1
Introduction to Lifespan Nutrition

Learning objectives
By the end of this chapter, the reader should be able to:
- Describe what is meant by a lifespan approach to the study of nutrition and health.
- Discuss the meaning of the term “nutritional status” and describe how optimal nutrition requires a balance of nutrient supply and demand for nutrients in physiological and metabolic processes.
- Show an awareness of the factors that contribute to undernutrition, including limited food supply and increased demands due to trauma or chronic illness.
- Discuss global strategies for the prevention of malnutrition.
- Describe how nutritional status is influenced by the stage of life due to the variation in specific factors controlling nutrient availability and requirements, as individuals develop from the fetal stage through to adulthood.
- Show an appreciation of how anthropometry, dietary assessment, measurements of biomarkers, and clinical examination can be used to study nutritional status in individuals and populations.
- Discuss the need for dietary standards in making assessments of the quality of diet or dietary provision, in individuals or populations.
- Describe the variation in the basis and usage of dietary reference value systems in different countries.

1.1 The lifespan approach to nutrition

The principal aim of this book is to explore relationships between nutrition and health, and the contribution of nutrition-related factors to disease. In tackling this subject, there are many different approaches that could be taken, for example, considering diet and cardiovascular disease, nutrition and diabetes, obesity or immune function as separate and discrete entities, each worthy of their own chapter. The view of this author, along with many others in recent times (Ben-Shlomo and Kuh, 2002) is that the final stages of life, that is, the elderly years, are effectively the products of events that occur through the full lifespan of an individual. Aging is in actuality a continual, lifelong process of ongoing change and development from the moment of conception until the point of death. It is therefore inappropriate to consider how diet relates to chronic diseases that affect adults without allowance for how the earlier life experiences have shaped physiology. The lifespan approach that is used to organize the material in this book essentially asserts three main points:

1. All stages of life from the moment of conception through to the elderly years are associated with a series of specific requirements for nutrition.
2. The consequences of less than optimal nutrition at each stage of life will vary, according to the life stage affected.
3. The nature of nutrition-related factors at earlier stages of life will determine how individuals grow and develop. As a result, the relationship between diet and health in later stages of adult life, to some extent, depends upon events earlier in life. As a result the nature of this relationship may be highly individual.

Although we tend to divide the lifespan into a series of distinct stages, such as infancy, adolescence, early adulthood, middle age, and older adulthood, few of these divisions have any real biological significance and they are therefore simply markers of particular periods within a continuum. There are, however, key events within these life stages, such as weaning, the achievement of puberty, or the menopause, which are significant milestones that mark profound physiological and endocrine changes and have implications for...
the nature of the nutrition and health relationship. On a continual basis, at each stage of life, individuals experience a series of biological challenges, such as infection or exposure to carcinogens that threaten to disturb normal physiology and compromise health. Within a lifespan approach, it is implicit that the response of the system to each challenge will influence how the body responds at later life stages. Variation in the quality and quantity of nutrition is one of the major challenges to the maintenance of optimal physiological function and is also one of the main determinants of how the body responds to other insults.

In considering the contribution of nutrition-related factors to health and disease across the lifespan, it is necessary to evaluate the full range of influences upon quality and quantity of nutrition and upon physiological processes. This book therefore takes a broad approach and includes consideration of social or cultural influences on nutrition and health, the metabolic and biochemical basis of the diet–disease relationships, the influence of genetics, and, where necessary, provides overviews of the main physiological and cellular processes that operate at each life stage. While the arbitrary distinctions of childhood, adolescence, and adulthood have been used to divide the chapters, it is hoped that the reader will consider this work as a whole. In this opening chapter, we consider some of the basic terms and definitions used in nutrition and lay the foundations for understanding more complex material in the following chapters.

1.2 The concept of balance

Balance is a term frequently used in nutrition and, unfortunately, the precise meaning of the term may differ according to the context and the individual using it. It is common to hear the phrase “a balanced diet” and, indeed, most health education literature that goes out to the general public urges the consumption of a diet that is “balanced.” In this context, we refer to a diet that provides neither too much nor too little of the nutrients and other components of food that are required for normal functioning of the body. A balanced diet may also be viewed as a diet providing foods of a varied nature, in proportions such that foods rich in some nutrients do not limit intakes of foods rich in others.

1.2.1 A supply and demand model

There is another way of viewing the meaning of balance or a balanced diet, whereby the relationship between nutrient intake and function is the main consideration. A diet that is in balance is one where the supply of nutrients is equal to the requirement of the body for those nutrients. Essentially, balance could be viewed as equivalent to an economic market, in which supply of goods or services needs to be sufficient to meet demands for those goods or services. Figure 1.1 summarizes the supply and demand model of nutritional balance.

Whether or not the diet is in balance will be a key determinant of the nutritional status of an individual. Nutritional status describes the state of a person’s health in relation to the nutrients in their diet and subsequently within their body. Good nutritional status would generally be associated with a diet that supplies nutrients at a level sufficient to meet requirements, without excessive storage. Poor nutritional status would generally (though not always) be associated with intakes that are insufficient to meet requirements.

The supply and demand model provides a useful framework for thinking about the relationship between diet and health. As shown in Figure 1.1, maintaining balance with respect to any given nutrient requires the supply of the nutrient to be equivalent to the overall demand for that nutrient. Demand comprises any physiological or metabolic process that utilizes the nutrient and may include use as an energy-releasing substrate, as an enzyme cofactor, as a structural component of tissues, a substrate for synthesis of macromolecules, as a transport element, or as a component of cell-cell signaling apparatus. The supply side of the balance model comprises any means through which nutrients are made available to meet demand. This goes beyond delivery through food intake and includes stores of the nutrient that can be mobilized within the body, and quantities of the nutrient that might be synthesized de novo (e.g., vitamin D is synthesized in the skin through the action of sunlight).

1.2.2 Overnutrition

When supply does not match demand for a nutrient, then the system is out of balance and this may have important consequences in terms of health and disease. Overnutrition (Figure 1.1) will generally arise...
because the supply of a nutrient is excessive relative to demand. This is either because intake of foods containing that nutrient increases, because the individual consumes supplements of that nutrient, or because demand for that nutrient declines with no equivalent adjustment occurring within the diet. The latter scenario particularly applies to the elderly, for whom energy requirements fall due to declining physical activity levels and resting metabolic rate (Rivlin, 2007). Commonly, intakes of energy that were appropriate in earlier adulthood will be maintained, resulting in excessive energy intake.

The consequences of overnutrition are generally not widely considered in the context of health and disease, unless the nutrient concerned is directly toxic or harmful when stored in high quantities. The obvious example here is, again, energy, where overnutrition will result in fat storage and obesity. For many nutrients, overnutrition within reasonable limits has no adverse effect as the excess material will either be stored or excreted. At megadoses, however, most nutrients have some capacity to cause harm. Accidental consumption of iron supplements or iron overload associated with inherited disorders is a cause of disease and death in children. At high doses, iron will impair oxidative phosphorylation and mitochondrial function, leading to cellular damage in the liver, heart, lungs, and kidneys. Excess consumption of vitamin A has been linked to development of birth defects in the unborn fetus (Martinez-Frias and Salvador, 1990).

Overnutrition for one nutrient can also have effects upon nutritional status with respect to other nutrients, and can impact on physiological processes involving a broader range of nutrients. For example, regular consumption of iron supplements can impact upon absorption of other metals such as zinc and copper, by competing for gastrointestinal transporters and hence promote undernutrition with respect to those trace elements. Having an excess of a particular nutrient within the body can also promote undernutrition with respect to another by increasing the demand associated with processing the excess. For
example, a diet rich in the amino acid methionine will tend to increase circulating and tissue concentrations of homocysteine. Processing of this damaging intermediate increases the demand for B vitamins, folic acid, vitamin B6, and vitamin B12, which are all involved in pathways that convert homocysteine to less harmful forms (Lonn et al., 2006).

1.2.3 Undernutrition

Undernutrition arises when the supply of nutrient fails to meet demand. This can occur if intakes are poor, or if demands are increased (Figure 1.1). In the short-medium term, low intakes are generally cushioned by the fact that the body has reserves of all nutrients that can be mobilized to meet demand. As such, for adults, it will usually require prolonged periods of low intake to have a significantly detrimental effect on nutritional status.

1.2.3.1 Increased demand

There are a number of situations that may arise to increase demand in such a way that undernutrition will arise if supply is not also increased accordingly. These include pregnancy, lactation, and trauma. Trauma encompasses a wide range of physical insults to the body, including infection, bone fracture, burns, surgery, and blood loss. Although diverse in nature, all of these physiological insults lead to the same metabolic response. This acute phase response (Table 1.1) is largely orchestrated by the cytokines including tumor necrosis factor-α, interleukin-6, and interleukin-1 (Grimble, 2001). Their net effect is to increase demand for protein and energy and yet paradoxically they have an anorectic effect. Thus, demand increases and supply will be impaired leading to protein-energy malnutrition. While in many developing countries, we associate protein-energy malnutrition with starvation in children, in developed countries such as the UK protein-energy malnutrition is most commonly noted in surgical patients and patients recovering from major injuries (Allison, 2005).

1.2.3.2 The metabolic response to trauma

The human body is able to adapt rates of metabolism and the nature of metabolic processes to ensure survival in response to adverse circumstances. The metabolic response to adverse challenges will depend upon the nature of the challenge. Starvation leads to increased metabolic efficiency, which allows reserves of fat and protein to be utilized at a controlled rate that prolongs survival time and hence maximizes the chances of the starved individual regaining access to food. In contrast, the physiological response to trauma generates a hypermetabolic state in which reserves of fat and protein are rapidly mobilized in order to fend off infection and promote tissue repair (Table 1.1). Physiological stresses to the body, including infection, bone fracture, burns, or other tissue injury, elicit a common metabolic response regardless of their nature. Thus, a minor surgical procedure will produce the same pattern of metabolic response as a viral infection. It is the magnitude of the response that is variable and this is largely determined by the severity of the trauma (Romijn, 2000).

The hypermetabolic response to trauma is driven by endocrine changes that promote the catabolism of

<table>
<thead>
<tr>
<th>Acute phase response</th>
<th>Markers of the response</th>
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<tbody>
<tr>
<td>Metabolic change</td>
<td>Catabolism of protein, muscle wastage. Amino acids converted to glucose for energy, or used to synthesize acute phase proteins. Catabolism of fat for energy</td>
</tr>
<tr>
<td>Fever</td>
<td>Body temperature rises to kill pathogens. Hypothalamic regulation of food intake disrupted, leading to loss of appetite</td>
</tr>
<tr>
<td>Hepatic protein synthesis</td>
<td>Acute phase proteins synthesized to combat infection (e.g., C reactive protein, α1-proteinase inhibitor, and ceruloplasmin). Liver reduces synthesis of other proteins, including transferrin and albumin</td>
</tr>
<tr>
<td>Sequestration of trace elements</td>
<td>Zinc and iron taken up by tissues to remove free elements that may be utilized by pathogens</td>
</tr>
<tr>
<td>Immune cell activation</td>
<td>B cells produce increased amounts of immunoglobulins. T cells release cytokines to orchestrate the inflammatory response</td>
</tr>
<tr>
<td>Cytokine production</td>
<td>Tumor necrosis factor-α and the interleukins 1, 2, 6, 8, and 10 work to produce a hypermetabolic state that favors production of substrates for immune function, but inhibits reproduction and spread of pathogens</td>
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protein and fat reserves. Following the initial physiological insult, there is an increase in circulating concentrations of the catecholamines, cortisol, and glucagon. Increased cortisol and glucagon serve to stimulate rates of gluconeogenesis and hepatic glucose output, thereby maintaining high concentrations of plasma glucose. The breakdown of protein to amino acids provides gluconeogenic substrates and also leads to greatly increased losses of nitrogen via the urine. Lipolysis is stimulated and circulating free fatty acid concentrations rise dramatically. These are used as energy substrates, along with glucose.

The response to trauma is essentially an inflammatory process and, as such, the same metabolic drives are noted in individuals suffering from long-term inflammatory diseases including cancer and inflammatory bowel disease (Richardson and Davidson, 2003). The inflammatory response serves two basic functions. Firstly, it activates the immune system, raises body temperature, and re-partitions micronutrients in order to create a hostile environment for invading pathogens (Table 1.1). Secondly, it allocates nutrients toward processes that will contribute to repair and healing.

The inflammatory response is orchestrated by the pro-inflammatory cytokines (e.g., TNF-α, IL-1, and IL-6) and the anti-inflammatory cytokines (e.g., IL-10). Whenever injury or infection occurs, the pro-inflammatory species are released by monocytes, macrophages, and T helper cells. The level of cytokines produced is closely related to the severity of the trauma (Lenz et al., 2007). The impact of pro-inflammatory cytokines is complex. On the one hand, they activate the immune system and protect the body from greater trauma. On the other, at the local level of any injury, they increase damage by stimulating the immune system to release damaging oxidants and other agents that indiscriminately destroy invading pathogens and the body’s own cells. The production of pro-inflammatory cytokines therefore has to be counterbalanced as an excessive response can lead to death (Grimble, 2001). This is the role of the anti-inflammatory cytokines and some of the acute phase response proteins, several of which inhibit the proteases released during inflammation and therefore limit the breakdown of host tissues.

In addition to stimulating proteolysis and lipolysis within muscle and adipose tissue, the cytokines have a number of actions that impact upon nutritional status. Firstly, they increase the basal metabolic rate. An element of creating a hostile environment for pathogens includes raising the core temperature of the body (fever). This greatly increases energy demands. The capacity to meet those demands through feeding is reduced as cytokines also act upon the gut and the centers of the hypothalamus that regulate appetite, effectively switching off the desire to eat. As can be seen in Table 1.2, the increased metabolic rate associated with the response to trauma greatly increases the demands of the body for both energy and protein. In severe cases, requirements can be doubled, even though the critically ill patient will be immobilized and not expending energy through physical activity. This can pose major challenges for clinicians managing such cases as the injured patient maybe unable to feed normally, and due to the anorectic influences of pro-inflammatory cytokines, the capacity to ingest sufficient energy, protein, and other nutrients is greatly reduced. Enteral or parenteral feeding are therefore a mainstay of managing major injuries.

With more severe trauma, the mobilization of reserves can produce marked changes in body composition. Muscle wasting may occur as the calcium-dependent calpains and ubiquitine-proteasome break Table 1.2 The metabolic response to injury and infection increases requirements for energy and protein

<table>
<thead>
<tr>
<th>Nature and severity of trauma</th>
<th>Increase in energy requirement (× basal)</th>
<th>Increase in protein requirement (× basal)</th>
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<tbody>
<tr>
<td>Minor surgery or infection</td>
<td>1.1</td>
<td>1.0–1.5</td>
</tr>
<tr>
<td>Major surgery or moderate infection</td>
<td>1.3–1.4</td>
<td>1.5–2.3</td>
</tr>
<tr>
<td>Severe infection, multiple or head injuries</td>
<td>1.8</td>
<td>2.0–2.8</td>
</tr>
<tr>
<td>Burns (20% BSAB)</td>
<td>1.5</td>
<td>–</td>
</tr>
<tr>
<td>Burns (30–40% BSAB)</td>
<td>1.8</td>
<td>2.0–2.8</td>
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BSAB, body surface area burned.
*Dependent upon level of nitrogen losses in tissue exudates and age of patient. Children with burns have higher requirements.
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down proteins rapidly to make amino acids available for gluconeogenesis and the synthesis of important antioxidants such as glutathione (Grimble, 2001). Body composition changes are beneficial to the injured patient as they primarily generate glucose. This is the optimal energy substrate for these circumstances, not least because it can be metabolized anaerobically to produce ATP in tissues where blood flow may be compromised and oxygen delivery impaired.

In the short term, the hypermetabolic response and the accompanying anorexia of illness are unlikely to impact significantly upon the nutritional status of an individual, although nutritional status prior to onset of trauma would be an important consideration. For example, the nutritional consequences of a fractured femur in a young, fit adult male may be dramatically different to those in a frail elderly woman. Prolonged periods of disease accompanied by inflammatory responses that drive hypermetabolism will, however, promote states of protein-energy malnutrition, such as kwashiorkor, or can produce the emaciated state of cachexia. Cachexia is characterized by loss of weight, decline in appetite, and muscle atrophy due to mobilization of muscle protein. It is generally associated with underlying chronic illnesses such as cancer, tuberculosis, or untreated AIDS. Nutritional support (i.e., supplemental feeding) of chronically ill individuals or those who have suffered more acute trauma can limit the impact of the hypermetabolic response upon body composition and overall nutritional status.

However, the catabolic metabolism cannot be reversed until the injury or illness is resolved, so the priority in these scenarios is limiting weight loss and loss of muscle mass, rather than achieving weight gain.

1.2.3.3 Compromised supply and deficiency

Clearly, there is a direct relationship between the supply of a nutrient to the body and the capacity of the body to carry out the physiological functions that depend upon the supply of that nutrient. As can be seen in Figure 1.2, the range of nutrient intakes over which optimal function is maintained is likely to be very broad and there are a number of stages before functionality is lost. It is only when function can no longer be maintained that the term nutritional deficiency can be accurately used.

A nutrient deficiency arises when the supply of a nutrient through food intake is compromised to the extent that clinical or metabolic symptoms appear. The simplest example to think of here relates to iron deficiency anemia in which low intakes of iron result in a failure to maintain effective concentrations of red blood cell hemoglobin, leading to compromised oxygen transport and hence the clinical symptoms of deficiency that include fatigue, irritability, dizziness, weakness, and shortness of breath. Iron deficiency anemia, like all deficiency disorders, reflects only the late stage of the process that begins with a failure of supply through intake to meet demands (Table 1.3).

Once the body can no longer maintain function using

<table>
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<th>Increasing nutrient intake</th>
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<tbody>
<tr>
<td>Danger of disease due to excess</td>
</tr>
<tr>
<td>Marginally high intake</td>
</tr>
<tr>
<td>Low risk of disease, Demands met</td>
</tr>
<tr>
<td>Marginally low intake</td>
</tr>
<tr>
<td>Danger of deficiency disease</td>
</tr>
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Figure 1.2 The association between nutrition and health. The requirements of the body for nutrients will be met by a broad range of intakes. Very low and very high intakes of any nutrient will be associated with ill health. The transition from intakes that are meeting demands and at which risk of disease is low to intakes that would be associated with disease is not abrupt.
Table 1.3 The three stages of iron deficiency

<table>
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<tr>
<th>Stage</th>
<th>Biochemical indicators and reference ranges</th>
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<tr>
<td>Normal iron status</td>
<td>Hemoglobin 14–18 g/dL (men), 12–16 g/dL (women). Serum ferritin 40–280 µg/L, transferrin saturation 31–60%</td>
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<tr>
<td>Depleted iron stores</td>
<td>Transferrin saturation falls as transport of iron declines. Hemoglobin normal. Serum ferritin &lt; 12 µg/L. Transferrin saturation &lt; 16%</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>Hemoglobin synthesis cannot be maintained and declines to &lt; 13.5 g/dL (men), &lt; 12 g/dL (women). Serum ferritin &lt; 10 µg/L. Transferrin saturation &lt; 15%</td>
</tr>
</tbody>
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In the case of iron, this will involve the release of iron bound to the protein, ferritin, to maintain hemoglobin concentrations. No change in function will occur at this stage but the individual will now be in a state of greater vulnerability to deficiency. A further decline in supply through intake may not be matched through mobilization of stores and so full deficiency becomes more likely. This situation in which intakes are sufficiently low that, although there are no signs of deficiency, biochemical indicators show that nutrition is subnormal is generally referred to as marginal nutrition, or subclinical malnutrition.

1.2.3.4 Malnutrition

Malnutrition describes the state where the level of nutrient supply has declined to the point of deficiency and normal physiological functions can no longer be maintained. The manifestations of malnutrition will vary depending on the type of nutrient deficiencies involved and the stage of life of the malnourished individual. In adults, malnutrition is often observed as unintentional weight loss or as clinical signs of specific deficiency. In children, it is more likely to manifest as growth faltering, with the affected child being either underweight for their age (termed wasted) or of short stature for their age (termed stunted). Specific patterns of growth are indicative of different forms of protein-energy malnutrition. Wasting is associated with marasmus where a weight less than 60% of standard for age is used as a cutoff. Edema with a weight less than 80% of standard for age is indicative of kwashiorkor.

From a clinical perspective, protein-energy malnutrition is the most serious undernutrition-related syndrome. Marasmus and kwashiorkor are classical definitions of this form of malnutrition. Historically, marasmus was considered to be a pure energy deficiency and kwashiorkor to be a protein deficiency, but it is now clear that the two are different manifestations of the same nutritional problems. Marasmic wasting is a sign of an effective physiological adaptation to long-term undernutrition. It is characterized by a depletion of fat reserves and muscle protein, along with adaptations to reduce energy expenditure. Children who become wasted in this way, if untreated, will generally die from infection as their immune functions cannot be maintained during the period of starvation. Kwashiorkor is a more rapid process, often triggered by infection alongside malnutrition. The metabolic changes with kwashiorkor are strikingly different to marasmus as the adaptation to starvation is ineffective. Fat accumulates in the liver and expansion of extracellular fluid volume, driven by low serum albumin concentrations, leads to edema. Micronutrient deficiencies often occur alongside protein-energy malnutrition and may partly explain why individuals with kwashiorkor, unlike those with marasmus, are unable to adapt successfully to malnutrition.

The causes of malnutrition are complex and are not simply related to a limited food intake. Where intake is reduced, this is often due to food insecurity associated with famine, poverty, war, or natural disasters. Reduced food intake can also arise due to chronic illness leading to loss of appetite or feeding difficulties. Malnutrition will also arise from malabsorption of nutrients from the digestive tract. This, again, could be a consequence of chronic disease or be driven by infection of the tract. Losses of nutrients are an important consequence of repeated diarrheal infections in areas where there is no access to clean water and adequate sanitation. Malnutrition may also be driven by situations that increase the demand for nutrients including trauma (as described above), pregnancy, and lactation, if those increased demands cannot be matched by intake.
Malnutrition is most common and most deadly in the developing countries, where it is the major cause of death in children. Stunting and wasting among malnourished children have long-term consequences too, as often the reduction in stature is not recovered, leading to reduced physical strength and capacity to work in adult life. As poverty is the most frequent cause of malnutrition, a self-perpetuating cycle can be established, as the stunted child becomes the adult with reduced earning capacity, whose children will live in poverty. Stunted, underweight women will also have children who are at risk due to lower weight at birth. Pregnancy is a time of high risk for malnutrition in women living in developing countries. Stunting is commonplace among women in South and South-east Asia, and is often accompanied by underweight. For example, in India and Bangladesh, up to 40% of women of childbearing age have a body mass index (BMI) of less than 18.5 kg/m² (Black et al., 2008). Iron deficiency anemia is endemic among pregnant women in developing countries, with prevalence of between 60% and 87% in the countries of southern Asia (Seshadri, 2001). Maternal and childhood malnutrition are believed to cause 3.5 million deaths among the under-fives every year (Black et al., 2008).

Developed countries also have a burden of malnutrition among vulnerable groups. At greatest risk are the elderly, who may develop protein-energy malnutrition or micronutrient deficiencies due to specific medical conditions, or through low intakes associated with frailty or loneliness. Surgical patients are at risk of protein-energy malnutrition as a result of the inflammatory response to trauma. As in the developing countries, poverty increases the risk of malnutrition among children and immigrant groups. There are many ways of targeting these at-risk groups, for example, monitoring the growth of infants, or including regular weighing and nutritional assessments of hospital patients. Malnutrition is easily treated through appropriate nutritional support.

The prevention of malnutrition is a major public health priority on a global scale. While a lack of food security and the risk of protein-energy malnutrition remains a major issue for many populations, there have been a number of success stories in the battle to prevent clinically significant malnutrition. The basic approaches that can be used to prevent nutrient deficiency are diet diversification, supplementation of at-risk individuals, and fortification. The basis for these approaches and their use in the attempt to eradicate vitamin A deficiency is described in Research highlight 1. Similar strategies have been used to reduce the occurrence of iodine and iron deficiency diseases. Iodine deficiency is an important issue for populations in all continents except Australasia. Availability of iodine is essentially limited by the iodine content of the soil and hence uptake by plants and animals. Iodine deficiency disorders, including cretinism and goiter, are a major manifestation of malnutrition, with approximately 740 million affected individuals worldwide. Fortification has been the cornerstone of the fight against iodine deficiency, with the Universal Salt Iodization program providing iodized salt (20–40 mg iodine per kg salt) to 70% of households in affected areas. Where the iodized salt is consumed, marked improvements in iodine status of the population are rapidly noted (Sebotsa et al., 2005). Although there are still significant numbers of individuals at risk of iodine deficiency disorders, due to lack of coverage of the USI program (Maberly et al., 2003), this fortification approach is widely considered to be a public health nutrition success for the World Health Organization (WHO).

1.2.4 Classical balance studies

Nutritional status with respect to a specific nutrient can be measured using balance studies. These have classically been used to determine requirements for some nutrients in humans. Essentially, the balance method involves the accurate measurement of nutrient intake, for comparison with accurate measures of all possible outputs of that nutrient via the urine, feces, and other potential routes of loss (Figure 1.3). If there is a state of balance, that is, intake and output are at equilibrium, it can be assumed that the body is saturated with respect to that nutrient and has no need for either uptake or storage. This technique can be applied to almost any nutrient and by repeating balance measures at different levels of intake it is possible to determine estimates of requirements for specific nutrients. The balance model works on the assumption that in healthy individuals of stable weight, the body pool of a nutrient will remain constant. Day-to-day variation in intake can be compensated by equivalent variation in excretion. The highest level of intake at which balance can no longer be maintained will indicate the actual requirement of an individual for that nutrient.

Nitrogen balance studies were used to determine human requirements for protein (Millward et al.,
Research Highlight 1 Strategies for combating vitamin A deficiency (VAD)

VAD is one of the most common forms of malnutrition on a global scale (West, 2003), with greatest prevalence in Africa, Central and South America, South and Southeast Asia. Subclinical VAD blights the lives of up to 200 million children every year and is a causal factor in up to a million cases of childhood blindness and up to a million deaths of children under the age of 5 years. VAD is also responsible for stunted growth in children and may cause blindness in women with increased demands for vitamin A, due to pregnancy or lactation. In 1990, the World Health Organization pledged itself to the virtual elimination of VAD by the year 2000. The strategies used to achieve this goal provide useful examples of how all common nutrient deficiencies might be prevented at a population level. Three main approaches have been used to tackle VAD:

1. Diet diversification. For many populations in areas where VAD is common, the range of staple foods consumed is very limited. For example, rice is the basis of most meals for many in Southeast Asia. Rice is a poor vitamin A source. Diversification programs include health education and promotion of consumption of a greater range of foodstuffs and the development of home gardening to provide vitamin A sources. Faber et al. (2002) showed that a home gardening program in South Africa increased knowledge and awareness of VAD, improved availability of vitamin A sources and increased serum retinol concentrations in young children.

2. Supplementation. In most countries where VAD is common, children are now supplemented with vitamin A, using an oil capsule, two or three times a year, often coupling supplement doses with other public health activities such as immunizations. Berger et al. (2008) highlighted the major disadvantage of supplementation, which is that it fails to reach all those in need of supplements. For VAD, those most at risk are preschool children who have less access to school-based supplementation programs. Often the poor and those most in need of supplements are least likely to receive them. Supplementation is expensive, which may reduce efficacy of the approach in impoverished countries (Neidecker-Gonzales et al., 2007).

3. Fortification. Fortification involves the addition of nutrients to staple foods at the point of their production, thereby increasing the amount of nutrient delivered to all consumers of that foodstuff. VAD in several countries has been tackled using this strategy. Red palm oil is widely available in many VAD-affected areas and is a rich source of ß-carotene. In India and parts of Africa, the addition of this oil to other oils traditionally used in cooking, and to snacks, has been shown to effectively increase vitamin A intake by the general population (Sanjivini et al., 1999). Zagri et al. (2003) showed that introducing red palm oil to a population in Burkina Faso was highly effective in reducing occurrence of VAD. A similar approach involves increasing the vitamin A content of crops such as rice, either through genetic modification (e.g., “golden rice”) or traditional plant breeding (Mayer, 2007).

Such studies involved experiments in which healthy subjects were recruited and allocated to consume dietary protein at specified levels of intake. After 4–6 days of habituation to these diets, urine and feces were collected for determination of nitrogen losses over periods of 2–3 days. On this basis, it was possible to state dietary protein requirements for different stages of life as being the lowest level of protein intake that maintained nitrogen balance in healthy individuals, maintaining body weight and engaging in modest levels of physical activity. Nitrogen balance studies are problematic in several respects, including the fact that 24-h urine collections used in such studies are often incomplete, because studies may fail to allow sufficient

Nutrient balance = Input − Output

Balance = 0 indicates that there is no net storage or loss of nutrient.
Positive balance indicates that there is net deposition of nutrient to the body pool.
Negative balance indicates that there is net loss of nutrient.

Figure 1.3 Determining nutrient requirements using the balance method. Precise measurements of nutrient intake and of output by all possible routes enable determination of nutrient requirements. The highest level of intake at which balance can no longer be maintained will indicate the actual requirement of an individual for that nutrient.
time for subjects to habituate to their experimental diet and because factors such as unobserved infection, stress, or exercise may increase demand for protein. It has also been impossible to use balance studies to examine protein requirements for all age groups and in all health situations, so requirements for pregnant and lactating women and for children are based on balance studies in young adults and make estimates of allowances for tissue deposition, growth, and milk synthesis and secretion.

1.2.5 Overall nutritional status

The diet delivers a multitude of components rather than single nutrients, and it is unlikely that any individual will have a diet that perfectly achieves balance for all of them. For example, an individual can be in balance for protein, while consuming more energy than is required and insufficient iron to meet demand. Hence, it is often not appropriate to discuss overall nutritional status of an individual without consideration of nutritional status with respect to specific nutrients.

Whether considering the overall nutritional status of an individual, examining nutritional status with respect to a specific nutrient, or investigating the nutritional status of a population, it is important to take into account a broad range of factors. It should be clear from the above discussions that intake is just one component of the supply side of the balance model. Nutritional status is only partly determined by the food that is being consumed. Nutritional status also depends upon the activities and health status of the individuals concerned. Trauma and high levels of physical activity will increase demand, while a sedentary lifestyle will decrease demand. Most important though is the stage of life of the individuals under consideration. Physiological demands for nutrients vary to a wide degree, depending on age, body size, and gender. The impact of variation within the diet upon health and well-being is largely, therefore, governed by age and sex.

1.3 Nutrition requirements change across the lifespan

Nutritional status is determined by the balance between the supply of nutrients and the demand for those nutrients in physiological and metabolic processes. So far in this chapter, we have seen that both sides of the supply–demand balance equation can be perturbed by a variety of different factors. Intake, for example, can be reduced in circumstances of poverty, while demand is elevated by physiological trauma. The main determinants of demand are, however, shaped by other factors such as the level of habitual physical activity (which will increase energy requirements), by gender, by body size, and by age. It is this latter factor that provides the focus of this book.

The demand for nutrients to sustain function begins from the moment of conception. The embryonic and fetal stages of life are the least understood in terms of the precise requirements for nutrition, but it is clear that they are the life stages that are most vulnerable in the face of any imbalance. Demands for nutrients are high in order to sustain the rapid growth and the process of development from a single-celled zygote to a fully formed human infant. An optimal balance of nutrients is essential, but the nature of what is truly optimal is difficult to dissect out from the competing demands of the maternal system and the capacity of the maternal system to deliver nutrients to the fetus. The embryo and fetus represent a unique life stage from a nutritional perspective, as there are no nutrient reserves and there is a total dependence upon delivery of nutrients, initially by the yolk sac and later by the placenta. The consequences of undernutrition at this stage can be catastrophic, leading to miscarriage, failure of growth, premature birth, low weight at birth, or birth defects (MRC Vitamin Study Group, 1991; Godfrey et al., 1996; El-Bastawissi et al., 2007). All of these are immediate threats to survival, but it is also becoming clear that less than optimal nutrition at this stage of life may also increase risk of disease later on in life (Langley-Evans, 2006).

After birth the newborn infant has incredibly high nutrient demands that, in proportion to body weight, may be two to three times greater than those of an adult. These demands are again related to growth and the maturation of organ systems as in fetal life. Growth rates in the first year of life are more rapid than at any other time, and the maturation of organs such as the brain and lung continues for the first 3–8 years of life. Initially, the demands for nutrients are met by a single food source, milk, with reserves accrued from the mother toward the end of fetal life compensating for any shortfall in supply of micronutrients. In later infancy, there is the challenge of the transition to a mixed diet of solids (weaning), which is
a key stage of physiological and metabolic development. The consequences of imbalances in nutrition can be severe. Infants are very vulnerable to protein-energy malnutrition and to micronutrient deficiencies, which will contribute to stunting of growth and other disorders. Iodine deficiency disorders and iron deficiency anemia can both impact upon brain development, producing irreversible impairment of the capacity to learn. Obesity is now recognized as a major threat to the health of children in the developed countries. In this age group, it is not simply a product of excessive energy intake and low-energy expenditure. Increasingly, we are seeing that the type or form of foods consumed at this time can influence long-term weight gain, with breast-fed infants showing a lower propensity for obesity than those who are fed artificial formula milks (Arenz et al., 2004; Bayol et al., 2007).

Beyond infancy, nutrient demands begin to fall relative to body weight, but still remain higher than seen in adulthood through the requirement for growth and maturation. These demands are at their greatest at the time of puberty when the adolescent growth spurt produces a dramatic increase in height and weight that is accompanied by a realignment of body composition. Proportions of body fat decline and patterns of fat deposition are altered in response to the metabolic influences of the sex hormones. Proportions of muscle increase and the skeleton increases in size and degree of mineralization. Nutrient supply must be of high quality to drive these processes, and in absolute terms (i.e., not considered in proportion to body size), the nutrient requirements of adolescence are the greatest of any life stage. However, adolescents normally have extensive nutrient stores and are therefore more tolerant of periods of undernutrition than preschool children (1–5 years).

The adult years have the lowest nutrient demands of any stage of life. As growth is complete, nutrients are required solely for the maintenance of physiological functions. The supply is well buffered through stores that protect those functions against adverse effects of undernutrition in the short term to medium term. In developed countries, and increasingly so in developing countries, the main nutritional threat is overweight and obesity, as it is difficult for adults to adjust energy intakes against declining physiological requirements and the usual fall in levels of physical activity that accompany aging. Reducing energy intake, while maintaining adequate intakes of micronutrients, is a major challenge in elderly individuals. Chronic illnesses associated with aging can promote undernutrition through increased nutrient demands, while limiting appetite and nutrient bioavailability.

For women, pregnancy and lactation represent special circumstances that may punctuate the adult years and which increase demands for energy and nutrients. Nutrition is in itself an important determinant of fertility and the ability to reproduce (Hassan and Killick, 2004). In pregnancy, provision of nutrients must be increased for the growth and development of the fetus and to drive the deposition of maternal tissues. For example, there are requirements for an increase in size of the uterus, for preparation of the breasts for lactation and for formation of the placenta. To some extent, the mobilization of stores and adaptations that increase absorption of nutrients from the gut serve to meet these increased demands, but as described above, imbalances in nutrition may adversely impact upon the outcome of pregnancy. Lactation is incredibly demanding in terms of the energy, protein, and micronutrient provision to the infant via the milk. As with pregnancy, not all of the increase in supply for this process depends upon increased maternal intakes, and in fact women can successfully maintain lactation even with subclinical malnutrition. Adaptations that support and maintain breast-feeding may impact upon maternal health. For example, calcium requirements for lactation may be met by mobilization of bone mineral, and if not replaced once lactation has ceased, could influence later bone health. However, although nutritionally challenging, most evidence suggests that lactation is of benefit for maternal health and actually contributes to reduced risk of certain cancers and osteoporosis (Ritchie et al., 1998; Danforth et al., 2007).

Lifespan factors clearly impact upon nutritional status as they are a key determinant of both nutrient requirements and the processes that determine nutrient supply. In studying relationships between diet, health, and disease, one of the major challenges is to assess the quality of nutrition in individuals and at the population level. Tools used for these nutritional assessments will be described in the next section.

1.4 Assessment of nutritional status

The assessment of nutritional status is necessary in a variety of different settings. Working with individuals
in a clinical setting, it may be necessary to assess dietary adequacy in order to plan the management of disease states, or to make clinical diagnoses. Public health nutritionists require data on dietary adequacy at a group level, in order to make assessments of the contribution of nutritional factors to disease risk in the population and to develop public health policies or intervention strategies. Nutritional assessment is also a critical research tool used in determining the relationships between diet and disease. These situations, which rely on considerations of the likelihood of nutritional deficit or excess at the individual or population level, use tools that aim either to measure intakes of nutrients, or the physiological manifestations of nutrient deficit or excess within the body. Tools for nutritional assessment include anthropometric measures, dietary assessments, determination of biomarkers, and clinical examination.

1.4.1 Anthropometric measures

Anthropometric methods make indirect measurements of the nutritional status of individuals and groups of individuals, as they are designed to estimate the composition of the body. Table 1.4 provides a summary of the commonly used anthropometric techniques. Information about relative fatness or leanness can be a useful indicator of nutritional status since excess fat will highlight storage of energy consumed in excess, while declining fat stores and loss of muscle mass are indicative of malnutrition. Extremes within anthropometric measures, for example, the emaciation of cachexia, or morbid obesity, are useful indicators of disease risk or progression in a clinical setting. In children, serial measures of height and weight can provide sensitive measures of growth and development that can be used to highlight and monitor nutritional problems.

1.4.2 Estimating dietary intakes

Estimation of dietary intakes, either to determine intakes of specific macro- or micronutrients, or to assess intakes of particular foods, is a mainstay of human nutrition research. A range of different methods are applied, depending on the level of detail required. All approaches are highly prone to measurement error.

1.4.2.1 Indirect measures

The least accurate measures of intake are those that make indirect estimates of the quantities of foodstuffs consumed by populations. These techniques are used to follow trends in consumption between national populations, or within a national population over a period of time.

Table 1.4 Anthropometric measures used to estimate body composition and nutritional status

<table>
<thead>
<tr>
<th>Technique</th>
<th>Component of body composition estimated</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (weight/height²)</td>
<td>Weight relative to height</td>
<td>Does not distinguish between lean and fat mass. Does not measure the composition of the body</td>
</tr>
<tr>
<td>Skinfold thicknesses</td>
<td>Fat mass</td>
<td>Requires skill in measurement. Makes assumptions about the even distribution of fat in the subcutaneous layer</td>
</tr>
<tr>
<td>Waist circumference or waist–hip ratio</td>
<td>Fat distribution</td>
<td>A good indicator of abdominal fat deposition. Requires set protocols for measurement</td>
</tr>
<tr>
<td>Mid-upper arm circumference</td>
<td>Muscle mass</td>
<td>Prone to measurement error. Unsuitable for some groups (e.g., adolescents) with rapidly changing fat and muscle patterns. Good indicator of acute malnutrition</td>
</tr>
<tr>
<td>Bioimpedance</td>
<td>Fat mass</td>
<td>Influenced by hydration status of subjects</td>
</tr>
<tr>
<td>Underwater weighing</td>
<td>Body density, fat, and lean mass</td>
<td>Requires subjects to undergo training for an unpleasant procedure. Underestimates fat mass in muscular individuals</td>
</tr>
<tr>
<td>Isotope dilution</td>
<td>Body water</td>
<td>Influenced by fluid intake of subject. Analytically difficult and expensive</td>
</tr>
<tr>
<td>Scanning techniques (NMR, DXA)</td>
<td>Proportions and distribution of lean and fat mass</td>
<td>Expensive, restricted access to scanners. Use ionizing radiation, so unsuitable for children and pregnant women</td>
</tr>
</tbody>
</table>
Food balance sheets are widely used by the United Nations Food and Agriculture Organization (FAO) to monitor the availability of foods, and hence nutrients, within most nations of the world and are published on an annual basis. They allow temporal trends to be monitored easily and apply a standardized methodology on a global scale. A food balance sheet is essentially compiled from government records of the total production, imports, and exports of specific foodstuffs. This allows the quantity of that foodstuff available to the population to be calculated (available food = production + imports − exports). Dividing that figure by the total number of people in the population allows the daily availability per capita to be estimated. Figure 1.4 shows data abstracted from the 2004 FAO food balance sheets, indicating how daily availability of protein from plant and animal sources varies with different regions of the world.

Food accounts are a similar approach to estimating food availability, but instead of collecting data on a national scale, they are used to measure the food available to a household or an institution (e.g., a nursing home). By compiling an inventory of food stored at the start of a survey, monitoring food entering the setting (often measured by looking at invoices and receipts from food shopping) and taking into account any food grown in the setting, it is possible to calculate the food available per person over the period of the survey. As with the food balance sheet, this method does not allow accurate estimation of individual food intakes and does not allow for food wastage, but the food account can provide data on dietary patterns of families or similar groups at low cost and over an extended period of time.

1.4.2.2 Direct measures

Direct measures of nutrient intake collect data from individuals or groups of individuals and, in addition to their obvious application to clinical circumstances, are well suited to research in human nutrition and epidemiology. Although more robust than the indirect estimates described above, all direct measures of intake are prone to bias and error and results must always be interpreted with caution.

**Dietary recall methods**

The dietary recall method is not only one of the best methods for examining nutrient intakes in a clinical setting, but it may also be used in research. One of the major disadvantages of the method is the need for a trained interviewer to spend a period of time with
the patient or research subject to elicit detailed information on all food and drink consumed over a recent period of time. Most dietary recalls will be based upon intake over the preceding 24 h, but in some cases may look at 48-h or 72-h periods. Information obtained in this way can then be coded for detailed analysis of energy and nutrient intakes using appropriate nutritional analysis software or food tables. Dietary recall methods can generate detailed information on types of food consumed and portion sizes. The use of photographic food atlases showing portion sizes for commonly consumed foods can enhance the quality of this quantitative information. Spending time interviewing a subject also makes it relatively easy to obtain recipes used in cooking, and information about cooking techniques (e.g., use of oils in frying). Like all methods of estimating nutrient intake, the dietary recall is prone to inaccuracy due to underreporting and overreporting of food intake by certain groups of people. It is also dependent upon the memory of the subject and so loses accuracy when attempting to estimate habitual intakes.

**Food record methods**

Food records, or diaries, administered to subjects for completion in their own time are widely regarded as the most powerful tool for estimation of nutrient intakes. Subjects keep records for extended periods of time (usually 3–7 days) and note down all foods and beverages consumed at the time they are consumed. Portion sizes can be recorded in a number of different ways, with the subject most frequently either noting an estimated intake in simple household measures (e.g., 2 tablespoons of rice, 1 cup of sugar), or an intake estimated through comparison to a pictorial atlas of portion sizes. To improve the quality of the data, intake can be accurately determined by weighing the food on standardized scales, taking into account any wastage (a weighed food record). Frohlich and Maxwell (2003) found that in studying intakes of children aged 6–16, a food record with a photographic atlas of portion sizes gave a good level of agreement with weighed records. In some settings, it is possible for a researcher to do the weighing, thereby reducing influences upon the subject consuming the food. Inaccuracies in estimates of portion sizes are a major problem associated with food record methods, particularly with some subgroups in the population, and methods should be chosen that best serve the purpose of the dietary survey. Surveys of small groups of well-motivated people in a metabolic unit lend themselves well to weighed record methods, while in large surveys of free-living individuals, these are rarely practical.

Food records have a number of strengths compared to other methods of estimating intake. Complex data on meal patterns and eating habits can be obtained through study of food diaries and this information can supplement estimates of nutrient intake. By obtaining records for periods of 5–7 days, the intakes of most micronutrients can be estimated with some degree of confidence, in addition to energy and macronutrients. For some nutrients, it is suggested that records of 14 or more days may be required (Block, 1989). The major disadvantage of the food record approach is the reliance upon the subject to complete the record fully and accurately. Maintaining a food record is burdensome and it is often noted that the degree of detail and hence accuracy will be greater in the first 2–3 days of a 7-day record compared to later days. The act of recording intake, especially if a weighed record is used, can change the eating behavior of subjects and hence lead to an underestimate of habitual intakes.

Like other direct methods, the food record is prone to underreporting and overreporting of energy and nutrient intakes among certain subgroups in the population, due to the tendency of individuals to report intakes that will reflect them in the best possible light to the researcher. Bazelmans et al. (2007) studied a group of elderly individuals, comparing self-reported intakes on a 24-h food record to estimates of likely energy intake based upon the subjects’ basal metabolic rates calculated using the Schofield equation. It was found that approximately 20% of men and 25% of women significantly underreported or overreported their energy intakes. Subjects with a BMI under 25 kg/m² (i.e., in the ideal weight range) were most likely to overreport, while 13% of those with BMI in the overweight range and 27% of those with a BMI in the obese range were found to have underreported their energy intake. Obese and overweight women are frequently found to underreport intakes in dietary surveys.

**Food frequency questionnaire methods**

Food frequency questionnaire methods involve the administration of food checklists to individuals, or groups of individuals, as a means of estimating their habitual intake of foods, or groups of foods. Subjects
work through the checklist and, for each foodstuff, indicate their level of consumption (i.e., number of portions) on a daily, weekly, or monthly basis. Semi-quantitative food frequency questionnaires also collect information on typical portion size.

Food frequency questionnaires can vary in their complexity and length. Often a questionnaire will consist of 100–150 food items and will therefore allow for a comprehensive coverage of the dietary patterns of a subject. Some questionnaires are much shorter and may be focused upon a particular food group or the main sources of a specific type of nutrient. For example, Block and colleagues (1989) developed a questionnaire with just 13 items in order to identify individuals who had high intakes of fat. This was used as a preliminary screening tool to select subjects for a more detailed investigation.

Food frequency questionnaires have many desirable attributes for researchers wishing to estimate intakes in large populations. They are self-administered by the subject, are generally not time consuming, and are unlikely to influence eating behaviors. Data entry can sometimes be automated, reducing the analytical burden for the researcher. Moreover, the food frequency questionnaire provides an estimate of habitual intake over a period of months or even years, as opposed to the snapshot obtained by looking at a food record representing just a few days. However, the food frequency questionnaire can be a weak tool when considering portion sizes and is therefore less effective for estimating micronutrient intakes than a food record. Food frequency questionnaires must also be valid for the population to be studied as the range of foods consumed will vary with age and various other social and demographic factors. For example, if attempting to survey nutrient intakes in a population with a wide ethnic diversity, the foods and food groups included on the questionnaire needs to reflect that level of diversity. A questionnaire that fails to include staple foods consumed by particular ethnic groups will inevitably underestimate their intake.

1.4.3 Biomarkers of nutritional status

Biomarkers of nutritional status are measures of either the biological function of a nutrient, or the nutrient itself, in an individual, or in samples taken from individuals. These measures can often provide the earliest indicator of a nutrient deficit as they register subnormal values ahead of any clinical symptoms. Biomarkers are therefore useful in monitoring the prevalence of nutrient deficiency, measuring the effectiveness of the treatment of deficiency, and assessing preventive strategies. Given the huge difficulties of making accurate assessments of dietary intakes, as described above, biomarkers provide a useful means of validating dietary data and are often measured as adjuncts to dietary surveys. For example, in the UK National Diet and Nutrition Survey of preschool children (Gregory et al., 1995), measurements of circulating iron status were used to back up food record data collected on iron intakes. The doubly labeled water method (Koebnick et al., 2005) can be used to validate energy intakes estimated using dietary records or other means.

Biomarkers of nutritional status are often regarded as being more objective than other indices. They include functional tests, and measurements of nutrient concentration in easily obtained body fluids or other material. The latter type of measurement can be a static test, which is performed on one occasion, or may be repeated at intervals to monitor change over time. The relative merits of these approaches will be discussed later in this section.

Functional tests measure biological processes that are dependent upon a specific nutrient. If that nutrient is present at suboptimal concentrations in the body, then it would be expected that the specific function would decline. The dark adaptation test is classic example of a functional test, which determines vitamin A status. The dark adaptation test measures visual acuity in dim light after exposure to a bright light that desensitizes the eye. Reformation of rhodopsin within the retina is dependent upon the generation of cis-retinol and thus the visual adaptation in the dark will be related to vitamin A status. Measurement of the excretion of xanthurenic acid is a functional test for vitamin B6 (pyridoxine) status. Xanthurenic acid is a breakdown product of tryptophan and kynurenic acid and is formed via pyridoxine-dependent reactions. Nonfunctional measures of biomarkers typically involve direct measures of specific nutrients in simply obtained samples from individuals. These are most commonly samples of blood (plasma, serum, or red cells), or urine, but could include feces, hair, or, more rarely, biopsy material from adipose tissue or muscle. Static tests provide a snapshot of the nutrient concentration in the sample at a given point in time and could be misleading as they often provide an indicator
of immediate intake rather than habitual intake. For example, plasma zinc concentrations will vary hugely from day to day, reflecting ongoing metabolic fluxes, and fall by up to 20% following a meal (King, 1990). Wherever possible, repeated tests should be taken to increase confidence in the measured biomarker, or tests should be performed in a sample that provides a stronger indicator of habitual intake. In the case of zinc, plasma measurements are of limited value as most zinc is held in functional forms within tissues and less than 1% of the total pool is in circulation. Red or white blood cell zinc concentrations could be used as a more robust biomarker, as could white cell metallothionein concentrations (metallothionein is a key zinc-binding protein). Hair zinc concentrations give a better intake of long-term status. Zinc is deposited in hair follicles slowly over time and so using this sample source removes the influence of shorter term fluctuations in status. Similarly, the EURAMIC study (Kardinaal et al., 1993) used measures of α-tocopherol and β-carotene in biopsies of adipose tissue to assess intakes of these vitamins. As fat-soluble vitamins are stored in this tissue, this gave an indicator of habitual intake over several weeks.

The levels of a measured biomarker are only useful in estimating nutritional status if there is a linear relationship between the measurement and intake. In addition to this, and the need to make measurements in a relevant sample, it is important to appreciate the nondietary influences on the biomarker that could skew the interpretation of any measurement. Some measurements could be perturbed by the presence of disease, or the use of medications to treat disease. For example, serum albumin concentration can be used as a marker of dietary protein intake. Serum albumin declines with low protein intakes and in clinical settings can provide a predictor of morbidity and mortality associated with protein-energy malnutrition. However, as described earlier in this chapter, serum albumin concentrations also fall with infection and inflammation, and in seriously ill patients, albumin could be administered as an element of any intravenous fluid infusion. Either situation would render albumin useless as a marker of nutritional status. Like any measure of nutritional status, biochemical indices can lack specificity and should ideally be used as part of a battery of tests based upon dietary assessments, biochemical measures, anthropometry, and, if appropriate, clinical assessment.

1.4.4 Clinical examination
Performing a thorough physical examination and obtaining a detailed patient history is an effective method of determining symptoms associated with malnutrition in individuals. This approach can be most useful when dealing with children, where the paucity of nutrient stores can mean that clinical symptoms develop very quickly, as opposed to adults where the symptoms are generally a sign of chronic malnutrition. Obtaining a patient history can highlight key points that are missed when assessing dietary intake, or using anthropometric measures. Reported loss of appetite, loss of blood, occurrence of diarrhea, steatorrhea, or nausea and vomiting may all be indicators of potential causes of malnutrition and should trigger further investigation. Physical examination can assess the degree of emaciation of a potentially malnourished individual. Careful assessment of the hair, skin, nails, eyes, lips, tongue, and mouth can also highlight specific nutrient deficiencies. Bleaching of the hair is indicative of protein malnutrition, while cracking of the lips can suggest deficiency of B vitamins such as riboflavin. Pallor of the skin and spooning of the nails are clinical signs of iron deficiency. Evidence of rough spots on the conjunctiva of the eye will accompany early stages of vitamin A deficiency.

1.5 Dietary reference values
Dietary reference values (DRVs) are standards that are set by the health departments of governments in a number of countries around the world. DRVs are guidelines that can be used to define the composition of diets that will maintain good health. There are many complex systems of DRVs used in different countries. These vary according to national health priorities and policies, according to predominant health status, socioeconomic status, body mass and rates of growth, and with local factors, for example, the composition of foods or other lifestyle influences, that determine the absorption and hence bioavailability of nutrients (Pavlovic et al., 2007). DRVs are used in a variety of different ways. While some systems, such as those developed for the UK, are generally intended to be used only with populations or subgroups within populations, others (e.g., the US Dietary Reference Intakes) are used in providing dietary guidance for individuals. On a population level,
the DRVs are useful yardsticks with which to assess the adequacy of the diet of a population and hence protect individuals within that population against the adverse consequences of either deficiency or excess. By using DRVs as standard measures against which dietary survey data can be compared, it is possible to estimate the prevalence of risk of deficiency for specific nutrients within a population.

In some countries, regular surveys of national dietary patterns among age and gender specific groups, for example, the UK National Diet and Nutrition Surveys (Gregory et al., 1995; Henderson et al., 2002) or the US National Health and Nutrition Examination Surveys, are compared to the DRVs in order to highlight potential nutrient deficiencies. In other countries, food supply data at the national level, such as the food balance sheets collected by the FAO, can be used to crudely estimate the average per capita availability of energy and the macronutrients and compared to international standards. Although such data are prone to error, as described above, they can be used for tracking trends in the food supply and determining availability of micronutrient-rich foods. By comparison of such data with DRVs, it is possible to uncover evidence of gross inadequacies in the quality of the diet across whole populations (but not sub-groups such as children or the elderly). Standards for nutrient provision based upon DRVs can also be used in the planning of food supplies to regions (e.g., in humanitarian aid), or in menu planning for caterers in hospitals, schools or other institutional settings. Many of the food labeling schemes used in supermarkets are based upon published DRVs for specific nutrients.

1.5.1 The UK dietary reference value system

In 1979, the UK set a series of DRVs termed the recommended daily amounts (RDAs). In 1991, a new series of DRVs were published to replace these RDA values, as they were considered to be prone to misunderstanding and misuse. The term “recommended” wrongly suggests a level of intake that an individual must consume on a daily basis in order to avoid adverse consequences. The new system of DRVs produced by the Committee on Medical Aspects of Food Policy (COMA, DoH, 1991) therefore dropped the word recommended and was developed to indicate different levels of intake that would be suitable for healthy populations, broken down by age and gender. In setting the DRVs, COMA reviewed research for each macro- and micronutrient in order to determine the levels of intake that are necessary to maintain normal health and physiological function. In considering the available evidence, the key issues to be explored for each nutrient were as follows: (1) What level of intake is necessary to maintain circulating or tissue concentrations within normal ranges? (2) What level of intake is necessary to avoid clinical deficiency in individuals or in populations? (3) What level of intake has been established as being effective in treating clinical deficiency? (4) What level of intake has been shown to maintain normality in a biomarker of adequacy?

As shown in Figure 1.5, the relationship between nutrient intake and disease risk is not linear. At low levels of intake, the probability of adverse consequences (deficiency disease, loss of physiological function) is elevated. With rising intakes, the probability of such consequences declines to zero as intakes provide the requirements of most of the individuals in a population. At higher intakes, the probability of adverse consequences associated with overnutrition begins to rise. In developing a set of DRVs appropriate for a population like the UK, in which the economic wealth of the population makes overnutrition more likely than undernutrition, this continuum between risk and intake must be recognized.

In common with the US and other countries (see below), the UK DRVs were developed to map onto the expected distribution of nutrient requirements in a population. As shown in Figure 1.6, this would usually be expected to follow a normal distribution, which actually relates to the left hand side of the distribution of risk plotted against intake (Figure 1.6). In this context, the mean value (midpoint) in a normal distribution represents the requirements of 50% of the population. At intakes close to the EAR, it can be assumed that for 50% of people, this will be sufficient, but that for up to 50%, nutritional status would be compromised. The other DRVs are set at points that are two standard deviations either side of the mean. The reference nutrient intake (RNI) is the upper value and within the normal distribution would represent a level of intake that should meet the requirements of 97.5% of the population. When a population is consuming a
nutrient at a level close to the RNI it can be assumed that for most individuals this intake will be sufficient or will exceed true requirements, but that for the 2.5% of individuals with extremely high requirements nutritional status would be compromised. The lower reference nutrient intake (LRNI) lies at the lower end of the normal distribution and represents a level of intake that would meet the requirements of just 2.5% of the population. If a population was consuming a nutrient at a level close to the LRNI, it could be assumed that for most individuals, this will be insufficient and that deficiency disease would be rife. For some nutrients (e.g., pantothenic acid, biotin, and molybdenum), COMA had insufficient data to be able to derive estimates of requirements, but recognized the biological importance of these compounds in the diet. In the absence of extensive information, the Safe Intake was set. This is an upper level of intake set at a point likely to prevent deficiency and avoid toxicity. Safe Intakes are of greatest importance to vulnerable groups in the population such as infants and children (DoH, 1991).

The DRVsa are published as a comprehensive series of tables (DoH, 1999), which, for most nutrients,
provide reference values for males and females separately and for different age groups (typically 0–12 months, 1–3 years, 4–6 years, 7–10 years, 11–14 years, 15–18 years, 19–50 years, and 50+ years). To reflect increased demands for nutrients during pregnancy and lactation, some tables show additional increments of intake for pregnant and breast-feeding women. For micronutrients and trace elements, published values include all three terms (LRNI, EAR, and RNI). With respect to protein, only EAR and RNI values were determined. Given that excess energy consumption is a driver of obesity and related disorders, it is undesirable to set reference values at an upper point such as the RNI, as a population that consumed energy at that level would be expected to have a high prevalence of related adverse effects such as obesity. DRV tables for energy therefore include only the EAR value, and include modifiers to allow for levels of physical activity.

Humans have a requirement for essential fatty acids and children can develop clinical deficiency of linoleic acid. There are DRVs that indicate minimum intakes of essential fatty acids, but as low intakes of the majority of lipids are not associated with adverse health effects, the three main DRV terms are not applied to fats. Instead, COMA set population average guidelines for consumption of saturated, monounsaturated, and polyunsaturated fats based on percentage of dietary energy intake. Population averages are designed to encourage lower intakes of non-milk extrinsic sugars and fats, while increasing intakes of starch and nonstarch polysaccharides (Whitbread, 1992).

In the UK, the DRVs are not intended to be guidelines for individuals. It is generally considered a fruitless activity to make estimates of nutrient intakes for individuals, given problems with obtaining accurate data on food intake and because it is impossible to estimate what the true requirements for any individual are likely to be. In making assessments of dietary intakes of groups within a population, the RNI is considered to be the most important benchmark for comparison. The nearer the average intake of a group within a survey is to the RNI, the less likely it is that any individual within that group will have an inadequate intake. However, the LRNI value provides a better indicator of the likely risk of widespread deficiency, whether clinical or subclinical. The nearer the average intake of the group is to the LRNI, the greater is the probability that some individuals within that group are not consuming that nutrient at a level adequate to meet their requirements. An example of the DRVs in use is provided by the study of Cowin and colleagues (2000). This group assessed the nutrient intakes of 1026 18-month-old infants living in the southwest of England, using a 3-day unweighed dietary record. By comparing recorded intakes with the RNI values for micronutrients, the survey concluded that intakes of most nutrients were adequate in this population group. However, for iron and vitamin D, it was noted that mean intakes were considerably below the RNI, suggesting that these nutrients could be a cause for concern in this population group. Indeed, for iron, where the LRNI is 3.7 mg/day for infants, it was noteworthy that the 2.5% of the population with the lowest intakes (i.e., the group who might be expected to be meeting their requirements despite low intake) consumed only 2.4 (girls) to 2.7 (boys) mg/day, figures well below the LRNI. Data of this kind can be the start point for further studies that identify the causes of deficiency and for formulating appropriate interventions and dietary recommendations (Cowin et al., 2001).

Although not intended for use with individuals, the DRVs could still be used in a clinical setting. When working with healthy individuals, assessments of dietary intakes that indicate intakes below or close to the LRNI could indicate a dietary problem and might be a stimulus for a more in-depth assessment of biochemical or clinical indicators of nutritional status. In planning a diet for an individual, delivery of nutrients at the level of the RNI would be a basic priority to ensure optimal health.

1.5.2 Dietary reference values in other countries

The UK system described above is just one example of DRVs defined with the purpose of guiding the provision of healthy nutrition on a population-wide scale. Many other countries use similar systems that have also been derived to map against the normal distribution of nutrient intake ranges for provision of nutrient demands. This approach is generally applicable for westernized countries where the nutrition-related
health concerns are usually focused on the consequences of nutrient excess rather than nutrient deficiency. Table 1.5 summarizes the dietary reference terms used in North America, Australia, and New Zealand.

Among the countries of the European Union, there is considerable variation in the terminology used to describe DRVs and in the precise nature of recommendations made for particular population groups, most particularly children. There are suggestions that the European countries should harmonize their DRV systems (Pavlovic et al., 2007), and that in the course of generating a common system, a further review of the evidence could be conducted to determine whether regional variation reflecting health status and other local issues is necessary or desirable. The Scientific Committee on Food of the EU has defined three levels of DRVs: average requirement, population reference intake, and lowest threshold intake. In general intent, these terms map against the UK EAR, RNI, and LRNI values.

As in the UK, the countries of North America reviewed their existing reference values, originally set in 1941, and replaced them with a new comprehensive format in the early 1990s (Kennedy and Meyers, 2005). In Canada and the US, the EAR and RDA terms are exact equivalents of the UK EAR and RNI terms, but are used in a different manner to that seen in the UK. EAR is a term that would be used to estimate the prevalence of inadequate intakes in a population, but RDA is a term specifically intended for use with individuals. A habitual intake below this level would be associated with increased risk of dietary inadequacy.

In population surveys, however, comparing mean intakes to the RDA would tend to overestimate the likely prevalence of deficiency, as it is a figure set at a level where the requirements of 97.5% of the population are being met. This means that a significant proportion of the population is likely to be exceeding requirement (Kennedy and Meyers, 2005). For example, if the RDA for iron intake in children is 11.2 mg/day and the mean intake for a population is found to be 8.4 mg/day, it should not be assumed that deficiency will have a high prevalence. The majority of children in the population may be consuming well below the RDA value and still be achieving requirement. This could also be seen as a problem with the UK RNI. The tolerable upper level (UL) term is defined as the highest average daily nutrient intake level that is unlikely to result in adverse health effects for almost all individuals in a population. Effectively, individuals could use this as a guide to limit their intake, and at the population level it provides a benchmark against which estimates can be made of the likelihood of problems related to overnutrition. The AI term is similar to the UK Safe Intake in that it is used only where there is insufficient data to determine the EAR for a particular nutrient.

In Australia and New Zealand, the system of DRVs is broadly similar to that used in North America, except a fifth term (EER) is defined for energy. The EER comprises two separate terms. The estimated energy requirement for maintenance (EERM) is the energy intake that is estimated to maintain balance in healthy individuals or populations at a given level of physical activity and body size. The desirable estimated energy requirement (DEER) is the level of energy intake that should maintain energy balance in healthy individuals or populations of a defined gender, age, weight, height, and level of physical activity, consistent with optimal health. Although complex, this is an important distinction as the EERM represents an actual energy requirement of an individual or group of individuals, while the DEER allows calculation of energy references that can be used to guide weight loss in a clinical situation (National Health and Medical Research Council of Australia, 2006).

In less affluent countries where there is a high burden of malnutrition-related disease, the priorities of governments are different, and DRVs are set at levels

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**Table 1.5 Definitions of DRV terms used in the UK, North America, and Oceania**

<table>
<thead>
<tr>
<th>Region</th>
<th>Dietary reference terms</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>LRNI</td>
<td>Lower reference nutrient intake</td>
</tr>
<tr>
<td></td>
<td>EAR</td>
<td>Estimated average requirement</td>
</tr>
<tr>
<td>Safe intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US/Canada</td>
<td>EAR</td>
<td>Estimated average requirement</td>
</tr>
<tr>
<td></td>
<td>RDA</td>
<td>Recommended daily allowance</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td>Adequate intake</td>
</tr>
<tr>
<td></td>
<td>UL</td>
<td>Tolerable upper limit</td>
</tr>
<tr>
<td>AustralianNZ</td>
<td>EAR</td>
<td>Estimated average requirement</td>
</tr>
<tr>
<td></td>
<td>RDI</td>
<td>Recommended daily intake</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td>Adequate intake</td>
</tr>
<tr>
<td></td>
<td>EER</td>
<td>Estimated energy requirement</td>
</tr>
<tr>
<td></td>
<td>UL</td>
<td>Upper level of intake</td>
</tr>
</tbody>
</table>
that are more appropriate for a setting where main-
taining and monitoring food security are the main
applications of the figures. Often the values used in these
situations are obtained from the FAO, and focus heav-
ily on setting levels of intake that will provide the basic
requirements of most of the population, and therefore
avoid widespread clinical nutrient deficiency.

Summary Box 1
Nutritional balance depends upon the supply of nutrients being
able to meet the physiological and metabolic demand for nutrients
to be used as structural components, or as substrates and cofac-
tors for metabolism. Undernutrition or overnutrition arises through
disturbance of this balance.

Undernutrition can result from either a decrease in intake or
an increase in the demand for nutrients. Increased demands are
often a consequence of physiological insult or stress, including
trauma, pregnancy, and lactation.

Prolonged undernutrition can lead to micronutrient deficiency
or malnutrition, which are common among infants and women in
developing countries and among the elderly and poor in developed
nations.

Stage of life is one of the most important determinants of
nutritional status, as the nature of demands for nutrients and the
way in which these demands are met undergo profound changes
over the human lifespan.

Nutritional status can be assessed using anthropometric meth-
ods, using different methods of measuring intake, through clinical
examination, or by measuring specific biomarkers. All methods are
limited in their scope and are prone to inaccuracy.

DRIs are standards for nutrient intake, which are set by gov-
ernments. They are used sexually as the basis of nutrition-related
advice and interventions. They can be used as research tools, as
guidance for meal planners and caterers, and for the monitoring
of food security at a national level.

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Nutrition: A Lifespan Approach


Self-Assessment Questions
Assess your understanding of the concepts outlined in this chapter using the following questions:

1. Explain why requirements for energy and protein increase following physical trauma.
2. Describe the main causes of malnutrition.
3. What is meant by the term nutritional status? How can it be assessed in individuals?
4. What are the main advantages and disadvantages of methods used to assess nutrient intakes in populations?
5. Describe the systems of DRVs currently used in the UK and the US.
6. Discuss how DRVs are intended to be interpreted and explain how they are used in practice.