

Paediatrics

Haematology

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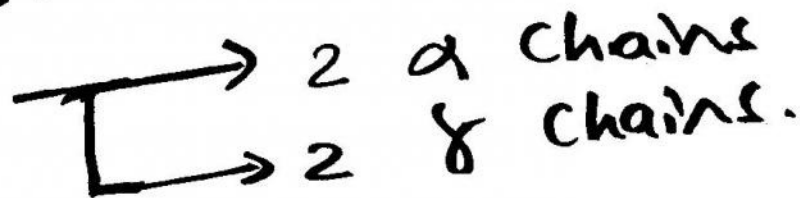
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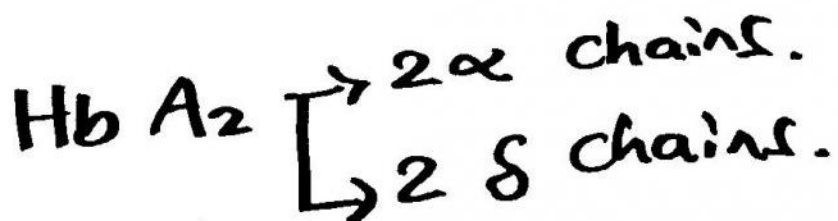
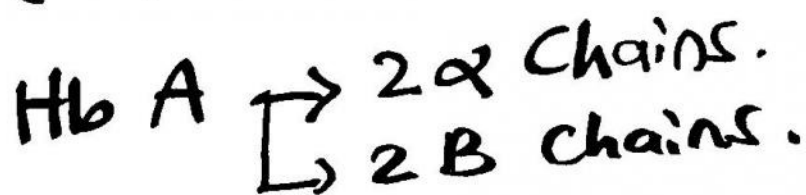
2017 - 2016

Types of Hb.

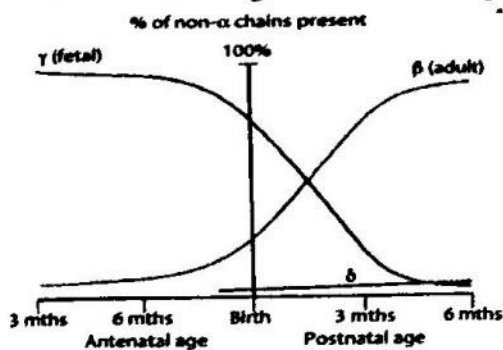
① Hb (F) Fetal haemoglobin



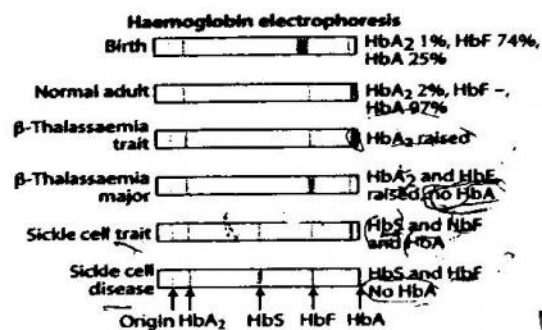
② Hb (A) (adult haemoglobin)



N.B :- In the intrauterine life the dominant Hb is HbF (It has a higher affinity for oxygen than adult Hb)



Changes in haemoglobin chains in the fetus and infancy.



Haemoglobins in sickle cell disease.

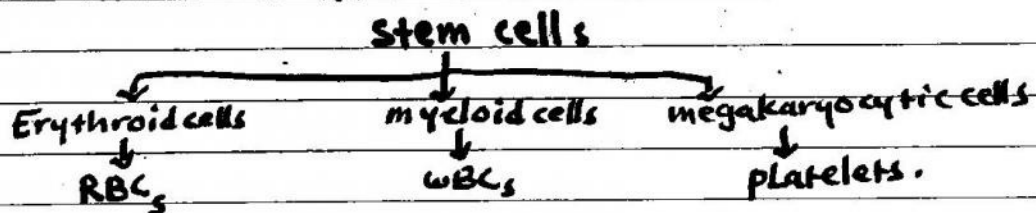
Introduction :-

* **Haematopoiesis** $\Rightarrow$ The process of blood formation.

* The main site of haemopoiesis in Fetal life is the Liver.

* " " " " " " " postnatal " " " bone marrow.

* The bone marrow contains



* Haemoglobin molecule:- 4 polypeptide chains attached to 4 heme group

* Types $\rightarrow$ $\square$ Hb F (Fetal haemoglobin) $\xrightarrow{is}$ made up of 2 α chain
2 γ chain

☐ Hb A (Adult haemoglobin)

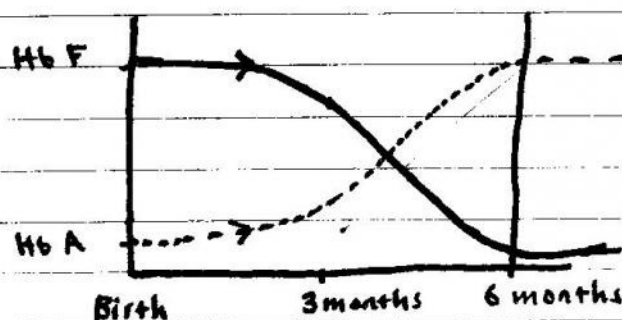
Hb A $\rightarrow$ 2 α chains.
2 β chains.

Ab $A_2 \rightarrow 2 \alpha$ chains.
2 δ chains.
(beta)

N.B :- In the intrauterine life the dominant Hb is $\rightarrow$ Hb F
(It has a higher affinity for oxygen than adult Hb)

At Birth $\rightarrow$ HbF 70-80% - HbA 25-30% - HbA₂ 1-3%

Adult $\rightarrow$ HbA 97% - HbA₂ 2%



* HbA is the main Hb after 6 months of age.

Blood indices:-

Date

No.

① Hemoglobin:-

* The Hb concentration at birth in term infant is high.

in 1st 2 weeks = 14 - 21.5 gm/dL.

* at age 2 months = 10 - 12 gm/dL. (why fall to this level)

* Adult life → ♀ = 11 - 15 gm/dL

♂ = 12 - 16 gm/dL.

② RBC count.

* In the Newborn = 6 million / mm³.

Afterwards = 4 - 6 " / "



③ Hematocrite Value - (packed red cell volume).

is the percentage of RBCs volume in 100 ml blood.

Normal = 40 - 50%.

IF Ht > 65% (polycythemia)

④ Mean Corpuscular Volume (MCV) N = 72 - 96 Femtolitre

No IF > 100 FL → macrocyte (RBCs are large).

IF < 70 FL → microcyte (" " small).

⑤ Mean corpuscular hemoglobin (MCH) N = 30 picogram

IF < 25 pg → hypochromic RBCs.

IF > 35 pg → hyperchromic RBCs.

⑥ WBC count = 4,000 - 10,000.

⑦ platelet count = 150,000 - 400,000 / mm³.

⑧ Reticulocyte count = 1% of RBCs.

IF > 1% reticulocytosis → D.R. ① Hemolytic anemia

② Hemorrhage ③ response to Iron & Folic

④ Recovery of bone marrow from suppression

Anemia.

Date

No.

Def :- it's reduction of hemoglobin and/or RBCs count below average value for age & sex interfering with O_2 carrying capacity of the blood.

Causes



I Decrease production

- ① Iron deficiency anemia.
- ② B_{12} & Folic acid deficiency anemia.
- ③ pure red cell anemia.
- ④ Aplastic anemia.
- ⑤ Anemia of chronic illness.
- ⑥ Bone marrow infiltration (leukemia)

II Increase destruction

(hemolytic anemia)



Intra capsular (RBC problem)

- ① membrane defect
 - ① Hereditary spherocytosis.
 - ② Hereditary elliptocytosis.
 - ③ paroxysmal nocturnal hemoglobinuria.
- ② Hemoglobinopathy
 - ① α thalassemia.
 - ② β thalassemia.
 - ③ sickle cell anemia.
- ③ Enzymatic defect
 - ① G-6-P-D deficiency.
 - ② pyruvate kinase deficiency.

Extra capsular

- ① Immune mediated (coombs +ve)
 - ① Autoimmune hemolytic anemia
 - ② Isoimmune hemolytic anemia
 - Hemolytic disease of newborn
 - Incompatible blood transfusion
- ② Non immune mediated (coombs -ve)
 - ① microangiopathic hemolytic anemia (MAHA)
 - HUS
 - DIC
 - ② septicemia
 - ③ Drugs & heavy metals.
 - ④ Hypersplenism (chronic hemolytic anemia)

Iron deficiency anemia. No.

Incidence → * The most common cause of anemia in pediatric
* The commonest cause of microcytic hypochromic anemia.

* **Peak Age** :- 6 months → 24 months.

Metabolism of Iron

Iron in diet (Ferric state) → Absorbed in the proximal small intestine (Duodenum & jejunum) in Ferrous state $Fe^{3+} \xrightarrow{HCl \& VitC} Fe^{2+}$ → then the absorbed iron is bound to serum Transferrin → & stored in the liver as Ferritin. → to be used in :-
RBC production in bone marrow. & in cell enzymes.

N.B. → Daily requirement of iron = 2-3 mg/kg/day of elemental iron.

→ Factors ↓ iron absorption ① antacid ② Tea ③ phytate.

* Causes of iron deficiency anemia

① Inadequate iron intake.

- ① prolonged breast feeding without supplementation.
- ② cow's milk feeders (low iron content, & poor absorption)

② Decrease iron absorption.

- ① malabsorption (celiac, cow's milk allergy)
- ② Excess Tea, phytate & antacid.

③ prolonged blood loss.

- ① overt blood loss → haematuria & epistaxis.
- ② occult blood loss → Hook worm infestation. → polyp & p.U
→ Meckles diverticulum. → GORD.
→ cow's milk protein allergy.

④ Increase requirement of iron.

- ① Rapid growth (preterm & twins).
- ② congenital cyanotic heart disease.

⑤ Decrease iron stores → ① Iron deficient mother. ② preterm & low birth wt baby.

④

pica → it's desire to eat unusual substances e.g. dirt

* Clinical picture :-

Date

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① may be asymptomatic (Mild anemia)

② symptoms → palor, ↓ appetite, breathlessness, palpitation, Fatigability, headache, Fainting.

+ Irritability, ↓ alertness, learning,

③ sign → ① palor, Tachycardia. & concentration
② Atrophic glossitis (pale smooth tongue)
③ spoon shaped nail (Koilonychia)
④ palpable spleen in 15% of cases.

* Investigation :- (History & Examination are very important)

① CBC → Hb = Low
MCH = Low
MCV = Low } → microcytic hypochromic anemia

+ plt = Normal or High (thrombocytosis)

② Blood Film → anisocytosis, poikilocytosis.
↑ red cell distribution width. (RDW)
target cell may be seen.

③ Iron study → serum iron → low. ↓
* Transferrin saturation → low. ↓
* Total iron binding capacity TIBC → ↑
* serum Ferritin → low ↓. (< 100 µg/ml)
(index of iron stores)

④ For diagnosis the cause.

- ① stool analysis for parasites.
- ② occult blood test
- ③ upper GI endoscopy.

Treatment of

Date

No.

① prophylaxis:-

oral iron supplement given at 4-6 months
For breast & cow's milk Feeders & preterm baby.

② curative:-

① Rx the cause.

② Diet rich in vit C, meat, fish

③ oral iron supplementation → Ferrous Sulphate.
Ferrous gluconate.
Ferrous Fumarate.

given for 8 weeks after blood values are
normalized to replenish the store (Total
duration 3-6 months)

S/E → GIT upset & dark stool.
constipation & metallic taste

④ parenteral iron. → IV venofer.

Iron dextran IM.

Indication → ① malabsorption.

② intolerance to oral iron.

S/E → staining, anaphylaxis.
IM → painful

⑤ packed red cell transfusion.

Indication ① severe anemia ($Hb < 6 \text{ g/dL}$)

② anemic heart failure.

* Response to therapy (Iron therapy)

① replaced cellular enzymes → ↓ irritability & ↑ appetite
(By 1st day)

② Erythroid hyperplasia in bone marrow (By 2nd day).

③ Reticulocytosis (good therapeutic test) (By 3rd day)
peak at 5-7 days.

④ increase Hb at rate 0.25 - 0.5 g/dL/day (by 1st month)

⑤ Repletion of iron stores (By 1-3 months)

Megaloblastic Anemia^{No.}

Def:- Anemia with megaloblasts in the bone marrow & macrocyte in the peripheral blood due to:-

- ① vit B₁₂ deficiency.
- ② Folic acid deficiency.

* Metabolism of vit B₁₂. (storage of vit B₁₂ → years)

• Source:- animal origin only eg milk, meat.

• Requirement:- 5-20 µg/day.

• Absorption:- in the Terminal ileum.

* Metabolism of Folic acid. (storage of Folic acid → 4m)

• Source:- animal & plant (green leaves & Fruits)

• Requirement:- 20-50 µg/day.

• Absorption:- in the proximal jejunum (need vit C)

* Causes of vit B₁₂ deficiency:-

- ① ↓ absorption → ① malabsorption disease as celiac disease.
② pernicious anemia (Rare in pediatric)
③ ileal disease as chron's or ileal resection.

② ↓ intake → very rare except for breast feeders of vegetarian mother.

③ others → ① Defect transport → Transcobalamin II ↓.

* Causes of Folic acid deficiency:-

- ① ↓ absorption → ① malabsorption disease as celiac disease
② vit C deficiency.

② ↓ intake → uncommon, May occur in infant fed on Goat's milk.

③ ↓ metabolism → ① cytotoxic drugs (methotrexate)

② Anti epileptic drugs → phenytoin, Na valproate

④ others → ① chronic hemolysis. (↑ requirement)

② prematures (↓ stores + rapid rate of growth)

Clinical picture of megaloblastic anemia.

- ① Feature of anemia. (Symptoms & signs).
(Fatigability, palor, breathlessness, palpitation, ↑HR.)
- ② GIT manifestation (especially in Folic acid deficiency).
 - ① Red glazed tongue & Glossitis.
 - ② poor feeding ③ abdominal pain.
- ③ Neurological Manifestation.
 - ① subacute combined degeneration. ^{NB} $\rightarrow$ in vit B₁₂ ↓ only
(sensory ataxia, delayed motor milestone.
 - ② optic atrophy ③ sexual dysfunction. ④ irritability.

Investigation:-

- ① CBC $\rightarrow$ Hb ↓ (anemia) ^{MC} $\rightarrow$ in severe case pancytopenia
MCV $>$ 100 fL (MCHC = Normal or ↑)
(type of anemia macrocytic hyperchromic)
- ② Blood Film. show $\rightarrow$ ① Hypersegmented neutrophils (4-5 lobes)
early finding.
 - ② macro-ovalocytosis
 - ③ anisocytosis & poikilocytosis.
 - ④ Reticulocytes low.
- ③ Bone marrow examination $\rightarrow$ megaloblasts.
- ④ IF vit B₁₂ deficiency is the cause:-
 - ① low serum vit B₁₂ < 100 pg/mL (Not specific)
 - ② schilling test. (to differentiate between IF deficiency.)
 - ③ others $\rightarrow$ IF Antibodies. & malabsorption disease
small bowel biopsy.
- ⑤ IF Folic acid deficiency is the cause.
 - ① low serum Folic acid.
 - ② Red cell Folate $\rightarrow$ ↓ (Reflect storage rather than serum level)

Treatment:- ① vit B₁₂ ↓ anemia. $\rightarrow$ vit B₁₂ 1mg IM monthly.
(if successful R_x $\rightarrow$ Reticulocytosis is seen in 2-4 d)

- ② Folic acid ↓ anemia $\rightarrow$ Folic acid tablets ⑧
if diagnosis is doubtful give vit B₁₂ then folic acid.

Hemolytic Anemia

Date

No.

Def:- anemia resulting from increased RBC destruction exceeding bone marrow capacity for compensation.

I Acute hemolytic anemia.

Causes → I Intracapsular causes. → G.6.p.D deficiency.
II Extra corpuscular causes.

Immunological (Coombs +ve)

- ① Autoimmune hemolytic anemia.
- ② Iso immune hemolytic anemia.
→ hemolytic disease of newborn.
→ incompatible blood transfusion.

Non-immunological (Coombs -ve)

- ① MAHA (DIC, HUS)
- ② septicemia.
- ③ malaria.
- ④ Drugs & heavy metals.

* C/P of acute hemolytic anemia.

- ① sudden pallor
- ② Jaundice.
- ③ Dark coloured urine.
- ④ pyrexia & rigors.
- ⑤ Loin pain.

* Investigation:-

- ① CBC → low Hb.
- ② decreased RBC survival → ↑ unconjugated bilirubine.
→ ↑ LDH
→ ↓ Haptoglobin.
→ Hemoglobinuria.
- ③ increased erythropoiesis → ↑ reticulocyte count.
- ④ specific test → Coomb's test
- ⑤ Blood Film → ① in G.6.p.D deficiency → Heinz bodies.
② in MAHA → Fragmented RBCs (schistocytes).

Glucose 6 phosphate dehydrogenase deficiency.

* It's X Linked recessive disorder (so occur mainly in male but may occur in Female).

* Pathogenesis:-

* Glucose 6 phosphate dehydrogenase enzyme. (G6PD) is the key enzyme in the pentose phosphate pathway $\rightarrow$ which produce reduced glutathione $\rightarrow$ which protect against oxidizing agents.

* people with G6PD deficiency are therefore at risk of hemolytic anemia in states of oxidative stress.

* Oxidizing agents:-

① Food $\rightarrow$ Fava beans. (Favism)

② Infection $\rightarrow$ Viral or bacterial.

③ Drugs $\rightarrow$ * Antimalarial (primaquine, chloroquine)

* Sulfonamides (sulphamethoxazole)

* Methylene blue.

* Analgesic as aspirin.

* Antibiotic as (Nitrofurantoin, Nalidixic acid, ciprofloxacin)

* C/P:- $\rightarrow$ most individuals with G6PD deficiency are asymptomatic

$\rightarrow$ ① may present with prolonged neonatal jaundice, possibly leading to kernicterus.

② Hemolytic crisis. $\rightarrow$ Feature of acute hemolysis. E out organomegally usually occur 24-48h after exposure to the oxidant.

* Investigation:-

① CBC $\rightarrow$ Low Hb (anemia) $\rightarrow$ Normocytic Normochromic anaemia.

② parameter for hemolysis $\rightarrow$ $\uparrow$ reticulocyte $\downarrow$ haptoglobin ---

③ Blood Film $\rightarrow$ Heinz bodies (intracellular inclusion bodies)

$\rightarrow$ Bite cells. (RBCs with bite of membrane missing)

④ enzyme assay (done 2-3 ^{weeks} months after acute attack) $\rightarrow$ to avoid False -ve Result

⑤ coomb's test - (-ve)

N.B → DD of Herz bodeis → ① thalassemia
② G6pD deficiency.
③ post splenectomy.
④ hemoglobinopathy.

Treatment →

prophylaxis → 1. avoid oxidant Food & drugs.
2. use antioxidant → vit E.

During attack → ① stop oxidant agent.
② packed RBC, transfusion.

* N.B patients with G6pD deficiency → are protected against malaria particularly malaria caused by plasmodium falciparum

(paroxysmal Nocturnal hemoglobinuria) (PNH)

⇒ it's Rare generally acquired life threatening disease of blood characterized by complement induced intravascular hemolytic anemia, red urine & thrombosis.

Treatment → oral iron, anticoagulants.
Bone marrow transplantation.

Chronic Hemolytic anemia.

Causes

I. Intra corpuscular causes.

- ① membrane defect →
 - ① Hereditary spherocytosis.
 - ② Hereditary elliptocytosis.
- ② Hemoglobinopathy →
 - ① α thalassemia.
 - ② β thalassemia.
 - ③ sickle cell anemia.
- ③ Enzymatic defects → ① pyruvate kinase deficiency.

II. extra corpuscular causes.

- ① Immunological (coomb's test +ve) → warm AIHA.
- ② Non immunological (coomb's test -ve) → Hypersplenism.

CIP:-

① Features of anemia (pallor ---)

② Jaundice.

③ Hepatosplenomegaly → due to extra medullary hemopoiesis.

④ skeletal changes → due to bone marrow expansion.

① Head → macrocephaly, depressed nasal bridge.
prominent maxilla, prognathism.

② Generalized osteoporosis (pathological #)

⑤ Gall bladder stones (ca bilirubin stones) if chronic hemolysis > 4y

⑥ Hematological crisis →

① Aplastic crisis.

② Hemolytic crisis.

③ Megaloblastic crisis.

General investigation:-

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- ① Anemia Hb ↓ Ht ↓
type of anemia [Normocytic Normochromic Anemia]

② evidence of hemolysis →

- ① ↑ reticulocytes (3-15%)
- ② ↑ LDH
- ③ ↓ Haptoglobin
- ④ ↑ unconjugated bilirubin.



③ Blood Film.

- ④ Skull X Ray → marrow space expansion.
→ macrocephaly & ↑ wide diploic space
(Hair on end appearance)

⑤ Hb electrophoresis. → For hemoglobinopathy.

Hereditary spherocytosis

Etiology → Inheritance is Autosomal dominant. 80%.
20% Autosomal recessive or New mutation.

* There is abnormality RBC membrane protein spectrin or ankyrin that cause RBC to become spherical in shape with ↑ rigidity.

Clinical picture:- (tue F/H usually present)

- ① Anemia (pallor - weakness, dyspnea, palpitation) } start early in life
- ② Jaundice + Splenomegally
- ③ pigmented gall stones occur in 50% of unsplenectomized cases by 4-5 years.

NB * 50% of cases presented by Neonatal anemia & jaundice.
* Neonatal Jaundice is most common presentation occurring especially in 1st 24 hr of life.
* splenomegally in majority of cases often present by age ⑬ or 1 year.

Investigation:-

Date

No.

- ① CBC $\rightarrow$ $\downarrow$ Hb & Normocytic Normochromic.
- ② chronic hemolysis $\rightarrow$
 - ① $\uparrow$ unconjugated bilirubin.
 - ② Reticulocytosis.
 - ③ $\uparrow$ LDH.
 - ④ $\downarrow$ haptoglobin.
- ③ Blood Film $\rightarrow$ spherocytes (RBCs are small, rounded) without central pallor
- ④ Osmotic Fragility test $\rightarrow$ +ve.
(when RBCs are added to hypotonic solution the RBCs are abnormally fragile (lysis).)
- ⑤ Coomb's test (-ve) to exclude immune mediated hemolytic anemia.

Treatment $\rightarrow$

- ① supportive $\rightarrow$ Folic acid 1mg/day
- ② in severe anemia $\rightarrow$ need packed RBC transfusion.
- ③ splenectomy $\rightarrow$ (it prevents crisis, hemolysis & G-B stones)
 - * splenectomy should be delayed until the child is >5 years to $\downarrow$ the risk of invasive infection caused by encapsulated bacteria
 - * vaccination:- pneumococcal haemophilus influenzae, meningococcal, influenza vaccines 2-3 week before splenectomy
 - * pneumococcal repeated every 5yr & influenza annually.
 - * Life long prophylactic penicillin.

Thalassemia

Date

No.

Definition → thalassemia is an **AR** syndromes of anemia characterized by defective synthesis of one of Hgb chains.

* pathophysiology →

* Normally the major Hgb in RBCs is hemoglobin A₁ [$2\alpha + 2\beta$]
other hemoglobins present in small amount are Hgb A₂ [$2\alpha + 2\delta$]
& Hgb F [$2\alpha + 2\gamma$]

* α thalassemia result from defective α globin chain synthesis
& β thalassemia result from defective β globin chain synthesis.

* Both types of thalassemia → hemolysis → ↑ bone marrow activity → bone marrow hyperplasia → ↑ in the size of bones in the face & skull.

α thalassemia

* more in Asian.

* is due to deletion of one or more of 4 α globin genes on chromosome 16

① silent carrier → 1 α globin gene is deleted
pts have No anemia (asymptomatic)

② α thalassemia minor → 2 α globin genes are deleted.
pts mildly anemic.

③ Hemoglobin H disease → 3 α globin genes are deleted.
mild to moderate anemia at birth.
electrophoresis → 15-30% bands Hb in neonate, Hb H [4 β chains] after 6 months.

Type of Anemia
microcytic hypochromic

④ Fetal hydrops → 4 α globin genes are deleted.
severe intra uterine anemia & anemic HF
→ Intrauterine fetal death & still birth.
or early neonatal death.

Treatment → ① Blood transfusion.

② Splenectomy if splenomegaly after 5yr

③ Non specific → Folic acid.

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B thalassemia.

No.

- . B thalassemia more in mediterranean.
- . it's due to mutation of one or more of the 2 B globin genes on chromosome 11.

I one gene mutation $\Rightarrow$ B thalassemia minor. B thalassemia trait.

- * it cause mild asymptomatic anemia.
- * most patients have short RBC survival but evidence of overt hemolysis (pt usually asymptomatic).
- * Investigation $\Rightarrow$ shows hypochromia and microcytosis with target cells.
- * To differentiate it from iron deficiency anemia.
 $\rightarrow$ Normal iron indices. & $\uparrow$ RBC count.
- * NO treatment is required.

II 2 gene mutation $\Rightarrow$ B thalassemia major $\rightarrow$ COOLEY'S anemia

- * It's the commonest cause of chronic hemolytic anemia in Libya & mediterranean.
- * B thalassemia is the most common cause of transfusion dependent anemia in childhood.

* pathogenesis $\Rightarrow$

III Impaired B chain production:-

- ① $\downarrow$ production of Hb A₁ ($\alpha_2\beta_2$)
- ② Deposition of excess unmatched α chain inside RBC.
 $\rightarrow$ hemolysis $\rightarrow$ anemia.
- ③ Compensatory production of other Hb contain non-Beta chains especially Hb F ($\alpha_2\gamma_2$) $\rightarrow$ $\uparrow$ Level of Hb F which has $\uparrow$ affinity to O_2 .
- ④ anemia & $\uparrow$ Hb F lead to tissue hypoxia
Compensatory $\uparrow$ RBC production $\rightarrow$ medullary (Bone marrow expansion)
 $\rightarrow$ extramedullary (splenomegaly & hepatomegaly)

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② iron overload due to :-

Date

No.

- ① chronic hemolysis.
- ② ↑ Iron absorption.
- ③ Repeated Blood transfusion

Iron deposition in Various organs.

* Clinical picture :-

① Features of anemia.

② " " chronic hemolysis.

③ poor growth & development (due to tissue hypoxia)

④ Hemosiderosis → iron deposition in

① Skin → Bronzed color.

② Heart → cardiomegally.

③ pancreas → DM.

④ Liver → cirrhosis.

⑤ pituitary → growth retardation & hypogonadism.

Begins in the infancy around 6 months of age.

⑤ **Thalassemia Facies** → mongloid Facies (Frontal bossing prominent cheek bones due to maxillary hyperplasia)

* Investigation :-

① all all hemolytic anemia (Anemia, Reticulocytosis, Indirect hyperbilirubinemia)

② CBC → microcytic hypochromic anemia.

③ Blood Film → ① microcytic hypochromic RBCs.

② Target cells.

③ Anisocytosis.

④ poikilocytosis.

④ Hb electrophoresis → Low or absent Hb A₁.
→ elevated Hb F (98%) & Hb A₂.

⑤ skull X Ray → shows 'hair on end' appearance

⑥ prenatal diagnosis is possible by (chorionic villous sampling)

* Treatment :-

① **Trans Fusion therapy** (Regular packed RBC transfusion)

* when Hb $\leq$ 6 g/dL over 3 consecutive months.

* aim → to maintain Hb 9-11 g/dL.

* Dose → 10-15 mL/kg packed RBC every 3-4 weeks.

(17)

[2] Iron chelation therapy:-

Date

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- * Start when serum Ferritin exceed 1000 ng/mL to avoid hemosiderosis.
- * Deferoxamine $\rightarrow$ 40-60 mg/kg/day (IM, IV, s.c)
- * Deferiprone oral

[3] Supportive treatment:-

- ① * $\downarrow$ Iron intake.
- ② * Folic acid 1mg/day
megaloblastic crisis.
- ③ * Hepatitis B vaccine.

[4] Splenectomy:-

* Indications

[1] Hypersplenism.

- * $\uparrow$ need for transfusion $\geq$ 50% than usual for more than 6 months
- * severe Leucopenia and/or $\downarrow$ plt.

[2] Huge spleen with pain or pressure symptoms

- * Age $\rightarrow$ preferred after the 5th yr.
- * Risk $\rightarrow$ overwhelming sepsis (esp if done $<$ 5yr)
- * 2 weeks before splenectomy $\rightarrow$ vaccination against

- ① $\rightarrow$ pneumococci
- ② $\rightarrow$ meningococci
- ③ $\rightarrow$ H. influenza.

* after splenectomy

$\rightarrow$ oral penicillin 250 mg 1x2.
till adulthood.

[5] Hydroxyurea $\rightarrow$ $\downarrow$ hemolysis $\rightarrow$ limited value due to serious side effect.

[6] Bone marrow transplantation.

[7] Gene therapy under research.

* Complication & causes of death.

- ① Heart Failure due to $\rightarrow$ under transfusion $\rightarrow$ anemia
 $\rightarrow$ over " $\rightarrow$ volume overload
 $\rightarrow$ cardiomyopathy $\rightarrow$ Hemosiderosis
- ② Hemosiderosis.
- ③ Hazards of frequent Bl transfusion.
- ④ Hypersplenism $\rightarrow$ pancytopenia.
- ⑤ post splenectomy complication $\rightarrow$ infection.
- ⑥ poor growth & development

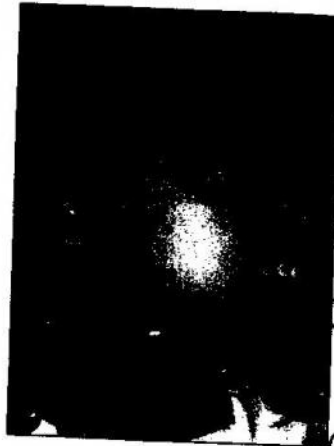
Pallor

Jaundice

Bossing of the skull
Maxillary overgrowth

Splenomegaly

Need for repeated
blood transfusions



Facies in β -thalassaemia showing maxillary overgrowth and skull bossing in a child who has not been adequately transfused.



Box 22.3 Complications of long-term blood transfusion in children

- Iron overload - the most common complication
- Iron overload may cause:
 - Liver damage
 - Heart failure
 - Endocrine disorders
- Allogeneic immune response - delayed growth and sexual maturation
- Alloimmunization

Antibody formation (in children)
All antibodies in the patient make finding compatible blood very difficult

Thrombotic microangiopathy (TMA) (<10%)



Frontal bossing

Depressed nasal bridge

Jaundice

Maxillary prominence

Protruding incisors

Pallor



Brownish pigmentation (hemosiderosis)

Sickle Cell disease.



* **Epidemiology:** - → More In Black.
→ Autosomal recessive.

* **Etiology & pathophysiology:** -

* SS disease is caused by a single amino acid substitution of valine for glutamic acid on the number 6 of the B-globin chain of Hb. → resulting in new Hb → Hb_s.

* when the RBC is exposed to low oxygen or acidosis → polymerization of Hgb lead to →

- ① sickle shaped RBC → ↓ RBC life span (Hemolysis)
- ② occlusion of small vessels → Ischemia & infarction.

* **2 clinical Forms.**

- ① SS disease → two genes for Hgb S (homozygous)
- ② SS trait → one gene for Hb S (heterozygous)
they have no anemia & the red cell morphology is normal but resistant to Falciparum malaria

* **Clinical picture:** - → crisis.
→ chronic hemolytic anemia.

① Feature of anemia.

② " " Chronic hemolysis } → start by 6 months.

③ crisis associated with sickle cell anemia:-

① **Aplastic crisis** →

* Transient sudden bone marrow hypoplasia → sudden low Hb
* caused by infection with parvo virus. → low retic count.

② **Hemolytic crisis** →

increased pallor, jaundice & ↑ reticulocyte count.

③ **Megaloblastic crisis** →

Due to Folate deficiency.

4 Hyperhemolytic Crisis :-

occur in case of sickle cell anemia + glucose 6 phosphate deficiency.

5 Vaso-occlusive crisis. (painful crisis)

* most common crisis. **

* Due to sickling $\rightarrow$ vascular occlusion $\rightarrow$ Ischemia & infarction $\rightarrow$ pain (sever).

* Clinically $\rightarrow$.

1 Hands & Feet (Dactylitis) $\rightarrow$ in young children.
symmetric bone pain & swelling.

2 Acute chest syndrome :-

$\rightarrow$ Bone marrow infarction (thrombotic crisis) $\rightarrow$ Fat emboli to the lungs $\rightarrow$ sickling & infarction of the lung

$\rightarrow$ Fatal if Not treated.

$\rightarrow$ clinically chest pain, Fever, Leucocytosis.

3 cerebro-vascular stroke.

4 Renal infarction $\rightarrow$ Hematuria.

5 priapism $\rightarrow$ painful sustained erection.

6 Leg ulcers.



6 Sequestration crisis :- Common < 2 years.

$\rightarrow$ Thrombosis of venous outflow $\rightarrow$ Acute painful enlargement

$\rightarrow$ In children the spleen is the most common site $\rightarrow$ splenomegaly

$\rightarrow$ C/P $\rightarrow$ acute pallor & hypovolemic shock, acute abdominal pain with splenomegaly $\pm$ hepatomegaly.

7 Infection Crisis :- Due to hyposplenism ($\downarrow$ antibodies, $\downarrow$ phagocytosis) & most common organism $\rightarrow$ encapsulated organism.
site $\rightarrow$ meningitis (pneumococci & Hib) $\rightarrow$ osteomyelitis (S. aureus)
& pneumonia (pneumococci)

sickling crisis may be precipitated by :-

- 1 Hypoxia
- 2 Dehydration.
- 3 Infection.
- 4 stress

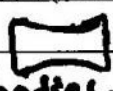
sickling crisis is treated by :-

- 1 Oxygen.
- 2 Intravenous Fluids.
- 3 opiate analgesia.
- 4 Antibiotic

NB → Splenic infarcts → Hyposplenism (autosplenectomy) * *

Investigation :-

① As all hemolytic anemia (Anemia, Reticulocytosis, ↑ Indirect Bilirubin)

② Blood Film → sickle cells  → 
→ Howell-Jolly bodies & submembranous pits.
may be seen indicating → Hyposplenism.
→ Target cells.

③ Hemoglobin electrophoresis → show HbS (90%) & HbF (2-10%)
↯ No normal HbA.

④ Neonatal screening → For early detection of sickle cell disease.

Treatment :-

① chronic Transfusion therapy & Iron chelation.

Indication :- ① pt with stroke.

- ② splenic sequestration crisis, aplastic crisis,
- ③ repeated episodes of acute chest syndrome.
- ④ pre-operation.

② Treatment of crisis :-

* Supportive care → ensure ABC & remove precipitating factors.

* vaso occlusive crisis → good hydration. (1.5 - 2 maintenance)
. Analgesia.

. if refractory → partial exchange Transfusion

* Sequestration crisis → Blood Transfusion.

. Exchange transfusion.

. If refractory → emergency splenectomy

* Aplastic crisis → Blood transfusion.

③ Control of infection → prophylactic penicillin up to 6 yr.
& vaccination against HI & pneumococci

④ Hydroxyurea chemotherapeutic agent that ↑ HbF.

⑤ Bone marrow Transplantation.

Regular
Folic acid
supplement

Aplastic Anemia

Definition:- A pancytopenia associated with hypoplastic Bone marrow.

Etiology:-

①. **congenital:-** Fanconi anemia.

②. **Acquired:-**

① Idiopathic (most common cause)

② Secondary:-

①. Radiation. carbamazepine, phenytoin

②. Drug induced (gold, chlorophenicol,

③. viral infection (parvo virus, CMV, EBV)

④. Diseases (paroxysmal nocturnal hemoglobin myelodysplastic syndroms.

clinical picture:-

* onset Rapid (over few days) or slow (over weeks or months)

① Anemia → pallor.

② thrombocytopenia → purpura.

③ Leukopenia → recurrent infection.

④ NO organomegaly, NO Lymphadenopathy

Investigation:-

① Anemia is Normocytic with low or absent reticulocyte

② Leukopenia & thrombocytopenia

③ Bone marrow Aspiration → is hypoplastic with ↑ Fat.

• No evidence of malignancy.

Treatment:-

* Supportive → RBC transfusion & prevention & Rx of infection.

* Immunosuppressive.

* Stem cell transplantation

Diamond-Blackfan Anemia

* Rare congenital erythroid aplasia (pure red cell aplasia)

* AD (Autosomal dominant)

* 25% Familial.

* C/P → Normocytic Anemia (in Infancy)

* WBC → Normal

* PLT → Normal

→ 25-50% ass $\bar{e}$ other congenital anomalies.

① CHD ② Craniofacial (snub nose, Hypertelorism)

③ Skeletal (triphalangeal thumbs)

④ Renal anomalies.

→ ↑ Risk to develop Leukemia.

* Diagnosis → ① CBC → Anemia + Hb

② Retic count → low

③ B1 Film

④ BM Aspiration

* Treatment → ① Blood transfusion

② C.S (oral prednisolone)

③ B.M.T.

① What? Shwachman-Diamond Syndrome?

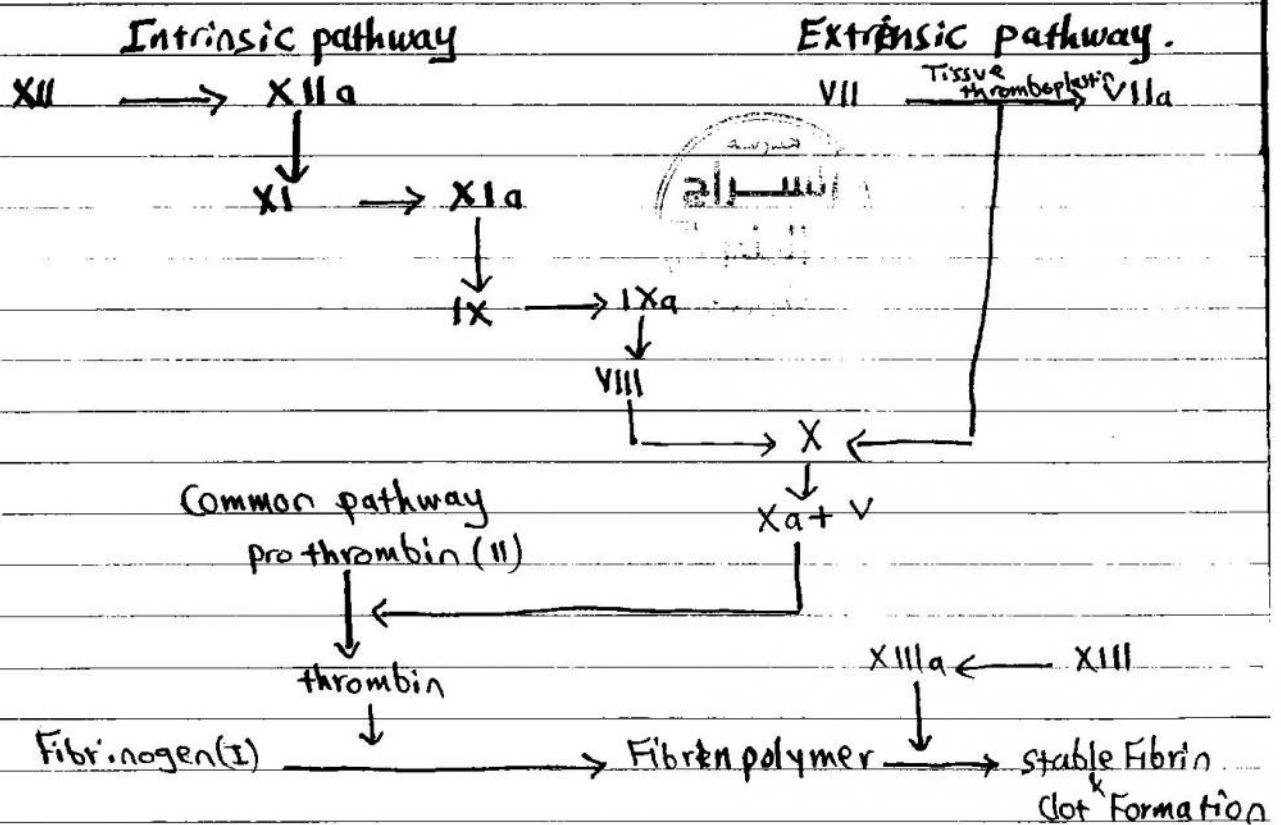
Disorders of Hemostasis.

Hemostasis $\Rightarrow$ is the mechanism of stoppage of bleeding after injury of blood vessels.

Hemostasis requires Normal Function of:-

- ① Blood vessels. $\downarrow$ Vasoconstriction
- ② platelets $\downarrow$ adhesion
- ③ clotting Factors.

* Coagulation Factors $\Rightarrow$ most coagulation factors are formed in the liver Except Factor VIII is formed by endothelial cells.

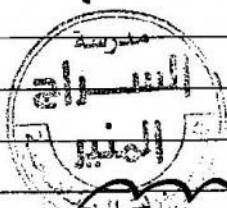


N.B. vit K dependent Factors 10, 9, 7, 2.

* Clotting time $\Rightarrow$ Normal 8-12 minutes
prolonged with defect in any phase.

* prothrombin time (PT) : Normal 12-14 second.
(* it's time needed to plasma to clot after addition of thromboplastin & Ca)

* partial Thromboplastin Time (PTT) : Normal 25-40 second.
(* it's time needed for plasma to clot after addition of Kaolin, Ca & platelets.
* it is a test for intrinsic & common pathway



Interpretation

Defect in	PT	PTT
Common pathway (X, V, II, I)	prolonged	prolonged.
Extrinsic pathway (VII)	prolonged	Normal.
Intrinsic pathway (XII, XI, VIII, IX)	Normal	prolonged

Differentiating between platelets disorders & clotting disorders.

	platelet disorders	clotting disorders.
① History $\Rightarrow$	Immediate mucocutaneous Bleeding $\Rightarrow$ epistaxis $\Rightarrow$ Gingival $\Rightarrow$ Gastrointestinal $\Rightarrow$ Menorrhagia	$\Rightarrow$ Delayed deep tissue bleeding & hemarthrosis
② Examination $\Rightarrow$	petechiae & purpura	$\Rightarrow$ Hematomas & hemarthrosis
③ Lab $\Rightarrow$	Bleeding time	PT & PTT

Hemophilia.

Date

No.

* Types:-

- ① Hemophilia A $\rightarrow$ classic hemophilia* is due to deficiency of Factor VIII.
- ② Hemophilia B (Christmas disease) due to deficiency of Factor IX.

* Epidemiology:-

- Hemophilia A & B are X Linked recessive disorder.
- up to 30% of patients have No Family history of the condition (New mutation)
- Hemophilia A represents 85% of all hemophilias.
- Hemophilia A & B have similar clinical picture, but hemophilia B is Four times less common & usually milder than hemophilia A.

* Clinical picture:-

* The severity of bleeding depends on plasma level of Factor VIII & severity of trauma.

- | | | | | |
|------------|---------------|--------|------------------------|--|
| ① - F VIII | $\rightarrow$ | $>5\%$ | $\rightarrow$ mild | $\rightarrow$ Bleeding with severe trauma |
| ② - F VIII | $\rightarrow$ | 1 - 5% | $\rightarrow$ moderate | $\rightarrow$ " " moderate " |
| ③ - F VIII | $\rightarrow$ | $<1\%$ | $\rightarrow$ severe | $\rightarrow$ " " minor " & spontaneous bleeding |

① at birth: $\rightarrow$ unusual bleeding from the umbilicus or Circumcision site, hematoma at site of vaccination.

② Later $\rightarrow$ ① external bleeding $\rightarrow$ epistaxis, dental bleeding, hematuria, gastrointestinal bleeding.

② Internal " $\rightarrow$ intracranial hemorrhage, muscle hematoma.

③ skin $\rightarrow$ ecchymosis, hematoma] (No petechiae)

④ Hemarthrosis $\rightarrow$ mainly in big joints of lower limbs. (joint become swollen, red, hot, Tender)
Later $\rightarrow$ Fibrosis & Ankylosis.

NB Hemophilia C $\rightarrow$ Factor XI $\downarrow$
 • A.R.
 R₁ $\rightarrow$ FFP

Investigation:-

- ① CBC $\rightarrow$ Normal
- ② Coagulation profile:-
 Bleeding time $\rightarrow$ Normal
 PT $\rightarrow$ Normal
 PTT $\rightarrow$ prolonged **
- ③ F VIII assay $\rightarrow$ Low
- ④ Detection of carrier state:- DNA analysis
- ⑤ prenatal diagnosis is also possible by amniocentesis or CVS & DNA analysis (at 19-20 week).



Treatment:-

I prophylactic treatment:-

Regular F VIII replacement 20 units/kg 3 times/week
 Avoid trauma, IM injections & aspirin.

II During bleeding attack:-

Factor VIII replacement:-

- ① recombinant Factor VIII.
- ② Fresh Frozen plasma.
- ③ Cryoprecipitate.
- ④ Factor VIII Concentrate.

III Adjuvant drugs:-

- ① Desmopressin (Vasopressin analogue) :- it $\uparrow$ endogenous Factor VIII, use in mild case.
- ② Anti Fibrinolytics (Tranexamic acid)
 used in $\rightarrow$ mucosal bleeding, menorrhagia.
- ③ prednisolone (short course) $\rightarrow$ in hemarthrosis & hematuria to minimize Fibrosis.

* In case of Hemarthrosis:-

- ① Local $\rightarrow$ Cold Sponge.
- ② Factor VIII replacement + prednisolone.
- ③ Rest for 48hr then physiotherapy to avoid ankylosis.

NB $\rightarrow$ Hemophilia B $\rightarrow$ C/P, Q & R similar to hemophilia A, except that Factor IX concentrate is used for R.

Von Willebrand's disease. (vWD)

Date



* **Epidemiology:-** vWD is the most common inherited bleeding disorder, affecting 1% of population.

* **pathophysiology:-**

The vWD is protein synthesized by endothelial cells & megacaryocytes & it has 2 functions:-

- ① platelets adhesion.
- ② carrier for FVIII protecting it from proteolysis.

* **Types of vWD:-**

Type I → partial deficiency of vWF (AD) most common.

Type II → Defect in vWF.

Type III → complete deficiency of vWF (AR) most severe.

* **Clinical picture:-**

- ① epistaxis, gum bleeding & menorrhagia.
- ② may be post operative bleeding.
- ③ very rarely purpura or hemarthrosis. (easily bruised)

* **Investigation:-** ① CBC → Normal.

② Coagulation profile:-

* Bleeding time → prolonged. (impaired platelet)

PT Normal

PPT → Prolonged
50%.

* PT → ~~prolonged~~ Normal Function

* PTT → ~~prolonged~~ Prolonged

③ Factor VIII assay → Low

④ vWF assay → Low (type I) Abnormal (type II) absent (type III).

* **Treatment :-**

- ① Desmopressin (IV / nasal spray)
- ② Factor VIII concentrate (containing FVIII & vWF)
- ③ Fresh Frozen plasma.
- ④ vWF

Purpura.

Date

No.

Definition :-

- ① multiple, spontaneous hemorrhages in the skin & mucous membrane
- ② Rang From pinpoint (petechiae) to several centimeter (Echymosis)
- ③ purple in colour, Not elevated, Not blanch on pressure, Not pruritic

Causes.

Thrombocytopenic purpura (↓ platelet count)

I Decreased production →

- ① Kongenital →
 - I Fanconi anemia
 - II TAR syndrome.
 - III Wiskott-Aldrich syndrome
 - IV osteopetrosis.

② Acquired

- I Aplastic anemia.
- II Bone marrow infiltration.
- III megaloblastic anemia.
- IV Drugs → as chemotherapy.

④ Increased destruction →

① Antibody mediated →

- ① **ITP** (the commonest)
- ② SLE
- ③ Drugs → phenytoin, sulpha.

② Non-immunologic →

- ① MAHA (eg HUS)
- ② sepsis
- ③ Hypersplenism.
- ④ Merritt-Kasabach syndrome.

Non thrombocytopenic purpura (Normal platelet count).

I vascular purpura.

- ① Hereditary Ehler Danlos syndrome
- ② Acquired → HSP

• scurvy
• sepsis.

② platelet dysfunction. (thrombasthenia)

① Hereditary

- ① Defect in Adhesion (von Will. brand)
- ② Defect in aggregation.
(Glanzmann disease)

② Acquired:

→ CRF
→ Aspirin.

Idiopathic Thrombocytopenic purpura. (I.T.P)

Definition:- is an immune mediated reduction in the platelet count & characterized by →



- ① shortened platelets survival.
- ② Thrombocytopenia.
- ③ Increased megakaryocytes in bone marrow.
- ④ Absence of other identifiable causes (Dx of exclusion).
- ⑤ otherwise healthy child.

Incidence:- * ITP is the most common bleeding disorder in children.

- * Age → 2-5 years & more in ♂ → URTI commonly
- * often follow infection (viral) as EBV, measles, Rubella.

Etiology:- * is an Autoimmune condition with Antibodies detectable against several platelet surface Antigens.

- * spleen is the primary site for antibodies production.
- * platelets destruction.

- C/p:-
- ① Bleeding → usually spontaneous but may be follow minor trauma usually acute onset & occurring 1-4 weeks after viral infection.
 - ① → purpura
 - ② External bleeding (epistaxis, oral bleeding)
 - ③ rarely Internal bleeding (Intracranial Hemorrhage) 1%
 - ② No significant organomegally & usually No splenomegally but tip of spleen may be palpable in <10% mcp
 - ③ No pallor except with significant bleeding.

Investigation:-

* ITP is a clinical diagnosis [thrombocytopenia in well appearing child & Normal CBC].

- ① CBC → WBC → Normal, RBC → Normal, platelet → ↓↓
Hb → Normal (unless severe bleeding)
- ② Bleeding time → prolonged
- ③ PT & PTT → Normal
- ④ Blood Film → to exclude leukemia.

- Done
- ⑤ Bone marrow examination $\rightarrow$ Normocellular Date (If diagnosis is in doubt)
- ① megakaryocytes.
 - ② Normal myeloid & erythroid cells.
- ⑥ urea & creatinin $\rightarrow$ Normal to (exclude HUS)
- ⑦ Antiplatelet auto antibodies $\rightarrow$ usually +ve highly sensitive but non specific (Not diagnostic)

Treatment:-

(with rare exception, there is usually No need to treat ITP based on platelet counts)

- ① observation & avoid trauma
- ② For moderate to severe clinical bleeding with severe thrombocytopenia $<10,000/mm^3$
 - ① $\rightarrow$ prednisolone 2-4 mg/kg/24hr.
 - ② Immunglobulin IV. 1gm/kg/24h For 1 to 2 days
- ③ splenectomy $\rightarrow$ in
 - ① Acute ITP & life threatening bleeding unresponsive to Ig & steroid.
 - ② chronic ITP in older children uncontrolled medically (chronic ITP $\rightarrow$ ITP persists longer than 6 months)
- ④ For resistant cases $\rightarrow$ Anti D & cytotoxic drugs are used.

prognosis:-

- ① spontaneous recovery occur in in 80% of cases over 6 months duration.
- ② 10-20% progress to chronic ITP.

N.B $\rightarrow$ ① platelet transfusion Not used in Rx of ITP.
 ② Evan's Syndrome (Hemolytic anemia + ITP)

Differential diagnosis:-

Date

No.

III Microcytic Hypochromic Anemia:-

- 1 Iron deficiency anemia.
- 2 Thalassemia.
- 3 sideroblastic anemia.
- 4 Lead poisoning.
- 5 Anemia of chronic disease.

Type of Anemia	serum iron	Transferrin saturation	serum Ferritin
Iron ↓ anemia	Low	Low	Low
Thalassemia	Low	Normal	High.
Sideroblastic anemia	Normal	Normal	Normal
Lead poisoning	High	High	High
Anemia of chronic illness	Low	Normal	High.

2 Normocytic Normochromic anemia:-

- 1 Anemia of chronic disease.
- 2 most hemolytic anemia.
- 3 Acute blood loss.
- 4 Bone marrow infiltration.

3 Howell-Jolly bodies (Basophilic cytoplasmic inclusion)

- 1 post splenectomy (Asplenic patient)
- 2 Megaloblastic anemia.
- 3 B thalassemia

4 poikilocytosis:- (variation in shape of erythrocyte)

- 1 sever Iron ↓ anemia.
- 2 B thalassemia.
- 3 Tear drop poikilocytosis seen in Myeloproliferative

[5] Heinz bodies:- (inclusion of precipitated hemoglobin)

- [1] G-6-p-D deficiency, & pyruvate kinase deficiency.
- [2] thalassemia.
- [3] Asplenic patient.

[6] Basophilic stippling:- (multiple small dots in red cell)

- [1] Lead poisoning.
- [2] B thalassemia.

[7] Target cell (central & outer rim of staining with intervening ring of paler)

- [1] thalassemia, [2] liver disease,
- [3] Iron deficiency, [4] Hyposplenism.

[8] Bite cells → G-6-p-D deficiency.

[9] schistocytosis → (Fragmented cells) → mechanical

[10] Acanthocytosis → (irregularly spiculated) Hemolysis

- [1] Abetalipoproteinemia. ** m/c
- [2] severe liver disease

*** Leukemoid Reaction:-** Extreme elevation of leukocyte count ($>50,000/\text{ML}$) composed of less mature white cells released prematurely from the bone marrow:-

R.D.

- [1] T.B [2] sepsis [3] Down syndrome.
- [4] systemic onset RA.

(Leukemia)

Date

No.

Definition:- group of malignant diseases of hematopoietic cells in bone marrow giving rise to uncontrolled clonal proliferation of cells with subsequent marrow failure.

*** Is the Commonest Tumor in pediatric age group.**
→ (25-30% of all childhood cancer)

*** Incidence:-**
* peak Age 2-5 years.
* More in ♂



*** Risk Factors:-** etiology → unknown.

- ① Genetic predisposition. (Identical twins → 20%)
- ② Chemicals (e.g Benzene in AML)
- ③ Ionizing radiation.
- ④ Drugs
- ⑤ chromosomal abnormalities:- as Down syndrome, Fanconi anemia, Ataxia Telangiectasia, Bloom syndrome, schwachman Diamond syndrome
- ⑥ Immune deficiency as wiskott aldrech syndrome.

*** Classification:-**

III Acute Leukemia (97%)

- ① Acute Lymphoblastic leukemia [ALL] → 75%
- ② Acute Non Lymphoblastic Leukemia [ANLL]
= Acute myeloblastic Leukemia → 20%

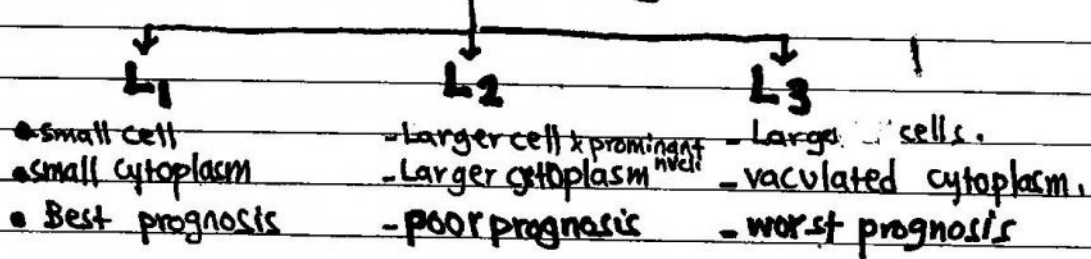
II Chronic Leukemia (3%)

- * Chronic myeloid Leukemia → ① philadelphia chromosome +ve myeloid Leukemia
- * ② Juvenile myelomonocytic Leukemia (JMNL)

Acute Lymphoblastic Leukemia. ALL

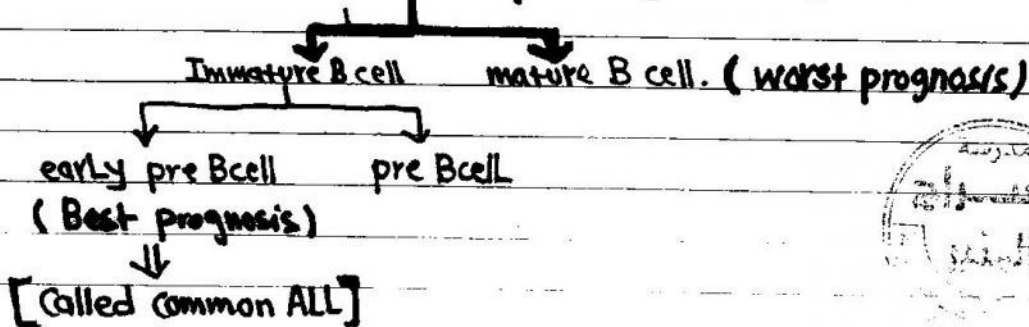
* Classification:-

① Morphological [FAB classification] French-American-British



② Immunophenotyping:- → Determine subtypes of ALL according to Blast cell membrane & cytoplasmic markers.

③ B cell type:- [$> 80\%$]



④ T cell type [Bad prognosis]

* clinical picture → peak Age [2-5 year] of life.

① Non specific symptoms:-

- ① Anorexia
- ② Irritability
- ③ Lethargy
- ④ wt Loss
- ⑤ Fever

② Manifestation of bone marrow Failure :-

- ① Anemia → pallor, Fatigability, ↑HR, dyspnea, HF.
- ② Neutropenia → Fever & infection.
- ③ Thrombocytopenia → petechiae, purpura, easy bruising, Bleeding

3] Manifestation of organ infiltration 8-

- ① generalized Lymphadenopathy. [25-50%]
- ② Hepato splenomegally [70%]
- ③ Mediastinal mass (with T cell type)
- ④ CNS involvement $\rightarrow$ $\leq 5\%$ in ALL
(sign of $\uparrow$ ICP & Fits & paresis)
- ⑤ Testis (painless enlargement of testis) 10-20% ^{in Boys}
- ⑥ Renal Involvement $\rightarrow$ Hematuria & Hypertension
- ⑦ Bone & Joint $\rightarrow$ Bone pain is one of the initial symptoms

Diagnosis $\rightarrow$

■ For Diagnosis

- 1] CBC $\rightarrow$ WBC $\rightarrow$ Low - Normal - Increased
Hb $\rightarrow$ Low [Anemia]
PLT $\rightarrow$ Low [thrombocytopenia]

- 2] Blood Film $\rightarrow$ Blast cell are present on blood smear.
 $> 2\%$, but absent of Blast cell does not exclude diagnosis.

3] Bone marrow examination

$> 25\%$

- * Bone marrow is usually replaced by 80-100% blasts.
- * Leukemia must be suspected when bone marrow contains more the 5% blast cells

* special Bone marrow studies help in detailed cell classification Include:-

- ① cytogenic study (Morphology)
- ② Immunophenotyping 80 in majority of cases have antigen on their surface of blast cell called common acute Lymphoblastic Leukemia.
- ③ Histochemistry.

■ To detect Infiltration

- ① chest X Ray. ② CT scan chest.
- ③ U/S abdomen ④ LP & CSF examination.
- ⑤ Renal & liver Function Test.
- ⑥ Bone survey.

(36)

* Treatment of ALL

Date

No.

① Specific Rx:-

1 Induction of Remission:-

* Aim $\rightarrow$ To eradicate malignant cells in bone marrow.

* Duration $\rightarrow$ 4-6 weeks

* Chemotherapy $\rightarrow$ ① Vincristine (weekly)

② prednisolone (Daily)

③ L-asparaginase

④ Intrathecal methotrexate.

* Criteria of remission are:-

① No hepatosplenomegaly, Lymphadenopathy.

② Normal CBC. ③ Bone marrow Blast $< 5\%$.

2 CNS prophylaxis [CNS therapy]

* Aim $\rightarrow$ prevent later CNS relapses.

* Duration $\rightarrow$ 4 weeks.

* Drugs $\rightarrow$ Intrathecal methotrexate.
Cranio spinal irradiation.

3 Maintenance phase:-

* Aim $\rightarrow$ maintain remission.

* Duration $\rightarrow$ 2-3 years.

* Drugs $\rightarrow$ Daily 6 mercaptopurine.
weekly methotrexate.

Intermittent dose of vincristine & steroids.

② Supportive Rx:-

① Control of infection $\rightarrow$ good hygiene, IV antibiotics
IF granulocytopenia (Neutrophils $< 500 \text{ cells/mm}^3$)
give $\rightarrow$ Granulocyte colony stimulating Factor (G-CSF)
 $\rightarrow$ = Transfusion

② Control bleeding $\rightarrow$ platelet transfusion.

③ Control Anemia $\rightarrow$ PRBC transfusion.

④ IF patient have Blast $> 50,000/\text{mm}^3$

$\rightarrow$ good hydration] To avoid Tumor lysis syndrome.
 $\rightarrow$ Allopurinol

(57)

* Complication of Leukemia

Date

No.

1] Tumour Lysis Syndrome:-

* IS group of metabolic complications that occur after treatment of cancer [Leukemia]

* Tumour cells very sensitive to chemotherapy $\rightarrow$ rapid lysis which contain high amount of uric acid + phosphate + K.

* Syndrome of $\Rightarrow$

• Hyperkalemia.

• Hyperphosphatemia.

• Hyperuricemia & Hyperuricosuria

• Hypocalcemia.

Leading to $\rightarrow$ Acute renal Failure

* Prevention:- ① over hydration (good hydration)

② Allopurinol IV (uric acid binding agent)
 $\rightarrow$ Rasburicase is alternative to allopurinol.

③ Alkalinization of the urine:-
By Na bicarbonate.

④ IF there's $\uparrow$ K $\rightarrow$ give Rx of Hyperkalemia

2] Relapsing ALL $\Rightarrow$ Common relapse $\rightarrow$ $\rightarrow$ $\rightarrow$ (Testes)
 $\rightarrow$ CNS

3] Complication of chemotherapy:-

① Bone marrow suppression. $\rightarrow$ pancytopenia.

② vincristine $\Rightarrow$ peripheral neuropathy

③ Methotrexate $\Rightarrow$ Renal Toxicity.

④ Adriamycin $\Rightarrow$ Cardiomypopathy.

(Philadelphia +ve ALL is present in 3-5% of children with ALL)

Prognosis :-

Date

No.

Good prognosis

Low Risk

Bad prognosis

High Risk

Initial CBC count

$< 50,000 / \text{mm}^3$

$> 50,000 / \text{mm}^3$

Age

$> 1 \text{ yr}, < 10 \text{ yr}$

$< 1 \text{ yr}, > 10 \text{ yr}$

Sex

Female

Male.

Race

White

black.

FAB classification

L_1

L_3

Immunophenotyping

Common ALL (pre B cell)

mature B cell & T cell

Cytogenetics

polyploidy

• Hypodiploidy

• Translocation t(9;22)

Philadelphia chromosome +ve

CNS Infiltration

-ve

Response to initial therapy

rapid response

Slow response

* **Congenital Leukemia** → [Leukemia diagnosed From Birth to 6 weeks.] It's rare & of unknown etiology.
It's associated with Trisomy 21, Turner syndrome

Lymphoma

Date

No.

Definition → Lymphoma is a neoplastic proliferation of lymphoid cells originating in lymph nodes or other lymphoid tissue

Types :-
 ① Hodgkin lymphoma. (mainly nodal)
 ② Non-Hodgkin lymphoma (common in pediatric age group) (mainly extranodal)

Etiology :- The cause is Not known. But may be. Risk Factors →

- ① * associated with EBV infection. (Burkitt's lymphoma)
- ② * Helicobacter pylori infection in (Gastric lymphoma)
- ③ * Radiation, drugs (phenytoin)
- ④ * Autoimmune disease as (celiac disease)
- ⑤ * Immuno suppression (AIDS)

* Histological classification :-

① Hodgkin Lymphoma →

* Reed-sternberg cells are characteristic

* Histological subtypes :-

prognosis ↓
 good ① Nodular sclerosing HL → [common 40-60%]
 ② Mixed cellularity HL. 20-40%
 ③ Lymphocyte rich HL. 10-20% [Bad prognosis]
 Bad ④ " depleted HL. 10-16% > 60yr

C/P :- → Bimodal age group

Hodgkin lymphoma
 60% of cases 10-16yr
 < 5yr → uncommon
 < 3yr → Rare

→ more common in ♂

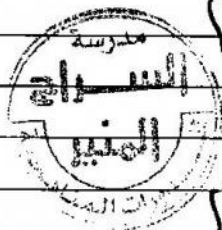
- ① enlarged painless cervical lymphadenopathy 70-80% or supraclavicular lymphadenopathy
- ② Constitutional symptoms (B symptoms) 30%
 [Fever - wt loss - night sweating]
- ③ Generalized pruritis (Itching)
- ④ splenomegally & hepatomegaly in advanced case
- ⑤ 50% have asymptomatic mediastinal disease.
- ⑥ Pel-Ebstein Fever.

Investigation:-

Date

No.

- ① CBC $\rightarrow$ usually normal. [Anemia & $\downarrow$ plt may be present]
- ② ESR & uric acid $\rightarrow$ High.
- ③ $\uparrow$ LDH
- ④ Radiology $\rightarrow$ chest X Ray & CT scan & MRI
- ⑤ Lymph Node biopsy:-



Indication:-

- ① Failed to resolve within 4-8 wk.

② Lymphadenopathy $\uparrow$ in size after 2wk.

③ Lack of infection.

④ Node size > 2 cm in diameter.

Biopsy show:- Reed sternberg cells $\rightarrow$



⑥ Bone marrow aspiration.

* Stages of Hodgkin lymphoma (Ann Arbor staging)

Stage I $\rightarrow$ Single lymph node region or single extra lymph node

Stage II $\rightarrow$ Two or more lymph node region at the same side of the diaphragm.

Stage III $\rightarrow$ Lymph node in both side of the diaphragm.

Stage IV $\rightarrow$ Diffuse involvement of an extra nodal organs

(Liver, Bone marrow) IV A $\rightarrow$ No B symptoms.

IV B $\rightarrow$ with B symptoms.

Treatment:- (Chemotherapy $\pm$ Radiotherapy)

* Stage I & II $\Rightarrow$ treated with local radiotherapy.

* Higher stages chemotherapy & radio therapy.

* Chemotherapeutic agent:-

ABVD Regim (Adriamycin + Bleomycin + Vinblastin +
Decarbazine).

[2] Non Hodgkin lymphoma:-

- (10-15% nodal)
- $\Rightarrow$ most common type (common in pediatric age group)
 - $\Rightarrow$ symptoms mainly extranodal. (compression symptoms)
 - $\Rightarrow$ D the same except in Biopsy (No Reed sternberg cell)
 - $\Rightarrow$ same staging & the same Rx.