trigger hemolysis
- ▶ “Bite” cells on peripheral smear and Heinz bodies (precipitated hemoglobin)
- ▶ Diagnosis made by level of G6PD, but may be normal in active hemolysis

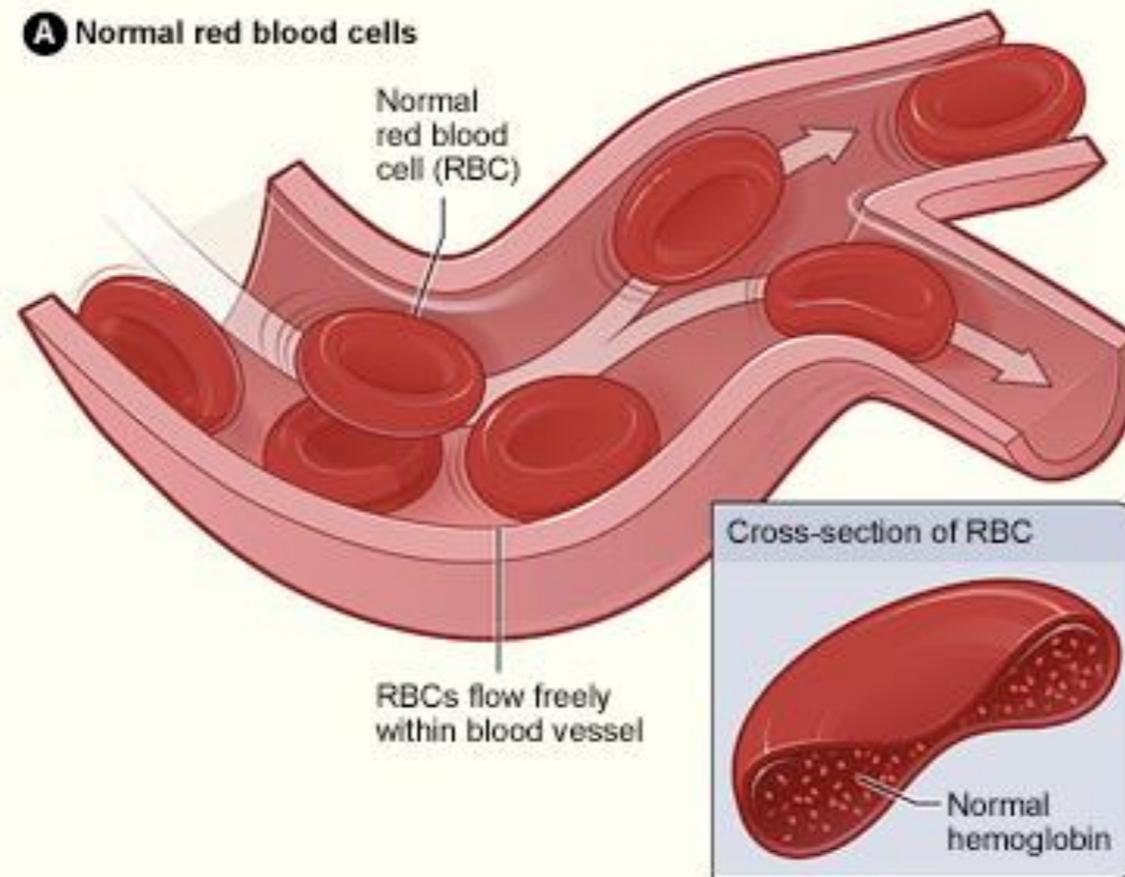
HEINZ BODIES & BITE CELLS



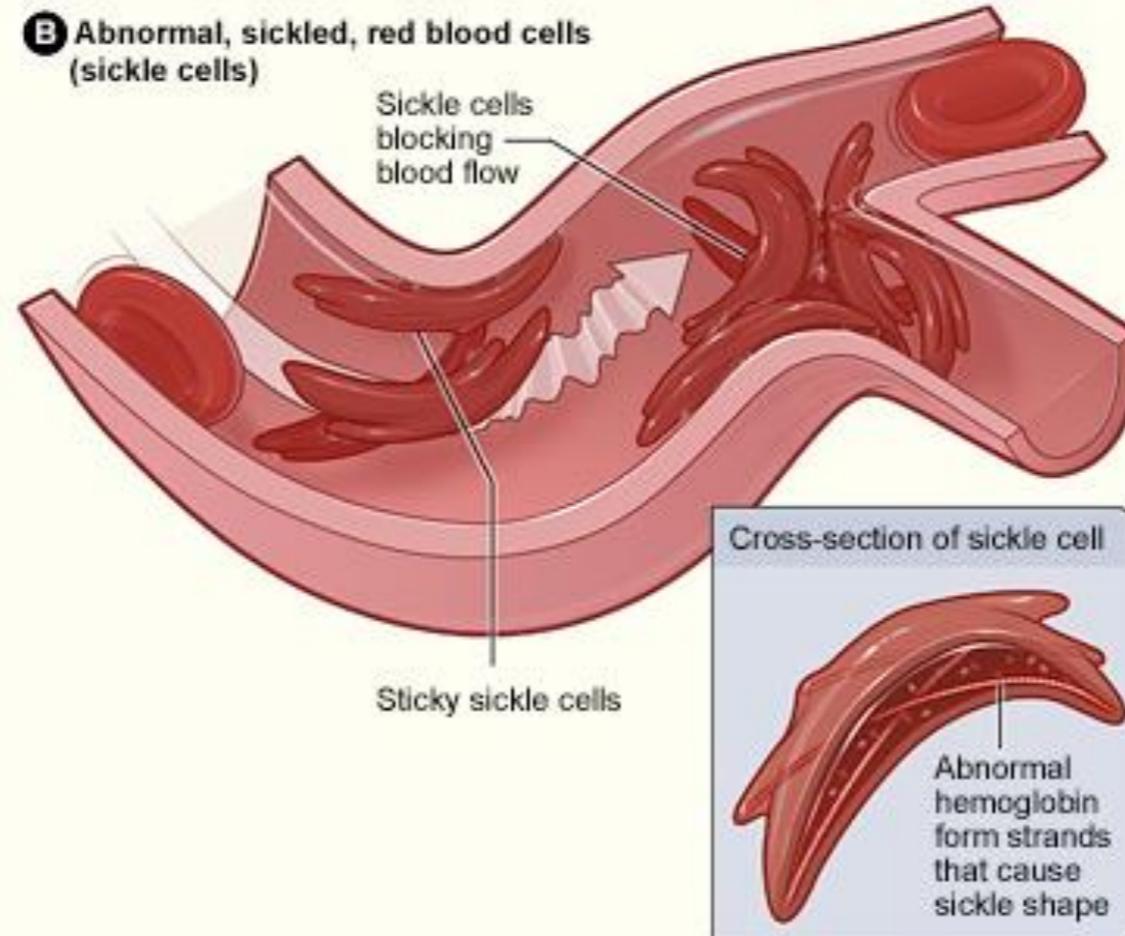
HEMOGLOBINOPATHIES

- ▶ SICKLE CELL DISEASE-the bone marrow makes sickle shaped red blood cells due to qualitative defects of globulin chain synthesis
 - HbS >50%
 - Multiple genotypes and phenotypes
 - Sickle Cell Trait is not a disease

A Normal red blood cells



B Abnormal, sickled, red blood cells (sickle cells)



SICKLE CELL ANEMIA: COMPLICATIONS

- ▶ Painful episode-most common
- ▶ Acute chest syndrome
- ▶ Stroke (10% children)
- ▶ Osteonecrosis
- ▶ Proliferative retinopathy
- ▶ Venocclusive complications
- ▶ Infectious complications

SICKLE CELL ANEMIA COMPLICATIONS

▶ HEMOLYSIS

-Gallstones

-Aplastic crisis

-Osteopenia

-Anemia

-Nutritional deficiencies

SICKLE CELL ANEMIA: TREATMENT

- ▶ General medical care
- ▶ Pain management: **AVOID MEPERIDINE!!**
- ▶ Hydroxyurea
- ▶ Transfusion-limited, maintaining at baseline
- ▶ Stem cell transplant

APLASTIC ANEMIA

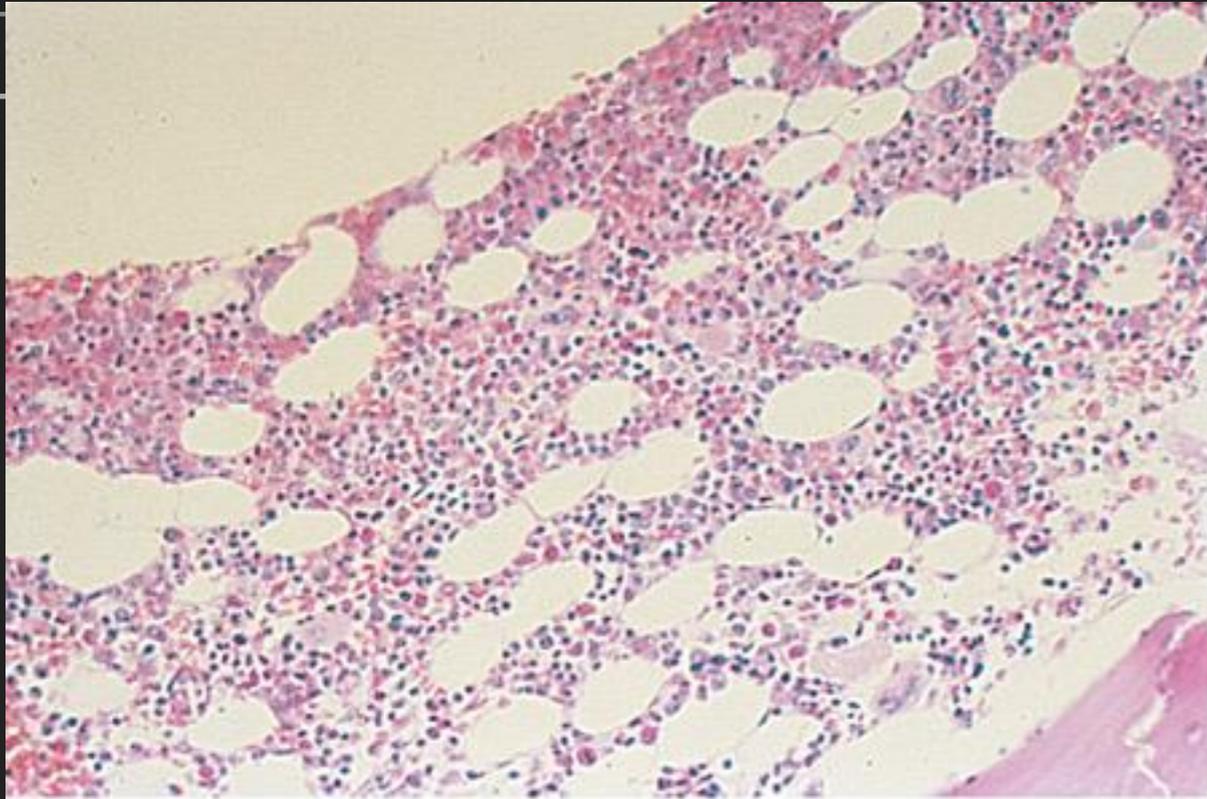
- ▶ Pure red cell aplasia
- ▶ Bicytopenia, pancytopenia
- ▶ Bone marrow failure

RED CELL APLASIA: CLASSIFICATION

- ▶ Congenital: Diamond Blackfan Syndrome
- ▶ Acquired: Idiopathic & Secondary
- ▶ Secondary:
 - Hematologic malignancies
 - Solid tumors
 - Immunologic disorders
 - Infectious diseases
 - Drugs

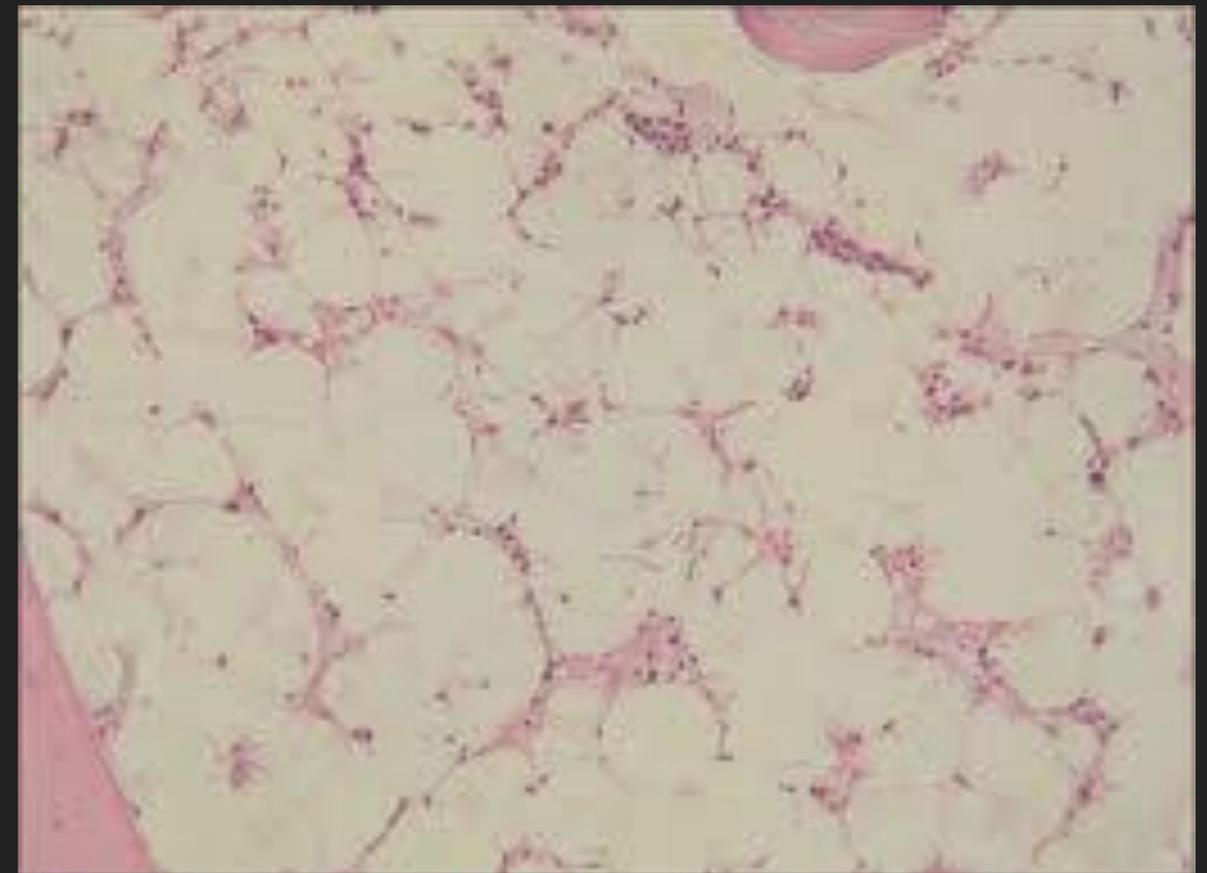
APLASTIC ANEMIA: DIAGNOSIS

- ▶ BONE MARROW BIOPSY: 4-5 cores showing cellularity of <30%
- ▶ Flow cytometry & cytogenetics to rule out the rarer variant - hypocellular MDS



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Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>
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APLASTIC ANEMIA: TREATMENT

- ▶ Antithymocyte globulin (ATG) & Cyclosporin (CSA)
- ▶ Stem Cell Transplant

Hemostasis

PHYSIOLOGICAL BLOOD CLOTTING IN RESPONSE TO INJURY OR LEAK
no disclosures

Disorders of Hemostasis

- Hemophilia
- von Willebrand Disease

HEMOPHILIA

A defect in the thrombin propagation phase of coagulation

HEMOPHILIA A or B

Diagnosis

Bleeding Time	Normal
PT	Normal
APTT	Prolonged
FVIII:c or FIX:c	<1% = severe 1-5% = moderate 6-30% = mild
vWF:Ag	Normal
vWF:Rco	Normal

HEMOPHILIA

Bleeding as a function of clinical severity

Concentration of factor %

50-100:	None
25-50:	Bleeding after sever trauma
6-25:	Severe bleeding after surgery Slight bleeding after minor trauma
1-5:	Severe bleeding after slight trauma
<1:	Spontaneous bleeding mainly in joints or muscles

HEMOPHILIA:

Clinical features

- Muco-cutaneous bleed
- Hemarthrosis
- Muscle bleeds
- Intra-cranial bleed
- Post-dental bleed
- Post surgical bleed

HEMOPHILIA TREATMENT

- Factor replacement
- DDAVP
- Amicar
- All patients should be cared for life long in bleeding disorder clinic

ACQUIRED HEMOPHILIA

CHARACTERISTICS

- AGE: MOST >50
- BLEEDING PATTERN: More severe soft tissue bleed
hemarthrosis less common
- INHIBITOR
- UNDERLYING DISORDER: usually none, but can be seen post partum, autoimmune disease, malignancy, drug reaction

ACQUIRED HEMOPHILIA

- Major bleeding requiring transfusion: >75%
- Death due to bleeding: >15%
- Immediate Rx with appropriate activated factor products
- Long term: Attempt suppression of inhibitor

VON WILLEBRAND DISEASE

- Most common inherited bleeding disorder presenting with:
mucocutaneous bleeds, nosebleeds, bleeding with dental work,
heavy menses
- Family history of bleeding
- Decreased levels of VWF
- Autosomal Dominant
- Bleeding usually mild to moderate

VON WILLEBRAND DISEASE

DIAGNOSIS:

- FVIII activity
- VWF antigen
- Ristocetin Cofactor
- PFA
- RIPA
- VWF Multimers

VWH Classification

Type 1: partial quantitative deficiency of VWF

Type 2: qualitative defect in VWF

Type 3: total deficiency of VWF

VWD Classification

TYPE	RIPA	Multimer Pattern	VWF:RCo/Ag
1 Partial Quantitative	decreased or normal	uniform decrease but all present	1:1
Qualitative 2A 2B	decreased increased	decrease large multimers decrease large multimers	decreased decreased
2M 2N	decreased normal	uniform decrease, all present normal multimers	decreased 1:1
3 Severe Deficiency	markedly decreased	Undetectable; usually cannot visualize	N/A

VWD TREATMENT

- DDAVP
- Factor VIII concentrates that contain vWF
- Antifibrinolytics (Amicar, gel foam w/thrombin)
- Severe types should be cared for lifelong at a bleeding disorder center

THROMBOSIS

Pathological Blood Clotting
no disclosures

HYPERCOAGUABLE STAGES

ACQUIRED:

- Advancing age
- Prior thrombosis
- Immobilization
- Major Surgery
- Malignancy
- Estrogens
- Pregnancy
- Trauma
- Paralysis
- Antiphospholipid Antibody Syndrome
- Myeloproliferative disorders
- PNH
- IBD
- Nephrotic syndrome
- HIT
- Prolonged air travel
- Central venous catheters
- Obesity

HYPERCOAGUABLE STAGES

INHERITED:

- Antithrombin III deficiency 20 fold RR
- Protein C deficiency 10 fold RR
- Protein S deficiency 10 fold RR
- Factor V leiden 3-8 fold RR
- Prothrombin gene mutation 3 fold RR

HYPERCOAGUABLE STAGES:

Who to test

Strongly Thrombophilic Clinical History

- **Age of onset <50**
- **Recurrent thrombosis**
- **Positive family h/o thrombosis, MI, CVA at young age**
- **Cerebral venous thrombosis**
- **Portal or mesenteric vein thrombosis (r/o MPD, PHN)**

**Consider: VTE associated with OCPs/HRT or pregnancy
Pregnancy loss in 2nd or 3rd trimester**

HYPERCOAGUABLE STAGES: Who to not test

- **Patients >50 with first spontaneous DVT**
- **VTE in patients with active cancer**
- **Elderly pts, especially post-op VTE**
- **Retinal vein thrombosis**
- **Arterial thrombosis**
- **Women starting OTCs with no personal or family history of VTE**

HYPERCOAGUABLE WORKUP

- **Prothrombin gene mutation**
- **Factor V Leiden (Activated Protein C resistance)**
- **Antithrombin III**
- **Protein C activity**
- **Protein S assay, total & free**
- **Tests for antiphospholipid antibody syndrome:**
 - **Lupus Anticoagulant**
 - **Anticardiolipin & B2-glycoprotein I antibodies**

TREATMENT OF DVT/PE

- **HEPARIN**

Unfractionated or LMW for 5 days

- **WARFARIN**

Start day 1

INR 2-3

Treat 3-6 months

DIRECT ORAL ANTICOAGULANTS

- **Rivaroxaban (Xarelto)**
- **Apixaban (Eliquis)**
- **Dabigatram (Pradaxa)**

- **KNOW YOUR DRUG**

NOACs: When not to use

- **Pregnancy associated with VTE**
- **Cancer associated VTE**
- **Obese patients (>275 lbs)**
- **Very frail patient (<100 lbs)**
- **Renal dysfunction-cr cl <30;
(use with caution in cr cl 30-40)**
- **Patients on medicine with major interactions**
- **Cautious with difficult patients, ie: recurrent DVT/PE on anticoagulation**
- **Ensure patients comply and can acquire med**

DURATION OF ANTICOAGULANT THERAPY

- **First isolated, unprovoked distal DVT or proximal DVT/PE secondary to a transient risk factor: 3 months**
- **Second unprovoked DVT/PE: long-term?**
- **VTE in setting of active cancer: LMWH at least 3 mos vs long-term**

DURATION OF ANTICOAGULANT THERAPY

SPECIAL SITUATIONS:

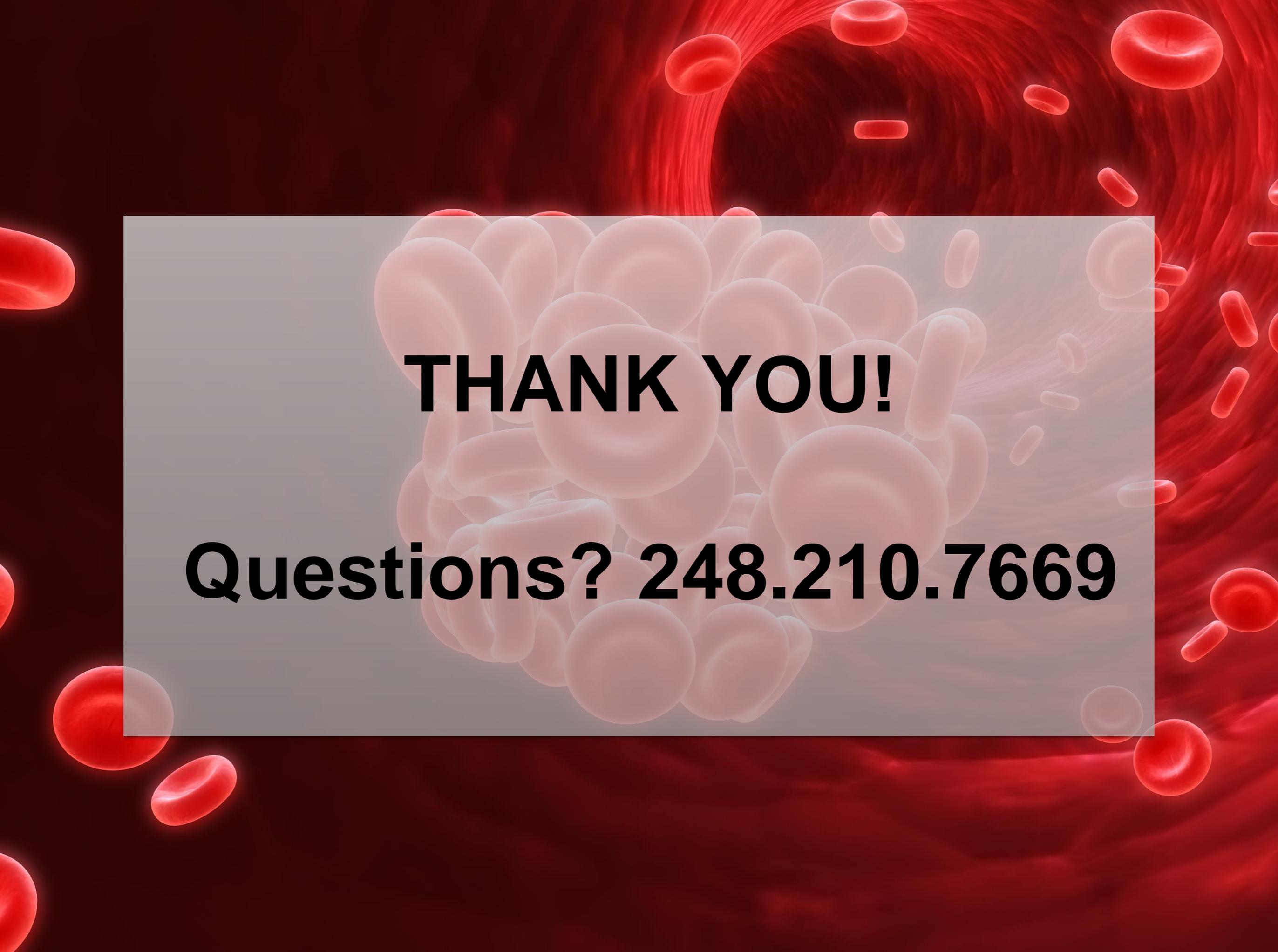
Consider indefinite anticoagulation after first event in following cases:

- **Cancer-until resolved (consider LMWH)**
- **Antiphospholipid antibody syndrome**
- **Antithrombin III deficiency**
- **Protein C or S deficiencies**
- **Multiple genetic defects**

DURATION OF ANTICOAGULANT THERAPY

Criteria for long term oral anticoagulation:

- **No resolution of triggering risk**
- **Sites and severity of thrombosis**
- **Identification of a prothrombotic defect**
- **Family thrombotic history**
- **Bleeding risk**
- **Patient preference (life style, occupation) with understanding of risks vs. benefits**



THANK YOU!

Questions? 248.210.7669