# 28. Understanding Blood Tests

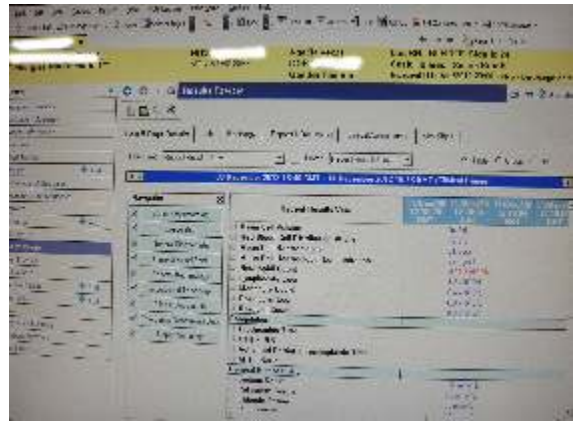
Introduction - Ordering and Interpretation

Blood tests are an essential tool for us in the management of patients treated in OMFS. Tests carried out in the haematology and biochemistry laboratories (recently combined and renamed Blood Sciences) can seem complicated but are much simpler when viewed from the perspective of the limited number of tests we use and the circumstances in which they may be useful. We will discuss the tests we commonly use, the basis for them and how they may help us.

The request form should be completed legibly and with care. In many hospitals requests must be made on- line; in this case the patient will be given a printed request for the phlebotomist with a bar code for exact identification. Outpatients and inpatients whose blood tests can be anticipated may be bled by a phlebotomist but you may have to do it yourself for urgent unplanned ward admissions if there is no clinical support worker available to do it. Request forms, if used, may be labelled with a sticky label from the patient's notes but blood specimen bottles should be identified with the patient's details in handwriting to reduce the risk of identity error. When requesting blood for transfusion both form and blood specimen bottle must be hand written.

The results will need to be interpreted intelligently and matched to the clinical problem being considered. Usually a reference range will accompany the result which does not necessarily equate with 'normal' in every case. The individual result may be affected by the patient's age, sex, ethnicity, medication, alcohol taken or the time of day; they may also be affected by pregnancy. The result obtained should be compared to the reference range which relates to the range of results for a normal population; this will therefore depend upon the population being compared. 2.5% of the normal population is removed from the top and bottom ends of the reference range so that a result just outside the range does not necessarily mean the patient is abnormal. 5% of the normal population will have a result outside the reference range or 1:20. Thus the result must be carefully considered with the patient's clinical condition and the results of other investigations.

All results should be followed up; it is unacceptable to request any investigation without looking at the results. For routine investigations the results should be



***You may have to order tests on a paper request form (as below) or more likely on an on-line clinical records system such as here.***

available on the hospital computer system the same day; others may take longer. Sometimes this will be followed by a printed report which should be signed to show it has been looked at and filed in the patient's notes or there may be just an electronic report on the clinical records system which is available for printing if desired. Where a result is outside the reference range a haematologist or biochemist may look at it and make suggestions for further action or investigation.

You should only order tests which are essential for the patient's management. Not only will this avoid incurring the expense of unnecessary tests but it will avoid the problem of trying to interpret the results that are outside the reference range, 5% of which may not represent an abnormality.

All investigations, including blood tests, should be subjected to the "so what" test before they are ordered. This means that you should be clear that the result will have some impact on the management of the patient before you tick the box on the request form or computer screen. You should be clear of the significance of a positive or negative result. Too many investigations are ordered by junior doctors without sufficient justification.

Heamatology tests

The most frequently used Haematology test in OMFS is the full blood count. This tells us the haemoglobin level and the quantity and proportions of the cellular component of the blood.

**Full Blood Count (FBC)**


**A.** The most usual need for a full blood count (FBC) is to estimate haemoglobin, most usually as part of pre-operative assessment for anaemia or for a base line assessment to compare with intra-operative measurements in a patient who we expect to lose a significant amount of blood. A low haemoglobin will compromise the oxygen carrying capacity of the blood, which may be important in anaesthesia and surgery for older patients. Any patient with pre-existing cardiac or respiratory disease will be more sensitive to low oxygen availability. An individual can adapt to a low haemoglobin which has been present for some time, for example if they have 'anaemia of chronic disease', especially so if they are fairly inactive. There is therefore no absolute lower haemoglobin level at which a patient can have an anaesthetic. However, a patient who has a low haemoglobin level consequent upon recent blood loss will be much more sensitive and may have a low tolerance to exertion or even be breathless at rest. Therefore patients who have suffered recent trauma and lost blood are more likely to benefit from having a full blood count. In practice we request it pre-operatively for only a few of our patients but we always would for those undergoing major surgery where a significant amount of blood may be lost, such as resection of oral cancer, orthognathic surgery or a major facial injury. The National Institute of Heath & Care (NICE) has published guidelines as to which patients we should request pre-operative investigations for; this guidance looks as if it has been written by a committee and is over complicated but it is potentially useful in preventing a lot of unnecessary tests.

Occasionally we may request an FBC (together with haematinics) if we see a patient with atrophic glossitis which may be a symptom of chronic iron deficiency anaemia and there is thought to be an association with angular chelitis. Our experience is that requesting an FBC for patients with sore tongues or angular chelitis produces an enormous number of normal results from the laboratory.

**B.** The red cell indices Mean Cell Volume (MCV), Haematocrit (Ht), Red Blood Cell Concentration (RBCC), Mean Cell Haemoglobin Concentration (MCHC) should be interpreted together. Some are not measured but are mathematically derived from the others. They can, when considered with the clinical picture, give an indication of the possible cause of anaemia. Anaemia with reduced MCV, MCH and MCHC is called hypochromic-microcytic. Iron deficiency anaemia and thalassaemia produce this blood picture as sometimes can 'anaemia of chronic disease'. A normal MCV and MCHC is called normocytic and normochromic anaemia. This will include most anaemias of chronic disease as well as anaemia resulting from blood loss, haemolysis and decreased RBC formation as a consequence of renal failure, aplastic and malignant disease of the marrow. A raised MCV is called macrocytic and mostly results from vitamin B12 and folate deficiency.

If the indices are abnormal the haematologist will examine cells under a microscope as their shape and staining characteristics may help in diagnosis; this will

be in the report. Anisocytosis means the red cells vary in size, Poikilocytosis, in shape. The other terms used, macro, micro and normo, you are familiar with.

An increase in the concentration of red cells may be caused by the rare condition polycythaemia ruba vera where there is over activity of the marrow, but it is more commonly caused as an adaption to chronic hypoxia related to lung disease and chronic smoking. A macrocytosis is often caused by excessive alcohol intake.

If haemoglobin and red cells are present in their normal absolute quantities they may still be shown to be in reduced concentration if there is an increase in the volume of the blood plasma; this may occur if a patient has been over-hydrated by intravenous fluids. Similarly, pregnancy increases plasma volume and therefore lower estimations for Hb. and RBC. If a patient is dehydrated then a corresponding increase in concentrations may be recorded.

**C**. The total white cell count is commonly increased in infection, inflammation or tissue damage. You can expect it to be increased if a patient has a large abscess, particularly if they are systemically unwell with pyrexia, after facial trauma or after major surgery. The count will return to normal as the patient recovers; occasionally serial white counts may be used to monitor recovery but this is unusual in our clinical practice as we can observe recovery directly. The white count may also increase in any malignant disease particularly of the bone marrow (leukaemia).

A decrease in white cells is uncommon but can occur in viral infections and when a patient is overwhelmed by acute sepsis or cancer. It can also occur as a result of chemotherapy. Very low levels will lead to infection from otherwise harmless bacteria and mucosal ulceration may occur. Candidiasis of the mouth is particularly associated with a low WBC.

**D**. Platelets, which are an essential part of haemostasis, may be decreased in numbers in aplastic anaemia, leukaemia and as a result of chemotherapy or radiotherapy. However, the most common cause of low platelets is autoimmune increased breakdown seen in idiopathic thrombocytopenia purpura (ITP). This may occur as a primary disease, mostly in women, or secondary to other disease processed or caused by some drugs. Most usually we will see patients with low platelets when they need dental extractions, usually because they have ITP or have recently had chemotherapy. However, platelet levels quickly recover after chemotherapy and fluctuate with ITP so the levels should be checked just beforehand. The level needs to be very low before there is a bleeding problem usually below about 60 x $10^9$/L.

**E**. The differential white cell count shows the number of the individual types of white cells in the blood. This is of infrequent use to us in OMFS. However we will briefly explain their significance. Neutrophils are the most numerous. They offer protection against bacteria and engage in phagocytosis. They are increased in acute infections, inflammation, tissue damage, where there are solid tumours and chronic myeloid leukaemia. The lymphocytes consist of 70% T – lymphocytes which destroy infected cells and 30% B – lymphocytes which produce antibodies. There are also a few 'Natural Killer' cells. Lymphocytes increase in infectious mononucleosis, several other viral infections, chronic bacterial infections and several rarer diseases which include toxoplasmosis which can present with enlarged lymph nodes in the neck. They are increased in chronic lymphatic leukaemia and non-Hodgkin's lymphoma. Monocytes phagocytose foreign material and have a role in presenting antigens to T lymphocytes; they are rarely increased in number. Eosinophils phagocytose larger foreign material and have a role in killing organisms larger than bacteria. They are present at the site of inflammation caused by allergic reactions such as allergic asthma and hay fever. They are increased in parasitic worm infections and allergic diseases as well as occasionally in Hodgkin's lymphoma. Basophils are rarely seen in the peripheral blood. They become Mast cells in the tissues which release mediators of acute

***Causes of Anaemia***

1. Iron deficiency
2. Chronic inflammation or infection (anaemia of chronic disease)
3. Blood loss
4. Deficiency of $B_{12}$ or folate
5. Deficiency of erythropoietin (most chronic renal failure)
6. Increased RBC destruction (haemolytic anaemias)
7. Marrow failure (aplastic, usually toxic drugs or radio therapy)
8. Malignant disease in marrow (leukaemia, myeloma)


***Blood for a full blood count is collected in a lavender topped colour coded bottle. It contains ethylene diamine tetra acetic acid (EDTA) which stops the sample from clotting by removing calcium ions from the plasma.***

***In the laboratory the full blood count is determined by one of these machines. The sample is shaken to ensure even distribution of cells and bottles are loaded in. It can process 120 samples per hour.***

inflammation; they are raised in chronic myeloid leukaemia but rarely otherwise.

Coagulation Studies

Intermittently patients with a history of prolonged or excessive bleeding present needing surgery or dental extraction. The most important part of the investigation is the clinical history but you will need to arrange a full blood count to check their platelet count and a coagulation screen.

The coagulation screen consists of three tests. The prothrombin time (PT) tests the extrinsic coagulation pathway clotting factors and the final common pathway as it forms fibrin. The activated partial thromboplastin time (APTT) assesses the intrinsic and final common pathways and the thrombin time (TT) the final pathway only. If all of these are normal then the coagulation cascade should be normal and produce normal fibrin for haemostasis. If any are abnormal the report will advise what to do next; to retest, do additional investigations or to refer the patient to a haematologist. If the patient is still bleeding a haematologist's help will be needed immediately.

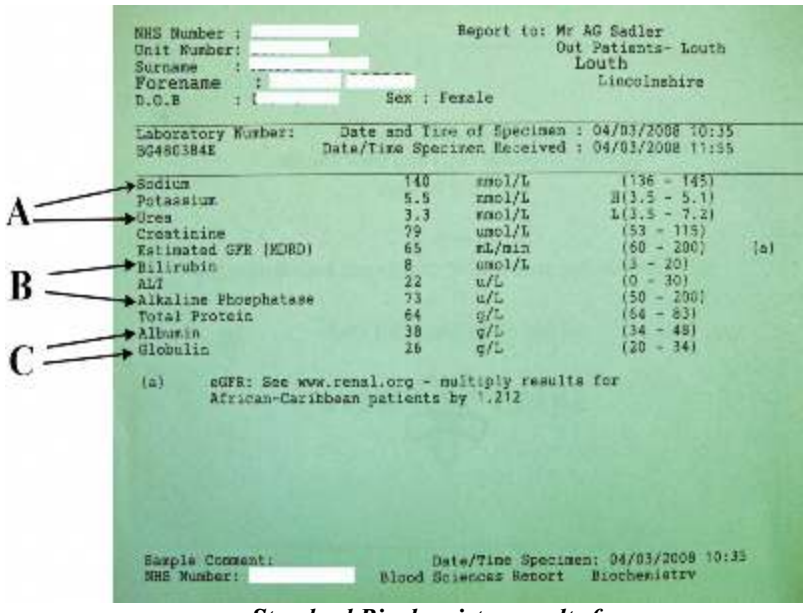
The most common inherited clotting defects are Haemophilia A, followed by Haemophilia B or Christmas Disease. These are caused by deficiency of factors 8 and 9 respectively. They are part of the intrinsic pathway so that the APTT will be prolonged, whereas PT and TT will be normal. More commonly, clotting factors are deficient due to liver disease, which is acquired. PT will be most sensitive to this but in severe liver disease PT and APTT will both be prolonged; it is unusual for the TT to be affected.

You will come across a lot of patients taking anti-coagulants, most frequently warfarin, which has a long half-life and is taken orally. This is used to prevent clots in patients who have had a deep vein thrombosis and pulmonary embolus and as primary prevention for patients at risk for several reasons, most commonly atrial fibrillation. Heparin is used in hospital for rapid anticoagulation of patients who have thrombosis. It has to be given subcutaneously or intra venously; it has a very short half-life and is therefore easily controlled. Warfarin therapy is monitored using the PT, Heparin with the APTT. The PT is expressed as the international normalized ratio (INR) which is the ratio of the patient's PT over the mean of the PT reference range using an international sensitivity index. This makes the result more standardized for comparison purposes.

Warfarin is the most commonly used anti-coagulant. An INR result of 2 means that the patient's blood will take twice as long to clot than the control. Patients who need anticoagulation have differing target values depending on their condition. Those who are taking it because they have atrial fibrillation or have had a recent deep vein thrombosis will have a target value of between 2 and 3 whereas those who have a mechanical heart valve replacement are at higher risk and will have a higher therapeutic range of between 3 and 4. We receive a large number of referrals for dental extractions for patients on warfarin but it has been shown repeatedly that if the INR is below 4 then if they are managed correctly with the sockets sutured and packed with oxidised cellulose gauze, then post extraction bleeding is no more of a problem than patients not on warfarin. If the INR is above 4 then this is outside the therapeutic range and the patients should see their GP to have their dose adjusted before the extractions.

Erythrocyte Sedimentation Rate and C Reactive Protein

Erythrocyte sedimentation rate (ESR) is a simple test in which anti-coagulated blood is left for the red




***Standard Biochemistry results form***

cells to sediment to the bottom of a tube. The result is expressed in the number of millimetres the red cells fall in an hour. The ESR will be increased in disease processes that increase certain plasma proteins, which cause aggregation of the red cells and in certain anaemias where the number of red cells is decreased. ESR is normally 1 – 10 mms/hour in males and 5-10 mms/hour in females. This increases with age by about 0.8 mms per 5 years. ESR is a very unspecific test; it is raised in pregnancy, where there is significant tissue damage, infection, malignancy and in certain individuals with no disease. A decrease in ESR is uncommon and usually of little clinical significance; it occurs in polycythaemia.

C reactive protein (CRP) is present normally in low concentration in the plasma and is a more modern non-specific test as an alternative to ESR. It is increased in inflammation, infection and malignancy, but is not affected by red cell numbers.

ESR and CRP are used to monitor treatment responses to patients with complicated and extensive disease processes e.g. inflammatory or infective.

Biochemistry tests

**A.** Urea and electrolytes (Us & Es) Sodium ($Na^+$), and Potassium ($K^+$) have been traditionally requested and analysed together. Nowadays, however, the analysing equipment will process multiple biochemical and immunological assays simultaneously on one sample.

$Na^+$ is the primary electrolyte in the blood; hypernatraemia may be due to a very high salt intake or dehydration from inadequate fluid intake or excessive fluid loss from sweating or diarrhoea. $Na^+$ concentration may be low in excessive fluid retention. Neither of these situations are of much relevance to us in everyday OMFS where, should we encounter patients with severe electrolyte or fluid balance abnormality, we would request the assistance of a physician.

Hyperkalaemia may be due to renal disease or diabetes. Hypokalaemia may be due to excessive $K^+$ loss in diarrhoea or from excessive loss due to diuretic medication. As surgeons our main concern with abnormal $K^+$ concentration will be the potential effect on cardiac muscle. Severe hyperkalaemia can result in instability of the cardiac muscle leading to cardiac arrest and in hypokalaemia cardiac arrhythmias may occur. We would therefore wish to test for $K^+$ concentration for any patient receiving a general anaesthetic if they have renal disease, poorly controlled diabetes or are taking diuretics. In general a narrow reference range for a blood test indicates potentially serious consequences when it is either too high or low and this is the case with potassium.

Urea is a waste product of normal metabolism. There is a gradual increase in the blood concentration with age due to gradual decline of renal function. Urea may be increased in more advanced renal disease but

not early on. It may also be increased in starvation and dehydration.

Creatinine is a waste product more specifically of muscle metabolism. Raised creatinine will be a more sensitive marker for early renal disease.

Estimated Glomerular Filtration Rate (eGFR) is calculated from the MDRD (Modification of Diet in Renal Disease study) formula; this includes creatinine level, age, sex and ethnicity. If the estimated glomerular filtration rate (eGFR) is decreased further investigation may be needed for chronic kidney disease. If a low eGFR is found on routine testing we should alert the patient's GP to deal with this later.

**B.** Bilirubin, alanine transferase (ALT) and alkaline phosphatase are together known as the liver function tests (LFTs). Bilirubin is derived from haemoglobin breakdown and is increased in liver disease, where there is obstruction to bile flow and in haemolytic anaemias where there is increased breakdown of red cells. If it is very high the patient may be clinically jaundiced. Alanine transferase and alkaline phosphatase are metabolic catalysts in liver cells. They are released into the blood stream, where they have no function, when liver cells are damaged and hence their presence usually indicates liver disease. However they are present in other tissues, notably the pancreas, kidney, heart and muscle. Alkaline phosphatase is present in osteoclasts and will be released into the plasma in any condition where there is high osteoclastic activity. This will include childhood growth spurts, Paget's disease of bone, healing fractures and bone cancer including metastatic disease. We may therefore wish to order these tests when a patient has a history of liver disease and is to receive an anaesthetic or if they have cancer and we want to know if metastatic disease has affected liver function or we wish to know if there might be bone involvement.

**C**. Albumin and globulin together make up the plasma proteins. Albumin is the more abundant, being about 60%; it is synthesised in the liver from amino acids. It acts as a transport medium for water insoluble substances in the blood and is important in maintaining blood plasma volume. Albumin may be low in chronic liver disease (cirrhosis) but not in acute; this will lead to increased fluid in the interstitial spaces and possibly oedema. It may be reduced in malnutrition due to inadequate amino acid intake or in severe burns. It will be raised in patients who are dehydrated. We will want to know the albumin level for new patients who present


***Combined clinical chemistry and immunology is tested on serum. Blood is taken into a tube which contains a gel, with silica in it; this activates coagulation. The tube is centrifuged to separate the serum; the gel moves up forming a barrier between serum and fibrin***

***The Abbott Architest integrated general chemistry & immunoassay analyser will process 1200 clinical chemistry and 200 immunoassays per hour. Only one serum specimen is needed for both.***

with advanced mouth cancer as they may have a low albumin from inadequate nutrition. Globulins make up the rest of the plasma proteins; they include the gamma globulins which are antibodies and they act as enzymes and carriers. They may be elevated in chronic infections and renal disease and may be decreased in renal disease which leads to protein loss, haemolytic anaemia, liver disease and hypogammaglobulinaemia.

Immunology tests

These are used infrequently in OMFS. However, we may occasionally test for antinuclear antibodies (ANA) in a patient with a dry mouth who we suspect may have Sjögren's syndrome (SS). ANA are raised in a variety of conditions such as systemic lupus, rheumatoid arthritis and chronic active hepatitis. About 70% of patients with SS will have raised titres of ANA. These are expressed as the dilution at which they may be detected; normal is 1:40. In addition 70% of SS patients will have a raised titre of the ANA sub types anti-SS-A (also known as anti-Ro) and 40% will have a raised titre of anti-SS-B (known as anti-La). Rheumatoid factor is also likely to be raised in 60% of these patients. The significance of SS (apart from the dry mouth) is that there is an increased incidence of

low grade lymphoma and this may be associated with a low level of complement C4.

Immunoglobulins may be tested in patients who have repeated infections. IgM will be raised in patients who have significant acute inflammation. IgE may be of help in supporting a diagnosis of an allergy. However, the normal range is very wide and it is possible to have a raised specific IgE against a single allergen when total IgE is normal; thus it is of limited use. Occasionally we see a patient with recurrent oedematous swelling around the face. A rare cause of this is hereditary angio-oedema due to complement C1 inhibitor deficiency. Patients with these clinical symptoms should have their complement C4 tested as a screening test. If this is normal then they will not have heredity angio-oedema and there is no need to test for complement C1 inhibitor levels.

***Blood tests used in Oral & Maxillofacial Surgery***

**Commonly**

**Full blood count**

• As a baseline measurement of haemoglobin in major cases where significant blood loss is expected.

• Where a patient has bled more than anticipated to check platelets.

• Occasionally if a patient has been anaemic in the past and is due for surgery under anaesthetic.

• Occasionally for a patient with stomatitis (see B12 etc. below).

**INR**

• Before surgery in a patient taking warfarin but check their anticoagulant card before testing.

**Coagulation screen**

• Where there has been inappropriate bleeding.

**Urea/Electrolytes**

• Diabetics and patients on diuretics before surgery under anaesthetic.

• Rarely in patients with renal disease who are due for surgery.

**Glucose**

• Diabetics due for surgery under anaesthetic.

• Patients who present with severe infections or unexplained candidiasis.

***Blood tests used in Oral & Maxillofacial Surgery***

**Sometimes**

**B12, folate ferritin**

• Patients with stomatitis; however, rarely abnormal and of dubious significance.

**LFTs**

• Patients who present with mouth cancer to check for compromised function which might be caused by metastatic disease or alcohol.

• To check for serum protein levels which might be decreased if nutrition has been compromised by difficulty with eating or high alcohol consumption.

• Patients who present with inappropriate bleeding whose liver dependent clotting factors may be reduced by alcohol or other liver disease.

**Occasionally**

**Anti-nuclear antibodies and Rheumatoid factor**

• If Sjögren's syndrome is suspected.

**Rarely**

**C4**

• As a screening test for hereditary angio-oedema.

**Bone and parathyroid hormone**

• Where a central giant cell granuloma is found in the jaw to exclude hyper-parathyroidism.