

DISORDERS OF BLOOD AND LYMPH & IT'S ORGANS



Presented By:

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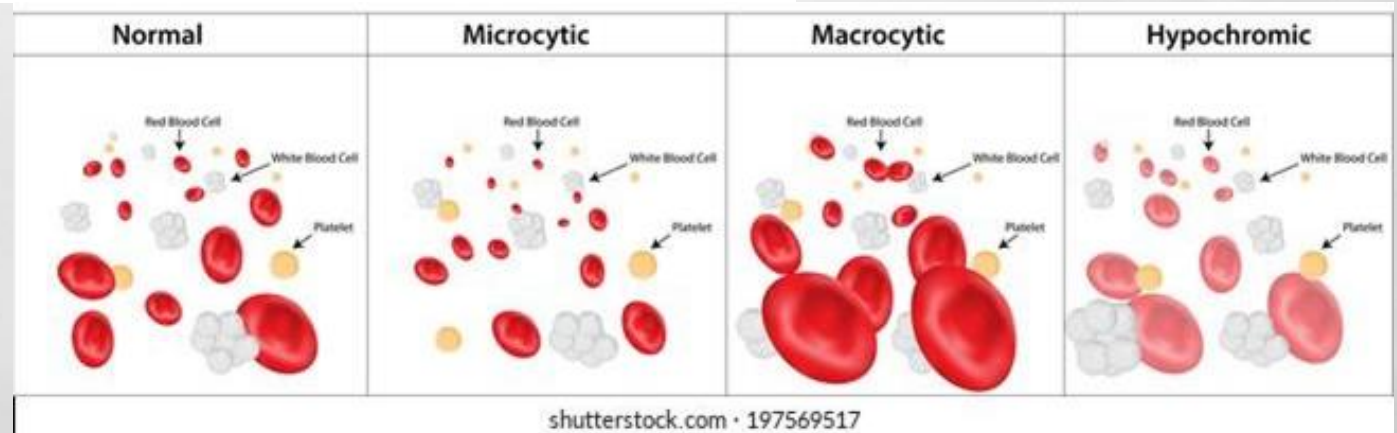
DISORDERS OF ERYTHROCYTES

Anaemias

- In anaemia there is not enough haemoglobin available to carry sufficient oxygen from the lungs to supply the needs of the tissues. It occurs when the rate of production of mature cells entering the blood from the red bone marrow does not keep pace with the rate of haemolysis.
- The classification of Anaemia is based on the cause:
 - Impaired erythrocyte production
 - – Iron deficiency
 - – Megaloblastic anaemias
 - – Hypoplastic anaemia
 - Increased erythrocyte loss
 - – Haemolytic anaemias
 - – Normocytic anaemia.
- Anaemia can cause abnormal changes in red cell size or colour, detectable microscopically.

Table 4.4 Terms used to describe red blood cell characteristics

Term	De finition
Normochromic	Cell colour normal
Normocytic	Cells normal sized
Microcytic	Cells smaller than normal
Macrocytic	Cells bigger than normal
Hypochromic	Cells paler than normal
Haemolytic	Rate of cell destruction raised
Megaloblastic	Cells large and immature



Iron deficiency anaemia

- ☐ This is the most common form of anaemia in many parts of the world.
- ☐ The normal daily requirement of iron intake in men is about 1 to 2 mg, mainly from eating meat and highly coloured vegetables.
- ☐ The normal daily requirement in women is 3 mg because of blood loss during menstruation and to meet the needs of the growing fetus during pregnancy.
- ☐ Children, during their period of rapid growth, require more than adults.
- ☐ The amount of haemoglobin in each cell is regarded as below normal when the MCH is less than 27 pg/cell.
- ☐ The anaemia is regarded as severe when the haemoglobin level is below 9 g/dl blood.
- ☐ It is caused by deficiency of iron in the bone marrow and may be due to dietary deficiency, excessively high requirements or malabsorption.
- ☐ In this type of anaemia erythrocytes are microcytic and hypochromic because their haemoglobin content is low.
- ☐ Iron deficiency anaemia can result from deficient intake, unusually high iron requirements, or poor absorption from the alimentary tract.

Deficient intake

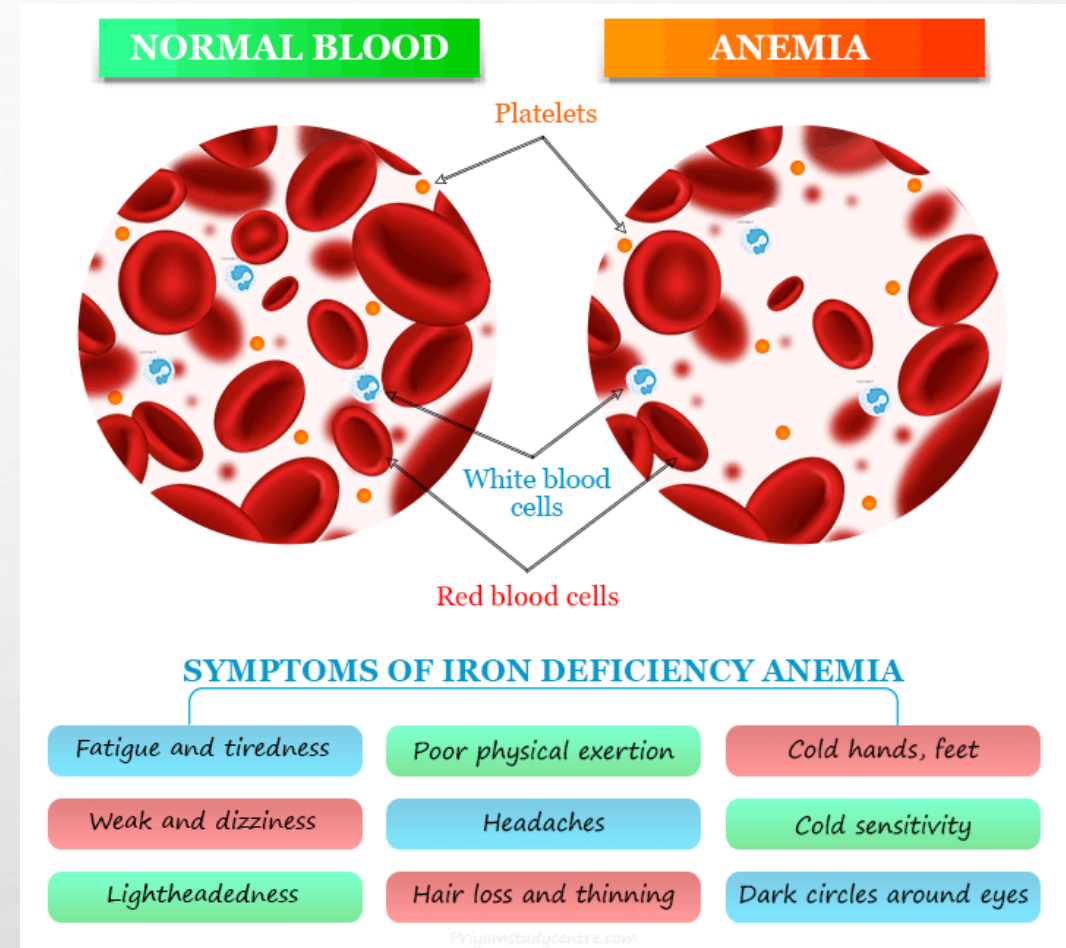
- Because of the relative inefficiency of iron absorption, deficiency occurs frequently, even in individuals whose requirements are normal.
- The risk of deficiency increases if the daily diet is restricted in some way, as in poorly planned vegetarian diets, or in weight-reducing diets where the range of foods eaten is small.
- Babies dependent on milk may also suffer mild iron deficiency anaemia if weaning on to a mixed diet is delayed much past the first year, since the liver carries only a few months' store and milk is a poor source of iron.

High requirements

- In pregnancy iron requirements are increased both for fetal growth and to support the additional load on the mother's cardiovascular system.
- Iron requirements also rise when there is chronic blood loss, the causes of which include peptic ulcers, heavy menstrual bleeding (menorrhagia), haemorrhoids or carcinoma of the GI tract

Malabsorption

- Iron absorption is usually increased following haemorrhage, but may be reduced in abnormalities of the stomach, duodenum or jejunum.
- Because iron absorption is dependent on an acid environment in the stomach, an increase in gastric pH may reduce it; this may follow removal of part of the stomach, or in pernicious anaemia, where the acid-releasing (parietal) cells of the stomach are destroyed.
- Loss of surface area for absorption in the intestine, e.g. after surgical removal, can also cause deficiency.



Megaloblastic anaemias

- ❑ Deficiency of vitamin B12 and/or folic acid impairs erythrocyte maturation and abnormally large erythrocytes (*megaloblasts*) are found in the blood.
- ❑ During normal erythropoiesis several cell divisions occur and the daughter cells at each stage are smaller than the parent cell because there is not much time for cell enlargement between divisions.
- ❑ When deficiency of vitamin B12 and/or folic acid occurs, the rate of DNA and RNA synthesis is reduced, delaying cell division.
- ❑ The cells can therefore grow larger than normal between divisions.
- ❑ Circulating cells are immature, larger than normal and some are nucleated (MCV > 94 fl).
- ❑ The haemoglobin content of each cell is normal or raised.
- ❑ The cells are fragile and their life span is reduced to between 40 and 50 days.
- ❑ Depressed production and early lysis cause anaemia.

Vitamin B12 deficiency anaemia

Pernicious anaemia: This is the most common form of vitamin B12 deficiency anaemia. It is commonest in females usually between 45 and 65 years of age. It is an autoimmune disease in which autoantibodies destroy intrinsic factor (IF) and parietal cells in the stomach.

Dietary deficiency of vitamin B12 This is rare, except in true vegans, i.e. when no animal products are included in the diet. The store of vitamin B12 is such that deficiency takes several years to appear.

Other causes of vitamin B12 deficiency

These include the following.

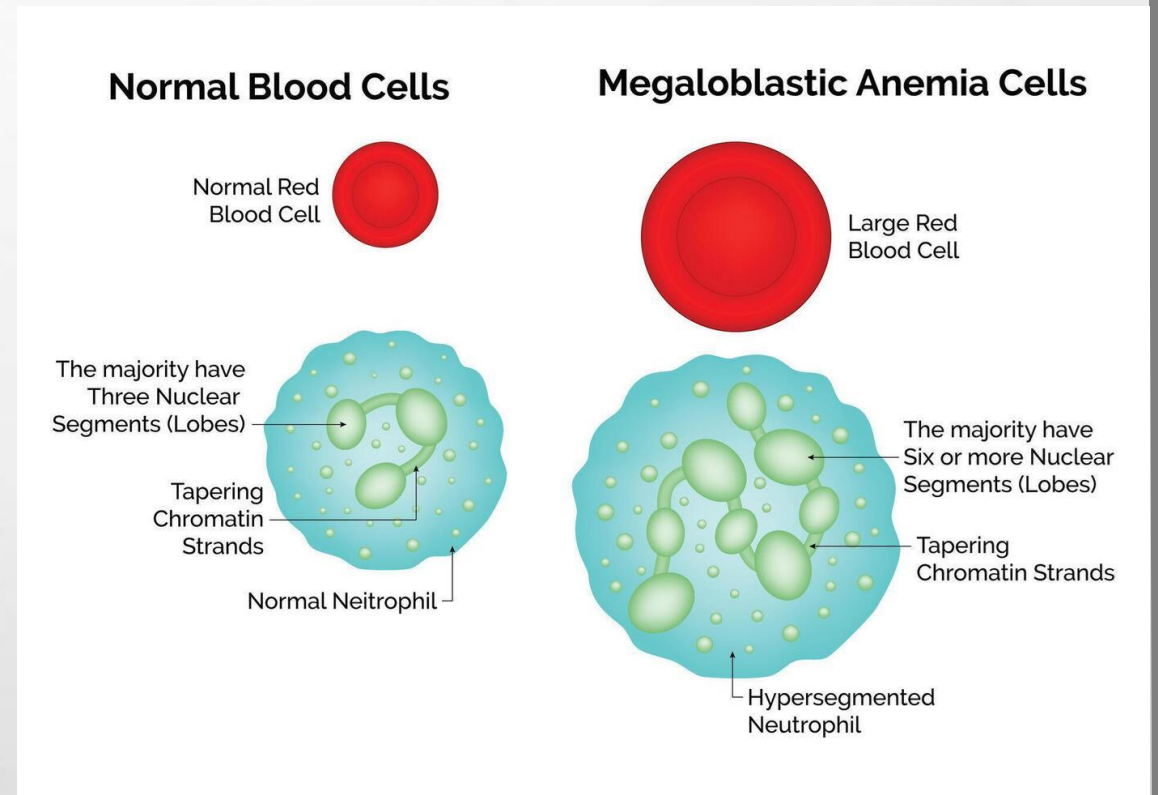
- Gastrectomy (removal of all or part of the stomach) – this leaves fewer cells available to produce IF.
- Chronic gastritis, malignant disease and ionising radiation – these damage the gastric mucosa including the parietal cells that produce IF.
- Malabsorption – if the terminal ileum is removed or inflamed, e.g. in Crohn's disease, the vitamin cannot be absorbed.

Complications of vitamin B12 deficiency anaemia

These may appear before the signs of anaemia. Because vitamin B12 is used in myelin production, deficiency leads to irreversible neurological damage, commonly in the spinal cord. Mucosal abnormalities, such as glossitis (inflammation of the tongue) are also common, although they are reversible.

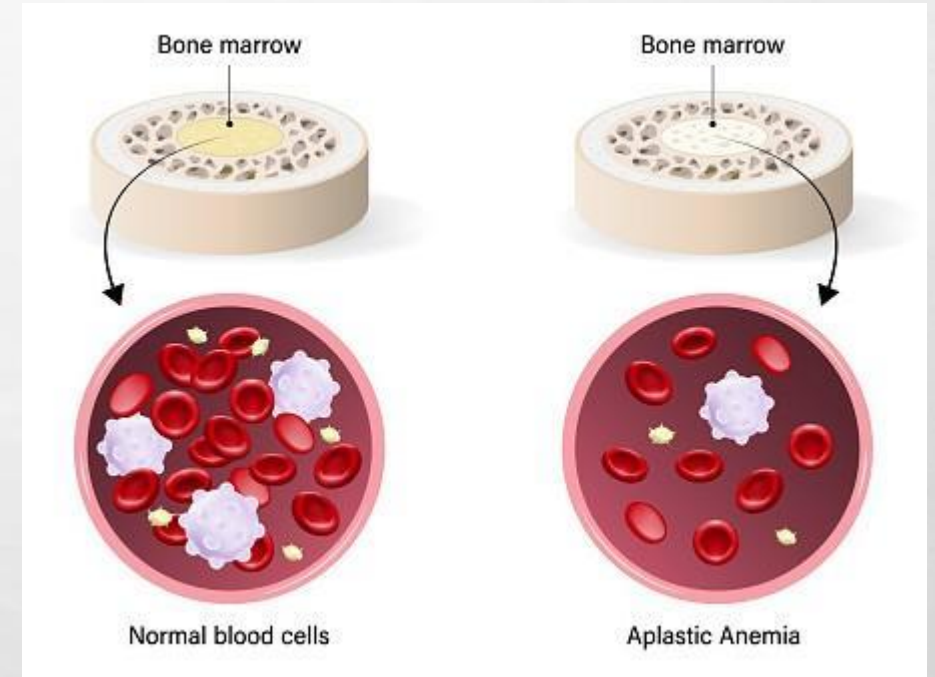
Folic acid deficiency anaemia

- Deficiency of folic acid causes a form of megaloblastic anaemia identical to that seen in vitamin B12 deficiency, but not associated with neurological damage.
- It may be due to: dietary deficiency, in alcoholism, in anorexia and in pregnancy malabsorption from the jejunum caused by, e.g., coeliac disease, tropical sprue or anticonvulsant drugs interference with folate metabolism by, e.g., cytotoxic and anticonvulsant drugs.



Aplastic anaemia

- Aplastic (hypoplastic) anaemia results from bone marrow failure.
- Erythrocyte numbers are reduced.
- Since the bone marrow also produces leukocytes and platelets, *leukopenia* (low white cell count) and *thrombocytopenia* (low platelet count) are likely to accompany diminished red cell numbers.
- When all three cell types are low, the condition is called *pancytopenia*, and is accompanied by anaemia, diminished immunity and a tendency to bleed.
- The condition is often idiopathic, but the known causes include: drugs, e.g. cytotoxic drugs, some anti-inflammatory and anticonvulsant drugs, some sulphonamides and Antibiotics ionising radiation some chemicals, e.g. benzene and its derivatives viral disease, including hepatitis.

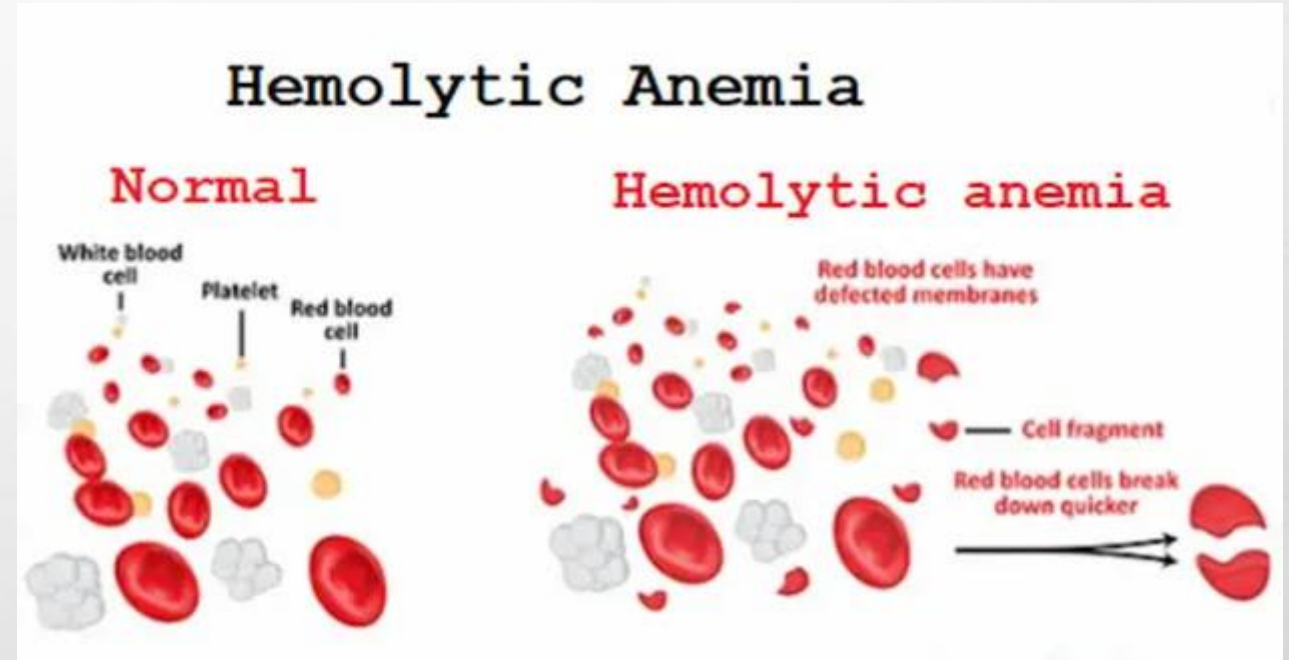


Haemolytic anaemias

These occur when circulating red cells are destroyed or are removed prematurely from the blood because the cells are abnormal or the spleen is overactive.

Congenital haemolytic anaemias

- In these diseases, genetic abnormality leads to the synthesis of abnormal haemoglobin and increased red cell membrane fragility, reducing their oxygen-carrying capacity and life span.
- The most common forms are sickle cell anaemia and thalassaemia.

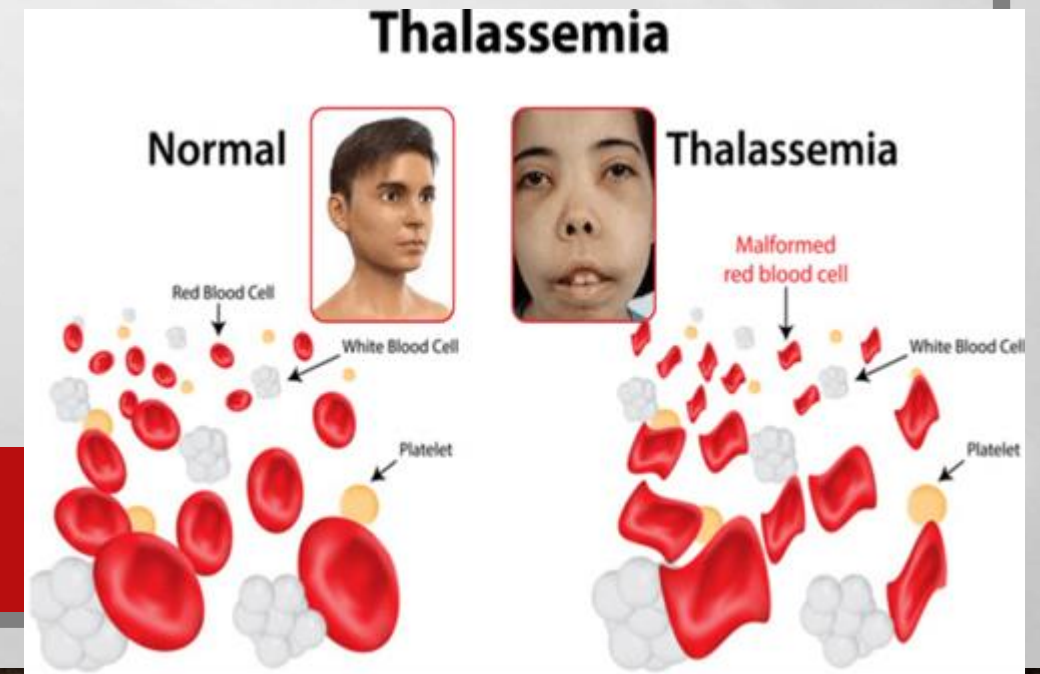
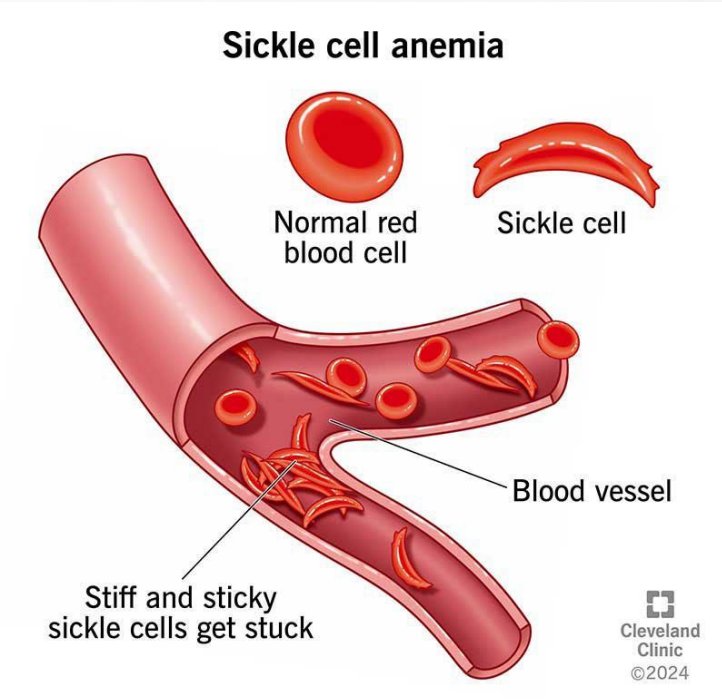


Sickle cell anaemia

- The abnormal haemoglobin molecules become misshapen when deoxygenated, making the erythrocytes sickle shaped.
- If the cells contain a high proportion of abnormal Hb, sickling is permanent.
- The life span of cells is reduced by early haemolysis, which causes anaemia.
- Sick cells do not move smoothly through the small blood vessels. This tends to increase the viscosity of the blood, reducing the rate of blood flow and leading to intravascular clotting, ischaemia and infarction.

Thalassaemia

- There is reduced globin synthesis with resultant reduced haemoglobin production and increased fragility of the cell membrane, leading to early haemolysis. Severe cases may cause death in infants or young children.



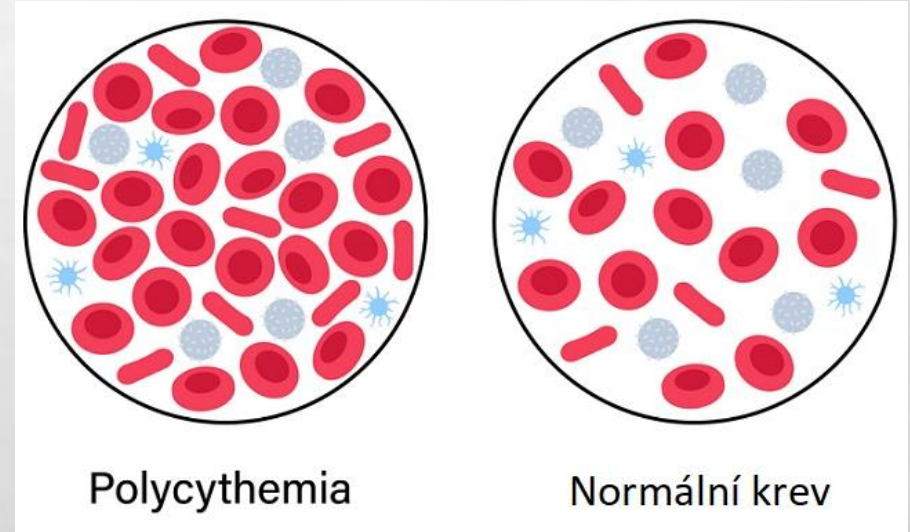
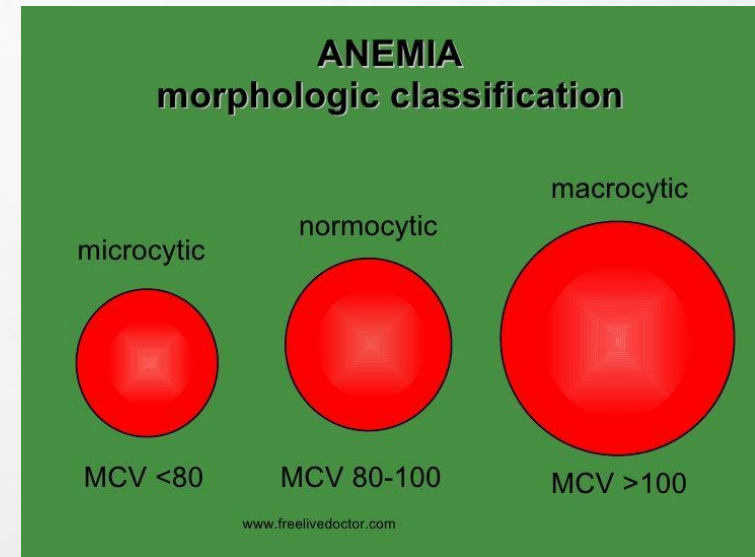
Normocytic normochromic anaemia

- In this type the cells are normal but the numbers are reduced, and the proportion of reticulocytes in the blood may be increased as the body tries to restore erythrocyte numbers to normal.
- This occurs: in many chronic conditions, e.g. in chronic inflammation following severe haemorrhage in haemolytic disease.

Polycythaemia: This means an abnormally large number of erythrocytes in the blood.

Relative increase in erythrocyte count This increases blood viscosity, slows the rate of flow and increases the risk of intravascular clotting, ischaemia and infarction.

True increase in erythrocyte count This occurs when the erythrocyte count is normal but the blood volume is reduced by fluid loss, e.g. excessive serum exudate from extensive burns.



Physiological

- Prolonged hypoxia stimulates erythropoiesis and the number of cells released into the normal volume of blood is increased.
- This occurs naturally in people living at high altitudes where the oxygen tension in the air is low and the partial pressure of oxygen in the alveoli of the lungs is correspondingly low. Each cell carries less oxygen so more cells are needed to meet the body's oxygen needs.

Pathological

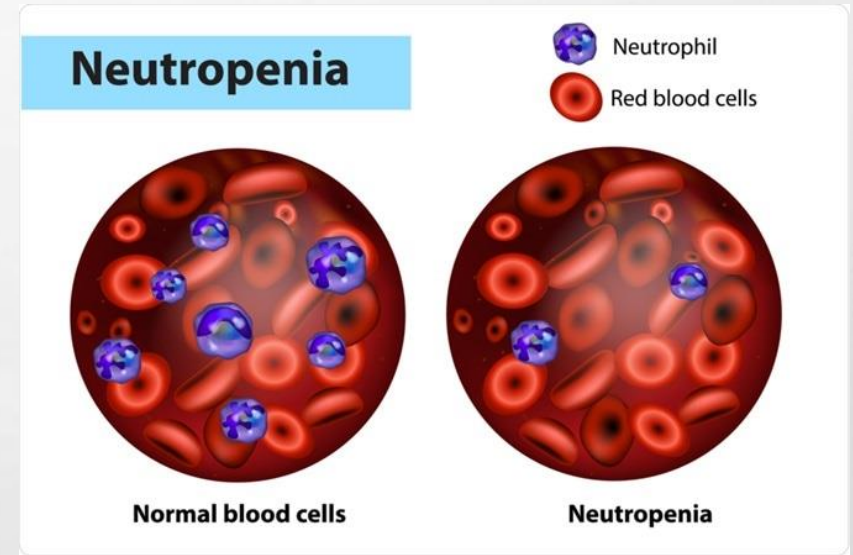
- The reason for this increase in circulating red cells, sometimes to twice the normal number, is not known.
- It may be secondary to other factors that cause hypoxia of the red bone marrow, e.g. cigarette smoking, pulmonary disease, bone marrow cancer.

DISORDERS OF LEUCOCYTES

Leukopenia In this condition, the total blood leukocyte count is less than $4 \times 10^9/l$ (4000/mm³).

Granulocytopenia (neutropenia)

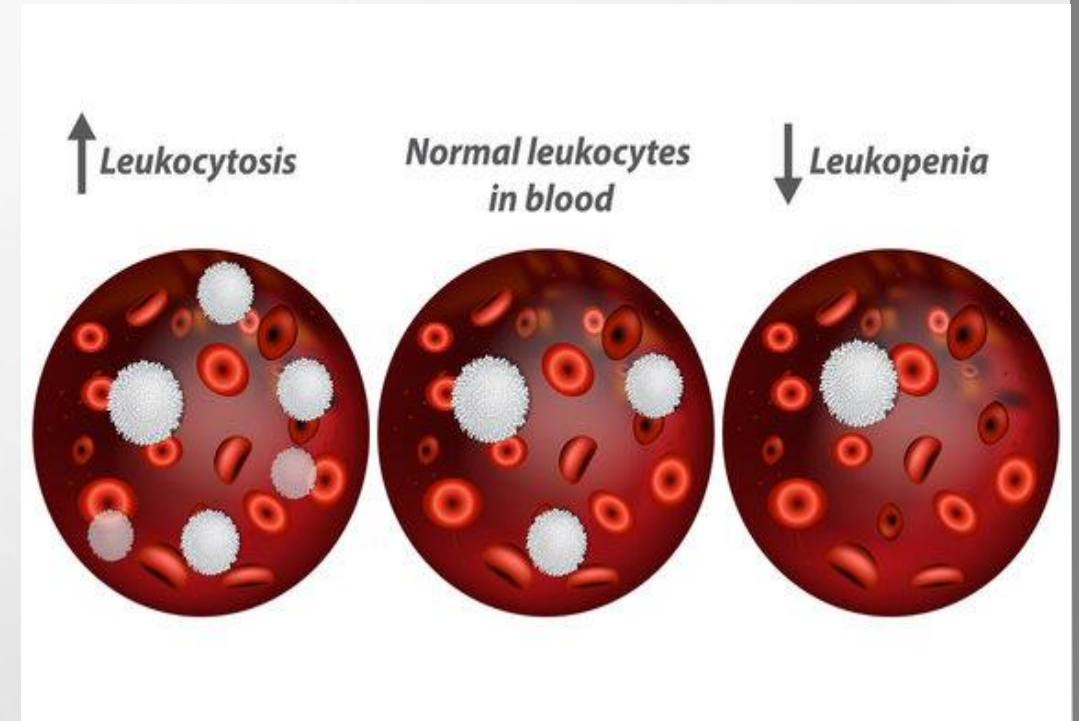
- This is a general term used to indicate an abnormal reduction in the numbers of circulating granulocytes (polymorphonuclear leukocytes), commonly called neutropenia because 40 to 75% of granulocytes are neutrophils.
- A reduction in the number of circulating granulocytes occurs when production does not keep pace with the normal removal of cells or when the life span of the cells is reduced.



- Extreme shortage or the absence of granulocytes is called *agranulocytosis*.
- A temporary reduction occurs in response to inflammation but the numbers are usually quickly restored.
- Inadequate granulopoiesis may be caused by:
 - drugs, e.g. cytotoxic drugs, phenothiazines, some sulphonamides and antibiotics
 - irradiation damage to granulocyte precursors in the bone marrow by, e.g., X-rays, radioactive isotopes
 - diseases of red bone marrow, e.g. leukaemias, some anaemias severe microbial infections.
- In conditions where the spleen is enlarged, excessive numbers of granulocytes are trapped, reducing the number in circulation.
- Neutropenia predisposes to severe infections that can lead to septicaemia and death.
- Septicaemia is the presence of significant numbers of active pathogens in the blood.

Leukocytosis

- An increase in the number of circulating leukocytes occurs as a normal protective reaction in a variety of pathological conditions, especially in response to infections.
- When the infection subsides the leukocyte count returns to normal.
- Pathological leukocytosis exists when a blood leukocyte count of more than $11 \times 10^9/l$ is sustained and is not consistent with the normal protective function.
- One or more of the different types of cell is involved.



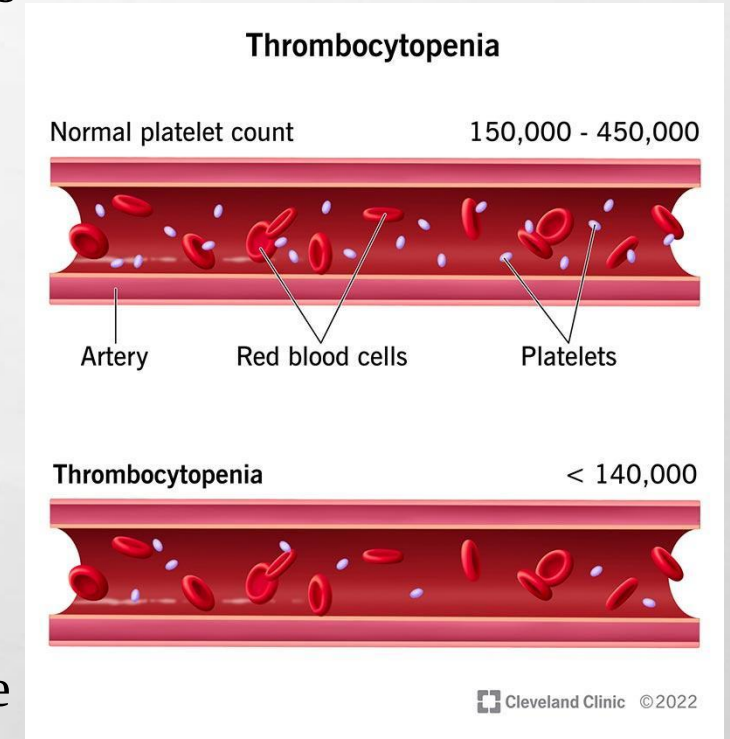
DISORDERS OF THROMBOCYTES

Thrombocytopenia: This is defined as a blood platelet count below $150 \times 10^9/l$ but spontaneous capillary bleeding does not usually occur unless the count falls below $30 \times 10^9/l$.

It may be due to a **reduced rate of platelet production or increased rate of destruction.**

1. Reduced platelet production

- This is usually due to bone marrow deficiencies, and therefore production of erythrocytes and leukocytes is also reduced, giving rise to pancytopenia.
- It is often due to:
 - platelets being crowded out of the bone marrow in bone marrow diseases, e.g. leukaemias, pernicious anaemia, malignant tumours
 - ionising radiation, e.g. X-rays or radioactive isotopes, which damage the rapidly dividing precursor cells in the bone marrow
 - drugs that can damage bone marrow, e.g. cytotoxic drugs, chloramphenicol, chlorpromazine, sulphonamides.



2. Increased platelet destruction

- A reduced platelet count occurs when production of new platelets does not keep pace with destruction of damaged and worn out ones.
- This occurs in disseminated intravascular coagulation and autoimmune thrombocytopenic purpura.

3. Autoimmune thrombocytopenic purpura

- This condition, which usually affects children and young adults, may be triggered by a viral infection such as measles.
- Antiplatelet antibodies are formed that coat platelets, leading to platelet destruction and their removal from the circulation.
- A significant feature of this disease is the presence of purpura, which are haemorrhages into the skin ranging in size from pinpoints to large blotches.
- The severity of the disease varies from mild bleeding into the skin to severe haemorrhage.
- When the platelet count is very low there may be severe bruising, haematuria, gastrointestinal or intracranial haemorrhages.

Vitamin K deficiency

Vitamin K is required by the liver for the synthesis of many clotting factors and therefore deficiency predisposes to abnormal clotting.

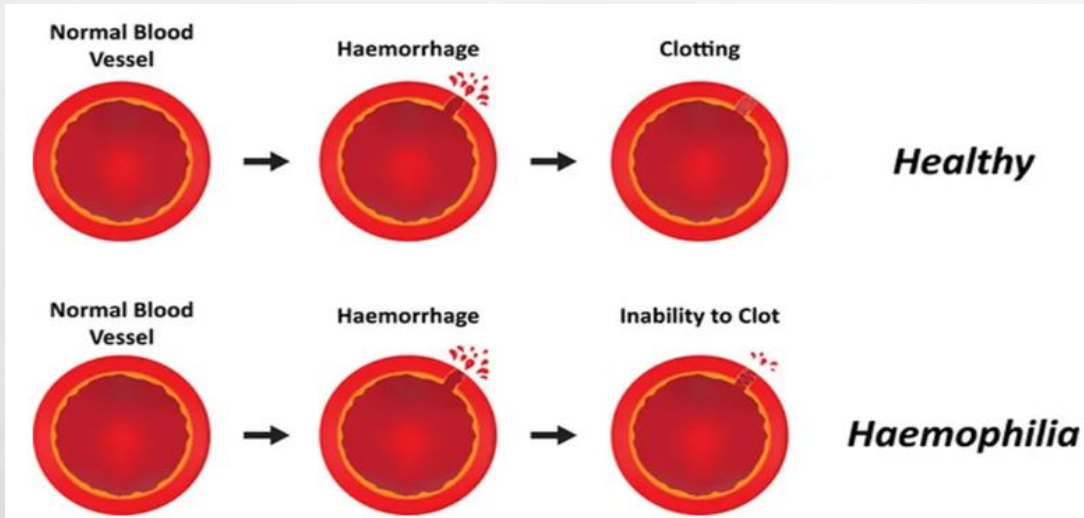
Haemorrhagic disease of the newborn

- Spontaneous haemorrhage from the umbilical cord and intestinal mucosa occurs in babies when the stored vitamin K obtained from the mother before birth has been used up and the intestinal bacteria needed for its synthesis in the infant's bowel are not yet established.
- This is most likely to occur when the baby is premature.

Deficiency in adults

- Vitamin K is fat soluble and bile salts are required in the colon for its absorption.
- Deficiency may occur when there is liver disease, prolonged obstruction to the biliary tract or in any other disease where fat absorption is impaired, e.g. coeliac disease.
- Dietary deficiency is rare because a sufficient supply of vitamin K is usually synthesised in the intestine by bacterial action.
- However, it may occur during treatment with drugs that sterilise the bowel.

Congenital disorders



The haemophilias

- The haemophilias are a group of inherited clotting disorders, carried by genes present on the X chromosome.
- The faulty genes code for abnormal clotting factors (Factor VIII and Factor IX), and if inherited by a male child always leads to expression of the disease.
- Women inheriting one copy are carriers, but, provided their second X chromosome bears a copy of the normal gene, their blood clotting is normal.
- Those who have haemophilia experience repeated episodes of severe and prolonged bleeding at any site, with little evidence of trauma.

- Recurrent bleeding into joints is common, causing severe pain and, in the long term, cartilage is damaged. The disease ranges in severity from mild forms, where the defective factor has partial activity, to extreme forms where bleeding can take days or weeks to control.
- The two main forms of haemophilia differ only in the clotting factor involved; the clinical picture in both is identical.
 - **Haemophilia A**. In this disease, factor VIII is abnormal and is less biologically active.
 - **Haemophilia B** (Christmas disease). This is less common and factor IX is deficient, resulting in deficiency of thromboplastin (clotting factor III).
- **Von Willebrand's disease :-** In this disease, a deficiency in the von Willebrand factor causes low levels of factor VIII. As the inheritance is not sex linked, haemorrhages due to impaired clotting occur equally in males and females.

DISORDERS OF LYMPH NODES

Lymphadenitis

- Acute lymphadenitis (acute infection of lymph nodes) is usually caused by microbes transported in lymph from other areas of infection.
- The nodes become inflamed, enlarged and congested with blood, and chemotaxis attracts large numbers of phagocytes.
- If lymph node defences (phagocytes and antibody production) are overwhelmed, the infection can cause abscess formation within the node.
- Adjacent tissues may become involved, and infected materials transported through other nodes and into the blood.



- Acute lymphadenitis is secondary to a number of conditions.
 - 1. Infectious mononucleosis (glandular fever)**
 - This is a highly contagious viral infection, usually of young adults, spread by direct contact.
 - During the incubation period of 7 to 10 days, viruses multiply in the epithelial cells of the pharynx.
 - They subsequently spread to cervical lymph nodes, then to lymphoid tissue throughout the body.
 - Clinical features include tonsillitis, lymphadenopathy and splenomegaly. A common complication is myalgic encephalitis. Clinical or subclinical infection confers lifelong immunity.
 - 2. Other diseases:**
 - Minor lymphadenitis accompanies many infections and indicates the mobilisation of normal protective mechanisms, e.g. proliferation of defence cells.
 - More serious infection occurs in, e.g. measles, typhoid and cat-scratch fever, and wound or skin infections. Chronic lymphadenitis occurs following unresolved acute infections, in tuberculosis, syphilis and some low-grade infections.

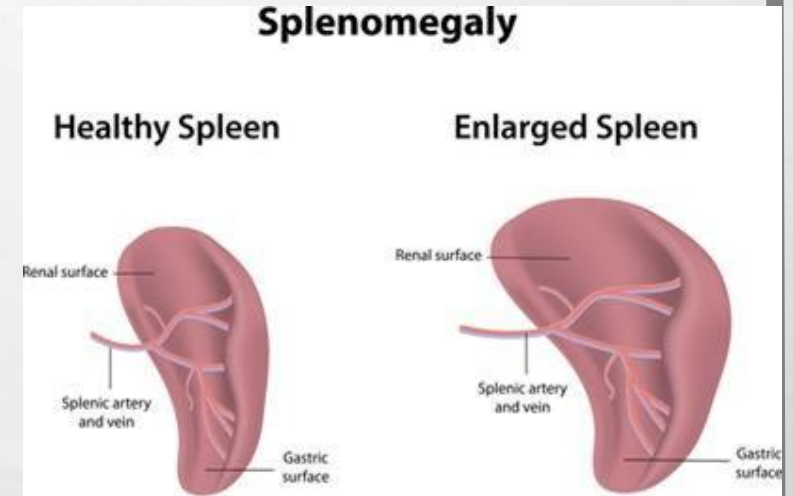
DISORDERS OF SPLEEN

Splenomegaly : This is enlargement of the spleen, and is usually secondary to other conditions, e.g. infections, circulatory disorders, blood diseases, malignant neoplasms.

A. Infections : The spleen may be infected by blood-borne microbes or by local spread of infection.

- The red pulp becomes congested with blood and there is an accumulation of phagocytes and plasma cells.
- Some chronic non-pyogenic infections cause splenomegaly, but this is usually less severe than in the case of acute infections.
- The most commonly occurring primary infections include: Tuberculosis, typhoid fever, malaria, brucellosis (undulant fever), infectious mononucleosis.

B. Circulatory disorders Splenomegaly due to congestion of blood occurs when the flow of blood through the liver is impeded by, e.g., fibrosis in liver cirrhosis, or portal venous congestion in right-sided heart failure.

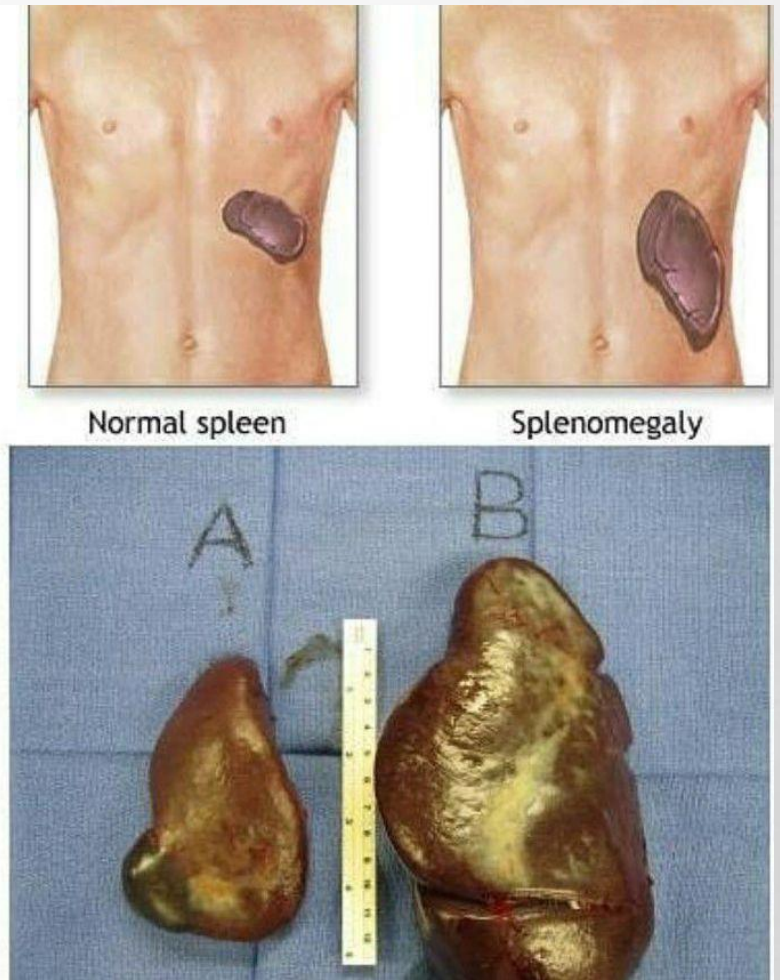


C. Blood disease Splenomegaly may be caused by blood disorders.

- The spleen enlarges to deal with the extra workload associated with removing damaged, worn out and abnormal blood cells in, e.g., haemolytic and macrocytic anaemia, polycythaemia and chronic myeloid leukaemia.
- When the spleen is enlarged for any reason, especially in portal hypertension, excessive and premature haemolysis of red cells or phagocytosis of normal white cells and platelets lead to marked anaemia, leukopenia and thrombocytopenia.

D. Tumours :-

- Benign and primary malignant tumours of the spleen are rare but blood-spread tumour fragments from elsewhere in the body may cause metastases.
- Splenomegaly caused by infiltration of malignant cells is characteristic of some conditions, especially chronic leukaemia, Hodgkin's disease and non- Hodgkin's lymphoma.



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