Therapeutic areas – Part 1

Haematology

Module 4 Topic 4_3

Haematology

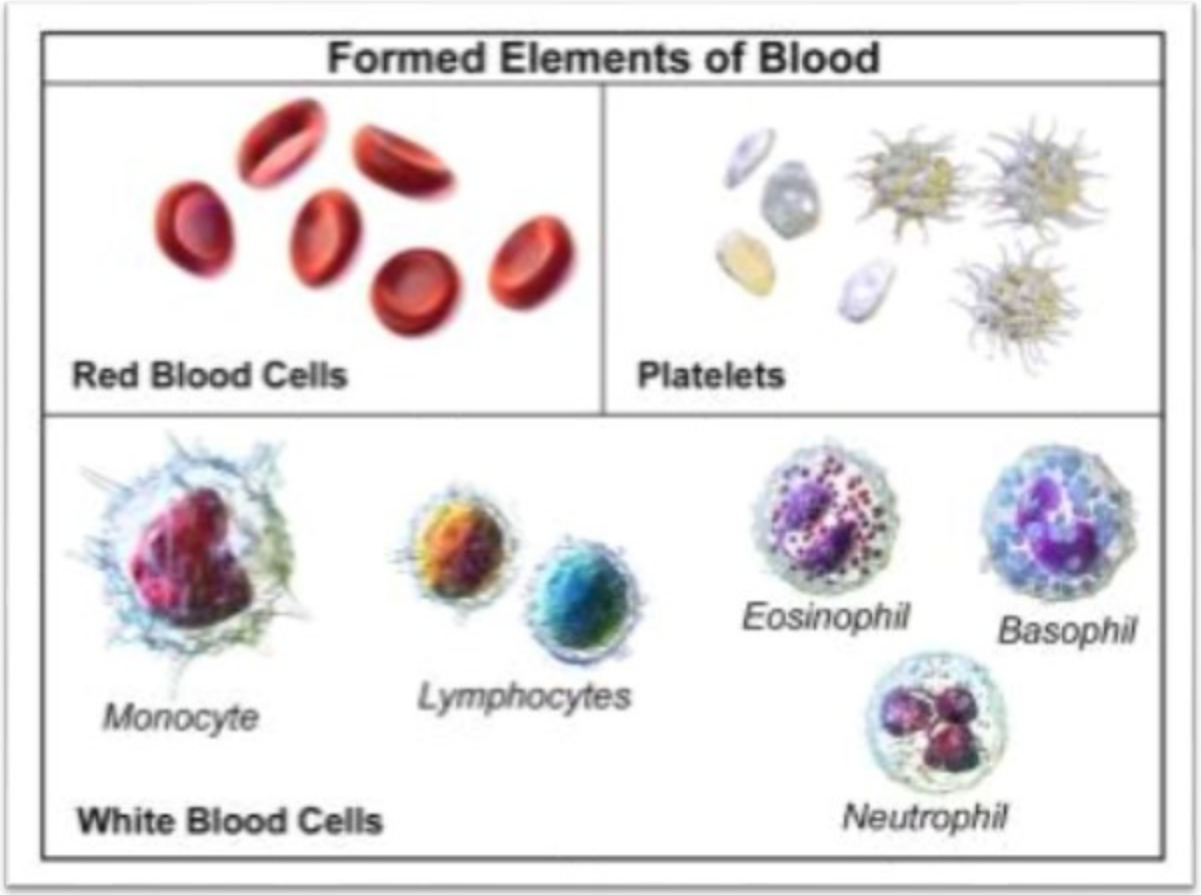
Blood is a complex mixture of

- Plasma (the liquid component)
- White blood cells (WBCs)
- Red blood cells (RBCs)
- Platelets

Haematology

- Functions of Blood
  - It delivers oxygen and essential nutrients (such as fats, sugars, minerals, and vitamins) to the body's tissues
  - It carries carbon dioxide to the lungs and other waste products to the kidneys for elimination from the body
  - It transports hormones (chemical messengers) to allow various parts of the body to communicate with each other
  - It also carries components that fight infection and stop bleeding

Haematology



Overview of Blood Disorders

- Some blood disorders cause the number of cells in the blood to decrease:
  - A decreased number of red blood cells is called anemia
  - A decreased number of white blood cells is called leukopenia
  - A decreased number of platelets is called thrombocytopenia
- Other blood disorders cause the numbers of blood cells to increase:
  - An increased number of red blood cells is called erythrocytosis
  - An increased number of white blood cells is called leukocytosis
  - An increased number of platelets is called thrombocytosis or thrombocythemia

Blood Disorders

- **Symptoms of Blood Disorders**
  - Decreased RBCs and hemoglobin can cause symptoms of anemia, such as fatigue, weakness, and shortness of breath
  - Decreased white blood cells or immune system proteins can cause recurrent fever and infections
  - Decreased platelets or blood clotting factors can cause abnormal bleeding and bruising

Blood Disorders

Symptoms suggestive of a blood disorder :

- Blood clot (phlebitis), usually in a leg causing swelling, redness, and/or warmth of the leg or shortness of breath
- Petechiae a fine pin-point red skin rash caused by low platelet count
- Blood blisters in the mouth caused by too few platelets or clotting problems
- Swollen lymph nodes caused by white blood cell cancers leukemias, lymphomas
- Pallor (pale skin) caused by anemia
- Pica (eating of ice, dirt, or clay) suggests iron deficiency anemia

Overview of Blood Disorders

Common Causes of Anemia

Mechanism	Examples
Decreased red blood cell production	Aplastic anemia Folate deficiency Iron deficiency Leukemia Lymphoma Myelodysplasia (abnormalities in bone marrow tissue) Vitamin B12 deficiency
Increased red blood cell destruction	Autoimmune reactions against red blood cells An enlarged spleen Glucose-6-phosphate dehydrogenase (G6PD) deficiency Sickle cell disease Thalassemia

Overview of Blood Disorders

Common Causes of Anemia

Mechanism	Examples
Chronic excessive bleeding	Bladder tumors Cancer in the digestive tract Heavy menstrual bleeding Hemorrhoids Kidney tumors Ulcers in the stomach or small intestine
Sudden excessive bleeding	Injuries Childbirth Surgery

Overview of Blood Disorders

Treatment for anaemia

- Depends on the type and cause of anaemia
- For iron deficiency anaemia, an iron preparation is given e.g. ferrous fumarate, ferrous sulphate etc.
  - initially to correct the deficiency and thereafter to replenish the body's stores
- Other ingredients like folic acid, vitamin B_{12}, vitamin C etc. may be included in the preparation to correct any coexisting dietary deficiency or help the intestinal absorption of iron

Overview of Blood Disorders

Treatment for anaemia (contd)

- Deworming with albendazole in patients with hookworm infestation
- Blood transfusion for patients with blood loss due to injury, childbirth or surgery

Leukemias

Leukemia

- Cancer of the WBCs involving bone marrow, circulating WBCs, and organs such as the spleen and lymph nodes
- Abnormal proliferation, clonal expansion at the pluripotent stem cell level, and diminished apoptosis (programmed cell death) lead to replacement of normal blood elements with malignant cells

Leukemias

Leukemia (contd)

- Inhibitory factors produced by leukemic cells suppress normal hematopoiesis, leading to anemia, thrombocytopenia, and granulocytopenia
- Organ infiltration results in enlargement of the liver, spleen, and lymph nodes

Leukemias

Types and features of leukemias

Feature	Acute Lymphocytic	Acute Myelogenous	Chronic Lymphocytic	Chronic Myelogenous
Peak age of incidence	Childhood	Any age	Middle and old age	Young adulthood
WBC count	High in 50% Normal or low in 50%	High in 60% Normal or low in 40%	High in 98% Normal or low in 2%	High in 100%
Differential WBC count	Many lymphoblasts	Many myeloblasts	Small lymphocytes	Entire myeloid series
Anemia	Severe in >90%	Severe in >90%	Mild in about 50%	Mild in 80%
Platelets	Low in > 80%	Low in > 90%	Low in 20 to 30%	High in 60% Low in 10%
Lymphadenopathy	Common	Occasional	Common	Infrequent
Splenomegaly	In 60%	In 50%	Usual and moderate	Usual and severe

Leukemias

Treatment	ALL	AML	CLL	CML
Chemotherapy Remission induction	1. daily oral prednisone and weekly IV vincristine with an anthracycline or asparaginase 2. cytarabine, etoposide and cyclophosphamide 3. IV methotrexate with leucovorin rescue	cytarabine by continuous IV infusion or high doses for 5 to 7 days; daunorubicin or idarubicin is given IV for 3 days during this time	1. Alkylating drugs, especially chlorambucil 2. Combination chemotherapy with fludarabine, cyclophosphamide, and rituximab	1. busulfan, hydroxyurea, and interferon for BCR-ABL–negative patients 2. Imatinib,a tyrosine kinase inhibitor
CNS prophylaxis	1. intrathecal methotrexate, cytarabine, and corticosteroids 2. methotrexate 3. cytarabine			
Consolidation	Drugs with different mechanisms of action than drugs used in induction	High-dose cytarabine regimens		
Maintenance	methotrexate and mercaptopurine			

Leukemias

Treatment	ALL	AML	CLL	CML
Corticosteroids			Prednisone 1 mg/kg po once/day in patients with immunohemolytic anemia and thrombocytopenia	
Monoclonal antibody therapy			Rituximab (combined with fludarabine/ with fludarabine and cyclophosphamide)	
Radiation therapy			Local irradiation for palliation in lymphadenopathy or for liver and spleen involvement	

Leukemias

Treatment	ALL	AML	CLL	CML
Supportive care	• Transfusions • Antibiotics or antifungal drugs • Hydration and urine alkalinization • Psychologic support	-do-	• Transfusions of packed RBCs or erythropoietin injections for anemia • Platelet transfusions for thrombocytopenia • Antimicrobials for bacterial, fungal, or viral infections	
Stem cell transplantation	✓	✓		✓*

* Except when stem cell transplantation is successful, treatment of CML is not known to be curative.

Lymphoma

Lymphoma

- A heterogeneous group of tumors arising in the reticuloendothelial and lymphatic systems
- The major types are -
  - Hodgkin lymphoma
  - Non-Hodgkin lymphoma

Lymphoma

Hodgkin Lymphoma

- Localized or disseminated malignant proliferation of cells of the lympho-reticular system, primarily involving lymph node tissue, spleen, liver, and bone marrow
- Symptoms include painless lymphadenopathy, fever, night sweats, weight loss, pruritus, splenomegaly, and hepatomegaly
- Results from the clonal transformation of cells of B-cell origin, giving rise to pathognomic binucleated Reed-Sternberg cells

Lymphoma

Treatment

- Chemotherapy
  - In early stage - abbreviated chemotherapy regimen of doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (ABVD) plus radiation therapy or with longer-course chemotherapy alone
  - In later stages - ABVD combination chemotherapy alone as standard
    - Other effective drugs include nitrosoureas, ifosfamide, procarbazine, cisplatin or carboplatin, and etoposide

Lymphoma

Treatment

- Chemotherapy (Contd)
  - Other drug combinations are - bleomycin, etoposide, doxorubicin (Adriamycin), cyclophosphamide, vincristine (Oncovin), procarbazine, and prednisone (known as BEACOPP)

    - and melchlorethamine, doxorubicin, vinblastine, vincristine, etoposide, bleomycin, and prednisone (known as Stanford V)
- Radiation therapy
- Surgery
- Sometimes hematopoietic stem cell transplantation

Lymphoma

Non-Hodgkin Lymphomas

- Heterogeneous group of disorders involving malignant monoclonal proliferation of lymphoid cells in lympho-reticular sites, including lymph nodes, bone marrow, the spleen, the liver, and the GI tract
- Most (80 to 85%) NHL arise from B lymphocytes; the remainder arise from T lymphocytes or natural killer cells

Lymphoma

Treatment

- Chemotherapy, radiation therapy, or both
  - External beam radiation therapy is used for stage I
- Immunotherapy with anti-CD20 monoclonal antibody, with or without chemotherapy
  - Standard drug combination is rituximab plus cyclophosphamide, hydroxydaunorubicin (doxorubicin), vincristine, and prednisone (R-CHOP) for patients with the aggressive B-cell lymphomas stage II to IV
- Sometimes hematopoietic stem cell transplantation for patients with peripheral T-cell NHL and primary CNS lymphoma

CBC

Complete blood count

- Red blood cell parameters evaluated by CBC include -
  - Number of red blood cells (red blood cell count, RBCs)
  - Proportion of blood made up of red blood cells (hematocrit, Hct)
  - Amount of hemoglobin (the oxygen-carrying protein in red blood cells) in the blood (hemoglobin, Hb)
  - Average size of red blood cells (mean cellular volume, MCV)
  - Amount of hemoglobin in an individual red blood cell (mean cellular hemoglobin, MCH)
  - Concentration of hemoglobin in an individual red blood cell (mean cellular hemoglobin concentration, MCHC)

CBC

White blood cell parameters evaluated by the CBC include -

- Total number of white blood cells
- Percentages and numbers of the different types of white blood cells
  - neutrophils, lymphocytes, monocytes, eosinophils, and basophils

Platelets are also counted as part of a CBC

Special tests

- Clotting tests
  - Bleeding time, clotting time
  - Prothrombin time (PT)
- Measurement of proteins e.g. Bence Jones proteins in Multiple Myeloma and other substances viz. iron, B-12, folate
- Blood typing - ABO System, Rh factor
- Bone Marrow Examination

Bone Marrow Examination

- **Bone marrow aspirate**: Removes fluid and cells by inserting a needle into the bone marrow and sucking out fluid and cells
- **Bone marrow core biopsy**: Removes an intact piece of bone marrow using a coring device (similar to a larger diameter needle)
- Samples are usually taken from the hipbone (iliac crest), rarely sternum (breastbone)