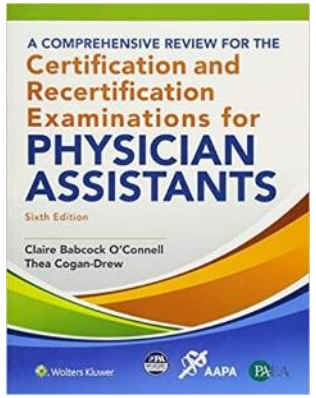
EMORY UNIVERSITY SCHOOL OF MEDICINE
Department of Family and Preventive Medicine
Physician Assistant Program

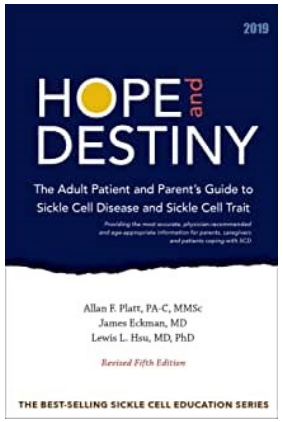
Anemia
Too Low, No Go

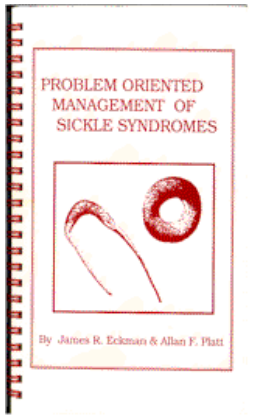
Allan Platt, PA-C, MMSc, DFAAPA
Assistant Professor
Emory University School of Medicine
Physician Assistant Program
Atlanta GA
aplatt@emory.edu www.EmoryPA.org

Disclosures

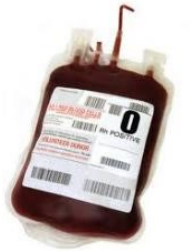


- Author of Chapter 4 – Hematology in **A Comprehensive Review for the Certification and Recertification Examinations for Physician Assistants Sixth Edition** by Claire O'Connell (Author)





- Co-Author of **Hope and Destiny 5th Edition: The Adult Patient and Parent's Guide to Sickle Cell Disease and Sickle Cell Trait** by Allan F. Platt Jr. P.A.-C. M.M.Sc., James Eckman M.D., et al. | May 12, 2019
- Sickle cell advisory board to a NIH funded project
- Webmaster of SCInfo.org website and monthly e-newsletter editor
- I do promote donating blood!!!

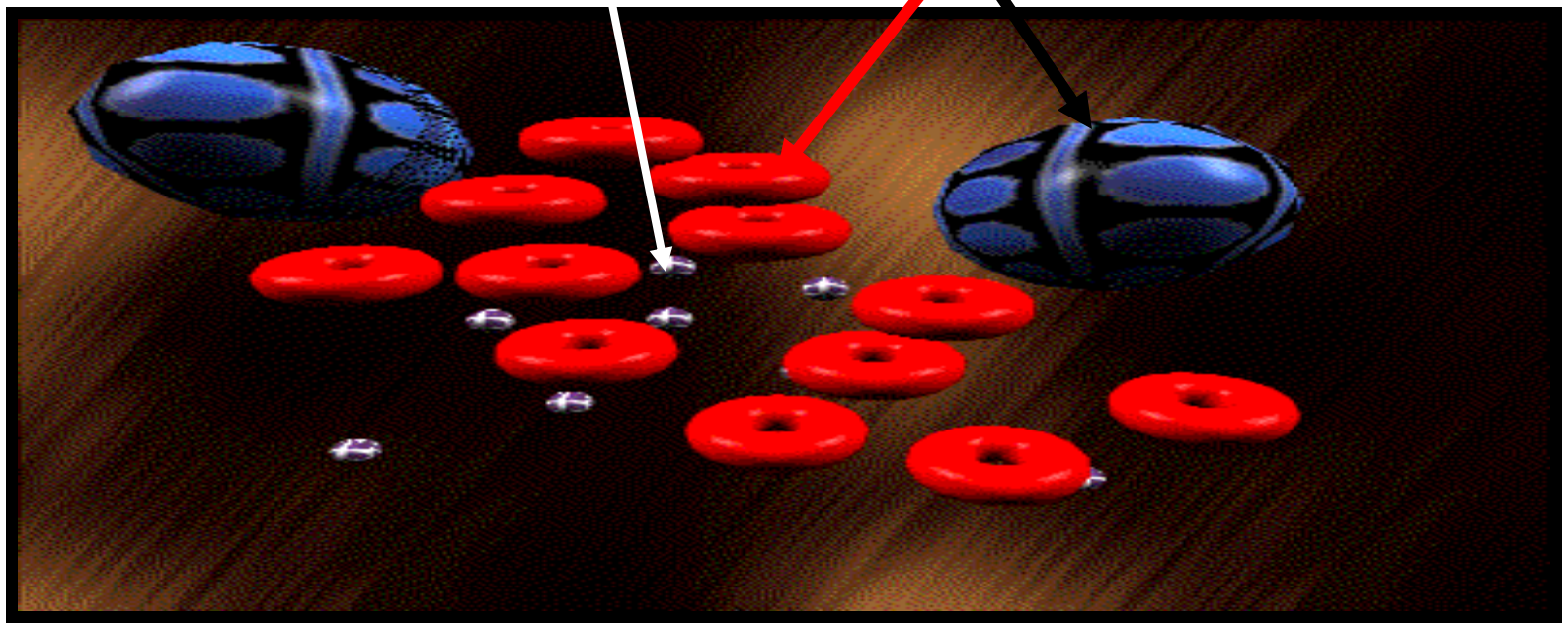


Objectives

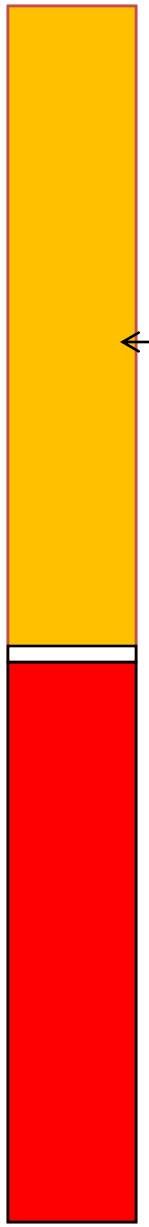
- At the end of this session, participants should be able to:
  - Explain the normal physiology of blood cells
  - Evaluate the common presentations and work-up of patients with anemia
  - Interpret the CBC and other common laboratory tests for anemia
  - Develop a differential diagnosis and work-up of microcytic, normocytic, macrocytic, and hemolytic anemias using common tests, treatment, and prevention

Blood

- Blood has red cells(erythrocyctes)
- White cells (leukocytes)
- Platelets (thrombocytes)



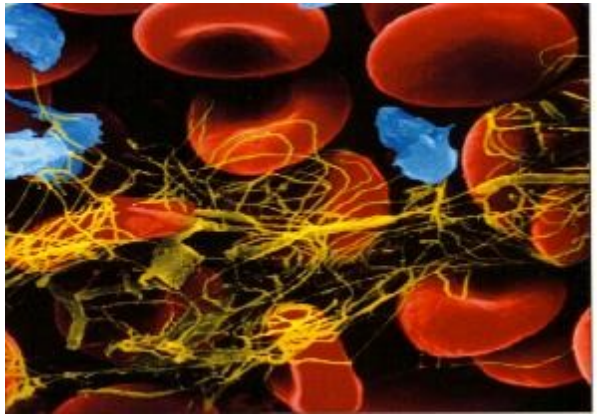
Blood Components

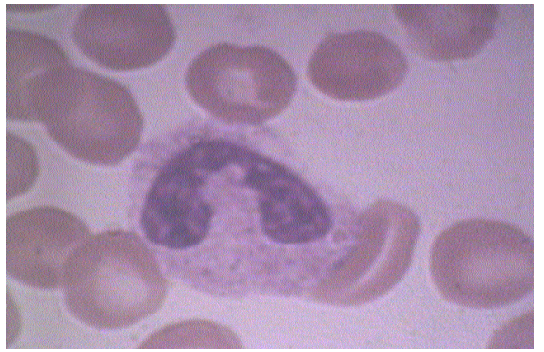


Plasma 54%

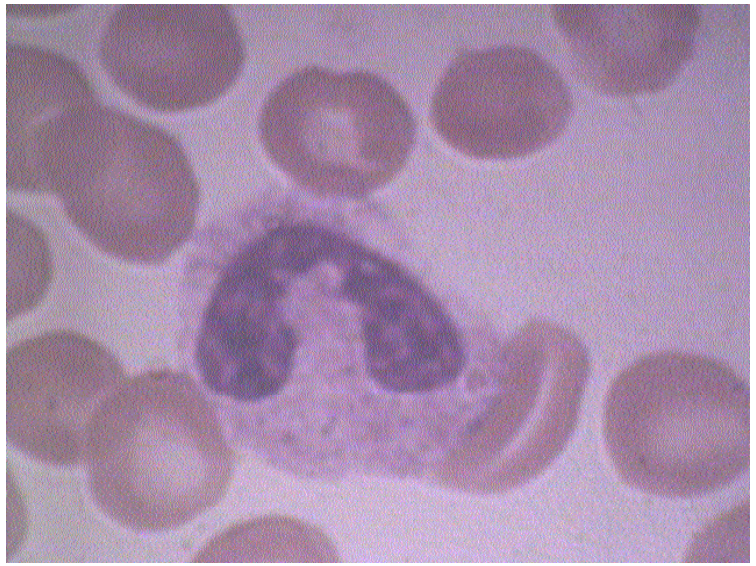
White cells and platelets 1%

Red Cells 45%



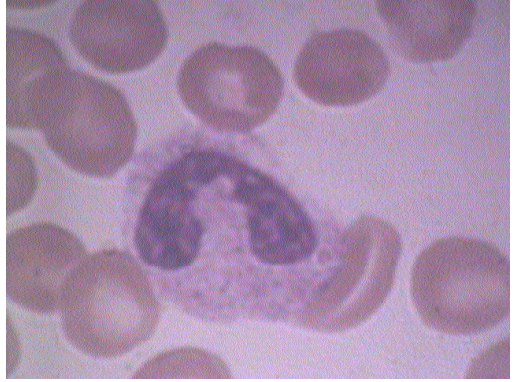


White Blood Cells



- Fight infections
- Are increased in infections
- Move inside and outside of blood vessels
- Are made in the bone marrow

White Blood Cells



WBC - White Blood Cell 4.5 - 11.0 K/uL High = Leukocytosis

WBC Differential

Neutrophils - Segs	54 -62%	Bacterial Infection
Neutrophils - Bands	3 -5 %	Acute Bacterial Infection
Lymphocytes - Lymphs	25 - 33%	Viral Infection (T, B cells)
Monocytes - Monos	3 - 7%	Chronic Infections TB,SBE..
Eosinophils - Eos	1 - 3%	Allergy, Parasites, Drugs
Basophils - Basos	0 - 0.75%	Allergy
Atypical Lymphs	0	Mono - EBV

Leukocytosis

- Over 11.0 K/uL but under 20.0 K/uL -
  - Infection
  - Pregnancy up to 13.2
  - Splenectomy
  - Hemolytic anemias
  - Chronic inflammation
  - Reactive – stress, seizure, post surgical
  - Meds - Corticosteroids, beta agonists, lithium, epinephrine, colony-stimulating factors
- 20,000 to 100,000 leukemoid reaction-
  - severe infections, such as Clostridium difficile infection, sepsis, organ rejection, or in patients with solid tumors, leukemias
- Over 100 - leukemias or myeloproliferative disorders.
- https://www.aafp.org/afp/2015/1201/p1004.html

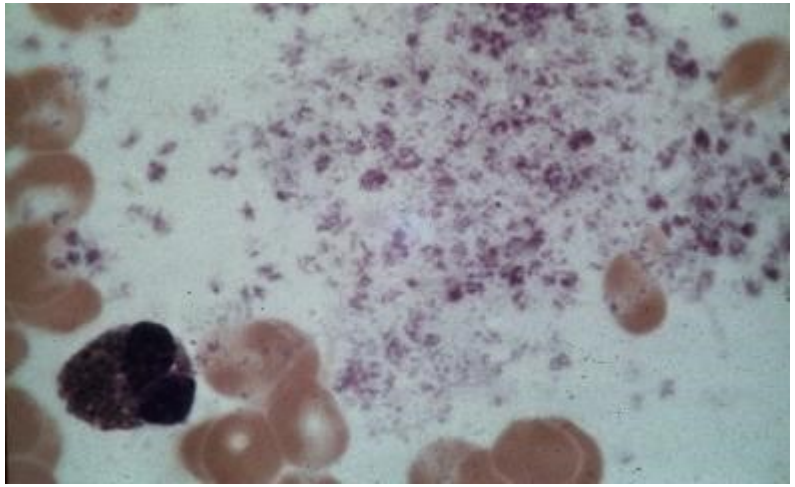
Leukopenia

- Under 4.5 K/uL
- Viral Infections
- Chemotherapy or radiation therapy
- Myelodysplastic syndrome - MDS
- Neutropenia less than 1.5×10^9
- African American “benign ethnic neutropenia.”

Myledysplastic Syndrome - MDS

- MDS - anemia, thrombocytopenia, and/or neutropenia on CBC
- May have Pancytopenia
- Needs Bone Marrow Biopsy
- Heme/Onc referral for supportive therapy with transfusions
- May be precursor to acute leukemia

Platelets



- Platelet Count 150 - 400 K cell/uL
- Primary Hemostasis
- Help clotting cascade
- Made in the bone marrow

Low = Thrombocytopenia

Destruction, Low production, Sequestration

High = Thrombocytosis

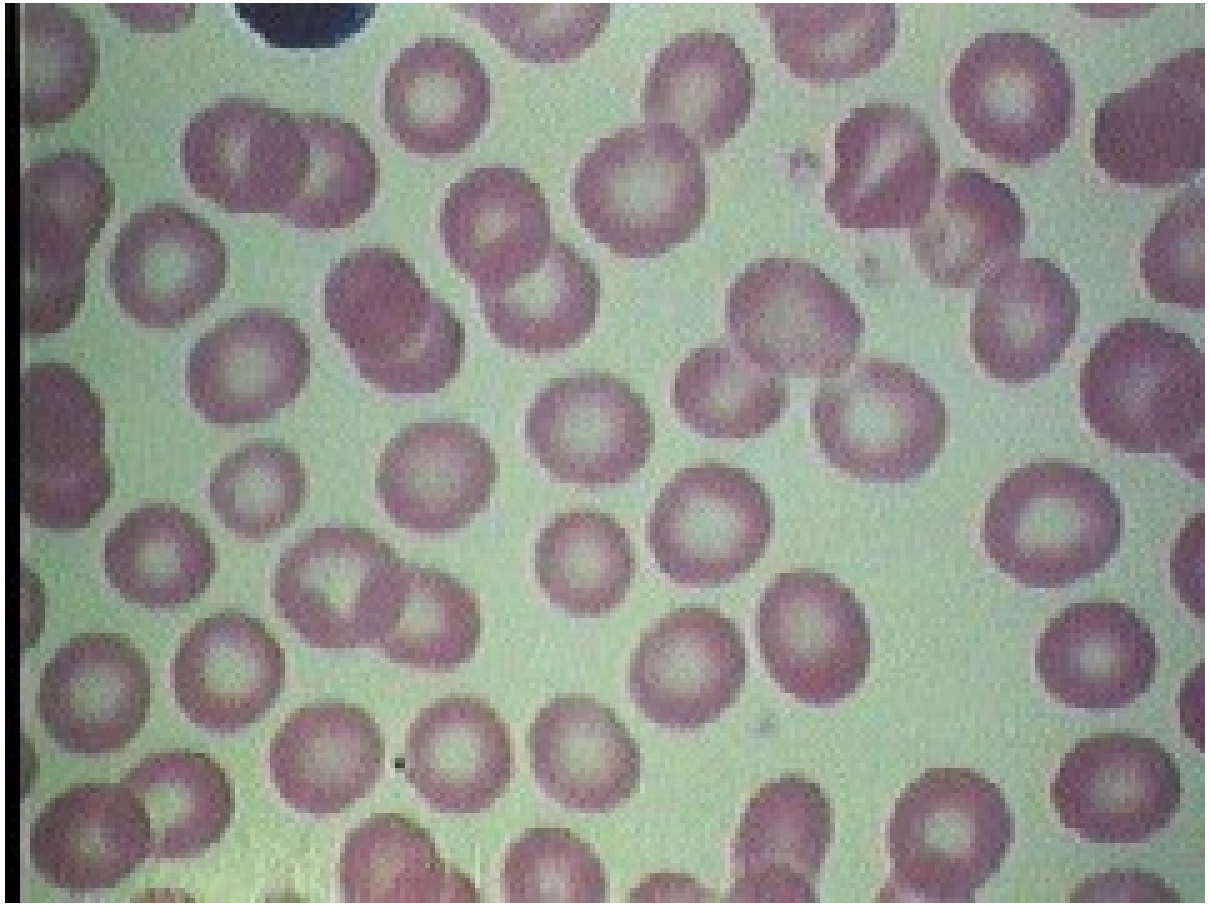
Polycythemia vera = All cells increased

Reactive thrombocytosis include iron deficiency, asplenia, cancer, chronic inflammatory, or infectious diseases, drugs, hemolysis, allergic reaction

Red Blood Cells

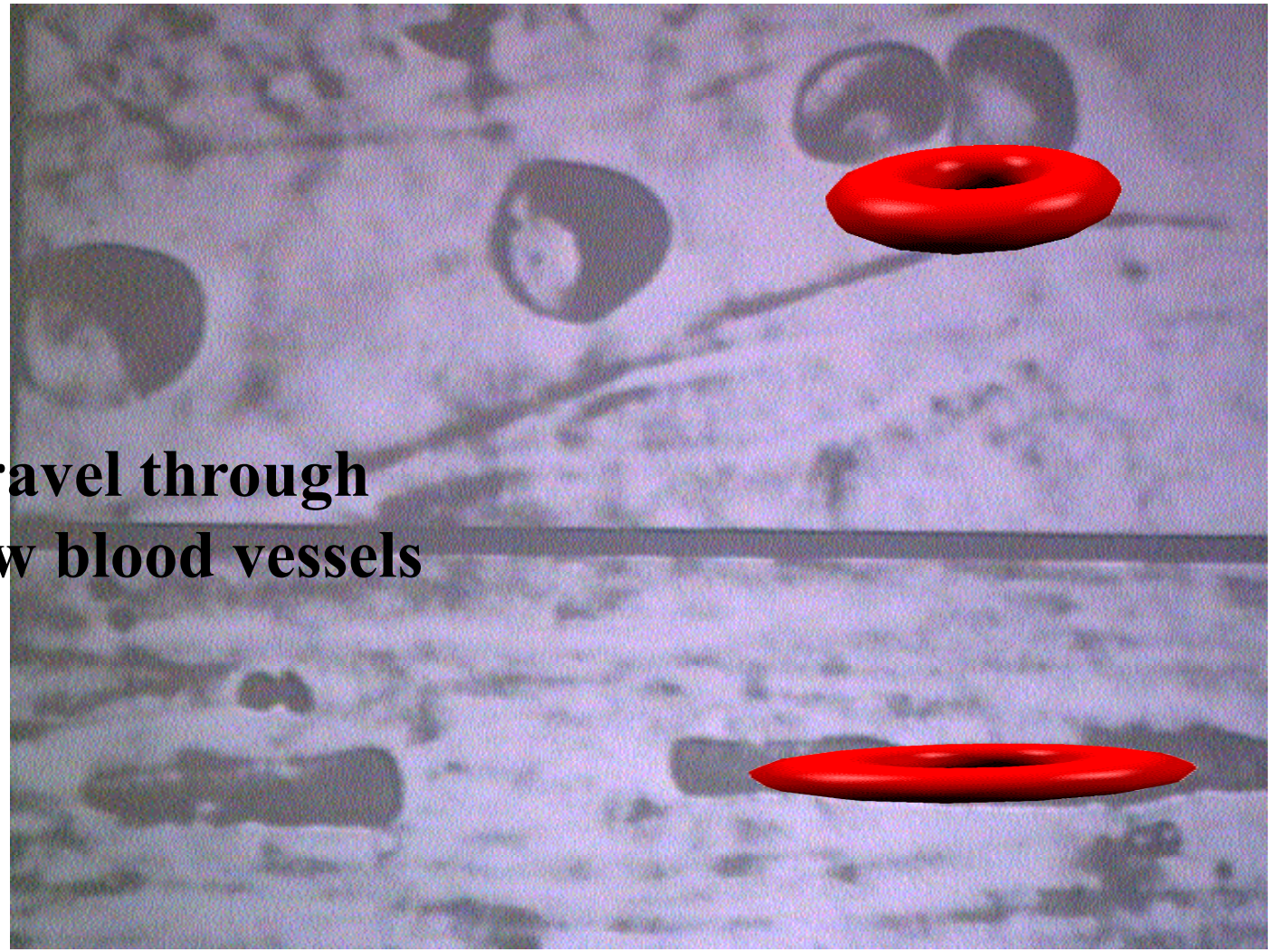
- Carry oxygen from the lungs
- Carry carbon dioxide back to the lungs
- Normally live 120 days
- Major acid buffer for pH
- Contains the protein hemoglobin
- Made from iron, folic acid, vitamin B12
- Made in the bone marrow

Microscope View



Red Blood Cells - Shape

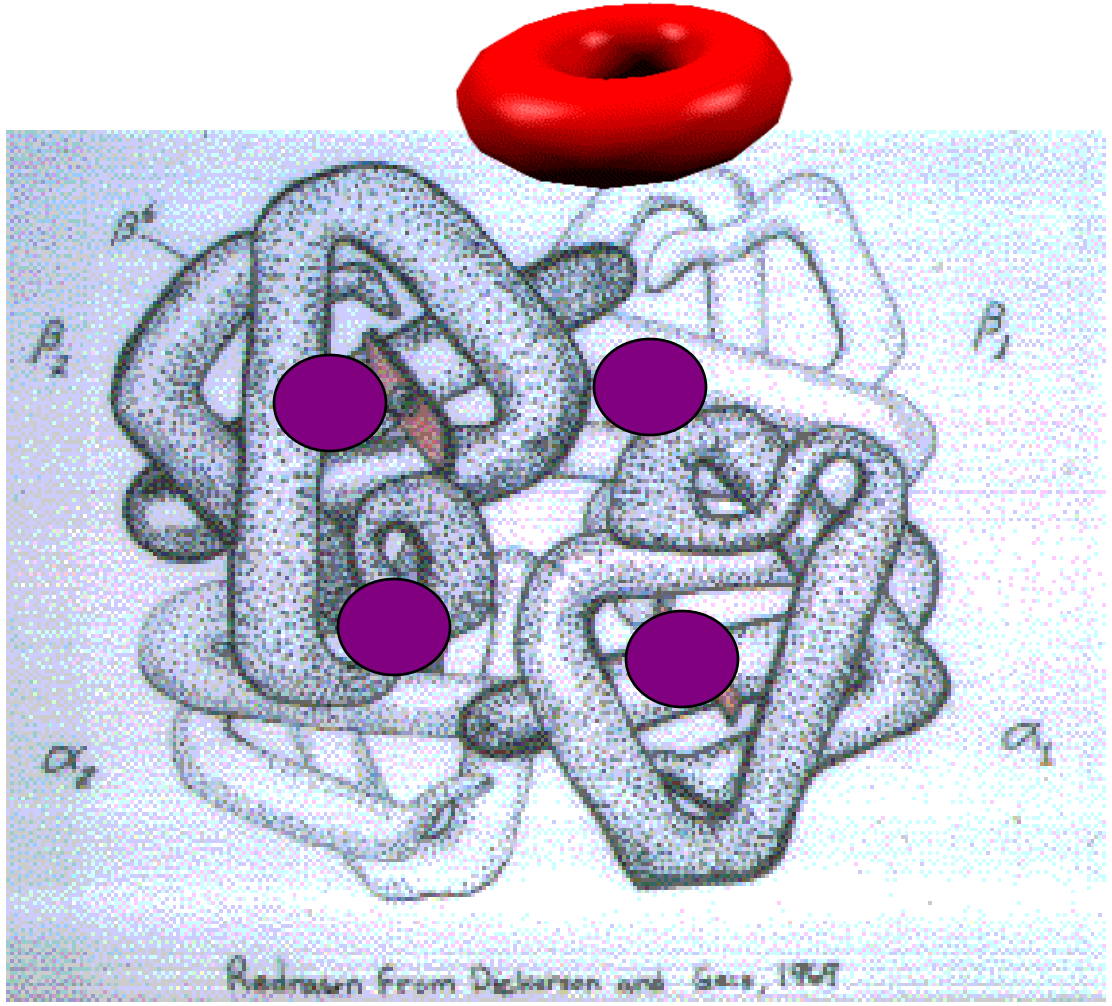
Red cells travel through very narrow blood vessels



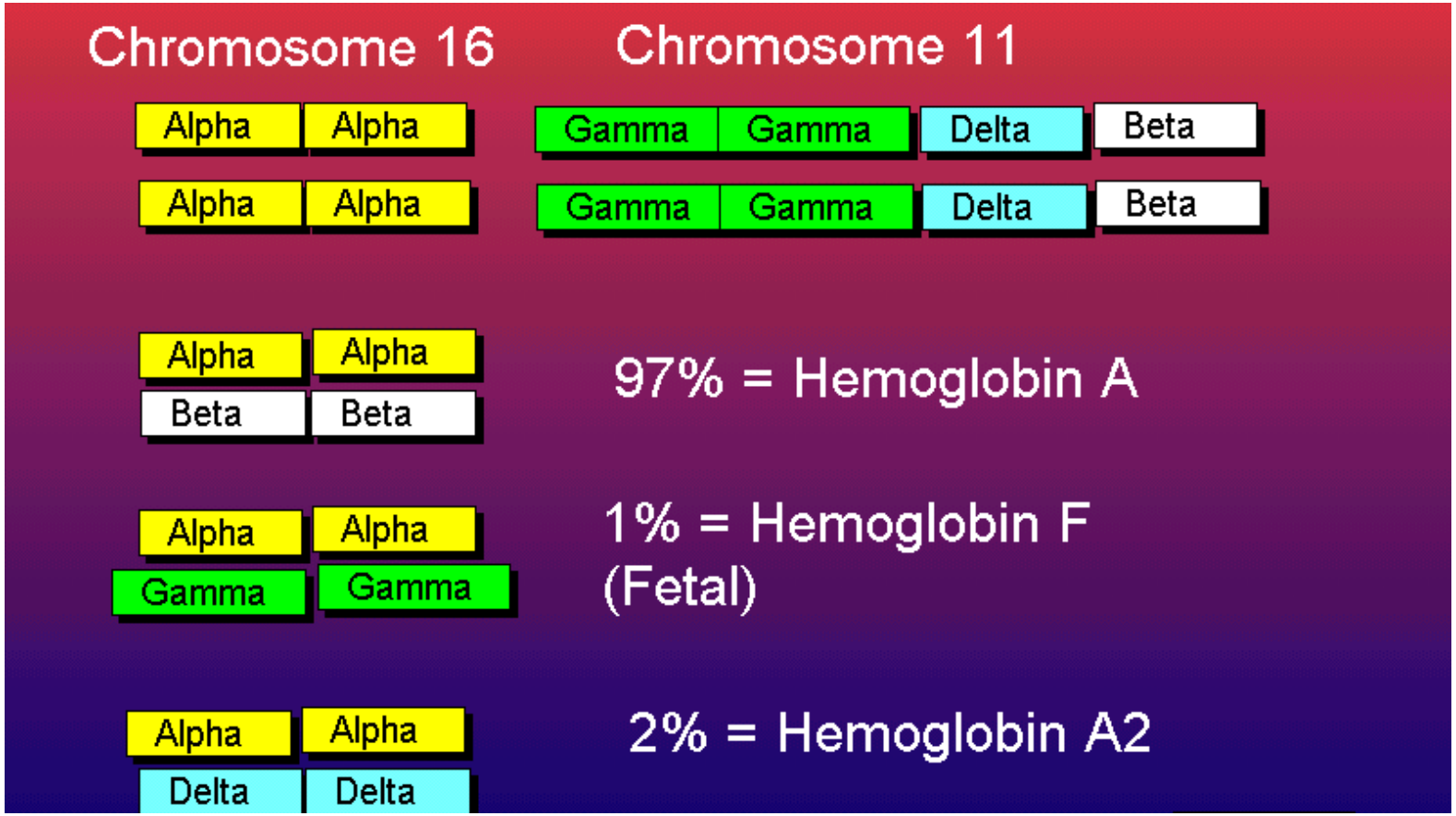
Red Blood Cells - Hemoglobin

Oxygen

Hemoglobin, the main protein in red cells made up of 2 alpha and 2 beta chains with 4 iron molecules holds four oxygen molecules

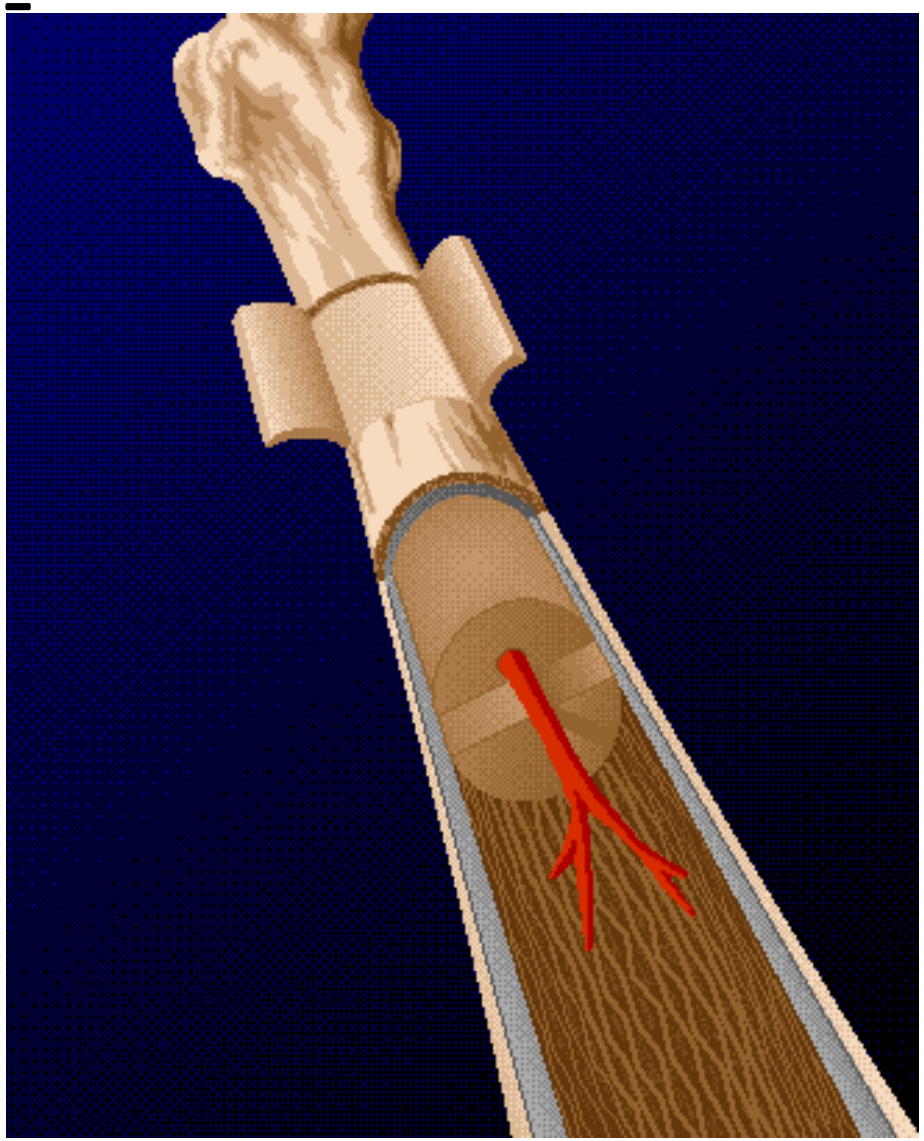


Red Blood Cells - Adult Hemoglobins
Hemoglobin electrophoresis



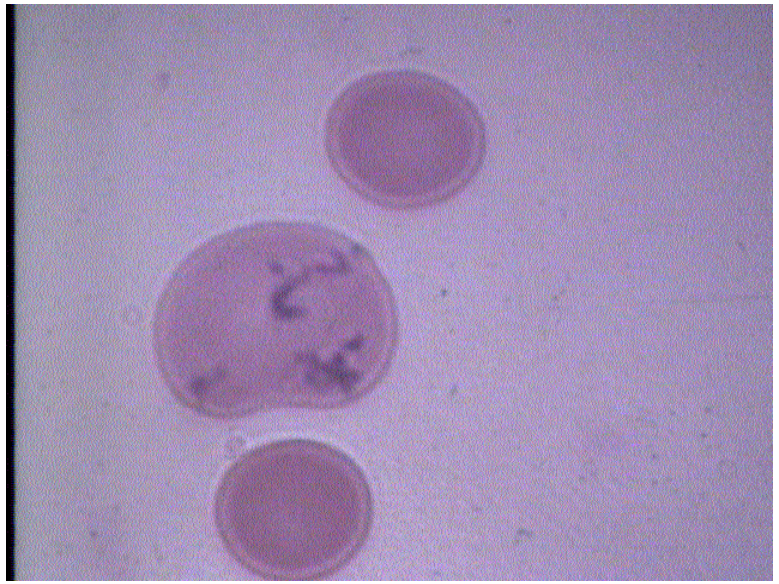
Red Blood Cells - Marrow

Red cells, white cells and platelets are made in the bone marrow of the axial skeleton



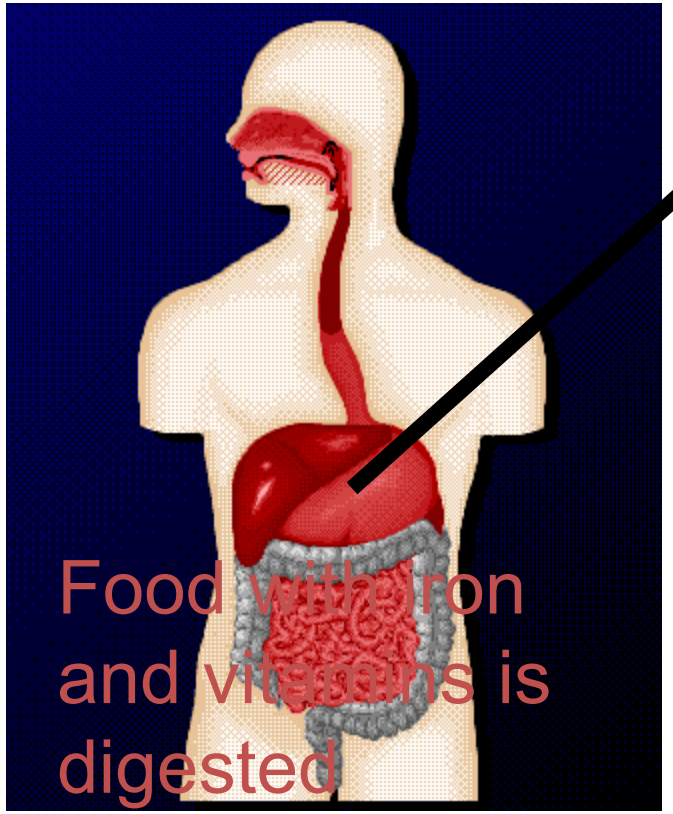
Red Blood Cells - Retics

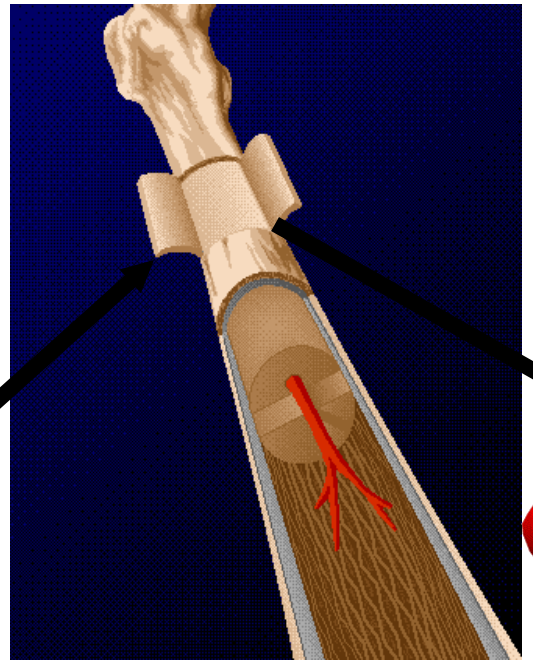
- Reticulocytes, or Retics are young red cells just released from the bone marrow. The Retic count is the best indicator about how the marrow factory is doing.

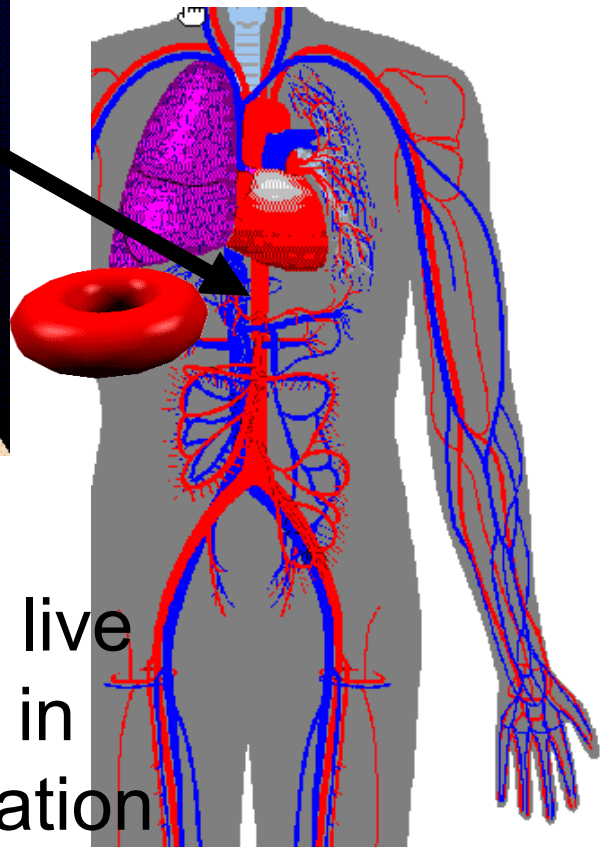


Red Blood Cells

Red cells are made in the bone marrow



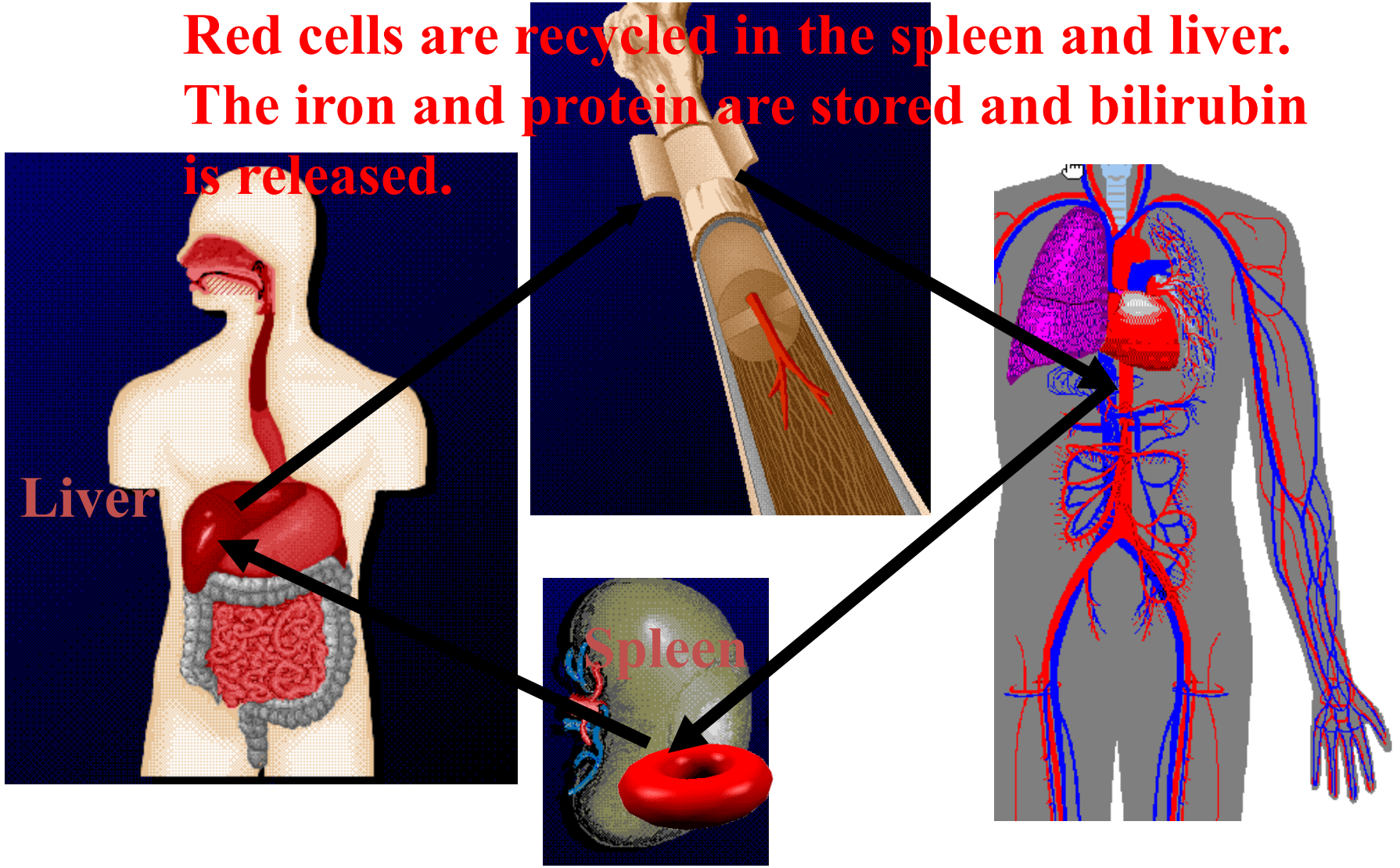




Red cells live 120 days in the circulation

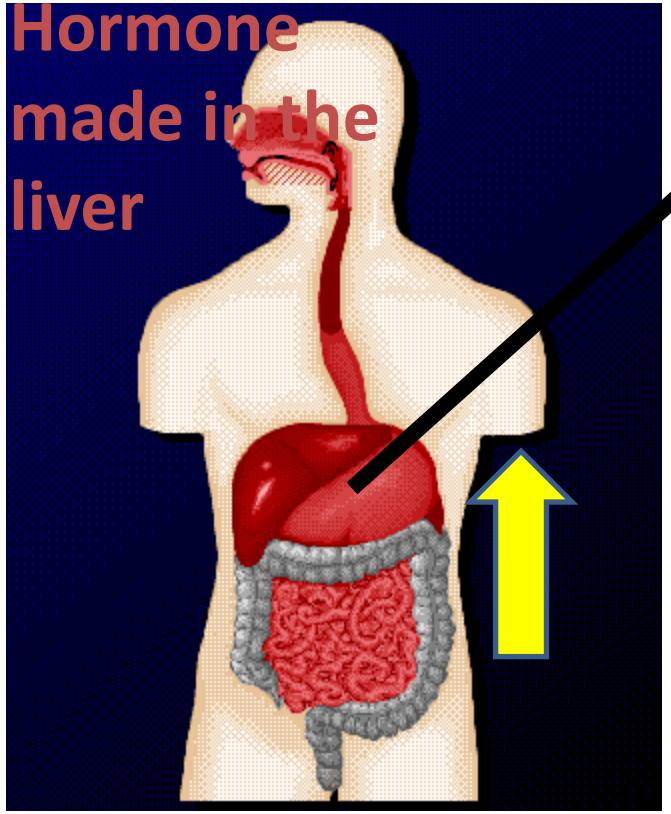
Red Blood Cells - Recycled

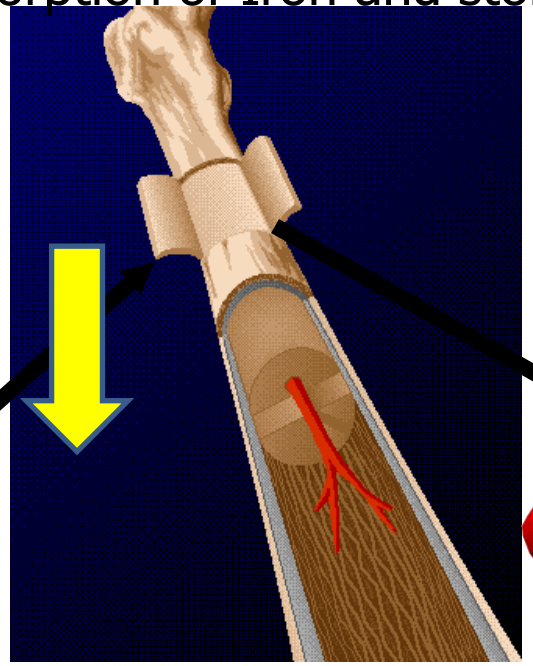
Red cells are recycled in the spleen and liver. The iron and protein are stored and bilirubin is released.



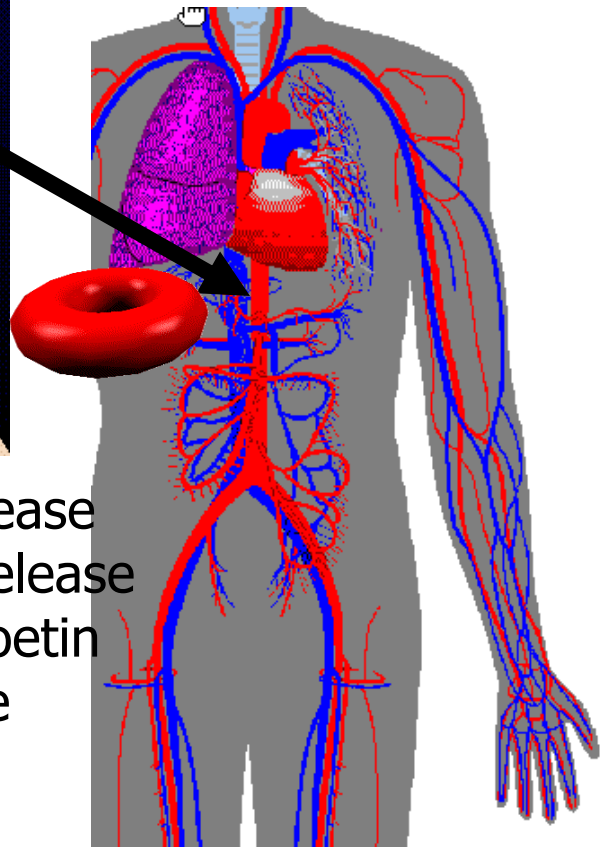
Hepcidin

Increased levels blocks absorption of Iron and storage release - inflammation IL6

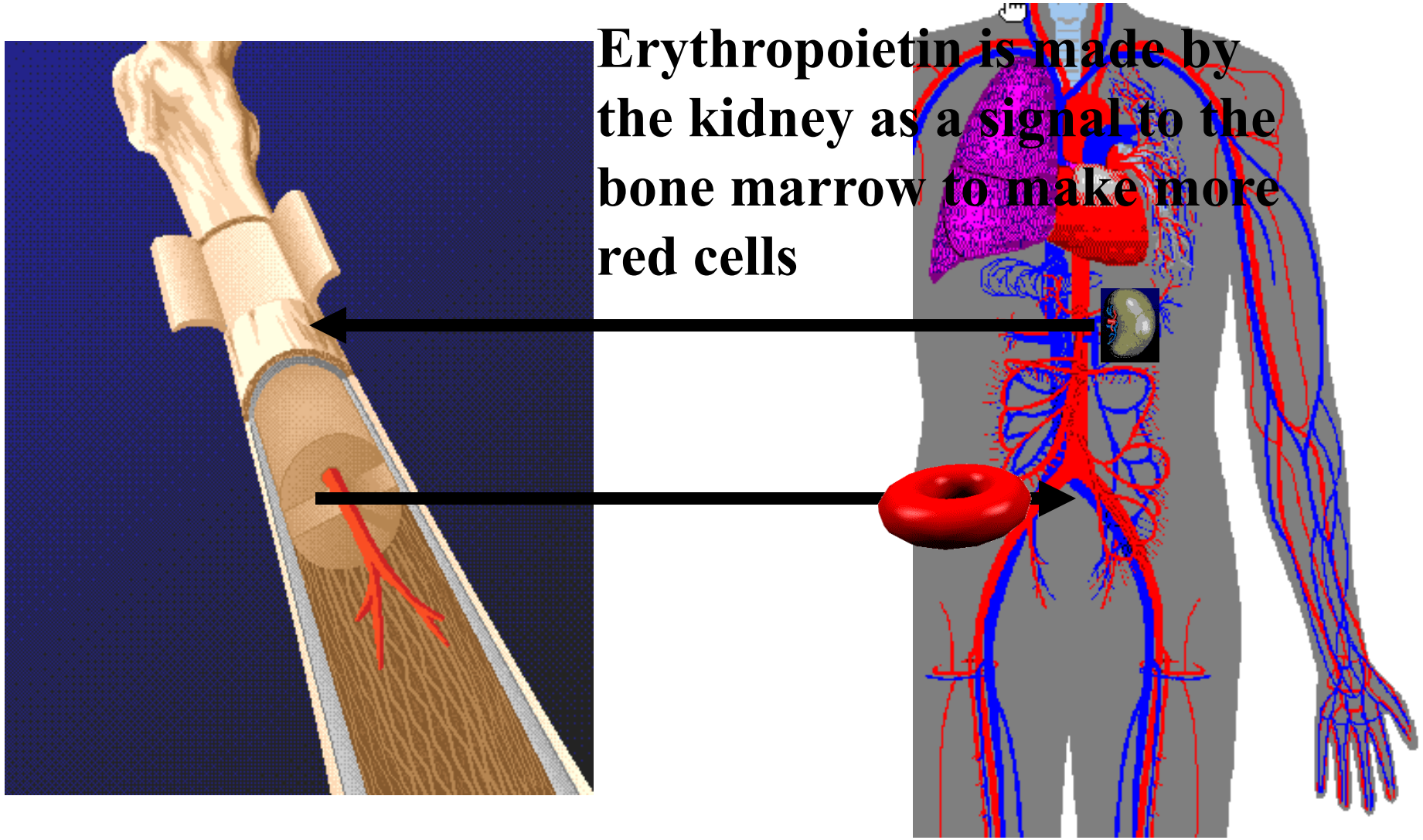




Decreased levels increase iron absorption and release from cells – Erythropoetin and low iron decrease Hepcidin



Red Blood Cells - The Kidney



Anemia Symptoms

- Generalized weakness
- Tiredness - Fatigue
- Dyspnea
- Dizzy – non vertigo
- Palpitations – rapid heart rate
- New angina
- Headache
- Cold extremities

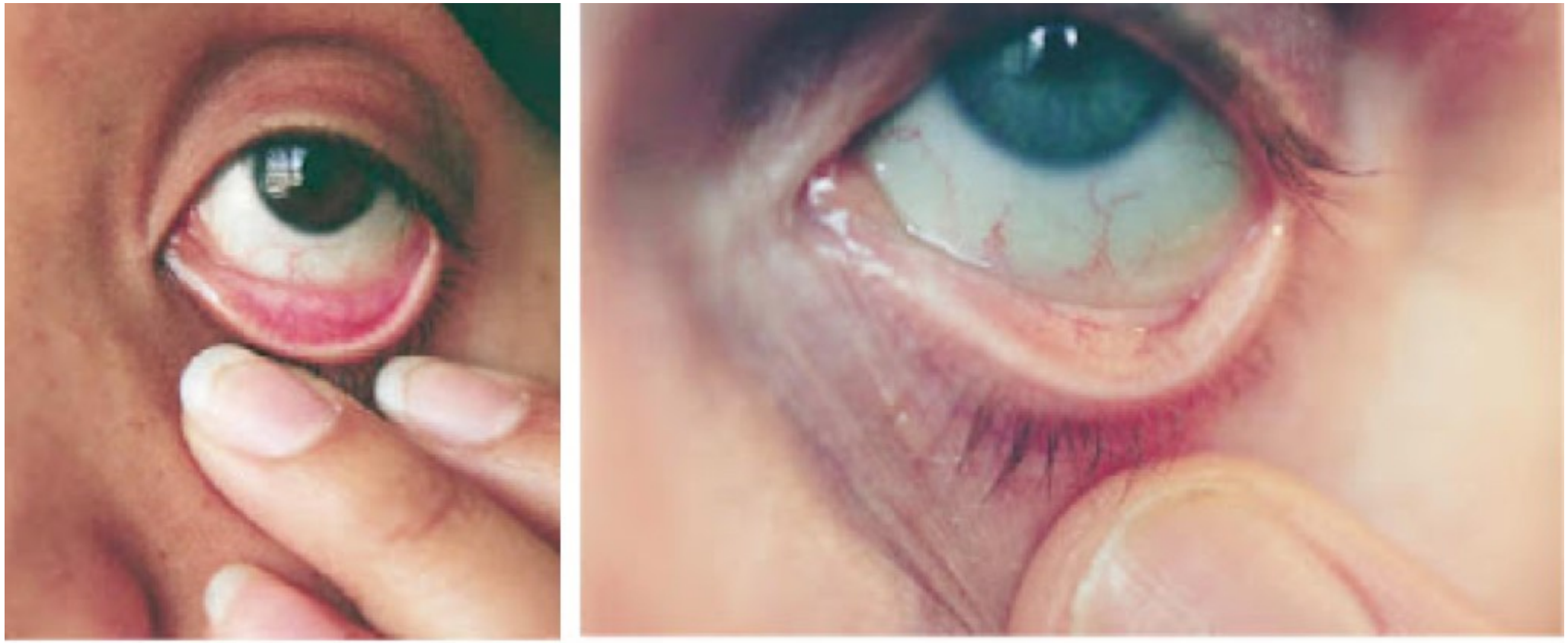
The History -2

- **- History of melena, abdominal pain, Aspirin or non-steroidal anti-inflammatory agents (NSAIDs) use, past peptic ulcer disease , then consider GI bleeding, platelet dysfunction.**
- **- In females the menstrual history quantifying the amount of bloodloss ,or possible pregnancy should be obtained.**
- **- History of pica or abnormal craving for ice, clay, starch...; dysphagia then consider iron deficiency.**
- **- Poor diet, then consider iron or folate deficiency, and general**
- **malnutrition**
- **- History of gastric surgery, distal paresthesias, gait problems - consider B12, Iron deficiency**
- **- History of alcohol abuse - consider folate deficiency or liver disease. If moonshine use or lead paint/pipe exposure, consider lead toxicity.**
-

The History -3

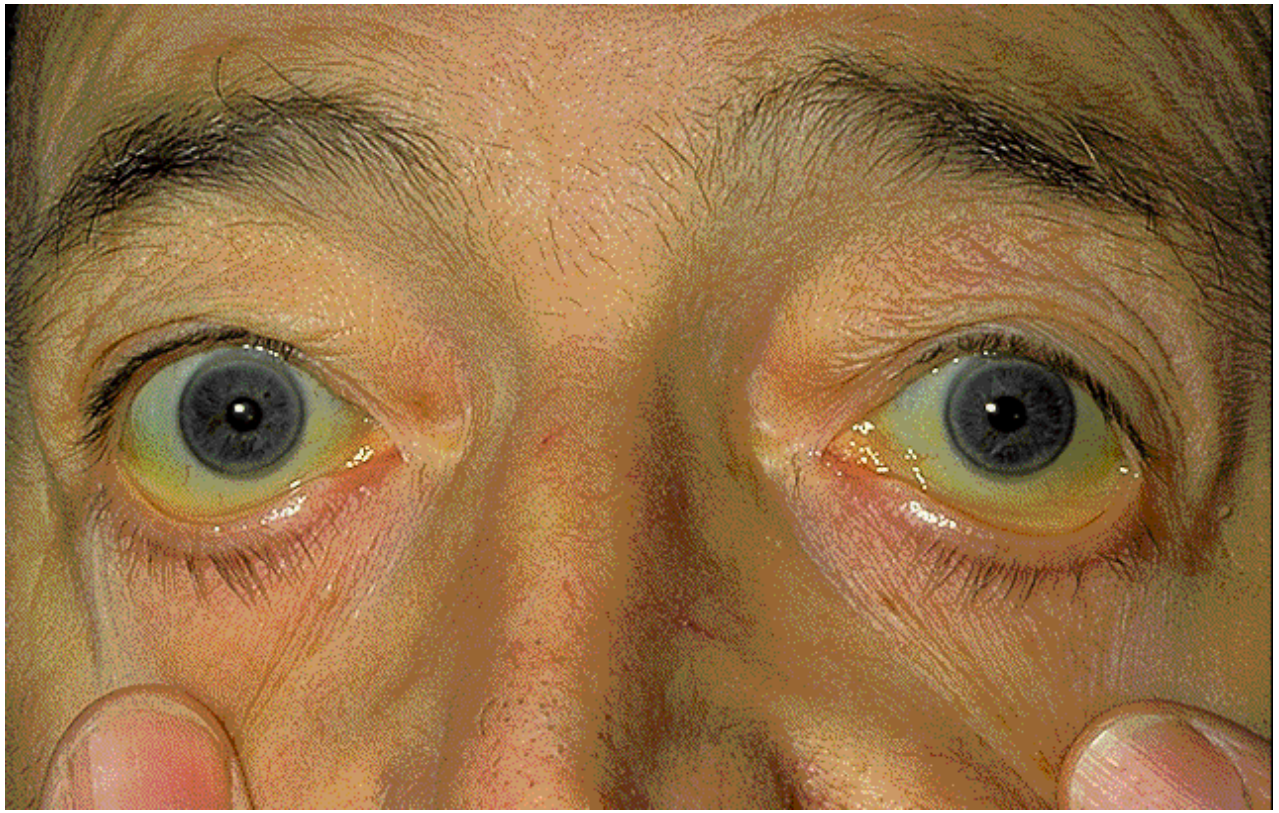
- **- Family history of blood cell or bleeding disorder: consider Sickle Cell disease, G6PD,Thalassemia, Hemophilia, von Willebrand**
- **- History of jaundice, transfusion, new medication, infection - consider hemolytic process**
- **- History of weight loss, Cancer, HIV, rheumatoid arthritis, thyroid disease, renal disease -then consider secondary cause**
- **- History of fever and chills, cough, dyspnea, then consider Infection.**

Physical Exam

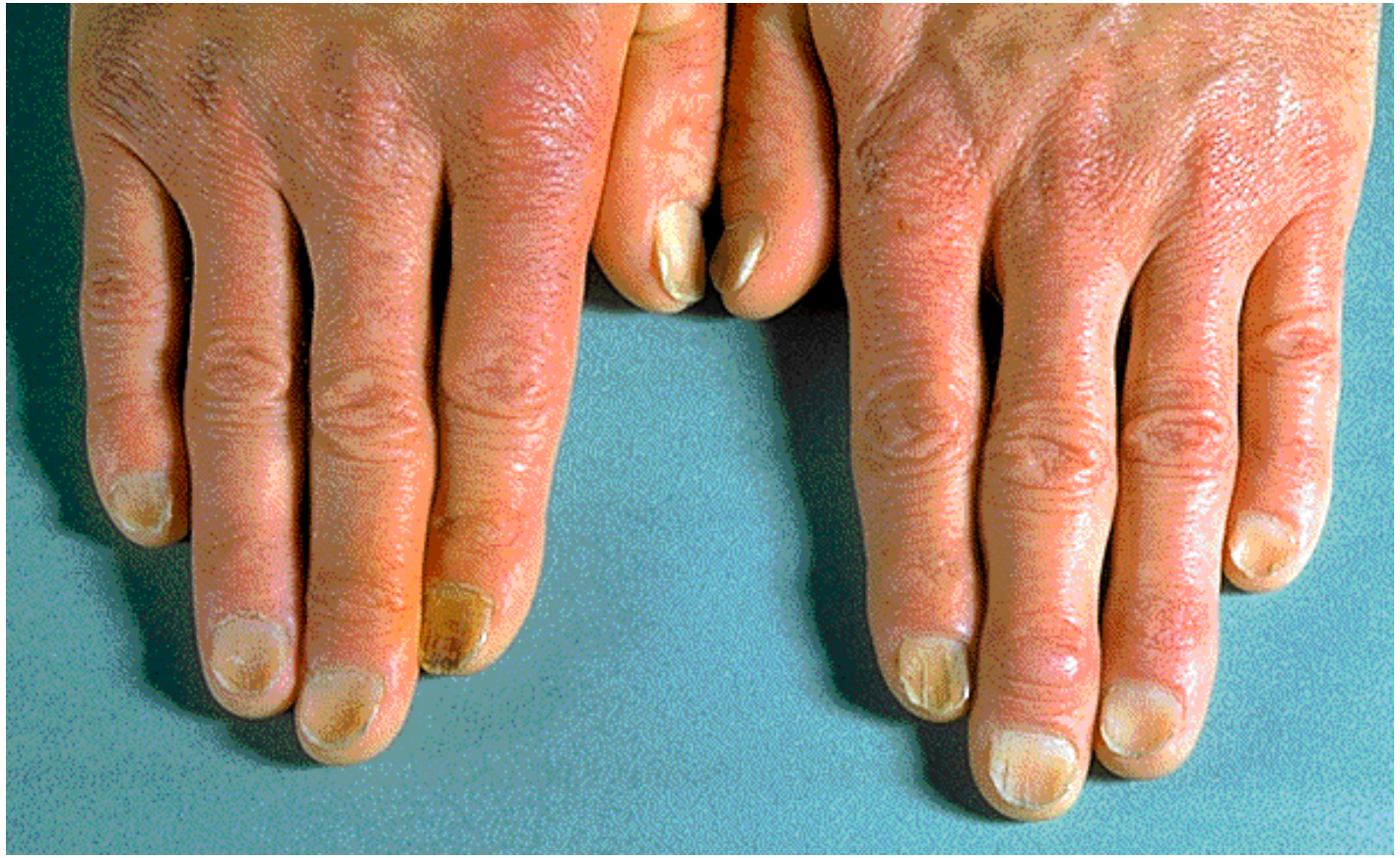


Look at the everted part of the lower eyelid

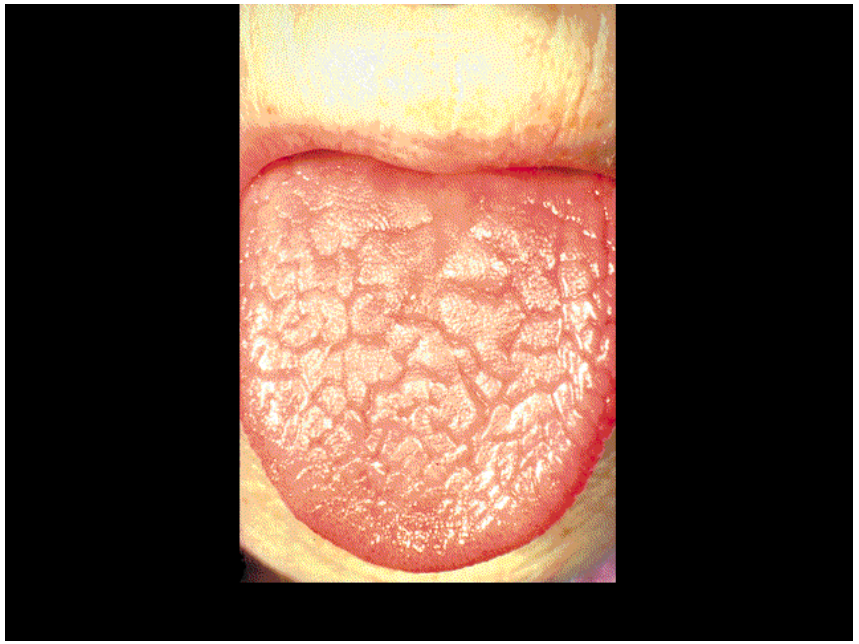
Sclera

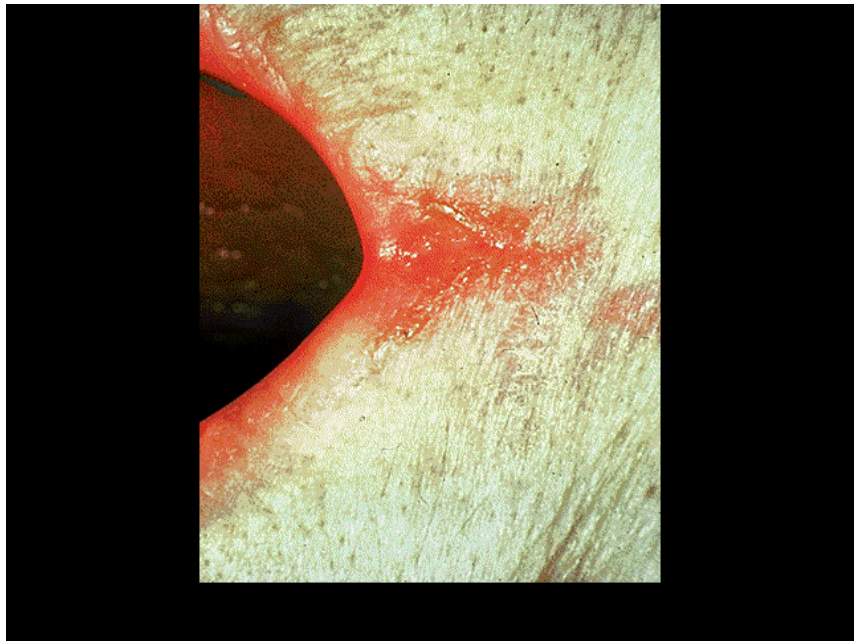


Spoon Nails – Fe Def.



Glossitis and Chelosis –
Fe and B12





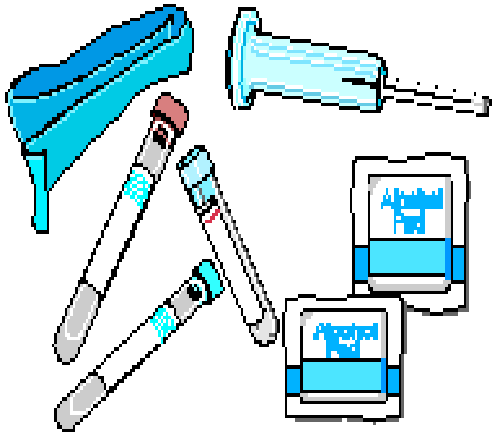
Physical Exam

- GENERAL INSPECTION- clubbing in TB or lung cancer
- Skin- Hypothyroid, SLE, Bruises, lesions, petechiae or purpura.
- Weight - Loss in Cancer, HIV, Chronic disease, gain in hypothyroid

- VITAL SIGNS- Pulse: Tachycardia from increased cardiac output
- Respirations: Tachypnea from decreased oxygen transport
- BP: Orthostatic if volume depleted
- Temp: Fever in infections and drug or transfusion reactions,
- HEENT- Eye: Jaundice if hemolysis, pallor in palpebral conjunctiva
- Mouth: Glossitis and angular stomatitis in iron or B12 deficiency
- NECK- Thyroid enlargement or nodules, lymph nodes
- HEART- Increased output/murmur- consider high output failure
- LUNG- consider infection, lesion
- ABDOMINAL- Liver/spleen size, masses, tenderness, surgical scars
- RECTAL- Stool guaiac, prostate exam in men
- PELVIC/BREAST- Uterine abnormality, Pap smear, Breast nodule
- LYMPHNODES- consider lymphoma, leukemia, infection, connective tissue disease
- NEUROLOGIC- Decreased vibratory and position sense in B12 deficiency

LAB- INITIAL SCREENING TESTS

- CBC, red cell morphology and white blood cell differential, Reticulocyte count
- Urinalysis- Hematuria/proteinuria in renal disease,hemoglobinuria in hemolysis.
- Chemistry profile (LDH, Bilirubin- Direct and Indirect, BUN, Creatinine, AST, ALT),
- Hemoglobin Electrophoresis if hereditary hemoglobinopathy is suspected
- C-Reactive Protein for inflammation
- IF BLEEDING - Platelet Count, PT, aPTT, PFA

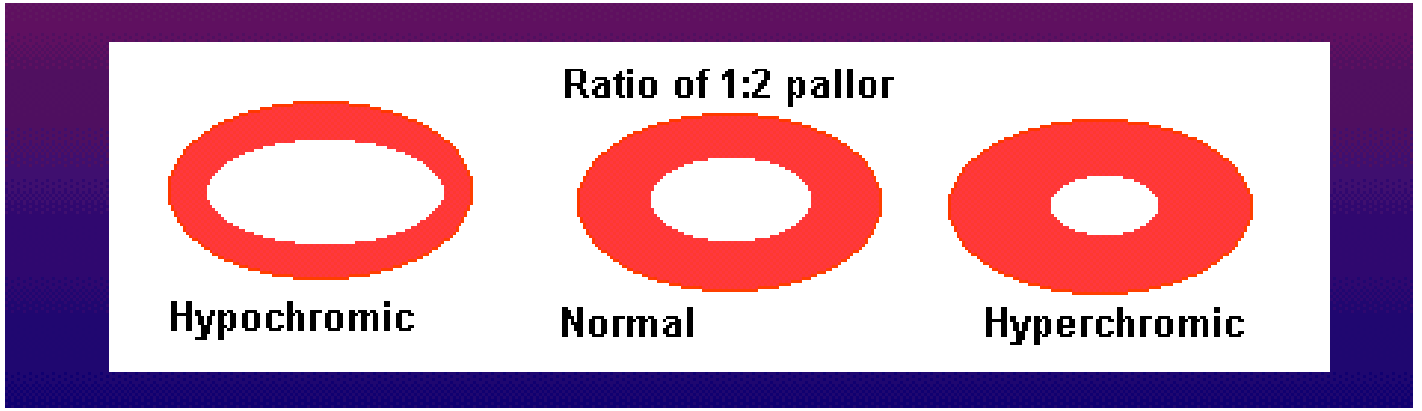


CBC- Red Cell Measures

PARAMETER	NORMAL ADULT	COMMENTS
HB - Hemoglobin	Male= 15.5 +/- 2 mg/dl	Low = Anemia
	Female = 13.5 +/- 2	High = polycythemia
HCT - Hematocrit	Male= 46.0 +/- 6%	
	Female= 41.0 +/- 6%	
RBC - Red Blood	Male = 4.3 - 5.9 Million/uL	
	Female = 4.0 - 5.2	

Red Cell Indices MCH, MCHC

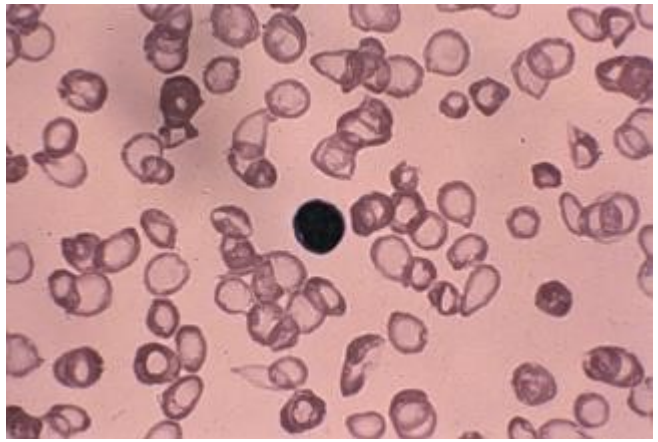
MCH - Mean Corpuscular Hemoglobin	27 -32 pg	Low = Hypochromic High = Hyperchromic
MCHC - Mean Corpuscular Hemoglobin Concentration	30 - 36 gm/dl	Low = R/O Fe def. High = Spherocytosis

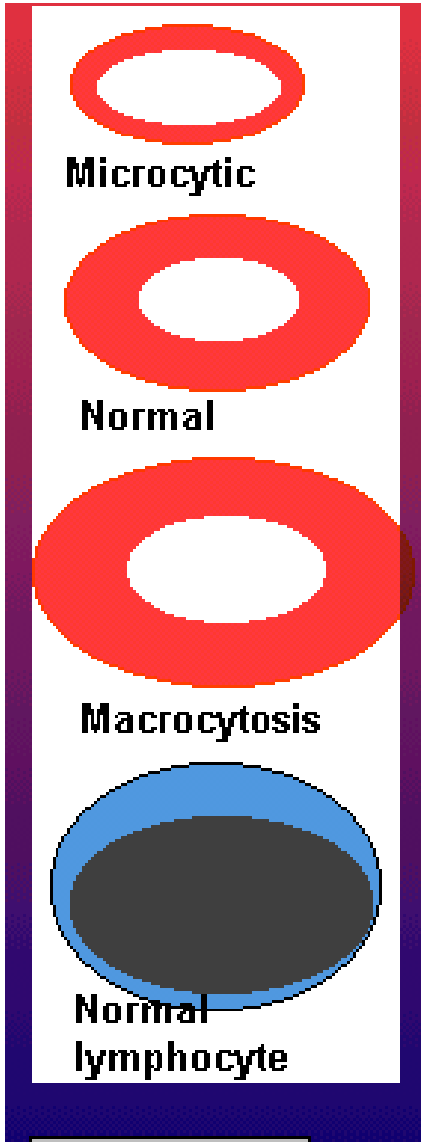


Red Cell Indices MCV - RDW

MCV - Mean Corpuscular Volume 80 - 94 fl
Low = Microcytosis High = Macrocytosis

RDW - Red Cell Distribution Width 11.5 - 14.5
Variation in RBC size (High in Iron deficiency)



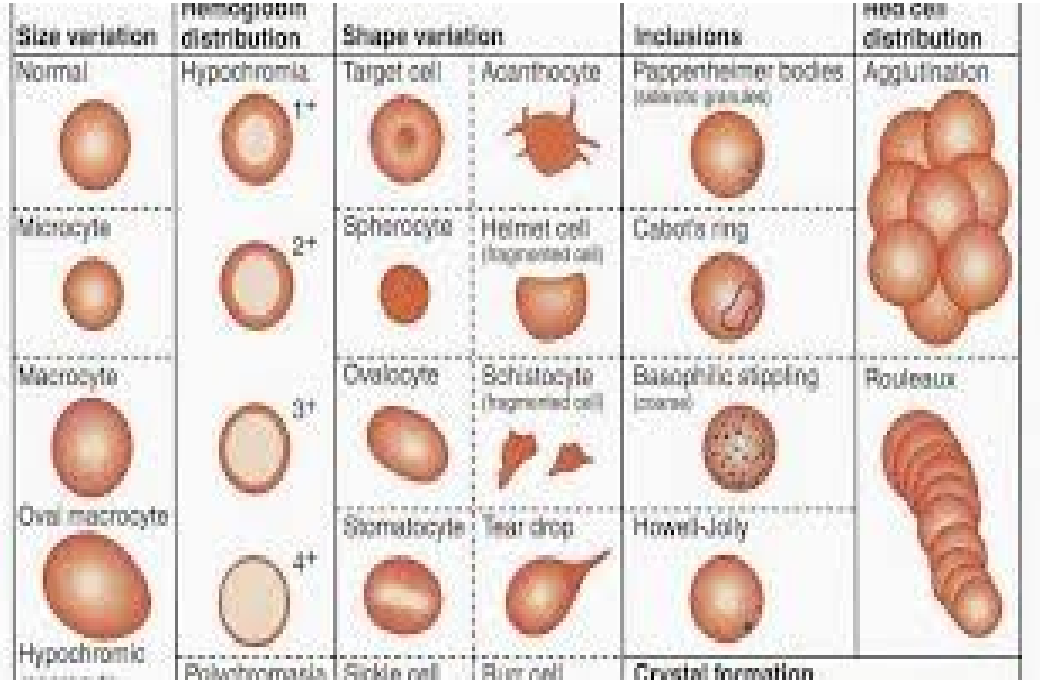


RBC Morphology

- **Red Cell Morphology** **SIGNIFICANCE**
- Burr Cells Uremia, Low K, artifact, Ca stomach, PUD
- Spur Cell Post-splenectomy, Alcoholic liver disease
- Stomatocyte Hereditary, Alcoholic liver disease,
- Spherocyte Hereditary, Immune hemolytic anemia,
- water dilution, post-transfusion
- Schistocyte –helmet cells-TTP, DIC, vasculitis, glomerulonephritis,
- heart valve, burns
- Elliptocyte – Ovalocyte -Hereditary, Thalassemia, Fe Def.,
- Myelophthistic, megaloblastic anemias
- Rouleaux formation -Multiple Myeloma
- Target Cells Thalassemias, hemoglobinopathies
- Microcytes Thalassemia, Iron Def., Lead Toxic,
- Macrocytes B12 of Folate Def.

Parasites Malaria, Babesiosis

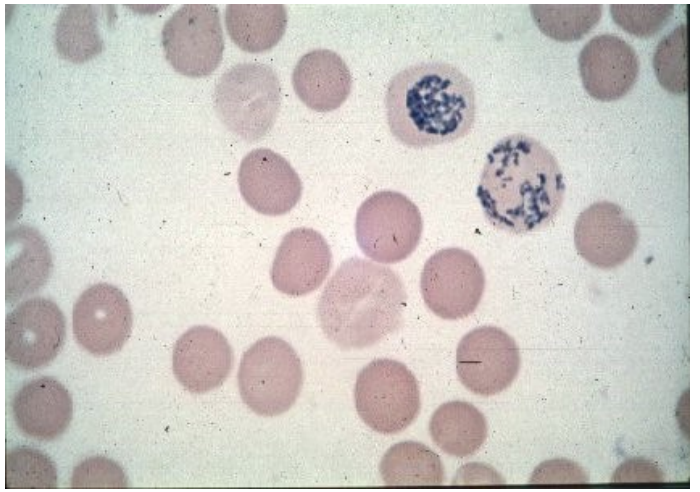
Basophilic Stippling – Lead Toxicity



Retics or Reticulocyte count

- Not a part of the CBC – must order separately
- Retic - Reticulocyte Count 0.5 -1.5 %
- Must be corrected for the patient's anemia = Reticulocyte index
- < 2 Low in anemia = low marrow output

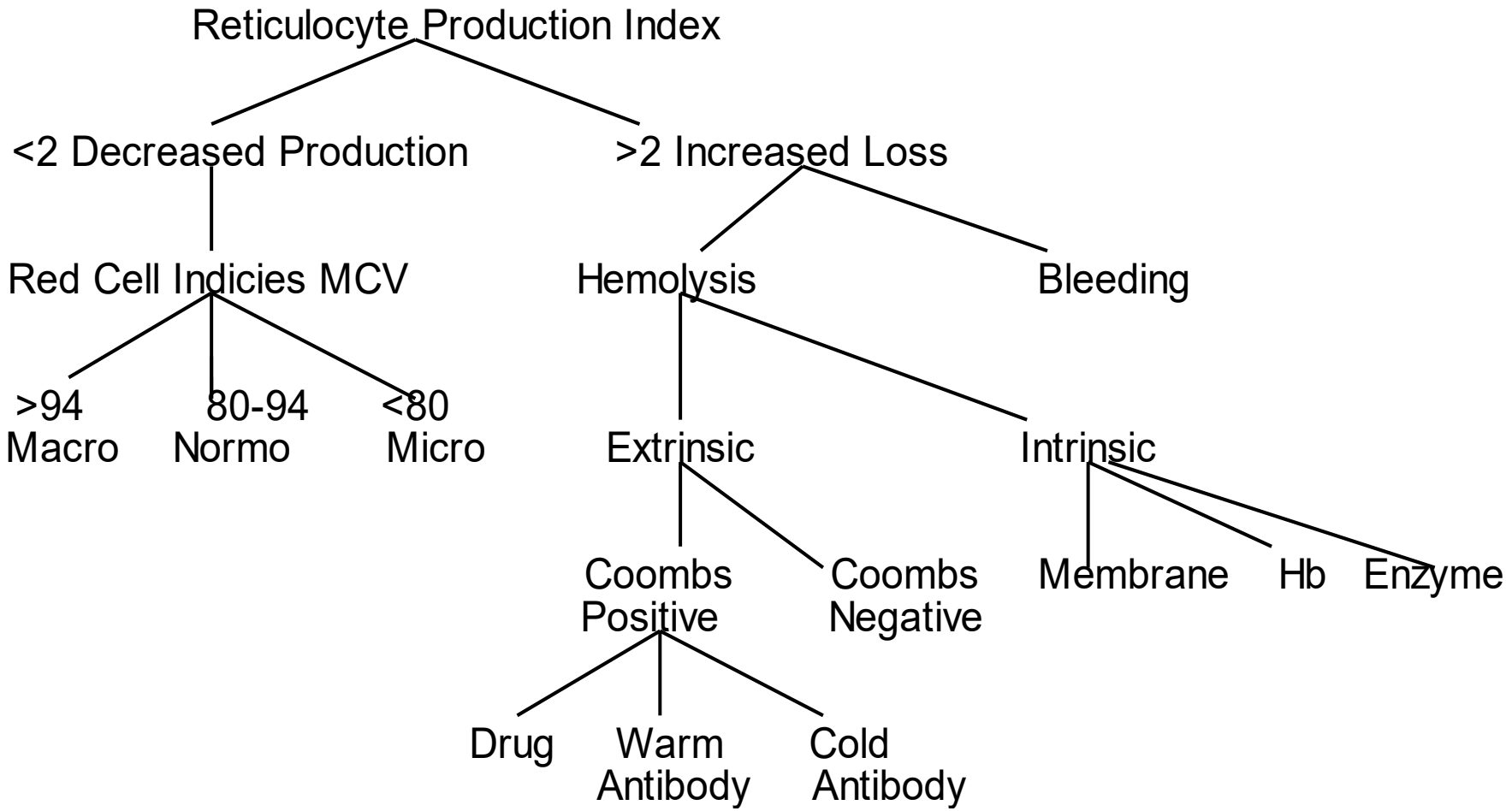
  > 2 High = RBC loss by bleeding or hemolysis



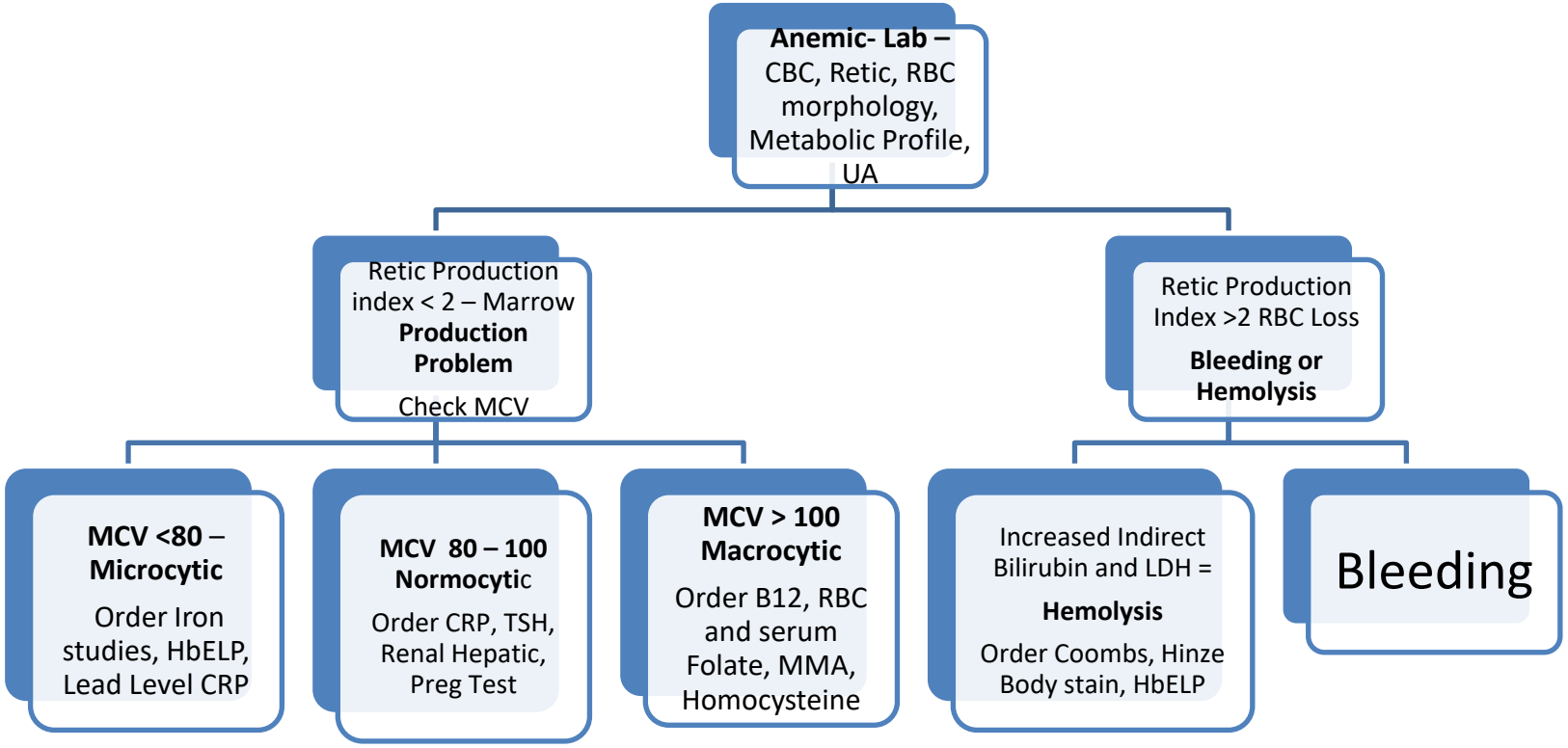
CBC and Retic Patterns

Hb	RBCs	WBCs	Platelets	Retics	MCV	Diagnosis to consider
low	low	high	low	low	normal	Leukemia
normal	normal	high	normal	normal	normal	Infection
low	low	high	normal	high	normal	Anemia -Malaria, infection
low	low	normal	normal	low	low	Anemia - TICS
low	low	normal	high	low	low	Anemia -Iron Def
low	high	normal	normal	high	low	Anemia-Thalassemia
high	high	high	high	normal	normal	Polycythemia Vera
high	high	normal	normal	high-normal	normal	Secondary polycythemia
low	low	low	low	low	normal	Pancytopenia - MDS

Diagnostic Pathway



Anemia – low Hb/Hct Lab work-up
BPH = Bleeding/Production/Hemolysis

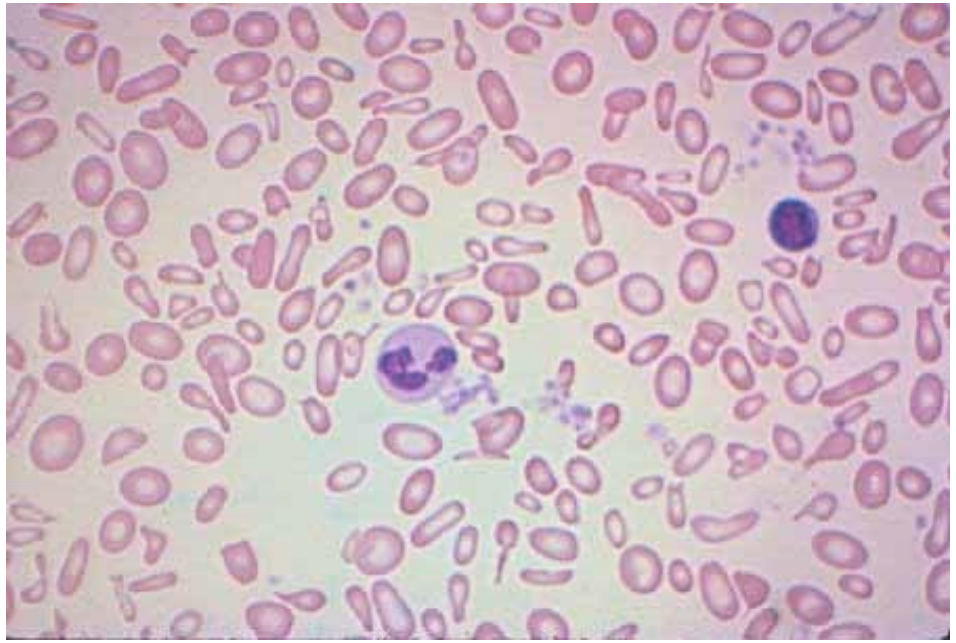


HbELP – Hemoglobin Electrophoresis, CRP – C-Reactive protein, MMA – Methymalonic acid level

Microcytic

- MICROCYTIC = "TICS"

- T-Thalassemias
- I-Iron Deficiency
- C-Chronic Inflammation
- S-Sideroblastic - lead, drug, or hereditary

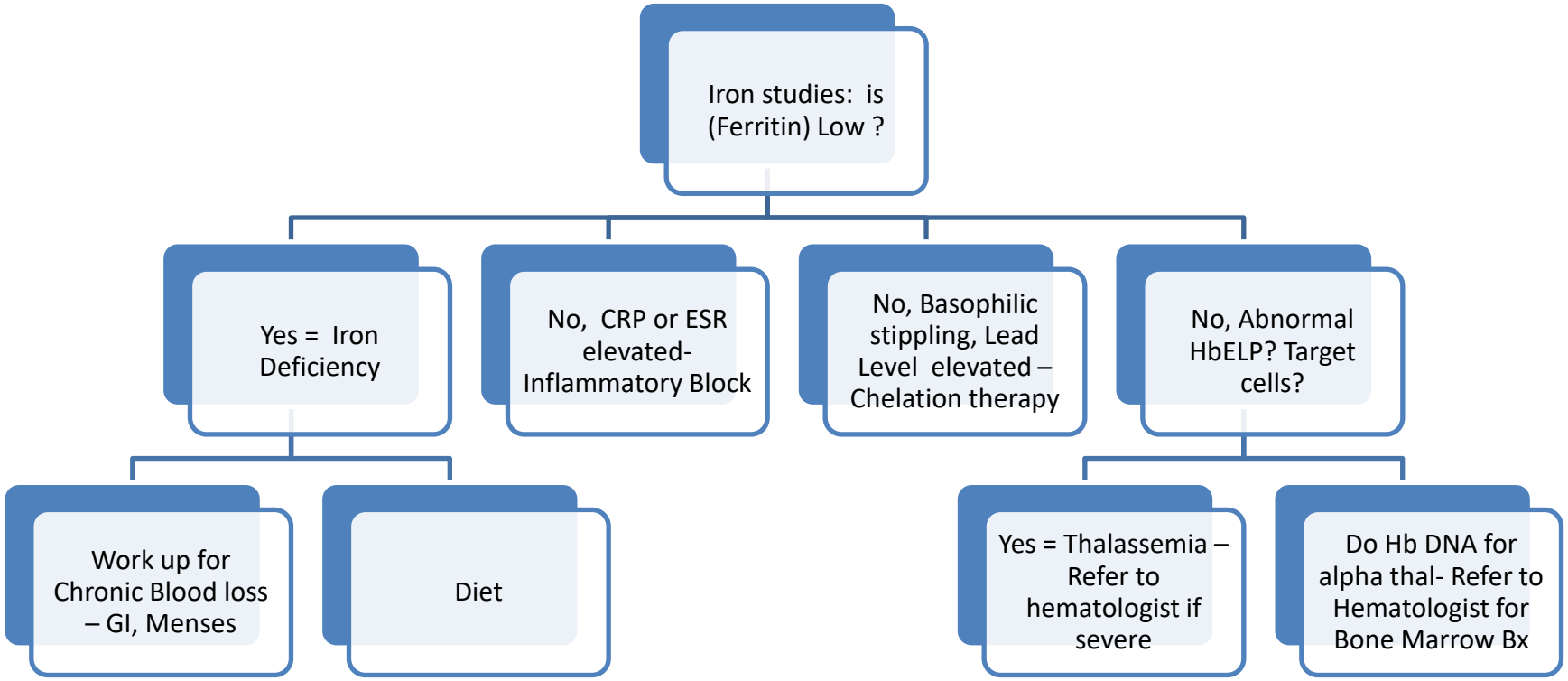


Microcytic Tests

- **TESTS TO ORDER:**
- **Iron studies with Serum Iron**
- **TIBC = Total Iron Binding Capacity =** Transferrin binding sites for transporting iron
- **% Saturation = Transferrin saturation with Iron**
- **Ferritin = Storage Iron-** Ferritin is also an acute phase reactant and can be elevated in patients with chronic inflammation or infection. In patients with chronic inflammation, iron deficiency anemia is likely when the ferritin level is less than 50 ng per mL
- **HBELP = Hemoglobin Electrophoresis**
- **Lead level if exposed**
- **C-Reactive Protein for inflammation**

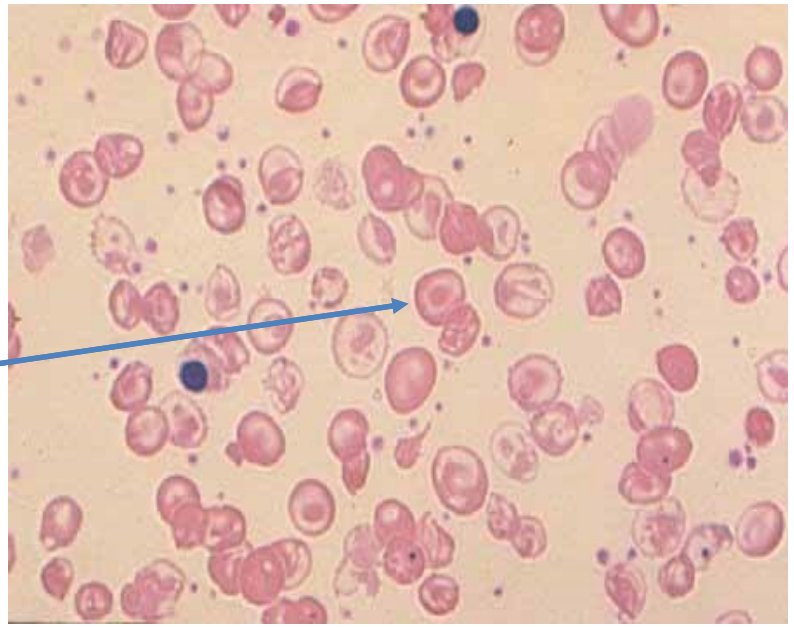
Microcytic workup

TICS – Thalassemia, Iron Deficiency, Chronic inflammation, Sideroblastic (Lead)



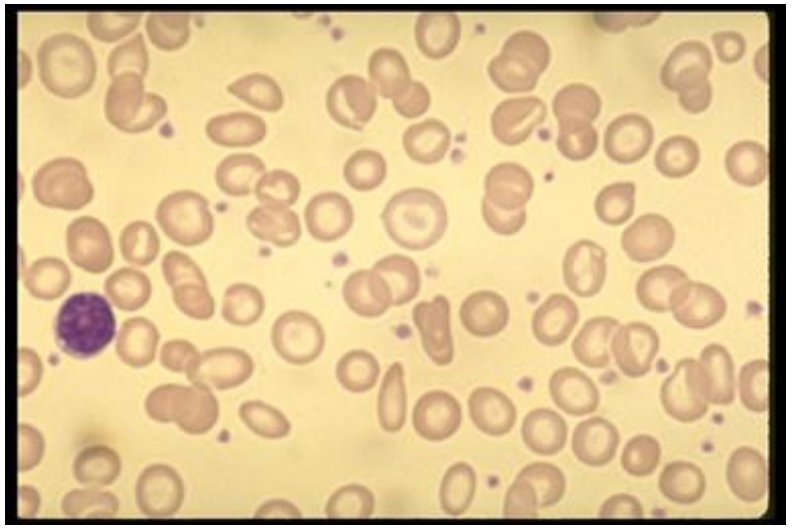
Thalassemia Syndromes.

- Hx - Hereditary – lifelong anemia from decreased Alpha or Beta chain production
- PE – May have jaundice if hemolysis
- Lab – Low Hb/HCT/MCV may have increased Retic and RBC, elevated Indirect Bili/LDH, Target Cells
- Hemoglobin ELP and normal Iron are diagnostic for Beta Thal, DNA studies for Alpha Thal
- Rx - Supportive therapy or BMT, gene therapy



Iron deficiency

- Hx – Pica, muscle cramps, dysphagia with solid foods (from esophageal webbing)
- PE – Spoon nails, cheilosis,
- LAB – Low HB/Hct/RBC/Retic/MCV, elevated platelets and RDW
- Low Serum iron, Low Ferritin, High TIBC
- Find out why –GI bleed, menses, diet, gastric bypass, celiac disease
- Rx - FeSO4 300 mg tid on empty stomach (acid needed to absorb)
- F/U in 2- 3 weeks for Retic and Ferritin levels

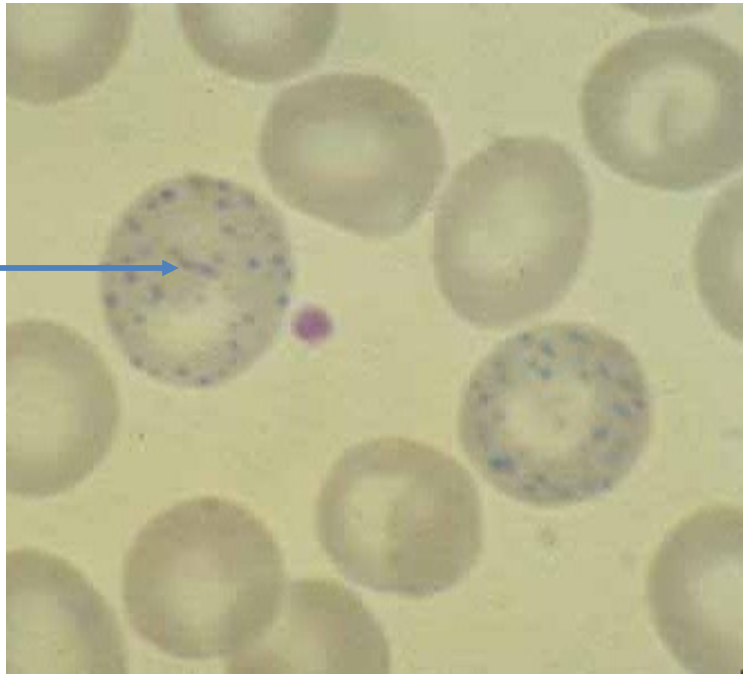


Chronic Inflammation

- Hx – fever , chills, fatigue, weight loss, chronic inflammatory disease, infection, autoimmune
- PE – evidence of inflammation or infection
- Lab – Low Hb/HCT/RBC/Retic, elevated Ferritin/WBC/Platelets, Serum iron and TIBC are low with a low saturation
- MCV - 30% Microcytic, 70% Normocytic
- High C-Reactive Protein = Inflammation
- Rx – reduce inflammation depending on cause

Sideroblastic (= Lead toxicity)

- Hx – Exposure to lead in water, paint, occupational, Abdominal cramps N/V/D, CNS/mood changes, neuropathy, headache, sleep disturbance
- PE – Neuro findings weakness of extensor muscles (eg, foot drop, wrist drop) Lead lines on gingiva
- Lab – Low Hb/HCT/RBC/MCV/Retic, normal Ferritin/WBC/Platelets, Serum iron and TIBC
- Basophilic stippling, Ring sideroblasts in bone marrow
- Serum lead level is diagnostic
- Rx - chelation agents succimer and penicillamine



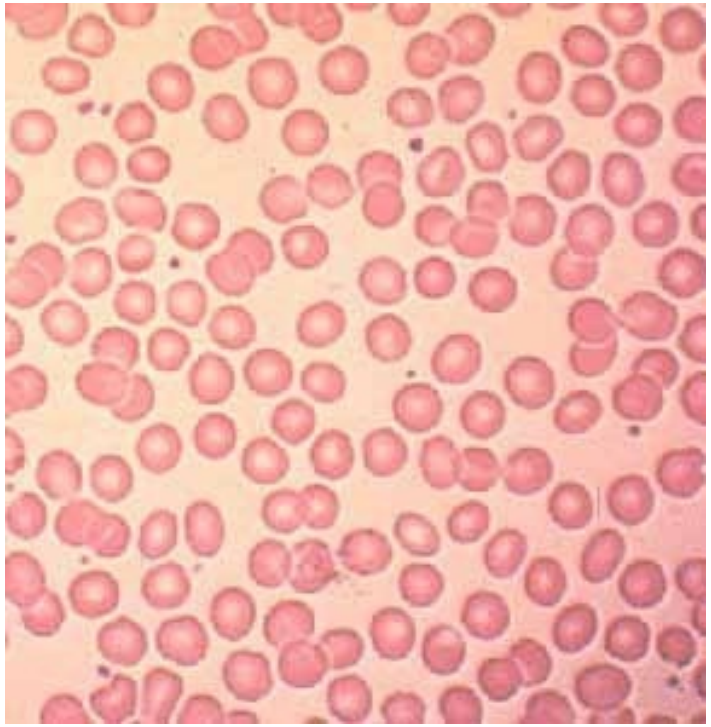
Lab Patterns

	Iron Deficiency	Chronic Inflammation	Sideroblastic Lead	Thalassemia
Red Cells	Microcytic Hypochromic	Normocytic Microcytic	Dimorphic Stippling	Microcytic Target cells
Serum Iron Iron	Decreased	Decreased	Normal or Increased	Normal or Increased
TIBC	Increased	Decreased	Normal	Normal
Saturation	< 16%	10-20%	50-100%	30-100%
Serum Ferritin	Decreased	Increased	Increased	Normal or Increased
HgbELP	Normal	Normal	Normal	Abnormal
Indirect Bilirubin LDH	Normal	Normal	Normal	Elevated
C-Reactive Protein	Normal	Elevated	Normal	Normal

Normocytic Anemia

- **NORMOCYTIC = "NORMAL SIZE“**
- N-Normal Pregnancy
- O-Over hydration
- **R-Renal Disease**
- M-Myelophthistic
- A-Acute Blood Loss
- L-Liver Disease

- S - Systemic Infection
- **I- Inflammatory Block**
- **Z-Zero Production- Aplastic anemia**
- E-Endocrine:Hypothyroid, hypoadrenal, hypoandrogen

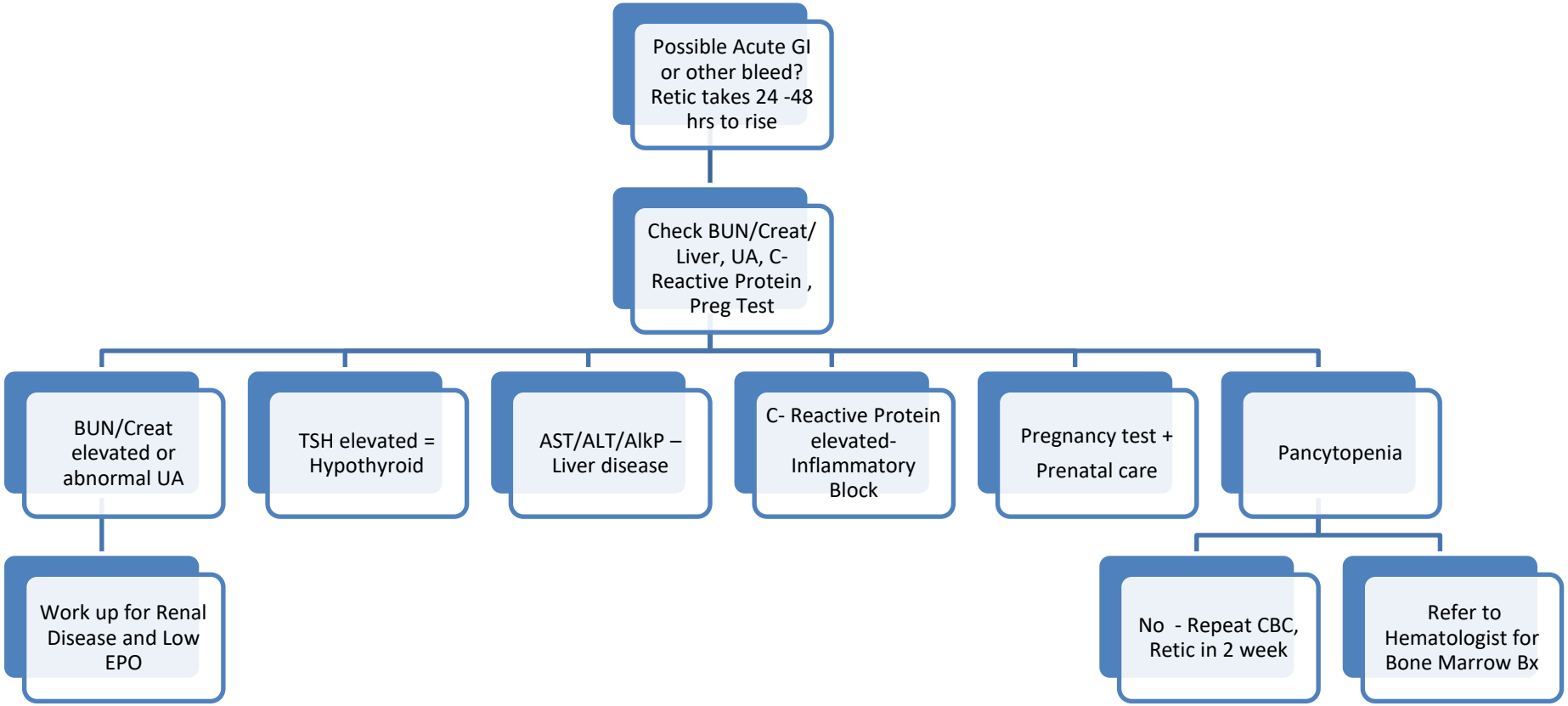


Normocytic Tests

- Blood Urea Nitrogen (BUN), Creatinine, SGOT, Alkaline Phosphatase, Bilirubin, C-Reactive Protein Urinalysis, and Thyroid profile
- Renal Function tests
- Pregnancy Test
- Bone Marrow Biopsy

Normocytic workup

“NORMAL SIZE”

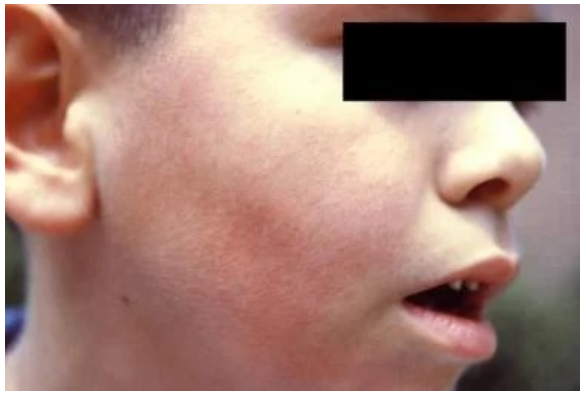


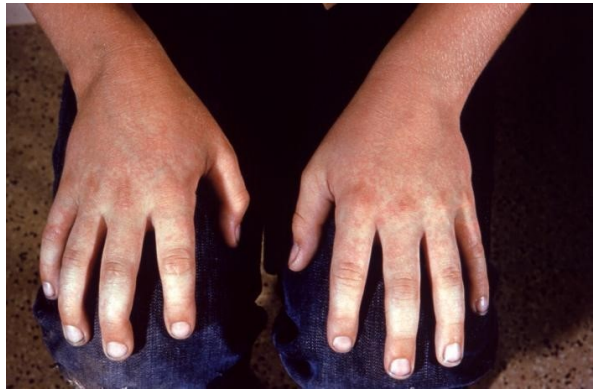
Normocytic - Renal Failure

- Hx – past hypertension, DM, urine changes
- PE – Lindsey's nails, elevated BP
- Lab - Low Hb/HCT/RBC/Retic, Normal WBC/Platelets/MCV, elevated BUN/Creat, low albumin/erythropoietin, proteinuria
- Anemia caused by decrease erythropoietin production causing decreased bone marrow production
- Rx - Erythropoetin-stimulating agents epoetin alfa and darbepoetin alfa

Aplastic Anemia

- Hx – Sx of anemia, bleeding, and infections. Medication review and sx of hepatitis, arthralgias in Parvo B19
- PE – Signs of anemia, low platelets and low WBCs, jaundice in hepatitis, rash on cheeks hands and feet in Parvo B19
- Lab – Low Hb/HCT/RBC/Platelets/WBCs/Retic, Normal MCV, PCR testing for parvovirus B19
- Causes: idiopathic (78% cases) hepatitis (5% cases) drugs (2% cases due to gold, 4% due to other drugs) Parvovirus B19 (Fifths disease)
- Rx –may need Bone Marrow Bx and supportive therapy including transfusion support



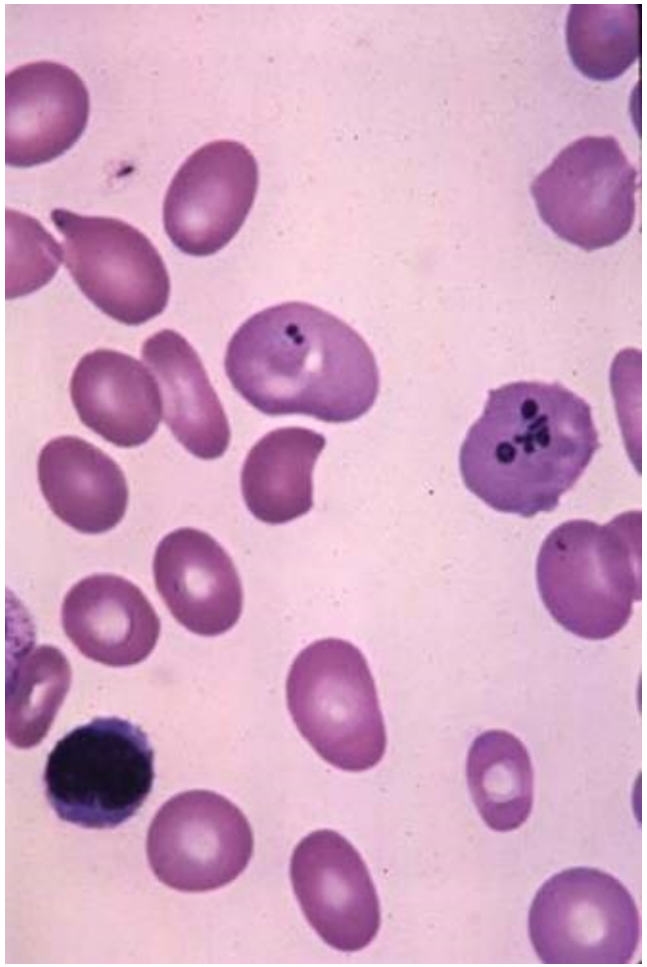


Macrocytic Anemia

- MACROCYTIC = "BIG FAT RED CELLS"

- **B-B12 Malabsorbtion**
- I-Inherited
- G-Gastrointestinal disease or surgery
-
- **F-Folic Acid Deficiency**
- A-Alcoholism
- T-Thiamine responsive
-
- R-Reticulocytes miscounted as large RBCs
- E- Endocrine - hypothyroid
- D-Dietary

- C-Chemotherapeutic Drugs
- E-Erythro Leukemia
- L- Liver Disease
- L- Lesch-Nyhan Syndrome
- S-Splenectomy

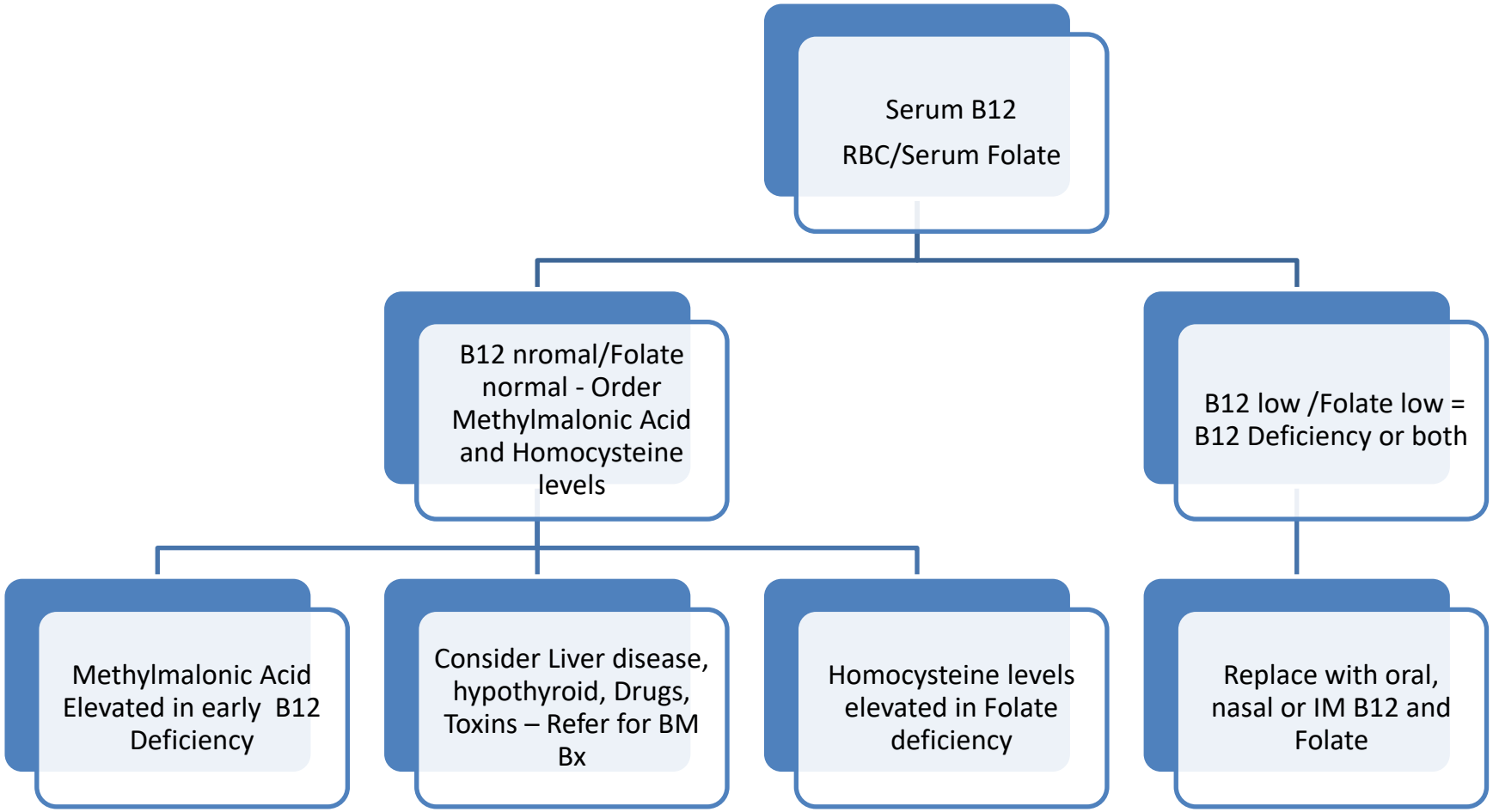


Macrocytic Tests

- The peripheral blood changes include:
- -Anemia with decreased reticulocyte count, -Increased MCV
- -Neutropenia with hypersegmented neutrophils
- -Thrombocytopenia with large platelets.

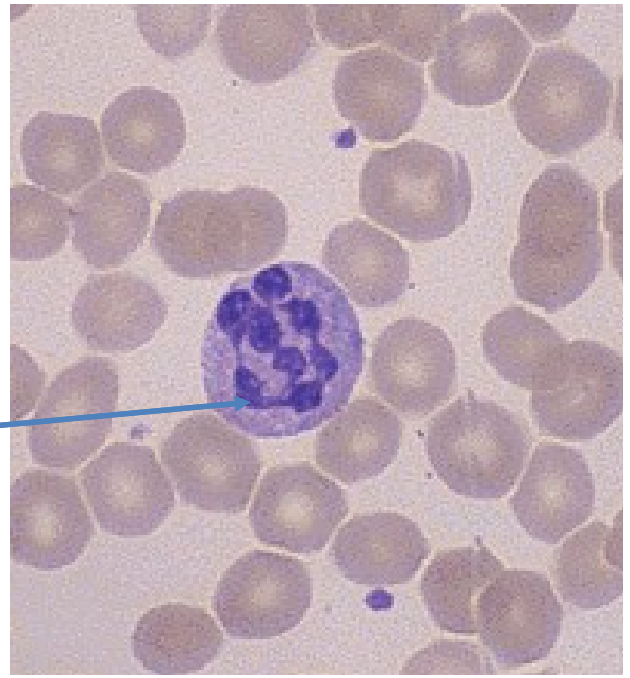
- LABS to order:
- B12, Serum Folate, RBC Folate
- Methylmalonic acid and homocysteine levels
- if all normal, consider TSH, and a Bone Marrow Bx.

Macrocytic Work-up



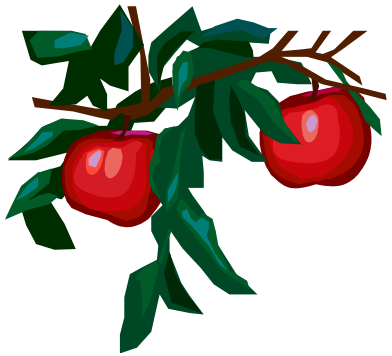
B12 Cobalamin Deficiency

- Hx – Stocking glove paresthesias, CNS changes, dementia, gait problems, anorexia and weight loss, sore tongue, metformin, gastric bypass, or PPI may block absorption
- PE - edema, pallor, jaundice, smooth tongue, decreased vibratory and position sensation, Romberg sign, hyperreflexia
- Lab – Low Hct/Hb/RBC/Platelets/Retics, elevated MCV, Large platelets/MPV, Hyper segmented polys
- May have hemolysis with elevated I Bili and LDH
- Low serum B12 level is diagnostic
- Methylmalonic acid (Specific to B12) and homocysteine levels elevate early
- Pernicious anemia - anti- intrinsic factor antibodies -Schilling's test
- Rx - cobalamin 1000 mg I.M. monthly, or oral 1000 mcg daily



Folate Deficiency

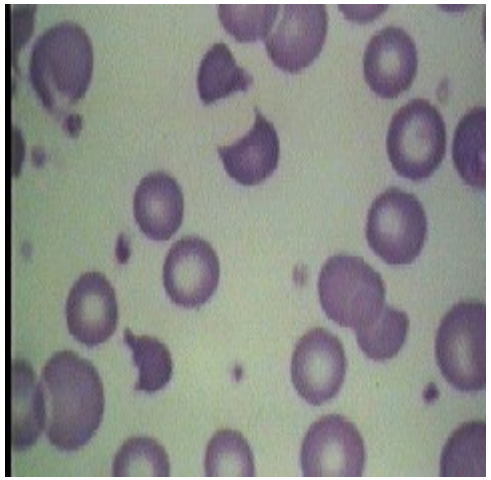
- Hx – Stocking glove paresthesias, cognitive impairment, dementia, and depression sore tongue, abdominal pain N/V/D, alcohol liver disease, diet vitamin B12 deficiency, and drugs such as methotrexate, and Dilantin
- PE - darkening of the skin and mucous membranes, particularly at the dorsal surfaces of the fingers, toes, and creases of palms and soles
- Lab – Low Hct/Hb/RBC/Retics, elevated MCV, low serum and RBC Folate - always check B12 elevated homocysteine not Methylmalonic acid
- Rx – Folate 1mg by mouth qD



Hemolytic Anemia

- HEMOLYTIC = "HEMATOLOGIST"

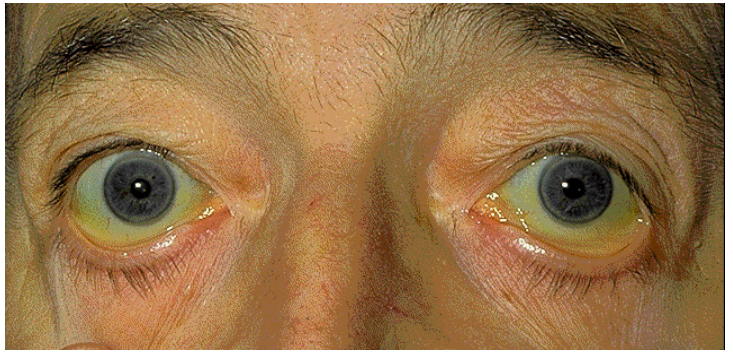
- **H-Hemoglobinopathy: sickle cell disease**
- - Hemoglobinuria: Paroxysmal Nocturnal Hemoglobinuria
- E-Enzyme Deficiency
- M-Medication - drug induced: aldomet, INH
- A-Antibodies - Immune attack
- T-Trauma to the red cells: D.I.C , artificial heart valves
- O-Ovalocytosis
- L-Liver disease
- O-Osmotic fragility in Hereditary spherocytosis
- and in Hereditary Eliptocytosis
- **G-G6PD Glucose-6-Phosphate Dehydrogenase Deficiency**
- I-Infection: malaria, babesiosis
- S-Splenic destruction in hypersplenism
- **T-Transfusion**
- - Thalassemias



Hemolysis (HIT)

- **Hereditary** (HEM)
  - Hemoglobin (sickle cell, thalassemia)
  - Enzyme (G6PD deficiency)
  - Membrane (Spherocytosis, Eliptocytosis)
- **Immune attack** – Coombs positive (transfusion, IgM – cold antibody-infections, IgG warm antibody – Drug induced, Paroxysmal Nocturnal Hemoglobinuria – complement induced)
- **Trauma**– Microangiopathic (TTP, ITP, HUS, DIC, HIT, HELLP- Eclampsia, Malaria, Splenomegaly)

Hemolytic Signs



1. Elevated reticulocyte count, with stable or falling hemoglobin.
2. Elevated indirect bilirubin -
3. Eevated serum lactate dehydrogenase (LDH)-
4. Decreased haptoglobin levels - haptoglobin binds hemoglobin released in the plasma from red cell breakdown.
5. Hemoglobinemia and hemoglobinuria (no RBCs)
6. Erythroid hyperplasia in bone marrow
7 Abnormal Hemoglobin Electrophoresis

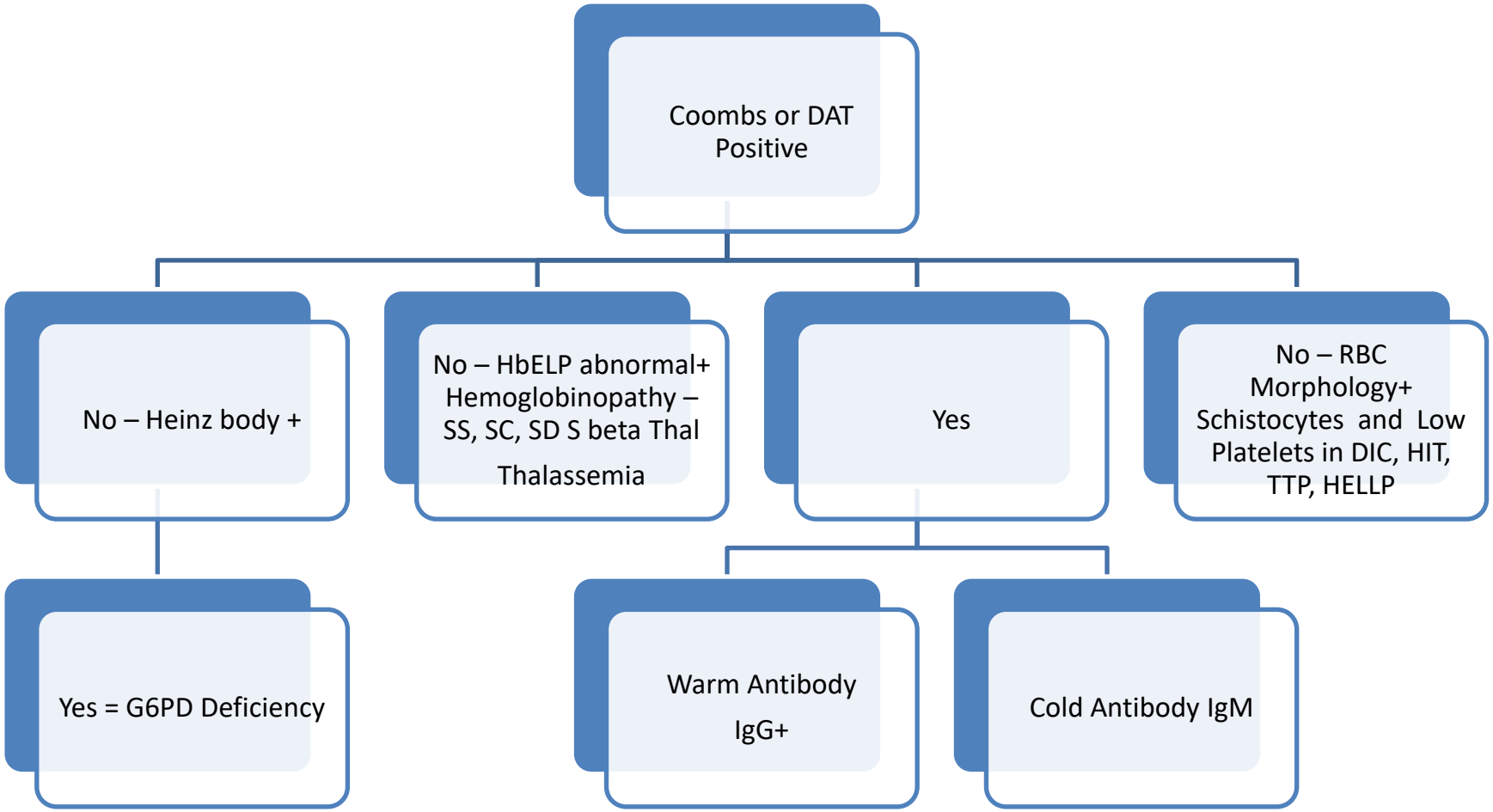
Hemolytic Tests

1. The direct antiglobulin (Coombs') test Direct Coombs test looks for antibody on the red cells. The Indirect Coombs looks for antibody in the serum.
2. Hemoglobin electrophoresis – Thalassemia, Sickle cell disease
3. Heinz body stain – G6PD deficiency
4. Osmotic fragility – RBC membrane
5. Blood smear – RBC morphology
6. Platelet count in the CBC - thrombocytopenia

Special - anti-CD59 and flow cytometry for Paroxysmal nocturnal hemoglobinuria

Hemolysis

Retic Production Index > 2, high LDH High indirect Bilirubin



Hemoglobinopathy

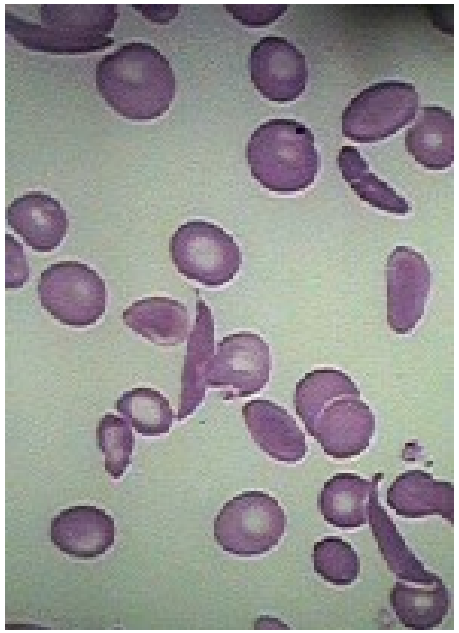
Sickle Cell Disease –autosomal recessive disorder: SS, SC, SD, SE, SO arab, S beta Thalassemia

Hx: Detected at newborn screening, recurrent pain events or complications

PE: Short stature, puberty delay, jaundice/pallor from chronic hemolysis

Lab: Low Hb/Hct/RBC, elevated Retic/WBC/platelets from increased marrow production elevated LDH/ I-Bili from chronic hemolysis. Low MCV in S Beta Thal

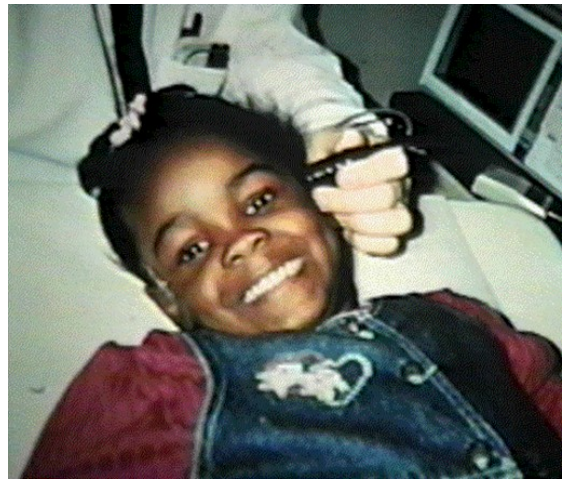
X-ray – Bone marrow hyperplasia from chronic hemolysis



Sickle Cell Disease Complications

- Sickle cells become trapped and destroyed in the spleen causing Splenic Sequestration (liver also)
- Anemia – chronic hemolysis or aplastic marrow
- Pain episodes acute and chronic
- Gall Stones bilirubin stones as child
- Strokes (children) or aneurysms (adults)
- Kidney failure
- Pneumonia or Chest Syndrome
- Increased Infections
- Bone infarctions – AVN of Hips and shoulder
- Retinopathy
- Priapism
- Iron Overload if transfused over 20 units

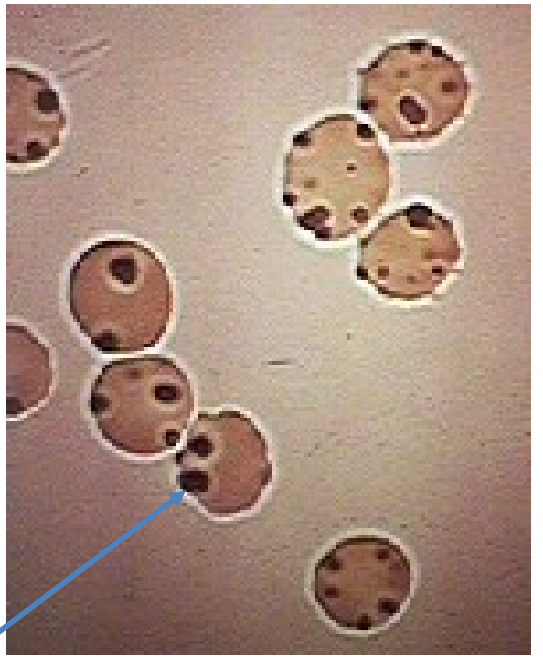
Sickle Cell Treatment

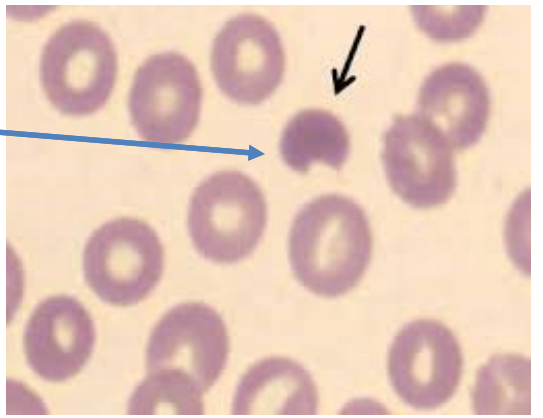


- Have patient referred to sickle cell center
- Daily low dose Penicillin –birth -6yo
- TCD screen to prevent strokes with chronic monthly transfusion
- Hydroxyurea (Hydrea) prolongs life, prevents pain and complications by half also adding oral Glutamine (Endari) as an antioxidant can help reduce episodes
- Prevent: infections, dehydration, temperature change
- New November 2019 - Crizanlizumab, a P-selectin inhibitor, Blocks red cell/platelet/endothelium adhesion, IV infusion monthly.
- Voxelotor is a daily oral hemoglobin S (HbS) polymerization inhibitor increasing the affinity of Hb for oxygen, Can be used with Hydrea.
- Curative – BMT, gene therapy
- Pain management – R/O other causes and then Hydration D5W, Oxygen if hypoxic, treat cause, good pain management

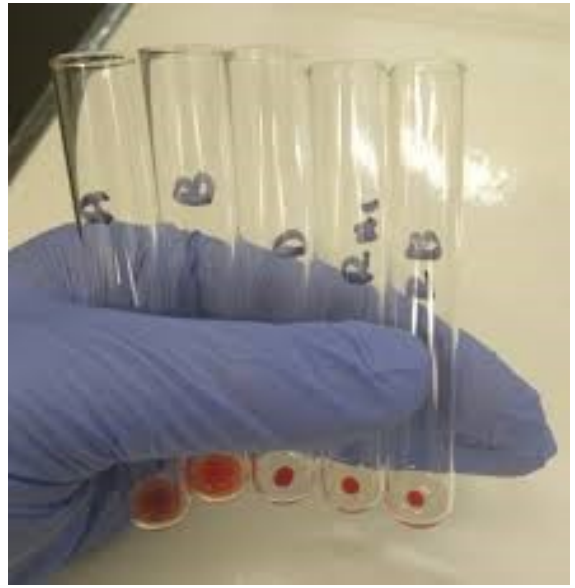
G6PD - Glucose - 6 - Phosphate Dehydrogenase Deficiency

- Hx: X linked genetic, family history of hemolysis with eating fava beans, sulfa or oxidant drugs
- PE: jaundice (hemolysis)
- Lab: Low Hb/Hct/RBC, elevated Retics/LDH/ I-Bili from hemolysis. Heinz body stain shows denatured Hb. Bite cells on regular RBC smear
- Rx: Avoid medications such as antimalarials, aspirin, sulfa drugs, and avoid eating fava beans.



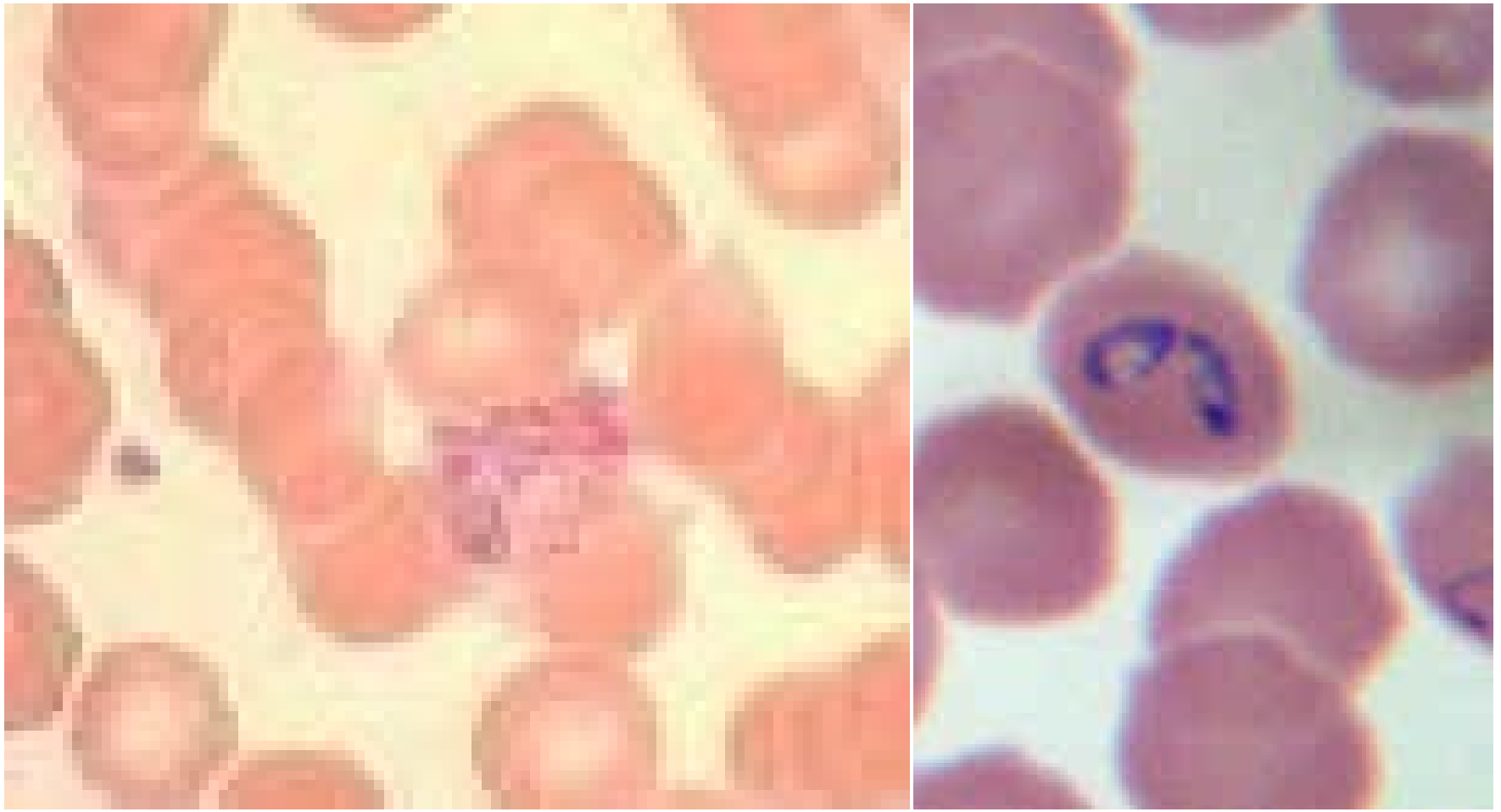


Immune Attack

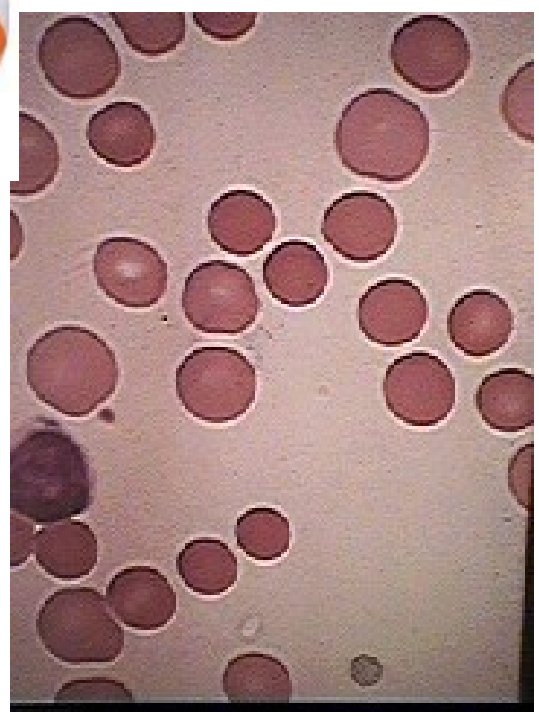


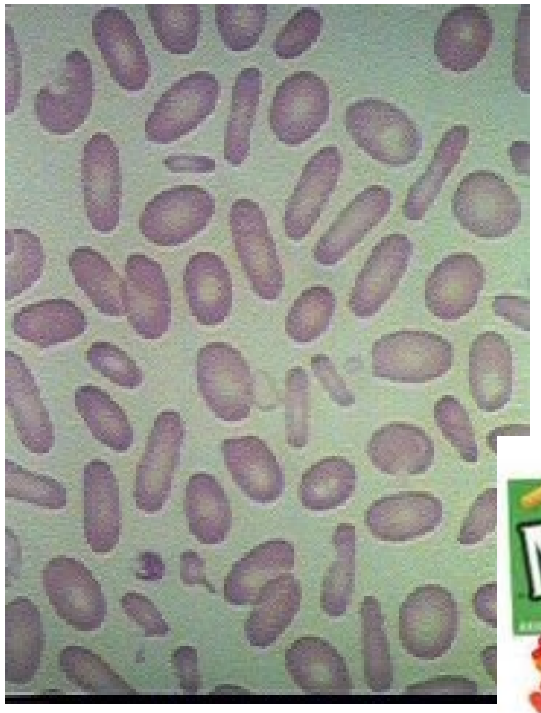
- Coombs Test: IgG and Compliment C3 +/-
- Direct – antibody on RBC. Indirect- antibody in plasma
- Transfusion reaction: immediate or delayed
- **IgM** – (IgG Neg Comp +) cold antibody-infections like, EBV (Mono), HIV, *Mycoplasma pneumoniae*, influenza B, Cytomegalovirus (CMV), rubella virus, varicella-zoster virus (VZV), parvovirus B19, and *Chlamydia psittaci*
- **IgG** warm antibody – Drug induced – Antibiotics, Ibuprofen, Autoimmune diseases
- **PNH** Paroxysmal Nocturnal Hemoglobinuria – Red cells attacked by complement. Lack of CD55 or CD59 on RBC surface

Parasites – Malaria - Babesiosis



Membrane problems Spherocytosis and Ovalocytosis





Anemia take home points

- A reticulocyte count is the best test to differentiate acute red cell loss from bone marrow production failure.
- Microcytic anemias - remember the causes as “TICS” Thalassemias, Iron deficiency, Chronic inflammation, and Sideroblastic (which is commonly lead toxicity).
- Vitamin B12 and Folate deficiency are the most common cause of macrocytic anemias.
- Vitamin 12 deficiency can cause loss of vibratory and position sense, hypersegmented PMNs, paresthesias, elevated methylmalonic acid levels, and dementia.
- Ferritin is the best peripheral indicator of stored body iron levels. If it is low, the cause must be determined: Diet, Menses, and GI bleeding are the most common causes worldwide.
- Anemia with high reticulocyte count, indirect bilirubin, and Lactate dehydrogenase (LDH) is most likely hemolysis.
- Hemolysis should be investigated with a Coombs test (autoimmune RBC attack) Heinze Body stain (G6PD Def.), Blood smear (Malaria, babesia, schistocytes, eliptocytes) Hb ELP (sickle cell and thalassemia.
- Sickle cell disease comprises a multitude of hemoglobin mutations, including types SS, SC, SD, SE, SOarab, S beta Thalassemia each with a different prognosis.
- Daily Hydroxyurea therapy reduces sickle cell pain events, blood transfusions, and hospitalizations by half. It prolongs life, and it is underused clinically.

References

- Labs: https://arupconsult.com/
- Anemias AAFP https://www.aafp.org/afp/topicModules/viewTopicModule.htm?topicModuleId=2
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Medscape links

- **Anemias**
  Aplastic anemia
  Vitamin B12 deficiency
  Folate deficiency
  Iron deficiency
  G6PD deficiency
  Hemolytic anemia
  Sickle cell anemia
  Thalassemia
- Leukopenia,
- Hemochromatosis,
- Transfusion reactions,
  Myelodysplasia, Polycythemia,