HEMOPOIESIS

- **Hemopoiesis** is the formation, development and specialization of cellular elements into mature functional cells.
- There are 3 basic stages of hemopoiesis:
    - **Mesoblastic:**
        - Begins at 2^{nd} to 7^{th} week of gestation.
        - Embryonic
        - In yolk sac
        - Condensation of mesenchymal cells to form blood islands
        - Nucleated blood cells form
    - **Hepatic:**
        - Begins at 12^{th} to 16^{th} week of gestation
        - In liver, thymus and spleen, lymph nodes somewhat latter
        - Forms anucleated RBCs
    - **Myeloid:**
        - 20^{th} week to adulthood
        - In bone marrow
        - Begins with establishment of ossification centres in bone
        - All blood cell types found in adults can be produced by the bone marrow.

Anatomy:

- Active marrow space in child of about 15kg is 1000 to 1400g, total marrow is 1600cc.
- Adult: active marrow space is 1200-1500 g, total marrow is 2600 to 4000cc.
- Large spaces in the neonate progressively decrease with age with the marrow becoming increasingly filled with fat.
- Function of fibroblastic cells:
    - Supportive framework
    - Production of essential hemopoietic colony stimulating factors.

Physiology:

- Maintenance of a constant number of red cells, white cells and platelets requires regulatory mechanisms:
    - $3\text{-}11 \times 10^{11}$ WBCs
    - $4.5\text{-}5.5 \times 10^{12}$ RBCs
    - $150\text{-}450 \times 10^{9}$ platelets

Origins of hemopoiesis:

- Single pluripotent (multipotent) stem cell is capable of:
  - Giving rise to many committed progenitor cells
  - Self-renewal
- Committed progenitor cells:
  - Form differentiated recognizable precursors of the specific types of blood cells
  - Are limited in proliferative potential and are not capable of indefinite self-renewal 'die by differentiation' and are repopulated on influx from pluripotent cell pool
  - Proliferative potential and differentiation of stem cells and committed progenitor influenced by:
    - Adventitial cells
    - Alpha HGF – produced in reaction to circulating levels of a particular differentiated cell type.

Regulation of hemopoiesis:

- Large reserve
  - 2 $x10^{11}$ RBC/day and increased x4 when required.
  - WBC capacity can be increased x12 in normal
- Maintenance by regulatory substances – HGF
  - Properties
  - Lineage map
  - Cytokine sources and actions
  - Various maturation pathways

Leucopoiesis:

1. Myeloblast
2. Promyelocyte
3. Metamyelocyte
4. Band/stab
5. Polymorphonuclear granulocyte
   - Eosinophil
   - Basophil
   - Neutrophil
   - Monocyte* (produced in this manner, but is not a granulocyte)

Erythropoiesis:

- Proerythroblast:
    - Loss of nucleolus, sideroblastic granules
- Basophilic erythroblast
- Polychromatic normoblast
- Intermediate (Orthochromatic)
    - Loss of nucleus
- Reticulocyte
    - Matures in 2-3 days
- Mature erythrocyte
    - No synthetic activity
    - Hemoglobinisation in 2 to 4 days.

Thrombopoiesis:

1. Pluripotent stem cell
    - Colony-forming unit (CFU)
    - Erythropoietin
    - Thrombopoietin
2. Megakaryocyte precursor
    - 4 to 8 to 16 to 32 nuclei
3. Megakaryocyte

Lymphopoiesis

1. Lymphoid stem cell
2. Prolymphoblast
3. Lymphoblast
4. Lymphocyte.

Hemopoietic growth factors:

- Colony stimulating factors:
- Cytokines
    - Interferons
    - Interleukins
- HGFs
    - FIK2 ligand
    - GM-CSF
    - G-CSF
    - M-CSF
    - Erythropoietin
    - Thrombopoietin

- Sources of HGFs
    - Fibroblasts
    - Endothelial cells epithelial cells
    - Activated T cells
    - Monocytes, macrophages