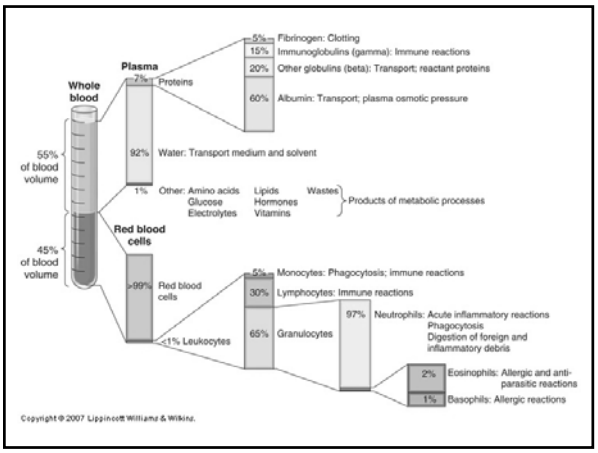
Disorders of Blood Cells & Blood Coagulation

HIHIM 409



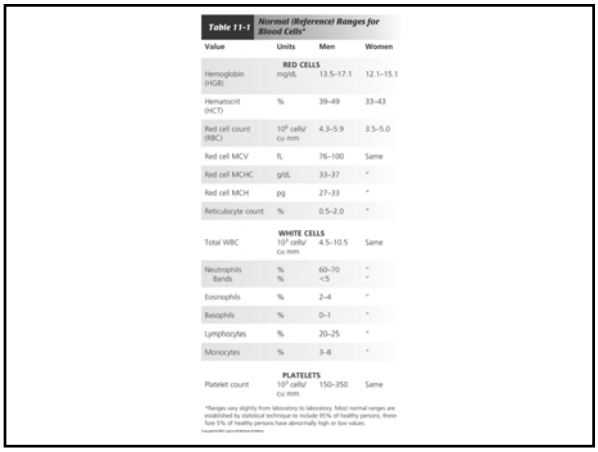
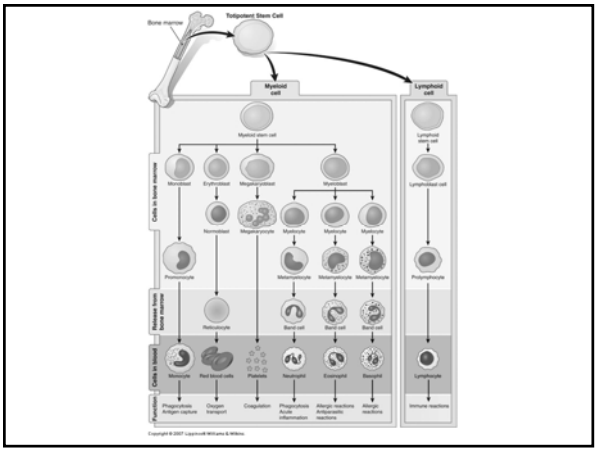


Table 11-1 Normal (Reference) Ranges for Blood Cells*

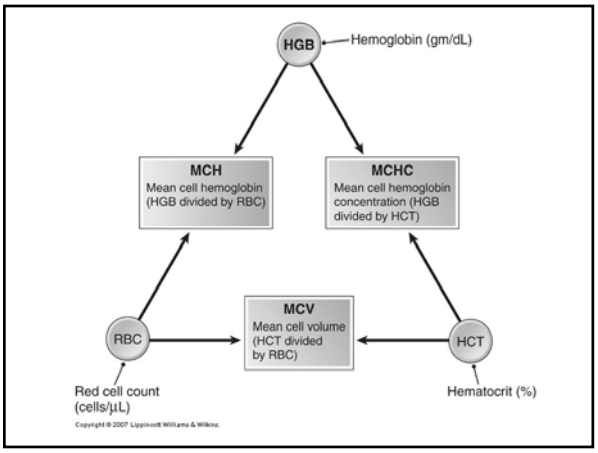
Value	Units	Men	Women
RED CELLS			
Hemoglobin (HGB)	mg/dL	13.5–17.1	12.1–15.1
Hematocrit (HCT)	%	39–49	33–43
Red cell count (RBC)	10^6 cells/cu mm	4.3–5.9	3.5–5.0
Red cell MCV	fL	76–100	Same
Red cell MCHC	g/dL	33–37	"
Red cell MCH	pg	27–33	"
Reticulocyte count	%	0.5–2.0	"
WHITE CELLS			
Total WBC	10^3 cells/cu mm	4.5–10.5	Same
Neutrophils Bands	% %	60–70 <5	" "
Eosinophils	%	2–4	"
Basophils	%	0–1	"
Lymphocytes	%	20–25	"
Monocytes	%	3–8	"
PLATELETS			
Platelet count	10^3 cells/cu mm	150–350	Same

*Ranges vary slightly from laboratory to laboratory. Most normal ranges are established by statistical technique to include 95% of healthy persons; therefore 5% of healthy persons have abnormally high or low values.



CBC

- WBC count
- RBC count
- WBC differential
- Hemoglobin (HGB)
- Hematocrit (HCT)
  - % of volume occupied by RBCs
- Red cell indices
  - Mean cell volume (MCV)
    - average size of RBC
  - Mean cell hemoglobin (MCH)
    - average amount of hemoglobin in an average RBC
  - Mean cell hemoglobin concentration (MCHC)
    - average concentration of hemoglobin/unit of volume in an average RBC

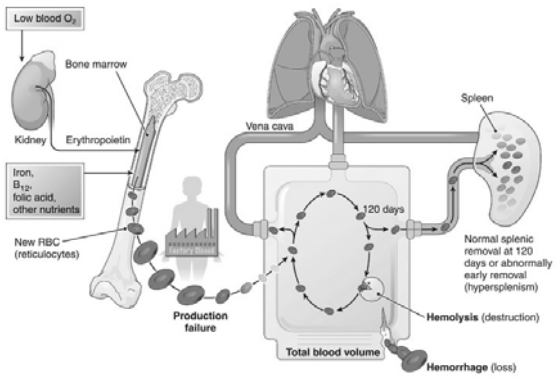


Major Determinants of Disease

- Blood cells have a short life span & require continuous replacement
- Most diseases of blood cells feature too many or too few cells because of an imbalance in the production or loss of cells
- Hemoglobin must be properly assembled & produced for effective O_2 transport
- White blood cells are critical in the defense against infection
- Diseases of lymphoid cells differ importantly from diseases of myeloid cells
- Malignancies of myeloid cells are associated with circulation of malignant cells in the blood (leukemia)
- Malignancies of lymphoid cells are associated with malignant cells in the blood (leukemia) or masses in lymph nodes & other tissue (lymphoma)
- Most diseases that affect platelets cause a low platelet count

Anemia

- Abnormally low hemoglobin
- Caused by
  - decreased numbers of RBCs
  - decreased amount of hemoglobin
  - both
- Sign of an underlying condition
- Diagnose
  - CBC



Hemorrhage

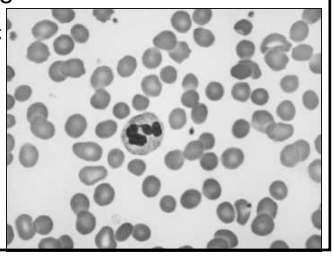
- Loss of O_2 carrying capacity
- Loss of iron
- Most common cause of iron deficiency anemia is chronic blood loss
  - abnormal menstrual bleeding
  - intestinal bleeding
- **IRON DEFICIENCY ANEMIA IN A MAN OR IN A POST-MENOPAUSAL WOMAN IS TO BE CONSIDERED BLEEDING FROM GI CANCER UNTIL PROVEN OTHERWISE**

Hemolytic Anemia

- Associated with
  - active, hypercellular bone marrow
  - high reticulocytes
  - increased LDH
  - low blood haptoglobin
  - increased bilirubin
- Genetic & non-genetic causes

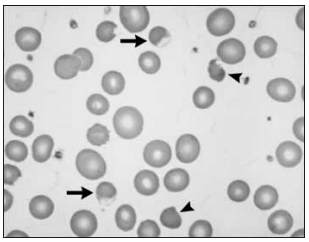
Hereditary Spherocytosis

- Disorder of a structural protein in the cell membrane
- Results in splenic hemolysis



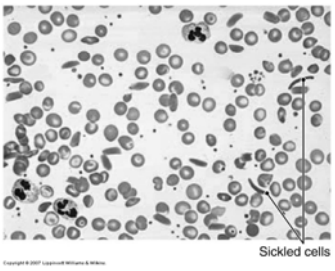
G6PD Deficiency

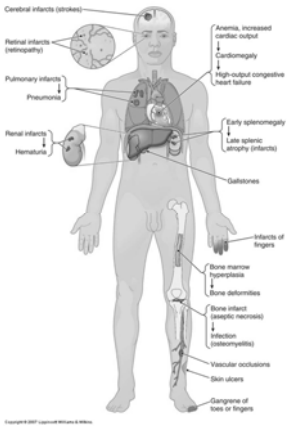
- Lacking enzyme that protects the RBC from oxidation



Sickle Cell Anemia

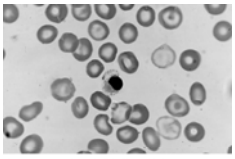
- Hemoglobin S
- Sickling precipitated by
  - low O_2 tension
  - infections
  - dehydration
  - acidosis

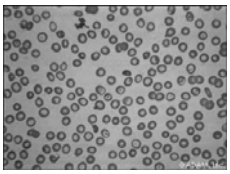




Thalassemias

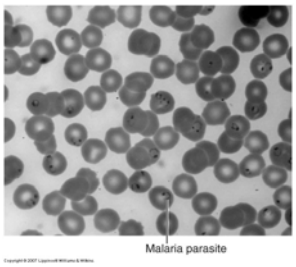
- Molecularly correct but not enough produced
- Several varieties
  - thalassemia major is most severe
  - most common type is a severe microcytic hypochromic anemia
    - stimulates iron absorption
    - can lead to hemachromatosis





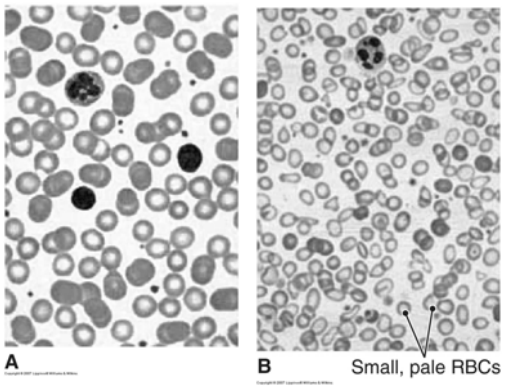
Non-Genetic Hemolytic Anemia

- Immune hemolytic anemia
  - antibodies directed against RBC antigens
- Mechanical hemolytic anemia
  - hemolyzed as they pass through mechanical devices such as artificial heart valves
- Associated with malaria



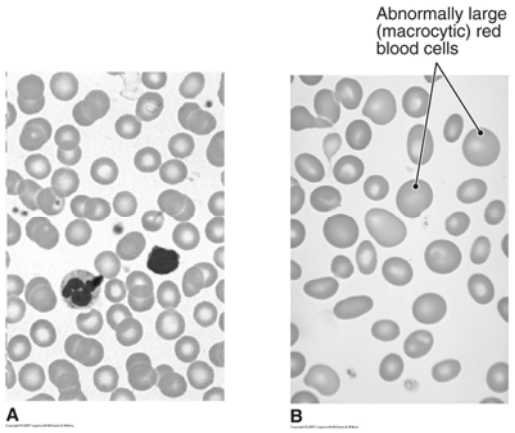
Iron Deficiency Anemia

- About 80% of iron is in hemoglobin with the rest stored as ferritin & hemosiderin
- Plasma ferritin levels vary directly with the amount of ferritin in bone marrow
- Transferrin transports iron
  - TIBC measures total transferrin
  - % saturation of TIBC is measuring how much iron is actually bound to the transferrin
- TIBC is high
- Plasma iron is low
- % saturation is low
- Most common cause is chronic blood loss
  - menstrual abnormalities
  - GI bleeding



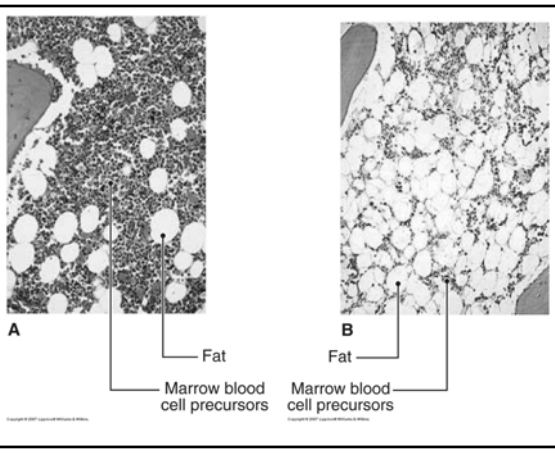
Macrocytic Anemia

- aka megaloblastic anemia
- Due to vitamin B_{12} or folic acid deficiencies
  - needed for DNA synthesis
- Hyperactive, hypercellular bone marrow
- Most common cause is defective intestinal absorption
  - intrinsic factor
  - gastrectomy
  - surgical resection of ileum
  - inflammatory bowel disease
- Pernicious anemia
  - autoimmune disease
  - associated with chronic atrophic gastritis



Aplastic Anemia

- Failure to produce all blood cells
- Idiopathic
- Results in pallor & fatigue
- Thrombocytopenia
- Low WBC count
- Hypocellular bone marrow

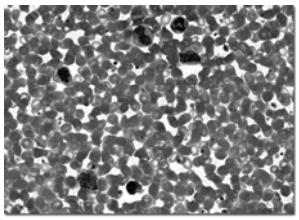


Myelophthisis

- Bone marrow replaced by tumor or fibrosis
- Fibrosis usually due to radiation but could be a manifestation of a myeloproliferative syndrome

Polycythemia

- Too many RBCs
- Relative
  - low plasma volume such as in dehydration
  - "stress polycythemia"
- Absolute
  - primary
    - polycythemia vera
  - secondary
    - due to
      - hypoxia from chronic lung disease
      - high altitude

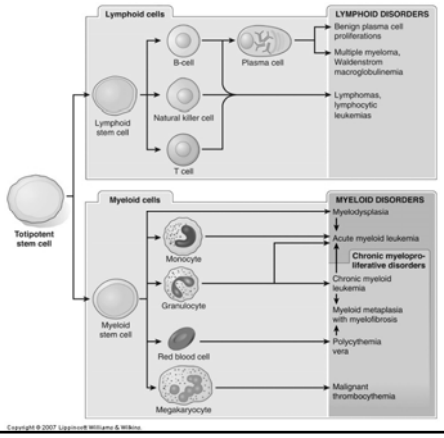


Leukopenia

- Low WBC count
- Caused by
  - hypersplenism
  - autoimmune disease
  - sepsis
  - bone marrow problem
- Agranulocytosis
  - severe neutropenia
  - caused mostly by drugs

Leukocytosis

- Too many WBCs
- Can be reactive or malignant

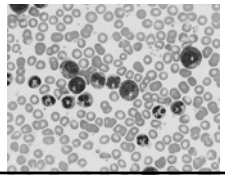


Leukemias

- Acute
  - immature cells
  - aggressive
  - short course
  - abrupt onset
  - symptoms include
    - anemia
    - infections
    - bleeding
    - bone pain
    - enlarged lymph nodes
- Chronic
  - mature cells
  - less aggressive
  - longer course
  - insidious onset
  - symptoms include
    - fatigue
    - pallor
    - night sweats
    - infections
    - splenomegaly
    - hepatomegaly

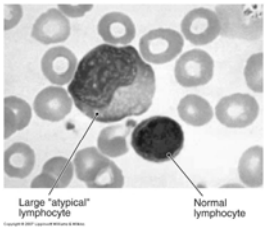
Reactive Leukocytosis

- Neutrophilia
  - bacterial infections
  - leukemoid reaction if count > 50,000
- Lymphocytosis
  - viral infections
- Eosinophilia
  - allergic reactions or parasitic infections
- "Bands"
  - when demand is great
  - "shift to the left"



Infectious Mononucleosis

- Acute, self-limited
- Atypical lymphocytes
- Epstein-Barr virus
  - infects B cells
  - heterophile antibodies
- Signs/symptoms
  - fever
  - sore throat
  - enlarged lymph nodes
- Monospot test

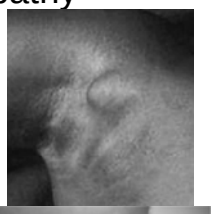


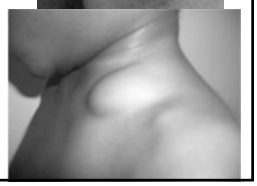
Lymph Node Response

- Infection
- Malignancy
- Immune reactions
- Autoimmune disease

Lymphadenopathy

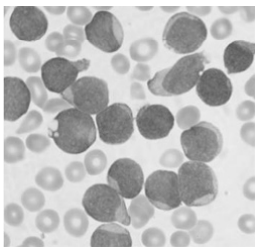
- Enlarged nodes
  - tender = infectious
  - non-tender = malignant
- Lymphadenitis
  - lymph node is infected
- Reactive hyperplasia
  - acute
    - dental infections, sore throat, genital infections
  - chronic
    - TB

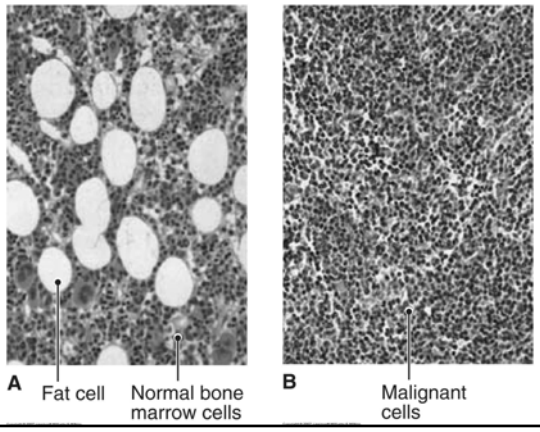




Acute Lymphocytic Leukemia

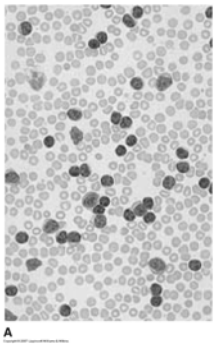
- ALL
- Uncommon
  - mostly in children & young adults
- Immature B cells
- Abrupt onset
- Results in
  - bone pain
  - lymphadenopathy
  - hepatosplenomegaly

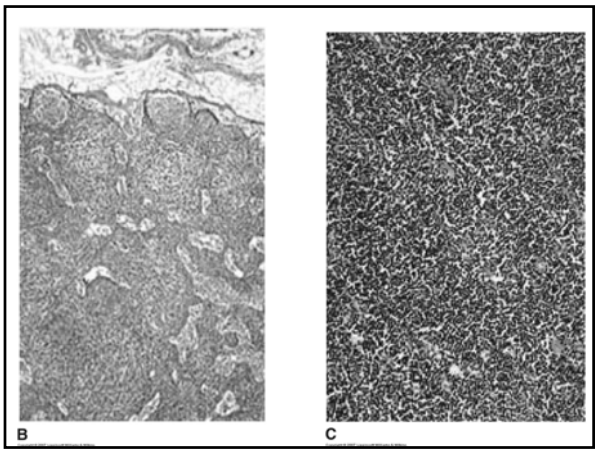




Chronic Lymphocytic Leukemia

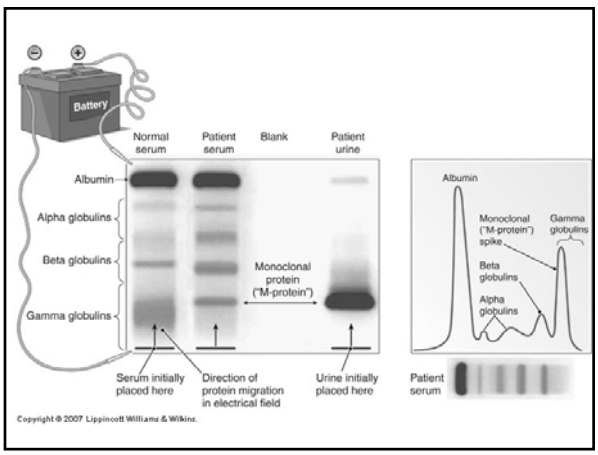
- CLL
- B cells
- About 1/3 of all leukemias
- Difficult to distinguish from small cell lymphocytic lymphoma
- Mostly in adults
- Slow developing





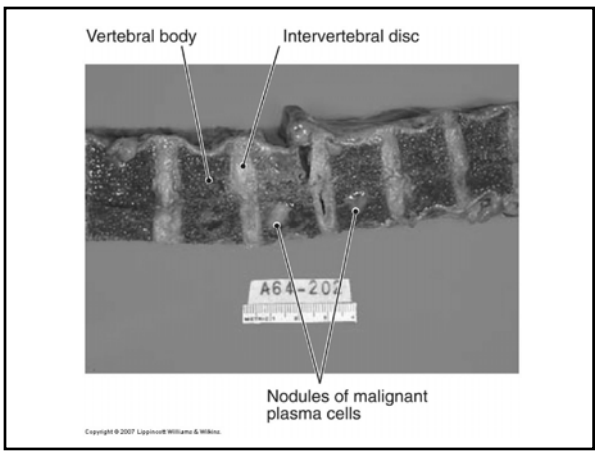
Plasma Cell Dyscrasias

- Activated B cells
- Make too much of a particular antibody
- On electrophoresis, appears as a dark band called an M-spike
- Light chains can pass through glomerulus & into urine
  - Bence-Jones proteins



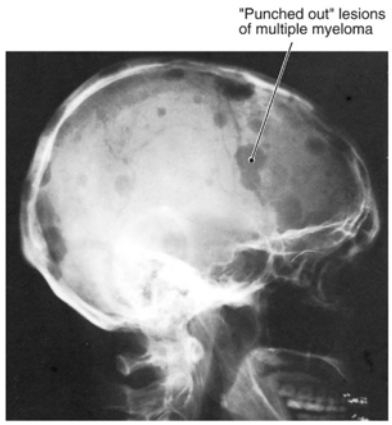
Multiple Myeloma

- Malignant cells appear as nodular masses in bone marrow



Multiple Myeloma

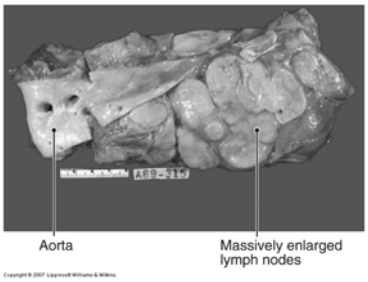
- Malignant cells appear as nodular masses in bone marrow
- "punched out" lesions in skull & spine



Multiple Myeloma

- Malignant cells appear as nodular masses in bone marrow
- “punched out” lesions in skull & spine
- Hypogammaglobinemia
- Susceptible to infections
- Elderly most commonly affected

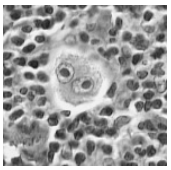
Lymphomas



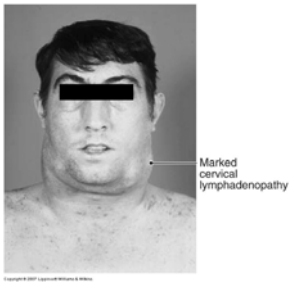
- Neoplasms of lymphocytes or lymphoblasts that grow as nodular masses usually in lymph nodes

Hodgkin Lymphoma

- EBV
- Characteristic cell is Reed-Sternberg (RS) cell
- Most common neoplasm between 10-30 yrs old
- Usually have poor T cell immunity
- Arises in a single lymph node or chain of nodes & spreads in an orderly manner
- Rarely involves anything but lymph nodes



- Usually painless, non-tender enlarged lymph node in neck
- Weight loss
- Night sweats
- Fever
- Fatigue
- Infection
- Good survival but at risk for other malignancies

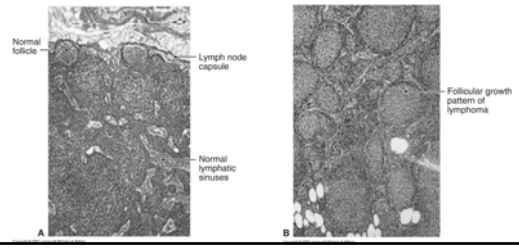


Non-Hodgkin Lymphomas

- B cells
- Aggressive
- Usually in advanced stage when diagnosed
- 1/3 arise in organs other than lymph nodes
- Tend to spread widely

Follicular Lymphoma

- About 50%
- Less aggressive
- Painless, enlarged lymph nodes

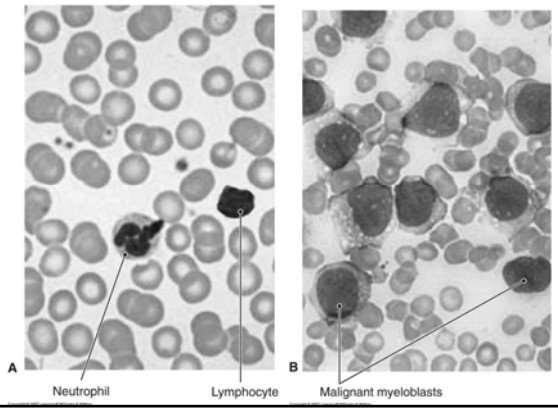


Diffuse Lymphomas

- About 50%
- No follicles
- Usually over 60 except for childhood lymphomas & those in AIDS
- Appear quickly & grow rapidly
- Lethal unless treated

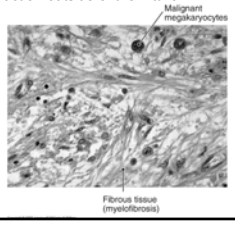
Acute Myelocytic Leukemia

- AML
- Myeloblasts
- Usually in middle age & older adults
- Sudden onset
- Marrow failure
  - anemia
  - infection
  - bleeding
  - bone pain
  - lymphadenopathy
  - hepatosplenomegaly



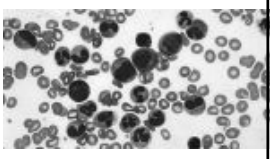
Chronic Myeloproliferative Disorders

- 2 features occur to some degree in each disorder
- Myelofibrosis
  - bone marrow replaced by fibrous tissue
  - due to fibrogenic factors released by megakaryocytes
- Extramedullary hematopoiesis
  - blood cell production outside of the marrow



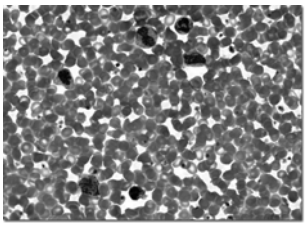
Chronic Myelocytic Leukemia

- CML
- Granulocytes
- Middle-aged adults usually
- About 15% of adult leukemias
- Slow onset but progressively worsens
- > 100,000 cells
- May end in a “blast crisis”



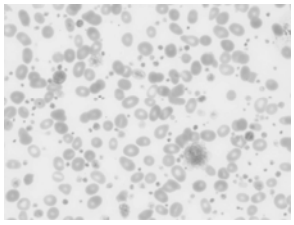
Polycythemia Vera

- Red cell precursors
- Middle-aged adults
- Appears slowly
- HCT > 60%
- High WBC count & platelet count
- May see giant platelets



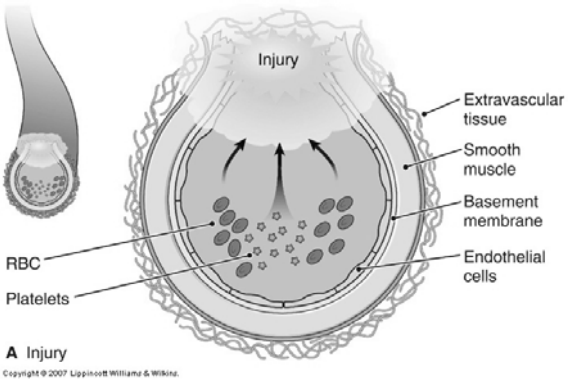
Malignant Thrombocythemia

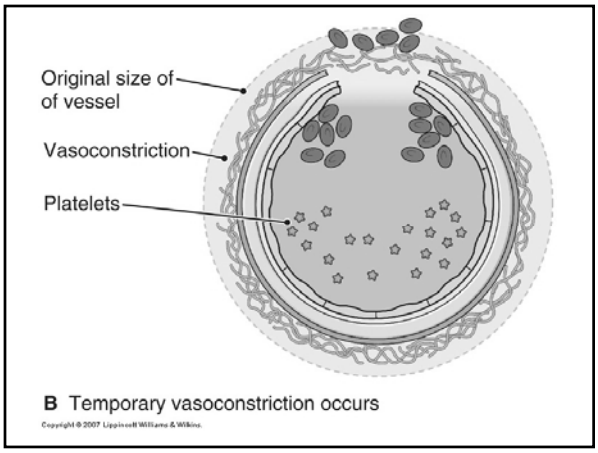
- aka essential thrombocythemia
- Rare
- 500,000/ml or greater
- Thrombosis & hemorrhage
- Survival is about 10-15 years

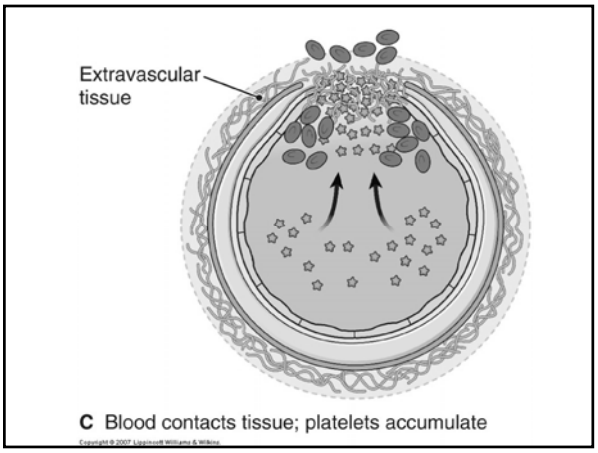


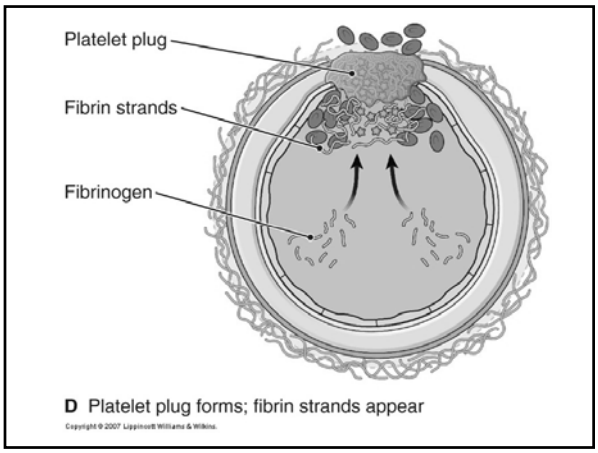
Myeloid Metaplasia with Myelofibrosis

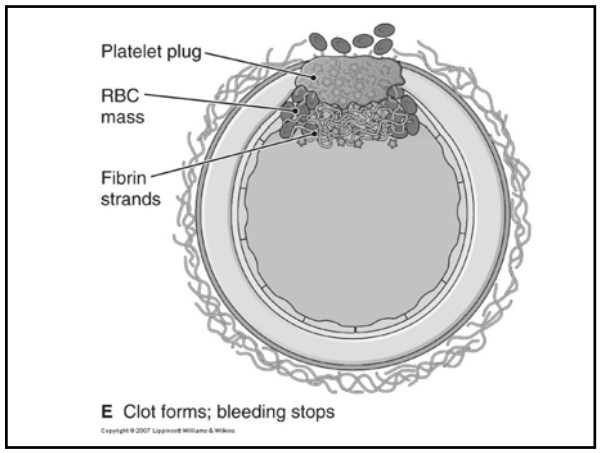
- Marrow fibrosis predominates
- Fibrogenic factors
- Older adults
- Extramedullary hematopoiesis
- Increased basophils
- Thrombosis & hemorrhage
- May end in “blast crisis”

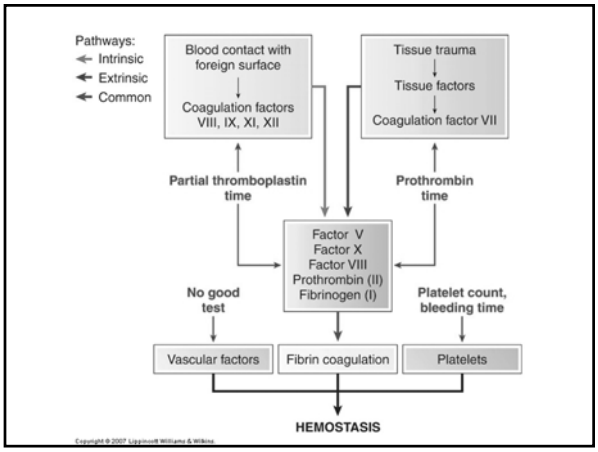












Major Determinants of Disease

- Excessive bleeding is always associated with at least 1 of 3 factors
  - fragile blood vessels
  - low platelet count or defective platelet function
  - decreased coagulation factor activity
- Bleeding related to platelet disorders usually occurs from capillary-sized blood vessels
- Bleeding related to coagulation factors usually occurs from larger vessels
- Most coagulation factors are proteins made by the liver, & severe liver disease is often accompanied by excessive bleeding
- Intravascular clotting is always abnormal & secondary to another disease

Hemorrhage

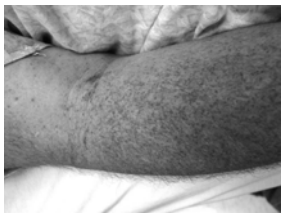
- Usually due to vascular injury
- If excessive, called hemorrhagic diathesis
- Platelet problems or fragile small blood vessels usually present as petechiae, nosebleed, hematuria, or excessive menses
- Coagulation factor deficiencies usually bleed into deep tissues, joints, & body spaces

Fragile Small Blood Vessels

- Usually trauma
- Seen in elderly
- Autoimmune vasculitis
- Scurvy

Thrombocytopenia

- Characterized by petechiae in skin or mucous membranes
- 130,000 – 400,000/ml is normal
- No concern until < 100,000/ml
- No excessive bleeding until < 50,000/ml
- Spontaneous hemorrhage at 20,000/ml
- Abnormal bleeding time
- Causes include
  - primary bone marrow disorder
  - toxicity due to drugs
  - nutritional deficiencies
  - hypersplenism



Immune Thrombocytopenic Purpura

- ITP
- Common cause of low platelet count
- Platelets destroyed by immune system
  - covered with antibodies & removed by spleen
- Insidious onset
- Usually presents as
  - easy bruising
  - epistaxis
  - bleeding gums
  - unusual bleeding after minor trauma
  - subungual or conjunctival petechiae

Classic Hemophilia

- aka Hemophilia A
- Factor VIII deficiency
- X linked
- Most common serious inherited coagulation disorder
- Normal bleeding time, PT, & platelet count
- PTT is prolonged

von Willebrand Disease

- Deficiency of von Willebrand factor (vWF)
  - made in endothelial cells & megakaryocytes
- One of the most common inherited coagulation disorders
- Prolonged bleeding time
- Normal platelet count
- Platelets cannot adhere to endothelium well

Severe Christmas Disease

- aka Hemophilia B
- Factor IX deficiency
- Named for 1st patient it was identified in
- X linked

Disseminated Intravascular Coagulation

- DIC
- Clotting inside vessels
- May cause obstruction in smaller vessels
- Eventually begin to bleed due to consumption of coagulation factors
  - consumptive coagulopathy
- Not a primary disease
- Anemia, thrombosis, & hemorrhage

- Initiated by
  - obstetrical complications
    - toxemia
    - abruptio placentae
  - infections
    - gram-negative sepsis
    - malaria
  - neoplasms
  - tissue trauma
    - crush injuries
    - burns
  - others
    - snakebite
    - heat stroke

Venous Thrombosis

- Usually due to local turbulence or endothelial injury
- Can be due to abnormalities of coagulation proteins
  - lupus anticoagulant
    - anti-phospholipid antibody
    - interferes with blood coagulation tests suggesting a deficit when there is not
    - suspect if PT or PTT is prolonged with no evidence of bleeding disorder
  - factor V Leiden
    - abnormal form of factor V
    - autosomal recessive