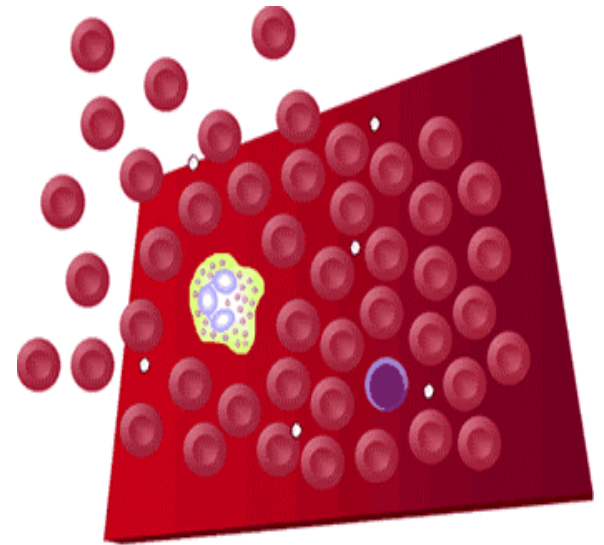
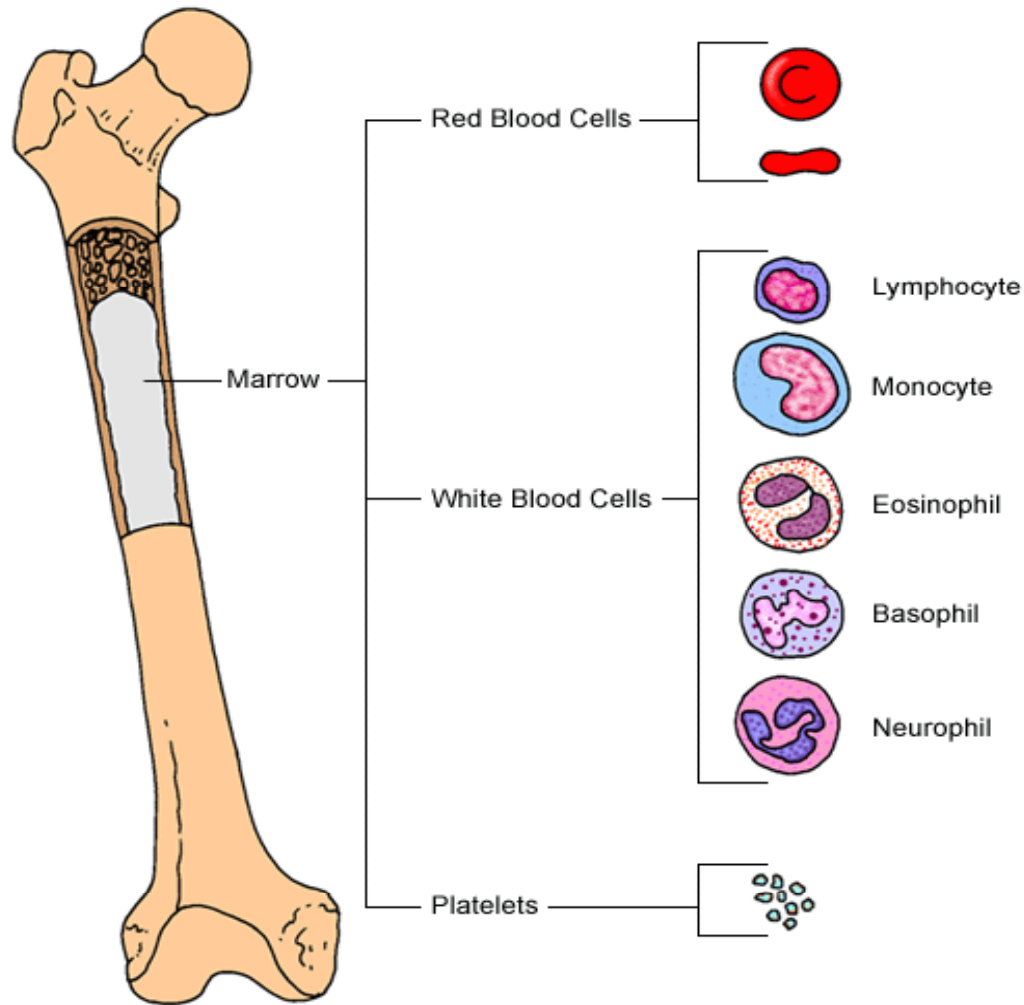

Hematology *review*

Mihaela Mates

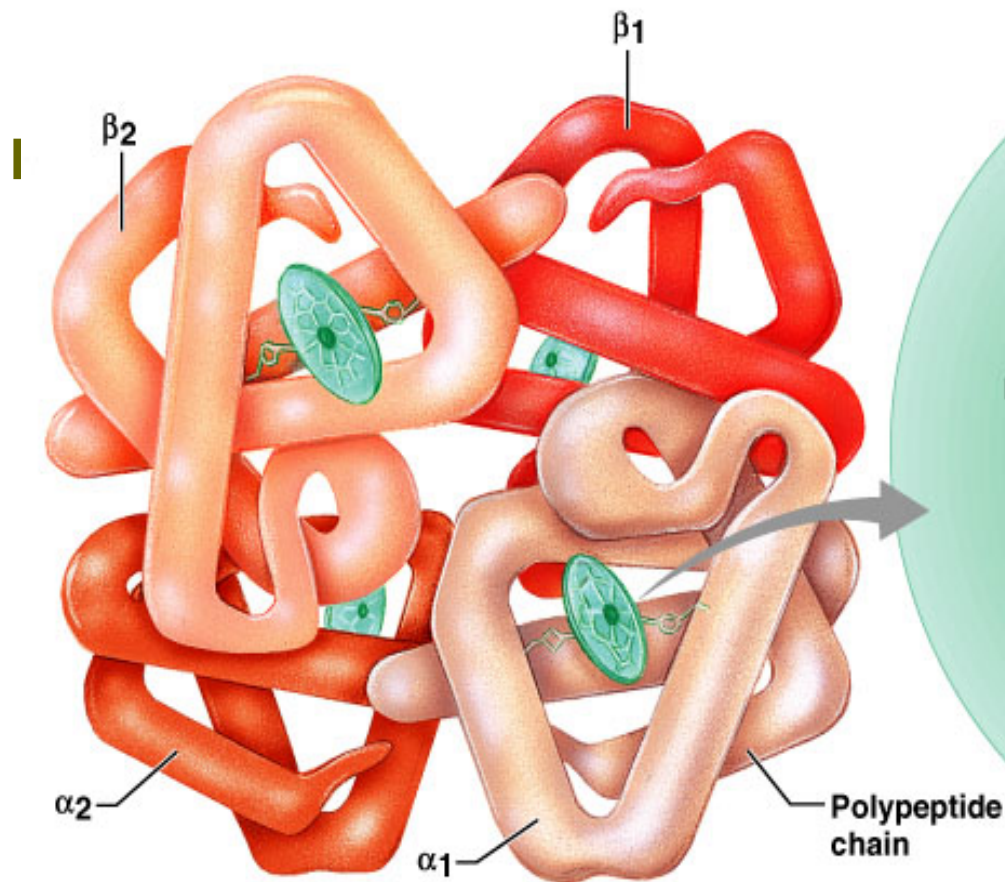
PGY3 – Internal Medicine



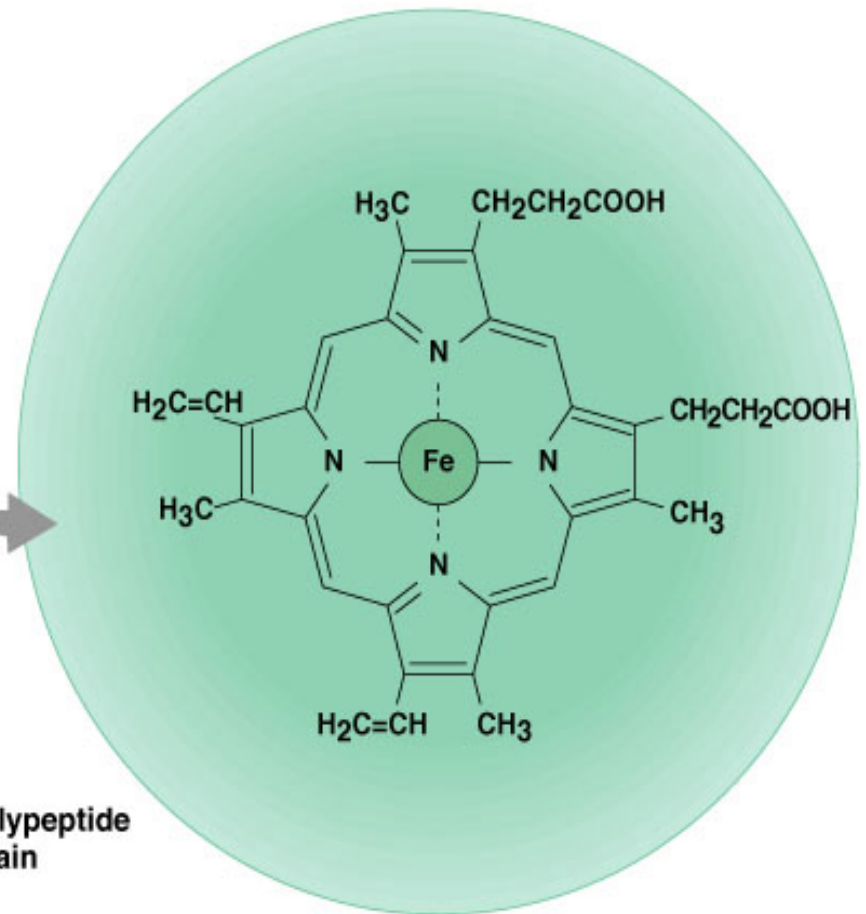
Normal hematopoiesis



Hemoglobin



(a) Hemoglobin



(b) Iron-containing heme group

Approach to anemia

- Definition (The WHO criteria):
 - Men: Hb <13.0 g/dL or Ht <40%
 - Women: Hb <12.0 g/dL or Ht <36%
- Useful measurements:
 - Mean corpuscular volume (MCV): 80 to 100 fl
 - RDW (red cell distribution width): increased RDW indicates the presence of cells of widely differing sizes
 - Reticulocytes: suggestive of regeneration

Approach to Anemia

□ Microcytic:

- MCV low, RDW high - iron deficiency
- MCV low, RDW normal – thalassemia

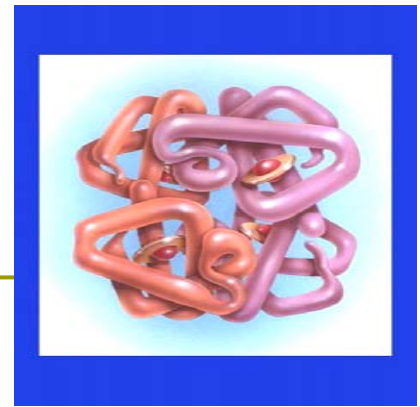
□ Macrocytic:

- MCV very high - B₁₂ or folate deficiency

□ Normocytic:

- MCV normal

Morphologic approach



- **Microcytic anemia** – $MCV < 80$ fl
 - Reduced iron availability — severe iron deficiency, the anemia of chronic disease, copper deficiency
 - Reduced heme synthesis — lead poisoning, congenital or acquired sideroblastic anemia
 - Reduced globin production — thalassemic states, other hemoglobinopathies

- The three most common causes of microcytosis in clinical practice are
 - iron deficiency (\downarrow iron stores)
 - alpha or beta thalassemia minor (often N or \uparrow iron stores)
 - anemia of chronic disease (hepatoma, RCC)

Morphologic approach

- **Macrocytic anemia** — $MCV > 100$ fL
 - Reticulocytosis
 - Abnormal nucleic acid metabolism of erythroid precursors (eg, folate or vitamin 12 deficiency and drugs interfering with nucleic acid synthesis, such as zidovudine, hydroxyurea and Septra)
 - Abnormal RBC maturation (eg, myelodysplastic syndrome, acute leukemia, LGL leukemia)
 - Other common causes:
 - alcohol abuse
 - liver disease
 - hypothyroidism

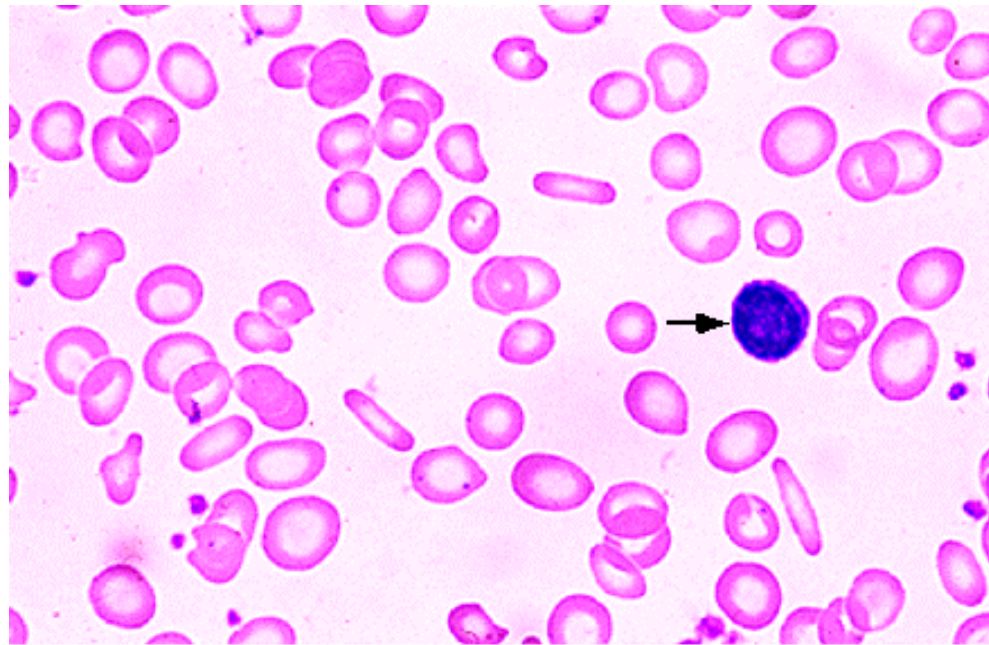
Morphologic approach

- **Normocytic anemia** – MCV normal
 - Increased destruction
 - Reduced production (bone marrow suppression):
 - Bone marrow invasion (myelofibrosis, multiple myeloma)
 - Myelodysplastic syndromes
 - Aplastic anemia
 - Acute blood loss
 - Chronic renal failure

Iron deficient anemia

- Diagnosis:
 - ↓ serum iron
 - ↑ **TIBC**
 - ↓ Transferrin saturation <20%
 - ↓ Ferritin < 10
- Iron replacement requires normalization of the hemoglobin and the body stores
- ALWAYS A SYMPTOM – LOOK FOR THE CAUSE

Iron deficient anemia



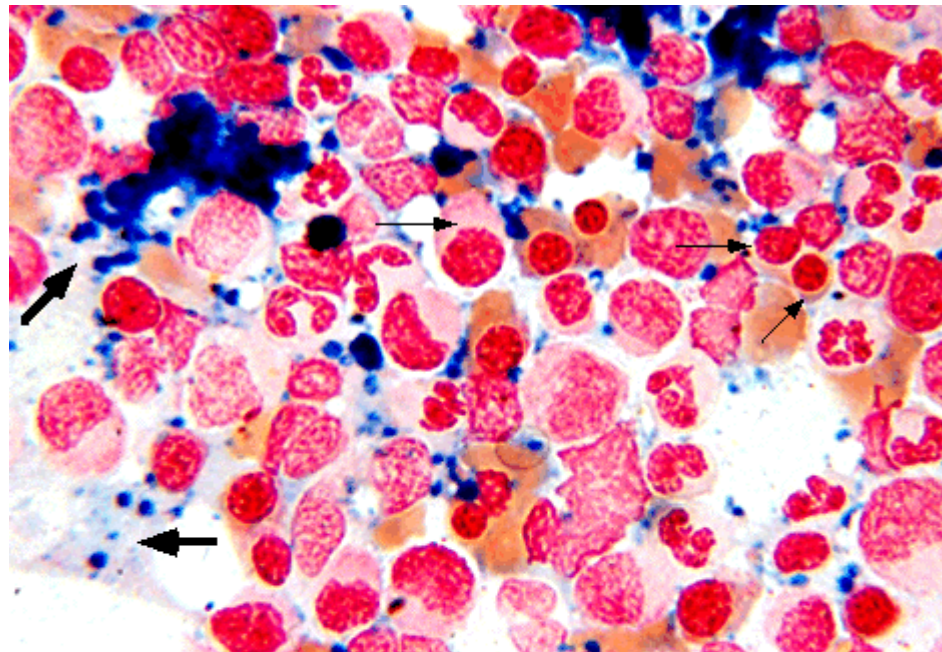
Microcytic hypochromic red cells Peripheral smear from a patient with iron deficiency shows pale small red cells with just a scant rim of pink hemoglobin; occasional "pencil" shaped cells are also present. Normal red cells are similar in size to the nucleus of a small lymphocyte (arrow); thus, many microcytic cells are present in this smear. Thalassemia can produce similar findings. Courtesy of Carola von Kapff, SH (ASCP).

Anemia of Chronic Disease

- ❑ Common in patients with infection, cancer, inflammatory and rheumatologic diseases
- ❑ Iron can not be remobilized from storage
- ❑ Blunted production of erythropoietin and response to erythropoietin
- ❑ Usually normocytic and normochromic but may be microcytic if severe

- ❑ **TIBC** ↓, Iron ↓, Transferrin saturation ↓, Ferritin↑

Anemia of Chronic Disease

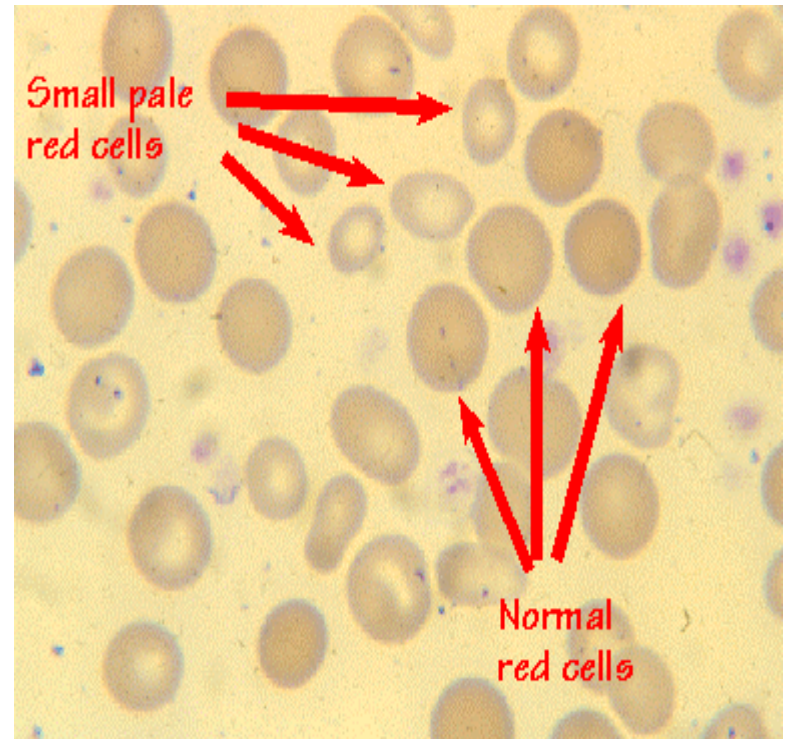


Anemia of chronic disease – bone marrow iron stain Section of a bone marrow aspirate taken from a patient with the anemia of chronic disease. The slide has been stained for iron (Prussian blue reaction) and counterstained with safranin to show nuclear detail. Note the increased iron staining within the voluminous cytoplasm of macrophages (thick black arrows), while there is no staining for iron within the cytoplasm of red blood cell precursors (thin black arrows). This pattern (abundant iron in macrophages and reduced to absent iron in red cell precursors) is quite typical for the anemia of chronic disease, and contrasts with iron deficiency, in which iron is absent from both macrophages and red cell precursors, while normal subjects demonstrate iron in macrophages and red cell precursors. Slide provided by Stanley L. Schrier, MD

Sideroblastic Anemia

- Two common features:
 - Ring sideroblasts in the bone marrow (abnormal normoblasts with excessive accumulation of iron in the mitochondria)
 - Impaired heme biosynthesis
- Produces a “dimorphic” blood film with microcytes and macrocytes
- Usually acquired:
 - Myelodysplastic syndrome
 - Drugs (Ethanol, INH)
 - Toxins (Lead, zinc)
 - Nutritional (Pyridoxine deficiency, copper deficiency)

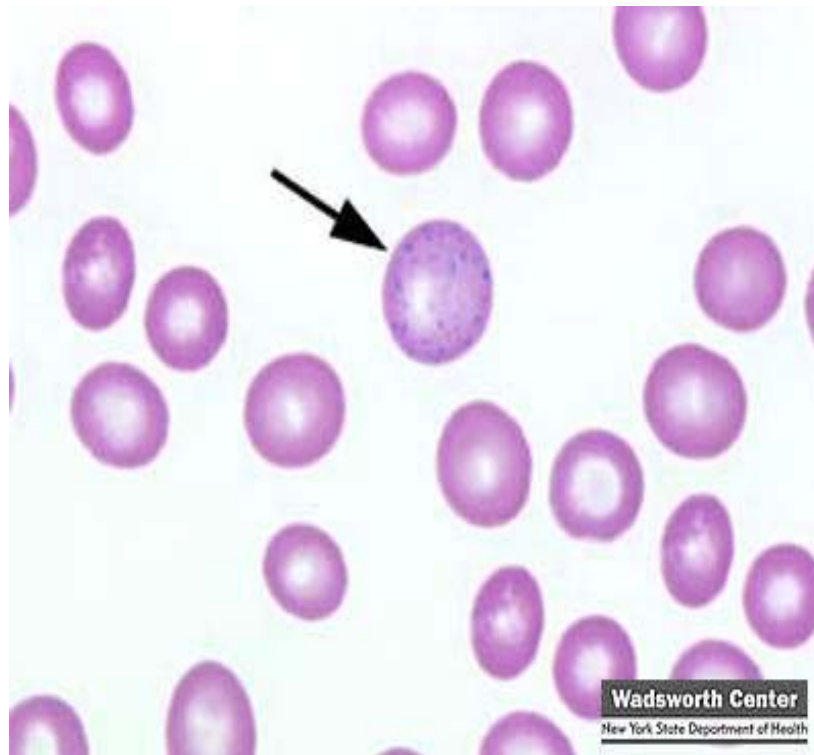
Sideroblastic Anemia



Thalassemia

- Anemia 2^o reduced or absent production of one or more globin chains
- Poikilocytosis (variation in shape) and basophilic stippling may be seen in the blood film
- Hemoglobin electrophoresis is only diagnostic for beta-thalassemia and may not be diagnostic if iron deficiency is also present
- Hb H (β -4) prep or DNA analysis is needed to diagnose alpha-thalassemia

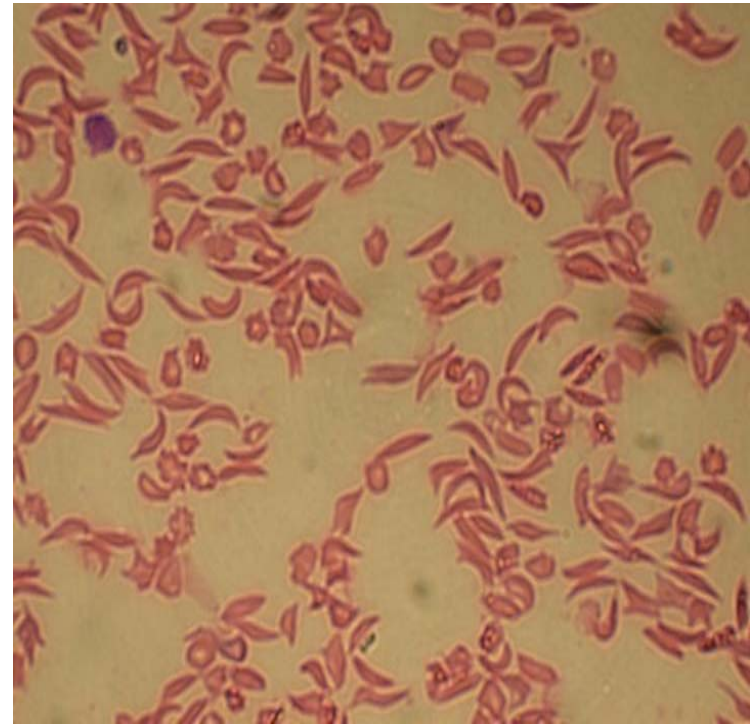
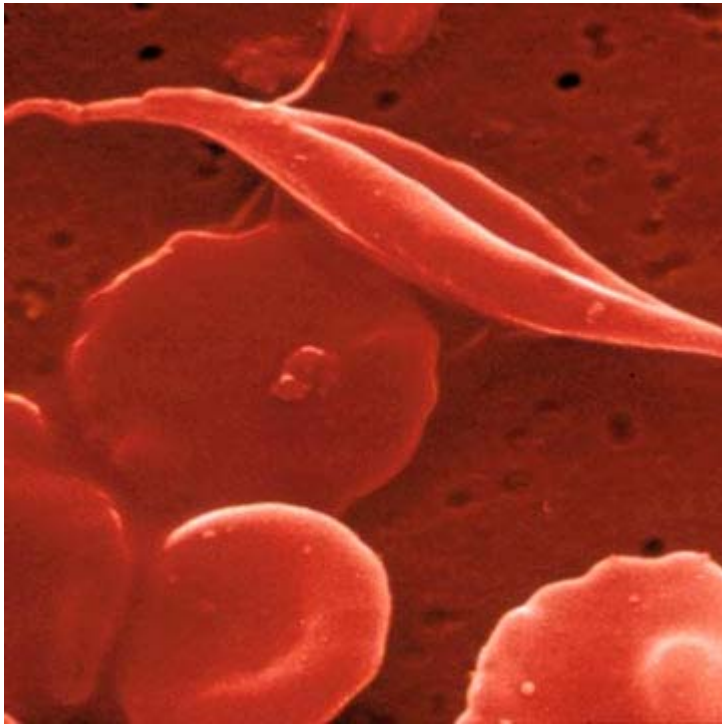
Basophilic stippling (ribosomal precipitates)



Sickle Cell Disease

- ❑ Inherited anemia (HbS)
- ❑ Acute crisis management includes fluids, oxygen and pain control +/- transfusion
- ❑ Transfusion therapy, hydroxyurea, magnesium and clotrimazole may reduce the frequency of vaso-occlusive crises
- ❑ Full vaccination program essential before functional hyposplenism develops
- ❑ Transplant may be curative

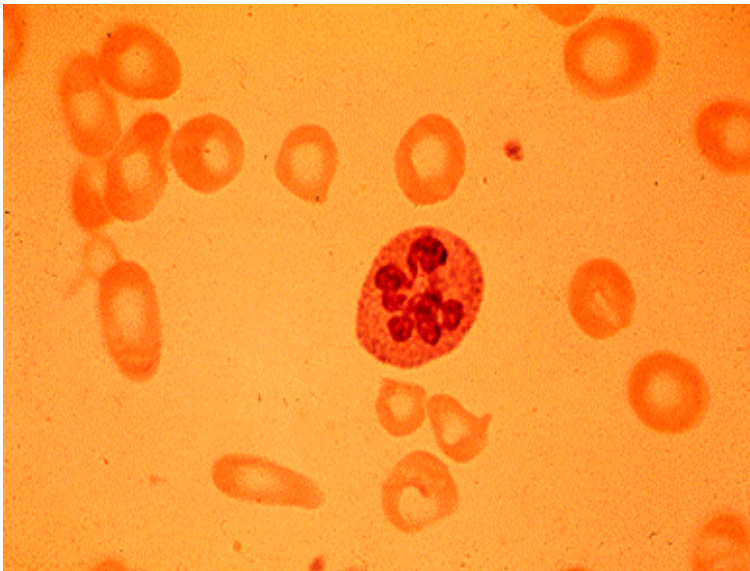
Sickle Cell Disease



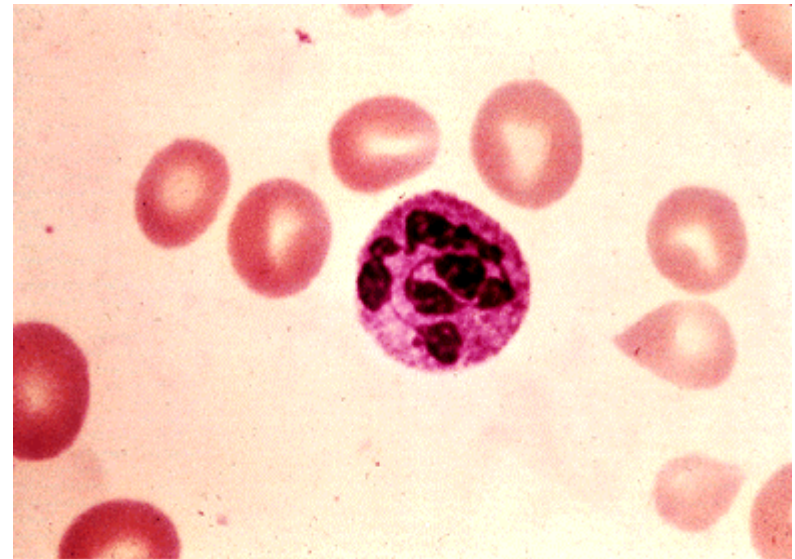
B₁₂ Deficiency

- Megaloblastic anemia (macrocytosis, hypersegmented neutrophils, abnormal megakaryocytes)
- Be aware of the neurological complications
- Never treat possible B₁₂ deficiency with folate - the CNS lesions may progress
- Schilling test distinguishes pernicious anemia from other causes

Megaloblastic smear



Megaloblastic blood picture Peripheral blood smear showing a hypersegmented neutrophil (7 lobes) and macroovalocytes, a pattern that can be seen with cobalamin or folate deficiency. Courtesy of Stanley L Schrier, MD.



Hypersegmented neutrophil Blood smear from a patient with megaloblastic anemia, showing a neutrophil with an increased number of nuclear lobes. At least six discrete lobes are present; normal neutrophils have five lobes or less. Courtesy of Stephen A. Landaw, MD, PhD.

Folic Acid Deficiency

- ❑ The peripheral blood film and bone marrow are identical to B₁₂ deficiency
- ❑ Women of childbearing age should take supplemental folate to prevent neural tube defects in their children
- ❑ Folate supplementation lowers homocysteine levels leading to less heart disease and stroke

Hemolytic anemia

- Extravascular hemolysis
 - Increased reticulocytes
 - Increased serum lactate dehydrogenase (LDH)
 - Increased indirect bilirubin concentration

- Intravascular hemolysis:
 - RBC fragments, hemoglobinuria, urinary hemosiderin, decreased haptoglobin

- Immune (positive direct antiglobulin test)
- Nonimmune (microangiopathic hemolytic anemia)

Hemolytic Anemia-Intravascular

Inherent RBC Defects:

- Enzyme defects - G6PD

Acquired Causes: Non-immune

- Drowning, burns, infections, PNH
- RBC fragmentation
 - DIC
 - prosthetic heart valves
 - vasculitis
 - TTP

Hemolytic Anemia-Extravascular

Inherited RBC Defects:

- ❑ Membrane defects - hereditary spherocytosis and elliptocytosis
- ❑ Hemoglobinopathy - Sickle Cell Disease, Thalassemia

Immune causes:

- ❑ Hemolytic transfusion reactions
- ❑ AIHA- primary or secondary
- ❑ Drugs eg. penicillin
- ❑ Cold agglutinins

Approach to Bruising & Bleeding

- ❑ Family history - bleeding or transfusion
- ❑ Drugs - ASA, NSAIDS and alcohol, steroids
- ❑ Other diseases - myeloma, renal or liver disease
- ❑ Pattern - lifelong or recent, deep seated bleeds or superficial bruising and petechiae
- ❑ Check for the spleen, petechiae, purpura and telangiectasia

Hemostasis Investigations

- ❑ Platelet count and platelet function studies
- ❑ INR, PTT, fibrinogen, FDP, bleeding time
- ❑ Thrombin time and reptilase time
- ❑ Euglobulin lysis time
- ❑ Inhibitor studies
- ❑ Factor assays
 - made in the liver, vitamin K dependent - 7
 - made in the liver, not vitamin K dependant - 5
 - made in endothelial cells -8

Platelets

- ❑ Acquired dysfunction is common in ill patients and DDAVP is often a valuable treatment
- ❑ The blood film helps differentiate ITP from the early phases of TTP. RBC fragments are present in TTP but not in ITP.
- ❑ Consider a bone marrow if platelet count is very low

Approach to thrombocytopenia

- Increase destruction (ITP, TTP, HIT)
- Decreased production (amegakaryocytic thrombocytopenia, aplastic anemia, acute leukemia, etc)

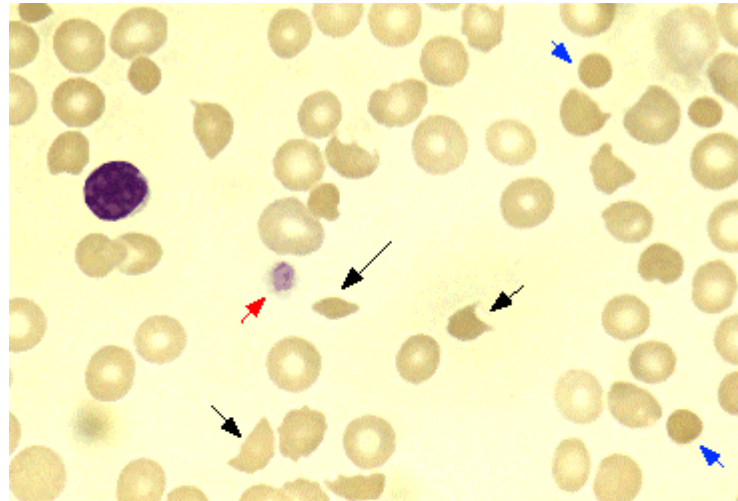
- Idiopathic (ITP)
- Secondary:
 - Drug toxicity
 - Connective tissue diseases
 - Infections: HIV
 - Hypersplenism

Thrombotic thrombocytopenic purpura

□ Diagnosis:

- Microangiopathic hemolytic anemia
=nonimmune hemolysis (negative direct antiglobulin test) with prominent red cell fragmentation (>1%)
- Thrombocytopenia
- Acute renal insufficiency
- Neurological abnormalities (fluctuating)
- Fever

Microangiopathic blood smear



Microangiopathic smear Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (small black arrows), other fragmented red cells (large black arrow); microspherocytes are also seen (blue arrows). The platelet number is reduced; the large platelet in the center (red arrow) suggests that the thrombocytopenia is due to enhanced destruction. Courtesy of Carola von Kapff, SH (ASCP).

Immune Thrombocytopenic Purpura

- Acquired: postviral infections in children (history of infection in the several weeks preceding the illness)
- Immune/Idiopathic:
 - Mainstem of treatment: steroids (response in up to 2 weeks)
 - If no response to steroids after 2 weeks consider splenectomy
 - In severe bleeding treat with IvIg (rapid response)

Disorders of Secondary Hemostasis

Hereditary

- Hemophilia A (factor VIII deficiency) and Hemophilia B (factor IX deficiency) are X-linked and produce hemarthroses and hematomas and are treated with recombinant factor concentrates and DDAVP (prolonged PTT)
- von Willebrand's disease (prolonged bleeding time and prolonged PTT)

Disorders of Secondary Hemostasis

Acquired

- ❑ Vitamin K deficiency (factors II, VII, IX and X)
- ❑ Liver disease (all factors other than VIII)
- ❑ Circulating anticoagulants (lupus anticoagulant)
- ❑ DIC

DIC

- DIC = uncontrolled THROMBIN and PLASMIN
- Excess thrombin leads to clotting, excess plasmin leads to bleeding
- Numerous disorders can trigger DIC ie. Sepsis, trauma, cancer, fat or amniotic fluid emboli, acute promyelocytic leukemia

DIC

- Can be acute or chronic
- Produces RBC fragmentation, confusion or coma, focal necrosis in the skin, ARDS, renal failure, bleeding and hypercoagulability

Management of DIC

- Treat the underlying cause
- Give cautious replacement therapy with FFP, cryoprecipitate and platelets
- Avoid products with activated factors
- In exceptional cases use low dose heparin

Approach to Neutropenia

- History - drugs, toxins, recurring mouth sores
- Physical - splenomegaly, bone pain
- Blood film - are granulocytic precursors or blasts present
- Bone marrow

Approach to Neutropenia

- Congenital
- Acquired
 - Immune Neutropenia
 - Neonatal Alloimmune Neutropenia
 - Primary Autoimmune Neutropenia
 - Secondary Autoimmune Neutropenia
 - Felty's syndrome (Rheumatoid arthritis, Splenomegaly, Neutropenia)
 - SLE-associated neutropenia
 - Drugs

Drug-Induced Neutropenia

- Antithyroid medications:
Carbamizole,
Methimazole,
Thiouracil
- Antibiotics:
Cephalosporins,
Penicillins,
Sulfonamides,
Chloramphenicol
- Ticlopidine
- Anticonvulsants:
Carbamazepine,
Valproic acid
- Antipsychotics:
Clozapine,
Olanzapine
- Antiarrhythmics:
Procainamide
- Sulpha drugs:
Sulfasalazine,
Sulfonamides

Leukemoid Reactions

- ❑ CML mimicked by acute bacterial infection inflammatory reactions, severe marrow stress such as bleeding, underlying tumors and treatment with G-CSF and GM-CSF
- ❑ CLL mimicked by pertussis, TB and mono
- ❑ CMMML and acute monoblastic leukemia mimicked by TB

Febrile Transfusion Reactions

- The most common reaction, non-immune
- Within 1-6 hours of transfusion
- Most often due to cytokines in the product
- Become more common as the product ages
- Treatment - Acetaminophen, Demerol and the transfusion of young products, washed products or leukodepleted products. The value of corticosteroids is less clear

Other Transfusion Reactions

- ❑ Urticaria (soluble plasma substances react with donor IgE) - treat with antihistamines
- ❑ Anaphylaxis (sec-min) 2° IgA deficiency - HISTORY! - only transfuse washed blood products
- ❑ Acute hemolytic (ABO mismatch)- recheck blood group and crossmatch - usually due to clerical error
- ❑ Delayed hemolytic (2-10 days) - mimics AIHA
- ❑ Citrate toxicity (hypocalcemia)- give calcium gluconate

Approach to pancytopenia

- Central
- Peripheral

Central causes

- Empty marrow: Aplastic anemia, Hypoplastic MDS, myelofibrosis
- Infiltration by abnormal cells: leukemia, lymphoma, solid tumors, TB
- Deranged marrow: Myelodysplastic syndrome
- Starved marrow: B12, folic acid
- Drug-induced: chemotherapy, antibiotics (sulpha), alcohol

Peripheral causes

- Hypersplenism
- Autoimmune
- Severe Sepsis

Aplastic Anemia

- Pancytopenia with "empty" marrow
- Most idiopathic cases are due to abnormal T cell inhibition of hematopoiesis
- Treatment:
 - Immunosuppression (Cyclosporin and antithymocyte globulin)
 - Allogeneic BMT
- Give irradiated, CMV negative blood products until CMV status is known

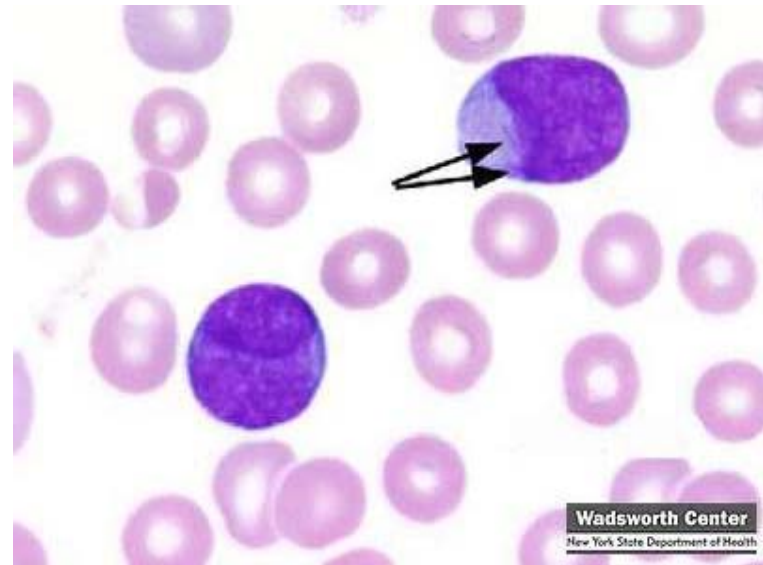
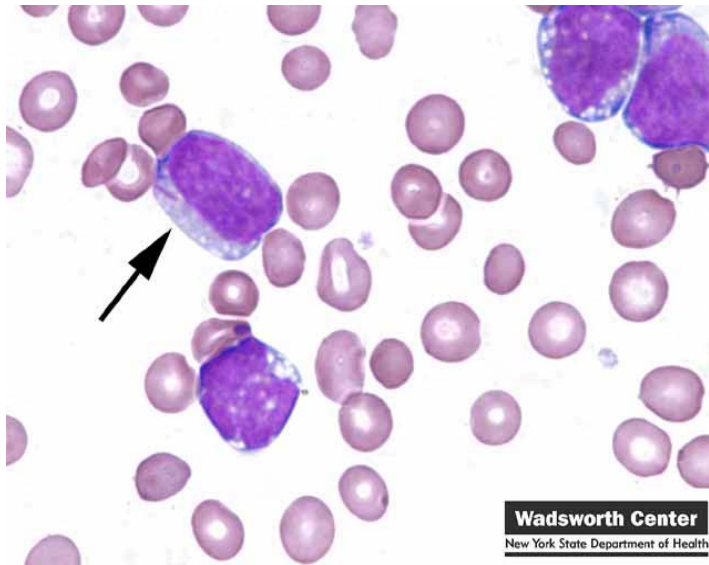
Myeloproliferative Disorders

- All are disorders of the pluripotent stem cell
- Acute Myelogenous Leukemia and Acute Lymphoblastic Leukemia
- Chronic Myeloproliferative Disorders
- Myelodysplastic Syndromes

Acute Myelogenous Leukemia

- Usually seen in adults
- Intensive, toxic treatment is needed to produce a complete remission
- Marrow transplantation may be curative
- Blasts are large with abundant cytoplasm
- Auer rods are diagnostic and granules are common

Auer Rods



Acute Lymphoblastic Leukemia

- Usually seen in children and adolescents
- Complete remission and cure rates are high
- Clinically: lymphadenopathy, hepatosplenomegaly
- Blasts are small, have scant cytoplasm, no granules and few nucleoli
- Some cases require marrow transplantation

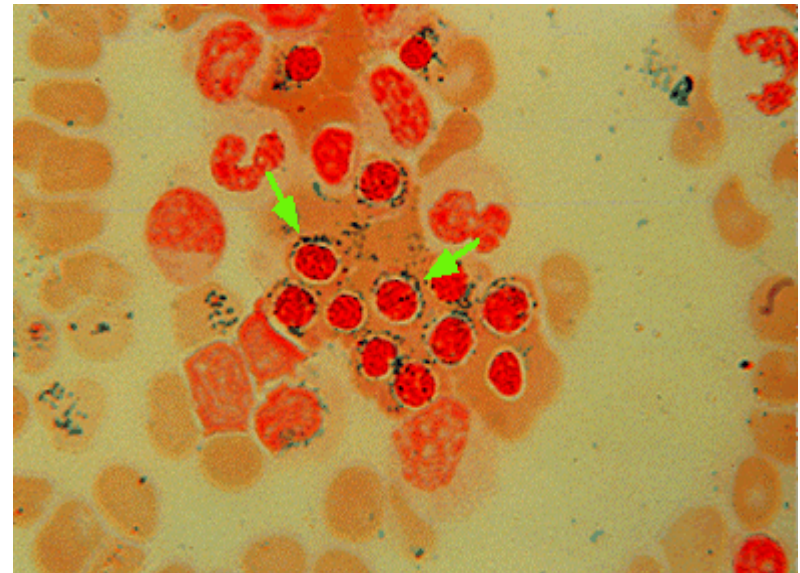
Myelodysplastic Syndromes

- Refractory anemia
- Refractory anemia with ring sideroblasts
- Refractory anemia with excess blasts
- Refractory anemia with excess blasts in transformation
- Chronic myelomonocytic leukemia

MDS



Pelger-Huet anomaly Peripheral blood smear from a patient with refractory anemia with excess blasts (RAEB) shows a neutrophil with a bilobed pseudo-Pelger-Huet (Pelgeroid) nucleus. The two lobes are connected by a thin strand (arrow) giving a "pince-nez" appearance. These nuclei look identical to the those seen in the inherited Pelger-Huet anomaly. This neutrophil also has markedly reduced granulation, a finding commonly seen in the myelodysplastic syndromes. (From Brunning, RD, McKenna, RW. Tumors of the bone marrow. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 9, 1994, Washington, DC. Armed Forces Institute of Pathology.)



Ringed sideroblasts Prussian blue stain of the bone marrow in a patient with refractory anemia and ringed sideroblasts (RARS). Blue-stained hemosiderin deposits in the mitochondria of erythroid precursors form an apparent ring around the nucleus (see arrows). Courtesy of Stanley L Schrier, MD.

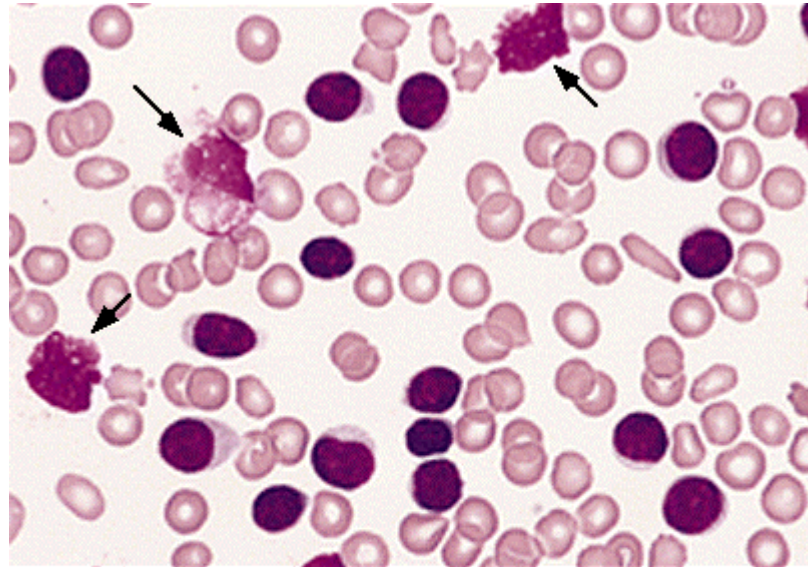
Chronic Myeloproliferative Disorders

- ❑ Polycythemia rubra vera (tx: phlebotomy, hydroxyurea)
- ❑ Chronic myeloid leukemia (tx: Gleevec, BMT)
- ❑ Idiopathic Myelofibrosis
- ❑ Essential thrombocythemia

Chronic Lymphocytic Leukemia

- ❑ Common in the elderly
- ❑ The blood film shows a lymphocytosis that may be extreme and smudge cells
- ❑ Lymphadenopathy and splenomegaly
- ❑ Autoimmune anemia and thrombocytopenia
- ❑ Treatment is observation, alkylating agents, fludarabine, steroids or radiation

CLL



B cell chronic lymphocytic leukemia Blood smear from a patient with B-cell CLL. The predominant lymphocytes have a very sparse cytoplasm, round to slightly oval nuclei, and no evident nucleoli. Damaged lymphocytes ("smudge cells") are present (arrows). (From Brunning, RD, McKenna, RW. Tumors of the bone marrow. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 9, 1994, Washington, DC. Armed Forces Institute of Pathology.)

Multiple Myeloma

- ❑ A monoclonal immunoglobulin in the serum or a single light chain in the urine is found (SPEP, UPEP) and marrow plasmocytosis
- ❑ Hypercalcemia and renal failure are frequent
- ❑ Lytic bone lesions are classical but osteoporosis is more common (alk phos is normal)
- ❑ The blood film shows rouleaux
- ❑ High ESR

MGUS

□ Characteristics:

- Presence of a monoclonal immunoglobulin < 3g/l (in 1% of people)
- Normal marrow (<10% plasma cells), normal chemistry (no anemia, hypercalcemia, no renal failure) and no lytic lesions
- The M-protein remains stable
- May transform to myeloma

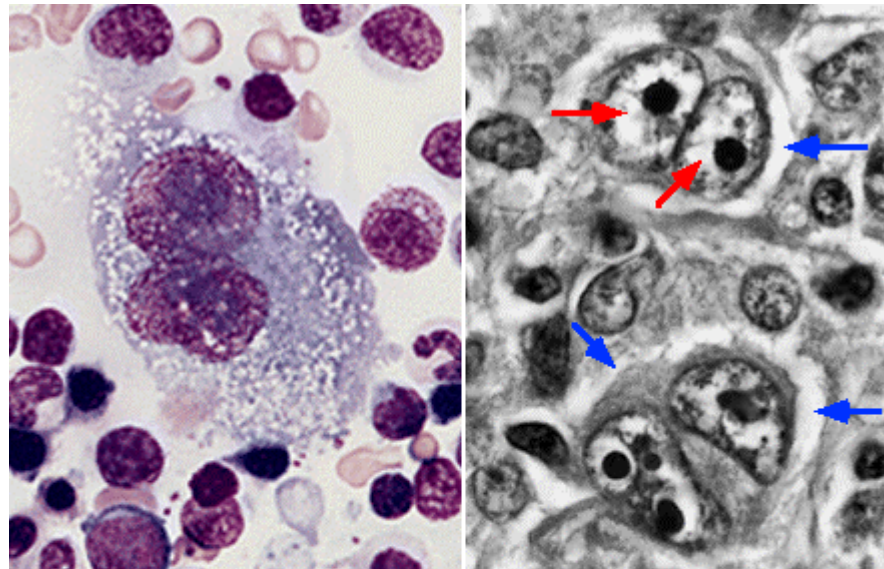
Macroglobulinemia

- Monoclonal IgM protein
- Clinically:
 - Lymphadenopathy
 - Hepatosplenomegaly
 - Hyperviscosity syndrome
- ESR may be very low
- Treat the hyperviscosity with plasmapheresis

Hodgkin's Disease

- The Reed-Sternberg cell is diagnostic
- The cure rate is high
- Long term complications are heart disease, hypothyroidism and secondary malignancies

Reed-Sternberg cell



Reed-Sternberg cells in Hodgkin's lymphoma Left panel: Reed-Sternberg cell as seen in a bone marrow specimen. Right panel: Reed-Sternberg cells in a lymph node section. Note the characteristic clear area surrounding the nucleoli in the right panel (red arrows), giving an "owl's eyes" appearance to the nuclei. Shrinkage artifact causes these cells to separate from the adjacent tissue, leaving a clear area surrounding these cells (ie, lacunar cells, blue arrows). (From Warnke, RA, Weiss, LM, Chan, JK, Cleary, ML, Dorfman, RF. Tumors of the lymph nodes and spleen. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 14, 1995, Washington, DC. Armed Forces Institute of Pathology.)

Non-Hodgkin's Lymphoma

- ❑ Numerous classification systems
- ❑ Low grade: Radiation +/- gentle chemotherapy does not cure but does produce long survival
- ❑ Intermediate and high grade: Radiation ± chemotherapy is used. Cure is possible
- ❑ Autoimmune hemolytic anemia and thrombocytopenia are common
- ❑ Hypersplenism is common
- ❑ Immunosuppression is frequent
 - never give live vaccines

Deep Vein Thrombosis and Pulmonary Embolism

- 1859 Rudolph Virchow described the major pathogenic determinants:
 - 1) Blood stasis
 - 2) Changes in the vessel wall
 - 3) Hypercoagulability

Thrombophilia

- Antiphospholipid antibodies
- Factor V Leiden
- G20210A prothrombin gene mutation
- Deficiency of protein C, protein S, and antithrombin
- Hyperhomocysteinemia

DVT/PE treatment

- Start LMWH (superior to UFH) if no contraindications
- Start Warfarin with LMWH
- Stop LMWH after 2 consecutive days of therapeutic INR (2-3)

- Thrombolytics indicated if circulatory collapse (shock)

Duration of anticoagulation

- Major transient risk factor (recent surgery): 3 months AVK
- Minor transient risk factor (immobilization): 6 months AVK
- Unprovoked thrombosis: longterm AVK
- Active cancer: longterm LMWH

Prophylaxis of VTE

□ **General surgery**

- Anticoagulant prophylaxis is recommended routinely
- UFH 5000 U administered 3 times daily is similarly effective as LMWH (Enoxaparin 40mg sc daily or Dalteparin 5000U sc daily)
- Fondaparinux - superior to other LMWH for DVT prophylaxis in orthopedic surgery

Prophylaxis of VTE

□ **Central venous catheters**

Based on recent data, the overall thrombotic risk of catheter-related thrombosis is low and probably insufficient to warrant routine prophylaxis

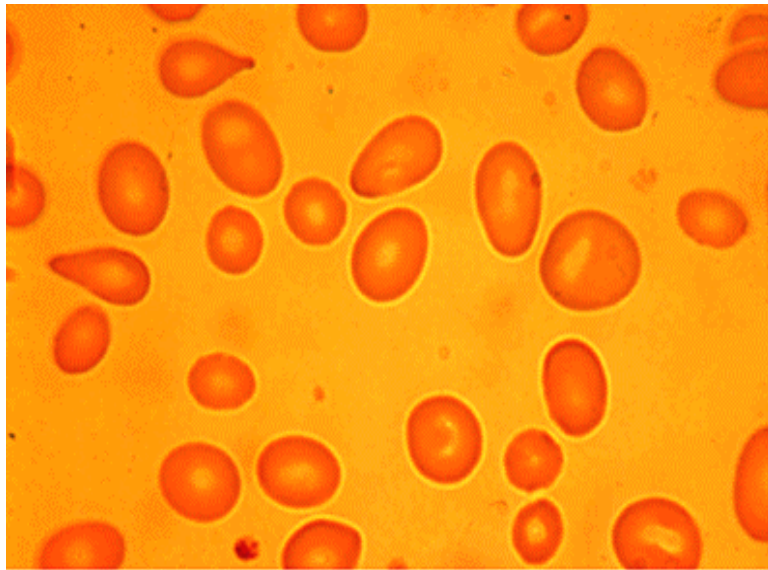
Case 1

- ❑ 63y F with severe fatigue and bruising
- ❑ O/E: T°=38.9°C, pale and slightly jaundiced, rest of examination normal
- ❑ PMHx: hypothyroidism
- ❑ Meds: thyroxine

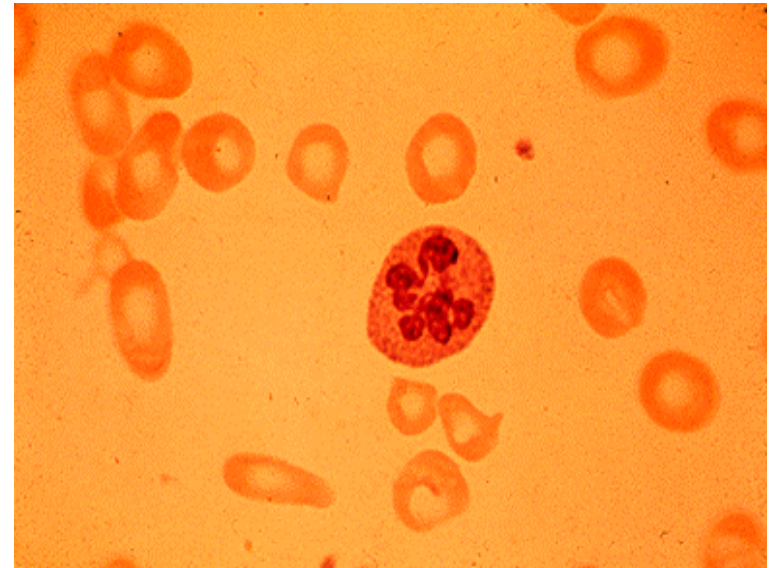
- ❑ WBC=1.9 x 10⁹/l
- ❑ Hb=53 g/l
- ❑ MCV=142 fl
- ❑ Plt=15 x 10⁹/l
- ❑ Retics=10 x 10⁹/l
- ❑ Neut=1.0 x 10⁹/l
- ❑ Ly=0.7 x 10⁹/l
- ❑ Mono=0.2 x 10⁹/l
- ❑ Film: Hypersegmented polymorphs. Oval macrocytes

- ❑ List 3 diagnosis in order of likelihood

Macrocytic anemia



Macroovalocytosis Peripheral smear shows marked macroovalocytosis in a patient with vitamin B12 deficiency. Courtesy of Stanley L Schrier, MD.



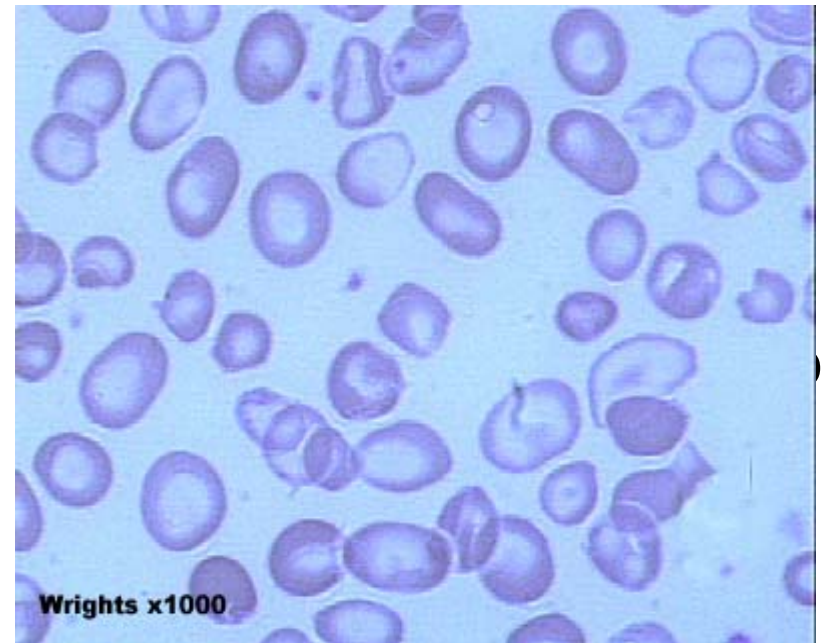
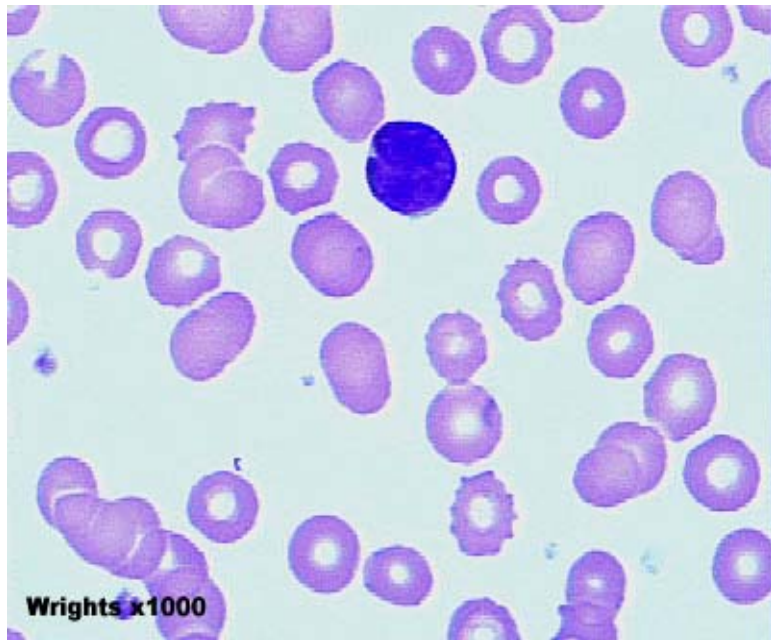
Megaloblastic blood picture Peripheral blood smear showing a hypersegmented neutrophil (7 lobes) and macroovalocytes, a pattern that can be seen with cobalamin or folate deficiency. Courtesy of Stanley L Schrier, MD.

Case 2

- ❑ 45y F on routine annual physical examination found to have following blood count (previously healthy, on no meds):
 - ❑ WBC: 7.5
 - ❑ Hb=61
 - ❑ MCV=58
 - ❑ Plt=345
 - ❑ Retics=10
 - ❑ Neut=4.3
 - ❑ Ly=2.7
 - ❑ Mono=0.5
 - ❑ Film: Hypochromia. Microcytosis.

- ❑ What is the most likely hematologic diagnosis?
- ❑ List 3 alternative possibilities.
- ❑ What tests would you order?
- ❑ Outline a management plan.

Hypochromic microcytic anemia



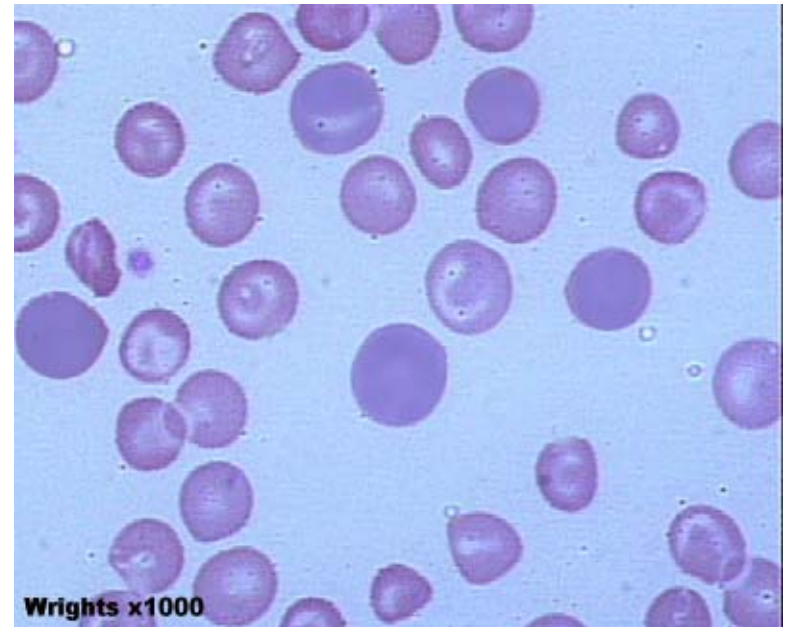
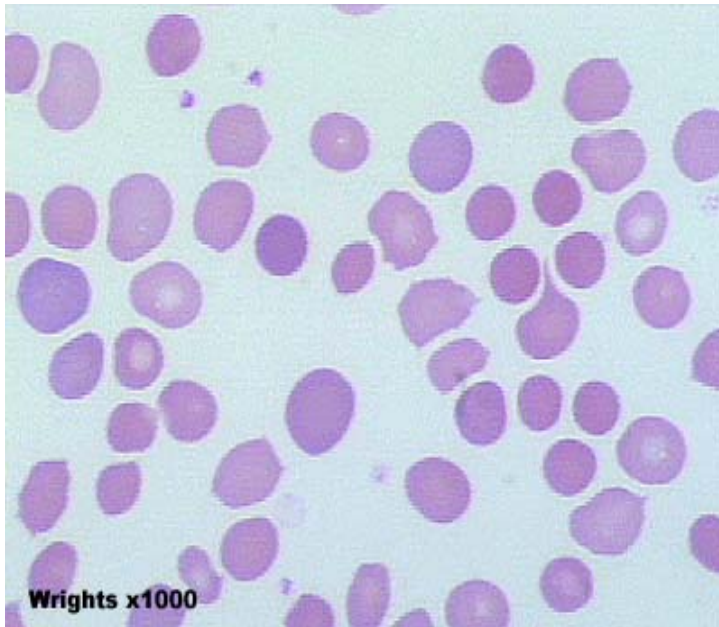
□ Microcytosis found in:
Iron deficiency anaemia
Thalassaemia
Sideroblastic anaemia
Lead poisoning
Anaemia of chronic disease

□ Hypochromia found in:
Iron deficiency
Thalassaemia
And any of the conditions leading to microcytosis

Case 3

- 59y F feeling “washed out”. Spleen palpable 4 cm BCM, jaundiced. Blood counts as follows:
 - WBC=8.5
 - Hb=61
 - MCV=110
 - Retics=560
 - Plt=156
 - Neut=4.5
 - Ly=3.0
 - Mono=0.8
 - Eo=0.2
 - Film: Spherocytes. Polychromasia.
- State the two most likely diagnoses, in order of probability
- Outline a plan of investigation and management

Hemolytic anemia



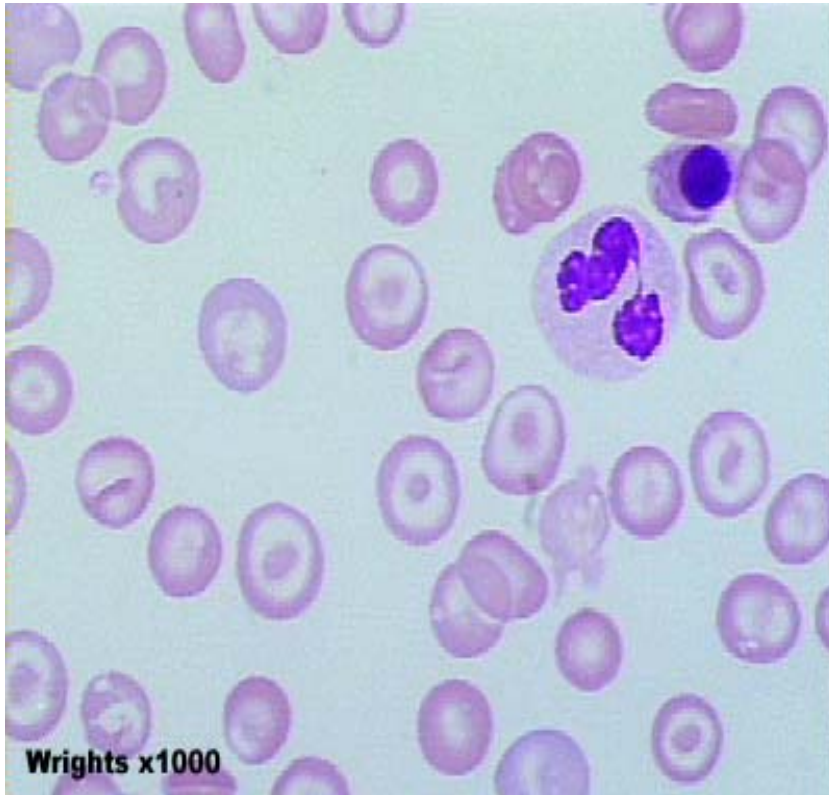
□ Spherocytosis found in:
Hereditary spherocytosis
Immune haemolytic anaemia
Zieve's syndrome
Microangiopathic haemolytic anaemia

□ Polychromasia found in:
Any situation with reticulocytosis
- for example bleeding,
haemolysis or response to
haematinic factor replacement

Case 4

- ❑ Black 56y M with splenomegaly (5cm BCM), no lymphadenopathy, non-drinker. Always had 'low blood', tx with several courses of iron with no difference on his health or blood counts. Upper and lower endoscopy – normal
- ❑ WBC=8.5
- ❑ Hb=106
- ❑ MCV=72
- ❑ Plt=254
- ❑ Retics=100
- ❑ Neut=4.5
- ❑ Ly=3.0
- ❑ Mono=0.8
- ❑ Eo=0.2
- ❑ Film: Target cells
- ❑ List the differential diagnosis

Target cells



Found in:

Obstructive liver disease

Severe iron deficiency

Thalassaemia

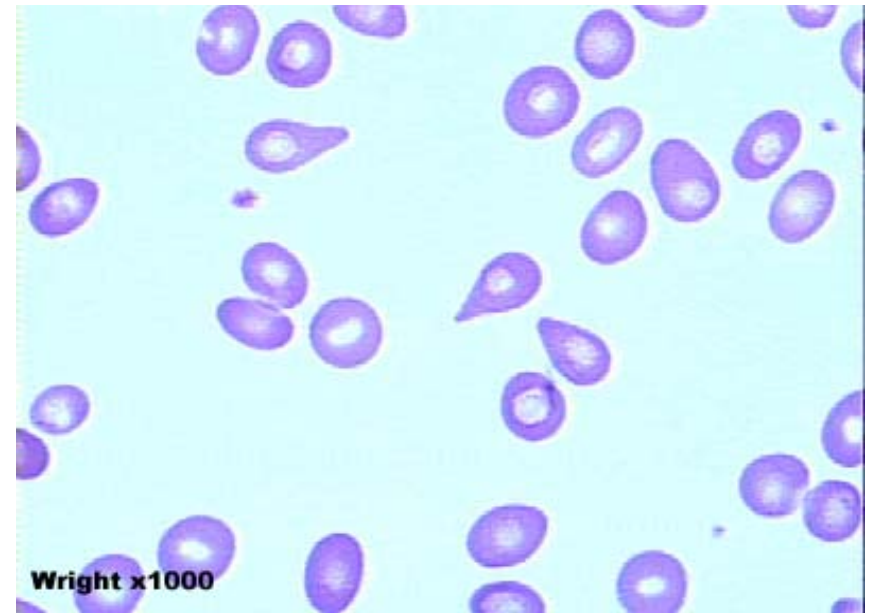
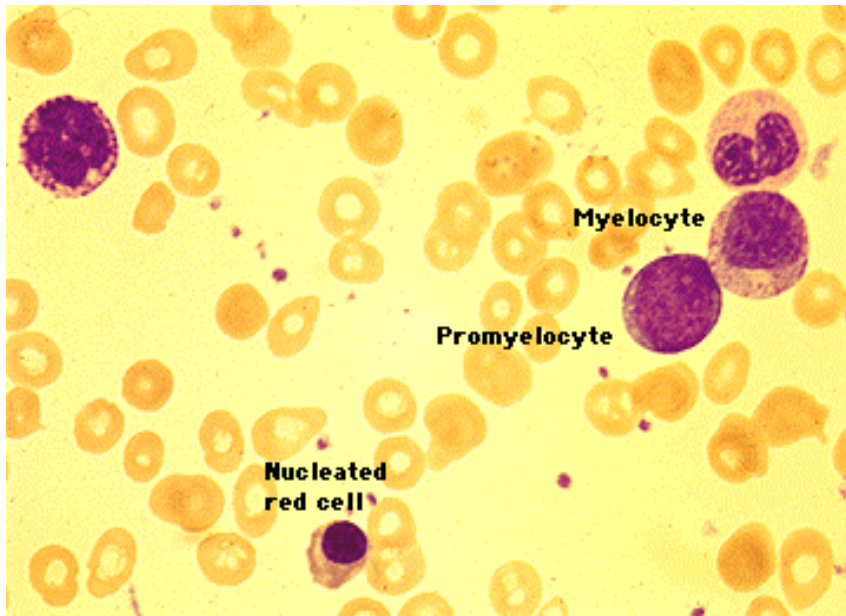
Haemoglobinopathies
(S and C)

Post splenectomy

Case 5

- 62y M on routine physical examination has a palpable spleen at 12cm BCM, no lymphadenopathy. He feels perfectly well, drinks a bottle of red wine every day for 10years. No signs suggestive of chronic liver disease
- WBC=2.5
- Hb=102
- MCV=93
- Plt=95
- Retics=60
- N=1.0
- Ly=2.0
- Mono=0.1
- Other: myelocytes 0.2, nucleated RBC 0.1, tear drop poikilocytes
- List the three most likely diagnoses
- Outline a plan of investigation

Erythroleukoblastic smear



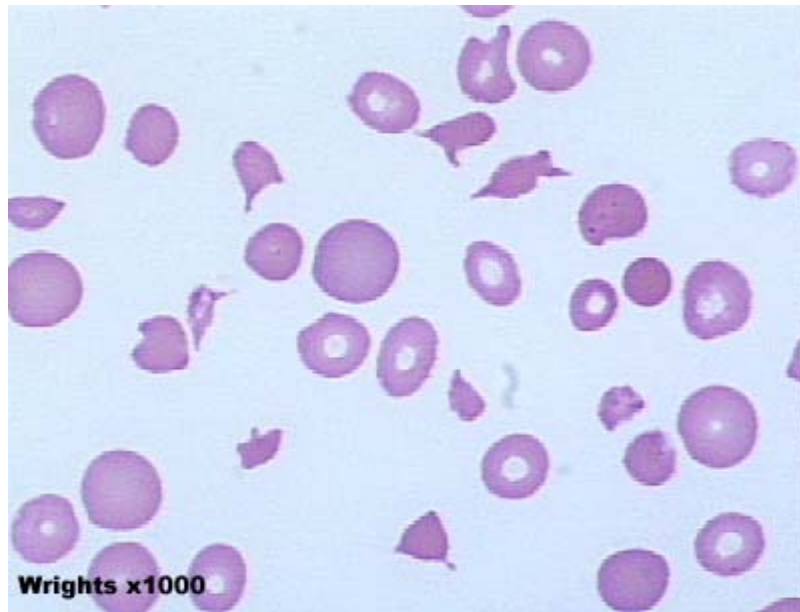
Leukoerythroblastic smear Leukoerythroblastic peripheral blood smear showing the presence of nucleated red cells and immature white cells. This pattern occurs with marrow replacement, usually due to fibrosis that may be idiopathic (eg, myelofibrosis with agnogenic myeloid metaplasia) or reactive to conditions such as metastatic cancer. Courtesy of Carola von Kapff, SH (ASCP).

- Found in:
 - Bone marrow fibrosis
 - Megaloblastic anaemia
 - Iron deficiency
 - Thalassaemia

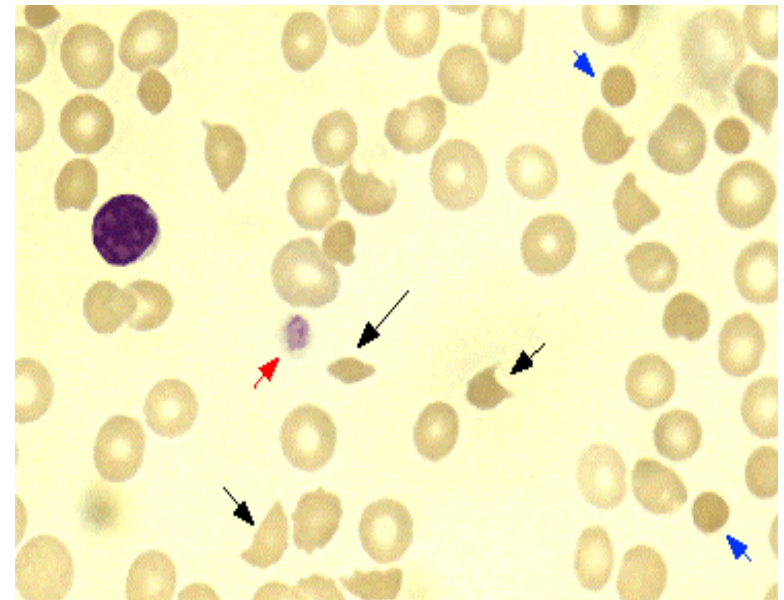
Case 6

- Patient with fatigue and bruising, present over the last 6-8 weeks. Otherwise well, on no medications. Has a history of CABG 3y ago, and at that time found to have AAA, 3cm in diameter. Chest x-ray shows a widened mediastinum
- WBC=4.6
- Hb=82
- MCV 101
- Plt=20
- Retics=390
- N=2.5
- Ly=1.8
- Mono=0.3
- Film: Schistocytes++
- What is the hematological diagnosis
- List 3 differential diagnoses
- Outline a plan of investigation and management

Schistocytosis



Schistocytes found in:
DIC
Micro angiopathic hemolytic anemia
Mechanical hemolytic anemia

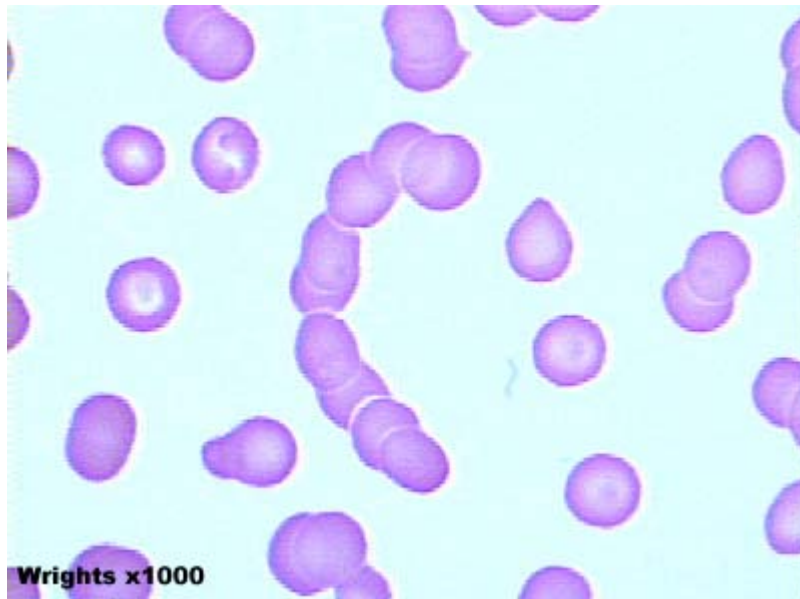


Microangiopathic smear Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (small black arrows), other fragmented red cells (large black arrow); microspherocytes are also seen (blue arrows). The platelet number is reduced; the large platelet in the center (red arrow) suggests that the thrombocytopenia is due to enhanced destruction. Courtesy of Carola von Kapff, SH (ASCP).

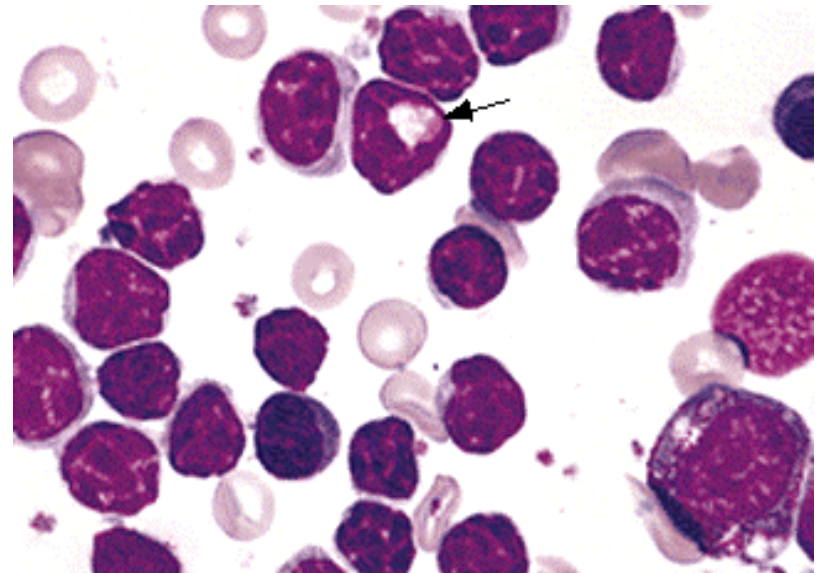
Case 7

- 65y F has headaches for about 3 weeks and gradually worsening drowsiness for 1 week. She comes to ER, is rousable, but sleepy. No neurological signs, generalized lymphadenopathy, up to approx 3cm in size. The spleen is felt at 7cm BCM
- WBC=3.1
- Hb=88
- MCV=87
- Plt=134
- Retics=27
- N=1.0
- Ly=2.0
- Mono=0.1
- Film: Rouleaux+++. Blue background staining
- What is the most likely diagnosis
- Outline a plan of investigation
- Outline a management plan

Rouleaux



Found in:
Hyperfibrinogenaemia
Hyperglobulinaemia



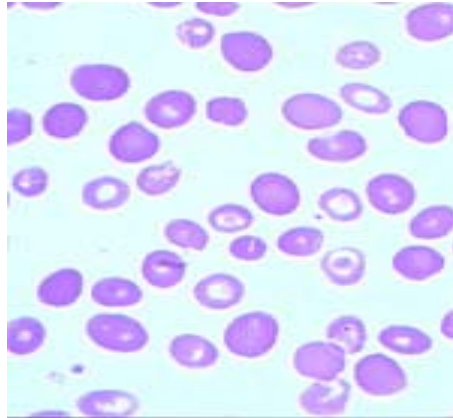
Dutcher body Bone marrow smear from a patient with lymphoplasmacytic lymphoma and an IgM spike. There is an intranuclear inclusion in a lymphocyte (arrow) that represents precipitated IgM. (From Brunning, RD, McKenna, RW. Tumors of the bone marrow. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 9, 1994, Washington, DC. Armed Forces Institute of Pathology.)

Case 8

- 76y F has an incidental blood count performed
- WBC=2.9
- Hb=88
- MCV=102
- Plt=75
- Retics=20
- N=1.0
- Ly=2.5
- Mono=0.4
- Film: dimorphic red blood cells

- What is the most likely diagnosis?
- How should it be investigated and managed?

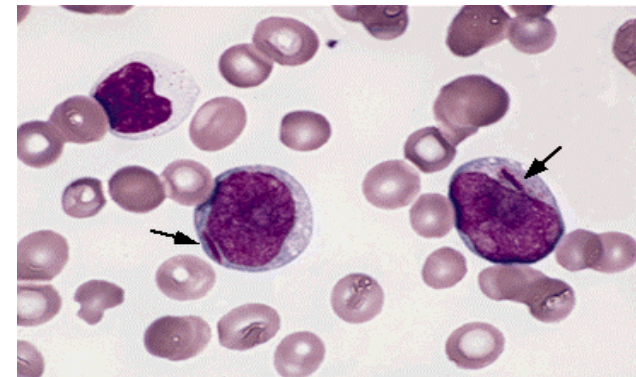
Myelodysplasia



- Dimorphic cells:
Two distinct populations of red cells. The populations may differ in size, shape or haemoglobin content.
- Found in:
Anemic patient after transfusion
Iron deficiency patient during therapy
Combined B12 / folate and iron deficiency
Sideroblastic anaemia



Pelger-Huet anomaly Peripheral blood smear from a patient with refractory anemia with excess blasts (RAEB) shows a neutrophil with a bilobed pseudo-Pelger-Huet (Pelgeroid) nucleus. The two lobes are connected by a thin strand (arrow) giving a "pince-nez" appearance. These nuclei look identical to the those seen in the inherited Pelger-Huet anomaly. This neutrophil also has markedly reduced granulation, a finding commonly seen in the myelodysplastic syndromes. (From Brunning, RD, McKenna, RW. Tumors of the bone marrow. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 9, 1994, Washington, DC. Armed Forces Institute of Pathology.)



Myeloblasts with Auer rod Peripheral smear from a patient with acute myeloid leukemia. There are two myeloblasts, which are large cells with high nuclear-to-cytoplasmic ratio and nucleoli. Each myeloblast has a pink/red rod-like structure (Auer rod) in the cytoplasm (arrows). (From Brunning, RD, McKenna, RW. Tumors of the bone marrow. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 9, 1994, Washington, DC. Armed Forces Institute of Pathology.)