NURS 821 Advanced Pathophysiology

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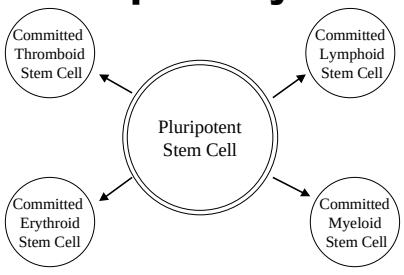
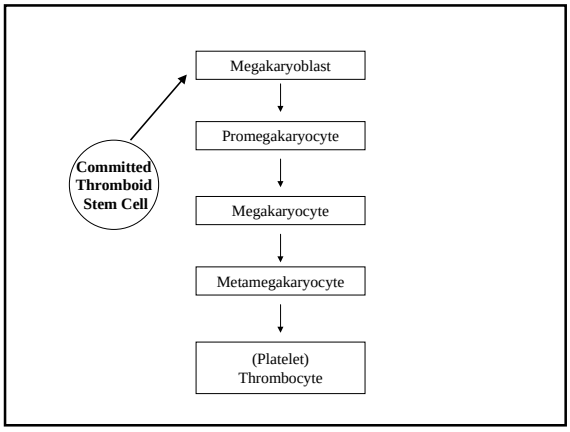
Lecture 5 Alterations in Blood Formation and Hemostasis

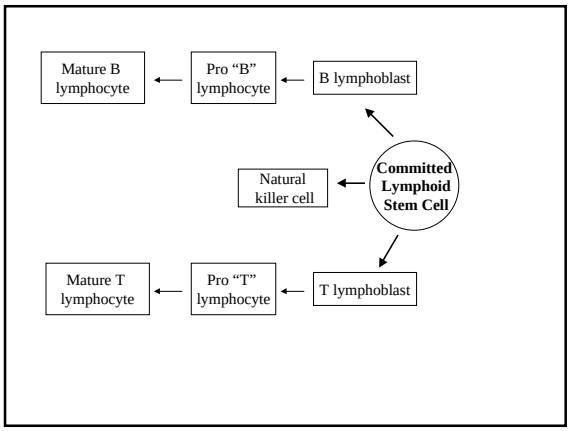
Alterations in Blood Formation and Hemostasis

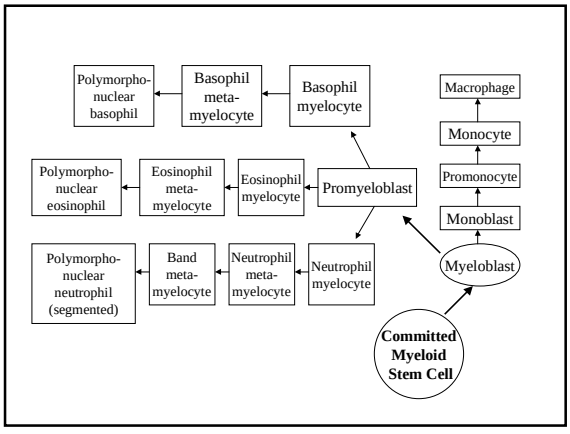
Part 1 Alterations in White Blood Cell Formation

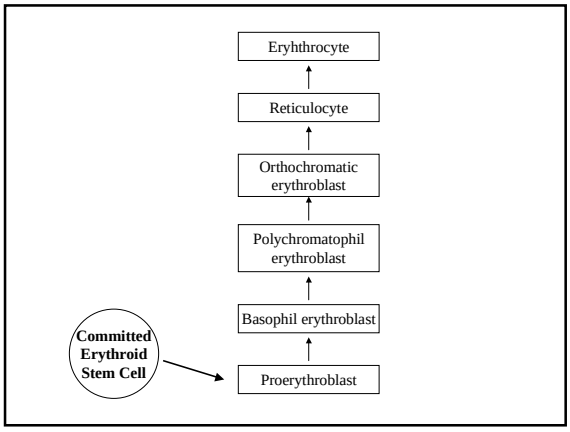
Stem cell differentiation and maturational pathways

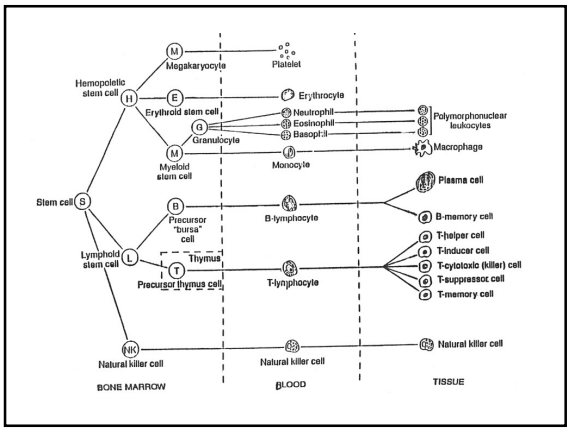



Megakaryoblast
Promegakaryocyte
Megakaryocyte
Metamegakaryocyte
(Platelet)
Thrombocyte
Committed
Thromboid
Stem Cell


Mature B
lymphocyte
Pro “B”
lymphocyte
B lymphoblast
Natural
killer cell
Committed
Lymphoid
Stem Cell
Mature T
lymphocyte
Pro “T”
lymphocyte
T lymphoblast


Polymorpho-
nuclear
basophil
Basophil
meta-
myelocyte
Basophil
myelocyte
Macrophage
Monocyte
Promonocyte
Monoblast
Polymorpho-
nuclear
eosinophil
Eosinophil
meta-
myelocyte
Eosinophil
myelocyte
Promyeloblast
Polymorpho-
nuclear
neutrophil
(segmented)
Band
meta-
myelocyte
Neutrophil
meta-
myelocyte
Neutrophil
myelocyte
Myeloblast
Committed
Myeloid
Stem Cell





Blood Functions

- Transport and distribute:
  - Respiratory gases
  - Hormones
  - Nutrients
  - Electrolytes
- Maintain homeostasis:
  - Acid-base balance
  - thermoregulation

Essential Nutrients for Erythropoiesis

- Fe-absorbed in duodenum; senescent RBCs-stored in liver
- B_{12}-need for DNA synthesis; Needs IF secreted by parietal cells; stored in liver
- Folic Acid-DNA synthesis and cell maturation
- Amino Acids
- Calcium
- Pyridoxine
- Cobalt
- Need erythropoietin from kidneys, stimulated by hypoxia and androgens

Leukemia

- Definition: …"malignant disorder of the blood and blood-forming organs: the bone marrow, spleen, and lymph nodes" (Schuber, 1997, p.1).
- Malignant stem cells in bone marrow lead to immature hamtopoietic cells without cell division regulation and ability to function; cells cram bone marrow space

Leukemia

- 5th leading cause of cancer death in males
- Leading site in children under 15; men 15-34
- Second to breast Ca in females 15-34
- 5th leading cancer deaths, men over 75
- 27,000adults diagnosed annually
- 2,000 children diagnosed
- (NCI, 2000; Schuber, 1997)

Leukemia Etiology

- Chemical and physical agent exposure
- Radiation
- Drugs (chloramphenicol, cytoxan)
- Viruses (in animals)- ? humans

Leukemia Etiology

- Genetic
  - Increased association with chromosomal abnormalities like Down's, Klinefelter's, Turner's Syndromes
  - Philadelphia chromosome-chromosome 22 found in CML
  - Chromosomal abnormalities found in 8 + 21-acute leukemias

Acquired Disorders Related to Leukemia

- Polycythemia vera
- Multiple myeloma
- Ovarian cancer
- Sideroblastic anemia

Leukemia Classification According to Cell Type

- Lympho-involving lymphoid tissue or lymphatics
  - Involve lymphoid precursors that originate in bone marrow, infiltrate spleen, lymph nodes, CNS, etc, l
- Myelo-originating in myeloid tissue or bone marrow
  - Interfere with maturation of all blood cells, including granulocytes, erythrocytes, thrombocytes

Leukemia Classification According to Maturity

- Blastic and acute-involving immature cells
- Cytic and chronic-involving mature cells

Leukemia Classification Examples

- Acute lymphoid leukemias-lymphatic, lymphoblastic, lymphoblastoid, stem cell, blast cell, etc.
- Acute nonlymphoid leukemias-granulocytic (neutrophils, eosinophils, basophils), myelocytic, monocytic, myelogenous, monoblastic, monomyeloblastic, etc.

Leukemia Classification

- Acute
  - Undifferentiated (immature) cells
  - Usually a blast cell
  - Massive number immature leukocytes
  - Abrupt, rapid onset with short survival
  - Severe thrombocytopenia
  - Increased fever, bleeding, infection
- Chronic
  - Mature but incorrect functioning cell
  - Gradual onset
  - Better prognosis

Leukemia

- Clinical manifestations based upon pathophysiology
- Complications

Leukemia Symptoms (NCI, 2000)

- Leukemia cells compete and block normal cell proliferation
- Chronic-may be asymptomatic
- Acute-quick symptoms and quick progression-varying systemic manifestations
- Low WBCs can not fight infection
- Low RBCs and platelets-anemia, bleeding, fatigue, bruising, petechiae

Leukemia Symptoms

- Cell mutation occuring very early in pluripotent stem cell-pancytopenia
- Flulike symptoms-f, chills; weakness, anorexia, weight loss, lymphadenopathy (testicles), swollen gums, bone or joint pain, night sweats
- CNS-HA, vomiting, confusion, seizures

Acute Leukemias

- Acute Lymphocytic Leukemia (ALL)
  - Increased incidence between 2-4,highest leukemia in kids
  - Also affects adults over 65
  - Abrupt onset-symptoms related to bone marrow depression: fatigue, f, bleeding, bone marrow changes, bone pain

Acute Myelogenous Leukemia

- Etiology-benzene, radiation, recreational drugs (?marijuana in pregnancy)
  - Auer rods seen in cytoplasm of myeloblasts
  - Both adults and children; Average age= 50, 15-39
  - Sometimes called acute nonlymphocytic leukemia (ANLL)
  - Abrupt onset
  - Hemorrhaging issues

Pathogenesis of AML

- Etiology-radiation, drugs, viruses, genetics
- Uniclonal neoplasm of myelopoietic stem cell
- Dev. Of leukemic cells (blasts) at myeloblastic stage
- Proliferation of blast cells

Blast cell proliferation:

- Inc. cell turnover
- Inc. purine catabolism—hyperuricemia—uric acid nephropathy
- Inc. BUN and Creatinine
- May lead to renal failure and anemia, etc.

Blast cell proliferation:

- Blast cell accumulation in BM
- Released into circulation-leukemic infiltration-splenomegally, lymphadenopathy, hepatomegally, CNS-HA, V, retinal hemorrhage, papilledema, cardiac conduction defects
- -crowds out developing erythrocytes, thrombocytes
  - Anemia, thrombocytopenia, granulocytopenia

Blast cell proliferation:

- Increased immature leukocye production
- Inc. metabolic rate
- Wt. Loss, weakness, pallor

Chronic Leukemia

- Lymphocytic (CLL)
  - Adults over 55
  - Sometimes occurs in younger adults
  - Rare in children
  - Present with lymphadenopathy, may be asymptomatic or a, fatigue, night sweats

Chronic Myelogenous Leukemia

- Myeloid (CML)
- Presence of Philadelphia chromosome
  - Mainly in adults, 30-50
  - Small number of children
  - B cells don't mature; may have decreased T_h
  - Present with fatigue, weight loss, weakness, anorexia