HEMATOLOGY [Dr. Lakshmy Maam]

28/11/2022 Monday

circulating body fluids

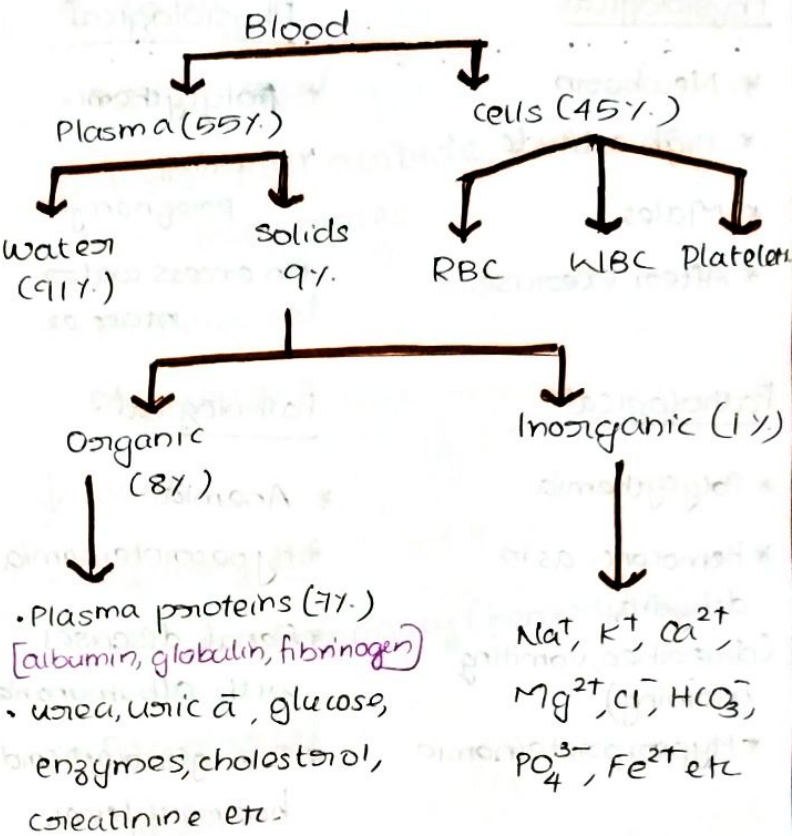
Blood — Lymph.

➡ Hematology: study of body fluids like blood & lymph.

➡ Functions of blood
- Transport of respiratory gases
- Nutritive fn
- Excretory fn
- Protective fn (Defense)
- ā-base balance
- water balance
- Transport of substances like hormones, enzymes, etc.
- Maintanence of bp & osmotic pressure
- storage fn (Reservoirs)
- Regulan of body temp

➡ Blood
- → unique CT : fluid
- → Red, opaque & alkaline [pH = 7.4] [7.38 - 7.42]
- → Blood
  - Arterial → Bright red → due to → Oxyhaemoglobin
  - Venous → Dark red → Reduced hemoglobin (slightly bigger RBC)
- → Vol. of blood = 5-6 L, ⇒ 8% of body wt.

Composn of blood



Physical properties of Blood
- → Red & opaque → pH = 7.4
- → Salty → Sp. gravity ↳ 1.050 - 1.060
- → viscosity - 3.5 - 5.4 times water.

➡ Specific gravity

⇒ $\frac{\text{wt. of blood}}{\text{wt. of equal vol. of water}}$ @ 4°C

[density of water max @ 4°C]

* determined by hemoglobin & plasma protein conc.

Factors affecting sp. gravity.
* RBC count
* Hemoglobin conc.
* Plasma protein conc.
* water content of blood

↑ sp gravity & viscosity

Physiological
* Newborn
* High altitude
* Males
* After exercise

Pathological
* Polycythemia
* Hemoconc. as in dehydration (diarrhoea, vomiting burning)
* Hyperproteinemia

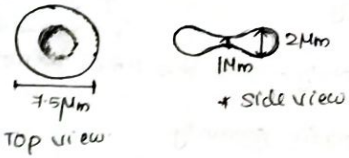
↓ sp gravity & viscosity.

Physiological
* Females
* During pregnancy
* In excess water intake ex.

Pathological.
* Anemia
* Hypoproteinemia
* Renal diseases with albuminuria
* ↑ in glucocorticoid hormone level.

RBC [Erythrocytes]

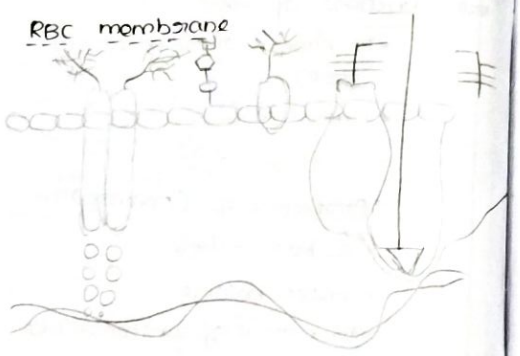
Morphology of RBC



→ Biconcave / dumbell shaped.
→ 7.2-7.5 μm in diameter, 2 μm thick @ periphery & 1 μm thick @ centre
→ non-nucleated, no organelles.
→ Red colour due to hemoglobin.
→ Blood gp. antigens present.
→ 1/3rd central pallore.

Advantages of biconcave shape
* ↑ SA to vol. ratio
* flexible, can squeeze through capillaries ≈ 3 μm in dia.
* mito. ⇒ x ⇒ does not consume O_2 they carry.
* can change vol. without affecting the integrity of membrane

RBC membrane



- lipid bilayer & protein layer
- lipid bilayer - phospholipid & cholesterol
- Integral proteins
- Band 3 protein [Cl -- HCO_3 - exchange]
- Glycophorins - rich in sialic ā, provide -ve charge to RBC.
- Blood gp antigens, Rh protein & various ion channels.
- Membrane skeleton - Spectrin, Ankyrin, actin.
- Structural integrity & maintain shape of RBC.
- Hereditary spherocytosis
  ↳ spectrin / ankyrin deficiency
- Spherical & fragile RBC - hemolysis

Composn of RBC
- 65% of water, 35-40% solids. 90% haemoglobin
- others: proteins, phospholipids, cholesterol & ions.
- Glutathione (antioxidant) : maintain integrity of RBC membrane
- No protein or enzyme synthesis/ no cell division
- Enzymes of glycolytic pathway (anaerobic - ATP)
  [2,3 DPG - formed in glycolytic pathway has got a role in O_2 transport]
- Enzymes like carbonic anhydrase, methemoglobin reductase
  Ferric ↓ → Ferrous

Fns of RBC
- Transport of respiratory gases
- Buffer system (Hb)
- Blood gp. antigen are present on the red CM.
- contributes to the viscosity of blood.

Metabolism of RBC (self study)

RBC count
- Birth :- 8 - 10 millions / cumm
- Infants :- 6 - 8 millions / cumm

Adults
- Male :- 4.5 - 5.5 millions (5.4)
- Female :- 4 - 5 millions (4.8)

Variations in count

↑ count
- Physiological
  at birth, high altitude, exercise, after food, males.
- Pathological
  Polycythemia.

↓ count
- Physiological
  Females, pregnancy (hemodilution)
- Pathological
  Anemia.

29/11/2022 Tuesday

Rouleaux formation
Tendency of RBC to pile one over other like a pile of coins; due to its particular disc shape.

Why RBC does not attain disc shape during blood flow?
→ constant flow
→ -ve charge repel (due to sialic ā) (zeta potential)

Properties of RBC
- Rouleaux formation
- ESR
- PCV
- Fragility of RBC.

→ Doesn't occur in normal circulation.

↳

ESR [Erythrocyte sedimentation rate]

It is the depth in mm of clear plasma measured when a vertical column of anticoagulated blood is kept undisturbed for a period of 1 hr.

- 3.8% of sodium citrate is used as anticoagulant
- Males - 3 - 5mm at the end of 1st hr.
- Females - 5 - 8 mm at the end of 1st hr.

ESR [stages]

Aggregation → Sedimentation → Packaging

RBC density is > plasma

ESR determinants

Rouleaux forma → RBC count

Factors affecting ESR

Plasma factors

- Plasma proteins
- Albumin : ↓ ESR
- Globulin & fibrinogen : ↑ ESR (favour RF)
- Cholesterol ↑ ESR
- Lecithin ↓ ESR

Cellular factor

- When RBC count ↑ ESR ↓
- In all anemias ESR ↑
- Except in sickle cell anaemia & Spherocytic anaemia [altered morphology ↓ ESR]

Technical factors

- ↑sed temp · slanting posn } ↑ ESR
  more than 1 hr.

Variation in ESR

↑ ESR	↓ ESR
Physiological	Physiological
• Females	• Males
• Pregnancy	• Newborns
Pathological	Pathological
• Anemia	• Polycythemia
• Infection, TB	• Sickle cell anemia
• Malignancies	• Spherocytosis
	• Hypofibrinogenimia

✕ Clinical significance of ESR

↳ has prognostic value.

↓

whether the treatment is effective & patient is improving his condn.

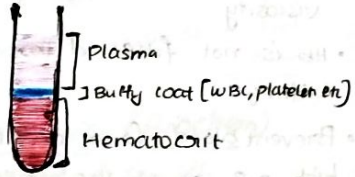
- Gravitational force helps in sedimentation

PCV [Packed cell volume]

- PCV refers to the cellular elements [RBCs, WBCs & platelets] in the whole blood.
- Ratio of vol. of RBCs to the vol. of whole blood.
- 3000 rpm for 30 mts - centrifuge
- "Double oxalate" - anticoagulant

ammonium oxalate → swelling of cell

Potassium oxalate → shrinking of cell



PCV (Hematocrit)

① Packed red cells in the bottom:

PCV

Males : 45 ± 7 %

Females : 42 ± 7%

② WBCs & platelets in middle

- Buffy coat normal : 1 mm
- 1mm almost equals to 10K WBCs

③ Plasma

- Topmost layer

Force : centrifugal force

~~Plasma layer~~ : ~~normal~~

Plasma layer

- Normal :- Straw coloured.
- Hemolysis :- Red (rupture of RBC)
- Jaundice :- Deep yellow.
- Lipemia :- Milky & opaque

PCV in ↑sed in :

- High altitude
- Newborns
- Males
- Polycythemia.

Hemoconcn :- Dehydration, diarrhoea [water content ↓]

PCV is ↓ed in pregnancy, females & Anemia.

FRAGILITY OF RBC

Due to endosmosis

- ↑ O. fragility - Hereditary spherocytosis
- ↓ O. fragility - sickle cell anemia, iron deficiency anemia. ⇓ microcytic anemia.

✕ Though O. fragility ↓ in sickle cell anemia, mechanical fragility is ↑.

"Fragility of RBCs means susceptibility of RBCs to break or burst

Hemolysis : rupture of RBCs & release of Hb.

Fragility may be of diff. types.

① Osmotic :- hypotonic soln [0.75% to 0.25%]

② Mechanical :- capillaries, membranes/ shape defects.

③ Chemical :- Ether, alkali, poison, toxins.

01/12/2022 Thursday

HEMOGLOBIN 8-9am

Oxygen carrying pigment in RBC.

- Non-protein part - Heme ↓ iron + porphyrin
- Protein part - Globin
- Globin part is formed by 4 polypeptide chains (2 pairs)
- 4 types of PP: α, β, γ, δ chains.

Normal values

In child & elderly present

- Male - 14-18 g/dl
- Female - 12-16 g/dl
- Newborn - 20-23 g/dl

Haemoglobin
- Haem
  - Iron
  - Porphyrin
- Globin
  - 2 α chains
  - 2 β chains.

Structure of Hemoglobin

Fe → normal → Ferrous
→ abnormal → Ferric
↳ methemoglobin

Functions of Hb

① Transport of O_2: from lungs to tissues. X fill in
(1 gm Hb carries 1.34 ml oxygen)
1 molecule of Hb can carry 4 molecules of O_2.
Hb combine loosely & reversibly with O_2

② Transport of CO_2 from tissues to the lungs.

③ Acid-base balance: Hb is an excellent buffer

What are the advantages of carrying Hb inside RBCs? Asked for practicals

- Prevents rapid destruction of Hb
- Prevent marked ↑ in plasma viscosity
- Hb is not filtered through the kidneys
- Prevent blood from exerting a high o.p across the capillary wall (osmotic pressure)

Types of Hb

A. Normal	B. Abnormal
Adult	HbS
Fetal	HbC
Embryonic	Hb D
	Hb E

Unstable Hb (Heinz bodies)

Hb A: 97% of adult Hb	$\alpha_2\beta_2$
HbA_2: <3% of adult Hb	$\alpha_2\delta_2$
Hb F: Fetal Hb	$\alpha_2\gamma_2$
Embryonic Hb -	
Gower 1	$\zeta_2\varepsilon_2$
Gower 2	$\alpha_2\varepsilon_2$
Hb Portland	$\zeta_2\gamma_2$

Fetal Hb

- Hemoglobin F is $\alpha_2\gamma_2$
- High O_2 affinity.
- Short ½ life span of 1-2 weeks.
- HbF disappears by age of 6 months
- Persistence after 6 months: disorders of HbA synthesis
- Minor fetal Hb - Hb Barts - γ_4 (chances of child death)

- 200-250 times more affinity to Hb than oxygen → hypoxia

⑤ Meth Hb: ~~Fe~~ ~~Fe~~

$Fe^{2+} + Fe^{3+}$ .... can't carry O_2 when Hb is exposed to drugs or oxidising agents like K^+ ferricyanide

⑥ Sulf Hb: Rn b/w Hb and H_2S (in drugs)

⑦ Glycosylated Hb (HbA1c)

- Glucose attatched to terminal valine of Beta chain of HbA
- Amount is proportional to blood glucose conc.
- Normal < 6%.
- Levels of HbA1C indicates glycemic state of an individual for the past 3 months.

6th lysine HbC
6th glutamine HbS

Heme synthesis - (Biochem)
Factors needed for Hb synthesis

- Amino ā - for globin formation
- Metals: Iron, Manganese, Copper, cobalt, Nickel
- Vit B_{12}, Folic ā - synthesis of NA (nucleic ā)
- Vit C helps in Fe absorption
- Heme catabolism → Biliverdin & Bilirubin

Derivatives of Hb (Rn of Hb)

practical X-Imp

① OXY Hb: $Hb + O_2 \rightarrow HbO_2$ (reversible)
* 1 Hb binds with 4 O_2 molecules.

② Deoxygenated Hb (Reduced Hb):
$HbO_2 \Rightarrow Hb + O_2$

③ Carbamino-Hb: $Hb + CO_2 \Rightarrow HbCO_2$

④ Carboxy Hb: $Hb + CO \rightarrow COHb$
CO binds to O_2 binding site of Hb

Abnormal Hb

At low conc. of O_2
↓
HbS precipitates into long crystals inside the RBC
↓
Elongate the cell and give it the appearance of a sickle
↓
Damages the CM, so the cells become highly fragile ... hemolysis & blockage of blood vessels. (mechanical fragility ↑)
↓
Anemia.
.... Once the process starts, it progresses rapidly.

- Defects in quality of structure of Hb.
  HbS, HbE, HbC, HbD
- Defects in quantity ↓ Thalassema.

Thalassemia

- Polypeptide chains are normal but ↓ in qty or absent
- α thalassemia – α chains ↓
- β thalassemia – β chains ↓
  - ↳ β Thalassemia Major [cooley's anaemia]
  - ↳ β Thalassemia Minor.

Erythropoiesis

INTERCELLULAR CONNECTIONS

Dr. Arisha

- In blw β cells
- Types of jn: Tight, Anchoring, gap
- Tight ↓ Zonula occludens
- found in the epithelium of GI Tract,
- protein contributing for their formation.
  Claudin, Occluden

6/12/22 Tuesday

Erythropoiesis

Haemopoiesis [SA topic] 15 marks

- Dvlpt of blood cells
- Erythropoiesis – RBCs

(Process of formation, dvlmt & maturation of RBCs)

- Leucopoiesis – WBCs
- Megakaryopoiesis – Platelets.

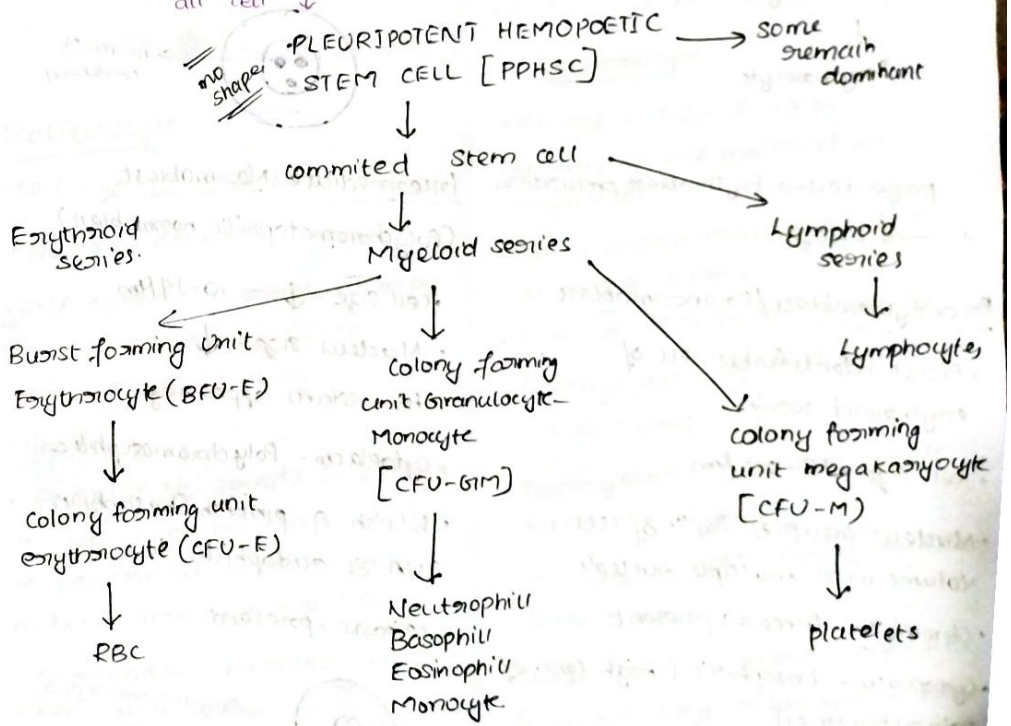
Sites of hemopoiesis

① Intrauterine life: 3 stages

(A) Mesoblastic stage	upto 3 week of foetal life	Mesoderm of the yolk sac
(B) Hepatic stage	From 3rd week to 6m	Liver, spleen
(C) Myeloid stage	From 6m – full term	Red Bone Marrow
(2) In children	upto 6 yrs	marrow of all bones
(3) In adults	upto 20 yrs	long bones, vertebrae, skull, Ribs, sternum, ilia
	After 20 yrs	Upper ends of long bones, vertebrae, ribs, sternum, ilia, skull

BONE MARROW

- The bone marrow – one of the most active organs.
- Active BM: red marrow – cells @ diff. stages of dvlmt
- Inactive BM infiltrated with fat – yellow BMarrow
- BM is aspirated from iliac bone/sternum... properly stained... examined under microscope.
- Indications: anemia... leukemia, lymphoma, pancytopenia (all cell ↓)
- 75% of the cells in the marrow belong to the myeloid series (for WBC & platelets)
- Only 25% – red cells (erythroid series)
- Normal myeloid – erythroid ratio is 3:1
- In circulation RBC count is 500 times more than WBC count... because of longer lifespan of RBCs.



PPHSC - committed stem cells.

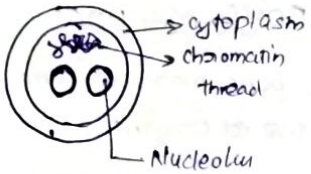
BFU-E
↓
CFU-E
↓
Proerythroblast
↓
early normoblast
↓
Intermediate normoblast
↓
Late normoblast
↓
Reticulocyte
↓
Erythrocyte

Stages of erythropoesis

progenitors → Erythroblast precursors → RBCs

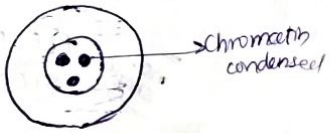
Proerythroblast/Pronormoblast

- First identifiable cell of erythroid series.
- cell size 15-20 μm
- Nucleus occupies 3/4th of cell volume with multiple nucleoli
- chromatin threads present
- cytoplasm - basophilic (high conc. of polyribosomes)
- Mitosis - present
- Hb - absent



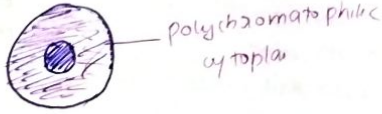
Early normoblast/Basophillic normoblast

- 14-16 μm
- Nucleus size - decrease - nucleoli absent
- chromatin condensation present
- cytoplasm - basophillic
- Mitosis - present
- Hb - absent



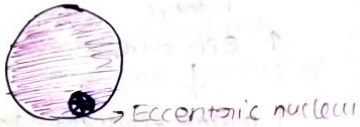
Intermediate Normoblast (Polychromatophilic normoblast)

- cell size - ↓ - 10-14 μm
- Nucleus size - ↓
- Hb - starts appearing
- cytoplasm - Polychromatophilic
- bluish & pinkish (basophillic RNA & acidophillic Hb)
- Mitosis - present.



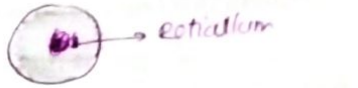
- Late Normoblast/Orthochromatic normoblast

- 8-10 μm
- Eccentric nucleus
- Pyknotic degeneration - clumping of the chromosomes, shrinking of the nucleus.
- cytoplasm - reddish (Acidophilic)
- No mitosis
- Hb - present
- Nucleus is extruded out later



Reticulocyte

- cell size ↓ 7-8 μm
- Nucleus absent
- RNA appears as a reticulum on supravital staining (with Brilliant cresyl Blue)
- Hb ↑
- Reticulocyte spends 1-2 days in bone marrow and 1-2 days in peripheral blood... spleen. matures into biconcave RBC.
- Mitochondria, ribosomes are lost when conv. to RBCs so RBC cannot synthesize proteins



- Normal count
- In new born : 2-6% of RBC count
- Adult - 0.5 to 1% RBC count

* Reticulocytosis
- Physiological - at birth, infants, ↑ altitude
- Pathological - after treatment for anemia, after hemorrhage, hemolytic anemia

* Reticulocytopenia - Aplastic anemia

Erythrocyte

- cell size - 7.2 - 7.5 μm
- Absence of RNA material, no organelles
- one pronormoblast give rise to at least 8-10 RBCs.
- 2 million RBCs produced each sec.
- Average duration of erythropoesis : 7 to 9 days
- Proerythroblast to reticulocyte takes 5 to 7 days
- Maturation of reticulocyte to RBC takes 2 days
- These are thus about 3×10^{13} RBC & about 900 g of hemoglobin in the circulating blood of an adult man
- Life span - 120 days

Draw, label various stages of erythropoiesis

sat

Factors affecting erythropoiesis

- General factors
  - Hypoxia → Erythropoietin
  - Growth inducers
  - Hormones
- Maturation factors
  - Iron, Vit B_{12}, folic ā
- Factors necessary for hemoglobin production

  Vit C → Helps in iron absorption ($Fe^{3+} \rightarrow Fe^{2+}$)
  - Proteins → a.ā for globin synthesis
  - Iron, copper, calcium, cobalt → Heme synthesis.

① Erythropoietin (EPO)

- Glycoprotein

Formation

- 85% formed in interstitial cells of the peritubular capillary bed of the renal tubule)
- 15% formed in liver.

Breakdown

- In liver. • $T_{1/2}$ = 5 hours.

Stimuli ↑sing EPO

- Hypoxia is the potent stimulus
  - High altitude
  - Anemia
  - chronic lung or heart dis
  - catecholamines
  - Prostaglandins
  - Androgens
- ↓sed by estrogen & Theophylline

↓ O_2 delivery to kidneys
↓
kidneys
↑ EPO secretion
↓
↑ plasma erythropoietin
↓
Bone marrow
↑ prodn of erythrocytes
↓
↑ Blood Hb conc.
↓
↑ Blood O_2 – carrying capacity
↓
Restoration of O_2 delivery

Functions of EPO

Erythropoietin ↑ RBC prodn.

- Stimulates stem cells towards erythroid series
- Promotes pronormoblast prodn from progenitor cells
- Enhances mitosis
- Accelerate Hb formation
- Promotes the early release of reticulocyte

Applied - EPO injections in treatment of anemia in renal failure

② Growth inducers/ Differentiation inducers

- Interleukin 1, 3, 5 (IL-3 is a growth inducer for all cells lines)

Acts on stem cells to convert them to progenitor cells

- Colony stimulating factors - produced from T cells, endothelial cells, fibroblasts stimulates produc of committed stem cells.

③ Hormones

- Androgens

Maturation factors

Role of iron, folic acid & vit B_{12}

- Iron - needed for Hb synthesis
- Folic ā & Vit B_{12} - required for the synthesis of DNA & maturation of nucleus & cell.
- Milk, meat, liver, green leafy vegetables.
- If deficiency occurs... failure of maturation of nucleus.
- There occurs redn in cell divn
- Cells remain large (megaloblasts) & become more fragile
- Intrinsic factor - needed for Vit B_{12} absorption

Role of folic ā & Vit B_{12}

* Folic ā & Vit B_{12} are necessary for maturation of nucleus

Other dietary factors

- Vit C → Helps in iron absorption ($Fe^{3+} \rightarrow Fe^{2+}$)
- Vit B6 (Pyridoxine - heme synthesis)
- Vit E anti oxidant
- Proteins → Amino ā for globin synthesis
- copper, calcium, cobalt → Heme synthesis.

13/12/22
Tuesday

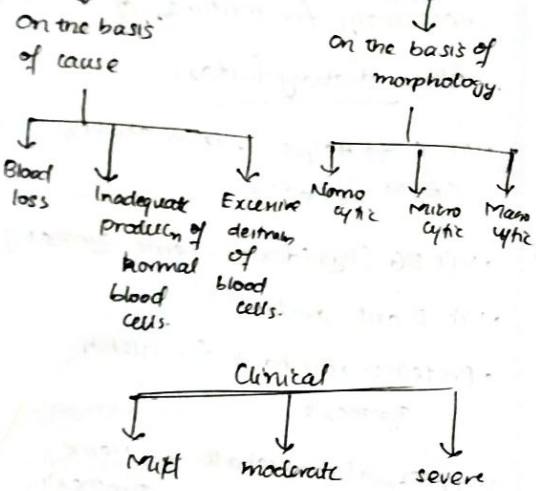
Blood indices

MCV	MCH	MCHC
* Mean corpuscular vol.	Mean corpuscular hemoglobin	Mean corp. hemoglobin conc.
Vol. of 1 RBC	Av. amt. of Hb in 1 RBC	Conc. of Hb in an RBC / degree of hemoglobinisation of RBC.
80-95 femto litre (87)	27-33 pg (29)	33-37 % (34)
Microcytic - Small Macrocytic - large RBC	Hypochromia Pale RBC	MCHC will never be more than 37% No hyperchromia

Anaemia.

• Defined as a condin where Hb content or the RBC count or both, is below normal for the age & sex of the individual.

Classificn of Anaemias



Classificn of Anaemia

A. Morphological classificn

1. Normocytic normochromic:
   Normal MCV & MCHC
   Acute post hemorrhagic anemia
   Hemolytic anemia
2. Microcytic hypochromic:
   ↓MCV & MCHC
   Fe deficiency anemia
   Chronic blood loss anemia
3. Macrocytic normochromic:
   MCV ↑ & MCHC normal
   Megaloblastic anemia

B. Etiological classi
[based on cause]

1. Anemia due to blood loss:
   Acute: accidents, surgery (normo-chromic normocytic)
   Chronic: bleeding piles, parasite
2. Excessive destrucn of RBCs- hemolysis
   • Hereditary or acquired
   • Intra corpuscular or extra corpuscular defect
   • sickle cell anemia, spherocytic anemia, thalassemia (intracorpuscular)
   • Malaria, incompatible blood transfusn, snake venom (extracorpu)
3. Abnormal prodn of RBCs.
   (a) Nutritional deficiency:
   - Fe Deficiency (microcytic)
   - vit B12 & Folic a def (macrocytic)

   (b) Aplastic anemia:
   failure to bone marrow to produce RBCs.

   (c) Anemia due to chronic diseases: chronic infecn like TB, malignancies...

C. Clinical classificn
- Mild anemia - Hb < 11%
- Moderate anemia - Hb < 9gm%
- Severe anemia - Hb < 6g%.

Physiological basis of symptoms

↓RBC count / ↓ Hb
↓
↓ O_2 carrying capacity of blood
↓
↓ tissue oxygenn → fatigue.

- Symptoms aggravate on exern
- Dyspnoea on exern, palpitans.
  ↓ (breathlessness)

General clinical features
- Either due to hypoxia or due to ~~other~~ the compensatory mechanisms..
- Pallor - pale skin & mucous membranes,
- Easy ~~fatag~~ fatiguability
- Respiratory symptoms: breathlessness (dyspnoea)
- Cardiovascular: tachycardia, palpitn.
- ↓ viscosity of blood & ↑ cardiac output → abnormal heart sounds (murmurs) ... cardiac failure...
- Nervous system: lethargy, drowsiness, confusn, fainting, visual disturbances...
- GIT: anorexia, indigestion. (Collapse/exertion)

Investigans
- Hb, RBC count, PCV
- Blood indices
- Reticulocyte count (may ↑ in all anemias except aplastic anemia)
- Peripheral smear
- Bone marrow examina... only for selected cases.
- Estimn of Fe content

Fe-storage
↳ Ferritin (plasma)
↳ Hemosiderin

Iron-deficiency anemia.

Commonest anemia in India... nutritional def. of Fe.

Causes:
- Chronic blood loss:
  bleeding piles, peptic ulcers
  hookworm infestn, menorrhagia

1 mg of Fe is lost from the body with every 2ml of blood
- Increased demand for Fe:
  infancy, childhood, pregnancy, menstrua
- ↓ dietary intake
- Decreased absorpn: disease of stomach & duodenum, after gastrectomy

14/12/2022 Wednesday

White Blood Cells.

- Leucopoiesis & its regulan
- Normal count & varian

Leucocytes / WBC
- Formed elements of blood
- Colorless
- Larger in size compared to RBCs.
- Nucleated
- Lesser in no:

Classifican

- Presence or absence of granules in cytoplasm

Granulocytes → Agranulocytes

- Staining property of granules
- Neutrophils: take up both acidic & basic stains
- Eosinophils: take up acidic stain
- Basophils: take up basic stain.

Life span of WBC

- 6-10 days in bone marrow
- 6-8 hrs in circulation
- 4-5 days in tissue phase.

Site - Red bone marrow

- Starts in 3-5 weeks of intrauterine life.
- In fetus: Liver, Spleen, Bone marrow
- In adults: only in Red marrow
- Usual site - iliac crest (flat bones, ends of long bones)

15/12/22

Clinical Features

(Chronic Anemia)

- General features:
- Characteristic features:
- Nails are dry, soft, brittle & spoon shaped (koilonychia)
- Atrophic glossitis (Hallerstein)
- Angular stomatitis
- Plummer Vinson syndrome: Membranous webs are formed in oesophagus causing dysphagia

Lab Findings

1. Hb ↓
2. Microcytic hypochromic anemia
3. Decreased MCV, MCH, MCHC.
4. Bone marrow shows erythroid hyperplasia (compensatory mechanism)
5. Serum Iron & Ferritin levels are ↓

Normal serum Fe: 60-160 microg/dl

Normal serum ferritin: 15-200 ng/ml in males

12-150 ng/ml in female

6. Serum Transferin (200-360 mg/dl)

... TIBC ↑

Total Iron binding capacity ↑

Treatment:

- Treat the cause
- Dietary modification
- Fe administration
- Oral (ferrous sulphate)
- Injection (intramuscular injection dextran complex) (Parenteral)
- Deworming

Fe metabolism

- 65-70% of total body Iron is present in Hb.
- Fe is needed for the formation of hemoglobin, myoglobin, cytochrome oxidase, peroxidase, catalase etc.
- Total body Fe: 3-5g
- Fe is absorbed from small intestine in ferrous form... Vit C & gastric HCl ... Fe^{3+} to Fe^{2+}
- Blood - iron binding... Transferrin
- Stored in liver as Ferritin & Hemosiderin
- When iron stores in the body ↓ its absorption ↑ & vice versa

— mucosal block theory —

Megaloblastic Anemia

[Macrocytic Anemia]

- Vit B_{12} def. & / Folic acid deficiency.

→ defective DNA synthesis

↓ multiplication of cells.

- Nuclear maturation lags behind cytoplasmic maturation
- Bone marrow shows abundant megaloblasts.
- 70% proerythroblasts & 30% IN (intermediate) & late normoblasts.
- Inadequate dietary intake; malabsorption, ↑ demand (preg, lactation) drugs (methotrexate)
- Pernicious anemia ... atrophy of gastric mucosa ... no IF ... Poor intrinsic factor

Vit B_{12} absorption ... inj. Vit B_{12}

- In B_{12} def. folic acid is not metabolised ... combined deficiency

~~Symptoms~~ Symptoms:

General features:

Special features:

- Glossitis, Angular stomatitis
- Loss of appetite... HCl ↓ in gastric cancer
- Neurological symptoms:
- Numbness of hands & feet
- Paraesthesia (pins & needles sensation) of fingers & toes
- Pain along peripheral nerves (neuritis)
- Sub acute combined degeneration of spinal cord: Demyelination of spinal cord fibres especially of dorsal column pathway
- ~~Peripheral sm~~

Lab Diagnosis

- Macrocytic normochromic anemia ↑ MCV & Normal MCHC
- Peripheral smear: Macrocytic RBC with anisocytosis & poikilocytosis
- ↑ reticulocyte count (>5%) (in 4-5 days) following treatment... Reticulocyte reponse

Classificaon

- Presence or absence of granules in cytoplasm

Granulocytes → Agranulocytes

- Staining property of granules
- Neutrophils: take up both ā & basic stains
- Eosinophils: take up ā stain.
- Basophils: take up basic stain.

Life span of WBC

- 6-10 days in bone marrow
- 6-8 hrs in circulaon
- 4-5 days in tissue phase.

Site - Red bone marrow

- Starts in 3-5 weeks of intrauterine life.
- In fetus: Liver, Spleen, Bone marrow
- In adults: only in Red marrow
- Usual site - iliac crest (flat bones, ends of long bones)

15/12/22

Clinical Features (Iron def Anemia)

- General features
- Characteristic Features:
  - Nails are dry, soft, brittle & spoon shaped (Koilonychia)
  - Atrophic glossitis (degeneraon)
  - Angular stomatitis
  - Plummer Vinson syndrome: Membranous webs are formed in oesophagus causing dysphagia

Lab Findings

1. Hb ↓
2. Microcytic hypochromic anemia
3. Decreased MCV, MCH, MCHC.
4. Bone marrow shows erythroid hyperplasia (compensatory mechanism)
5. serum Iron & Ferritin levels are ↓
6. Normal serum Fe: 60-160 microg/dl
   Normal serum ferritin: 15-200 ng/ml in males
   12-150 ng/ml in female
7. Serum Transferrin (200-360 mg/dl)

... TIBC ↑
Total Iron binding capacity ↑

Treatment:

- Treat the cause
- Dietary modificaon
- Fe administraon
  - Oral (Ferrous sulphate)
- Injecon (intramuscular injen
  iron dextran complex) (Parenteral)
- Deworming

Fe metabolism

- 65-70% of total body iron is present in Hb.
- Fe is needed for the formaon of hemoglobin, myoglobin, cytochrome oxidase, peroxidase, catalase etc.
- Total body Fe: 3-5g
- Fe is absorbed from small intestine in ferrous form... Vit C & gastric HCl ... Fe^{3+} to Fe^{2+}
- Blood - iron binding .. Transferrin
- Stored in liver as Ferritin & Hemosiderin
- When iron stores in the body ↓ its absorpn ↑ & vice versa

— mucosal block theory —

Megaloblastic Anemia [Macrocytic Anemia]

- Vit B_{12} def. & / Folic ā deficiency
- → defective DNA synthesis
  ↓ multiplicaon of cells.
- Nuclear maturaon lags behind cytoplasmic maturaon
- Bone marrow shows abundant megaloblasts.
- 70% proerythroblasts & 30% (N (intermediate) & late normoblasts
- Inadequate dietary intake, mal absorpn, ↑ demand (preg, lactaon) drugs (methotrexate)
- Pernicious anemia ... atrophy of gastric mucosa ... no IF ... poor intrinsic factor
  Vit B_{12} absorpn ... inj Vit B_{12}
- In B_{12} def. folic ā is not metabolised ... combined deficiency

Symptoms

General features:
Special features:

- Glossitis, Angular stomatitis
- Loss of appetite .. HCl ↓ in gastric causes.
- Neurological symptoms:
- Numbness of hands & feet
- Paraesthesia (pins & needles sensaon) of fingers & toes
- Pain along peripheral nerves (neuritis)
- Sub acute combined degeneraon of spinal cord: Demyelinaon of spinal cord fibres especially of dorsal column pathway
- ~~Peripheral sm~~

Lab Diagnosis

- Macrocytic normochromic anemia ↑MCV & Normal MCHC
- Peripheral smear: Macrocytic RBC with anisocytosis & poikilocytosis
- ↑ reticulocyte count (>5%) (in 4-5 days following treatment ... Reticulocyte reponse

- ↑ bilirubin (due to ↑ hemolysis of large cells)
- ↓ plasma conc. of B_{12} (normally above 400 pg/ml) ... (if < 180 pg/ml ↪ deficiency)

Congenital Spherocytosis

- Inherited as autosomal dominant disorder
- Genetic defect in formation of glycoprotein ⟶ Spectrin
- RBCs are spherical .. Biconcavity is lost ... easily destroyed.
- The blood picture typically shows anemia with spherocytosis, ↑ osmotic fragility, hyperbilirubinemia & reticulocytosis.

Aplastic Anemia.

There is suppression of bone marrow .. Fat / fibrosis.

There is decreased production of all blood cells like RBCs, WBCs & platelets .. Pancytopenia.

Types:

- 1° : idiopathic (65%) ... unknown cause
- 2° : radiation exposure, chemicals like benzene, bacterial toxins, anticancer drugs.

Features: Normocytic Anemia
: Absence of reticulocytes
: ↓ WBCs & platelets.

Hemolytic Anemia

- Excess hemolysis
- Normocytic normochromic anemia.
- ↑ sod serum Bilirubin (UCB) unconjugated bilirubin

Hemolytic Anemia

- Membrane Defect
  Spherocytosis
- Enzyme Defects
  G6PD & Pyruvate kinase def
- Infections
  malaria
- Antibody Induced
  AIHA, HDN
  (Auto Immune Hemolytic Anemia; Hemolytic Dis of newborn)
- Abnormal Hb
  HbS
- Chemicals, drugs

Thalassemia.

- Polypeptide chains are normal but ↓ in qty or absent
- α thalassemia - α chains ↓
- β thalassemia - β chains ↓
  → β Thalassemia Major [Cooley's anemia]
  → β Thalassemia Minor
- Anemia, hepatosplenomegaly, jaundice
- Microcytic hypochromic anemia
- Rx - blood transfusion
  ↳ Treatment

Polycythemia

- 1° : Polycythemia Rubra Vera
  Myeloproliferative disorder like malignancies of the bone marrow. The RBC count is persistently above 4 million / μL
- 2° : hypoxia producing condn.
- high altitude, chronic lung disease, congenital heart disease
- Plethora (↑ sod redness of skin & face), pruritis (release of histamine), headache
- Treatment - Phlebotomy (removal of blood ... 500 ml every 2-4 days)
  Myelosuppressive drugs like Hydroxyurea & Busulfan.

Heme metabolism. (catabolism)

Hb → Globin
↓
Heme
↓ (CO)
Heme Oxygenase
↓
Biliverdin
↓
Biliverdin reductase
↓
Bilirubin

Hemolysis / breakdown of RBC
↓
unconjugated bilirubin + albumin
(Blood; Hepatic sinusoid)

Unconjugated bilirubin
↓ transported with ligandin / Z protein
↓ conjugated to glucuronic acid
conjugated bilirubin
↓
Biliary system
↓
conjugated bilirubin
↓ 10%
Urobilinogen → 90% → Feces
↳ stercobilinogen - Stercobilin

Urobilinogen → kidney → excreted in urine

Jaundice.

Yellowish discolouration of skin, mucus membranes & deeper tissues due to ↑ bilirubin in blood > 2 mg/dl

- Normal serum bilirubin is 0.2 - 0.8 mg/dl

Types of jaundice.

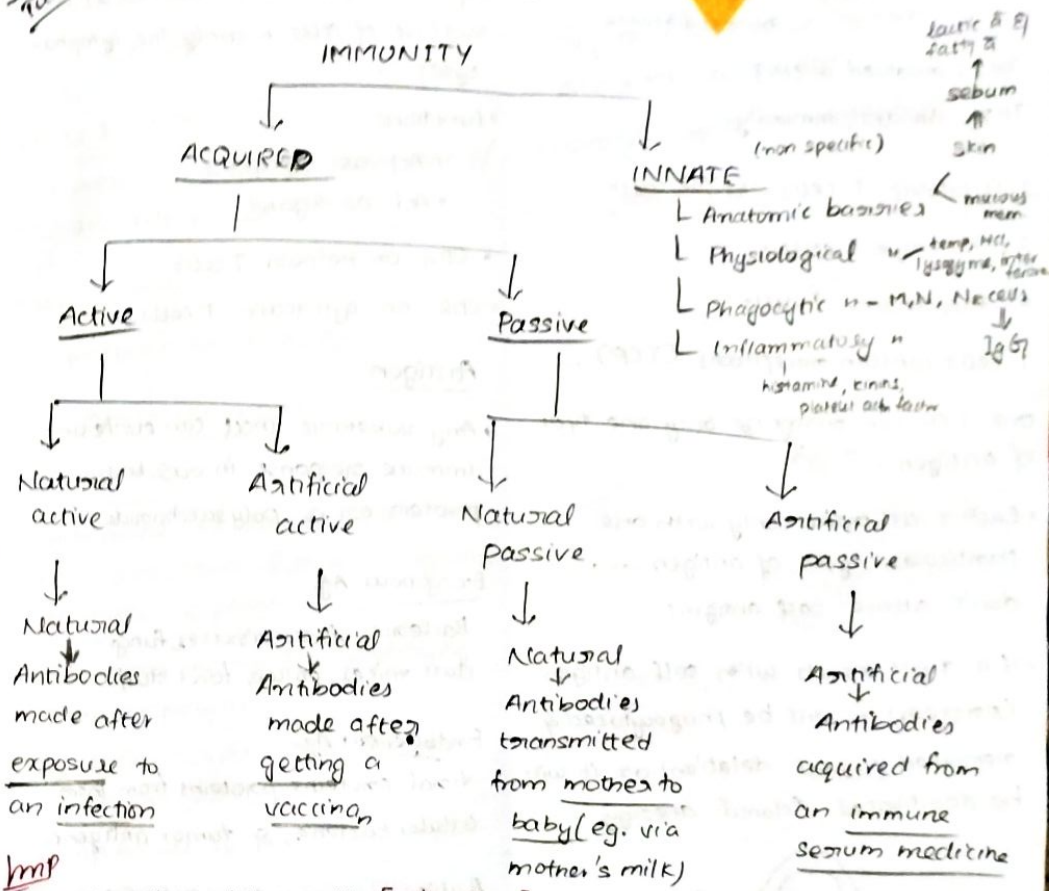
1. Prehepatic or hemolytic jaundice
2. Hepatic or hepatocellular
3. Post hepatic or obstructive

Physiological jaundice of new born

- Reduced activity of the enzyme glucuronyl transferase
- less conjugan of bilirubin in hepatocyte
- Appears after 2nd day
- Rx - Phototherapy
- Uncony. Bilirubin - Lumirubin
  - Poor feeding
  - Excessive crying
  - Yellow skin
  - sleepiness

20/12/2022 Tuesday

IMMUNITY



imp

① cell mediated immunity - [T-lymphocytes] & macrophages

- Forms defense against viruses, fungi, intracellular bacteria like TB bacilli, tumor cells ...
- Transplanted tissue rejections & delayed allergic reactions.

② Humoral immunity [B-lymphocytes]

Most effective against extracellular bacterial infections

Involves antibodies

MHC - major histocompatibility complex

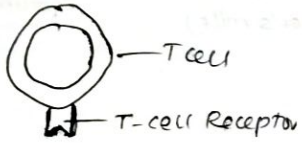
T cells

1. Helper T cells (CD_4 cells)
   cluster of differentiation
   TH1 : involved in CMI
   TH2 : Humoral immunity.
2. Cytotoxic T cells – (CD8 cells)
3. Memory T cells.
4. Suppressor T cells

T cells contain receptors (TCR)...

one TCR can recognize only one type of antigen..." ✗

- Each T cell react only with one particular type of antigen .... don't attack self antigens.
- If a T cell reacts with self antigen (protein) it will be phagocytosed & removed (clonal deletion) or it will be deactivated (clonal anergy



B cells

- Humoral immunity
  2 types:
  - Plasma cells
  - Memory cells
- Plasma cell : produce antibodies
- BCR are present on the surface of B cells.
- Antigenic specificity is present

Cluster of differentiation

- Special molecules identified on surface of cells mainly the lympho-cytes...
- Functions:
  - Act as receptor
  - Act as ligand
- CD4 on Helper T cells
- CD8 on cytotoxic T cells.

Antigen

- Any substance that can evoke an immune response in our body- protein or a polysaccharide

Exogenous Ag

Bacteria, free viruses, fungi... dust mites, pollen, food stuff.

Endogenous Ag

Viral proteins, proteins from intra-cellular bacteria, & tumor antigens.

Antigen presenting cells (APC)

Specialised cells which present antigen to lymphocytes.

1. Macrophages
2. Dendritic cells (lymph node, spleen)
3. B lymphocyte
4. Langerhans cell of skin.

Role in both cell mediated & humoral immunity [But must in CMI]

Antigens are presented to lymphocytes after coupling it with some protein products of MHC genes

Major histo compatibility complex

↳ Human leukocyte antigen (HLA)

Class 1 MHC

- present in the cell membrane of all cells except RBCs.

Class 2 MHC

- present in all APCs.

Other components

cytokines

- Hormone like substances that act in a paracrine fashion to regulate immune response...
- secreted mainly by lymphocytes & macrophages
- Eg: Interleukins, TNF_α (Tumour necrosis factor)

complement system:

- Another group of proenzymes present in the plasma, which get activated during immune response.
- Help in killing of invading organisms

NK cells (Natural killer cells)

- Large granular lymphocytes
- Null cells (neither B nor T cells)..
  spleen, lymph nodes, bone marrow & blood.
- contribute first line defense against viral infect & tumor cells.
- Non specifically kill viruses (which are coated with IgG antibodies)
- They don't mature in Thymus...
  APC & MHC not needed
- osmotylic lysis or phagocytosis.

[Immunity PPt]