Type of Human Stem Cells

① Totipotent - cells present a few hours after fertilization
↳ can develop into any cell type, incl. embryo → fetus
★ most versatile type of stem cell

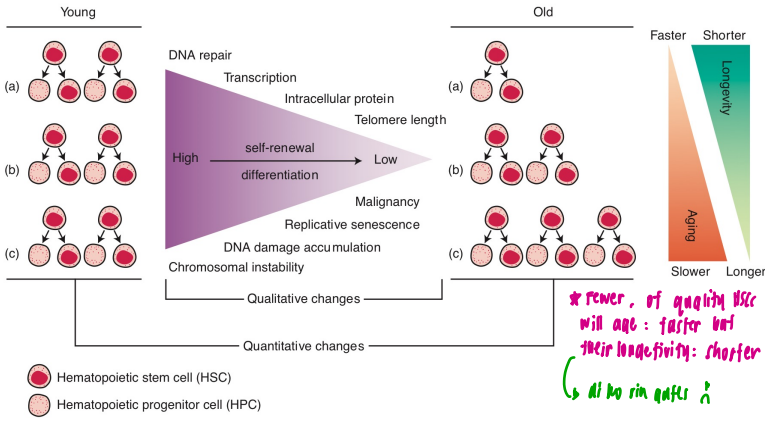
② Pluripotent - cells present several days after fertilization
↳ can develop into any cell type, exc. fetus

③ Multipotent - derived from pluripotent cells
↳ found in adults → limited to specific types of cells to form tissues

★ HSCs: self-renew & multipotential differentiation

Cellular elements of BM

- Stem cell plasticity - stem cells are capable of making replacement cells
  ↳ adults have a reservoir of "master cells" inside the BM that are capable of rebuilding any damaged tissue → Multipotent Adult Progenitor Cells (MAPC)
  ★ Telomerase keep MAPCs from aging
- Pluripotent stem cell - first in the sequence of hematopoietic cell generation and maturation
- multipotent hematopoietic stem cell - progenitor of all blood cells



★ fewer, of quality HSC will age: faster but their longevity: shorter
↳ dl bo rin gatis ?

★ Quantitative changes ← a: decrease; b: remains the same; c: increases

★ Qualitative changes: HSC quality decreases w/ age due to:
- ↓ capacity for DNA repair & transcription
- ↓ [intracellular proteins]
- cross-linking of intracellular molecules
- shortened telomere

Hematopoietic growth factors

- Each HGF is encoded by a single gene

EPO: Chr 7

GM-CSF, IL-3, M-CSF: Chr 5q

G-CSF: Chr 17

TABLE 4.2 Characteristics of Human Hematopoietic Growth Factors

Growth Factor	Cellular Source	Progenitor Cell Target	Mature Cell Target
Erythropoietin	Peritubular cells of the kidney, Kupffer cells	CFU-E, late BFU-E, CFU-Meg	None
IL-3	Activated T lymphocytes	CFU-blast, CFU-GEMM, CFU-GM, CFU-G, CFU-M, CFU-Eo, CFU-Meg, CFU-Baso, BFU-E	Eosinophils, monocytes
G-CSF	Monocytes, fibroblasts, endothelial cells	CFU-G	Granulocytes
M-CSF	Monocytes, fibroblasts, endothelial cells	CFU-M	Monocytes
GM-CSF	T lymphocytes, monocytes, eosinophils, monocytes, fibroblasts, endothelial cells	CFU-blast, CFU-GEMM, CFU-GM, CFU-G, CFU-M, CFU-Eo, CFU-Meg, BFU-E	granulocytes

G-CSF, granulocyte colony-stimulating factor; M-CSF, macrophage colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; CFU-blast, colony-forming unit-blast; CFU-GEMM, colony-forming unit granulocyte, erythrocyte, monocyte, and megakaryocyte; CFU-GM, colony-forming unit-granulocyte and macrophage; CFU-EO, colony-forming unit-eosinophil; CFU-Meg, colony-forming unit-megakaryocyte; BFU-E, burst-forming unit-erythroid; CFU-G, colony-forming unit-granulocyte; CFU-M, colony-forming unit-macrophage; CFU-E, colony-forming unit-erythroid; CFU-Baso, colony-forming unit-basophil.

Bone marrow exam

- In adults, accounts for: 3.4-6.9% of body weight
  1600 to 3700 g
  30-50 mL / kg

★ produces ~ 6 billion blood cells / kg per day

TABLE 14.1 Indications for Bone Marrow Examination

Indication	Examples
Neoplasia diagnosis	Acute leukemias Myeloproliferative neoplasms such as chronic leukemias, myelofibrosis Myelodysplastic neoplasms such as refractory anemia Lymphoproliferative disorders such as acute lymphoblastic leukemia Immunoglobulin disorders such as plasma cell myeloma, macroglobulinemia Metastatic tumors
Neoplasia diagnosis and staging	Hodgkin and non-Hodgkin lymphoma
Marrow failure: cytopenias	Hypoplastic or aplastic anemia Pure red cell aplasia Idiosyncratic drug-induced marrow suppression Myelodysplastic syndromes such as refractory anemia Marrow necrosis secondary to tumor Marrow necrosis secondary to severe infection such as parvovirus B19 infection Immune versus amegakaryocytic thrombocytopenia Sickle cell crisis Differentiation of megaloblastic, iron deficiency, sideroblastic, hemolytic, and blood loss anemia Estimation of storage iron to assess for iron deficiency Infiltrative processes or fibrosis
Metabolic disorders	Gaucher disease Mast cell disease
Infections	Granulomatous disease Miliary tuberculosis Fungal infections Hemophagocytic syndromes
Monitoring of treatment	After chemotherapy or radiation therapy to assess minimal residual disease After stem cell transplantation to assess engraftment

- Bone marrow puncture is prohibited in px w/ coagulopathies, exc. thrombocytopenia

★ Red marrow is gelatinous & amenable to sampling

Bone marrow spx

① BM aspirate - obtained by BM aspiration
- ✓ identify the types & proportions of hematologic cells
- ✓ look for morphologic variance

② Core biopsy - obtained by trephine biopsy
- ✓ BM architecture: spatial relation bet. hematologic cells to fat connective tissue bony stroma
- ✓ cellularity estimation

TABLE 14.2 Advantages and Disadvantages of the Marrow Aspirate Smear and Marrow Core Biopsy

	Marrow Aspirate Smear	Marrow Core Biopsy
Advantages	Fast No need for decalcification of the specimen Quantification of cell type differential count Material for ancillary studies (flow, molecular)	Ability to analyze both cells and stroma Represents all cells Explains dry taps ★ focal lesions bony spicules
Disadvantages	May not represent all cells Dry tap in cases of fibrosis or hypocellularity Does not represent architecture Inability to analyze the stroma	Slow processing Decalcification precludes certain ancillary studies Inability to perform quantitative differential count

Collection sites

- Posterior iliac crest - adequate red marrow isolated from other structures
  ★ preferred
  ✓ aspiration
  ✓ core biopsy
- Anterior iliac crest - same as posterior cortical bone is thicker for px who can only lie supine
- Sternum - only 1cm thick
  risk of piercing through the sternum
  ✓ aspiration
  x core biopsy
- Anterior medial surface of tibia - children younger than 2 years old
  ✓ aspiration
  x core biopsy
- Spinous process of vertebrae, ribs - only used when suspicious lesions are noted w/ a radiograph