CHAPTER 3

Anaemia

Learning objectives

After studying this chapter you should confidently be able to:

- **Define anaemia**
  Anaemia is functionally defined as an insufficient red cell mass to adequately deliver sufficient oxygen to peripheral tissues to meet physiological needs. However, this is impractical to measure so, in practice, anaemia is frequently defined as a haemoglobin concentration ([Hb]), red blood cell count (RBC) or haematocrit (Hct) outside of the reference range.
- **Explain the relationship between anaemia and the reference range for haemoglobin**
  Defining anaemia simply as a blood parameter value outside of the reference range can be misleading in several ways (e.g. following acute blood loss, in pregnancy, following severe burns, in dehydration, with chronic hypoxia, in inherited haemoglobin disorders or due to postural changes). The astute haematologist needs to be aware of these situations to avoid misdiagnosis.
- **Describe in outline the broad morphological classes of anaemia**
  In morphological terms, anaemia can be described in terms of red cell size (as microcytic, normocytic or macrocytic) and in terms of colour intensity (as hypochromic or normochromic; the term hyperchromic is not used). Variation in red cell size, colour and shape are known as anisocytosis, polychromasia and poikilocytosis respectively. Many abnormal cell shapes have specific descriptive names, e.g. spherocyte, ovalocyte, sickle cell and target cell.
- **Outline the pathophysiology of anaemia**
  The basic problem in all anaemias is the inability to deliver sufficient oxygen to permit normal function. The most common presenting features are reduced exercise tolerance, shortness of breath after minimal exertion and palpitations. The severity of these symptoms is related to the severity of the anaemia, the speed with which anaemia developed and the presence of co-morbidity. Acute anaemia may be associated with obvious, acute symptoms such as shortness of breath, tachycardia, vertigo, orthostatic hypotension and a sensation of extreme fatigue. Conversely, very gradual onset of anaemia can permit gradual physiological compensation to offset the development of symptoms.
- **Outline the mechanisms leading to microcytic, hypochromic anaemia and macrocytic, normochromic anaemia**
  Red cell size is determined by the number of mitotic divisions during development. Broadly, cell size decreases with each mitotic division and maturation phase. Intracellular haemoglobin concentration increases with red cell maturity but synthesis stops when a critical intranuclear concentration is reached. Macrocytic anaemias result when nuclear maturation is retarded, leading to fewer cell divisions before maturity. Conversely, microcytic, hypochromic anaemias arise when haemoglobin synthesis is retarded, allowing more cell divisions before maturity.

3.1 DEFINING ANAEMIA

The definition of anaemia is not as simple as it might at first appear. Anaemia is functionally defined as an insufficient red cell mass to adequately deliver sufficient oxygen to peripheral tissues to meet physiological needs. However, this is impractical to measure so, in practice, anaemia is frequently defined as a haemoglobin concentration ([Hb]), red cell count (RBC) or haematocrit (Hct) outside of the reference range (see *Box 3.1*). For the most part, this definition serves as a useful screening tool to identify people with anaemia, but there are many circumstances in which a single measurement of Hb, RBC or Hct can be misleading. The astute haematologist must be aware of these circumstances to avoid misinterpretation and hence missed diagnosis.

Box 3.1 Reference values

Subject	Hb (g/dl)	RBC (x 10^{12}/l)	Hct (l/l)
Neonate	13.5–19.5	3.9–5.3	0.42–0.60
Infant	9.5–13.5	3.1–4.5	0.29–0.41
Adolescent	11.5–14.5	4.0–5.2	0.35–0.45
Adult male	13.3–17.7	4.4–5.9	0.37–0.49
Adult female*	11.7–15.7	3.8–5.2	0.36–0.46

*Values are for females of child-bearing age

[Hb] and acute blood loss

Acute blood loss is a common reason for requesting a full blood count, and this provides an excellent example of the need for careful interpretation of isolated haemoglobin measurements. The immediate response to significant acute blood loss is vasoconstriction, so an early haemoglobin measurement may be normal. After about six hours, there is a shift of tissue fluid into the bloodstream to restore the total blood volume, so a haemoglobin measurement will be reduced due to the dilution effect. A reticulocyte response will be seen in healthy individuals after 24–48 hours and the red cell count and haemoglobin level will be restored gradually. So which of these haemoglobin values is 'correct' and can be used to determine the presence and severity of anaemia?

In reality, determination of anaemia in the presence of acute blood loss should be based on symptoms and signs of decreased tissue oxygen supply, because none of the haemoglobin values on their own will truly reflect the clinical state of the patient. In an otherwise healthy individual, acute blood loss of up to 20% of their total blood volume can be compensated for without significant reduction in tissue oxygen delivery. The body possesses several compensatory mechanisms, including shifting the haemoglobin oxygen dissociation curve (see *Chapter 6*) to increase oxygen delivery, increased synthesis of intracellular 2,3-DPG (see *Chapter 8*), decreasing vascular resistance and increasing cardiac rate and stroke volume. In practice, the maintenance of circulatory pressure through rapid restoration of blood volume with colloid solutions is more important than the correction of haemoglobin concentration. In patients with co-morbidity such as cardiopulmonary disease, hypertension or a history of heavy smoking, physiological compensation may be impaired and blood transfusion may be appropriate.

In summary, diagnosis of anaemia must be made only after considering the blood count, other haematological signs of anaemia (see later in this chapter) and the clinical picture. An isolated haemoglobin measurement can be seriously misleading.