Full blood count

Introduction

The full blood count is a fast readily available investigation which adds essential information to clinical assessment of a patient. Interpretation of the blood count is an important skill, requiring knowledge of causes of individual abnormalities and the ability to recognize patterns associated with certain conditions.

A quantitative value is provided for the blood's cellular components: white cells (including differential), red cells and platelets. For red cells, additional useful readings include total haemoglobin, measures of red cell size (mean cell volume) and range of different red cell sizes (red cell distribution width), and sometimes a reticulocyte (newly formed red cells) count is given. The mean cell haemoglobin and mean cell haemoglobin concentration are derived values which are not very useful clinically. All these data are produced by an automated analyser which scans the sample identity, extracts and aliquot of blood and performs analyses of varying complexity (*Figure 1*). Examples of clinical scenarios are provided in *Figures 2* and *3*.

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Red cell abnormalities

Low haemoglobin

Anaemia, whether this is acute or chronic, may be apparent from the patient's history; a very low haemoglobin in the absence of breathlessness is probably chronic. Another clue is the reticulocyte count. An acute anaemia is often accompanied by a vigorous attempt by the bone marrow to compensate, leading to a high reticulocyte count. Thus the mean cell volume is often high in acute anaemia whatever the cause, as reticulocytes are bigger than mature red cells. A low reticulocyte count may imply potential bone marrow pathology.

Acute anaemia

The commonest causes of this are acute bleeding and haemolysis. There may be clues from clinical assessment favouring one, although acute bleeding into the gastrointestinal tract or a body compartment may not be obvious. Dark urine and jaundice suggest haemolysis, which can be confirmed by testing unconjugated bilirubin (which will be high), lactate dehydrogenase (which will be high as it is released from red cells), haptoglobin (which will be low, especially in intravascular haemolysis, as it binds free haemoglobin and is broken down) and Coombs' test (or direct antiglobulin test) which will be positive in autoimmune haemolysis.

Chronic anaemia

The causes of chronic anaemia are numerous but finding the cause is often easy, usually they are divided by the size of the red cells. A microcytic anaemia (mean cell volume <80 fl) is generally caused by defective haemoglobin production: often iron deficiency or a haemoglobinopathy such as thalassaemia. Iron deficiency can be confirmed by testing serum ferritin or iron levels (remembering that both these may be abnormal in the face of inflammation), and unless a cause is apparent, endo-

Figure 1. Once loaded onto an analyser an aliquot of the blood sample is removed automatically and diluted, the blood then moves through a tube thin enough that cells pass by one at a time. Characteristics of the cell are measured using lasers (fluorescence flow cytometry) or electrical impedance. The haemoglobin level is determined after lysing the red cells. The results are checked by a qualified biomedical scientist who will decide if the machine is performing adequately and if, for example, a blood film is required.

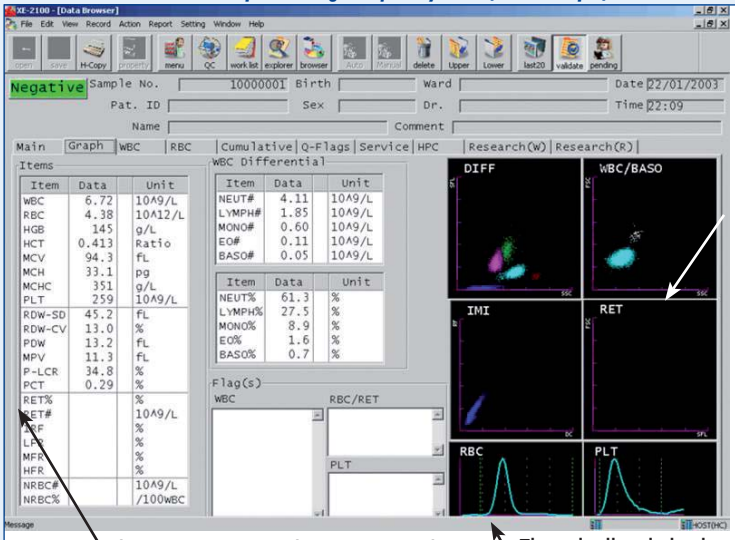

Figure 2. Clinical scenario.

Patient 1

A 42-year-old man had been unwell for 3 days with fevers, he had a convulsion today. He is unresponsive, febrile, tachycardic, and is jaundiced. His full blood count results are:

Haemoglobin = 6.2 g/dl; mean cell volume = 104 fl; platelets = 32 x 10^9/litre; white cell count = 6.2 x 10^9/litre, neutrophils = 3.8 x 10^9/litre, lymphocytes = 1.5 x 10^9/litre

Clinical comment:

Anaemia with a high mean cell volume could either indicate a chronic macrocytic anaemia or an acute anaemia with reticulocytosis; the acute history favours the latter, jaundice and lack of any signs of bleeding make haemolysis likely. In combination with low platelet count, microangiopathic haemolytic anaemia and malaria are possible.

In this patient with fever and neurological impairment, cerebral malaria and thrombotic thrombocytopenic purpura are the most likely causes. The next step would be to request that a blood film is made urgently

Patient 2

A 34-year-old woman has been unwell for 2 days with cough and breathlessness. She looks very unwell, is bald, febrile and hypoxaemic, and has widespread bruising. Her full blood count results are:

Haemoglobin = 7.8 g/dl; mean cell volume = 84 fl; platelets = 7 x 10^9/litre; white cell count = 0.3 x 10^9/litre, neutrophils = 0.1 x 10^9/litre, lymphocytes = 0.1 x 10^9/litre

Clinical comment:

The severe pancytopenia strongly suggests bone marrow failure. She has febrile neutropenia and requires immediate intravenous broad spectrum antibiotics and supportive care including fluid resuscitation and oxygen. Platelet transfusion should be given. In the absence of an obvious cause for this (e.g. recent chemotherapy) urgent haematology consultation should be obtained to establish diagnosis

Figure 3. Clinical scenario.

scopies are advisable. Most common haemoglobinopathies can be detected on haemoglobin electrophoresis.

Chronic macrocytic anaemia (mean cell volume >100 fl) is generally caused by defective DNA synthesis – often caused by deficiencies in either vitamin B_{12} or folate. Macrocytosis is also seen in people with a chronically high alcohol intake, hypothyroidism or who are taking certain drugs, including methotrexate and azathioprine. If vitamin B_{12} or folate deficiency is found the cause of this should be identified; gastrointestinal malabsorbtion (e.g. from pernicious anaemia) is common. When both vitamin B_{12} or folate and iron deficiency are present, a chronic anaemia with normal mean cell volume can result. In this situation there may be both microcytic and macrocytic red cells, reflected in increased red cell distribution width.

A chronic normocytic anaemia may also be the result of chronic inflammatory disease or reduced erythropoietin production in renal failure. However, even if one of these seems likely, haematinic assays are still recommended because anaemia is often multifactorial.

High haemoglobin: polycythaemia

Polycythaemia (best determined by elevated haematocrit or packed cell volume >0.51 in males and >0.48 in females) is usually secondary: a result of dehydration, poor sampling technique or excess erythropoietin production, caused for example by chronic hypoxia or renal tumours. A less common cause is polycythaemia vera. It is not usually necessary to distinguish these in an acute situation, but it is important to recognize that all patients with polycythaemia are at increased risk of thrombosis – such as stroke or myocardial infarction.

Abnormalities of the white cell count

When interpreting the white cell count, it is important to remember that the normal ranges are different for different ages and racial groups. For example, babies have higher lymphocyte counts and lower neutrophil counts than adults, and Afro-Caribbeans have lower white cell, neutrophil and platelet counts than Caucasians.

High white cell count: leukocytosis

A high white cell count is most often caused by infection, but this should not be assumed to be the cause – other illnesses including cancer, myocardial infarction, autoimmune disease and primary haematological conditions cause leukocytosis.

Taken with other signs of infection (fever, focal signs) a leukocytosis can help confirm clinical suspicion of infection, and the differential white cell count can suggest the likely type of organism, for example neutrophilia may indicate a bacterial infection (except at extremes of age and with some atypical organisms); lymphocytosis may indicate acute viral infections, or haematological causes such as chronic lymphocytic leukaemia which may occur especially where the lymphocyte count is very high and in the elderly; and eosinophilia may indicate a parasitic infection (e.g. schistosomiasis), inflammatory disease (e.g. Churg–Strauss), allergies or neoplasia.

Low white cell count: leukopenia

When all the types of white cells are low (taking into account age and ethnicity), a cause of 'pancytopenia' (see below) is likely. Causes of low levels of individual white cells are as follows: neutropenia may be caused by an acute viral infection, drugs (most notorious being carbimazole and clozapine – always check in the British National Formulary), or at extremes of age by bacterial sepsis. Importantly, patients with a neutrophil count of less than 0.5, whatever the cause, have severely compromised ability to fight bacterial and fungal infections. If there is a fever or other signs of infection, treatment with intravenous broad spectrum antibiotics should be started right away and is life-saving.

Lymphopenia may be associated with acute bacterial infections, drugs, particularly those targeting the immune system, autoimmune disorders like lupus and advanced human immunodeficiency virus infection all commonly cause lymphopenia. Prolonged lymphopenia is associated with compromised immunity and a broader range of pathogens than normal need to be considered – for example pneumocystis pneumonia, cytomegalovirus infection and mycobacterial infection should be considered in a patient presenting with respiratory symptoms.

Abnormalities of the platelet count

High platelet count: thrombocytosis

Secondary causes are infection, inflammatory disorders, malignancy and iron deficiency. Primary (essential) thrombocytosis is a rare myeloproliferative condition. Importantly patients with a high platelet count, and especially those with myeloproliferative disorders, are at risk of thrombotic events such as myocardial infarction or stroke. Paradoxically, haemorrhage may also occur as the platelets may be dysfunctional.

Low platelet count: thrombocytopenia

Isolated thrombocytopenia may be normal in patients of Afro-Caribbean origin (acceptable for platelets >80x10^9/litre), or may be caused by blood clots in the sample, bacterial sepsis, viral infections, malaria and a range of drugs. Thrombocytopenia caused by heparin is potentially serious and advice should be sought straight away if this occurs. It may also be caused by autoimmune destruction – in a condition called idiopathic thrombocytopenic purpura. Any

patient with severe thrombocytopenia should be discussed with a haematologist. A platelet transfusion is contraindicated in thrombotic thrombocytopenic purpura, but otherwise should be considered in a stable patient with a platelet count <$10x10^9$/litre (<$20x10^9$/litre if unstable).

When thrombocytopenia is seen in combination with anaemia, the possibility of a microangiopathic haemolytic anaemia needs to be considered (*Table 2*) – this is a type of haemolysis caused by mechanical fragmentation of red cells in small blood vessels which is a medical emergency.

Table 1. Causes of concurrent anaemia and thrombocytopenia

Evans syndrome – autoimmune haemolytic anaemia and immune thrombocytopenia	
Bleeding in a patient with thrombocytopenia	
Microangiopathic haemolytic anaemia	+ Thrombotic thrombocytopenic purpura (normal coagulation screen, fever renal impairment and neurological symptoms)
	+ Haemolytic uraemic syndrome: normal coagulation, severe renal failure +/- diarrhoea often associated with *Escherichia coli* 0157
	+ Pre-eclampsia or HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome in pregnancy
	+ Disseminated intravascular coagulation
	+ Malaria

Pancytopenia

This may either be caused by failure of the bone marrow to produce blood cells or excessive destruction of blood cells by an overactive spleen (hypersplenism).

Pancytopenia in hypersplenism is not usually very severe, and examination may provide evidence of splenomegaly or liver disease, portal hypertension or perhaps rheumatoid arthritis (Felty's syndrome). Severe pancytopenia is usually caused by bone marrow failure: this could be as a result of drug toxicity, acute leukaemia, aplastic anaemia, marrow infiltration by carcinoma, a myelodysplastic syndrome or severe haematinic deficiency. Haematology advice should always be sought.

Conclusions

The full blood count, correctly interpreted, can give a great deal of information. To develop this skill, it is necessary both to learn common causes of individual abnormalities and to try to recognize patterns in abnormal results. **BJHM**

Conflict of interest: none.

Further reading

Hoffbrand AV, Moss PAH, Pettit JE (2006) *Essential Haematology.* Blackwell, Oxford

Provan D (2007) *ABC of Clinical Haematology.* Blackwell, Oxford

KEY POINTS

- Anaemia may be acute or chronic – acute anaemia usually being caused by either bleeding or haemolysis. It is important to send tests to establish the cause of chronic anaemias before transfusion.
- High white cell, red cell and platelet counts may be caused by primary haematological conditions, but they are more commonly reactive to other pathologies.
- It is important to recognize patterns such as pancytopenia, microangiopathic haemolytic anaemia and severe neutropenia as these conditions require urgent investigation and treatment.