



The Red Blood Cell

The role of the red blood cell is to carry oxygen bound to haemoglobin around the body to organs of the body.

They are a biconcave disc in shape to allow the largest surface area for exchange.

The red blood cell is made in the bone marrow from stem cells which divide and differentiate to become reticulocytes (once the nucleus has been extruded) which then become erythrocytes (once the ribosomes have been lost) in a process called 'erythropoiesis'.

Stem cells	->	Erythroblasts	->	Reticulocyte	->	Mature erythrocyte
		Dark blue cytoplasm		Nucleus extruded (so unable to divide)		Lost ribosomes

Red blood cells then circulate in the blood for 120 days.

The production of red blood cells is regulated by erythropoietin (EPO) made by the kidneys in response to low blood oxygen levels.

The red cells are removed from the blood by the reticulo-endothelial system as blood passes through the bone marrow, liver and spleen. The iron from the red blood cells is then recycled so that it can be used to create new red blood cells. The rest of the recycled haemoglobin gets converted into bilirubin which is excreted via the liver in bile, faeces and urine.

Red Blood Cell count (RBC)

The number of red cells in the blood.

Normal range $4.3-5.7 \times 10^{12}/L$

We use Hb more commonly to assess for anaemia

Hb

The Hb is the concentration of the protein haemoglobin in the blood and therefore is a measure of the number of red bloods full of haemoglobin circulating at that point in time.

Too low Hb is called anaemia and can result in symptoms of anaemia depending on the severity of the anaemia (<60 will usually be symptomatic) and the speed of onset (rapid onset being more symptomatic).

Fundamentally the cause of anaemia can be due to:

1. Reduced production of red blood cells e.g due to bone marrow disorders
2. Increased loss/removal of red blood cells e.g. acute bleeding, haemolysis

Symptoms/signs of anaemia:

- Pallor
- Fatigue
- SOB
- Headaches
- Tachycardia and palpitations
- Dizziness and fainting
- Chest pain

To start investigate why the patient may have a low Hb you can look at the MCV.

Mean cell volume (MCV)

Tells you the average volume, or size, of the red blood cells.

Normal range 77-98 fL





Small red blood cells = 'microcytic'
 Normal sized red blood cells = 'normocytic'
 Large red blood cells = 'macrocytic'

The size of the red blood cells can help to point you in the direction of the cause of the anaemia, for example:

Microcytic anaemia	Normocytic anaemia	Macrocytic anaemia
Iron deficiency	Chronic renal disease (low EPO)	B12/folate deficiency
Thalassemia	Chronic disease	Alcohol excess
Sideroblastic anaemia	Acute bleeding	Chronic liver disease
Chronic disease	Marrow infiltration	Hypothyroidism
	Aplastic anaemia	Anti-folate medications e.g. MTX, hydroxycarbamide

Packed cell volume (PCV) or Haematocrit (Hct)

This is a measure of the % of the blood sample made up of red blood cells (compared to other components of the plasma, WCCs, platelets, proteins etc)

Normal range Hct 0.39-0.50 L/L

PCV normal range males 04.0-0.53 i.e. 40-53%, females 0.36-0.48 i.e. 36-48%

Critical values <20% or >60%

This is therefore a particularly useful measure of a patient's hydration status:

- A dehydrated patient will have a high Hb, high PCV/haematocrit and RBC as the plasma is concentrated
- An over-hydrated patient, given too much IVFs for example, will have a low Hb, low PCV/haematocrit and RBC due to the dilutional effect of the fluids.

Causes of an increase in PCV	Causes of a decrease in PCV
Increased number of red blood cells e.g. polycythaemia	Reduced number of red blood cells e.g. anaemia from iron deficiency
Fall in plasma volume e.g. dehydration	Rise in plasma volume e.g. high WCC

Its therefore important to interpret the Hb in the context of the PCV/haematocrit.

Mean Cell Haemoglobin (MCH) and Mean Cell Haemoglobin Concentration (MCHC)

MCH is a measure of the average amount of haemoglobin in each red blood cell.

Normal range is 27.3-32.6 pg

MCHC is a measure of the average concentration of haemoglobin in red blood cells.

Normal range is 316-349 g/L

Both of these measures are a reflection of the 'health' of the haemoglobin in the blood.

A low MCV reflects that there is not enough haemoglobin in each red cell which is commonly due to iron deficiency or thalassemia's.

A high MCV is seen in B12/folate deficiency and haemolytic anaemia due to breakdown/loss of red blood cells or issues with red blood cell production without an issue with the haemoglobin production per se.





Red Cell Distribution Width (RDW)

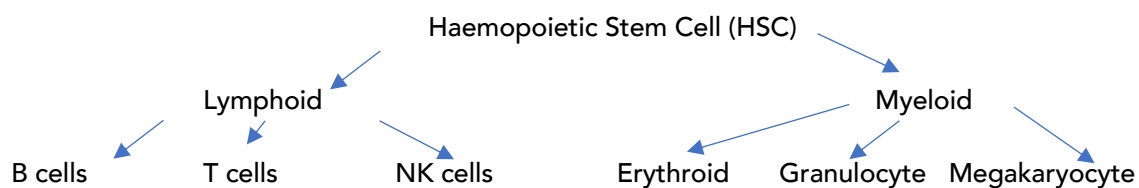
RDW is a measure of the range of widths of the red blood cells i.e. the variation in the red blood cell sizes.

A high RDW may indicate the presence of fragments, groups of red blood cells agglutinated and/or abnormal shapes of red blood cells e.g. in iron deficiency or B12/folate deficiency.

The White Blood Cell

The role of white blood cells is to fight infection and the bone marrow increased their production in response to infection and inflammation.

White blood cells (leukocytes) are also made from the bone marrow stem cell.



Granulocytes include:

- Neutrophils
- Macrophages
- Eosinophils
- Basophils

Test	% of total white cells	Normal Values
Total white cell count (WCC)		3.7-9.5 x10 ⁹ /L
Neutrophils	40-75%	1.7-7.5 x10 ⁹ /L
Lymphocytes (B and T cells)	20-40%	1.5-4.0 x 10 ⁹ /L
Monocytes	2-10%	0.2-0.8 x 10 ⁹ /L
Eosinophils	1-5%	0.04-0.44 x 10 ⁹ /L
Basophils	<1%	0.01 – 0.1x10 ⁹ /L

Neutrophils

Neutrophils, or 'phagocytes' are the most abundant of all white blood cells in the blood. They surround and engulf bacterial predominantly in a process known as phagocytosis.

Neutrophilia – high neutrophils

The cause of high neutrophils will usually be infection however some autoimmune inflammatory conditions can cause a high neutrophil count.

Causes of neutrophilia:

1. Bacterial infection (look at CRP)
2. Inflammation secondary to tissue damage e.g. after surgery, burns.
3. Corticosteroid use
4. Smoking
5. Chronic myelomonocytic leukaemia
6. Chronic myeloid leukaemia

Neutropenia – low neutrophils





Neutropenia is defined as when neutrophils are $<1.5 \times 10^9/L$. If the patient has signs of infection with neutropenia they are at risk of life threatening sepsis so this must be acted on urgently.

Mild	$1-1.5 \times 10^9/L$
Moderate	$0.5-1 \times 10^9/L$
Severe	$<0.5 \times 10^9/L$

Causes of neutropenia are most commonly secondary to chemotherapy (usually 10-14 days post chemotherapy) but can also be due to radiotherapy and marrow infiltration with disease (both haematological and solid cancers).

Causes of neutropenia:

1. Viral infection (transient) – check HIV, Hep B,C
2. Drugs
3. Autoimmune diseases
4. B12/folate deficiency
5. Felty's syndrome
6. Thyroid disease
7. Bone marrow failure (in the context of a pancytopenia)

Lymphocytes

Lymphocytes are divided into:

- B cells – which make antibody against infectious agents e.g. bacteria
- T cells – which destroy virally infected cells (through an education process in the gland known as the thymus hence 'T' cells)

Causes of elevated lymphocyte count include viral illnesses (esp glandular fever caused by Epstein-Barr virus) or malignant haematological conditions e.g. CLL.

Very high lymphocyte counts rarely cause issues by virtue of their high count in the blood, such as hyper-viscosity symptoms, because the lymphocytes are very small.

Causes of low lymphocytes include bacterial infection, age, HIV, autoimmune diseases, drugs and bone marrow disease.

Monocytes

These are cells that migrate to the tissues after a short circulation in the blood (20-40 hours) where they mature into cells called macrophages.

They therefore defend from infection within the tissues mainly through phagocytosis but they also present antigens (foreign bits from invading pathogens) to induce further immune response ('antigen presenting cells').

Monocytes can therefore also be increased in infection (e.g. TB) but an important differential would be haematological malignancies e.g. CMML

Basophils

These are rare cells but can rise in acute hypersensitivity reactions. They migrate into tissues and mature into mast cells.

High levels of basophils are highly suspicious of haematological malignancy especially CML.

Eosinophils





These cells defend against parasites. They are also raised in atopic conditions such as asthma, eczema, autoimmune disease (eosinophilic granulomatosis with polyangiitis, PAN), medications and haematological malignancy.

The Platelet

Platelets are produced from stem cells that differentiate into megakaryocytes which are giant cells that replicate their DNA without dividing to produce a mature cytoplasm which then releases 1000s of platelets in a process called fragmentation leaving a bare nucleus.

Platelets only last 10 days in circulation. The production of platelets is controlled by the hormone thrombopoietin produced by the liver.

The primary role of platelets is to form a haemostatic plug where injury has occurred to prevent bleeding.

The normal range of the platelet count is $150-400 \times 10^9/L$.

Thrombocytosis (high platelets)

A moderate platelet increase ($400-1000 \times 10^9/L$) is relatively common among acutely ill patients caused by the bone marrow being stimulated by infection or tissue damage e.g. after surgery, sepsis, acute bleed. This is called a 'reactive thrombocytosis'.

Other causes include:

- Essential thrombocythaemia (or as part of another myeloproliferative disorder e.g. PRV)
- Iron deficiency
- Hyposplenism or post-splenectomy

Thrombocytopenia (low platelets)

A low platelet count can be due to:

- Reduced bone marrow production (secondary to medications, bone marrow disease)
- Increased platelet destruction (E.g. immune thrombocytopenic purpura, ITP)
- Increased rate of platelet consumption (E.g. Disseminated intravascular coagulation, microangiopathic haemolytic anaemias)

Features of low platelets include bruising and petechial haemorrhages, bleeding gums, nose bleeds.

We aim for a minimum platelet count of 10 in most haematology patients and 20 in febrile patients.

