Hematology : Lec 1.

* Body fluids :

amount depends on age, gender & amount of adipose tissue. In the average 70 kg man, the amount of body fluids = 60% of body weight (42L)

Fluids → $\frac{2}{3}$ Intracellular , $\frac{1}{3}$ Extracellular [80% Interstitium, 20% blood.

↳ a comparison between the composition of IC & EC fluids.

ECF : most abundant → cation : Na^+ , anion : Cl^-

ICF : most abundant → cation : k^+ , anion : proteins and phosphates.

] this difference is maintained thro the action of Na^+/k^+ pump (keeping Na^+ out and k^+ in).

- usually both parts of ECF (interstitial & plasma) are very similar in their components except in protein content.
  plasma has much more protein anions
  the difference is due to capillaries' impermeability to proteins which contains them in the plasma.
  As a result to this difference, colloid osmotic pressure is exerted by blood plasma.

↳ fluid filtration and reabsorption at the level of capillaries.

At the arterial end : Blood hydrostatic pressure pushes fluids out of capillaries mainly
↳ BCOP is too small to reverse the filtration, we also have IFOP favoring filtration but its too small so it's effect isn't major.

At the venous end : BCOP pulls fluid into capillaries (reabsorption).
↳ there's BHP at the venous end by it can't counteract BCOP.

this process of reabsorption & filtration, diffusion & osmosis allows for continual exchange of water and solutes between body compartments yet the volume of fluid in each compartment remains stable.

* Blood Components :

slide 7-10. (check from slides)

Plasma Proteins : imp. for creating colloid osmotic pressure and plasma's buffer capacity.

Albumin : non specific binding (bilirubin).

Fibrinogen: clotting

Globulins: α & β : specific binding (thyroid hormone, cholesterol & iron).
blood clotting & Angiotensinogen.
γ : Antibodies → only plasma protein synthesised by WBCs not the liver like all the others.

* Hematocrit or Packed Red Cell Volume = $\frac{\text{volume of RBCs}}{\text{volume of blood}} \times 100\%$ → fraction of blood composed of RBCs.

males : 40-54 %.
females : 38-46 %.
→ difference is due : 1. testosterone stimulating hematopoeisis.
2. women lose blood during menstruation.

↳ Conditions that mess up the hematocrit.

higher in dehydration
lower in pregnancy due to higher plasma volumes, RBCs volume increases but less than plasma.

] low hematocrit = Anemia
high hematocrit = polycythemia.

→ HCT < PCV (slightly less).

In hematocrit calculation (automated) there's no trapped plasma which can occur in spun PCVs.

* General Roles of Blood:

Transport : gases, nutrients, hormones & waste.
Regulate : pH, temperature, water content (osmotic pressure).
Protect : clotting, WBCs, antibodies

* Hemopoiesis

Early fetal life : yolk sac, later : liver, spleen, thymus & lymph nodes.
3rd trimester & : Red bone marrow
throughout life with age, red bone marrow is restricted in the axial skeleton, pectoral & pelvic girdles and proximal epiphyses of humerus & femur.

pluripotent hematopoietic stem cells → myeloid SC → different CFU

population of adult SCs found in bone marrow that are multipotent and able to self-renew.

myeloid SC: RBCs, platelets, monocytes, neutrophils, eosinophils & basophils.

lymphoid SC: lymphocytes and NK cells.

- similar to pluripotent SCs, but they're committed to certain cell linage
- when cultured they give colonies of specific types of blood cells.

↳ stem cells in bone marrow : reproduce themselves, proliferate & differentiate
formed element won't divide once they leave the bone marrow except lymphocytes.

- Growth and reproduction of different types of SCs are controlled by proteins called growth inducers.
  ex IL-3 : promotes growth of committed SCs.
  Hemopoietic GFs for each cell type
  RBCs : Erythropoietin
  WBCs : Colony stimulating factors and ILs.
  platelets : Thrombopoietin.

Hematology : Lec 2

* Red Blood Cells

general features : lack nucleus , mitochondria and other organelles → can't synthesize new components.
key enzymes : carbonic anhydrase. ⅓ glycolytic enzymes → has glycogen.
Oligosaccharides in plasma membrane → ABO and Rh blood typing.
Production = destruction (2 million / sec).
5.2 million / mm^3 in men , 4.7 million / mm^3 in women.

features that help in gas exchange : Hemoglobin : O_2 carrying protein.
Biconcave : ↑ S.A , makes the cell thinner so O_2 would diffuse rapidly from innermost pt. to exterior
strong + flexible plasma membrane : go thro narrow capillaries without rupturing
extremely pliant.

8 um in diameter.

* Function of RBCs :

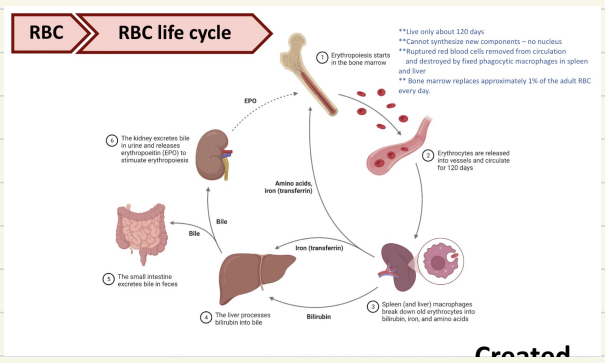
Oxygen and CO_2 transport thro hemoglobin.
Contains a large amount of carbonic anhydrase which increases the rate of its rxn multiple folds [$CO_2 + H_2O \rightleftharpoons HCO_3^- + H^+$]
- RBCs contribute to the transport of CO_2 in 2 ways : carrying it on hemoglobin , converting it rapidly into HCO_3^- which allows the water of the blood to transport large amounts of CO_2 as HCO_3^- to the lungs to be expelled.

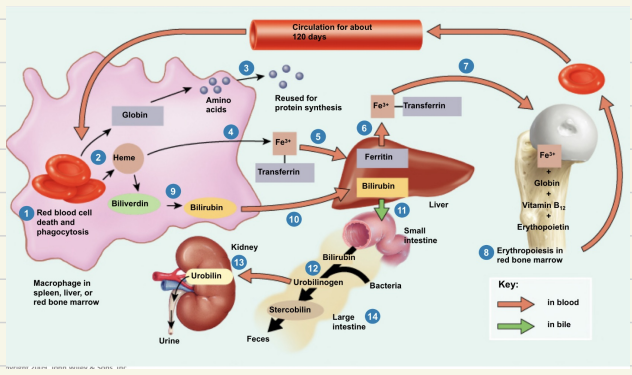
Hemoglobin (as most proteins) is responsible for the buffering power of the blood.

* Hemoglobin.

- a pigment / naturally coloured : due to iron its reddish w/ O_2 and bluish when deoxygenated.
- made of 2 α-β globulin units combined with heme (porphyrin ring + iron). → most common adult form (hemoglobin A).
- Iron binds O_2 reversibly.
- transport 23% of CO_2 as it bind to A.A of hemoglobin.
- normal range 14 g/dL female , 15.5 g/dL male.

* RBCs life cycle.





RBCs rupture when they pass thro narrow spots bcuz the membrane becomes fragile. they can self destruct in the spleen as they pass thro its red pulp (3 um).

Break down products.
Globin's AA. reused.
iron reused
heme → bilirubin in urine
stercobilin in feaces.

↳ overview : Erythropoiesis

Red bone marrow as proerythroblast , near the end the cell ejects the nucleus → reticulocyte — 1-2 days → RBC.
During reticulocyte maturation : remaining basophilic material disappears , and it continues to make hemoglobin for the 1-2 days period.
Total changes: Hemoglobin accumulation , nuclear condensation and reabsorption of ER.

↳ Reticulocyte count < 2 % in adults.

$$= \frac{\text{no. of Reticulocytes}}{\text{no. of RBCs}} \times 100\%$$

it helps in diagnosing and typing Anemia :- Decreased : Aplastic Anemia
Increased : Hemolytic Anemia , post hemorrhage.

↳ in the state of anemia , reticulocyte % is not a true reflection of production.
we can't apply a correction factor as the percentage is already increased
→ new reticulocytes added to low Hct → increasing the percentage.

↳ Corrected Reticulocyte count = Reticulocyte * $\frac{\text{Act. Hct}}{\text{Nor. Hct}}$

↳ Vitamin Requirements :-

maturation of RBCs requires vit B_{12} + folic acid which are essential for synthesis of TTP
deficiency in either one → abnormal or diminished DNA → failure of nuclear maturation & cell division during erythropoiesis.
resulting in the production of large cells (macrocytes) w/ flimsy membranes.
↳ capable of carrying O_2 but short life span due to their fragility.

↳ Regulation of Erythropoiesis : Erythropoietin.

Low O_2 levels don't act directly on red bone marrow to increase RBCs production , instead hypoxia stimulates the kidneys to produce EPO.
EPO is a glycoprotein (90% in kidneys , 10% in liver) that stimulates production of proerythroblasts from hematopoietic SCs more rapidly.
↳ hypoxia → ↑ EPO so tissue oxygenation is an essential regulator of RBC production yet not directly.
conditions that cause hypoxia : Anemia (hemorrhage) , high altitudes , prolonged cardiac failure and lung disease [failure of O_2 absorption from blood as it passes in the lungs due to decreased blood flow.
↳ renal failure slows EPO release → ↓ Hct.
Usually negative feedback balances production and destruction

Hematology : Lec 3

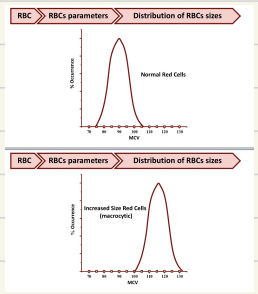
* Hb , RBC count , Hct decline after birth due to decreased EPO + transient hemolysis.
* Hemoglobin decrease in older adults is due to ↓ androgen in males and ↓ estrogen in females.
* Asymptomatic elderly adults with anemia → iron deficiency and anemia of chronic disease.

* RBCs parameters

1. MCV : mean cell volume → avg volume (size) of RBCs

$$= \frac{\text{Hct [\%] x10}}{\text{RBC count million/uL}}$$

80 - 100 normocytic
> 100 macrocytic , < 80 microcytic.



bell - shaped distribution.

2. RDW : RBC distribution width → RBC size variation.

$$= \frac{sd}{MCV} * 100$$

high RDW → large variation in sizes
low RDW → homogenous sizes.

- high RDW associated w/ anemias of iron , B12 and folate deficiency.

3. MCH : mean cell Hb → avg. Hb content in an RBC.

$$= \frac{Hb * 10}{RBC\ count}$$

normochromic 30 - 34
hypochromic < 30

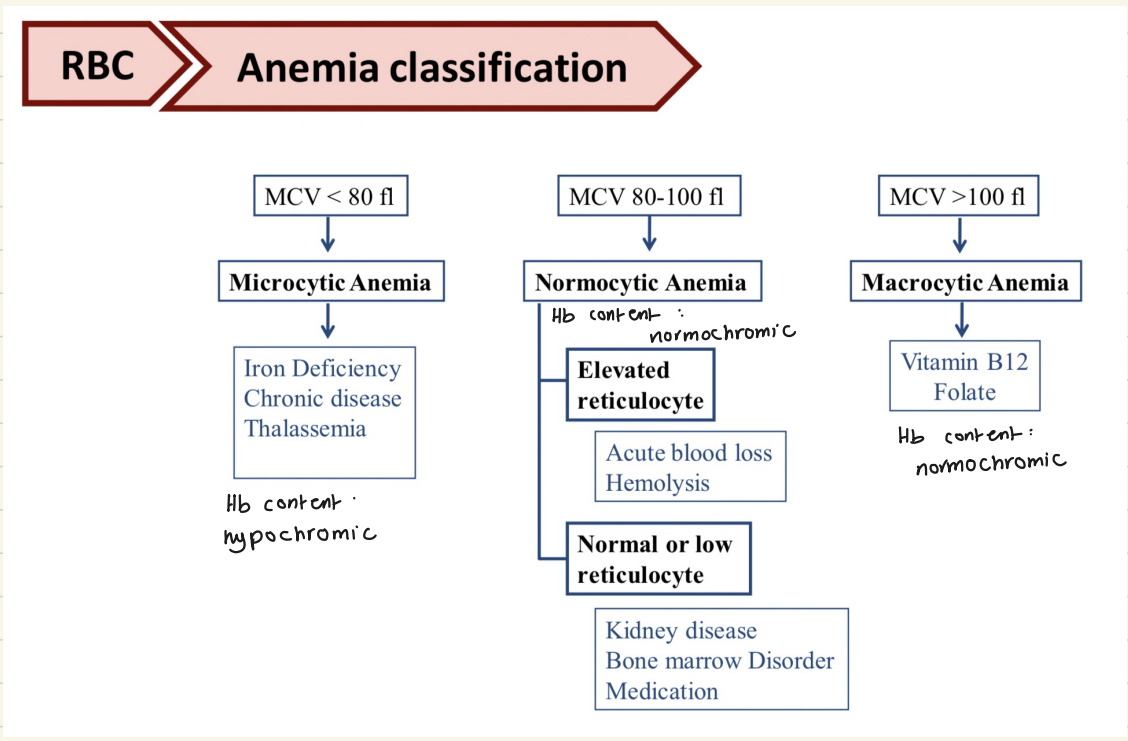
- low MCH is seen as large central pale area (more than one third).

4. MCHC : mean cell Hb concentration → avg. Hb concentration in an RBC

$$= \frac{Hb * 10}{Hct}$$

it's a ratio between amount of Hb to cell volume.
normochromic 30 - 36
hypochromic < 30

* Anemia → ↓ Production → less EPO , BM damage , Iron deficiency. low RI
→ ↑ Destruction → Blood loss and hemolysis high RI



↳ effects of Anemia on CVS

↓ blood viscosity and resistance to blood flow on peripheral BV.
then greater quantities of blood return to the heart
↳ greater cardiac output
↳ more pumping workload on the heart.

Hematology : Lec 4

* Thrombocytes

- formed in BM from megakaryocytes.
- ½-life in blood is 8-12 days with normal concentration of 150 000 - 450 000 /μL
  then they get eliminated from blood by tissue macrophages in spleen.

→ cytoplasmic characteristics :-

- no nuclei
- Residues of ER and Golgi's apparatus.
- Enzyme systems for PG synthesis.
- GF for vascular endothelial cells, vascular smooth muscle cells and fibroblasts.
- contractile proteins : actin, myosin ⅓ thrombosthenin.
- Mitochondria for ATP
- Fibrin stabalizing factor.

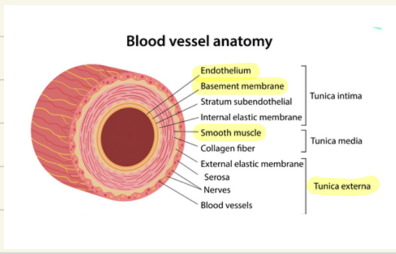
→ membrane characteristics.

- coat of glycoproteins → repels adherance to normal endothelium but causes adherance to injured areas of vessel wall.
- alot of phospholipids → activate many steps of blood-clotting process.

* Thrombocytopenia : decreased platelets.

- thousands of small hemorrhagic areas develop under the skin and throughout internal tissue, they appear red or purple.

symptoms :- cutaneous and mucosal bleeding, easy bruising, petechiae, ↑ bleeding time.



* Hemostasis : prevention of blood loss thro :

1. vascular constriction.
2. Platelet plug
3. blood clot as a result of coagulation.
4. Growth of fibrous tissue into the clot to close the hole permenantly.

- if the hole is small it's closed by a platelet plug rather than clot.

* bleeding occurs when there's a defect in B.V wall and pressure inside must be greater than outside for blood to flow out.
* small vessels are ruptured by minor traumas daily but it's handled by inherent body hemostatic mechanisms.
  ↳ if the vessel is larger these mechanisms are not adequate.
* bleeding from severed arteries is worse than venous bleeding, as arterial blood has higher pressure so the bleeding is more profuse.

First Aid → Arterial bleeding : apply pressure that is more than arterial blood pressure to minimize bleeding until it's fixed surgically.

→ Venous bleeding : raise bleeding part to minimize gravity's effect. If not enough, add mild external pressure

[1] vascular constriction

immediatly after trauma → S.M contraction to reduce blood flow out of the vessel.

contraction results from :

local myogenic spasm, nerve reflexes, local autocoid factors from injured tissue, vascular endothelium ⅓ platelets.

this spasm lasts for minutes - hours until platelet plug and coagulation take place.

[2] Platelet Plug formation

1. Adhesion : platelets don't adhere to intact endothelium, only to damaged endothelial cells and collagen on subendothelium.
   adherance occurs thro a plasma protein called vWF → bridge between platelets and injured vessels.
   ↳ vWF : secreted by megakaryocytes, platelets and endothelial cells.
2. Secretion : release of platelet granules thro formation of numerous irradiating pseudopods
   they secrete large amounts of ADP and thromboxane A2 [which activates platelets and cause vasoconstriction] respectively.
   → ADP + TXA2 also activate adjacent normal endothelium to produce prostacyclin and NO
   these compounds inhibit platelets so that the PLug is restricted to the lesion.
3. Aggregation : Platelet to Platelet cohesion

Imp. roles of platelet plug aside from physically sealing the tear :-

1. Actin-myosin complex in aggregated platelets contracts to compact ⅓ strengthen the plug
2. Release powerful vasoconstrictors.
3. other chemicals to enhance blood coagulation.