Chapter IV

Summary And Conclusions

SUMMARY

Haemopoiesis

Haemopoiesis may be medullary or extramedullary. The bone marrow produces each day about 2.1 x 10 red cells, it has also large reserve capacity in response to increased demands Extramedullary haemopoiesis is a term applied to blood formation in organs other than the marrow e.g. the spleen, liver and the lymph nodes, they are the site of myeloid metaplasia in response to increased demand for cells following haemorrhage or haemolysis (De Gruchy, 1972).

Erythropoiesis

Erythropoiesis comprises these biological processes of cell differentiation, proliferation, biosynthetic activities and maturation which provide erythrocytes and hemoglobin (Hb) in appropriate amounts for the respiratory gas transport requirements of the organisms (Douglas 1974). All the blood cells are developed in the bone marrow from one stem cell called colony forming unit which proliferates and differentiates to give different series of bl. cells.

Factors that determine erythropoiesis.

(1) Arterial O_2 content and tissue O_2 tension.

A decrease in O_2 content stimulates erythropoiesis while an increase depresses it.

(2) Erythropoietin.

The effect of O_2 tension on the rate of erythropoiesis occurs through the erythropoietin produced in response to O_2 lack, the kidney is the site of its production or activation (Talaat, 1973).

(3) Dietary factors

Proteins, iron, vitamin B_{12}, folic acid, cobalt,copper, vitamin c and hormones as thyroxine.

Physiology of red blood cells

The adult red blood cell is a non nucleated cell, shaped as flat biconcave disc, it is pliable and flexible. It may be regarded as a frame work of protein in which is contained the Hb and at its outer surface is the red cell membrane. The red cell membrane is semipermeable, it is consisted of bimolecular leaflet of lipids covered externally and internally by a layer of protein changes in its lipid composition influence its flexibility (Cooper et.al., 1975) The bl. group antigens are situated on the surface Hb is conjugated protein consisted of 4 molecules of haem attached to each molecule of globin, Haem is composed of protoporphyrin and ferrous iron it is a red pigment (De Gruchy 1972) Normal human Hb exists in 2 main forms mainly adult and foetal Hb (HbA & HF) and in small quantities HbA_2 is present, they differ in the structure of the Hb moeity.

Function of the red cells

The primary role of the red cell is to transport O_2, a function, made possible by the Hb within the erythrocyte. The amount of O_2 delivered to tissues by oxygenated blood is dependent on Hb content, the rate of bl. flow, and on the affinity of Hb for O_2 that can be significantly reduced by certain phosphate compounds as 2,3 DPG, (Kerr, 1970).

Red cell breakdown

The normal red cell has a definite life span in the circulation of 120 ± 20 days. As the cell becomes older enzymatic activity is decreased membrane is lost and cell pliability is decreased the red cell is no longer able to traverse the microvasculature and is phagocytosed by the RE tissues especially the spleen (Weiss, 1972) The Hb is broken down, the globin is splitted off from the haem, the globin is reutilised and the haem is broken into iron and Porphyrin. The iron passes to blood stream to be either reutilised or stored. The prophyrin is broken down to bilirubin.

Anaemia

Anaemia may be defined as a reduction in the concentration of Hb in the peripheral blood below the normal for the age and sex of the patient. Following the reduction

in the O_2 carrying capacity of the blood, the body brings to play several compensatory mechanisms to make the most effective use of the available Hb:

(1) An increase in the cardiac output and in the rate of blood circulation, with a state of hyperkinetic circulation.

(2) The Hb delivers to the tissues more than the usual proportion of its oxygen, this is aided by a shift to the right in the O_2 dissociation curve.

(3) The blood volume is kept at normal by expansion of plasma volume to maintain an adequate circulation.

(4) There is some deviation of blood flow from tissues with lesser O_2 requirements to those with greater requirements. So the compensatory mechanisns commonly allow the patient to be symptom-free at rest, but exertion causes symptoms by increasing O_2 requirements (Oski and Delivoria 1970).

Classification of anaemia (Michael Beard 1977)

(A) Aetiological classification

(1) Due to diminished production of normal Rb.c.

- Deficiency of iron, vitamin B_{12}, C, folic acid and thyroxine.
- Pancytopenia "aplastic anaemia.

(2) Due to excessive blood destruction "haemolytic anaemia Hereditary red cell defects.

(1) Membrane e.g.

Hereditary spherocytosis, elliptocytosis

(2) Metabolism e.g.

G.6.P, pyruvate kinase deficiency.

(3) Haemoglobin. e.g.

- Sickle cell disorders.
- Unstable haemoglobins.
- Thalassaemic disorders.

2) Acquired membrane defects.

Paroxysmal nocturnal haemoglobinuria.

3) Extracorpuscular abnormality.

- Immune haemolytic anaemia.
- Autoimmune, drug induced.
- Red cell fragmentation syndromes.
- Hypersplenism.
- Miscellaneous drugs, chemicals, toxins.

II. Morphological classification

a) Macrocytic anaemia e.g. megaloblastic anaemia.

b) Normacytic anaemia e.g. bl. loss, haemolytic anaemia.

c) Microcytic hypochromic anaemia, iron deficiency, thalassaemia.

Clinical features of anaemia

Many of signs and symptoms are related to tissue hypoxia (Michael C. Brain, 1980) Pallor, Lassitude and easy fatiguability are the earliest and most common symptoms

- Cardiovascular system.

Dyspnea and palpitation on exertion, soft mid systolic haemic murmur that disappears on correction of the anaemia.

- Central nervous system.

Giddiness, faintness, headache, lack of concentration.

- Renal system.

Slight proteinuria and impairement of the concentrating power of the kidney are not uncommon in severe anaemia.

- Gastro-intestinal system.

Anorexia, nausea, and constipation may occur splenomegaly and slight to moderate hepatomegaly are common.

The principles in the diagnesis of anaemia

- From the detection of signs of anaemia, its presence and degree can be established only by Hb estimation.
- The cause of anaemia is determined from

(a) The history: Rapid onset (acute bleeding or haemolysis or acute leukemia).

(b) Complete physical examination

- Skin: pallor, petechiae and ecchymosis
- Nails: koilonychia and brittleness
- Conjunctiva pallor and icterus

- Abdomen: Hepatomegaly, splenomegaly
- Bones: tenderness especially of sternum.

(c) The blood examination

Hb estimation, blood film examination, white cell count, PCV, reticulocyte count and ESR.

(d) When necessary further special investigations.

Management of an anaemic patient

The principles of management are:-

(1) Treatment of the disorder causing anaemia.

(2) Administration of specific haematinics when indicated.

(3) treatment of symptoms.

1) Treatment of the disorder causing anaemia

a) Arrest of blood loss as it is the commonest cause of anaemia.

b) Correction of a dietary deficiency as anorexia, bad habits.

c) Treatment of an underlying systemic disorder as infection, renal failure, malignancy.

d) Removal of a toxic chemical agent or drug.

2) The administration of haematinics

- Iron can be administred orally e.g. ferrous sulphate gluconate or succinate.
- Vit B_{12} and folic acid in case of megaloblastic anaemia.

3) Symptomatic and supportive treatment

Well balanced diet, blood transfusion is the most important supportive measure in treatment of anaemia

Polycythaemia

An increase in the number of red cells per c.mm blood above the normal for the age and sex of the patient. Erythrocytosis means an increase in the red cells secondary to some underlying disorder and erythraemia is a term used to describe idiopathic polycythaemia vera.

- Secondary polycythaemia

A polycythaemia resulting from some known primary disorders, the increase in the red cell values relates to one of the following:-

1) Compensation for generalised hypoxia: accompanied living in high altitudes, congenital heart diseases chronic pulmonary diseases.
2) Abnormalities of O_2 transport.
3) Renal diseases with inappropriate erythropoietin.

The clinical pictures are those of the causative. disorder together with cyanosis of varying degrees and headache, tinnitus and vomiting.

- Polycythaemia vera:-

It is a disease of unknown cause characterised by hyperplasia of all the cellular elements of the bone marrow, with resultant sustained elevation of the

erythrocyte count and the Hb. and to a lesser extent leucocytosis and thrombocytosis. It may be regarded as a neoplastic disease of the erythropoietic tissue.

The clinical manifestations include headache, dizziness ringing in the ears or visual disturbances they are associated with hypertension. The increased PCV and viscosity tends to slow the blood flow rate that predisposes to thrombosis, Pruritis may be atroublesome, the spleen is palpable in 75% of patients and less commonly the liver may be enlarged the major causes of death are thrombosis, haemorrhage, congestive heart failure and leukaemia.

Treatment

1) Venesection for rapid relief of symptoms
2) Radioactive phosphorous P^{32}
3) Myelosuppressive drugs e.g. chlorambucil
4) Symptomatic measures.

Relative polycythaemia

In relative polycythaemia, the total number of red cells in the body is not increased, but the raised cell values are due to haemoconcentration resulting from a decrease in the total plasma volume or sometimes its redistribution. (Harrit 1973).