Routine Blood Results Explained

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By

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PREFACE

The past two decades have seen a huge expansion in the responsibilities of a host of health care workers, especially in clinical practice. These expanded roles include:

- examining the patient
- proposing a diagnosis
- venesection (taking blood)
- ordering blood tests
- interpreting the results
- managing the condition.

Previously, these roles were undertaken by medical staff only, but it is now clear that appropriately trained professionals can be equipped to carry out these tasks.

This slim volume has been written to provide help in understanding and interpreting the majority of the normal blood results found in most NHS Hospitals and in General Practice. The text, based on the routine blood report forms sent out from Pathology Departments, has evolved from lecture notes given to various Health Care Professionals (Nurses, Phlebotomists, Pharmacists, Radiographers, and Physiotherapists etc.) attending day-long courses on exactly these topics.

An additional objective is to keep the material simple and focused. Thus, the reader seeking a comprehensive in-depth explanation of a wide number of tests and their exact relationship to various clinical diseases will be disappointed. However, it is impossible to fully understand pathology without a sure grounding in physiology. Hence there will be an adequate and clear explanation of those aspects of the body that are necessary to understand a particular test and its associated problems. Examples are provided that will illustrate particular points; it must be stressed that these are not exact and perfect case reports, merely aids in understanding the concepts developed in the text.

Focusing on 'routine' blood tests therefore, by definition, excludes tests less frequently reported. In this volume, tests that will be absent from the general discussion are, for example, platelet volume, red cell mass, magnesium, and reproductive hormones. These omissions are not indicative of lack of importance, merely lack of regular requesting. The emphasis is also on the adult, so that paediatric tests (by and large) will not be covered, but reference ranges are provided.

The objective of this book is to support and enable these professionals to be successful in their new roles. In recognising these roles, wherever possible, each chapter will conclude with a brief case study. However, more complete case reports reflecting the different aspects of primary and secondary care are presented in the concluding chapters.

Acknowledgements

ABBREVIATIONS

ACPA	Anti-citrullinated protein antibodies
ALL	Acute lymphoblastic leukaemia
AML	Acute myeloid leukaemia
ANA	Antinuclear antibodies
APTT	Activated partial thromboplastin time
ARF	Acute renal failure
CKD	Chronic kidney disease
CK	Creatine kinase
CLL	Chronic lymphocytic leukaemia
CML	Chronic myeloid leukaemia
CRP	C-reactive protein
DKA	Diabetic ketoacidosis
DVT	Deep vein thrombosis
ECG	Electrocardiogram
EDTA	Ethylene diamine tetra-acetic acid
ESR	Erythrocyte sedimentation rate
FBC	Full blood count
GFR	Glomerular filtration rate
Hct	Haematocrit
Hb	Haemoglobin
HbA_{1c}	Glycated haemoglobin
HDL-cholesterol	High density lipoprotein cholesterol
INR	International normalised ratio
LDL-cholesterol	Low density lipoprotein cholesterol
LFT	Liver function tests
LMWH	Low molecular weight heparin
MCH	Mean cell haemoglobin
MCHC	Mean cell haemoglobin concentration
MCV	Mean cell volume
NICE	National Institute for Health and Care Excellence
OGTT	Oral glucose tolerance test
PTH	Parathyroid hormone
PSA	Prostate specific antigen
PT	Prothrombin time
PTT	Partial thromboplastin time
PE	Pulmonary embolus
RBCC/RCC	Red blood cell count/red cell count
RhF	Rheumatoid factor
TSH	Thyroid stimulating hormone
U&E	Urea and electrolytes
VTE	Venous thromboembolism
WBCC/WCC	White blood cell count/white cell count

INTRODUCTION:
ROUTINE BLOOD RESULTS EXPLAINED

> "…it is estimated that the data received by clinicians from Medical Laboratories constitutes 70 – 80% of the information they rely on to make major medical decisions"
>
> The Biomedical Scientist 2005:49; page 38

Blood tests are important as they provide three times as much information as do all other sources (history, examination, symptoms, imaging etc.) combined. Fortunately, the vast majority of routine blood tests, certainly in routine, emergency, and critical care medicine, fall easily into defined groups – haematology (with blood transfusion), immunology, and biochemistry, together often described as Blood Science. The layout of the volume will therefore follow this pattern. Each of the major sections breaks down into individual chapters and concludes with a dedicated example.

Knowledge is nothing without practice. Therefore, the book will conclude with case studies designed to help the practitioner. These cases will look at both primary and secondary care.

What is done where?

In some Pathology Departments, certain tests are done in the Haematology Laboratory, whilst in other Hospitals the same test may be performed in the Biochemistry or Immunology Laboratory, or perhaps a Department of Blood Science. Examples of this include iron studies, immunoglobulins, C-reactive protein (CRP), and testing for vitamin B_{12}. These latter tests are done on serum obtained from whole blood that has not been anticoagulated, but some tests are performed on blood where clotting has

been prevented by anticoagulants. The reader is referred to their own Pathology Service for the correct tube for the test and the destination of these requests.

Overall, our colleagues in the Pathology Department, regardless of discipline, would far rather set the position clear in a phone call than go through the bother of phoning back that a fresh sample in the correct tube must be obtained.

If in doubt – PHONE!

A note on units. In the real world, of course, results are almost always described as the numbers themselves (e.g., a haemoglobin of 125 or a cholesterol of 5) instead of the more correct way its unit (i.e., 125 g/L and 8 mmol/L). This shorthand is generally accepted, and generally makes life considerable easier. It matters not so much that the correct unit of the average size of a red blood cell is described fully, for example, as 112 fL, or in shorthand simply as 112, but it does matter that the particular cell is much larger than can be expected in health, implying come pathological condition.

The reference ranges

In defining ill-health, we generally use good health as a comparator. Thus, a healthy person can be expected to have a certain blood result profile. However, sometimes these values are not well established and are subject to variation. Furthermore, there are many normal (healthy) people whose blood result may not be in the expected range of values – this does not necessarily mean they are ill. Therefore, the concept of being 'normal' may as well be 'desirable'. So, you could use a 'reference' range, or perhaps a 'target' range. However, for the purposes of this volume, the reference range will be cited.

Haematology, biochemistry, and immunology are very quantitative sciences. Consequently, the reference range is important. The precise definition of the reference range in use at a particular hospital is crucial and may not be transferable to another hospital. This may be because of small differences in the technical manner in which tests are derived. Furthermore, reference ranges may well (or actually should) reflect the local population that the hospital serves, and this is important as different catchment populations may well vary considerably, especially in race and ethnicity.

Reference ranges should also be relevant for the demography of the particular patient, i.e., a male reference range for blood from a man, a paediatric reference range for an infant etc. Therefore, care must be taken when comparing samples and reference ranges. In the future it can be predicted that an age-specific and race-specific reference range may also be produced.

Interpretation

In haematology, biochemistry and immunology, the numbers mean something. Many will seek guidance from, and will base treatment on, these results. One of the first questions is therefore 'is the result acceptable?' This in turn begs the question of acceptability, which in many cases boils down to the reference range, presumably derived from normal, i.e., healthy, individuals. However, merely having a result a fraction outside the reference range does not necessarily imply a serious pathology. Conversely, a result very far from the reference range carries with it an implication of a problem. Several tests, as well as clinical signs, history, etc. are needed to be sure of a particular diagnosis.

Near Patient Testing

Not all routine blood tests are performed in the laboratory. With advances in technology, small analysers have been developed suitable for use literally near the patient (hence NPT). This is also known as point-of-care testing (POTC). Found in locations such as Accident and Emergency, Coronary Care Units and Intensive Care Units, these analysers offer rapid results on almost all routine tests. However, the laboratory is the gold standard, and also offers advice on interpretation.

Key point: The purpose of the laboratory is to provide assistance in the diagnosis and management of disease

PART 1:

HAEMATOLOGY AND BLOOD TRANSFUSION

Objectives and Scope

These are listed in Table 1. The purpose of the Haematology Laboratory is to provide information on blood cells and the ability of the blood to form a clot. The Blood Transfusion Laboratory provides blood components (mostly red cells, but also coagulation factors and the blood protein albumin) for patients at risk of potentially life-threatening situations.

In order to do this, the components of the blood are analysed, almost always in custom-designed equipment. It is taken as understood that all blood tubes and forms must be fully labelled by those taking the blood in order to minimise the risk of (possible fatal) error. Indeed, the laboratory will be well within its rights to decline to test a sample that is incorrectly or inadequately labelled.

There are three basic blood tubes that are used in these disciplines. A full blood count (FBC) is performed on blood that is anticoagulated with ethylene diamine tetra-acetic acid (EDTA). Coagulation tests are invariably done on plasma that is obtained from whole blood anticoagulated with sodium citrate. The erythrocyte sedimentation rate (ESR) may be assessed on blood that is held within its own dedicated glass tube: blood clotting in this tube is also prevented by sodium citrate. However, in some cases, the ESR can be measured on the same sample as is the FBC. For blood transfusion, an EDTA or a tube free of an anticoagulant (providing serum) are often used. Immunologists can work with serum or plasma, but for cell work, the blood must be anticoagulated. Once more, if even in the slightest doubt about which vacutainer to take for whichever test – PHONE!

This is because testing can only be performed on blood that is collected in the correct tube. Failure to do so will, at best, result in a polite phone call from the lab explaining the problem and its remedy. At worse, a report will be returned a day or so later with a comment such as 'inappropriate

blood sample received, please repeat'. Fortunately, many blood tubes have different coloured tops to help this process and minimise errors.

Fortunately, Haematology can be divided very easily into three different areas. These are the red blood cell (often just described as red cell), the white blood cell (or white cell), coagulation. The most important aspects of each of these are, in turn, anaemia, infection and neoplasia, and thrombosis and haemorrhage. Blood transfusion is easily addressed in its own Chapter, where the avoidance of a transfusion reaction is crucial.

Table 1: Learning Objectives – Haematology and Blood Transfusion

Having completed these notes in a satisfactory manner, the reader will….

1. Appreciate the importance of different anticoagulants and tubes for the different blood tests requested:

    - EDTA (ethylene diamine tetra-acetic acid) for a full blood count

    - Sodium citrate for coagulation

    - The ESR may require its own tube, or the same as the full blood count

    - The blood bank generally needs a sample of clotted blood, taken into a tube with no anticoagulant, or blood taken into EDTA

2. Recognise major areas of interest, i.e.

    - The red blood cell

    - The white blood cell

    - Coagulation

    - Blood transfusion

3. Describe major problems associated with each of these areas, e.g., respectively

    - Anaemia

    - Leukaemia, lymphoma, and myeloma

    - Thrombosis/haemorrhage

    - An incompatible blood transfusion

4. Interpret simple haematological results, e.g.

    - A haemoglobin of 84 g/L

    - A white cell count of 15 x 10^9/L

    - A prothrombin time of 25 seconds

CHAPTER 1

THE RED BLOOD CELL

Key words:

Haemoglobin (Hb)
Red blood cell count (RBCC)
Haematocrit (Hct)

Mean cell volume (MCV)
Mean cell haemoglobin (MCH)
Mean cell haemoglobin concentration (MCHC)

Red cell distribution width (RDW)
Erythrocyte sedimentation rate (ESR)

Key pathological expressions:

Anaemia   Polycythaemia
Thalassaemia   Sickle cell disease

1.1: An explanation of terms

Haemoglobin (Hb): reference range 133-167 in men, 118-148 in women

Haemoglobin is undoubtedly the index most frequently referred to in clinical haematology. It is a protein designed to carry oxygen from the lungs to the tissues, where the oxygen is given up to participate in respiration, the process by which energy is obtained.

The reference range varies between the sexes. Lower levels in menstruating women seem obvious, but in post-menopausal women levels are still lower than age-matched men as the latter produce testosterone to stimulate red

cell production. We know this because men who have lost their testes to accident or disease see their haemoglobin levels fall.

The red blood cell count (RBCC): reference range 4.3-5.7 in men, 3.9-5.0 in women

Haemoglobin is carried in the blood in red cells. These are unusual as they lack a nucleus, thus providing additional flexibility to penetrate the smallest capillaries and so deliver oxygen to distant cells and tissues. They are the most abundant cell in the blood, are often called erythrocytes, and numbers can also vary between the sexes for the same reason as does haemoglobin.

Haematocrit (Hct): reference range 0.35-0.53 in men, 0.33-0.47 in women

This index expresses that proportion, as a decimal (say 0.43) of whole blood that is taken up by all the blood cells. Since there are approximately a thousand more red cells per unit volume than white cells, and twenty times as many (tiny) platelets, the red cells make up the major proportion of the haematocrit. Consequently, at the practical level, it provides an idea of the proportion of red cells that makes up the whole blood pool. The haematocrit also varies with sex.

Mean cell volume (MCV): reference range 77-98

The size of the average red blood cell.

Mean cell haemoglobin (MCH): reference range 26-33

The average amount (mass) of haemoglobin in the cell. It does not take into account the size of the cell.

Mean cell haemoglobin concentration (MCHC): reference range 330-370

The average concentration of haemoglobin inside the average size cell, therefore merging the MCV and MCH.

These three are often described as the red cell indices. Because several of the red cell values are mathematically derived from some of the others, it is entirely possible for any one of them to be outside the reference range whilst the other five are apparently normal. Thus, one must consider all six (and possibly some others) together to obtain a full picture. In most labs, the haematology analyser provides the Hb, RBCC and MCV directly from the blood provided to it, then (simply speaking) calculates the Hct from the RBCC times the MCV, the MCH by the Hb divided by the RBCC, and the MCHC by the Hb divided by the Hct, with adjustments (e.g., multiply or divide by 10 or 100).

Red cell distribution width (RDW): reference range 10-15%

One of the problems with the MCV is that it can mask a number of abnormalities. Being the mean of millions of cells, some are smaller than the mean size, some larger than the mean size. In health, is variation is quite small, so that an MCV of 90 fL may represent a true range in the size of cells from 85 to 95 fL. This variation is quantified as the red cell distribution width (the RDW). An increased RDW, perhaps 20%, shows a wider range of the size of the red cells, with more smaller and large cells than normal, that in turn indicates a pathological state such anaemia.

Erythrocyte sedimentation rate (ESR): reference range <10 mm/hour

The ESR is also a global score of physical aspects of the blood and is simple to understand. The result is obtained by allowing a thin column of blood to settle down under the influence of gravity. As it does so, the red blood cells will separate from the plasma, so that after an hour, a band of clear plasma will sit atop the red cells. The fall in the level of the red cells is then recorded as mm/hour. The effects of platelets and white cells are minimal and are ignored. It is therefore unique in requiring no sophisticated machinery and few technical skills.

An increased ESR can be caused by many factors, including cancer, infections, anaemia, inflammation, renal failure, rheumatoid arthritis, multiple myeloma, and tuberculosis. It is increased soon after myocardial infarction and is also heavily influenced by plasma proteins. Some laboratories have a higher reference range, e.g., <20 mm/hour, especially in the elderly.

Other haematology tests

These include plasma and blood viscosity, iron, ferritin, transferrin, and vitamin B_{12}, although some of these may be performed by biochemists. Reticulocytes (immature red cells) may be increased in anaemia, reflecting the bone marrow's increased red cell production, but not when the bone marrow is seriously suppressed.

1.2: What are red cells for?

The answer to this question is easy: to carry oxygen. This gas is required in the process of respiration, where energy is obtained from molecules such as glucose and certain fatty acids. So, muscles require oxygen for the energy needed to contract, and if this oxygen is insufficient, there may be pain. In the case of muscles of the intestines this may be manifest as abdominal discomfort and cramps: if muscle of the rib cage and diaphragm fails to get enough oxygen this may lead to problems with breathing and shortness of breath. Insufficient oxygen to the brain may lead to forgetfulness, personality changes and what may seem to be early Alzheimer's disease. General symptoms include tiredness and lethargy.

These symptoms of insufficient oxygen (hypoxia) may be due any combination of pathologies. Oxygen in the inhaled air must first cross the alveoli and enter the pulmonary circulation, a process that will be impaired by lung disease such as COPD, emphysema, and pneumonia. But even well oxygenated blood may not be delivered to the body is the heart is functioning poorly, perhaps because of valve disease, cardiomyopathy, heart failure (with an inadequate ejection fraction), left ventricular aneurysm, and the consequences of myocardial infarction. Blood passage around the body may be impaired by atherosclerosis, and in the tissues the movement of oxygen to the cells may be impaired by oedema and cellulitis.

However, if lung function is good, the heart is working well and there is no barrier to blood or oxygen moving into the cells, and the patient still complains of tiredness, lethargy, and shortness of breath etc., then only one major pathology remains.

1.3: Anaemia – an introduction

The oxygen-carrying capacity of the blood is a function not only of the amount of haemoglobin in each cell, but also the number of red cells and,

to a lesser extent, the Hct. In this way someone with a low MCH but a high RBCC may well have the same oxygen-carrying capacity as someone else with a higher MCH but a lower RBCC. Red cells can also contribute to clotting.

Haemoglobin, RBCC, Hct and the three red cell indices MCV, MCH and MCHC are requested to obtain a view of the individual's oxygen carrying capacity. When an individual is having difficulty performing their most basic physiological and lifestyle demands, they could be anaemic. Some authorities define anaemia as a level of haemoglobin below a certain level. However, a haemoglobin value of, say, 115 g/L may well be perfectly adequate for an elderly person with few physiological requirements and a relatively quiet life. Conversely, the same haemoglobin level in a younger person with a very active lifestyle, perhaps including sports, will be inadequate. Thus, the medical state of the individual as a whole person should be considered, not merely an arbitrary number at which one acts. An alternative view of anaemia may be the level at which concern arises, and at which further investigations are considered. Certainly, anaemia should not be seen merely as that level that automatically requires a blood transfusion, a therapy that many consider should be reserved only for life-saving situations (see Chapter 4).

This brings us to an important equation:

Abnormal results x symptoms = disease

What this means if someone has a low haemoglobin (perhaps 115 as above) but is asymptomatic, then they don't have a disease (in this case, anaemia). Conversely, if the patient is tired, lethargic, pale, and short of breath (Table 2) with a haemoglobin of 140, they can't possibly be anaemic. Therefore, their symptoms must be due to some other pathology, maybe several pathologies. However, if the patient does indeed exhibit all those symptoms, and has a low haemoglobin, then they are anaemic, and so warrant further investigation and possibly restorative treatment.

More serious signs of anaemia include jaundice, splenomegaly (a large spleen), hepatomegaly (a large liver), angina, heart failure, and fever, although these may of course arise from other conditions. But first we need more information about the type of anaemia, and how it came about.

Table 2: Signs and symptoms of anaemia

Signs

Pallor (especially of the conjunctiva)
Tachycardia (pulse rate over 100 beats per minute)
Glossitis (swollen and painful tongue)
Koilonychia (spoon nails
Dark urine (a sign of red cell destruction)

Symptoms

Decreased work and/or exercise capacity
Fatigue, lethargy, 'Tired all the time'
Weakness, Dizziness, Palpitations
Shortness of breath (especially on exertion)
Rarely: headaches, tinnitus, taste disturbance

1.4: The aetiology and classification of anaemia

Anaemia may be classified in many ways.

Since red cells are produced in the bone marrow, infiltration by cancer or other cells will inevitably lead to a reduction in the production of the red cells, thus anaemia. Anaemia is also a fundamental aspect of aplastic anaemia, where the other functions of the bone marrow (i.e., the production of platelets and normal white blood cells) are also depressed.

As we shall see, this is also the case in leukaemia, where many abnormal white blood cells make up the tumour. Our present view of medicine offers various drugs in an attempt to solve many problems. However, few, if any, drugs are free of undesirable side effects, and one can be bone marrow suppression. Thus, use of many drugs will call for frequent monitoring to check for the development of, for example, low levels of red blood cells. Azathioprine, for example, is linked to an increase in the size of the red cell.

Poor nutrition will also result in anaemia, and a diet lacking essential factors such as iron, vitamin B_{12} or folate are good examples. However, the diet itself may be adequate, but other factors may cause anaemia, such

as failure to produce special proteins to aid the passage of the minerals and vitamins across the gut wall and into the blood (i.e., malabsorption).

Problems with other organs may also contribute to anaemia. Chronic liver disease may be a factor in anaemia as it produces molecules that store and others that transport essential iron and vitamins around the body (such as the specialised protein transferrin for carrying iron). Intestinal disease or malabsorption may also lead to anaemia, as the ability to absorb essential minerals and vitamins will be impaired. The kidney produces a hormone, erythropoietin, to stimulate the bone marrow to produce red blood cells. Thus, chronic renal failure (chapter 10) may contribute to an anaemia.
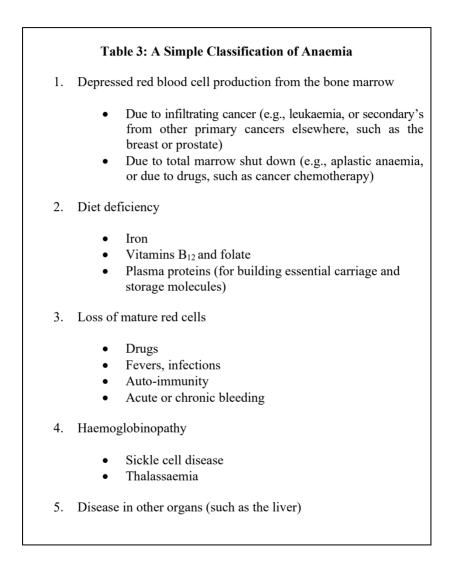
Haemolytic anaemia is the bursting, destruction, or inappropriate break-up of red blood cells. Possible mechanisms for this include physical destruction by, for example, a poorly functioning mechanical heart valve, prolonged heavy exercise, or long marches undertaken by the armed forces. Certain individuals are sensitive to drugs (such as antibiotics) that stick onto the surface of red blood cells and render them more susceptible to attack and degradation. High fever may also destroy fragile red cells, as will infections such as malaria.

A sub-type of haemolytic anaemia occurs when antibodies are produced which (erroneously) bind to red blood cells. This is therefore called autoimmune haemolytic anaemia (chapter 6). These autoantibodies will make the cell a target of the immune system and will lead to their elimination, often in the spleen. Indeed, a treatment for certain types of haemolytic anaemia includes splenectomy.

Red cells may be lost by an acute or chronic bleed. The former may include bleeding after surgery, heavy menstrual bleeding, or bleeding by a ruptured blood vessel that may leak into the intestines. If this process is occult, or prolonged, it may lead to a chronic state of blood loss. In these types of anaemia, there is nothing intrinsically wrong with the red cells themselves.

The most common congenital haemoglobinopathies (=disease of haemoglobin) are sickle cell disease and thalassaemia, genetic conditions characterised by qualitative changes in the haemoglobin molecule that severely reduce its ability to transport oxygen. These cells also have a shorter lifespan than cells carrying normal haemoglobin, and both conditions are associated with a variety of clinical conditions such as jaundice and skin ulcers.

There are, of course, many more possible types of anaemia. The above, summarised in Table 3, simply lists major causes.

Table 3: A Simple Classification of Anaemia

1. Depressed red blood cell production from the bone marrow

    - Due to infiltrating cancer (e.g., leukaemia, or secondary's from other primary cancers elsewhere, such as the breast or prostate)
    - Due to total marrow shut down (e.g., aplastic anaemia, or due to drugs, such as cancer chemotherapy)

2. Diet deficiency

    - Iron
    - Vitamins B_{12} and folate
    - Plasma proteins (for building essential carriage and storage molecules)

3. Loss of mature red cells

    - Drugs
    - Fevers, infections
    - Auto-immunity
    - Acute or chronic bleeding

4. Haemoglobinopathy

    - Sickle cell disease
    - Thalassaemia

5. Disease in other organs (such as the liver)

A Cautionary Tale – 1

In the past there was great debate as to the definition of anaemia, such as the haemoglobin count being less than a pre-defined level of 80, 90, 100 g/L or even (marginally) below the reference range. Consider this case report.

The case is a woman in her 30s with homozygous sickle cell disease. She was a fully-trained pharmacist, had worked full-time, had one uneventful and successful pregnancy, and had never received a blood transfusion. When was she last seen in her Clinic in Jamaica her haemoglobin was 39 g/L. Was she anaemic?

In 1997 she emigrated to the USA, and two years later was seen routinely by her family doctor who found a haemoglobin result of 38 g/L. Again – was she anaemic? Her family doctor and colleagues apparently believed so, and she was transfused with six units of blood within 24 hours. This increased her haematocrit from 0.11 to 0.31, but also increased her systolic and diastolic blood pressures by 30 mm Hg each. Nine hours after the last transfusion she reported a headache, subsequently developed cerebral haemorrhage, and later died.

I will not discuss this case further as, I believe, it is self-explanatory. However, the report concludes with '... The award of US $11.5 million recommended by the jury in this case could have been avoided'. Other comments on blood transfusion follow in Chapter 4.

Source: Serjeant, G. Blood transfusion in sickle cell disease: a cautionary tale. Lancet 2003; 361:1659–60.
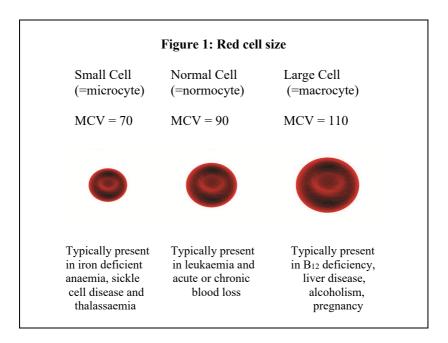
1.5: Size matters!

The red cell index MCV can also be used to further classify anaemia. For example, in the anaemia that follows problems with vitamin B_{12}, the red blood cells are larger than normal (e.g., greater than 98 fL), and are said to be macrocytes, and if the Hb is low and the patient is symptomatic, they

have macrocytic anaemia. Conversely, some haemoglobinopathies and iron deficient states often lead to microcytic anaemia because the red cells are small (e.g., less than 80 fL) and are called microcytes. Finally, a normocytic anaemia may be associated with a normal sized red cell (a normocyte, between 80 and 98 fL) but a lower overall Hb level (figure 1).

A prime reason for a normocytic anaemia will be the sudden loss of a large number of (healthy) red cells, perhaps by an accident, through a perforated duodenal ulcer, or bleeding gastrointestinal cancer. Here, there is nothing intrinsically wrong with the red cells themselves, the anaemia follows from another problem. Treatment therefore follows aetiology: more iron in the diet will not help an anaemia based on malabsorption, but intravenous iron may increase the haemoglobin level.

Figure 1: Red cell size

Small Cell (=microcyte)	Normal Cell (=normocyte)	Large Cell (=macrocyte)
MCV = 70	MCV = 90	MCV = 110
Typically present in iron deficient anaemia, sickle cell disease and thalassaemia	Typically present in leukaemia and acute or chronic blood loss	Typically present in B_{12} deficiency, liver disease, alcoholism, pregnancy

This illustrates how the three red cell indices can vary. Taking the Hb to be 130 g/L and the red cell count 4.5 x 10^{12} cells/mL in each of these cases with different MCVs, then the MCHC is 412 pg/L in the microcyte, 320 pg/L in the normocyte and 262 pg/L in the macrocyte. This may well be important in certain conditions.

Key point: The most common blood disease is anaemia; its diagnosis and management require regular full blood counts.

1.6: Increased levels of red cell indices

Ideally, the healthy body tightly regulates the numbers and quality of the various aspects of red cells. However, in rare instances, high levels are reported.

Polycythaemia is an excess overall red cell mass and is generally associated with a high haemoglobin, RBCC and haematocrit. This condition may arise from a rare kind of malignancy or over-activity of the bone marrow and is more correctly called polycythaemia rubra vera.

A second cause of increased red cell indices is the response of the bone marrow to reduced levels of oxygen, and is called erythrocytosis. This is understandable in those people living at a very high altitude (up mountains) where the air is very thin and of low oxygen content, but in the UK, this cannot be the case.

The most common form of erythrocytosis is low level of oxygen (hypoxia), and (until recently) the dominant form of this is an unhealthy lifestyle with heavy smoking. A contributing factor is that tobacco smoke contains carbon monoxide, which binds irreversibly to haemoglobin and prevents it carrying oxygen, leading to poor oxygen carrying capacity and thus a pseudo-anaemia. It is also possibly that the low grade pulmonary damage caused by tobacco smoke causes poor oxygen movement across the alveoli. The bone marrow responds by producing high numbers of excess red blood cells in an attempt to improve (restore) oxygen-carrying capacity. Consequently, this places an extra strain on the heart and circulation. Fortunately, the reduction in the rate of smoking means that we are seeing less and less of this problem.

Possibly for the same reason (response to hypoxia), an increased red cell count can be seen in chronic anaemia such as thalassaemia, as the bone marrow attempts to improve the ability of the blood to carry oxygen.

Recommended websites

www.pernicious-anaemia-society.org/
www.nhs.uk/conditions/Anaemia-iron-deficiency-/
www.hbregistry.org.uk/information/haemoglobinopathies.html

Summary of red blood cells

- Haemoglobin (Hb) is the key index used to investigate the major disease of red cells: anaemia.

- To aid precise diagnosis, the causes of the anaemia, and directions for treatment, RBCC, Hct and MCV are frequently referred to.

- Often less useful, but occasionally very enlightening, are MCH and MCHC.

- ESR is a non-specific marker: an abnormal result could reflect a variety of different pathologies.

- The MCV tells us whether the anaemia is microcytic, normocytic, or macrocytic, and so is likely to point to the aetiology and guide therapy.

Case Report 1

A 20-year old female and her family recently moved to this country from the Far East. Following a few weeks' acclimatisation and recovery from jet lag, it became clear to her family that she was consistently tired and lethargic, more so than her siblings, but had no symptoms of infection (e.g., a fever). Blood results were as follows.

	Result (unit)	Reference range
Haemoglobin	108 g/L	118 - 148
RCC	5.2 x 10^{12}/L	3.9 – 5.0
MCH	20.8 pg	27 – 33
MCV	68 fL	77 - 98
MCHC	330 pg/L	316 - 349
Hct	0.33	0.33 – 0.47
ESR	4 mm/hour	<10
RDW	10-15%	16%

Interpretation

The abnormal results are reduced haemoglobin, MCV, MCH, Hct and RDW, with raised a red cell count. The ESR is within the reference range. With a haemoglobin level below the bottom of the reference range, and the symptoms, we would have little difficulty in describing her result as concerning and would therefore probably label her as anaemic. Very heavy menstrual periods may possibly produce this picture, but as the red blood cells are not simply small (i.e., MCV <77), but are very small (<70), we would have no hesitation in describing a microcytic anaemia, not an anaemia due to simple blood loss by itself. High numbers of red cells may well be a response to the oxygen-carrying problem.

The most common reasons for microcytic anaemia are iron deficiency, sickle cell disease and thalassaemia. Iron status can be easily tested for, and a test for sickle cell disease is also very simple to perform. However, both types of haemoglobinopathies are ultimately diagnosed by another test (chromatography, HPLC). Thus, with a normal iron profile and negative sickle test, thalassaemia would seem to be an appropriate diagnosis.