Blood cells

Part two – Red blood cells

**Author** Ken Campbell, FIMBS, CertHMS, is clinical information officer, Leukaemia Research Foundation (written in a private capacity).

This article, the second in our series on blood cells, describes red blood cells, also known as erythrocytes or red corpuscles and commonly abbreviated as RBCs.

**Structure**

RBCs are biconcave, anucleate discs 7-8µm in diameter (Fig 1). Their shape and the absence of a nucleus allow RBCs to be deformed to pass through capillaries (Fig 2). This shape also offers the maximum surface area relative to volume for gas exchange.

The RBC is not simply a ‘bag’ of haemoglobin (Hb) – it has a complex membrane structure and multiple glycolytic pathways to supply energy and maintain Hb and membrane proteins in a reduced state (Kern, 2002a).

A trade-off against the benefits of losing the nucleus is that the cell can no longer synthesise protein. Unlike other cells, RBCs have no pathways for repair or to stave off ageing. Therefore, the cells only have a short lifespan of about 120 days. They are then destroyed by the liver and spleen, with most of the iron in the Hb being reclaimed.

**Source**

RBCs are produced and mature within the bone marrow as described in the first article in this series (Campbell, 2005a). After expulsion of the nucleus there is a stage during which the immature RBC contains residual protein-production machinery and mRNA. Such cells are called reticulocytes and they can be seen using special staining methods. Reticulocytes tend to be larger than RBCs and have a bluish tinge; an increased number of such cells on the blood film is termed polychromasia.

The normal reticulocyte level is about 0.2–2 per cent of the total RBC count. Modern cell counters normally give an absolute reticulocyte count. If none is present this is abnormal and indicative of disease.

An increase in reticulocyte number is often the first indication of successful treatment of deficiency anaemia – this is particularly true of vitamin B₁₂ or folate deficiencies.
RBC production is regulated by levels of the growth factor erythropoietin (EPO). This is produced mainly in the kidney in response to tissue hypoxia (Kern, 2002b).

The role of the kidney in regulating RBC synthesis means anaemia is a common consequence of renal disease; recombinant EPO has been used successfully to treat anaemia in renal failure, cancer and other conditions. In treating renal patients with cardiac disease, target Hb levels must be chosen carefully to avoid increased mortality (Strippoli et al, 2003).

Function

Although metabolically active, the only function of RBCs is to contain and transport the respiratory pigment Hb, which makes up 95 per cent of the content of a mature RBC. To consider RBCs’ function, the structure and function of the Hb molecule need to be considered (Kern, 2002b).

Hb is a complex of four protein chains (globins) each complexed with a haem group (Fig 3). Haem is an iron-containing ring molecule, which can differentially bind and release oxygen (O2) in response to O2 saturation, pH and temperature. The differential binding capacity enables Hb to bind to O2 in the pulmonary alveoli and then release O2 in peripheral vessels. Secondary functions of Hb include transport of carbon dioxide from the tissues to the lung for excretion, and a buffer effect to help control blood pH.

The chains of the Hb molecule act cooperatively in binding and releasing O2. When a fully deoxygenated Hb molecule binds a single molecule of O2, the shape of the entire Hb molecule changes to assist binding of the second O2 molecule. A similar process occurs in binding the third and fourth molecules of O2.

This process is reversed in tissue so that release of each O2 molecule triggers the easier release of each subsequent one. Because of this, the O2 affinity curve of Hb has a distinct sigmoid shape. Hb binds easily to O2 at high O2 concentrations (in the pulmonary alveoli) and O2 release is efficient at low O2 concentrations (in hypoxic tissues).

Oxygen affinity is determined by which globin chains are present and their configuration. The presence of different globin chains results in subtypes of Hb. All normal haemoglobin variants contain two α-chains and two non-α chains, which may be β, δ or γ.

The most abundant variant of Hb in adults is HbA, which consists of two α-chains and two β-chains, and makes up over 95 per cent of normal adult haemoglobin. Most of the rest is HbA2, which consists of two α-chains and two δ-chains. The remainder is HbF, the predominant haemoglobin during foetal life, which consists of two α-chains and two γ-chains.

A number of inherited haemolytic anaemias involve synthesis of defective Hb (haemoglobinopathy) or imbalanced globin chain production (thalassaemia).

**Clinical significance**

Normal blood test values (Table 1) vary according to age and sex in adults (Bain, 1996). A reduced number of RBCs is termed anaemia, and may result from many underlying processes (Campbell, 2004). An excess of RBCs is termed polycythaemia – this may be primary, which is a myeloproliferative disorder (Campbell, 2005b) or secondary to another pathology (Provan and Weatherall, 2000).

In each case it is necessary to first determine the underlying mechanisms of disease. Only in primary polycythaemia is it appropriate, or indeed feasible, to treat the blood disease directly. If the cause of a patient’s iron-deficiency anaemia is a bleeding gastrointestinal lesion or hookworm parasitaemia, there is no point administering iron tablets and even RBC transfusions will only offer temporary respite.

If the underlying cause is not treatable, for example an inoperable malignancy, then attention must focus on the best possible supportive care. In the case of renal disease, EPO supplements may promote adequate erythropoiesis if, and only if, the patient has adequate levels of substances required for blood cell production, collectively known as haematins.

Primary dietary anaemia may occasionally be seen in older people, those who self-neglect or those who adopt extreme dietary fads. Iron is poorly absorbed from a vegetarian diet and vitamin B12 cannot be synthesised by humans and is chiefly absorbed from meat and dairy products. Strict vegetarianism, veganism and similar dietary practices can lead to anaemia unless appropriate supplements are taken.

Under normal conditions, nucleated RBCs (NRBCs) are found in the blood only in the foetus and neonate. In any other case, the presence of NRBCs in the blood is an indicator of pathology, either an increase in erythropoietic activity or damage to the marrow microarchitecture (Schafer and Rowan, 2000). Many automated cell counters cannot reliably distinguish between NRBCs and small lymphocytes – in cases of thalassaemia, there may be so many NRBCs present that it is necessary to correct the machine-determined total white cell count.

### Table 1. Typical normal values for blood test results

<table>
<thead>
<tr>
<th></th>
<th>RBC x 10^12/L</th>
<th>Hb g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult male</td>
<td>4.3 to 5.7</td>
<td>13.3 to 16.7</td>
</tr>
<tr>
<td>Adult female</td>
<td>3.9 to 5.0</td>
<td>11.8 to 14.8</td>
</tr>
<tr>
<td>Child 2–5 years</td>
<td>4.2 to 5.0</td>
<td>11 to 14</td>
</tr>
<tr>
<td>Child 6–9 years</td>
<td>4.3 to 5.1</td>
<td>11 to 14</td>
</tr>
<tr>
<td>Child 9–12 years</td>
<td>4.3 to 5.1</td>
<td>11.5 to 15.5</td>
</tr>
</tbody>
</table>

This article has been double-blind peer-reviewed.

For related articles on this subject and links to relevant websites see www.nursingtimes.net

### REFERENCES


