Focus on blood tests used for monitoring haematological conditions

Different haematological diseases can result in similar symptoms so it is essential to carry out a full blood screen to distinguish between different conditions and treat these appropriately. Hibo Osman and Richard Mellor describe the tests that comprise a full blood count and explain how the profile changes with disease.

Introduction

Haematological diseases can be loosely defined as disorders of blood and its components, which include red cells, white cells, platelets and plasma. These diseases range from the very common, such as anaemia (disorder of red blood cells) to the rare, such as thalassaemia (inherited mutations in genes that code for haemoglobin).

This article will concentrate on those haematological conditions most commonly seen in practice and the monitoring required for treatment of these conditions. (Management of malignant haematological diseases will not be included.) We envisage the following learning objectives will be achieved after reading this article:

- ☐ Be able to outline the common blood tests — discuss the range and implications of abnormal results.
- ☐ Understand how to treat and monitor the more common haematological conditions seen in clinical practice.

Full blood count

A full blood count (FBC) is an essential investigation that is routinely conducted on most patients. An understanding of the profile of FBC results is central to the monitoring of many conditions — not just those that are haematological in origin. Typical results that might be reported as part of an FBC are shown in Table 1.

Red blood cell count

Red blood cell count (RBC) is the concentration of red blood cells in a given volume of blood. This can be low because of blood loss (which can take up to 24 hours to show on FBC) or because of anaemia. It is lower in women because of menstrual blood loss (see Table 1). A raised RBC can be caused by increased red cell production, as occurs in hypoxia in airways disease and in men by hormonal differences (for example, testosterone has been reported to stimulate the production of red blood cells).

Haemoglobin — Hb. Oxygen, bound to haemoglobin, is transported around the body by red blood cells. Haemoglobin measurements are used in the detection and classification of anaemias. Low concentrations may also be indicative of other conditions, such as leukaemia and liver disease.

Mean corpuscular volume — MCV. This is the average volume of a single red blood cell. MCV is used in the identification of different types of anaemias. Low MCV is described as microcytic anaemia while a high MCV is macrocytic anaemia.

Mean corpuscular haemoglobin — MCH. This is the average amount of haemoglobin in a red blood cell. Low MCH is often accompanied by microcytosis (low MCV), and this is seen in iron deficiency anaemia.

Mean corpuscular haemoglobin concentration — MCHC. This is the average concentration of haemoglobin per 100ml of red blood cells (and it is a measure of how tightly packed with Hb the red blood cells are). Hypochromic red blood cells are pale coloured with low Hb concentration, which occurs in iron deficiency anaemia.

Erythrocyte sedimentation rate — ESR. The ESR is a measure of the rate at which

Table 1. Typical full blood count test results

Red blood cell count (RBC)	3.9–5.6 x 10^{12}/L (female) 4.5–6.5 x 10^{12}/L (male)
Haemoglobin (Hb)	115–155 g/L (female) 135–175 g/L (male)
Mean corpuscular volume (MCV)	80–100 fL
Mean corpuscular haemoglobin (MCH)	27–33
Mean corpuscular haemoglobin concentration (MCHC)	30–35 g/dL
White cell count (WCC)	4–11 x 10^9/L
Neutrophils	2.5–7.5 x 10^3/L
Lymphocytes	1.5–3 x 10^9/L
Monocytes	0.2–0.8 x 10^9/L
Eosinophils	0.04–0.4 x 10^9/L
Basophils	0.01–0.1 x 10^9/L
Platelets	150–400 x 10^9/L

Learning points

An understanding of the profile of FBC results is central to the monitoring of many conditions — not just those that are haematological in origin.

red blood cells settle in a sample of anti-coagulated blood. It is a relatively non-specific test, which can be used to monitor acute response to infection or disease.

White blood cells

The various types of white blood cells — or leukocytes — found in the blood and their cellular origins are shown in Figure 1. The white cell count (WCC) includes a measurement of the total number of white blood cells (WBC) and a differential count of the five different types of WBC. WCC is used in the diagnosis of infections because it may be raised in the body's response to infection, although a low WCC can result in poor resistance to infection.

Lymphocytes. Lymphocytes comprise the second highest proportion of the WBCs — nearly half of the total WCC — and are an integral component of the body's immune response. Viral infections, such as glandular fever, often result in a rise in their number.

Neutrophils. Neutrophils are the most plentiful type of WBC and they play a major role in the body's immune system by ingesting and killing bacteria, fungi and damaged cells. The neutrophil count is therefore raised in the presence of infection, tissue damage and inflammation. Neutrophils are also described as granulocytic WBCs (Figure 1). Therefore, severe neutropenia (low neutrophil count) and the absence of neutrophils is called agranulocytosis. Neutropenia can be acquired (for example, caused by drug toxicity, such as sulphonamides) or it can be inherited.

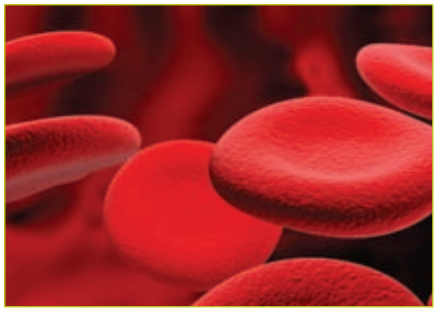
Eosinophils. Eosinophils are involved in the body's allergic response and can be raised (eosinophilia) in conditions such as asthma and drug sensitivity reactions.

Basophils. Basophils form a relatively small part of the WCC. Their physiological role is poorly understood. However, they can be raised (basophilia) in myeloproliferative disorders, such as leukaemia.

Monocytes. Monocytes are macrophages (scavenger cells) and monocytosis (raised monocyte count) can occur in chronic bacterial infections, such as tuberculosis.

Platelets

Platelets are responsible for the clotting of blood. Thrombocytopenia (low platelet count) can be caused by reduced platelet synthesis in the bone marrow and destruction or consumption of formed platelets. This can be idiopathic, drug induced (by low molecular weight heparins for example) or as a result of disease (such as malignancy or sepsis). Thrombocytopenia caused by drugs usually resolves fairly quickly after withdrawal of the causative agent. Thrombocytosis (raised platelet count) can occur in response to blood loss or in patients with malignancy.



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Anaemia

Anaemia is not a disease *per se*. Rather, it is a clinical feature often associated with other conditions. It is characterised by a reduction in the concentration of haemoglobin or red blood cells in the blood. Anaemia can be classified according to its causes, for example: iron deficiency, folate and vitamin B deficiency, and chronic disease. It can also be classified according to the cell size involved, for example: macrocytic, microcytic or normocytic anaemia. These classifications are necessary because treatment varies according to cause — particularly because most anaemias have similar signs and symptoms (Table 2.) The World Health Organization estimates that two billion of the world's population is anaemic with nearly 50% being attributed to iron deficiency.[1]

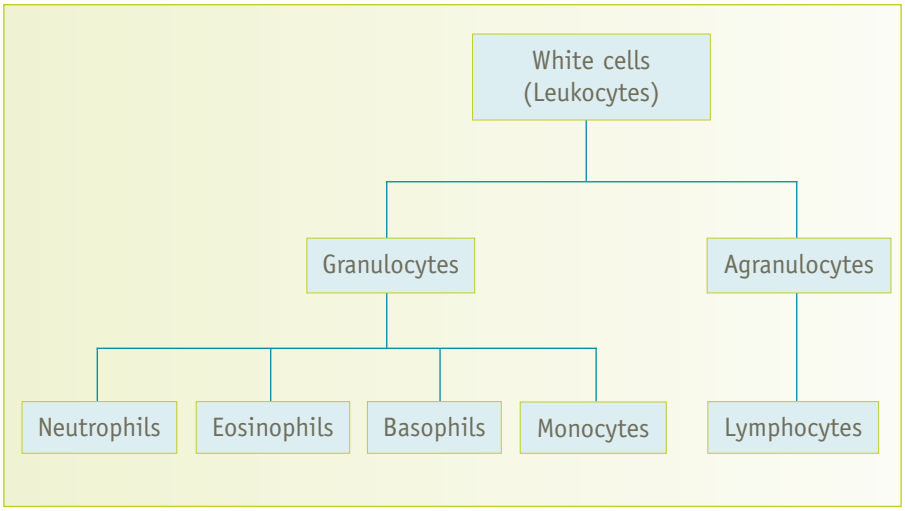

Figure 1. The types of white blood cells found in the blood and their cellular origins

Table 2. Signs and symptoms of anaemia

- ☐ Fatigue
- ☐ Headaches
- ☐ Faintness
- ☐ Breathlessness
- ☐ Insomnia
- ☐ Pallor
- ☐ Palpitations
- ☐ Angina
- ☐ Tachycardia

Iron deficiency anaemia

Iron deficiency anaemia occurs as a result of inadequate iron being available for haemoglobin production. This anaemia is characterised by small (microcytic), pale (hypochromic) red blood cells, which are deficient in haemoglobin. This is translated into reduced Hb, MCV, MCH and MCHC. Further tests will be needed to more accurately identify the type of anaemia present. These are discussed below.

Serum ferritin is a measure of total stored iron and it is usually low in people with iron deficiency anaemia. It is also used monitor iron therapy. It is an acute phase protein so can be raised in the presence of inflammatory or malignant disease and therefore should be interpreted in conjunction with other measurements.

The serum iron level is the concentration of circulating iron bound to transferrin (a serum protein). This will be low in cases of iron deficiency anaemia. Only one third of transferrin is usually bound with iron. The total iron binding capacity (TIBC) is a measure of transferrin's ability to bind to iron. In iron deficiency anaemia there is less iron available to bind to transferrin. This means there is more free transferrin available thus increasing its capacity to bind to iron (Table 3).

Treatment of any anaemia should start with identification of the underlying cause. Causes of iron deficiency anaemia can include reduced iron intake from the diet, increased requirements (such as during pregnancy), decreased absorption or increased loss (for example, through a gastrointestinal bleed). Iron replacement therapy is needed in most cases. This usually involves oral iron therapy, which replenishes iron stores thereby restoring haemoglobin levels. In general, 100–200mg of elemental iron should be given daily, and this should be given for long enough to correct the haemoglobin level and replenish the iron stores. This can take up to six months.

Although there is no evidence to support the use of any particular oral iron preparation, ferrous sulphate 200mg is the preparation most commonly used. Ideally this should be given three times daily; however, it can be used less frequently if side-effects occur. With successful treatment the haemoglobin concentration should increase by 1–2g/L per day.[2] Once in range treatment should continue for a further three months to ensure iron stores are fully replenished.[2]

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Oral therapy is the treatment of choice for iron deficiency anaemia. Treatment failure may arise through reduced compliance, malabsorption, intolerance or continuing blood loss. In these circumstances parenteral iron may be necessary. Iron dextran (Cosmofer®) or iron sucrose (Venofer®) are the two preparation available. Although these do restore iron reserves faster than oral therapy the haematological response is no faster. Blood transfusions are used only if Hb falls below a critical level, and this is a clinical decision, which is based on severity and the cause of anaemia.

Macrocytic anaemia

Vitamin B12 and folate deficiency anaemia are characterised by large red blood cells (MCV>100fl) and are described as macrocytic anaemias. In addition to those general signs and symptoms of anaemia described in Table 2, there are some specific clinical features of macrocytic anaemias. These include jaundice (caused by increased breakdown of haemoglobin in the large red blood cells) and glossitis (sore, pale and shiny tongue).

Anaemia can be classified according to its causes, for example: iron deficiency, folate and vitamin B deficiency and chronic disease.

Vitamin B12 deficiency anaemia (see Table 4) is typically caused by low dietary vitamin B12 (for example, by following a strict vegan diet) or malabsoprtion of vitamin B12 (such as in pernicious anaemia). In Britain vitamin B12 deficiency is usually the result of pernicious anaemia,[3] which is an autoimmune disorder that results in atrophic gastritis and consequently an absence of intrinsic factor. This lack of intrinsic factor leads to malabsorption and hence deficiency of vitamin B12. Total and partial gastrectomies also lead to a lack of intrinsic factor. As well as the general features of anaemia described in Table 2 and those of macrocytic anaemias described above, patients with vitamin B12 deficiency may also develop a progressive neuropathy.

Vitamin B12 deficiency is diagnosed by a low serum vitamin B12 concentration, while pernicious anaemia is identified by the presence of intrinsic factor antibodies.

The treatment of vitamin B12 deficiency starts with identifying the underlying cause;

Table 3. Predicted FBC changes in iron deficiency anaemia

Haemoglobin	↓
MCV	↓
MCH	↓
MCHC	↓
Serum ferritin	↓
Serum iron	↓
TIBC	↑

Table 4. Predicted FBC changes in vitamin B12 deficiency

Haemoglobin	↓
MCV	↑
MCHC	↔
RBC	↓
Platelets	↓ /↔
Serum B12	↓
Serum folate	↔/ ↓

Learning points

Treatment for any anaemia should start with identification of the underlying cause. Causes of iron deficiency anaemia can include reduced intake from the diet, increased requirements (such as during pregnancy), decreased absorption or increased loss (for example, through a gastrointestinal bleed).

if the deficiency is caused through diet then oral preparations and dietary advice may be given. All other causes of vitamin B12 deficiency arise from malabsorption from the gastrointestinal tract and parenteral administration may be necessary. The standard treatment is six doses of intramuscular hydroxycobalamin over two weeks followed by three monthly injections for life. Clinical improvement can be seen within 48 hours and haemoglobin levels should rise by 2–3g/dL every two weeks. Potassium levels should be monitored during initial therapy because hypokalaemia can develop as new cells are produced. Similarly, iron deficiency may occur as iron is incorporated into haemoglobin in the new cells.

Folate deficiency anaemia is caused by poor intake (through diet or anorexia), increased use (in pregnancy or while breastfeeding), malabsorption (such as in small bowel disease) or anti-folate drugs (methotrexate, trimethoprim). Folate deficiency may be asymptomatic or have those symptoms described above for macrocytic anaemias. Neuropathy, however, does not occur. Low serum and red cell folate is an indication of folate deficiency anaemia (although they can also be low in severe vitamin B12 deficiency).

Table 5. Predicted FBC changes in folate deficiency

Haemoglobin	↓
MCV	↑
MCHC	↔
RBC	↓
Platelets	↓ /↔
Serum folate	↓
Serum B12	↔

Folate deficiency is usually self-limiting or responds to short courses of oral treatment. It can take up to four months of treatment with 5mg of folic acid to replenish body stores. Long-term therapy is only indicated in cases where the underlying condition cannot be eradicated or as prophylaxis in renal dialysis or with anti-folate drugs. Note that macrocytic anaemia of both folate and vitamin B12 deficiency may respond to folate therapy.

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However, vitamin B12 should also be corrected to reduce the risk of neuropathy.

Anaemia of chronic disease

Anaemia of chronic disease is associated with systemic diseases such as rheumatoid arthritis, renal failure and heart failure. This is a normocytic anaemia, which can arise from a number of causes. Inflammatory processes can reduce iron absorption, use and erythropoesis (production of red blood cells). Erythropoietin (EPO), the hormone responsible for red blood cell production, may also be deficient.

Anaemia of chronic disease is corrected by treating the underlying cause. The administration of recombinant EPO (such as NeoRecormon®) may be necessary for those conditions with EPO deficiency, such as occurs in renal disease.

Summary

Haematological diseases are very diverse, ranging from red blood cell anaemias to rare, inherited gene mutations that lead to abnormalities in haemoglobin synthesis. To correctly identify the cause of anaemia it is essential to perform a full blood count. This routine screen allows us to gain an understanding of the number and type of cells within a given volume of blood, their relative cell sizes and the amount of haemoglobin bound to red blood cells. By comparing a patient's FBC results with the typical population ranges in conjunction with their clinical history and symptoms we are able to pinpoint the likely source of anaemia and recommend suitable treatments. ✣

Declarations of interest

The authors have no interests to declare.

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