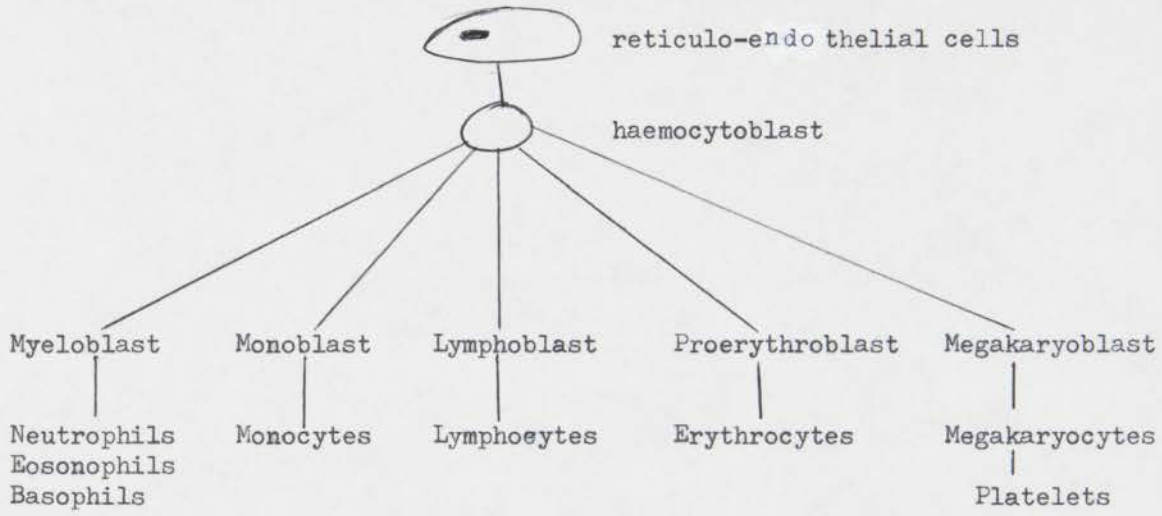
PATHOLOGY OF THE HAEMAPOIETIC SYSTEM

Normal Function:

1. Red cells: haemopoiesis in the marrow cavity of bones occurs from the fifth month of intra-uterine life and continues thereafter. Extra-medullary haemopoiesis occurs in the liver and spleen, and in lymphatic tissues when there is a sustained large demand for blood cells, e.g. haemolytic anaemia.

2. White Cells (leucocytes)
Just like erythrocytes, white cells are derived from the reticulo-endothelial cells which give rise to haemocytoblasts:



It is not known what factors control the production of the different cell lives except that the spleen influences the total quantities of leucocytes produced, and that adrenal steroids cause over-production of neutrophils and a relative deficiency of lymphocytes and eosonophils.

Functions of normal adult leucocytes:

Normal count: 5-10,000 cu.mm.

Neutrophils: phagocytose, destroy, and digest, with the aid of specialised enzymes, infecting micro-organisms and harmful products present as a result of injury, inflammation, vascular and metabolic disturbances. Count raised insevere infections.

Basophils: contain large amounts of histamine and heparin; believed to discharge heparin at sites of inflammatory lesions to facilitate phagocytosis of particles.

Eosinophils: motile, phagocytic - detoxify foreign proteins. Raised in people suffering from chronic allergic conditions such as asthma, and in patients affected by tropical parasites.

Lymphocytes: motile, initiate antibody formation - surround chronic inflammatory lesions.

Monocytes: motile, phagocytic - scavengers, ingesting larger particulate matter and organisms, e.g. protozoa.

Erythrocytes - control and functions:

Function: transport of respiratory gases in the circulation.

Control: (1) erythropoietin, produced by the kidney, stimulates erythrocyte production.

(2) anoxia stimulates erythrocyte production, e.g. high altitude.

(3) secretion of the endocrine glands, particularly adrenals and thyroid.

Normal Values: Hb. ♂'s: 13-17.0 gm/100 ml.
♀'s: 12-15.0 "

Measurements (indices) expressed as the erythrocyte count (4.2-6.4 million), the mean corpuscular volume (80-94 cμ), the mean corpuscular haemoglobin concentration (32-26%), the packed cell volume (38-54%), and the total blood volume (6-8%/body weight).

♀ 's : 3-4.9 litres (44-85 ml/kg.)
♂ 's : 4-7 litres (60-95 ml/kg.)

Disorders of Erythropoiesis

1) Anaemia: too few erythrocytes.

2) Polycythaemia: too many erythrocytes.

3) Erythroleukaemia (rare): malignant proliferative disorder of erythroblastic tissue.

Platelets:

Play an important role in haemostasis.

Normal count: 200,000-500,000/cu.mm.

Disorders:

1) Thrombocytopenia - too few platelets.

2) Thrombocythaemia - too many platelets.

3) Thrombasthenia - defective platelet function.

Abnormalities of the White Cell count.

Leucocytosis: (too many white cells)

1) Neutrophil leucocytosis:

(a) Infections (particularly bacterial)
(b) Collagen diseases
(c) Diabetic coma
(d) Poisoning
(e) Tissue damage: crush injuries, infarcts, surgical operations &c.
(f) Acute haemorrhage
(g) Mismatched blood transfusion
(h) Malignant diseases, e.g. leukaemia.

2) Eosinophils:

(a) parasitic infections, e.g. intestinal worms.
(b) allergic conditions, e.g. asthma
(c) infections, e.g. TB.
(d) skin diseases, e.g. eczema.

3) Basophils: disorders of lymphatic tissue, e.g. Hodgkin's disease.

Lymphocytosis:

(a) virus infections, e.g. glandular fever
(b) bacterial infections, e.g. TB, whooping-cough
(c) thyroid diseases
(d) lymphatic leukaemia

Monocytosis:

(a) convalescence
(b) protozoal and rickettsial infections, e.g. malaria
(c) chronic bacterial infections, e.g. TB.
(d) Hodgkin's disease.

Leucopenia (too few white cells)

Types: (a) Reduction of granulocytes (neutrophils, eosinophils and basophils) - granulocytopenia).
(b) Reduction of all white cell types - leucopenia.

Granulocytopenia

(1) Overwhelming infections, e.g. TB, typhoid.
(2) Virus infection, e.g. influenza.
(3) Protozoal infection - malaria
(4) Fungal infections.
(5) Haemopoietic disorders: (i) all severe anaemias
(ii) leukaemias
(6) Disseminated lupus erythematosis (D.L.E.)
(7) Drugs, chemical and physical agents: e.g. X-rays, cytotoxic drugs, numerous other drugs causing individual hypersensitivity reactions (chlorpromazine, sulphonamides, chloramphenicol).

Mechanism of leucopenia :

(1) decreased production: e.g. direct bone-marrow poisons
(2) increased destruction: by bacterial toxins etc.

Agranulocytosis (Pancytopenia)

Sudden onset of pyrexia, with necrotising ulceration of the mouth and throat - progresses to septicaemia and death. Usually due to a bone-marrow poison, e.g. irradiation.

Infectious Mononucleosis (Glandular Fever)

An absolute lymphacytosis caused by a viral agent - incubation may be as long as six months, and the infection may last up to 12 weeks. Can be followed by depression. Self-limiting. Can occasionally produce disorders of the white cell count that mimic leukaemia.

The Leukaemias:

Definition: disorderly proliferation of all leucopoietic tissues associated with quantitative and qualitative changes in the circulating blood.
Incidence: rising (local "epidemics")
Age: can occur at any age but incidence highest over 45 years.
Aetology: still unknown but following factors contribute -
(i) viral infections
(ii) irradiation.

Classification: (i) Acute, e.g. myeloblastic leukaemia in the elderly
lymphoblastic leukaemia in the young (5-15 yrs)
(ii) Chronic, e.g. chronic lymphatic in the elderly.

R_x : Vincristine, vinblastine) cytotoxic agents.
6-mercaptopurine)

BLOOD GROUPS

Nine main antigen systems but usually only ABO and Rh systems are important.

(1) The ABO system: AB, BO, OO, AO.

The antigens all form part of the surface of the erythrocyte and each system of antigens is quite distinct.

(2) Rhesus Group system: Cc Dd Ee - D^+ve - 83%
Cc dd Ee D^-ve - 17%

(3 pairs allelomorphic genes)

The ABO group: unique because the antibodies or agglutinins are naturally found in normal individuals:
AB - no serum agglutinins
BO - serum contains Anti-A
OO - serum contains Anti-A and Anti-B
A - serum contains Anti-B

The Rhesus blood group: antibodies to the antigens are not present in normal individuals and can only occur as a result of iso-immunisation. 95% of persons developing antibodies to the Rh antigens lack D antigen, i.e. D-ve or Rh- ve. Those possessing the D antigen are known as D+ve or Rh+ve.

Blood Transfusion

Blood to be transfused should be of the same ABO group and Rh group as the recipient.
It is essential before any blood-transfusion is undertaken, to establish that the recipient possesses no antibodies in his plasma which could react with the erythrocytes of the donor; that is the purpose of the direct compatability or "cross-matching" test.

Indications for blood-transfusion:

To restore blood volume and O_2 carrying capacity of the bloodstream.

(i) acute haemorrhage from any cause.
(ii) correction of severe anaemia due to other medical disorders, e.g. thalassanaemia.

Danger of blood transfusion: undesirable reactions in 20% of recipients.

(i) febrile reaction - infected apparatus
inadequately stored blood
antibodies in the recipient

(ii) air embolism - air enters the patient's circulation via the infusion apparatus;(10 mls) can be fatal

(iii) allergic reactions.

(iv) overloading of the circulation - easily produced in elderly patients and those requiring large transfusion minimise by using "packed cells" (the plasma has been removed).

(v) K^+ and citrate toxicity (contained within anticoagulated blood)

(vi) transfusion of incompatible blood - rigors, severe loin pain, circulatory collapse, renal failure.

Haemolytic Disease of the Newborn

An haemolytic anaemia of the foetus which commences in utero due to excessive destruction of its erythrocytes.
Caused by iso-immunisation of the mother to blood group antigens as a result of a previous blood transfusion or pregnancy.
Mother is D -ve (Rh -ve) and the antibody to D antigen is responsible.
Maternal antibodies cross the placenta into the foetal circulation and if the baby is D +ve (Rh +ve), the erythrocytes are haemolysed.

Babies of Rh -ve mothers are grouped at birth (cord blood sample) and if they are Rh +ve, mother is given "anti-D" to destroy, any D antigen that may immunise her.

The Anaemias

Definition: A deficiency in the quantity or quality of erythrocytes in the circulating blood.

Classification: (i) Haemorrhagic - anaemia due to excessive blood loss.
(ii) Dyshaemopoietic: due to defective production of erythrocytes
(iii) Haemolytic: due to excessive destruction of erythrocytes

(1) Acute Haemorrhage:

Up to 600 mls. - no symptoms
" " 1200 mls. - No symptoms recumbent but faintness on rising.
" " 2000 mls. - General weakness - requires urgent medication.

The body reacts by an increase in vascular tone (peripheral vasoconstriction). Peripheral blood vessels are systematically shut down, to sustain the blood pressure (perfusion pressure) to the brain and kidneys. Given optimistic circumstances, blood volume is restored in 1-2 days, erythrocyte numbers in six weeks.

Clinical: fall in blood pressure, prostration, thirst, rapid pulse rate, rapid, shallow breathing; the skin is cold, pale and sweaty.

R i) arrest the haemorrhage
ii) restore blood volume - plasma expanders
blood transfusion
packed cells.
iii) convalescent R_x with oral iron, high protein, diet and rest.

(2) Chronic haemorrhagic anaemia, due torepeated small blood loss. e.g. peptic ulceration, haemorrhoids, menorrhagia, etc.

Clinical: i) the primary condition
ii) signs of anaemia
iii) evidence of iron deficiency

Dyshaemopoietic Anaemias: anaemias resulting from deficiency of factors essential for red cell production:

(1) Iron deficiency: (the body normally compensates for routine physiological loss of iron, e.g. during menstruation, pregnancy, etc.)
See format from beginning of last term.

(2) Vitamin B_{12} deficiency:

(a) inadequate intake of B_{12} (liver, kidney, meats, seafoods, eggs, milk and dairy products).
e.g. chronic alcoholism.

(b) lack of secretion of intrinsic factor - pernicious anaemia. Failure of the intrinsic factor means that B_{12} cannot be absorbed. The disorder is characterised by weakness and neurological signs, particularly in the legs (peripheral neuritis) leads to megaloblastic changes on the blood film. R_x: replacement of B_{12} by monthly injections (life-long).

(c) Inadequate absorption secondary to partial gastrectomy.

(3) Folic Acid deficiency:

Similar to B_{12} deficiency but not so severe.
Often associated with iron deficiency.
There is a greatly increased demand for folic acid during pregnancy, hence folic acid is often administered with iron in a combined preparation.
Provided malabsorption is not present, folic acid is given by mouth.

Dyshaemopoietic anaemias may also be caused by toxins and poisons, e.g. lead and metabolic diseases such as hyperthyroidism. Aplastic anaemia (extreme anaemia, leucopenia and thrombocytopenia due to severe hypoplasia of the bone marrow) can be caused by drugs and radiation, e.g. cytotoxic drugs, chloramphenicol, gold.

Haemolytic Anaemias:

Definition: Anaemia caused by an abnormally high rate of erythrocyte destruction. There is anaemia, raised reticulocyte count, raised serum bilirubin, excess urobilinogen in the urine and faeces.

Types: (1) inherited.
(2) acquired.

(1) Inherited: familial defects of haemoglobin synthesis:

(a) e.g. Sickle cell anaemia and sickle cell trait

(homozygotes)	(heterozygotes)
HbS/Hbs	(HbA/HbS)

Sickle cell trait affects up to 40% of African negroes within the tropics and 8% of negroes in the West Indies.
Reduced oxygen carrying capacity - important in conditions of low oxygen e.g. high altitudes, anaesthesia.
Sickle cell anaemia is much more severe; generalised thrombotic incidents due to clumping of the abnormal red cells, from 6/12 of age
Prognosis is very poor.

(b)

Thalassaemia Major (homozygotes)	Thalassaemia minor (heterozygotes)

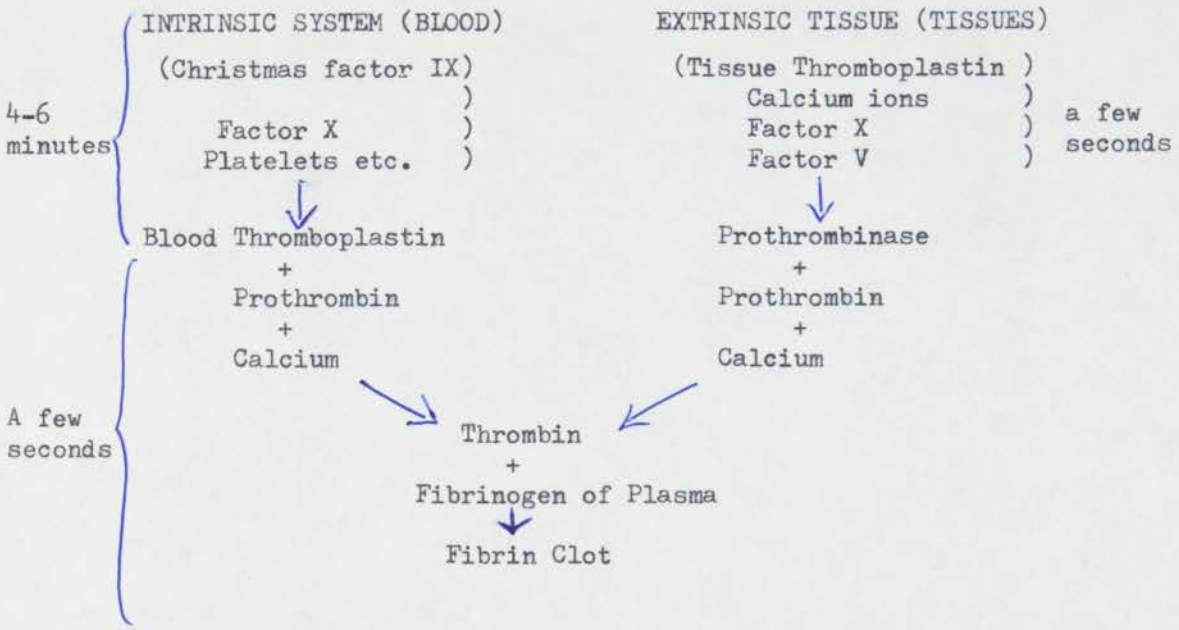
Common in Mediterranean peoples. Thalassaemia minor causes a mild, chronic anaemia, often asymptomatic, and which does not respond to iron. Thalassaemia major is a severe anaemia, in childhood, with a poor prognosis.

(2) Acquired:
(i) Infections - e.g. clostridium welchii (cause of gangrene)
(ii) Protozoal infection - e.g. malaria.
(iii) Virus infection - e.g. glandular fever, atypical virus pneumonia.
(iv) chemicals and drugs, e.g. lead.
(v) circulating antibodies, e.g. Hodgkin's disease, lymphatic leukaemia.

Investigation: Electrophoresis of blood; abnormal haemoglobins separate out.

Haemorrhagic Diseases:

Mechanism of blood coagulation:



Natural blood coagulation and onset of haemorrhage requires both extrinsic and intrinsic symptoms.

Necessary factors:

1) Platelets. If the count is 100,000/cu.mm., thrombocytopenia is present but thromboplastin formation is deficient.
2) Calcium.
3) Factor V. Only deficient in severe debilitating liver disease or carcinomatous.
4) Plasma thromboplastin antecedent. Deficiency rare.
5) Factor X. Deficient in liver disease.
6) Anti-haemophiliac globulin. A.H.G. Factor VIII. Deficiency - sex-linked congenital defect of males - haemophilia and Von Willebrand's disease - prolonged coagulation time.
7) Christmas factor. Factor IX. Sex-linked congenital defect of males - prolonged coagulation time. Christmas Disease or Haemophilia B. May also occur in liver disease and with anti-coagulants.
8) Factor VII. Deficient in liver disease.
9) Tissue thromboplastin.
10) Prothrombin: deficient in oral anticoagulant therapy.
11) Thrombin.
12) Fibrinogen: deficient in severe liver disease.

Haemorrhagic Diseases

1. Abnormalities of platelets and/or capillaries:

(a) Purpura; extravasation of blood into the skin and mucous membranes due to capillary haemorrhage, with low platelet count.

Haemorrhagic Diseases

1. Abnormalities of platelets and/or capillaries:

   (a) Purpura; extravasation of blood into the skin and mucous membranes due to capillary haemorrhage, with low platelet count. Causes: leukaemia, virus infections, X-rays, massive blood transfusion, poison and drugs.

   (b) Henoch-Schonlein Purpura: Hypersensitivity to B-haemolytic streptococci, seen in children. Causes rapid renal failure.

2. Coagulation defects:

   (a) Haemophilia: X-linked gene recessive.
   Prolonged coagulation time - life-long tendency to excessive haemorrhage.

Polycythaemia

An increase in the total number of erythrocytes in the circulating blood. A rise in Hb level, packed cell volume, and erythrocyte count.

Causes:
(a) Newborn
(b) High altitude
(c) Cardiovascular disease (lowered oxygen tension of altered blood).
(d) Pulmonary disease. Emphysema and chronic bronchitis.

Causes recurrent vascular thromboses because of the high red cell density.
Repeated