**Haemolytic anaemia**

**Objectives:**

 1-Define the defect in G6PD deficiency and mode of inheritance.

2-Enumerate the main clinical syndrome associated withG6PD

 deficiency

3-What are the diagnostic test of G6PD deficiency.

4-Define red cell fragmentation syndrome and its causes.

5-Know the types of autoimmune haemolytic anaemia and the features

 of each type.

6-Define pancytopenia and its causes.

7-Define aplastic anaemia and its classification.

**GIucose-6-phosphate dehydrogenase deficiency**

-Deficiency in glucose -6- phosphate dehydrogenase renders the red cell susceptible to oxidant stress .

- The inheritance is sex-linked, affecting males, and carried by females who show approximately half the normal red cell G6PD values.

- The degree of deficiency varies, often being mild in black Africans, more severe in orientals and most severe in Mediterraneans, Severe deficiency occurs occasionally in white people.

- It is *usually asymptomatic*.

- **The main syndromes that occur are as follows:**

**( i. )Acute haemolytic anaemia**

 in response to oxidant stress, e.g. drugs( e.g. antimalarials, aspirin

 (high doses) , Phenazopyridine, Cotrimoxazole ,Sulfadiazine) , fava

 beans or infections. The acute haemolytic anaemia is caused by

 rapidly developing intravascular haemolysis with haemoglobinuria.

**(ii) Neonatal jaundice.**

**(iii)** Rarely, **a chronic nonspherocytic haemolytic anaemia**.

-***Diagnosis***

 -Between crises the blood Count is normal.

**-Blood film** :During a crisis may show contracted and fragmented cells, 'bite' cells and 'blister' cells.

 Heinz bodies (oxidized, denatured haemoglobin) may be seen in the reticulocyte preparation., particularly if the spleen is absent.

There are also features of intravascular haemolysis: (Haemoglobinaemia , haemoglobinuria and Haemosiderinuria).

-Red cell enzyme assay may give a 'false' normal level in the phase of acute haemolysis with a reticulocyte response because of the higher enzyme level in young red cells,.

**-To confirm diagnosis, subsequent enzyme assay after the acute**

 **phase reveals the low G6PD level .**

 **Acquired Haemolytic Anaemia:**

* **Autoimmune haemolytic anaemias**

-Autoimmune haemolytic anaemias (AIHAs) are caused by

 antibody production by the body against its own red cells.

- They are characterized by a positive direct antiglobulin test (DAT).

- **'Warm' and 'Cold'** **types according to whether the antibody reacts more strongly with red cells at 37°C or 4°C.**

* ***Warm autoimmune haemolytic anaemias***

The autoantibody is usually IgG and binds to red cells best at 37 °C.

The red cells are coated with immunoglobulin (Ig), usually immunoglobulin G (IgG) alone or with complement, and are therefore taken up by RE macrophages which have receptors for the Ig Fc fragment. Part of the coated membrane is lost so the cell becomes progressively more spherical to maintain the same volume and is ultimately prematurely destroyed, predominantly in the spleen.

***Clinical features:***

 -The disease occur at any age, in either sex.

- It presents as a haemolytic anaemia of varying severity.

-Jaundice.

-Enlarged spleen.

--The disease tends to remit and relapse.

**- It can occur as :**

 **- Idiopathic** (alone)

Or

- **Secondary** (in association with other diseases ) : SLE, CLL, lymphomas , Drugs (e.g. methyldopa)

***Laboratory findings*:**

-Anaemia and reticulocytosis.

**-**Blood film: spherocytes with polychromasia.

-Biochemical evidence of haemolysis is present.

-The diagnosis is confirmed by positive direct antiglobulin test( coombs' test).

The antibodies bare best detected at 37°C.

* ***Cold autoimmune haemolytic anaemias :***

-The antibody is usually IgM and binds to red cells best at 4°C.

-Both intravascular and extravascular haemolysis.

-The autoantibody attaches to red cells mainly in the peripheral circulation where the blood temperature is cooled.

- It can occur as :

***Idiopathic***

 *or*

***Secondary:***

Infections- :Mycoplasma **pneumonia** , infectious mononucleosis. Lymphoma

***Clinical features***

-The patient may have a chronic haemolytic anaemia aggravated by

 the cold and often 'associated with intravascular haemolysis.

-Mild jaundice and splenomegaly

-Acrocyanosis (purplish skin discoloration) at the tip of the nose, ears,

 fingers and toes caused by the agglutination of red cells in small

 vessels.

**Laboratory findings**:

-Anaemia and reticulocytosis.

**-**Blood film: spherocytes but is less marked than warm type,

 red cells agglutinate in the cold.

-The diagnosis is confirmed by positive direct antiglobulin test

 ( coombs' test) . DAT reveals complement only on the red cell

 surface.

 **Red cell fragmentation syndromes**

 These arise through physical damage to red cells either on :

 1- abnormal surfaces (e.g. artificial heart valves or arterial grafts),

 arteriovenous malformations .

 2- a microangiopathic haemolytic anaemia . This is caused by red cells passing through abnormal small vessels. The latter may be caused by deposition of fibrin strands, often associated with disseminated intravascular coagulation (DIC), or platelet adherence as in thrombotic thrombocytopenic purpura (TTP) or vasculitis (e.g. polyarteritis nodosa) .

**The peripheral blood** contains many deeply staining red cell fragments

**Pancytopenia:**

Pancytopenia describes a reduction in the blood count of all the major cell lines-red cells, white cells and platelets.

***--Causes:***

*1.Bone marrow suppression by drugs (anti cancer drugs,*

 *immunosuppressive agents) or radiation.*

*2. megaloblastic anaemia.*

*3.Acute leukaemia.*

*4.Infilteration of bone marrow by lymphoma ,metastatic carcinoma, tuberculosis.*

*5.Aplastic anaemia.*

*6.Myelofibrosis.*

*7. Splenomegally .*

**Aplastic anaemia**

Aplastic (hypoplastic) anaemia is defined as pancytopenia resulting from aplasia of the bone marrow.

**Laboratory findings:**

-Pancytopenia.

- Reduced reticulocyte count.

-**Blood film**: show no specific morphological abnormality.

-**Bone marrow Biopsy** : hypocellular , haemopoeitic marrow is

 replaced by fat cells.

**It is classified into:**

 **i-Primary:** either congenital or acquired

-**Congenital** e.g. Fanconi anaemia.

-**Acquired** idiopathic

**ii-Secondary types*.***

-Ionizing radiation

-Chemicals: benzene, organophosphates, DDT

-Drugs e.g. busulfan, cyclophosphamide, chloramphenicol, gold

-Viruses: viral hepatitis (non-A, **non- B, non-C, in** most cases) , EBV.

**Iron overload**

There is no physiological mechanism for eliminating excess iron from the body and so iron absorption is normally carefully regulated to avoid accumulation.

 Iron overload can occur in disorders associated with excessive absorption or chronic blood transfusion.

 Excessive iron deposition in tissues can cause serious damage to organs, particularly the heart, liver and endocrine organs

**The causes of iron overload:**

**1-Increased iron absorption**: Hereditary (primary) haemochr-omatosis, This is a group of diseases in which there is excessive

absorption of iron from the gastrointestinal tract leading to iron overload of the parenchymal cells of the liver, of the endocrine organs and, in severe cases, of the heart.

**2-Increased iron intake:** This occurs in sub –Saharan African through a combination of increased iron absorption because of genetic defect ,and a dietary increased iron overload caused by consumption of beverages of high iron content because of the use of iron cooking pots.

**3-Repeated red cell transfusion:** as in thalassemia**.** Each 450 ml of transfused blood contains approximately 200-250 mg of iron.Iron damage the liver,and the endocrine organs with failure of growth ,delayed or abscent puberty ,diabetes mellitus, hypothyroidism and hypoparathyrodism ,also skin pigmentation.