Interpretation of the Full Blood Count

Red Blood Cells

Constituents of the red cell count

Most important

- **Haemoglobin (Hb)**: *concentration* of haemoglobin within the blood. Hb is the protein which carries oxygen in the blood and, hence, is the most important value to look at. Low haemoglobin = "anaemia".
- **Mean cell volume (MCV):** mean *volume* of the red blood cells ("-cytic"). This is the main method used to classify anaemia.
- **Reticulocyte count:** concentration of immature red blood cells – increased in blood loss and haemolytic anaemia because the bone marrow works harder to replace lost cells.

Less important

- **Red cell count (RCC)**: the *concentration* of the red blood cells within the blood.
- **Haematocrit (HCT)/ packed cell volume (PCV)**: volume *percentage* of red blood cells in the blood.
- **Mean corpuscular haemoglobin (MCH)**: mean haemoglobin *quantity* within the bloods cells – affects the colour of the cells ("-chromic")
    - most normocytic and macrocytic anaemias are normochromic
    - most microcytic anaemias are hypochromic (except anaemia of chronic disease)
- **Mean corpuscular haemoglobin concentration (MCHC)**: mean haemoglobin *concentration* within the bloods cells.
- **Red blood cell distribution width (RDW):** measure of the variation of red blood cell volumes. It is used in conjunction with MCV to determine if anaemia is due to a mixed cause or a single cause. Raised RDW = "anisocytosis".

Anaemia

Anaemia = "a reduced concentration of haemoglobin within the blood"

Other relevant tests

- **WCC and platelet count:** if both also abnormal, a bone marrow cause is likely
- **Reticulocyte count:** if raised, the cause is blood loss or haemolytic anaemia
- **Mean cell volume (MCV):**

Table 1: Causes of anaemia by MCV

Microcytic (SIT)	Normocytic	Macrocytic
Sideroblastic	Acute blood loss	Megaloblastic
Iron deficiency	Haemolytic anaemia	↓B_{12}
Thalassaemia	Sickle cell	↓folate
		Non-megaloblastic
		Alcohol
		Reticulocytosis
		Liver disease
		Pregnancy
Chronic disease	Hypothyroidism	
	Bone marrow failure (aplastic anaemia, myelodysplasia, leukaemia, myelofibrosis)	

Tests for specific causes

- **Haematinics**: B_{12} & folate, ferritin *(NB. ferritin is also an acute phase protein)*
- **Iron studies**: iron, transferrin/ total iron binding capacity (TIBC), transferrin saturation, ferritin, soluble transferrin receptor
- **TFTs**
- **Blood film ± bone marrow biopsy** (if bone marrow cause/haemolytic anaemia/sideroblastic anaemia suspected)
- **Hb electrophoresis** (if thalassaemia/ sickle cell suspected)
- **Bilirubin** (raised in haemolysis)

Commonest causes

- **Iron-deficiency anaemia**
    - Physiology: iron is found in red meats (haem iron) and cereal (non-haem iron). In humans, $^2/_3$ is stored as haem, $^2/_9$ as ferritin, $^1/_9$ as haemosiderin. Fe^{2+} (ferrous) is absorbed; Fe^{3+} (ferric) is consumed and used.
    - Causes:
        - Chronic blood loss (1. Menstrual loss; 2. GI tract loss e.g. malignancy, any '-itis', ulcers, varices; 3. Urinary tract loss)
        - ↑demand (pregnancy, growth)
        - ↓absorption (coeliacs, gastrectomy)
        - Poor intake

    Check urea (↑in upper GI bleeding)
    - Investigations if no clear cause: upper GI endoscopy + colonoscopy, coeliacs screen, urine dipstick
    - Treatment: treat cause, ferrous sulphate tablets, transfusion if Hb<70
- **B_{12}-deficiency anaemia**
    - Physiology: vitamin B_{12} is found in meat and dairy products. The stomach produces *intrinsic factor* which binds to B_{12}, allowing it to be absorbed in the *terminal ileum*. Body stores last up to 4 years.

- Causes: pernicious anaemia, malabsorption (e.g. after gastrectomy or terminal ileum disease/resection)
- Investigations for pernicious anaemia: parietal cell antibodies, intrinsic factor antibodies, Schilling's test
- Treatment: treat cause, hydroxocobalamin (B_{12}) injections 3-monthly

- **Folate-deficiency anaemia**
  - Physiology: folate is found in green vegetables. Body stores only last 4 months (therefore deficiency develops earlier in malabsorption/pregnancy).
  - Causes:
    - Dietary (alcoholism, neglect)
    - ↑requirements (pregnancy, haematopoiesis)
    - Malabsorption (coeliacs, pancreatic insufficiency, gastrectomy, crohns)
    - Drugs interfere with metabolism (phenytoin, methotrexate, trimethoprim)
  - Treatment: treat cause, oral folic acid supplements
- **Anaemia of chronic disease**
  - Causes: any chronic disease
  - Classically: iron ↓, TIBC ↓, ferritin normal (vs. iron deficiency anaemia: iron ↓, TIBC ↑, ferritin ↓)
  - Treatment: treat cause, transfuse if Hb<70
- **Haemolytic anaemia**
  - Physiology:
    - When red cells are destroyed extravascularly by macrophages (normal process):
      1. Hb → globulin (which is broken down to amino acids) + haem (which is broken down to bilirubin)
      2. Bilirubin is then conjugated by the liver (a rate limited process) and passed to the bowel in bile, where it is converted to urobilinogen
      3. Some of this urobilinogen is passed in stool and some is reabsorbed and excreted in urine as urinary urobilinogen
    - When red cells are destroyed intravascularly (abnormal process) – free Hb follows one of three pathways:
      - Some binds to haptoglobin (and is removed by liver)
      - Some is filtered by the glomerulus and passed as haemoglobinuria or haemosiderinuria
      - Some is oxidised to methaemoglobulin which dissociates to globin + ferrihaem (most ferrihaem then binds to albumin → methaemalbuminaemia)
  - Inherited causes:
    - Haemoglobinopathies: sickle cell, thalassaemia
    - Membrane defects: hereditary spherocytosis, elliptocytosis
    - Enzyme defects: G6PD deficiency, pyruvate kinase deficiency
  - Acquired causes:
    - Immune mediated: autoimmune haemolytic anaemia, drug-induced haemolytic anaemia, alloimmune haemolytic anaemia
    - Non-immune mediated: DIC, TTP, physical damage by e.g. heart valves, toxins such as lead/uraemia/drugs, malaria, paroxysmal nocturnal haemoglobinuria
  - Investigations to confirm haemolysis:
    - Increased Hb breakdown: ↑unconjugated bilirubin, ↑LDH (from red cells), ↑urinary urobilinogen (on urine dipstick)
    - Increased Hb production: ↑reticulocytes
    - Intravascular haemolysis: ↓free haptoglobin, haemoglobinuria (on haematuric urine microscopy), ↑urinary haemosiderin, red cell fragments on blood film
  - Investigations to find cause:
    - Blood film: sickle cells, schistocytes (microangiopathic haemolytic anaemia), inclusion bodies (malaria), spherocytes/ elliptocytes (hereditary spherocytosis/ elliptocytosis), Heinz bodies (G6PD), bite/blister cells (G6PD), distorted 'prickle' cells (pyruvate kinase deficiency)
    - Direct antiglobulin (Coombs') test (for autoimmune haemolytic anaemia)
    - Osmotic fragility testing (for membrane abnormalities)
    - Hb electrophoresis (for haemoglobinopathies)
    - Enzyme assays (for enzyme defects)

Polycythaemia

Polycythaemia = "increased concentration of red blood cells within the blood"

Causes

- **Relative polycythaemia** (i.e. ↓plasma volume)
  - Acute dehydration
  - Chronic (associated with obesity, hypertension, alcohol excess, smoking)
- **Absolute polycythaemia** (i.e. ↑RBC mass)
  - Primary = polycythaemia ruba vera
  - Secondary = due to increased EPO (e.g. RCC) or chronic hypoxia (e.g. COPD, altitude, congenital cyanotic heart disease)

Investigations

- **WCC and platelet count** (both also raised in primary absolute polycythaemia, but not in secondary absolute polycythaemia)
- **^{51}Cr Red cell mass study** (normal red cell mass in relative polycythaemia; raised red cell mass in absolute polycythaemia)
- **Erythropoietin level**
- If polycythaemia ruba vera suspected: bone marrow biopsy, JAK-2 mutation

White Blood Cells

Table 2: Causes white blood cell abnormalities		
Constituents of the white cell count	**High**	**Low**
Neutrophil count	**Bacterial infection** Inflammation Necrosis Corticosteroids Malignancy/ myeloproliferative disorder Stress (trauma, surgery, burns)	**Post-chemotherapy** Agranulocytosis causing drugs (4C's: **C**arbamazepine, **C**lozapine, **C**olchicine, **C**arbimazole) Viral infection Hypersplenism Bone marrow failure (e.g. in leukaemia) Felty's syndrome
Lymphocyte count	**Viral infection** Chronic infections CLL/ lymphoma	**Viral infection** HIV Post-chemotherapy Bone marrow failure (e.g. in leukaemia) Whole body radiation
Monocyte count	Bacterial infection Autoimmune diseases Leukaemias/ Hodgkin's disease	Acute infections Corticosteroids Leukaemias
Eosinophil count	**Allergy** (inc. eczema, ABPA) **Parasite infection** **Drug reactions** Hypereosinophilic syndrome Skin diseases Malignancy e.g. Hodgkin's disease	n/a
Basophil count	Some leukaemias/ lymphomas IgE mediated hypersensitivity Inflammatory disorders Myeloproliferative disorders Viral infection	n/a

Platelets

Thrombocytopenia

Causes

- **Decreased production**: bone marrow failure, aplastic anaemia, megaloblastic anaemia, myelosuppression
- **Increased destruction/ consumption**
    - **Non-immune**: DIC, TTP, HUS, sequestration in hypersplenism (including portal hypertension e.g. in liver disease)
    - **Primary immune**: ITP
    - **Secondary immune**: SLE, CLL, viruses, drugs, alloimmune

Possible investigations

- **Blood film ± bone marrow biopsy**
- **Infection screen** e.g. HIV, hepatitis C
- **LFTs** (live dysfunction can also cause thrombocytopenia)
- **LDH** (increased in haemolysis and lymphoproliferative disorders)
- **Serum vitamin B12** and **folate**
- **Coagulation screen** including fibrinogen and D-dimer (if suspect DIC)
- **Acute phase reactants** (look for evidence of infection)

Treatment

- Treat cause
    - Immunosuppressants if autoimmune e.g. prednisolone, azathioprine, cyclophosphamide
    - Plasmapheresis for TTP/HUS
- Platelet concentrate transfusion
- Splenectomy

Thrombocythemia

Causes

- **Primary**: essential thrombocythaemia, other myeloproliferative disorders
- **Secondary**: bleeding, inflammation, infection, malignancy, post-splenectomy

Possible investigations

- **Blood film ± bone marrow biopsy**
- **Acute phase reactants** (look for evidence of infection)
- **JAK2 mutation** (myloproliferative diseases)

Treatment

- Aspirin (to prevent thromboembolic disease)
- Hydroxycarbamide (if primary cause)