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Blood and the classification of anaemia

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Aims and intended learning outcomes

Blood circulates throughout the body and is central to maintaining homeostasis of many bodily processes. It has a wide range of vital functions and transports a variety of different substances that are involved in cellular metabolism. After reading this article, you should be able to:

- State the functions of blood.
- List the major components of blood.
- Demonstrate understanding of how blood cells are formed.
- List the components required for normal red blood cell formation.
- Describe the various types of anaemia and the reasons why they occur.
- Explain the blood tests undertaken and their rationale in the context of anaemia.
- Discuss the nursing care that might be required for patients with each type of anaemia.

Functions of blood

As blood flows through the tissues it transports a variety of substances that ensure nutrition, respiration, excretion, physiological regulation and defence processes occur. Effective internal transport is vital to homeostasis – a process where constant levels of substances in the body are regulated, to attain optimal cell functioning. As blood passes through the capillaries, it delivers nutrients absorbed from the

small intestine and oxygen from the lungs to the cells. The cells use oxygen and glucose to form adenosine triphosphate (ATP), the substance that provides cellular energy. Blood also removes the toxic waste products of cellular metabolism, such as urea and carbon dioxide, from the cellular environment. These waste products are then excreted from the body in accordance with the body's needs. For example, the liver metabolises bile pigments, hormones and drugs; the kidney excretes excess water, acid, electrolytes, and urea; while the lungs eliminate carbon dioxide.

Regulation of body temperature is another important function of blood. Stable body temperature is vital for normal enzyme function. The body regulates loss or retention of heat by dilating or constricting blood vessels. Blood also assists in the regulation of osmotic pressure, where plasma proteins, such as albumin and globulin, draw fluid back into the blood stream. Blood also affects the movement of hormones and all endocrine functioning is, therefore, dependent on the blood flow. The pH of the blood is crucial to cellular function and must be strictly regulated. The blood has a buffer mechanism that helps to maintain the blood pH within the appropriate range (7.35-7.45).

The ability of the blood to form a clot, and thus stem bleeding and prevent haemorrhage, is one of its main protective functions. The inflammatory response is mediated by substances dissolved in the plasma, such as hormones and bilirubin, and plays a minor role in the deregulation of acid-base balance (Porth 1998). Other components

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In brief

Author

Helen Hand BSc(Hons), MA(Ed), RGN, is Lecturer, School of Nursing and Midwifery, University of Sheffield. Email: h.e.hand@sheffield.ac.uk

Summary

This article gives a brief overview of the function and composition of blood, focusing on the red blood cell and the development of the various types of anaemia. Good patient care and effective treatment of this complex condition is dependent on informed nursing practice.

Key words

- Blood
- Blood disorders

These key words are based on subject headings from the British Nursing Index. This article has been subject to double-blind review.

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of blood include white cells or leucocytes, which protect the body against disease and convey long-term immunity against invading micro-organisms.

Blood composition

Blood is a viscous substance that varies in colour depending on how much oxygen it is carrying. Arterial blood is well oxygenated and, therefore, bright red, while venous blood is less well oxygenated and is a much darker colour. Blood constitutes approximately 6-8 per cent of total body weight (Hinchliff and Montague 1988). On average, men have more blood (5.6 litres) than women (4.5 litres), although blood volume increases during pregnancy (Kapit *et al* 1987). Blood is made up of two components: fluid, known as plasma; and cells that float freely in the plasma. Plasma accounts for 55-60 per cent of the blood volume and is 91 per cent water, which helps to dissolve blood proteins. The blood proteins constitute 7 per cent of plasma volume (Huether and McCance 1996). Plasma proteins, such as albumin, globulin and fibrinogen, are the most abundant solutes in the plasma. Most plasma proteins are formed in the liver and have a variety of functions.

Albumin is the main plasma protein, making up 54 per cent of the plasma proteins (Porth 1998). The movement of albumin across the capillary wall is severely restricted because of its large size, and, therefore, it contributes to effective osmotic pressure. Osmotic pressure is a major factor in determining the balance between interstitial fluid (the extracellular fluid surrounding the cells) and plasma volume. Albumin also transports fatty acids and other substances dissolved in the plasma, such as hormones and bilirubin, and plays a minor role in the regulation of acid-base balance (Porth 1998).

Globulins are large protein molecules representing 38 per cent of the plasma proteins (Porth 1998), and function as carrier molecules for bilirubin and steroids. Gamma globulins synthesised by B lymphocytes contain antibodies released by plasma cells. Fibrinogen makes up around 7 per cent of the plasma proteins and is converted to fibrin during the clotting process. The remaining 1 per cent of plasma proteins consists of hormones, enzymes, complement and carriers for lipids (Porth 1998).

Other substances in the plasma are electrolytes, mainly sodium, potassium, chloride, calcium, magnesium and bicarbonate, and larger molecules including nutrients (such as glucose and

amino acids), drugs, vitamins, waste products, enzymes and hormones. Glucose is absorbed from the small intestine after digestion. It is stored in the liver and released in accordance with the body's need for energy. Amino acids, which are the end products of protein metabolism, are also absorbed from the small intestine. Lipids constitute a small percentage of blood plasma; lipid components include fats, cholesterol and lipoproteins, which are proteins bound to cholesterol. The amount of water in the plasma is kept constant by the kidneys. This is important, as the ratio of plasma to formed elements must be maintained so that the blood does not become too thick or too dilute. The levels of the other substances dissolved in the plasma must also be carefully regulated within a normal reference range, regardless of variations in lifestyle, food and water intake, and activity levels. For example, a person who puts salt on every meal will maintain the same range of plasma sodium as the person who eats little.

TIME OUT 1

Complete the following table by finding the reference range for each of the constituents of plasma:



Substance	Reference range
pH	
Sodium	
Potassium	
Chloride	
Bicarbonate	
Calcium	
Albumin	
Urea	
Phosphate	

The remaining 40-45 per cent of blood consists mainly of red blood cells (erythrocytes) (Kapit *et al* 1987). The volume of red cells in 100ml of blood is known as the haematocrit. White blood cells (leucocytes) and platelets (thrombocytes), constitute only a small fraction of the blood.

Blood cells are formed mainly in the bone marrow. Although the mass of bone marrow in a single bone might be small, the total mass of bone marrow in the body is large. In an adult, active bone marrow can be found in the sternum, ribs, vertebra and skull. The red marrow in these bones provides the primary source for red cells. In growing children, red marrow is also found in the femur and tibia. In adults, these bones provide secondary sources and are activated only when the primary sources are unable to keep up



with demand. Under extreme conditions, such as massive blood loss because of haemorrhage or destruction of marrow cells because of exposure to ionising radiation, the liver and spleen also make blood cells.

Blood cells are formed from the proliferation and differentiation of stem cells. All cell types have the same origin. Stem cells differentiate into lymphoid stem cells that produce lymphocytes and myeloid stem cells that produce red cells, white cells and platelets. A variety of hormonal and humoral controls adjust the production rate of blood cells according to the body's needs.

White blood cells White blood cells (WBCs) (leucocytes) are vital to human survival. The number of circulating white cells is 4,000-11,000 per mm³ blood (Marieb 1995), which is relatively low when compared to the number of red cells. Leucocytes remain in the blood for six to eight hours, or they might enter the tissues and survive for days, months, or even years. The need for constant replacement and, therefore, the need for healthy bone marrow activity, is vital to survival. There are several different types of WBCs that protect the body against disease. Granular white cells (those with visible granules in the cytoplasm) include: neutrophils, which are phagocytes, and directly destroy invading micro-organisms; eosinophils which are particularly effective against parasitic worm invasion; and basophils, which are effective in allergic reactions and the production of the inflammatory response. Agranular white cells (no visible granules) include lymphocytes and monocytes. Lymphocytes are the second most numerous white cells and have two forms: T and B cells. The T cells attack invading micro-organisms, while B cells produce antibodies against them. B cells are responsible for cell-mediated immunity – the ability to produce an immune response. Contact with a foreign antigen stimulates the B cells to differentiate, giving rise to plasma cells and memory cells, making long-term immunity possible. Monocytes are the largest white cells and function as phagocytes, which engulf and digest micro-organisms and cellular debris. The relative percentages of white cells in a healthy adult are outlined in Table 1.

Platelets Of all the formed elements, platelets are the smallest and are not cells, but cell fragments. They have a lifespan of approximately ten days. The circulating number of platelets ranges from 150,000 to 450,000 per mm³. Platelets are essential for blood clotting. When as a result of injury, blood comes into contact with any tissue other than the lining of the blood vessel, platelets stick together and form a

Table 1. Relative percentages of white blood cells

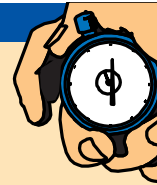
Cell type	Relative percentage	Function
<i>Granulocytes</i> Neutrophils Eosinophils	60-70 2-4	Phagocytosis Allergic reaction, defence against parasites
Basophils	0.5-1.0	Allergic and inflammatory response
<i>Agranulocytes</i> Lymphocytes Monocytes <small>(Bastian 1993)</small>	20-25 3-8	Immunity (T and B cells) Phagocytosis

plug that seals the wound. Platelets then release chemicals that participate in coagulation to stop blood loss.

TIME OUT 2

From what you have read so far, answer the following questions:

- What does the blood transport?
- What does the blood assist in regulating?
- How do blood cells protect us?



Red blood cells Red blood cells (RBCs) (erythrocytes) are the most abundant cells in the blood (up to 30 thousand billion per person). Their shape – biconcave disc – is highly adapted to their function of transporting respiratory gases, particularly oxygen, around the body. As red cells move through different width vessels and capillaries, their shape and size changes: in veins they inflate and in capillaries they bend. The biconcave shape enables oxygen and carbon dioxide diffusion into the cell and maximises the probability of binding with haemoglobin molecules inside the cell. Mature circulating RBCs contain no nucleus, all available space is filled with haemoglobin molecules so that as much oxygen as possible can be transported. The cytoplasm of a single red cell can carry 300 haemoglobin molecules (Huether and McCance 1996). Haemoglobin contains a protein part (globin) and four pigment (haem) molecules. Each of the four haem units is associated with one of the chains of the globin. Each haem contains an iron atom that binds reversibly with an oxygen molecule. Each molecule of haemoglobin can potentially carry four molecules of oxygen. Haemoglobin that is carrying oxygen is called oxyhaemoglobin.



Box 1. Classification of anaemia

- Hypoproliferative anaemia resulting from defective red cell production
- Anaemia due to haemorrhage and, therefore, loss of red cells
- Haemolytic anaemia, resulting from excessive destruction of red cells (haemolysis)

Oxyhaemoglobin gives oxygenated blood its typical bright red colour.

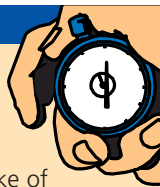
Erythrocytes develop from myeloid stem cells. The cell begins as an erythroblast (a nucleated cell) which as it matures to form a reticulocyte, accumulates haemoglobin and gradually loses its nucleus. Under conditions of rapid erythropoiesis (red cell production), reticulocytes and other immature cells (such as erythroblasts) might be released prematurely into the circulation. Differentiation of the primitive myeloid stem cell into an erythroblast is stimulated by the hormone erythropoetin produced primarily by the kidney. If the kidney detects low levels of oxygen, for example at high altitude, the release of erythropoetin is enhanced. This stimulates the bone marrow to increase production. The entire process typically takes five days.

In red cell production, iron is required for the haem part of haemoglobin; vitamin B₁₂ and folic acid are needed for synthesis of DNA; vitamins B₆, riboflavin and vitamin E are essential for normal erythropoiesis; vitamin C enables the absorption of iron; protein is needed for the globin part of haemoglobin; and copper and cobalt are required for haemoglobin synthesis.

Red cells survive for approximately 120 days after which they are removed from the circulation by the reticuloendothelial system (Kupffer cells in the liver and reticulum cells in the spleen, lymph nodes and lungs), and are ingested and destroyed by phagocytes. Approximately 1 per cent of red cells are removed and replaced each day (Porth 1998). The haemoglobin is largely recycled, but some breaks down to form bilirubin. Most of the iron is recycled to form new haemoglobin molecules in the bone marrow. Small amounts are lost in the faeces, urine and in menstrual flow.

TIME OUT 3

Make a list of the nutrients necessary for red blood cell formation. Describe the various types of food patients might eat to increase their intake of each of these nutrients.



Blood testing for anaemia

Anaemia is defined as a: '... decrease in haemoglobin in the blood, below the normal reference range for the age and sex of the individual' (Kumar and Clark 1990). Although there are many kinds of anaemia, there are three main classifications (Box 1).

There are a variety of tests that can be performed to provide information on the type and severity of anaemia. A full blood count (FBC) examines bone marrow function, RBCs, WBCs and platelets. The red blood count is specifically important in anaemia, as the red cells carry haemoglobin. The haemoglobin (Hb) level is also included in the FBC, and this level confirms the diagnosis of anaemia. The haematocrit calculation indicates the relative proportion of plasma and red blood cells. Men's blood contains about 47 per cent haematocrit compared to 42 per cent in women and children (Kapit *et al* 1987). This indicates a higher concentration of red cells, which is probably in response to a higher metabolic rate and increased oxygen need in males. A reduced haematocrit is indicative of anaemia or haemodilution, whereas an increased haematocrit is indicative of dehydration or polycythaemia.

The mean corpuscular volume (MCV), which indicates the average size of the red cells, is used to help differentiate between the various types of anaemia. Cells of normal size are known as normocytic, large cells as macrocytic, and small cells are called microcytic. The mean corpuscular haemoglobin concentration (MCHC) tests the average concentration of Hb in red cells irrespective of size. The appearance of the red cells in terms of colour is also an important part of testing for anaemia. Cells of normal colour are termed 'normochromic' and cells with little colour are hypochromic.

Once a diagnosis of anaemia has been confirmed, the next step is to discover the cause. This might be obvious or might need further investigation and there are a number of other blood tests that can be performed. The levels of substances such as iron, vitamin B₁₂ and folate can be ascertained. A reticulocyte count is also a useful tool in diagnosing the type of anaemia. The number of circulating reticulocytes should remain constant, but in certain anaemias the amount might increase as the body tries to compensate for low levels of circulating oxygen. Investigations of suspected sites of internal bleeding might also aid diagnosis and subsequent treatment.

Hypoproliferative anaemia

In hypoproliferative anaemia the red cells usually survive normally, but the bone marrow cannot produce adequate numbers of these cells. Decreased production will be reflected in a low blood reticulocyte count. Inadequate production of red cells can result from damage to the bone marrow, chemotherapy or other medication, a



lack of iron, vitamin B₁₂, and folic acid, or a lack of stimulation by erythropoietin.

The most common types of anaemia in this classification are iron deficiency anaemia, vitamin B₁₂ deficiency anaemia, folate deficiency anaemia and aplastic anaemia.

Iron deficiency anaemia Iron deficiency anaemia is caused by inadequate iron availability for normal red cell formation. It is the commonest type of anaemia (Higgins 1995), with a prevalence of 11 per cent worldwide (Hansen 1998). In haemoglobin there is an atom of iron at the centre of each haem group, which the oxygen molecule binds to. In iron deficiency anaemia, the body's stores of iron become depleted leading to impaired haemoglobin synthesis.

Kumar and Clark (1990) suggest that a normal diet contains 10-15mg of iron per day and that only 5-10 per cent of this is absorbed. For this reason, dietary deficiency is rarely the cause of iron deficiency anaemia. The cause is likely to be loss of iron through chronic bleeding, such as occurs with excessive menstruation, haemorrhoids, carcinoma and gastrointestinal bleeding.

Blood tests will reveal that the cells are microcytic and hypochromic, as they are unable to transport as much oxygen. The red cell count and the reticulocyte count will be slightly low. MCHC and MCV will also be reduced. The serum iron level is low, but the levels of other substances involved in red cell formation, such as vitamin B₁₂ and folate, will remain within the normal range.

Symptoms of iron deficiency anaemia do not often develop until the haemoglobin has fallen to around 9-10g/100ml of blood (Kumar and Clark 1990). This low level of Hb means that the tissues will not receive sufficient oxygen, resulting in symptoms of tiredness, headaches and breathlessness on exertion. Other symptoms are dizziness, tachycardia and palpitations due to increased cardiac work to pump the remaining oxygen around the body, and pale mucous membranes. These symptoms appear in all classifications of anaemia. Symptoms specific to iron deficiency anaemia result from epithelial cell atrophy in the presence of reduced oxygen. Depending on the severity of the condition, the symptoms can include brittle, spoon-shaped nails (koilonychia), decreased acid production, sores in the corners of the mouth, a smooth sore tongue, and sometimes dysphagia. One of the more bizarre symptoms is that of excessive eating of ice, dirt or other abnormal substances.

Locating the site of bleeding (if this is the cause) is a priority and the patient will need to

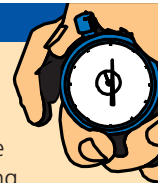
be thoroughly assessed. Questions should be asked regarding the colour and consistency of vomit and faeces. Patients might experience 'coffee-ground' vomit and dark stools indicate the presence of blood. A stool specimen should be tested for occult blood. Women should also be asked about their menstrual flow particularly in relation to the amount and time between each period. Patients of both sexes are prone to haemorrhoids and should be asked about them during assessment.

A full nutritional assessment is important in patients with iron deficiency anaemia to determine their understanding of the principles of diet and to identify any deficiencies. Cardiac status should also be assessed, as the heart will have been compensating for reduced oxygen levels in the blood by beating faster. Without treatment, this can lead to heart failure, which can be detected by the presence of cardiomegaly, hepatomegaly and peripheral oedema.

Before commencing treatment, it is important to exclude any serious underlying cause of anaemia, such as gastrointestinal cancer or uterine fibroid tumour, which might necessitate radiographic or endoscopic investigation. Treatment of iron deficiency anaemia involves replenishing the patients' iron stores, usually by giving oral medication, in the form of ferrous sulphate 200mg three times daily. The haemoglobin concentration should begin to rise by about 100-200mg per 100ml per day over three to four weeks (BNF 2001). Although an increase in Hb might occur, Smeltzer and Bare (2000) suggest that treatment needs to continue for 6-12 months to ensure that iron stores in the liver are adequate. Some people do not absorb or tolerate oral iron and might require intramuscular injection. Great care needs to be taken with this form of administration as it causes local pain and can stain the skin.

TIME OUT 4

- Mr Jones has been admitted to your ward for investigations of anaemia. His Hb is 7g/100ml. Describe the specific aspects of nursing care he will require during his admission
- He has been prescribed oral iron tablets. What advice and information would you give him about taking this medication?



Vitamin B₁₂ deficiency anaemia A deficiency in vitamin B₁₂ can result from a dietary deficiency or an inability of the body to absorb vitamin B₁₂ from ingested food. Vitamin B₁₂ is found in fish, meat, eggs and milk. The



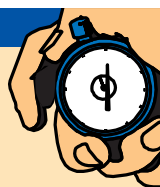
commonest cause of B₁₂ deficiency is pernicious anaemia. This condition occurs when the gastric mucosa atrophies leading to subsequent failure of the stomach to produce intrinsic factor, which results in malabsorption of B₁₂. It occurs mainly in older people, and affects one in 8,000 people over the age of 60 in the UK (Kumar and Clark 1990).

Other causative factors include low dietary intake (vegetarians in particular are at risk), impaired absorption as a result of gastrectomy, ileal disease or resection, coeliac disease, and chronic pancreatic disease. Patients with pernicious anaemia might present with bilateral paraesthesia of the fingers and toes, early loss of vibration sensation and proprioception, progressive weakness and ataxia. This occurs because a lack of B₁₂ impairs DNA synthesis and cell division, with significant effects on erythropoiesis and nerve myelination. Lack of myelin affects nerve impulse transmission, leading to abnormality of sensation or movement in affected tissues. Abnormal erythropoiesis results from impaired folic acid metabolism due to lack of vitamin B₁₂. If not treated, pernicious anaemia can be fatal, as patients can develop heart failure.

Pernicious anaemia is treated by giving the patient intramuscular hydroxocobalamin for the rest of his or her life. The usual prescription is an initial dose of 0.25-1mg on alternate days for one to two weeks, followed by 250µg weekly until the blood count is in the normal range (BNF 2001). This is then followed by 1mg every two to three months to maintain appropriate levels. The side effects of the medication include dizziness, hot flushes, fever, nausea and hypokalaemia. Clinical improvement might occur soon after treatment commences, although the neurological problems, such as the numbness and tingling in the feet, could take up to 6-12 months to resolve and some long-standing lesions might be irreversible (Smeltzer and Bare 2000).

TIME OUT 5

Mrs Smith had a blood test for pernicious anaemia and the diagnosis has been confirmed based on the following results: low Hb, low haematocrit, low reticulocyte count, raised MCV and a low serum B₁₂. The blood cells are described as macrocytic and normochromic. In your own words explain what these results mean.



Folate deficiency anaemia The main cause of folate deficiency is inadequate dietary intake (Kumar and Clark 1990). Absorption of folate

occurs in the upper small intestine. Folate is stored in the liver. Folate stores are not usually reduced by excessive use or malabsorption, but both these mechanisms can precipitate folate deficiency in a patient with an inadequate diet. Unlike vitamin B₁₂, body stores of folic acid are low and on a deficient diet folate deficiency develops rapidly over a period of four months. Other factors associated with folate deficiency include poverty, old age, alcohol misuse, or regular use of antiepileptic drugs, such as phenytoin.

Patients with folate deficiency are often asymptomatic; however, symptoms are similar to those in pernicious anaemia, with the exception of neurological symptoms which are not experienced. Diagnosis is based on blood testing and measurement of serum folate. Low Hb will initially indicate anaemia; this will be accompanied by a low haematocrit, low reticulocyte and a high MCV (indicating a macrocytic anaemia), normochromic cells and a low level of folate. Oral folic acid is the treatment and prophylactic folic acid is often recommended in pregnancy and in chronic haematological disorders where there is a rapid cell turnover.

Aplastic anaemia This is a primary condition of bone marrow stem cells that results in a reduction of red cells, white cells and platelets, with fatty replacement of the bone marrow. Failure of the bone marrow to replace cells that have been destroyed results in anaemia – the demand for cells outstrips the body's ability to produce them. The remaining cells are normochromic and normocytic, and because all cells are affected, deficiencies in white cells (particularly neutrophils) and platelets usually occur before the anaemia becomes severe. Causes include exposure to high dose radiation, chemicals and toxins that suppress haematopoiesis, for example, the antibiotic chloramphenicol and certain drugs used in cancer treatment. Aplastic anaemia might develop during certain infections and has been reported as a complication of viral hepatitis and AIDS (Porth 1998).

Onset might be insidious or sudden, and can occur at any age. Initial symptoms include weakness, fatigue and pallor. These can be accompanied by bruising, petechiae (small skin haemorrhages), and bleeding from the nose, gums or gastrointestinal tract, as a result of low circulating platelets. In idiopathic aplastic anaemia the cause is unknown. Treatment includes bone marrow transplant and immunosuppressive therapy. Transfusion of blood and components such as platelets might also be



indicated. Blood results indicate a low Hb, haematocrit, and reticulocyte count, normal or slightly raised MCV and raised plasma iron levels.

Anaemia due to major haemorrhage

It is important to distinguish between anaemia resulting from inadequate or deficient red cell formation and that resulting from excessive blood loss through acute haemorrhage, usually as a result of a traumatic episode. Because acute blood loss carries the risk of hypovolaemia and shock, nursing priorities will be focused on the trauma (Porth 1998). Once the bleeding has been stopped, blood volume should be returned to normal limits to adequately oxygenate the tissues. After a major bleed, anaemia might not be evident for several days until the blood plasma volume has returned to normal (Kumar and Clark 1990). The red cells will be normocytic and normochromic as there has not been a problem with their formation or rate of production. The number of circulating reticulocytes will be raised as the bone marrow attempts to increase the oxygen content of the blood by releasing more immature red cells into the circulation. Hb levels and the haematocrit will fall as fluid is drawn out of the cells into the vascular compartment to maintain the plasma volume, thus diluting the blood. The hypoxia that results from blood loss stimulates red cell production in the bone marrow via erythropoetin, and if bleeding is stopped and sufficient iron stores are available in the body, the RBC concentration should return to normal in three to four weeks.

Haemolytic anaemia

Haemolytic anaemia is characterised by the premature destruction of red cells and the retention in the body of iron and other products of red cell breakdown. Red cells in almost all types of haemolytic anaemia are of normal size and colour. Because of the short life of red cells, the bone marrow is usually hyperactive resulting in an increase in the number of reticulocytes circulating in the blood. Because of this, the patient will experience symptoms of fatigue, breathlessness, and other signs of reduced oxygen transport. The patient with haemolytic anaemia might also have mild jaundice from the accumulation of broken down red cell components in the blood.

The cause of haemolytic anaemia can be intrinsic or extrinsic to the red cell. Intrinsic factors include defects of the cell membrane, haemoglobinopathies and inherited disorders. Extrinsic

factors include certain medications, chemicals, toxins and infections, such as malaria, mechanical factors, such as prosthetic heart valves, and severe burns. Obstructions in the microcirculation as occur in disseminating intravascular coagulation (DIC), thrombotic thrombocytopenic purpura and renal disease might also traumatise red cells leading to early destruction. Some of these factors can be treated by splenectomy, while others respond to steroid treatment and others will not resolve until the primary cause is corrected. Sickle cell anaemia and thalassaemia are the two most well known haemolytic disorders.

TIME OUT 6

Think of a patient with sickle cell disease and briefly describe the condition. Make a list of the complications that might occur and give the rationale for each.



Sickle cell anaemia Sickle cell anaemia is a severe haemolytic anaemia resulting from the inheritance of the sickle cell haemoglobin gene (HbS). It causes faulty haemoglobin production, resulting in tissue hypoxia and circulatory obstruction. Sickle cell anaemia occurs almost exclusively in people of African descent, and to a lesser extent in those of the Middle East and Mediterranean countries (Smeltzer and Bare 2000). The condition is genetically transmitted, and can manifest as either sickle cell trait or sickle cell disease. The disease in its homozygous state (where both sickle cell genes are present, one from each parent), is serious. However, in the heterozygous state where only one gene for sickle cell anaemia is inherited, a condition called sickle cell trait results, which is less severe.

In sickle cell trait around 50 per cent of the haemoglobin is HbS (Smeltzer and Bare 2000). People with sickle trait can have a normal life expectancy and have no problem with activities of daily living (Huether and McCance 1996). Certain factors including anaesthesia, severe hypoxia caused by shock, and vigorous exercise at high altitude can trigger an attack. Although less severe, patients with sickle cell trait should receive counselling. If two people with the trait have children, these children could inherit two abnormal genes making them homozygous for the disease. The chances of this occurring are one in four (Kumar and Clarke 1990). Both forms of sickle cell are lifelong conditions.

A patient with sickle cell disease has a low haematocrit, raised reticulocyte count, low Hb,



Box 2. Complications of sickle cell anaemia

- Hypoxia
- Ischaemia
- Infection
- Poor wound healing leading to skin breakdown and ulcers
- Dehydration
- Stroke
- Anaemia
- Renal dysfunction
- Heart failure and pulmonary hypertension
- Priapism and impotence

(Smeltzer and Bare 2000)

Box 3. Sickle cell crises

- Vaso-occlusive or pain crisis – pain originates from an area of occlusion, but there are no haematological changes
- Aplastic crisis – some pain might be experienced, but the predominant sign is bone marrow hypoplasia with increased reticulocytes and decreased haemoglobin
- Haemolytic crisis – fever will be present and red cell destruction increases
- Sequestration crisis characterised by sudden and massive red cell trapping by the visceral organs, especially the spleen
- A mixed crisis – manifestations of more than one crisis occur

(Hansen 1998)

usually around 6-8g/100ml (Kumar and Clark 1990), and sickled cells evident on a blood smear. Patients with sickle cell trait have a normal Hb, haematocrit and blood smear. If blood testing confirms the presence of HbS, haemoglobin electrophoresis (a technique used to separate and identify serum proteins and other substances) can provide additional information about the amount of HbS in the erythrocytes. Treatment consists of supportive care aimed at preventing the consequences of the disease and avoiding crises.

HbS acquires a crystal-like formation when exposed to low oxygen tensions; the oxygen level in venous blood can be low enough to cause this change. In such conditions, the cell containing HbS loses its round, pliable, concave disc shape, and becomes deformed, rigid and sickle shaped. The long rigid flattened cells can become trapped in small blood vessels and pile up against each other, resulting in reduced blood flow to tissues and organs. The resulting ischaemia or infarction causes pain, swelling and fever, and stimulates further erythropoiesis, which increases the viscosity of the blood. Sickle cells have a reduced lifespan. The phagocytic cells in the spleen remove the sickled cells from the circulation, anaemia results, which further exacerbates tissue hypoxia. The sickling process takes time and if red cells are exposed to an adequate amount of oxygen before they become too rigid, they can revert to their normal shape. Kumar and Clark (1990) suggest that after repeated episodes of deoxygenation, the cells eventually lose their membrane flexibility and remain sickled. The course of the disease is characterised by periods of remission and exacerbation (crisis). Cold temperatures exacerbate the sickling process – vasoconstriction occurs in response to lower temperatures and slows the blood flow. Sickling is precipitated by infection, dehydration, acidosis, and reduced oxygen tension during sleep (Kumar and Clarke 1990).

Signs and symptoms of the disease are not seen in children under the age of six months as foetal Hb (HbF) persists. After this HbS predominates and clinical manifestations are evident. A sickle cell crisis is usually precipitated by infection of the respiratory or gastrointestinal tract towards the end of the first year of life, but according to Smeltzer and Bare (2000) the use of antibiotics and parent and patient teaching have greatly improved outcomes for these children. Anaemia is usually severe, resulting in weakness, fatigue and growth impairment. The spleen will be enlarged early on in the disease process but tends to atrophy as a result of infarction

(autosplenectomy) by the time children reach school age. As the microvasculature becomes obstructed, the blood supply is reduced causing ischaemia, which leads to painful hands and feet. Blood vessel obstruction can, unless treated, damage the lungs, kidneys, heart and central nervous system, sometimes irreversibly. There are several complications associated with sickle cell anaemia (Box 2).

Respiratory infections and other stressors that reduce oxygen tension below normal can cause an acute exacerbation or crisis. There are five types of crisis (Box 3).

Treatment involves counselling patients about the factors that exacerbate the condition, and premarital screening might be appropriate. Immunisations and prompt treatment of infections is also recommended. Pain is one of the most distressing symptoms for patients but can usually be well-controlled using appropriate analgesics. Patients are given intravenous fluids to reduce blood viscosity, oxygen therapy to reduce hypoxia, and antibiotics are prescribed to manage infection.

Blood transfusion is the cornerstone of sickle cell management; research indicates that transfusion can prevent the occurrence of strokes in children (Olujohungbe *et al* 2001). Blood transfusions are indicated when the Hb falls more than 2g/100ml below normal (Hansen 1998). However, it is often difficult to obtain suitable blood in sufficient quantities.

Hydroxyurea – a drug used in the treatment of chronic myeloid leukaemia and polycythaemia – can reduce the frequency of painful crises and the incidence of complications by almost 50 per cent (Charache *et al* 1995). It is not a cure, however, and to date bone marrow transplantation is the only available treatment option that offers the prospect of a cure. This should be undertaken early on in the disease process before the onset of organ damage, which reduces the chances of success.

Thalassaemia In contrast to sickle cell anaemia, thalassaemia results from absent or defective synthesis of the alpha- or beta-globin chains of haemoglobin. α -thalassaemia is a defective alpha chain, and β -thalassaemia results from a defective beta chain. This defect is inherited and a person might be homozygous and have the severe form of the disease, or heterozygous and have a milder form of the disease. Like sickle cell, thalassaemia occurs more frequently in certain populations. β -thalassaemia, also called thalassaemia major or Cooley's anaemia, affects populations of southern Italy and Greece. In Britain most people with thalassaemia are

Greek, Greek Cypriot or Indian (Hinchliff *et al* 1996). α -thalassaemia is more common among Asians; both α - and β -forms affect Africans and black Americans (Porth 1998).

Each haemoglobin molecule should consist of two α - and two β -globin chains. Each of these chains is attached to a haem unit that surrounds an iron atom, which binds to oxygen. If the globin chains are not formed correctly, oxygen carriage is severely affected, resulting in hypochromic and microcytic red cells. The unaffected chain will continue to be synthesised and accumulates in the red cell, contributing to red cell destruction and anaemia.

Beta-thalassaemia In β -thalassaemia, the excess α -chains that have been formed are denatured and form precipitates (Heinz bodies), within the bone marrow. These Heinz bodies impair DNA synthesis and cause damage to the red cell membrane. Severely affected red cell precursors are destroyed in the bone marrow, and the spleen usually destroys those that escape. Clinical signs and symptoms depend on the severity of the anaemia. The presence of the trait usually means that there is sufficient normal haemoglobin to prevent severe anaemia. Homozygous individuals will be dependent on blood transfusions because of the severity of the anaemia. Erythropoetin production by the kidney increases in the presence of hypoxia, which stimulates haematopoiesis. This leads to bone marrow expansion and increased iron absorption. The iron is deposited in the myocardium, liver and pancreas inducing organ injury and heart failure.

Death in patients with β -thalassaemia used to be caused by heart failure. However, blood transfusions have increased the lifespan of these patients by a decade or two. Death now results from haemochromatosis as a result of repeated blood transfusions (Huether and McCance 1996). The only current treatment for thalassaemia is regular blood transfusion, usually every three to four weeks. After each blood transfusion, the red cells in the blood are broken down slowly over the next four months. The iron from the red cells stays in the body and if not removed, builds up and causes damage to the liver, heart and other organs. Most children who have transfusions can live normally until their early twenties, but to live longer requires other treatment as well. Iron can be removed from the body by the use of subcutaneous injections of the iron-chelating agent deferoxamine mesylate. The chelate bonds with iron and excretes it via the urine. This substance is infused over 8-12

hours, three to seven times each week. The dose reflects the degree of iron overload.

Growth and maturation is often retarded in patients with β -thalassaemia and some people develop 'chipmunk-like' deformities caused by bone expansion to accommodate hyperplastic marrow.

Alpha-thalassaemia People who inherit α -thalassaemia trait are usually symptom free, or might have mild symptoms similar to those of β -thalassaemia trait. These include microcytic, hypochromic cells, bone marrow hyperplasia, increased serum iron concentrations and slight splenomegaly. Those with the disease have similar but milder symptoms to those with β -thalassaemia. Moderate microcytic, hypochromic cells are accompanied by spleen and liver enlargement, and marrow hyperplasia. α -thalassaemia also causes major fetal problems including oedema, ascites and congestive heart failure. The fetus will have a grossly enlarged heart and liver leading to premature death.

TIME OUT 7

If you have access to the internet, have a look at the following websites:
<http://www.sicklecellsociety.org/>
<http://www.ukts.org/thalweb.html>



Conclusion

Anaemia is a complex condition and many nurses working in different clinical areas will encounter patients with various types of anaemia. It is important that nurses are knowledgeable about the composition and characteristics of blood, so that they can understand the process and consequences of anaemia. Anaemia might be the primary reason for admission or it might be secondary to the condition the patient is in hospital for. Some types of anaemia such as sickle cell disease and thalassaemia are not common. However, the information provided in this article should help nurses across a wide range of care settings to understand more about the different types, causes and treatment of anaemia ■

TIME OUT 8

Now that you have completed the article, you might like to think about writing a practice profile. Guidelines to help you are on page 55.



Further information

UK Thalassaemia Society
 19 The Broadway
 Southgate Circus
 London
 N14 6PH
 Tel: 020 8882 0011

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