2: Benign Leukocytosis

Neutrophilia

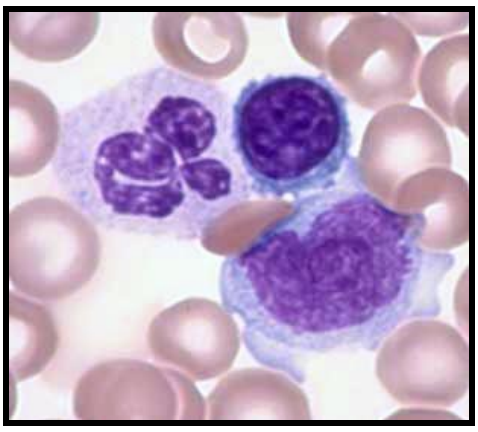
- Neutrophils fight infection, participate in inflammatory response, grow up and live in bone marrow, only 5% are in blood, normally only segmented neutrophils, half are marginated (cover around the vessel wall)
- Mature: segmented neutrophils
- Immature neutrophils (big blob of a cell)

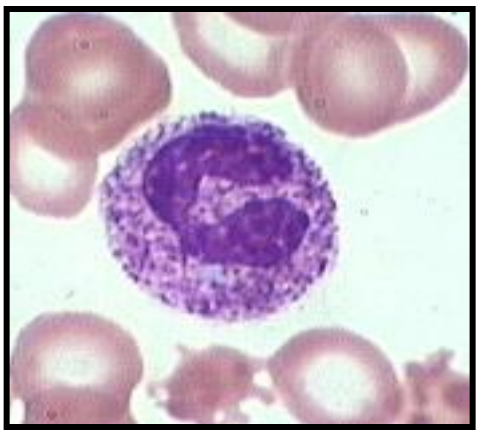
Causes of Mature Neutrophilia:

- Infection (bacterial)
- Inflammation
- Physical things (stress, hormones)

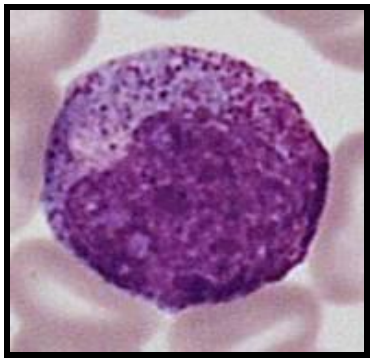
Toxic Changes:

- Seen only in infection
- 3 changes: toxic granulation, Dohle bodies (*dark blue/sky blue cause of RNA in cytoplasm*), cytoplasmic vacuolization (vacuoles that look like fat in cytoplasm, severe change, life threatening)
- Scariest: cytoplasmic vacuolization (left normal, right toxic)





Promyelocyte: just matures, won't divide, high concentration of granules



Causes of Immature Neutrophilia:

- Infection (bacterial)
- Inflammation
- Severe anemia
- Something filling up the marrow (can be bad)

3 Forms of Immature Neutrophilia:

- **Left Shift** (immature cells in the blood that shouldn't be there)
- **Leukemoid Reaction**
- **Leukoerythroblastotic reaction**
    - Due to something malignant or benign

Lymphocytosis

- Lymphocytes fight infection, participate in immunologic responses
- You'll have normal lymphocyte count! Varies a lot with age, bigger normal range in infants
- Normal immunophenotype in blood: T cell: 80%, B cell: 15%, NK cell: 5%

Types of Lymphocytosis: Mature and Reactive (funny looking)

Causes of Mature Lymphocytosis:

- Infectious lymphocytosis
- Bordetella pertussis (whooping cough)
- Transient stress

Causes of Reactive Lymphocytosis:

- Infectious MONO (Downey cells)
- Pediatric viral infection
- Viral Hep
- Immune disorders

Basophilia (BCML) BC…Mark's Love!

- **ALWAYS** due to **CML** (Chronic Myeloid Leukemia)

Eosinophilia

- **Esi the SAD Parasite**
- Skin disease, Asthma, Drugs, Parasite

Monocytosis (MIA)

- Infection, autoimmune disease, malignancy

3: Acute Leukemia

Hematologic Malignancies

Leukemia:

- Malignancy of hematopoietic cells
- Starts in the bone marrow, can spread to blood, nodes
- **Myeloid or lymphoid**
- **Acute Leukemia:**
    - Sudden onset, can occur in either kids or adults, fatal quickly without treatment, composed on immature cells (BLASTS)
    - Malignant proliferation of immature myeloid or lymphoid cells in the bone marrow cause by clonal expansion and maturation failure
    - Bad cause crowd out normal cells, inhibit function and attack into other organs
    - Symptoms of bone marrow failure are fatigue, infections, bleeding. Bone pain due to expanding marrow, organ infiltration (liver, spleen, brain)
    - Lab findings: blasts, leukocytosis, anemia, thrombocytopenia
- **Chronic Leukemia:**
    - Slow onset, ONLY adults, longer course, mature cells

Lymphoma:

- Malignancy of hematopoietic cells
- Starts in the lymph nodes, can spread to blood, marrow
- Lymphoid only
- Hodgkin (owl) or non-Hodgkin

Plasma cell disorders:

- Multiple myeloma (lots of plasma cells)

Diagnosis:

- Clinincal setting, morphology, immunophenotyping, molecular studies, cytogenetics
- Bone marrow biopsy
- Acute leukemias: mainly young cells, not many mature
- Chronic leukemias: a lot but look mature

AML Acute Myloid Leukemia

- Malignant proliferation of myeloid blasts in blood and bone marrow
- 20% cut off for diagnosis
- Many subtypes
- BAD PROGNOSIS

- AUER RODS (AML RODS)

M0 – M3 = Neutrophilic
M4 – M5 = Monocytic = brain involvement, gum involvment
M6 = RBC
M7 = Megakars (platelets)

Treatment of AML

- Chemo, bone marrow transplant

Prognosis

- Not good

Myelodysplastic Syndrome:

- Dysmyelopoiesis (cells look funny) and increased blasts
- May evolve into AML
- Usually older patients
- Asymptomatic or marrow failure
- Macrocytic anemia

ALL Acute Lymphoblastic Leukemia

- Malignant proliferation of lymphoid blasts in blood and bone marrow
- Classified by immunophenotype (B vs T)
- Common in children and prognosis is GOOD!
- T-lineage: bad
- B-lineage
    - B cell precursor ALL: better (most kids get this)
    - B cell ALL: bad (same thing as Burketts lymphoma) = starry sky pattern
- **Prognosis:** hyperdiploidy good!, under 1 and older than 10 bad, T is bad

4: Chronic Leukemia

CHRONIC MYELOPROLIFERATIVE DISORDERS:

- Malignant proliferation of myeoild cells (NOT blasts, but maturing cells) in blood/bone marrow
- 4 disorders: CML, PV, ET, MF
- Features common to all 4 disorders: occur only in adults, long clinical course, increase WBC with left shift, hypercellular marrow (stuffed wt cells), big spleen, Occurs only in adults, Long course

    - **Chronic Myeloid leukemia (most common)**
        - Neutrophilic leukocytosis, basophilia, philli chromosome, 3 clinical phases

- 3 Phases:
    - Chronic: 3-4 yrs, easily controlled, stable counts
    - Accelerated Phase: dead in months, unstable counts
    - Blast Crisis: now is acute leukemia, lots of blasts, dead in weeks
- Treatment of CML: Gleevec
- Prognosis: used to be 506 yrs but now who knows??

Polycythemia vera

- High RBC, make blood sludgy, different from secondary polycythemia

Essential thrombocythemia

- Very high platelet count in blood, different from secondary thrombocythemia

Myelofibrosis

- Panmyelosis (all myeloid cells proliferating like crazy), marrow fibrosis, extramedullary hematopoiesis, teardrop cells (spleen gets huge)

CHRONIC LYMPHOPROLIFERATIVE DISORDERS:

- Malignant proliferation of lymphocytes in blood/bone marrow, many disorders, CLL most important, ONLY in adults, long course (indolent but incurable) Difficult to treat with chemo since not dividing often/regularly

Chronic Lymphocytic Leukimea:

- Small, mature lymphocytes, WEIRD: B cells but CD5+
- Die usually from infection

5: Lymphoma and Myeloma

Lymphoma:

- Malignancy of hematopoitetic cells, starts in lymph nodes, spreads to blood, marrow. Lymphoid only. Hodgkin or non-Hodgkin.

Causes of Lymphadenopathy:

- Most common cause overall: benign reaction to infection
- Most common malignant cause: metastatic carcinoma

Non-Hodgkin Lymphoma:

- Malignant proliferation of lymphoid cells in lymph nodes, skips around, many subtypes, most are B cells
- Painless, firm lymphadenopathy, B symptoms weight loss, night sweats, fever
- Gingival/papaltal lesions
- LOW GRADE: older, incurable, small mature cells, non-destructive
- HIGH GRADE: children, aggressive, big ugly cells, destructive

Types of NHL

Low Grade:

Small Lymphocytic Lymphoma:

- Small mature lymphocytes, same thing as CLL, CD5+, long course, death from infection

MALT Lymphoma:

- Occurs in mucosa-associated lymphoid tissue, associated with Helicobacter pylori, early on can be treated with antibiotics.

Follicular Lymphoma:

- Small cleaved cells, grade 1,2,3, t(14:18) – IgH and bcl-2

Mycosis Fungoides / Sezary Syndrome:

- Skin lesions, blood involvement, cerebriform lymphocytes, T-cell immunophenotype

High Grade:

Diffuse Large-Cell Lymphoma:

- Large B cells, extranodal involvement, grows rapidly, bad prognosis

Lymphoblastic Lymphoma:

- Typical patient teenage male with mediastinal mass, lymphoblasts in diffuse pattern, same as ALL

Burkitt Lymphoma:

- Children, fast growing, starry-sky pattern, same as B-cell ALL

Hodgkins Lymphoma:

- Younger, contiguous spread, five suntypes, Reed-Sternberg cell, disease often localized, prognosis very good, danger is second malignacies

MULTIPLE MYELOMA:

- Malignant proliferation of plasma cells, monoclonal gammopathy, decreased normal immunoglobulins, osteolytic lesions
- Clinical features: weakness, infections, renal failure, bone pain, hypercalcemia
- Serum protein electrophoresis
- Treatment: chemo and radiation, bone marrow transplant, 5 yr survival with chemo only (20%)