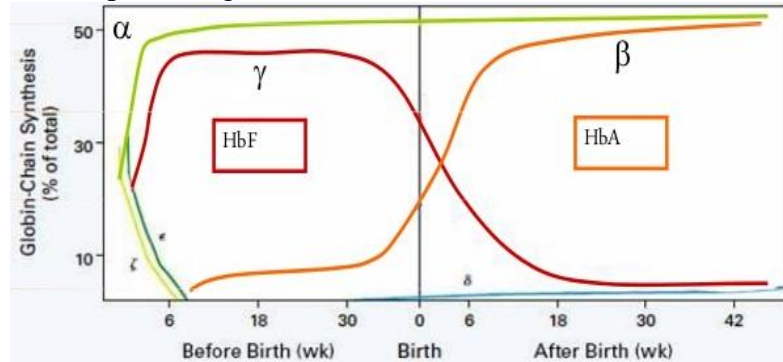
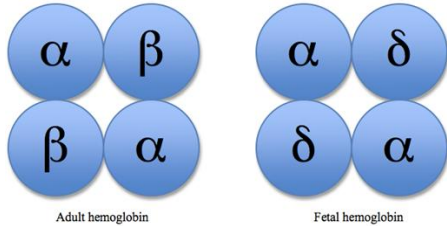


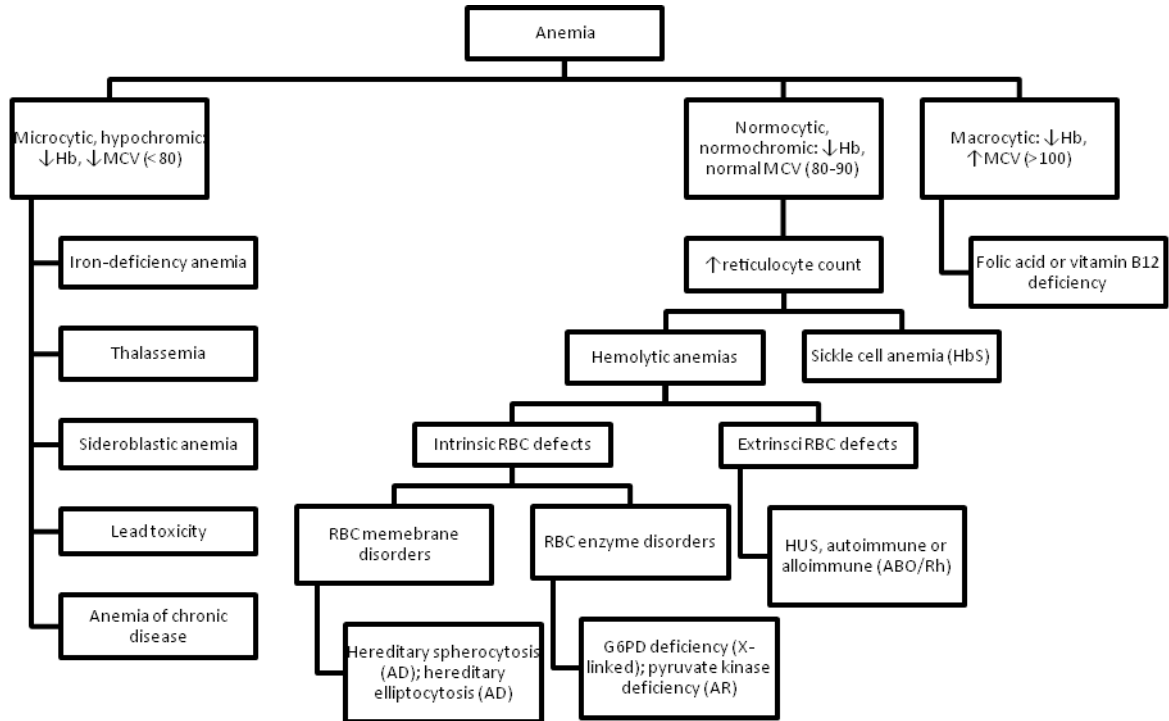


- **Anemia:**

- It is a reduction in number of RBCs or Hb concentration > 2 SD below the mean for a corresponding age and sex.
- **HbF:** has a higher affinity to oxygen but it reduces and disappears by 6 months of age. Thus infants with SCD will not experience crisis until that age.
- 80% of children in developing countries will experience anemia sometime during their childhood.
- **Reticulocyte count:** represents immature RBCs in the circulation (normally 1%). Increased count indicates active hemolysis while decreased count with anemia indicates bone marrow failure in producing new RBCs.



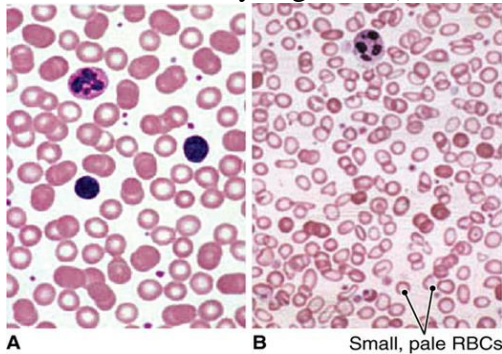
• **Classification of anemia:**





• **Iron-deficiency anemia:**

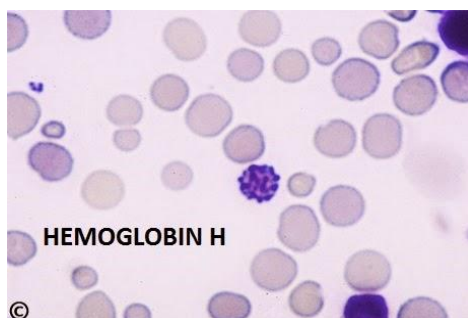
- ✓ It is microcytic, hypochromic and is the most common blood disease during infancy and childhood.
- ✓ Causes:
 - ❖ *Nutritional deficiency:* iron stores are depleted by 6 months of age thus iron-fortified cereals must be added at that time to prevent anemia. Notice that cow's milk is deficient in iron.
 - ❖ *Increased demand (especially in adolescent females):* due to blood loss during menstruation or pregnancy.
 - ❖ *Blood loss:* PUD (in developed countries); hookworms (developing countries).
- ✓ Clinical features: pallor (of skin and conjunctiva), weakness and fatigue, koilonychia (spoon-shaped nails) and pica (desire to eat unusual substances such as ice).
- ✓ Investigations: CBC (\downarrow Hb, \downarrow MCV), \downarrow ferritin, \downarrow serum iron, \uparrow TIBC, \uparrow reticulocyte count.
- ✓ Management: iron supplementation with vitamin C (orange juice) to enhance intestinal iron absorption + increase iron intake from diet (red meat and green leafy vegetables).



• **α -thalassemia:**

- ✓ It is an inherited disease in which there is deletion in α -globin chain on chromosome 16 resulting in deficiency in synthesis of α -globin chain.
- ✓ Severity of the disease depend on the number of genes deleted (normally there are 4 genes):

Silent carrier	<ul style="list-style-type: none"> • 1 gene is deleted • Patient is asymptomatic
α-thalassemia minor	<ul style="list-style-type: none"> • 2 genes are deleted • There is mild anemia
HbH disease	<ul style="list-style-type: none"> • 3 genes are deleted • Severe anemia at birth with \uparrow Hb Bart's
Hydrops fetalis	<ul style="list-style-type: none"> • 4 genes are deleted • Incompatible with life





• **β-thalassemia:**

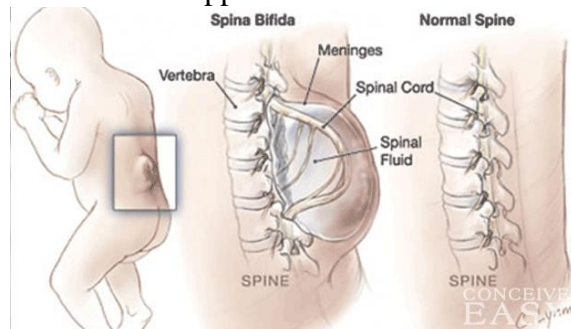
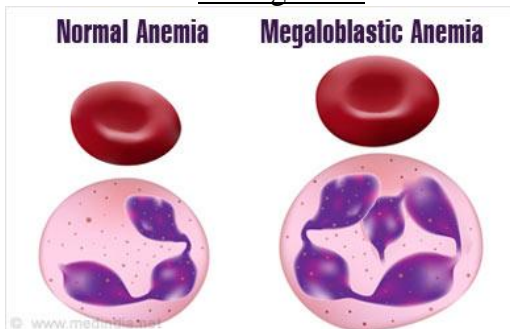
β-thalassemia major	B-thalassemia minor (trait)
<ul style="list-style-type: none"> • There is total absence of β-globin chains (genes are present on chromosome 11) • <u>Clinical features</u>: severe hemolysis, hepatosplenomegaly, bone marrow hyperplasia with thalassemia facies (chipmunk's face) and hair-on-end on skull x-ray • <u>Investigations</u>: ↓Hb, ↓MCV, ↑indirect bilirubin, target cells on peripheral blood smear and Hb electrophoresis shows (↓HbA, ↑HbF) • <u>Management</u>: lifelong transfusion which might be complicated with hemochromatosis (deposition of iron in liver, pancreas and skin) → iron chelation therapy with deferoxamine 	<ul style="list-style-type: none"> • <u>Investigations</u>: ↓Hb, ↓MCV, ↑HbA₂ on Hb electrophoresis and target cells on peripheral blood smear... but notice that this is a mild asymptomatic anemia. • No treatment is required.

Beta Thalassemia Major – bone changes



• **Folic acid deficiency:**

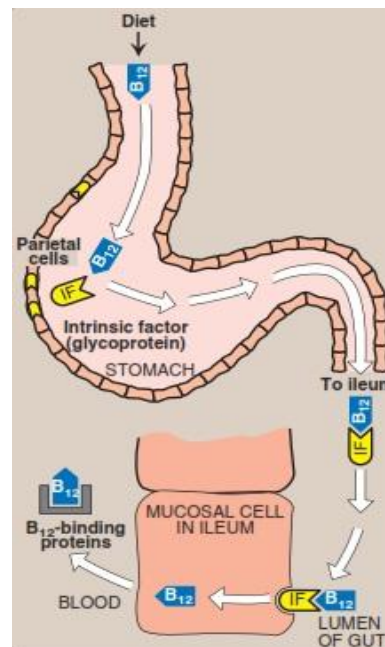
- ✓ It causes megaloblastic anemia and occurs due to:
 - ❖ *Nutritional deficiency*: no green leafy vegetables in diet; exclusive feeding with goat's milk.
 - ❖ *Decreased absorption of folate from intestine*.
- ✓ Clinical features: pallor (of skin and conjunctiva), weakness and fatigue. Notice that folate deficiency in pregnant women might result in neural tube defects in the fetus.
- ✓ Investigations: ↓Hb, ↑MCV and ↓serum folate.
- ✓ Management: increased intake of folate or supplements.





- **Vitamin B12 deficiency:**

- ✓ Normal absorption: dietary vitamin B12 must bind to intrinsic factor (which is produced by parietal cells of the stomach) and then absorbed in terminal ileum.
- ✓ Causes of deficiency:
 - ❖ Nutritional deficiency (strict vegetarian diet).
 - ❖ Inability to secrete intrinsic factor.
 - ❖ Inability to absorb vitamin B12 (Crohn's disease).
- ✓ Clinical features: pallor, fatigue and weakness, smooth red tongue (glossitis) and neurologic manifestations (sub-acute combined degeneration of the spinal cord).
- ✓ Investigations: ↓Hb, ↑MCV and ↓serum vitamin B12
- ✓ Management: monthly IM injection of vitamin B12.

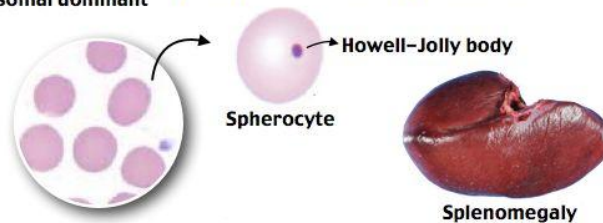


- **Hereditary spherocytosis:**

- ✓ It is an AD inherited defect in RBC membrane protein (spectrin) resulting in the spherical shape of RBCs that will lead to their destruction as they pass through the spleen.
- ✓ Clinical features: pallor, weakness and fatigue, splenomegaly, pigmentary gallstones and aplastic crisis (associated with parvovirus B19 infection).
- ✓ Investigations: ↓Hb, normal MCV, spherocytes on peripheral blood smear and abnormal RBC fragility with osmotic fragility test.
- ✓ Management: splenectomy (but this is delayed until after 5 years of age to avoid decreased immunity and subsequent infections).

Hereditary Spherocytosis

Autosomal dominant



Dense and hyperchromic
Autoimmune hemolytic anemia

- **Pyruvate kinase deficiency:**

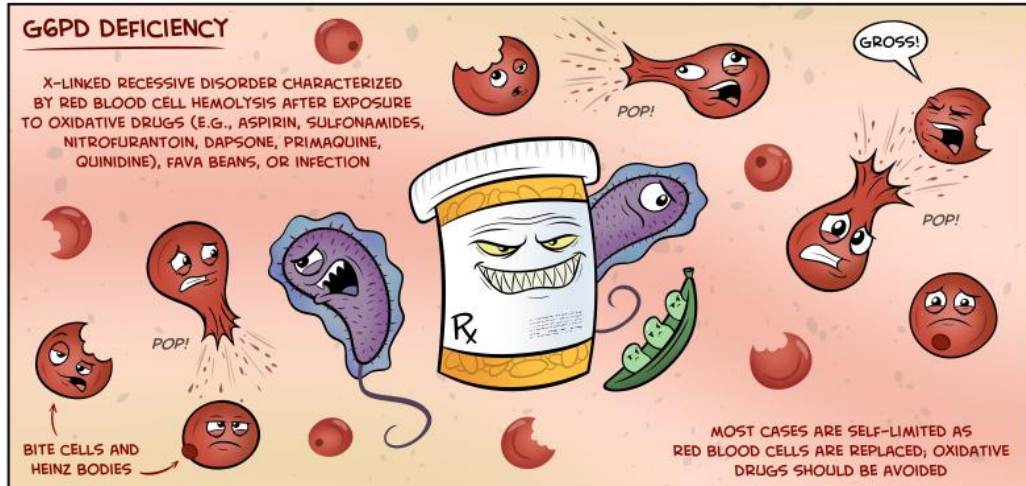
- ✓ It is an AR disorder which is characterized by decreased pyruvate kinase production resulting in decreased survival of RBCs.
- ✓ Clinical features: pallor, jaundice and splenomegaly.
- ✓ Investigations: polychromatic RBCs on peripheral blood smear and decreased enzyme activity in RBCs.
- ✓ Management: blood transfusions. Notice that splenectomy is done in severe disease.

- **G6PD deficiency:**

- ✓ It is an X-linked recessive disorder in which there is deficiency of the enzyme Glucose-6-Phosphate Dehydrogenase (G6PD) resulting in decreased formation of reduced glutathione which will predispose RBCs to oxidative stress caused by Reactive Oxygen Species (ROS). They will cause hemolysis of RBC membrane producing what is known as Heinz bodies.
- ✓ Hemolysis attack is triggered by: fava beans, infections and anti-malarial drugs.



- ✓ Clinical features: hemolysis, hemoglobinuria and jaundice.
- ✓ Investigations: ↓Hb, ↑reticulocyte count, bite cell on peripheral blood smears, ↑indirect bilirubin and ↓G6PD in RBCs.
- ✓ Management: blood transfusions (as needed).



- **Autoimmune Hemolytic Anemia (AIHA):**

- ✓ In this condition there are autoantibodies directed against RBCs.
- ✓ Classification and clinical features:

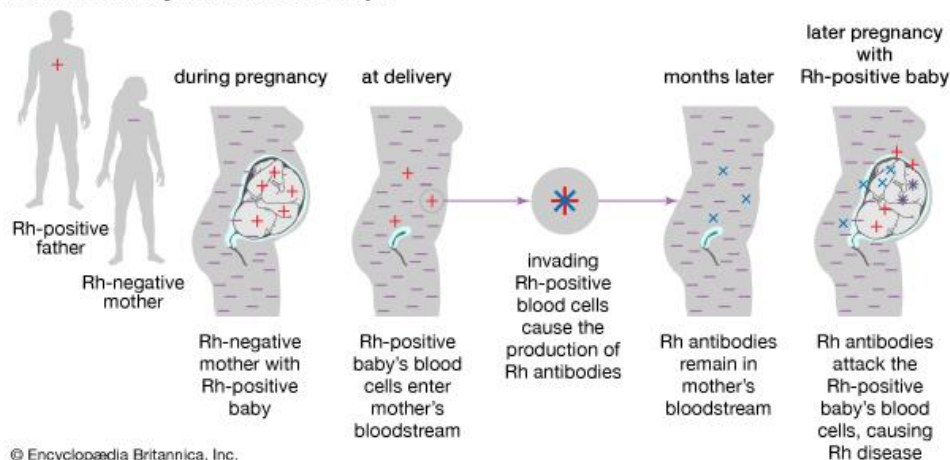
Primary	Secondary
<ul style="list-style-type: none"> • Idiopathic but can be associated with viral infections or drugs • Pallor, jaundice, hemoglobinuria and splenomegaly. • A complete recovery is expected 	<ul style="list-style-type: none"> • There is an underlying disease such as SLE, lymphoma or immunodeficiency disease • Associated with high mortality.

- ✓ Investigations: ↓Hb, ↑reticulocyte count, ↑WBCs, (+) direct Coomb's test and spherocytes on peripheral blood smear.
- ✓ Management: corticosteroids.

- **Alloimmune hemolytic anemia:**

- ✓ Rh hemolytic disease: an Rh (-) mother will produce antibodies against RBCs of an Rh (+) fetus. In subsequent pregnancies, these antibodies will cross from the mother to the fetus causing hydrops fetalis (hemolysis, jaundice and hepatosplenomegaly). There is (+) direct Coomb's test.

How Rh hemolytic disease develops



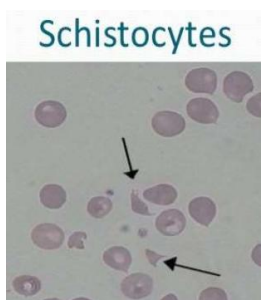
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- ✓ ABO hemolytic disease: this occur when the mother is blood group O and her fetus is blood group A or B or AB. This can occur in first pregnancy. Direct Coomb's test is weakly positive.



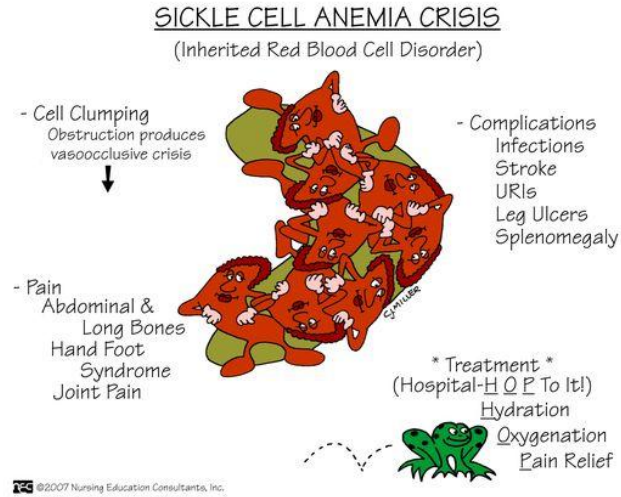
• **Microangiopathic hemolytic anemia:**

- ✓ In this condition there is an injury to vascular endothelium (such as in hypertension) and as RBCs pass through → hemolysis and fragmentation will occur.
- ✓ Investigations: ↓Hb (anemia) and ↓platelet count (thrombocytopenia).
- ✓ Management: supportive with treatment of underlying cause.



• **Sickle Cell Disease (SCD):**

- ✓ It is an AR disease in which there is single amino acid substitution (valine instead of glutamic acid) in the 6th amino acid position of β-globin chain. This will produce the abnormal hemoglobin (HbS). When a person experiences hypoxic conditions, RBCs will polymerize thus occluding small blood vessels and resulting in ischemia and infarction of different organs.



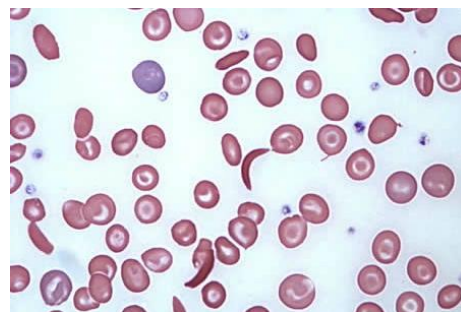
- ✓ There are 5 main types of crisis:

Crisis	Clinical features	Management
Vasocclusive crisis (also known as painful bone crisis)	<ul style="list-style-type: none"> • Most common. • Ischemia/infarction of bones (patient usually presenting with pain in limbs) • Differential diagnosis: osteomyelitis especially if there is fever and signs of inflammation 	<ul style="list-style-type: none"> • Analgesia (IV paracetamol or morphine). • Hydration (1 ½ maintenance)
Acute Chest Syndrome (ACS)	<ul style="list-style-type: none"> • Patient has cough, chest pain and SOB due to infection with S.pneumoniae 	<ul style="list-style-type: none"> • Analgesia. • Hydration. • Oxygen. • Antibiotics (cefuroxime and azithromycin)
Sequestration crisis	<ul style="list-style-type: none"> • There is rapid accumulation of RBCs in the spleen. • Patient has pallor, abdominal pain and abdominal distention • Labs: ↓Hb, ↑retics 	<ul style="list-style-type: none"> • Analgesia. • Hydration. • Blood transfusion



Anaplastic crisis	<ul style="list-style-type: none"> • Bone marrow failure mainly due to infection with parvovirus B19 • Labs: ↓Hb, ↓retics 	<ul style="list-style-type: none"> • Analgesia. • Hydration. • Blood transfusion
Hemolytic crisis	<ul style="list-style-type: none"> • Rapid hemolysis often occurring in patients with other hemolytic disease (such as G6PD deficiency) • Labs: ↓Hb, ↑retics, ↑bilirubin 	<ul style="list-style-type: none"> • Analgesia • Hydration • Blood transfusion

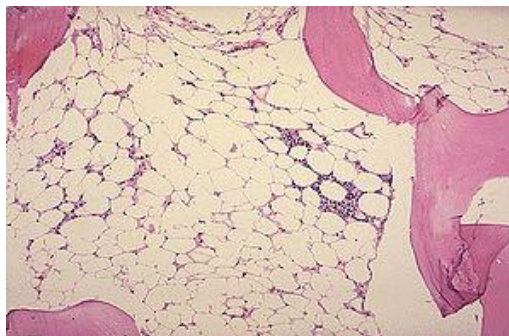
- ✓ Peripheral blood smear shows: sickled cells and sometimes Howell-Jolly bodies (if there is hyposplenism).
- ✓ Complications: infection with encapsulated bacteria: H. influenza, S.pneumoniae and Salmonella (which causes osteomyelitis).
- ✓ Preventive care: hydroxyuria (which is increasing HbF levels thus lowering the chances of hypoxia and subsequent crisis), daily folic acid and immunization especially against encapsulated bacteria.



- **Pancytopenia:**

- **It is bone marrow failure with:** ↓RBCs, ↓WBCs and ↓platelets.
- **Classification:**

Congenital aplastic anemia (Fanconi anemia)	Acquired aplastic anemia
<ul style="list-style-type: none"> • <u>AR</u> characterized by: petechiae and ecchymosis, short stature, absence/hypoplasia of thumb and radius, renal abnormalities and skin hyperpigmentation. 	<u>Caused by:</u> chemicals, radiation, infections (HIV, EBV or CMV) or drugs. Therefore, you have to stop the causative agent
<u>Investigations:</u> pancytopenia, ↓reticulocyte count and bone marrow hypocellularity	
<u>Management:</u> transfusion of RBCs and platelets (as needed) and bone marrow transplantation as a definitive treatment	

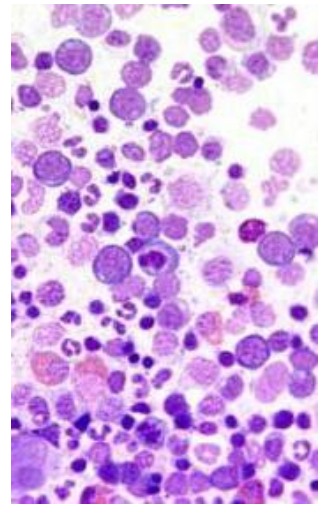


- **Polycythemia:**

- **It is an increase in RBCs relative to total blood volume. Hct is > 60%**
- **Classification:**
 - ✓ Primary polycythemia (polycythemia vera): it is malignancy involving RBC precursor.
 - ✓ Secondary polycythemia: due to increase in erythropoietin production. This is further classified to be:



- ❖ *Appropriate secretion*: caused by chronic hypoxemia due to cyanotic congenital heart disease (most common cause of polycythemia in childhood).
- ❖ *Inappropriate secretion*: caused by benign or malignant tumors of the kidney.
- ✓ Clinical features: red face with no organomegaly.
- ✓ Investigations: ↑Hb, ↑Hct, ↑erythropoietin.
- ✓ Management: treatment of underlying cause and phlebotomy (withdrawal of blood to lower the concentration of RBCs).
- ✓ Relative polycythemia: increase in RBCs when there is decreased plasma volume (in dehydration).
- ✓ Complications: thrombosis (stroke, MI) or bleeding.



- **Disorders of hemostasis:**

• **Hemophilia-A:**

- ✓ It is an X-linked recessive disorder which occurs in males and is characterized by deficiency of factor VIII.
- ✓ The main clinical features which occur are: hemarthrosis (in elbows, knees and ankles) and deep soft tissue bleeding. There is a complication of CNS bleeding which is life-threatening. Features depend on activity of factor VIII:

Severe (< 1%)	Spontaneous bleeding
Moderate (5%)	Bleeding after trauma
Mild (> 5%)	Bleeding after surgery or major trauma

- ✓ Investigations:

aPTT	PT	Bleeding time	Platelets	Petechiae	Hemarthrosis
Prolonged	Normal	Normal	Normal	No	Yes

❖ *It is differentiated from von Willebrand's disease in that bleeding time is normal and von Willebrand's factor is normal.*

- ✓ Management: recombinant factor VIII (notice that antibodies might develop against it as a complication). DDAVP can be used with mild hemophilia.

HEMOPHILIA
(Inherited Blood Disorder
Factor VIII, Classic, or Type A)

- No Cure
- Avoid Injury & Meds That Promote Bleeding
- Good Nutrition
- Good Dental Hygiene
- IV Administration Of Deficient Clotting Factor

- Intracranial Hemorrhage
- Prolonged Nosebleeds
- Bruises Easily
- Warm, Painful, Swollen Joints With ↓ Movement
- GI Hemorrhage

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• **von Willebrand's disease:**

- ✓ It is an AD disorder which is characterized by deficiency of von Willebrand's factor (vWf) of factor VIII complex.
- ✓ Clinical features: mild to moderate mucocutaneous bleeding (epistaxis; bleeding after dental extraction or tonsillectomy; menorrhagia).

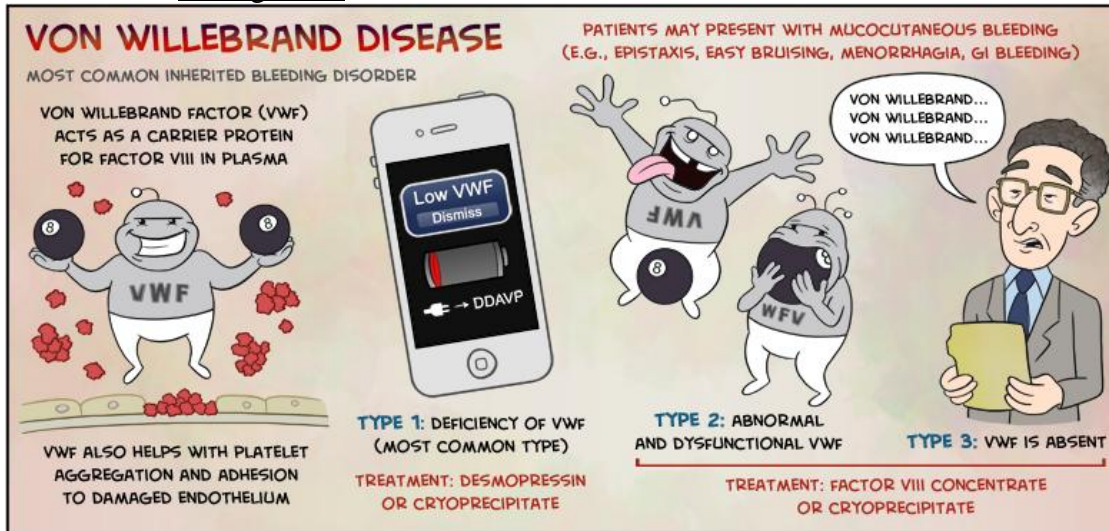


✓ Investigations:

aPTT	PT	Bleeding time	Platelets	Petechiae	Hemarthrosis
Prolonged	Normal	Prolonged	Normal	No	Rare

❖ (vWf) is reduced by ristocetin test.

✓ Management: DDAVP.



• **Vitamin K deficiency:**

✓ Vitamin K is a fat-soluble vitamin (other fat-soluble vitamins are A, D and E) which is essential for synthesis of factors II, VII, IX, X, protein C and protein S.

✓ Causes of vitamin K deficiency:

- ❖ *Nutritional deficiency is unusual.*
- ❖ *Hemorrhagic disease of newborn:* which occurs between 2-7 days (at day 1 there is still vitamin K derived from the mother; at day 7 intestinal bacteria will start producing vitamin K). This now rarely occurs because neonates are routinely given vitamin K IM injection as they are born to prevent this complication.
- ❖ *Pancreatic insufficiency, biliary obstruction or inability to absorb vitamin K.*
- ❖ *Medications interfering with vitamin K metabolism (such as warfarin).*

✓ Clinical features: bruising, oozing from skin puncture wounds and bleeding into organs.

✓ Investigations:

aPTT	PT	Bleeding time	Platelets	Petechiae	Hemarthrosis
Prolonged	Prolonged	Normal	Normal	Yes	Yes

✓ Management: administration of vitamin K

• **Disseminated Intravascular Coagulation (DIC):**

✓ It is a secondary phenomena to: malignancy, sepsis, burns, snake bites... etc.

✓ Clinical features: bleeding from venepuncture sites.

✓ Investigations:

aPTT	PT	Bleeding time	Platelets	Petechiae	Hemarthrosis
Prolonged	Prolonged	Prolonged	↓	Yes	Sometimes

❖ *In addition, there will be:* ↓fibrinogen and ↑D-dimer

✓ Management: treatment of underlying cause, FFP and platelets (as needed).



- **Quantitative platelet disorders:** thrombocytopenia ($<100,000/\mu\text{L}$) either due to decreased production or increased destruction by the spleen
 - ✓ Decreased platelet production:
 - ❖ *Wiskott-Aldrich syndrome:* it is an X-linked disorder which is characterized by the triad of thrombocytopenia, eczema and defects in T and B-cell immunity.
 - ❖ *Thrombocytopenia-absent radius syndrome:* it is AR and differentiated from Fanconi anemia in that the thumb is present.
 - ✓ Increased platelet destruction (Immune Thrombocytopenic Purpura ITP):
 - ❖ It is a disorders which can be idiopathic (most common) or preceded by a viral infection which will trigger the production of autoantibodies against Gp IIb/IIIa of platelets. This will lead to destruction of platelets by macrophages in the spleen.
 - ❖ *Clinical features (the following can occur):* petechiae and bruising, epistaxis, gingival bleeding and menorrhagia in adolescent females.
 - ❖ *Investigations:* \downarrow platelet count.
 - ❖ *Management:* IV immunoglobulin or corticosteroids. Platelets transfusion is generally of no benefit.
 - ❖ *Prognosis:* 80% will resolve within months. Chronic ITP persists > 6 months for which splenectomy can be done.
- **Qualitative platelet disorders:** there is no thrombocytopenia but there is deficiency in platelet function:
 - ✓ Congenital:
 - ❖ *Glanzmann's thrombasthenia:* AR; deficiency in GP IIb/IIIa
 - ❖ *Bernard-Soulier syndrome:* AR; absence of platelet membrane glycoproteins.
 - ✓ Acquired:
 - ❖ Aspirin which is affecting the production of thromboxane A_2 .

- **Neutropenia:**

- It is defined as low Absolute Neutrophil Count (ANC) $< 1500 \text{ cells}/\text{mm}^3$
- Classification:

Mild neutropenia	1000-1500 cells/mm ³
Moderate neutropenia	500-1000 cells/mm ³ ; associated with infections of skin and mucous membranes
Severe neutropenia	$<500 \text{ cells}/\text{mm}^3$; associated with severe infections such as sepsis, meningitis and pneumonia.

- **Neutropenia caused by decreased production:**
 - ✓ Infections are the most common cause of neutropenia in childhood:
 - ❖ *Viruses:* CMV, EBV and HIV.
 - ❖ *Bacteria:* typhus.
 - ❖ *Protozoa:* malaria.
 - ✓ Chronic Benign Neutropenia of childhood (CBN): occurring in children < 4 years of age and associated with mild infections. It will resolve spontaneously within months to years.
 - ✓ Severe congenital agranulocytosis (Kostmann syndrome): AR; ANC $< 300 \text{ cells}/\text{mm}^3$ with life-threatening pyogenic bacterial infections.
 - ✓ Chediak-Higashi syndrome: AR; characterized by the trial of: oculocutaneous albinism, neutropenia and blond hair with silver streaks.