chapter 10:

DIET AND DISEASE

OBJECTIVES

After studying this chapter you should be able to:

- define the term *nutrient*;
- outline the types and roles of nutrients;
- list some of the common nutritional disorders;
- explain the causes of some common nutritional disorders;
- review the general methods for investigating nutritional disorders;
- discuss the treatment and management of some common nutritional disorders.

10.1 INTRODUCTION

Nutrition is concerned with food and how the body uses it. All nutrients must be ingested, and most of them digested, before they can be assimilated and used by the body. Carbohydrates, lipids and proteins are nutrients that are required in comparatively large amounts. Others, such as vitamins, minerals and trace elements, are also necessary but are required in much smaller quantities. Water is also necessary to support life. Nutrients have a variety of metabolic roles and are needed for normal growth, development and the maintenance of health. The body can make some nutrients from others that must be supplied in the diet; the former are **nonessential**, the latter **essential nutrients**. Specific daily nutritional requirements are determined by a number of factors and, indeed, vary throughout the life of any individual. The major factors concerned include the age, sex, physical activity and the general well-being of the person concerned and, in the case of females, menstruation, pregnancy and lactation. Good nutrition is essential for health and the prevention of diseases. Nutritional disorders may arise from a deficiency or, in some cases, an excess of some component of the diet.

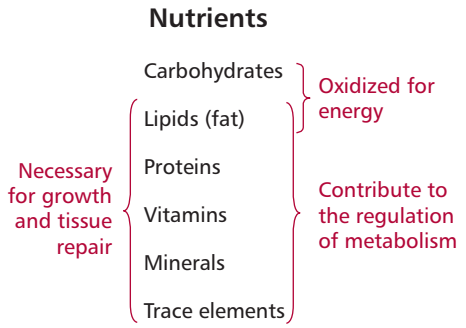


Figure 10.1 Overview of the general roles of nutrients.

10.2 DIET AND NUTRITION

Food is obviously needed to sustain life but a balanced diet is vital for good health. General evidence for good nutrition is a well developed body with an ideal weight (*Section 10.3*), good skin, including hair, and muscle tone, and physical and mental alertness. The food eaten by an individual constitutes the diet and it should supply appropriate amounts and proportions of a variety of substances, usually called nutrients. Some nutrients, the macronutrients, such as carbohydrates, lipids and proteins, are required in amounts that are large compared with the micronutrients, such as vitamins, minerals and trace elements, which are needed in much smaller quantities. Nutrients are needed to sustain a number of activities within the body if good health is to be maintained. They supply the raw materials required for growth and maintenance of tissues, include substances that help regulate metabolism, for example the cofactors and coenzymes necessary for enzyme activities and provide the energy to drive metabolism and maintain homeothermy. Nutrients vary in their contributions to these roles and there is also overlap between their contributions to each (*Figure 10.1*).

NUTRIENTS AND ENERGY

Diets are often described in terms of their energy content, despite the fact that they need to supply materials for needs other than just their energy provision (*Figure 10.1*). It is possible for a diet to supply an adequate amount of energy but be deficient in some essential raw materials, such as vitamins and minerals needed by the individual. A **balanced diet** is one that supplies adequate energy distributed appropriately between carbohydrates, lipids, and proteins and contains the necessary amounts of vitamins, minerals, trace elements, water and nondigestible fiber.

Nutritional energy is usually measured in joules or kilojoules. The number of joules required by any one person needs to be matched to their energy output (*Table 10.1*). The term **recommended daily amount (RDA)** was originally used by the UK Department of Health in 1979 to define the amounts of certain nutrients needed by different groups within the population.

Group	Approximate daily energy requirements /kJ required per kg desirable body weight
Babies up to one year old	500
Children one to 10 years old	335–420
Male children 11–15 years old	270
Female children 11–15 years old	145
Sedentary males and most females	117
Physically active males and females	125
Males and females over 55 years old	117
Pregnant females (first trimester)	117–134
Pregnant females (second and third trimesters)	150–159
Lactating females	150–159

Table 10.1 Energy required to maintain body functions. For example, a physically active man weighing 70 kg requires $70 \times 125 = 875$ kJ (or 2080 kcalories) daily.

Unfortunately, RDAs were often used inappropriately to assess the dietary needs of individuals. Accordingly, in 1991, they were replaced with **dietary reference values** (**DRVs**) that are guidance values as to the amounts of energy and nutrients that should be ingested, rather than exact recommendations. Dietary reference values indicate the amount of energy or amount of an individual nutrient required by a group of a certain age range and sex for good health. The value of any DRV is given as a daily intake. However, in practice DRVs must be determined from the energy and nutrient intakes averaged from several days eating, because food intake and appetite vary from day to day. Groups for which DRVs have been set include seven groups of infants of both sexes from birth to age 10 years, four groups each for males and females between the ages of 11 and 50-plus, with extra groups for women who are pregnant or are lactating. The value of a DRV applies to healthy people, since patients who are unwell for whatever reason may have differing nutritional requirements. Dietary terms that are related to DRVs are the **estimated average requirement** (**EAR**), **reference nutrient intake** (**RNI**) and **lower reference nutrient intake** (**LRNI**). The EAR is the mean amount of energy or nutrient needed by a population, while the RNI is an amount of a nutrient that is greater than the dietary needs of 97.5% of that group. The LRNI is the amount of a nutrient sufficient to meet the requirements of 2.5% of a population. Note that most people will need more than the LRNI. *Figure 10.2* shows how EAR, RNI and LRNI are related. Finally, the **safe intake** is the amount judged to be sufficient for the needs of most people and anything below this level could be undesirable. This arbitrary value is given when there is simply insufficient evidence to establish reliable values for EAR, RNI or LRNI.

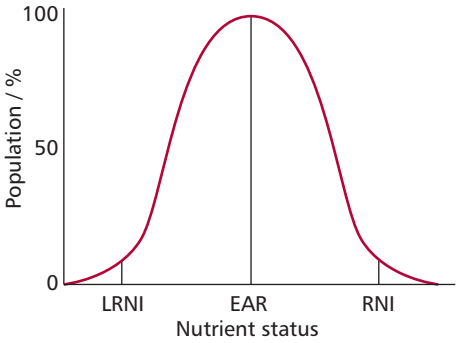


Figure 10.2 The relationships between EAR, RNI and LRNI.

CARBOHYDRATES

Carbohydrates have the general formula $(CH_2O)_n$. The main dietary carbohydrates (*Figure 10.3*) are mono- and disaccharide sugars, for example fructose, glucose, lactose and sucrose, and polysaccharides, mainly starch, and these are usually the major suppliers of energy. Current recommendations from the WHO suggest that 55% of dietary energy should be in the form of carbohydrates. Most of the carbohydrates should be in the form of starch with no more than 10–15% of energy intake in the form of sugars. However, dietary fiber or roughage largely consists of cellulose, a polysaccharide that cannot be digested and absorbed, although it may be metabolized by bacteria in the large intestine (*Chapter 11*). Foods rich in fiber include wholemeal cereals, flour, root vegetables, nuts and fruits. Dietary fiber stimulates peristalsis and protects against constipation and is known to reduce blood cholesterol and glucose and the incidence of colorectal cancers (*Chapter 17*). Communities that consume high fiber diets have relatively low incidences of these cancers.

Carbohydrates
bread
cereals
pasta
peas
potatoes
rice

Fats
butter
cheese
cooking oils
cream
lard
margarine
milk
nuts
oily fish
suet

Proteins
cheese
eggs
fish
meat
milk
potatoes
pulses

Figure 10.3 A selection of carbohydrate, fat and protein rich foods. Some foods, of course, contain more than one of these macronutrients.

LIPIDS

Dietary lipids are the fats and oils, both of which contain fatty acids that are concentrated sources of energy. Fats are also needed as carriers for the fat-soluble vitamins A, D, E and K. Fatty acids may be saturated or unsaturated, that is, they lack or contain double bonds respectively. The only difference between fats and oils is in their melting points which are related to their degree of unsaturation and chain length: oils are liquid at room temperatures, indicating a higher degree of unsaturation than fats which are solid at these temperatures. Dietary fats (*Figure 10.3*) consist largely of triacylglycerols together with small amounts of phospholipids and cholesterol. The WHO has recommended that total fats should not supply more than 30% of the energy intake of the diet.

Essential fatty acids

Humans lack the enzymes necessary for synthesizing certain unsaturated fatty acids necessary for health and these are **essential fatty acids** (**EFAs**).

Figure 10.4 A computer generated model of arachidonic acid. Oxygen atoms are shown in red, carbon in black and hydrogen in gray.

A number of fatty acids cannot be synthesized by the body including linoleic, linolenic and arachidonic acid (*Figure 10.4*) and are precursors of many biologically active and clinically relevant molecules, such as the eicosanoids (prostaglandins, thromboxanes, prostacyclins and leukotrienes). These molecules act like hormones and mediate a wide range of physiological activities affecting, for example inflammatory responses, blood pressure and clotting, reproductive activities and the sleep–wake cycle. Their actions are local, affecting only cells near their sites of production, and they act at low concentrations via second messengers (*Chapter 7*).

Humans, like all mammals, lack the enzymes needed to form a double bond beyond C-9 or within the terminal seven carbon atoms of a fatty acid (*Figure 10.5*). Rather than the strict chemical convention of numbering carbon atoms in fatty acids from the carboxyl group, the double bonds in fatty acids are often numbered from the terminal or ω carbon atom, giving rise to three families of fatty acids with their first double bond occurring at positions ω-3, ω-6 and ω-9. These three families cannot be metabolically interconverted. The term omega fatty acid has entered everyday English and the structures of a number of examples are shown in *Figure 10.6*. Linoleic acid is an ω-6 acid. Two forms of linolenic acid occur, a ω-3 type called α linolenic acid (ALA) and the ω-6 form, γ linolenic acid (GLA). Other ω-3 EFAs are eicosapentaenoic acid (EPA) and

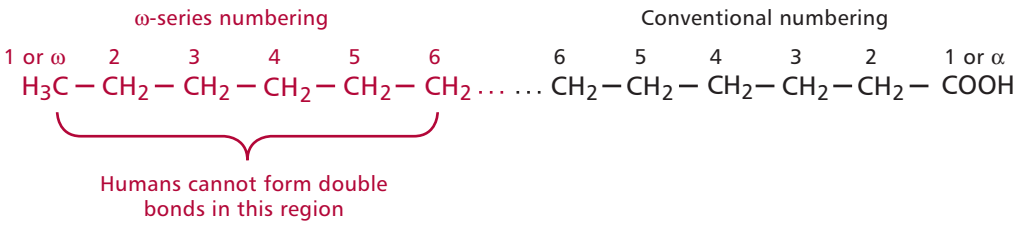


Figure 10.5 The numbering and terminal unsaturation of fatty acids.

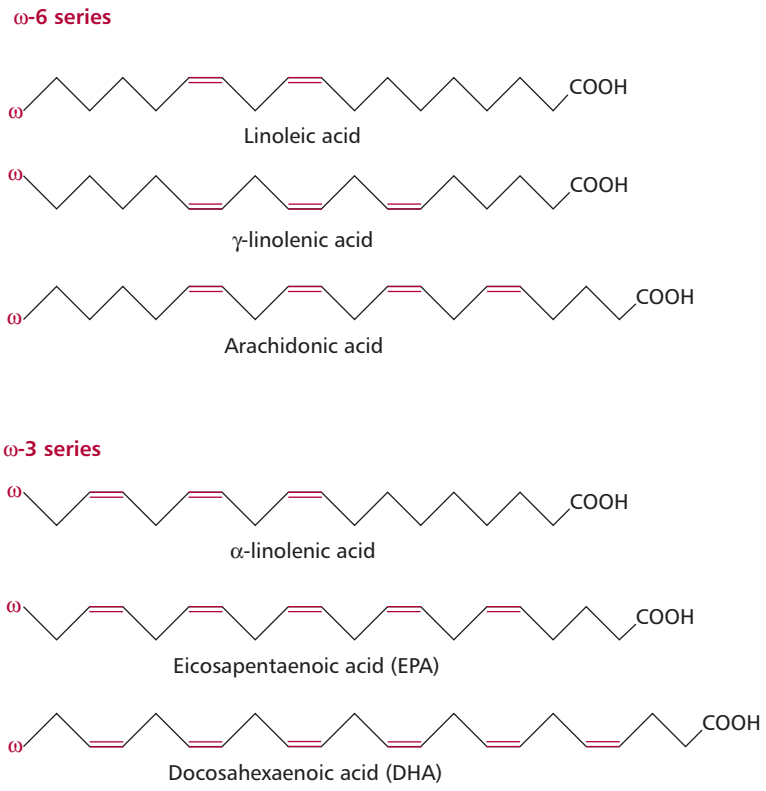


Figure 10.6 The structures of some unsaturated fatty acids.

docosahexaenoic acid (DHA). Omega-3 and ω-6 fatty acids are EFAs because they are not synthesized by the body but must be obtained in the diet. Seeds and vegetable oils are excellent dietary sources of ω-6 EFAs and the body is able to convert linoleic acid to GLA and arachidonic acid. Many vegetable oils contain only low amounts of ALA since this is normally present in the chloroplasts of plants and may only be a significant dietary constituent if green leafy vegetables are consumed. However, ALA can be used to synthesize EPA and DHA by body tissues. Rich sources of the ω-3 EFAs, EPA and DHA are in the oils from the muscles and skins of a number of cold deepwater fishes, such as herring, mackerel, salmon, sardines and tuna (*Figure 10.7*). Cod, which live in similar environments, store fat in the liver: hence cod liver oil is also an excellent source of EPA and DHA.

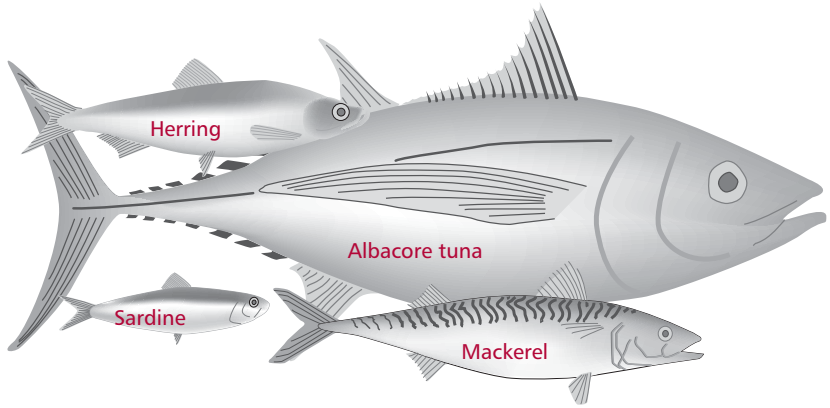


Figure 10.7 A selection of fish rich in essential fatty acids.

A dietary deficiency of EFAs leads to a dry scaly skin subject to erythema, poor healing of wounds and hair loss and a failure to thrive in infants. The first associations between ω fatty acids and health came from studying Greenland Inuit (Eskimo) and inhabitants of fishing villages in Japan and people of Okinawa. These groups have much lower incidences of diseases, such as coronary heart disease (CHD, *Chapter 14*), rheumatoid arthritis (*Chapters 5* and *18*) and diabetes mellitus (*Chapter 7*), than their European or USA counterparts, even though their diets are high in fat from eating seal and fish. However, these organisms are rich in ω-3 fatty acids that have been shown subsequently to provide significant health benefits. The metabolites of ω-3 fatty acids decrease platelet function, reduce the risk from sudden death caused by cardiac arrhythmias and slow the progress of atherosclerosis. Modest decreases in blood pressure also occur with high intakes of ω-3 fatty acids. Some studies have indicated that ω-3 fatty acids inhibit the synthesis of very low density lipoprotein (VLDL) and triacylglycerols (TAGs) and so decrease their concentration in plasma, particularly in patients suffering from hypertriglyceridemia (*Chapters 13* and *14*). Furthermore, they have been associated with reducing morning stiffness and the number of tender joints in patients with rheumatoid arthritis. There is, however, no established recommended daily intake for ω-3s although it has been suggested that 1–2% of the total daily energy intake should be in the form of EFAs. Human adults are thought to require up to 10 g of linolenic acid daily.

The eicosanoids formed from ω-6 fatty acids, although produced by many of the same enzymes as those from ω-3 acids, have different physiological functions and effects. For example, the ω-3 group is antithrombic and anti-inflammatory, both processes promoted by ω-6 acid derived metabolites. Thus a balancing of the intakes of ω-3 and ω-6 fatty acids in the diet is thought to be of importance. The diet typical of the developed world is far richer in ω-6 than ω-3 fatty acids; it has been suggested that ratios of

Essential	Nonessential
His	Ala
Ile	Arg[1]
Leu	Asn
Lys	Asp
Met[2]	Cys
Phe[3]	Glu
Thr	Gln
Trp	Gly
Val	Pro
	Ser
	Tyr

[1]Arg can be synthesized by tissues but not in sufficient amounts to support growth in children.
[2]Met is required in substantial dietary quantities to form Cys if this is not ingested in adequate amounts.
[3]Increased quantities of Phe are needed to form Tyr if this is not ingested in adequate quantities.

Table 10.2 Essential and nonessential amino acids

Margin Note 10.1 Selenocysteine

The amino acid selenocysteine (*Figure 10.8*) is a component of a number of selenoproteins, including the enzymes glutathione peroxidase, tetraiodothyronine 5′ deiodinase, thioredoxin reductase, formate dehydrogenase, glycine reductase and a number of hydrogenases. Selenocysteine is specified by the codon UGA that would normally function as a termination codon in protein synthesis. However, in the presence of a selenocysteine insertion sequence element (SECIS) in the mRNA, UGA specifies selenocysteine. Characteristic nucleotide sequence and base-pairing patterns in the SECISs form secondary structures that lead to the change in codon specificity.

ω-3:ω-6 of 2:1 or 1:1 are a healthier balance. The American Heart Association and the UK Food Standards Agency recommends that people without a history of CHD should consume two servings of fish weekly and those with known CHD should eat one serving of fish daily. More than these amounts are not recommended because, unfortunately, significant amounts of environmental contaminants, such as methylmercury, polychlorinated biphenyls and dioxins, are concentrated in some species of fish. For the same reason, young children and women who may become pregnant, who are pregnant or who are breastfeeding should avoid eating excessive amounts of fish and shellfish. Omega-3 fatty acids exert a dose related effect on bleeding time and it has been suggested that care be applied to their excessive intake, particularly when combined with anticoagulant medications, such as warfarin or heparin (*Chapter 13*). In general, however, their ingestion is well tolerated, although side effects can include a fishy aftertaste and gastrointestinal tract (GIT) disturbances, for example nausea, bloating, belching, all of which appear to be dose dependent.

PROTEINS

Dietary proteins (*Figure 10.3*) are necessary to supply the amino acids needed for growth and the general repair and maintenance of tissues. A daily intake of about 65 g and 50 g of dietary protein is required in males and females respectively, which provides about 10–15% of the total energy in a balanced diet, although only about 5% of body energy comes from their catabolism under normal circumstances. Protein must be obtained from a variety of sources to supply all essential amino acids. Humans are unable to synthesize nine of the 20 amino acids found in proteins that have codons in the genetic code and these are therefore essential dietary constituents (*Table 10.2*).

However, the nonessential amino acids can be synthesized if the supply of the essential ones is adequate. The 'quality' of dietary protein is important and protein intake needs to be varied, particularly as some plant proteins lack one or more of the essential amino acids.

WATER

Water is vital for life because it helps stabilize the structures of large molecules, such as proteins and starch, functions as a medium for most biochemical reactions, acts as a solvent for electrolytes, glucose, vitamins, minerals and numerous other small molecules and transports nutrients to, and waste products away from, cells as well as around the whole body. The GIT (*Chapter 11*) secretes some 7–9 dm^3 of water that aids the digestion and absorption of nutrients. To maintain these functions, loss of body water should match intake to ensure water balance (*Chapter 8*). It is recommended that two to three dm^3 of water should be consumed daily, of which about 60% should be liquid water and the rest obtained from seemingly solid foods. The homeostasis of water has been described in *Chapter 8*.

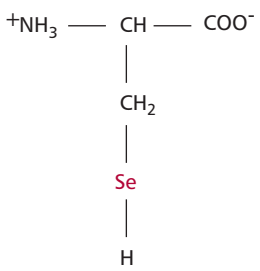


Figure 10.8 The structure of selenocysteine.

VITAMINS

Vitamins are organic substances that the body cannot synthesize or can make only from chemically closely related compounds. They are needed in the diet but only in relatively small amounts (*Table 10.3*).

Vitamins may be classified as water soluble, such as the B group and vitamin C (*Figure 10.9*) and fat soluble, such as the vitamins A, D, E and K. Some of the B vitamins and, in general, each fat soluble vitamin comprise a group of closely related compounds called **vitamers**. In such cases, the name of the vitamin is used as a collective descriptor. Vitamins have specific biochemical roles and are essential for normal metabolism, growth and good health.

Vitamin or related compounds	Recommended intake / mg day^{-1}	Sources
Vitamin B_1 Thiamin	1.0 in males 0.8 in females	yeast, eggs, milk, cheese and cereals
Vitamin B_2 Riboflavin	1.3 in males 1.1 in females	liver, milk, cereals, mushrooms and eggs
Niacin or nicotinic acid Nicotinamide	17 in males 13 in females	meat, fish, pulses, cereals and synthesized endogenously from tryptophan
Vitamin B_5 Pantothenic acid	3–7 is normally provided in diet and appears more than adequate	meats, offal, eggs, green vegetables, whole grains
Vitamin B_6 Pyridoxine Pyridoxal Pyridoxamine	1.4 in males 1.2 in female	vegetables, fruit, cereals, eggs, milk and nuts
Vitamin H Biotin	0.01–0.2 in adults	eggs, pulses, liver, yeast, milk, dried fruit and can be synthesized by intestinal bacteria in the GIT
Folic acid	0.2 in adults 0.4 in pregnancy	liver, spinach, cabbage, peas, bananas and oranges
Vitamin B_{12} Cobalamin	0.0015 in adults	liver, egg and milk
Vitamin C Ascorbic acid	40 in adults	green vegetables and citrus fruits
Vitamin A Retinol Retinal β carotene	0.7 in males 0.6 in females	liver, fish oils, eggs, cheese and can be synthesized from carotene in the diet
Vitamin D Cholecalciferol Ergocalciferol	0.01 in pregnancy	liver and dairy products and endogenous synthesis in the skin if there is adequate exposure to sunlight.
Vitamin E Tocopherol Tocotrienols	4 in males 3 in females	vegetable oils, nuts and wheat germ
Vitamin K Phylloquinone, Menaquinones	0.001 in adults	leafy vegetables, cheese or synthesized by colon bacteria

Table 10.3 Recommended intakes of vitamins and some of their sources

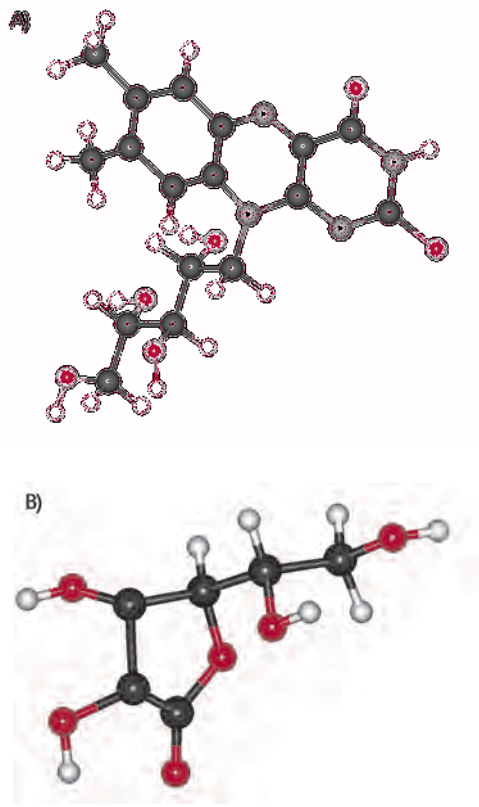


Figure 10.9 Computer generated models of the water soluble vitamins (A) B_2 and (B) C. Oxygen atoms are shown in red, carbon in black, nitrogen in gray and hydrogen are colorless.

Vitamin B_1 or thiamin is an essential component of the coenzyme or prosthetic group, thiamin pyrophosphate (TPP, *Figure 10.10*). This is necessary for the actions of some enzymes, for example transketolase activity of the pentose phosphate pathway for oxidizing glucose and oxidative decarboxylations catalyzed by pyruvate and 2-oxoglutarate dehydrogenases in carbohydrate metabolism. Thiamin is therefore necessary for the metabolic formation of ATP, the major energy carrier in metabolism, and NADPH. Thiamin pyrophosphate is also known to function in nerve conductance. Vitamin B_2 or riboflavin is also required to form coenzymes or prosthetic groups, in this case flavin mononucleotide (FMN, *Figure 10.11 (A)*) and flavin dinucleotide (FAD, *Figure 10.11 (B)*), which function as electron carriers in flavoproteins. The flavoproteins are extremely numerous and include renal L-amino acid oxidase, NADH reductase, 2-hydroxyacid oxidase (FMN) and D- and L-amino acid oxidases, succinate dehydrogenase and glutathione reductases (FAD). Hence riboflavin is essential to many oxidation and reduction reactions in, for example, the TCA cycle, electron transport and the oxidation of fatty acids in mitochondria.

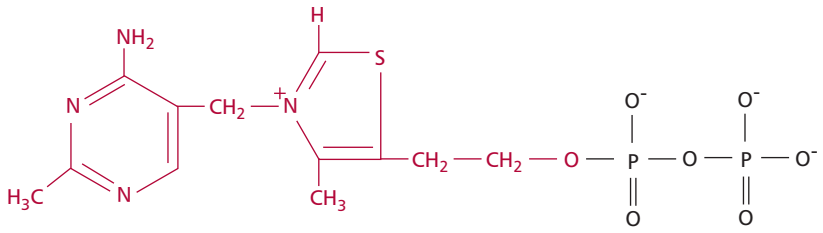


Figure 10.10 The structure of TPP.

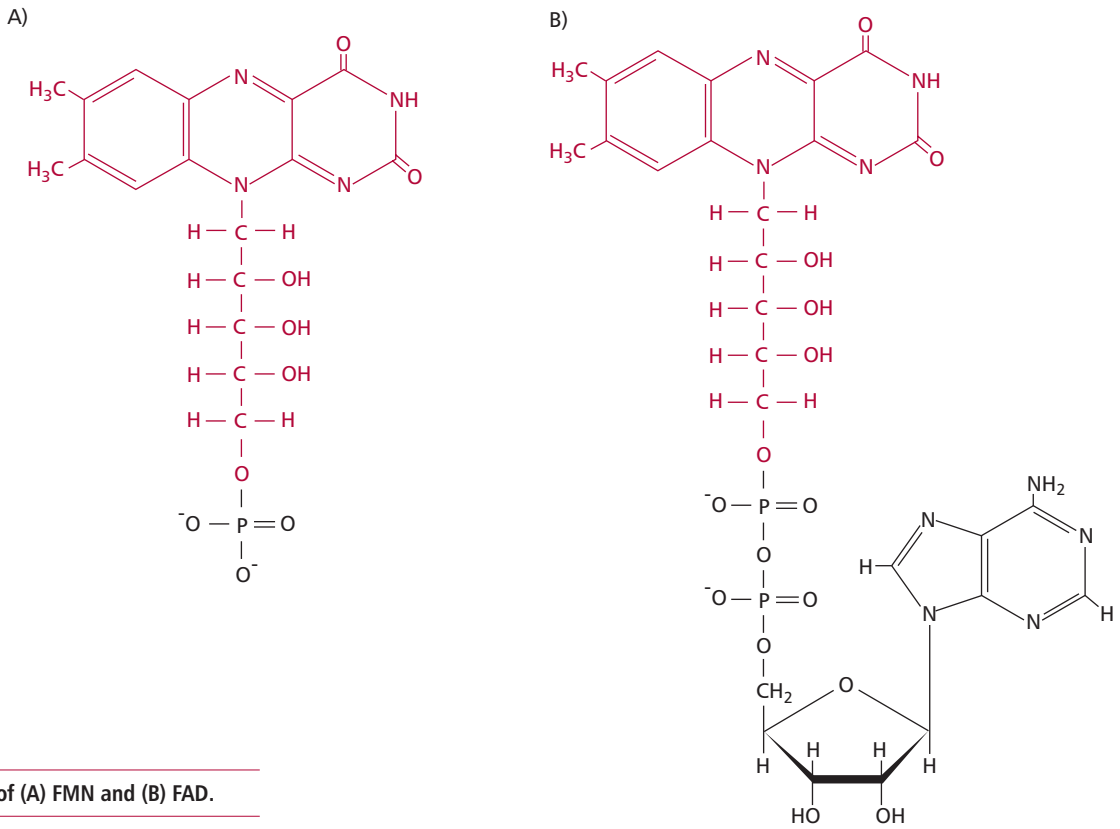


Figure 10.11 The structures of (A) FMN and (B) FAD.

Nicotinic acid and nicotinamide are vitamers of niacin, which strictly is not a vitamin since limited amounts of it can be synthesized from tryptophan. Niacin is required to form coenzymes NAD^+ and $NADP^+$ (*Figure 10.12*) which

are electron and hydrogen carriers. The former is crucial in electron transport associated with oxidative phosphorylation and ATP formation, the reduced form of NADPH is essential to the biosynthesis of, for example sugars, lipids, amino acids and nucleotides.

Vitamin B_5 or pantothenic acid is an essential part of coenzyme A (*Figure 10.13*), which is the major carrier of metabolically active acyl (fatty acid residues) in metabolism. Thus it is essential to many of the reactions involved in the oxidation of lipids and in the synthesis of lipids including steroid hormones, some neurotransmitters and hemoglobin.

The vitamers pyridoxine, pyridoxal and pyridoxamine all have vitamin B_6 activity (*Figure 10.14*), forming pyridoxal 5-phosphate, which is a cofactor for a number of enzymes. These include glutamate decarboxylase that catalyzes the formation of γ aminobutyric acid, a neurotransmitter of the central nervous system, and enzymes that catalyze transamination and decarboxylation reactions of amino acids. Vitamin B_6 is therefore essential for the synthesis of nonessential amino acids and in the catabolism of amino acids. Pyridoxal 5-phosphate is also a cofactor for glycogen phosphorylase of liver and muscle tissues and helps regulate the actions of steroid hormones (*Chapter 7*) by participating in the dissociation of hormone–receptor complexes from DNA.

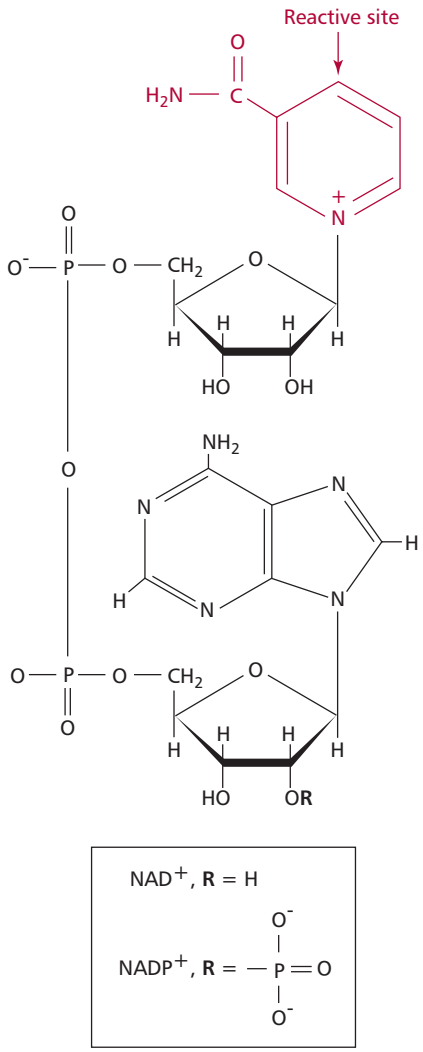


Figure 10.12 The structures of NAD^+ and $NADP^+$.

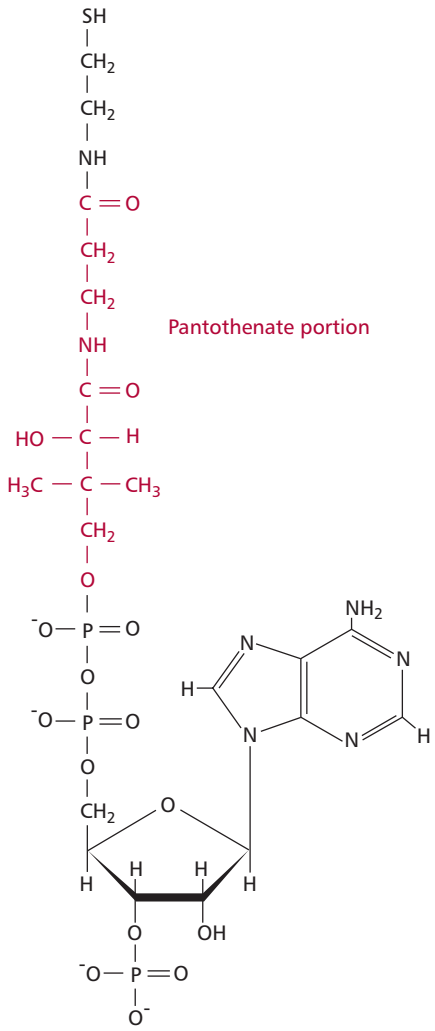


Figure 10.13 The structure of coenzyme A.

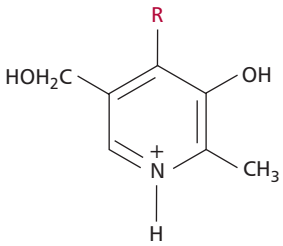


Figure 10.14 The structures of vitamin B_6.

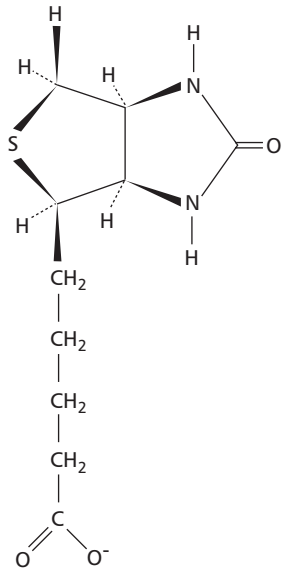


Figure 10.15 The structure of vitamin H (biotin).

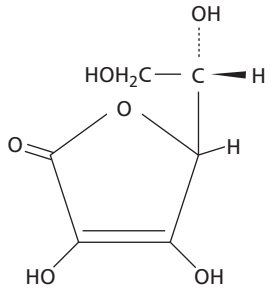


Figure 10.16 The structure of vitamin C (ascorbic acid).

Vitamin B_{12} or cobalamin is an unusual molecule in that it contains an organometallic bond between cobalt and carbon (*Figure 13.18 (A)*). A close relationship exists between the functions of vitamin B_{12} and folic acid and, to some extent at least, they depend on each other for activation. Organic one carbon groups, for example methyl (CH_3–), methylene (–CH_2-), methenyl (–CH=), formyl (–CHO), formate ($–COO^-$) and formino (–CHNH), are generally toxic. In metabolism, they are bound to carriers derived from vitamin B_{12} and folic acid, which allows them to be converted to different oxidation states and used in a variety of different reactions in a nontoxic manner. These reactions are necessary for the catabolism of some amino acids, for the formation of a number of proteins and the synthesis of purine and pyrimidine bases and therefore nucleotides and nucleic acids. Unlike vitamin B_{12} and folic acid that carry organic one carbon compounds, vitamin H or biotin (*Figure 10.15*) is required to form the prosthetic group that carries CO_2 in a number of enzymes. These include acetyl CoA carboxylase and pyruvate decarboxylase which are key enzymes of fatty acid synthesis and gluconeogenesis, the production of glucose from noncarbohydrate precursors.

Vitamin C or ascorbic acid (*Figure 10.16*) is required to reduce metal ions in a number of enzymes following catalysis. Prolyl and lysyl hydroxylases contain Fe^{2+}(II) which is oxidized to Fe^{3+}(III) during hydroxylation reactions involved in cross-linking collagen molecules, which adds strength to connective tissues. Ascorbate reduces their iron back to the ferrous state, regenerating an active enzyme. Similarly, the Cu^{2+}(II) in enzymes involved in synthesis of catecholamine hormones (*Chapter 7*) is returned to the Cu^{+}(I) state following the oxidation of the copper during catalysis. The antioxidant properties of ascorbic acid, in association with vitamin E, help protect lipids in the cell membranes and blood lipoproteins from oxidative damage. It also enhances the absorption of iron and regulates the absorption of copper from the GIT.

Several vitamers, retinol, retinaldehyde or retinal and retinoic acid, show vitamin A activities. Retinol (*Figure 10.17 (A)*) can be metabolically converted to retinaldehyde, which, in turn can be oxidized to retinoic acid. In addition, the provitamin A carotenoids, for example β carotene (*Figure 10.17 (B)*), can be converted to active forms in the liver. Retinoic acid helps regulate the proliferation and development of cells in a tissue specific manner that resembles the actions of steroid hormones (*Chapter 7*). It binds to nuclear receptors, which then interact with DNA and activate specific genes. Vitamin A is associated with the development of epithelial cells, such as the skin and the mucosal membranes that cover internal and external surfaces of the body and have numerous functions, for example, as structural barriers that

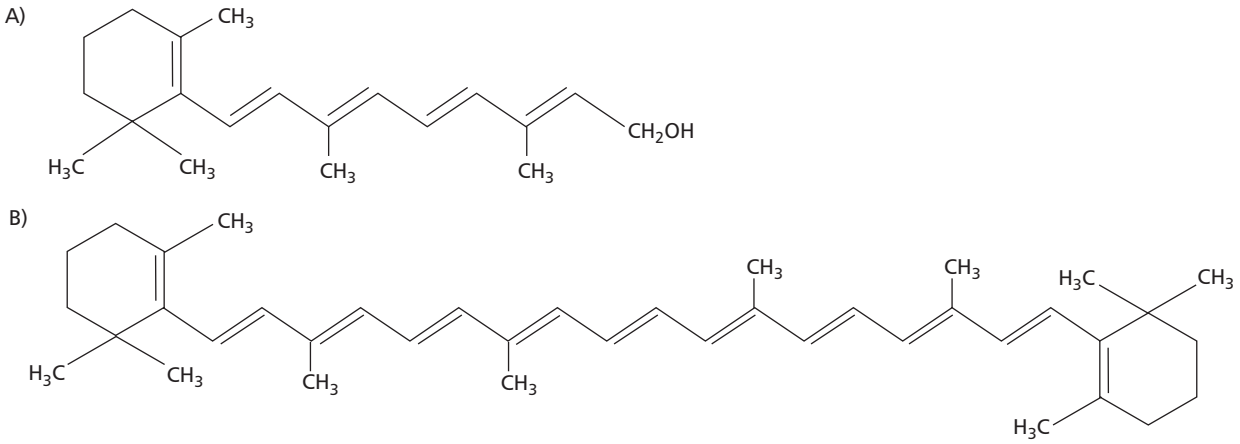


Figure 10.17 The structures of (A) vitamin A (retinol) and (B) β carotene.

prevent microorganisms from entering the body (*Chapter 4*). Retinaldehyde is necessary for vision and functions as the prosthetic group (visual pigments) of opsin proteins in light-sensitive retinal cells. Vitamin A is a weak antioxidant that can protect against free radical damage. There is some evidence that β carotene reduces the incidence of cardiovascular disease and some forms of cancer.

The usual dietary form of vitamin D is cholecalciferol (*Figure 10.18*), although this is not strictly a vitamin since it can be formed by ultraviolet irradiation of the skin from 7-dehydrocholesterol. Foods are sometimes fortified with the synthetic ergocalciferol, which has the same biological activity as cholecalciferol. Enzyme-catalyzed hydroxylations yield the active metabolites 1α, 25 dihydroxycholecalciferol (*Chapter 8*) and calcitriol respectively. Vitamin D mainly functions in the homeostasis of calcium as described in *Chapter 8*.

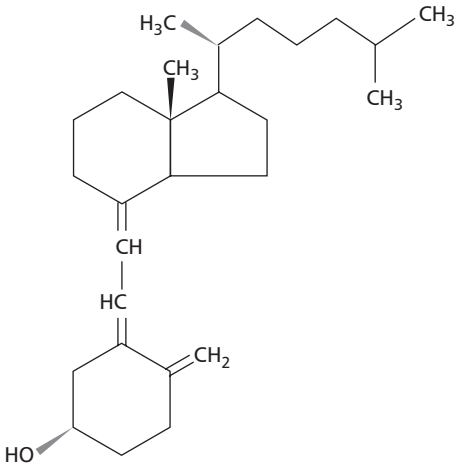


Figure 10.18 The structure of vitamin D (cholecalciferol).

Vitamin E is generally used to describe the tocopherols and tocotrienols that comprise a number of vitamers of differing biological potencies, of which the most active is α tocopherol (*Figure 10.19 (A)* and *(B)*). Like vitamins A and D, vitamin E also has a role in regulating gene expression, although a receptor has yet to be found, and also in signal transduction. A major function generally ascribed to vitamin E is to protect cellular membranes against free radicals (described in *Chapters 12* and *18*) and prevent the oxidation of plasma lipoproteins, especially low density lipoproteins (*Chapter 14*). The corresponding reduction of the vitamin produces a relatively unreactive and therefore less damaging tocopheroxyl radical. This is also relatively long lived and so persists sufficiently long to be reoxidized back to the active form by vitamin C or glutathione peroxidases. However, the utility of this mechanism has been challenged and it has been suggested that the antioxidant role is more restricted and arises from an inhibition of NADPH oxidase and so reduces the production of radicals, such as superoxide.

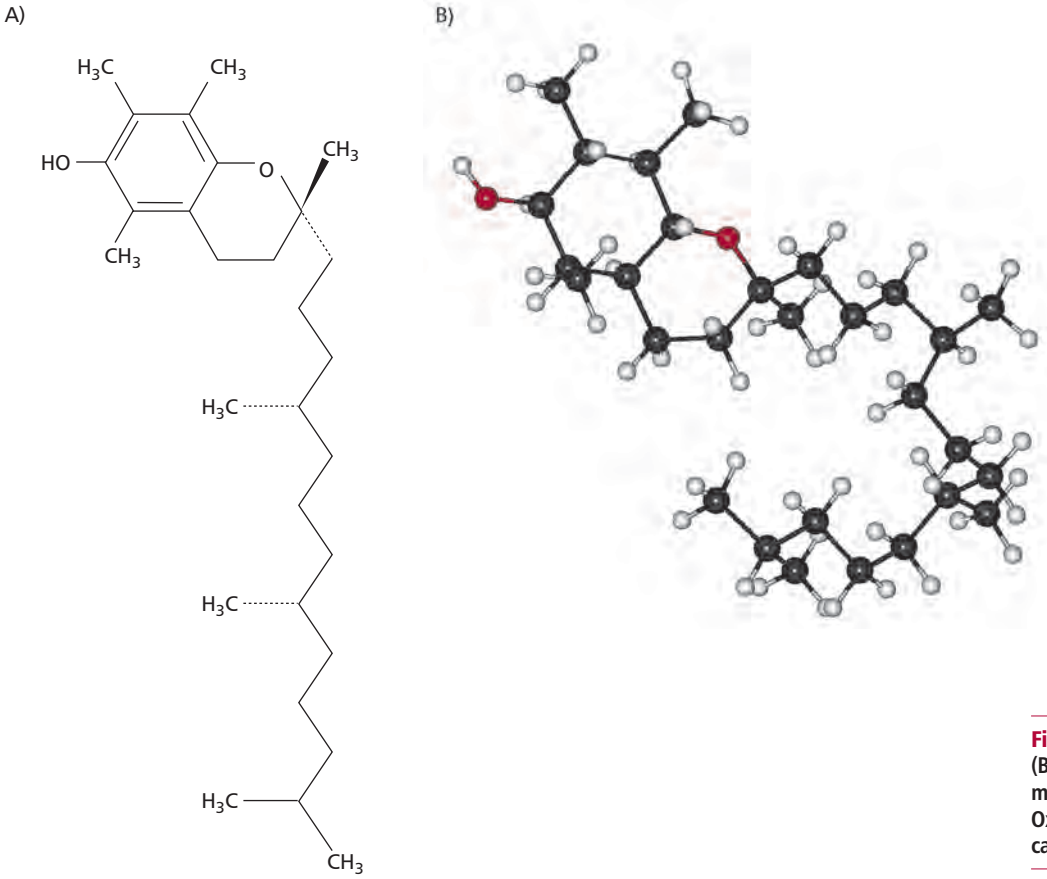


Figure 10.19 (A) The structure and (B) a computer generated molecular model of vitamin E (α tocopherol). Oxygen atoms are shown in red, carbon in black and hydrogen in gray.

A number of compounds are possible vitamers of vitamin K, including phylloquinone and the menaquinones. The first is the normal dietary source, while the menaquinones are a group of compounds with similar structures synthesized by GIT bacteria. Phylloquinone (*Figure 10.20*) is metabolically necessary for the conversion of glutamate residues in some proteins to γ carboxyglutamates. This is necessary for the synthesis of some blood clotting factors, which are described in *Chapter 13*, and some proteins of the bone matrix. The ability of menaquinones to function as vitamin K is unclear; they may partially satisfy the human requirements for vitamin K but their contribution is probably much less than previously thought.

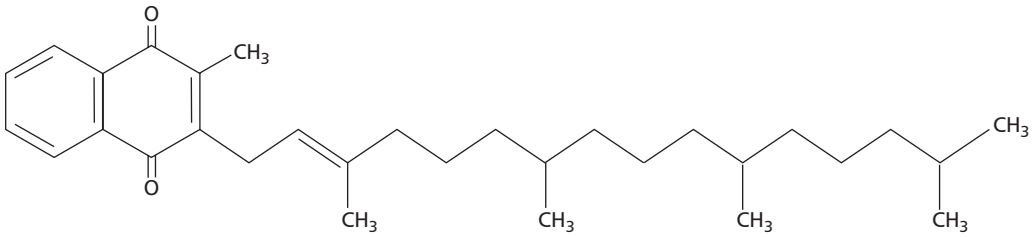


Figure 10.20 The structure of vitamin K (phylloquinone).

MINERALS AND TRACE ELEMENTS

Minerals and trace elements are inorganic dietary substances required to maintain good health. Minerals include calcium, magnesium, sodium, potassium, phosphate, chloride and sulfate. They are present in the body in amounts larger than 5 g and some are required in dietary quantities of more than 100 mg per day and are provided by a variety of foods (*Table 10.4*).

Both groups have diverse functions. Minerals play roles in promoting growth and are important constituents of body tissues such as bone, teeth, hair, skin and nails, and as cofactors in some enzymes and other proteins. Sodium, potassium and chloride are required to maintain the electrolyte and osmotic composition of intra- and extracellular fluids, generate electrochemical gradients across plasma membranes and for nerve conductance and muscle contraction. Calcium is an essential component of bone and teeth, is required for muscle contraction and is a second messenger for some hormones and neurotransmitters. Magnesium is a cofactor for many enzymes, especially those utilizing nucleotides involved in energy metabolism and nucleic acid synthesis. Like calcium, phosphate is needed for bone and teeth formation and is also a component of nucleic acids and phospholipids. It activates a number of enzymes, especially some involved in energy metabolism and is

Mineral	Recommended daily intake / mg day^{-1}	Sources
Sodium and chloride	< 6000 in adults	milk, cheese, salt
Potassium	3500 in adults	bananas, vegetables, nuts, fish, pulses, poultry
Calcium	700 in adults	milk, cheese, vegetables, nuts, fish
Magnesium	300 in males 270 in females	vegetables, nuts, bread, fish, meat
Phosphate	550 in adults	meat, fish, poultry, rice, oats
Sulfate	balanced diet adequate	milk, meat, legumes, eggs

Table 10.4 Recommended intakes and sources of minerals

an important renal buffer. Sulfate is required for the synthesis of cartilage and other components of the extracellular matrix.

Compared with minerals, trace elements are required in much smaller quantities, but like them are supplied by a variety of foods (*Table 10.5*). Trace elements include iron, cobalt, copper, molybdenum, chromium, manganese, zinc, selenium, iodide and fluoride. They are present in the body at concentrations less than 100 parts per million and are required in milligrams or even micrograms per day and a number are toxic in excess.

Trace elements have specific and diverse functions. Chromium helps maintain blood glucose concentration by acting as a cofactor for insulin activity. The role of cobalt as a component of vitamin B_{12}, has already been mentioned. Copper is also an essential cofactor for a number of enzymes, including those involved in collagen and elastin synthesis and some redox proteins. Copper is also required for iron absorption and metabolism and hemoglobin synthesis. Fluoride is necessary for the 'hardening' of bone and teeth. All the thyroid hormones contain iodine as described in *Chapter 7*. Iron is a component of the prosthetic group, heme found in hemoglobin and myoglobin, where it maintains its oxidation state and binds a dioxygen molecule. Iron is also found in the heme of cytochromes and in nonheme iron proteins involved in electron transfer, where, of course, its oxidation state does alter. Manganese is essential for the activities of a number of enzymes. For example, pyruvate carboxylase and phosphoenolpyruvate carboxykinase function in gluconeogenesis; arginase is a key enzyme of the urea cycle that detoxifies ammonia produced during amino acid metabolism and superoxide dismutase is a major antioxidant defence. Enzymes that contain molybdenum are common and catalyze several reactions in purine metabolism, for example xanthine oxidase, and maintains the synthesis of sex hormones. Selenium is a cofactor in, for example, glutathione peroxidases, and zinc in carbonic anhydrase and RNA polymerase.

Trace element	Recommended intake /mg day^{-1}	Sources
Chromium	0.025 in adults	meats, cheese, water, whole grains, lentils, spices
Cobalt	0.0015 in adults	beef, eggs, offal, fish, milk products, nuts, vegetables, cereals
Copper	1.2 in adults	offal, fish, nuts
Fluoride	diet generally adequate	present in drinking water in many areas of the world
Iodide	0.14 in adults	fish, milk, eggs , cereals, iodized salt
Iron	8.7 in males 14.8 in females	liver, meat, eggs, beans, nuts, dried fruit, brown rice, green vegetables and fortified cereals
Manganese	diet generally adequate	bananas, egg yolk, bread, nuts, cereals, vegetables, tea
Molybdenum	diet generally adequate	whole grains, leguminous vegetables, meats
Selenium	0.075 in males 0.06 in females	fish, meat, offal, Brazil nuts and eggs
Zinc	5.5 to 9.5 in males 4.0 to 7.0 in females	meat, offal, eggs, fish, cereals, milk, cheese, spinach, beans

Table 10.5 Recommended intakes and sources of trace elements

BOX 10.1 Inherited disorders of copper metabolism

Menkes or kinky hair disease is a neurodegenerative disease of impaired copper transport that results in extreme tissue copper deficiency and was first described in 1962. It is a sex-linked inherited disorder that only affects male children (*Chapter 15*). Babies born with classic Menkes disease appear normal at birth and symptoms typically begin about three months later. The disease is characterized by a failure to thrive, psychomotor deterioration, seizures, hypothermia and strikingly peculiar hair, which is characteristically kinky, stubby, tangled, sparse or steely and easily broken and is often white, ivory or gray colored. Brain problems, such as blood clots at the base of the brain (subdural hematoma) and/or rupture or thrombosis of arteries in the brain may occur. Recurrent respiratory and urinary tract infections are common and weakened bones (osteoporosis) may result in fractures. Menkes disease has an incidence of 1 in 50 000 to 250 000.

The condition arises from mutations in the *ATP7A* gene found on the X chromosome, the product of which is a copper transporting adenosine triphosphatase (ATPase). Transport of dietary copper from intestinal cells is impaired, leading to the low serum copper levels and poor incorporation of copper into cuproproteins. Copper accumulates in excessive amounts in the liver, but is deficient in most other tissues and impairs the functions of a number of essential enzymes, including tyrosinase, monoamine oxidase, cytochrome *c* oxidase, lysyl oxidase and ascorbic acid oxidase. Low activities of tyrosinase leads to depigmentation of hair, while monoamine oxidase results in kinky hair. Impaired lysyl oxidase leads to defects in elastin and collagen, resulting in vascular weaknesses and cytochrome *c* oxidase malfunction results in hypothermia. A defective ascorbate oxidase leads to skeletal demineralization and osteoporosis.

A diagnosis of Menkes disease in neonates could be based on high concentrations of copper levels in the placenta. However, this would be unusual, given a general absence of signs and symptoms at this age. After six weeks, low serum levels of copper and the copper binding protein, ceruloplasmin, are indicative of the condition. A microscopic examination of hair samples shows characteristic Menkes abnormalities and a skin biopsy can be used to assess copper metabolism. There is no effective treatment for Menkes disease and prognosis is poor. Milder forms of the disease respond to intramuscular injections of copper, but the severe form does not show much change. Other treatments are focused on relieving the symptoms. Most patients die within the first decade of life, however, survival to the late 20s has been reported. Genetic screening of the individual's family can identify carriers and provide guidance for counseling on recurrence risks.

Wilson's disease is characterized by an excessive accumulation of copper, although patients have normal or even low concentrations of copper in their blood and increased urinary excretion, and was first described in 1912. It is an autosomal

Margin Note 10.2 Kwashiorkor in the developed world

Kwashiorkor is rarely seen in developed countries except in neglected children, the very elderly or as a consequence of nutritional ignorance. For example, cases of kwashiorkor have been reported in the USA in a small number of children fed somewhat idiosyncratic diets. Most of these cases were not associated with poverty and about half were associated with perceived or presumed food allergies. A significant portion of the food of some of these children was rice-based beverages, popularly referred to as 'rice milk', which contain less than half the amount of protein of breast milk. Other patients were fed brown rice emulsion, goat's milk or atole, a liquid emulsion of barley, water, and sugar.

10.3 NUTRITIONAL DISORDERS

Nutritional disorders can arise from a deficiency or excess of nutrients and may affect growth or cause specific diseases and even death. They are proving to be major health issues. Nutritional disorders can arise from an inadequate intake of food, such as protein-energy malnutrition, or an excessive intake, for example obesity, or due to an inadequate amount of a specific dietary nutrient, such as scurvy in vitamin C deficiency.

PROTEIN-ENERGY MALNUTRITION

Protein-energy malnutrition (PEM) is the name for a spectrum of disorders that arise due to lack of food. Despite the name, affected individuals may not be suffering from a lack of protein, however, because of their deficiency of total energy, dietary proteins that would normally be used for tissue repair or growth are used as a fuel. In addition, vitamin and mineral intakes are usually inadequate. In the developed world, PEM is rare and is usually associated with solitary elderly patients who are malnourished or with children suffering from neglect. The clinical features of PEM vary depending upon the severity, from the merely underweight to two major conditions, **marasmus** and **kwashiorkor** (*Margin Note 10.2* and *Table 10.6*). Protein-energy malnutrition can also be life threatening in that it increases susceptibility to infectious diseases that would not normally be lethal.

Marasmus is a chronic disorder that develops over a period of months to years and is caused by an inadequate energy intake (*Figure 10.21*). It occurs

recessive condition caused by mutations to the *ATP7B* gene located on chromosome 13 that, like *ATP7A*, encodes a copper transporting ATPase. Indeed, the two proteins are 55% homologous in amino acid sequence. However, *ATP7A* is predominantly expressed in the placenta, GIT and blood–brain barrier, *ATP7B* expression is mainly hepatic. In contrast to *ATP7A*, mutations lead to an accumulation of copper in the liver and brain and damage to other tissues also. The first symptoms shown by about 50% of patients with Wilson's disease are swelling and tenderness of the liver and sometimes fever; this resembles more common disorders, such as viral hepatitis. Abnormal levels of circulating liver enzyme activities can indicate serious liver damage, which can progress to cirrhosis. Other symptoms may include jaundice, abdominal swelling and abdominal pain. An extremely severe hepatitis called fulminant hepatitis may occur in about 5% of patients with jaundice, fluid leaking into the abdomen, low blood protein content and clotting abnormalities, swelling of the brain and damage to erythrocytes causing hemolytic anemia. There may also be difficulties with speech, swallowing and coordination resulting in trembling, an unsteady walk and writing problems. A characteristic brown pigmentation in the cornea of the eye, called Kayser-Fleischer rings may occur. Decreased renal functions and osteoporosis may occur prematurely in some patients. Associated psychiatric problems include severe insomnia, poor concentration, depression and suicidal impulses. Wilson's disease, though more common than Menkes disease, is still rare with an incidence of 1 in 30 000.

Wilson's disease is diagnosed by a combination of blood and urine tests, eye examination and liver biopsy. A decrease in serum ceruloplasmin is seen in 95% of patients and an increased urinary excretion of copper is present in most, but not all, symptomatic patients. Kayser-Fleischer rings are visible with a slit-lamp examination performed by an optometrist or ophthalmologist in about 50% of patients presenting with liver disease. The definitive test is the demonstration of a high copper content in liver tissue obtained by biopsy.

Long-term maintenance therapy of Wilson's disease is possible with D-penicillamine, trientine or zinc treatments. Penicillamine and trientine chelates copper, leading to an increased urinary excretion and reduced tissue levels. Zinc, with vitamin B_6 (pyridoxine) supplements, reduces copper absorption and promotes its loss from the GIT. Foods high in copper, such as shellfish, nuts, liver, chocolate and mushrooms should be avoided, as should alcohol. Medical therapies must be continued for life. Patients with acute liver failure or those with advanced liver disease who do not respond to medical therapy should be considered for liver transplantation, which effectively cures the condition and results in long-term survival of approximately 80%. Genetic testing can be used to assist counseling and to screen siblings of an identified patient.

Condition	Expected weight for age/%	Edema
Underweight	60–80	not present
Marasmus	< 60	not present
Kwashiorkor	60–80	present
Marasmic kwashiorkor	< 60	present

Table 10.6 Distinguishing features of different types of protein-energy malnutrition

in epidemics due to famine and is endemic in many areas of Africa, Asia and South America, and in patients with long-term illnesses, such as chronic pulmonary disease and anorexia nervosa (*see later*). Children with marasmus fail to thrive, are emaciated and lack subcutaneous fat. Cachexia, muscle wastage associated with some chronic infections, such as tuberculosis (*Chapter 4*), or the severe and prolonged weight loss seen in some cancers (*Chapter 17*) produces similar clinical features to marasmus but the etiologies are different.

The name, **kwashiorkor** is derived from one of the Kwa languages of Ghana and means 'the one who is displaced' and reflects the development of a nutritional condition in children typically three to five years old who have been abruptly weaned when a new sibling is born (*Figure 10.22*). Kwashiorkor

Figure 10.21 An Ethiopian child of the early 1980s showing signs typical of marasmus. Courtesy of Catholic Fund for Overseas Development, London.

Figure 10.22 Child showing severe signs of kwashiorkor. Courtesy of Catholic Fund for Overseas Development, London.

Margin Note 10.3 BMI and IBW

The generally accepted way to assess the weight of patients is to determine their **body mass index (BMI)** where

$$BMI = \text{weight (kg)} / \text{height (m)}^2$$

Health risks associated with weight are lowest for a BMI of 20–25 kg m^{-2}. A BMI of less than 18.5 kg m^{-2} is underweight, one of greater than 30 kg m^{-2} is defined as obese. **Ideal body weight (IBW)** is another index that can be useful in assessing the nutritional status of a patient. This index is defined differently for men and women. The IBW of a man 5 feet tall is 106 pounds and this increases by an additional six pounds for each inch over the height of 5 feet. For a woman, the IBW at 5 feet tall is 100 pounds and this increases by five extra pounds for each additional inch.

is common in parts of the world affected by famine and where there is poor education and knowledge of nutrition. In the original description of kwashiorkor in children of the Gambia reported in 1932, Williams (1894–1992) implied that a deficiency of protein was its major cause, even when the energy input was adequate. Since then, a number of explanations for the development of kwashiorkor have been proposed. Environmental toxins, such as aflatoxins from moldy foods, general conditions of overcrowding and poverty, a lack of other key nutrients and high rates of disease have all been implicated. A combined protein and energy deficiency, although important, is not the key factor and it is generally accepted that the condition is likely to be due to deficiency of one of several nutrients, including copper, selenium, zinc and the vitamins folic acid, C, A, β carotene and E that are associated with oxidative stress management. It is likely that infectious diseases are the precipitating factor because children with reduced antioxidant status exposed to the stress of an infection are most liable to develop kwashiorkor. Further, kwashiorkor usually occurs following infectious conditions, such as diarrhea, or diseases, for example measles, indicating that its causes are not purely nutritional. Invading pathogens trigger a macrophage respiratory burst (*Chapters 4* and *5*) that considerably increases the total free radical load of the patient and this may be the start of events that result in kwashiorkor. Unfortunately, its causes are still not fully known; siblings in the same household and on the same type of diet may develop marasmus or kwashiorkor. However, lower concentrations of the antioxidants β carotene, glutathione and vitamin E are observed in children suffering from kwashiorkor than in those affected by marasmus; both of course, have reduced levels compared with healthy children.

A significant feature of kwashiorkor is a large protruding abdomen due to edema and an enlarged liver. The edema is traditionally thought to occur because an inadequate intake of protein leads to a reduced plasma albumin concentration, which in turn causes edema, although electrolyte disturbances, such as potassium deficiency and sodium retention, are also thought to play a role. The hepatomegaly occurs from a large infusion of fats into the liver; the cause of which is unknown. Early features of kwashiorkor include fatigue, irritability, lethargy, stunted growth, muscular wasting, edema in the lower limbs and impaired neurological development. The skin may be affected by dermatitis and have areas of hypo- or hyperpigmentation and thin, brittle, light colored hair that is easily pluckable. The patients may also present with delayed wound healing and anemia. If untreated, kwashiorkor can result in shock, coma and death, with a mortality rate as high as 60%. In the long term, it can lead to impaired physical and mental development.

OBESITY

Obesity is diagnosed when the patient's BMI is greater than 30 kg m^{-2} (*Margin Note 10.3*). It is characterized by an excess of fat in the body, particularly under the skin and is generally recognizable when a person is 20% above their IBW. Environmental and genetic factors can determine body weight, but overeating combined with lack of exercise are its usual causes (*Box 10.2*). Very rarely, obesity may be secondary to endocrine disease (*Chapter 7*), for example hypothyroidism that decreases energy requirements, Cushing's syndrome where the distribution of body fat is altered, and some hypothalamic disorders that are associated with overeating.

BOX 10.2 Leptin and *obese/OBESE*

In 1994, the **obese* gene was discovered in mice. Its expression in adipocytes produces the hormone leptin, a polypeptide of 146 amino acid residues (*Figure 10.23*), which is secreted in amounts that are proportional to the mass of body fat. Among the effects of leptin are to decrease adiposity or total body fat and to pass through the blood–brain barrier and act on the hypothalamus to inhibit eating. It also stimulates the oxidation of fatty stores and prevents lipid accumulating in nonadipose tissues and so protects the individual against some of the adverse effects of fat accumulation, for example coronary artery disease. During periods when more energy is used than ingested, that is the starved state, adipose tissue is metabolized and the amount of leptin secreted declines. Hence, the mouse is stimulated to eat more. When more energy is consumed than used, the converse holds. Mutations to the gene or its absence in mice can lead to excessive overeating and morbid obesity (*Figure 10.24 (A)* and *(B)*). Injections of synthetic leptin to obese mice cause a weight loss. These findings led to great excitement that obesity in humans could be a genetic phenomenon and controllable by leptin therapy. However, although the physiological effects of leptin are similar in humans and mice, mutations in the **OBESE* gene have been discovered in only a handful of obese humans. Two of these patients were members of the same highly consanguineous family and weighed 29 and 86 kg at the ages of two and eight years respectively. Their *OBESE* genes had a deletion mutation of a single guanine nucleotide at codon 133 leading to a biologically inactive leptin. Injections of leptin relieved their symptoms. However, most obese people, in fact, secrete leptin in amounts that exceed its production in thinner people because they have a greater mass of fat. Unfortunately, they appear to be less sensitive to its effects.

*The convention is to write mice genes in lower case italic letters and humans in upper case italics.

Figure 10.23 Molecular model of a leptin molecule. PDB file 1AX8.

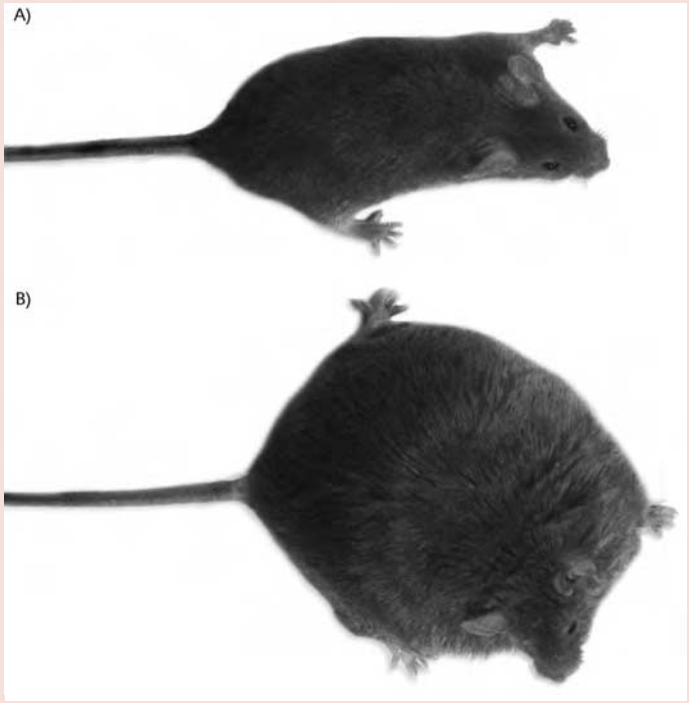


Figure 10.24 (A) Normal and (B) genetically obese mice.

A number of diseases occur more frequently in obese individuals (*Figure 10.25*), including type 2 diabetes mellitus (*Chapter 7*), coronary heart disease, hypertension (*Chapter 14*), cholelithiasis (*Chapter 11*) and osteoarthritis (*Chapter 18*). Not surprisingly, mortality rates are also greater as body weight increases. Some of the complications of obesity are listed in the *Table 10.7*.

The increasing incidence of obesity in many developed countries (*Figure 10.26 (A)*), and particularly in children of the USA and UK (*Figure 10.26 (B)*), is of concern.

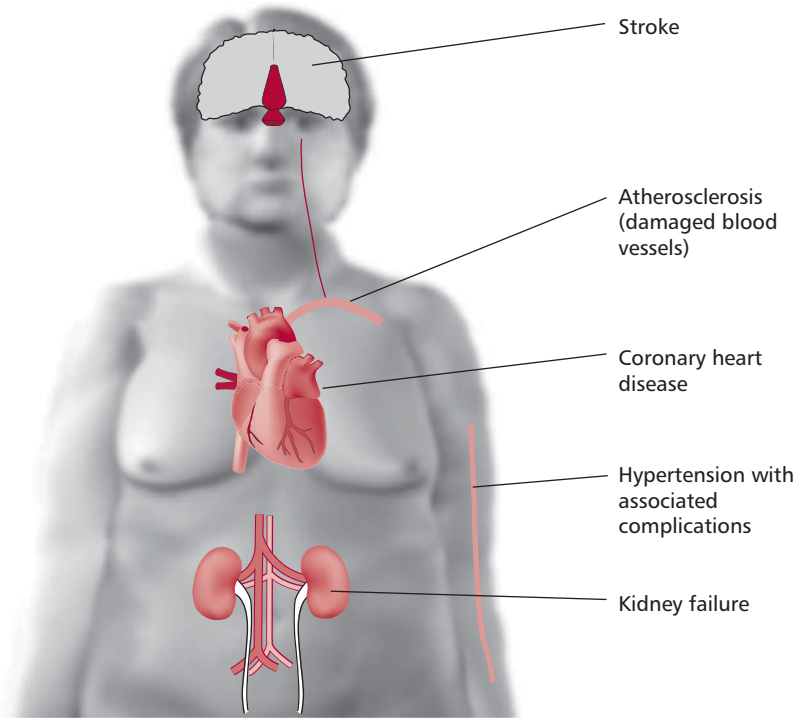
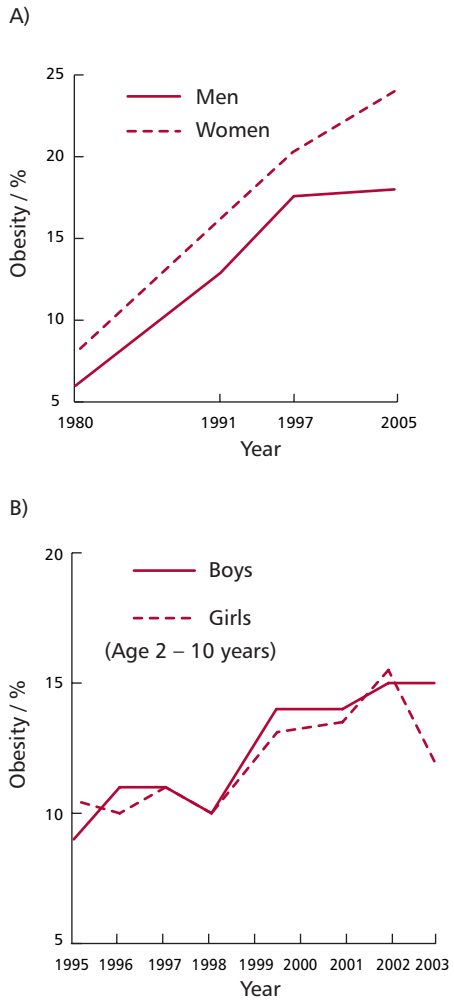


Figure 10.25 Schematic indicating the characteristic shape of an obese person with some of the associated complications indicated.



Disease	Pathophysiology
Cholelithiasis	increased cholesterol, bile stasis
Diabetes mellitus	insulin resistance
Hypertension	obesity, inappropriate lifestyle
Osteoarthritis	increased wear and tear of joints
Respiratory disorder	impaired lung ventilation
Vascular disease	hypertension, dyslipidemia, diabetes

Table 10.7 Complications associated with obesity

Figure 10.26 The increasing incidences of obesity in (A) adults and (B) children in the UK. Data from a variety of sources.

BOX 10.3 The Atkins Diet

The Atkins diet is a high protein, high fat and low carbohydrate slimming diet (*Figure 10.27*) introduced by Atkins (1930–2003) in 1972. The Atkins diet has received much publicity, and is one of the more popular of those diets in which carbohydrate intake is restricted. Individuals on the Atkins diet exclude most cereal-based foods, beans, fruits and starchy vegetables. Instead they eat generous amounts of meat, poultry, eggs, cream and butter. Carbohydrates promote insulin production that, in turn, causes weight gain because of the growth promoting effects of insulin (*Chapter 7*). A low carbohydrate diet will therefore reduce insulin production leading to a loss of weight. When the intake of carbohydrates is reduced, the body responds quickly by utilizing stored glycogen for energy, reducing body weight as the glycogen and its associated water are lost. Muscle, lean body mass, is not depleted because of the high intake of dietary proteins but body fats are used for energy. The oxidation of fats produces ketone bodies (ketosis) that are lost in the urine, although this condition is much less severe than the ketoacidosis of diabetes mellitus (*Chapter 7*). A number of tissues, for example brain, utilize glucose in preference to other fuels and this can be produced by gluconeogenesis in the liver using amino acids when the dietary intake of carbohydrate is low. The glucose 6-phosphate supplied from gluconeogenesis also partially replenishes glycogen stores (*Figure 10.28*). The high protein and fat intakes and the circulating ketone bodies have satiating effects that suppress appetite, reduce food intake and aid weight loss.

The program for a typical Atkins diet consists of four phases: induction, ongoing weight loss (OWL), premaintenance and a final or lifetime maintenance phase. In the induction phase, carbohydrate intake is limited to 20 g daily and is associated with the greatest weight loss, which can be as high as 3–4 kg per week. In the OWL phase, carbohydrate intake is increased by 5 g per day each week, with the goal of finding the intake of carbohydrates that will maintain weight reduction. The OWL phase continues until weight is within 4.5 kg of the set target. In the premaintenance phase, carbohydrate intake is further increased with the aim of finding the maximum amount of carbohydrate intake that can be consumed each day without causing a weight gain. The final or lifetime maintenance phase continues the dietary plan of the previous phase and also aims to avoid a return to previous dietary habits.

It has been shown that the weight losses in the first six months on the Atkins diet are greater than conventional diets but there is little difference between them over a one-year period. Supporters of the Atkins diet claim that the ketosis produced during low carbohydrate diets is a safe and natural condition necessary for weight loss. Surprisingly given the high fat intake, some studies have indicated that individuals on the Atkins diet have higher levels of HDL, the so-called 'good' cholesterol and lower levels of triacylglycerols in their blood and that levels of LDL cholesterol (*Chapter 14*) and glucose remain unchanged. Some studies have shown these reductions are attributable to the initial weight loss and concentrations often return to levels that are higher than before the diet. Critics have also expressed concerns that diets high in saturated fats may increase the risk of cardiovascular diseases. The ketosis can result in bad breath, tiredness, weakness, dizziness, insomnia and nausea. Constipation may also occur as a consequence of avoiding high-fiber foods such as fruit, vegetables, rice and cereals. There are also concerns that the unbalanced nature of the diet may lead to nutritional deficiencies with undesirable effects. For example, poor intakes of calcium may increase the risk of developing osteoporosis. The high protein intake can also produce acidosis that can leach calcium from bones and increase the likelihood of kidney stones leading to osteoporosis and kidney problems respectively. The poor intakes of antioxidants, found in fruit and vegetables, increase susceptibility to heart disease and cancers. Whether the Atkins diet should be recommended for weight loss is a controversial issue. Long-term studies are required to assess nutritional status, body composition and cardiovascular risk factors in individuals on the diet.

Figure 10.27 An example of a meal on the Atkins diet!

BOX 10.3 *continued*

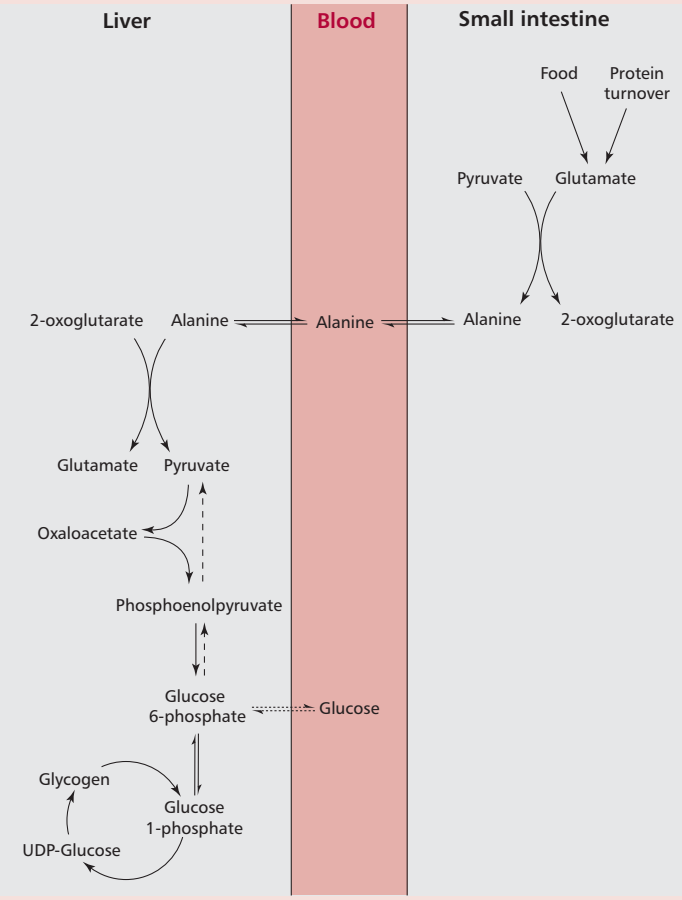


Figure 10.28 An overview of how dietary proteins can be metabolized to support gluconeogenesis to provide glucose during a low dietary intake of carbohydrates.

ANOREXIA NERVOSA AND BULIMIA NERVOSA

Anorexia nervosa (AN) and bulimia nervosa (BN) are both disorders of eating behavior and body weight regulation. Anorexia is simply a lack of appetite; bulimia is derived, in part, from the Greek word *limos* meaning hunger. Both have received considerable publicity in recent years although they were reported many centuries ago. The prevalence rate for AN in young females is estimated to be 0.3% and for BN 1% and 0.1% in young women and young men respectively. The incidence in the general population is much lower with the incidences of AN and BN being approximately 8 and 12 cases per 100 000 respectively.

Anorexia nervosa is an extreme refusal or reluctance to eat and associated psychological problems, leading to a severe weight loss. Compulsive exercising and the abuse of laxatives and diuretics often compound the reduced input of dietary energy. Patients are therefore normally extremely hungry and are obsessed with food but they avoid eating, especially carbohydrates. The signs and symptoms of AN include a body weight at least 15% below the recommended weight, a 'wasted' appearance with reduced muscle mass, and swelling of the joints. In younger females, puberty is delayed; an older female is likely to become amenorrhetic and infertile because her body weight reduces to less than 45 kg and/or fat content becomes less than 22% of body weight. The skin is dry, hair thin and the nails brittle. Constipation and decreased heart rate and blood pressure are common. If left untreated, long-term damage to the skeleton and cardiac systems are likely and death can

result from starvation, cardiac arrest or other complications. Sufferers of AN are often of above average intelligence but generally have a grossly dysmorphic view of their own bodies, seeing themselves as obese, even though they 'know' they are underweight. It is unclear as to what causes this view. It has been suggested that overreactions to relatively mild obesity, peer or social pressures regarding an ideal human shape or a wish to delay the onset of menarche may all be linked to the condition.

Bulimia nervosa is characterized by episodes of excessive or 'binge' eating that induce feelings of guilt such that sufferers induce vomiting to void the food. This cycle of eating and induced vomiting can be repeated many times. As with anorexics, the use of laxatives, diuretics and dieting pills may be abused. The condition tends to affect older patients than those with anorexia. The signs and symptoms of BN include puffy cheeks due to enlarged salivary glands and often severely damaged tooth enamel because of the excessive vomiting. Electrolyte imbalance, such as loss of potassium, can cause health problems and increases the risk of cardiac arrest (*Chapters 8* and *13*). However, patients generally manage to maintain their weight at an appropriate value and so the condition may not be noticed and can remain undetected for many years.

DISORDERS OF VITAMIN NUTRITION

An inadequate dietary intake of a vitamin, its impaired absorption, or insufficient utilization of an adequate intake, increased dietary requirements, for example in pregnancy, without a corresponding increased intake or an increased excretion of a vitamin give rise to **hypovitaminoses**. In many cases, the symptoms of a hypovitaminosis can be correlated with the known functions of the vitamin (*Section 10.2*), although in other cases they are rather generalized. Hypovitaminoses often develop over an extended period. Initially there is depletion of body stores with a biochemical impairment, that is a subclinical deficiency. This eventually results in an overt deficiency with frank signs and symptoms and is usually accompanied by other evidence of malnutrition, for example PEM. A covert deficiency does not present with clinical features under normal conditions, but any trauma or stress may precipitate the hypovitaminosis. Starving individuals will suffer from multiple vitamin deficiencies. At the other extreme, an excess of the vitamin can be toxic and may result in a **hypervitaminosis**.

Hypovitaminoses

A deficiency of vitamin B_1 or thiamin in some developing countries is common because of the high consumption of foods, such as polished rice, where the vitamin is lost during milling, and in chronic alcoholics, who often have a poor diet. The consequences of a deficiency are depression, irritability, defective memory, peripheral neuropathy and beriberi. Beriberi, which literally means 'I cannot, I cannot' in Singhalese, occurs in two forms, which affect different body systems. Dry beriberi mainly affects the nervous system, wet beriberi the heart and circulation; both types usually occur in the same patient but one set of symptoms predominates. Patients with the dry form may present late, with polyneuropathy and Wernicke-Korsakoff syndrome (*Box 10.4*). The polyneuropathy is characterized initially by heavy, stiff legs, then weakness, numbness and paresthesia and absent ankle jerks. Later stages involve the trunk and arms. Wet beriberi, also known as shoshin, from the Japanese for acute heart damage, is less common and characterized by edema. Symptoms appear rapidly with acute heart failure in addition to the polyneuropathy. It is highly fatal and known to cause sudden deaths in young migrant laborers in Asia whose diet consists of white rice.

Vitamin B_2 (riboflavin) deficiency is rare in the developed world and usually only seen in alcoholics who normally have diets lacking other nutrients or

BOX 10.4 Wernicke-Korsakoff syndrome or cerebral beriberi

Wernicke-Korsakoff syndrome or cerebral beriberi, also known as Wernicke's disease or Korsakoff psychosis, is a brain disorder with the loss of specific functions. The term Gayet disease is applied when lesions are more extensive than those in the Wernicke type. The condition is primarily due to a deficiency of vitamin B_1 (thiamin) or secondary to alcoholism and/or starvation. Even in alcoholics on a balanced diet, which is very unusual (*Chapter 12*), the heavy drinking interferes with the absorption of thiamin from the GIT. The syndrome includes two separate conditions. The first, Wernicke's encephalopathy, involves damage to nerves of the central and peripheral nervous systems. Korsakoff syndrome, or Korsakoff psychosis, begins as Wernicke's symptoms diminish and involves damage to areas of the brain involved with memory. Patients often attempt to hide the memory loss by confabulating, that is telling detailed and credible stories that are untrue, although these are not usually deliberate attempts at deception because the patient often believes them to be factual. Other symptoms include double vision and other eye abnormalities, a loss of muscle coordination, unsteady gait and hallucinations. Many of these symptoms are indicative of alcohol withdrawal and may also be present or develop even when Wernicke-Korsakoff syndrome is not present. Other disorders related to the abuse of alcohol may also be apparent. Incidence and prevalence data for Wernicke-Korsakoff syndrome are poorly reported although one study has indicated a prevalence of 1 to 3%.

Abstinence from alcohol or moderate intake together with adequate nutrition reduces the risk of developing Wernicke-Korsakoff syndrome. Thiamin supplements and a good diet may also help prevent the condition occurring in a heavy drinker but not if damage has already occurred. The syndrome is diagnosed following an examination of the nervous and muscular systems that demonstrates polyneuropathy or damage to multiple nerves and decreased or abnormal reflexes. Testing of gait and coordination can indicate damage to the parts of

suffer malabsorption. However, it is a major problem globally affecting some 200 million people, especially children, in developing countries. Other susceptible people include the elderly with a poor diet and regular laxative users. The main metabolic effects are on lipid metabolism, which leads to clinical features of weakness, dermatitis, glossitis, insomnia and sensitivity to bright light, normochromic and normocytic anemia. A deficiency of vitamin B_2 is rarely fatal because it is present in most foods, which provide adequate amounts to maintain function, and there is efficient reutilization of the vitamin during the turnover of flavoproteins, so that little is lost.

A deficiency of niacin causes pellagra, where the patients present with weight loss, anemia, dementia, dermatitis and diarrhea. Pellagra can be primary when the diet is deficient in nicotinic acid, such as when maize is the staple, but it can be secondary, where other diseases interfere with absorption. Causes of secondary pellagra include prolonged diarrhea, cirrhosis of the liver, alcoholism (**Chapter 12**) and use of isoniazid (*Figure 10.29*) to treat TB. Isoniazid reacts with vitamin B_6 to form an inactive hydrazone and can lead to a deficiency.

A deficiency of vitamin B_5 (pantothenic acid) is rare but has been induced experimentally in animals by feeding a diet virtually devoid of the vitamin or by giving metabolic antagonists, such as ω methylpantothenic acid. Symptoms included irritability, fatigue, malaise, GIT problems, muscle cramps and paresthesia. Historically, pantothenic acid deficiency has been implicated in the 'burning feet' syndrome experienced by severely malnourished prisoners of war.

A deficiency of vitamin B_6 impairs the synthesis of γ aminobutyric acid and amino acid metabolism and may be implicated in the development of some cancers (*Chapter 17*). Clinical features associated with a deficiency of vitamin B_6 include peripheral neuropathy. However, deficiencies are uncommon because it is widely available. Cases have been reported in infants fed overheated and inadequately fortified milk formula who developed severe symptoms: irritability, **opisthotonos**, which is an arching of the head, neck and spine backwards, and convulsions that were relieved by vitamin B_6 supplements.

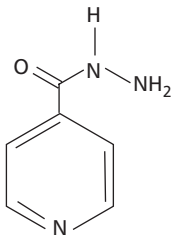


Figure 10.29 Isoniazid.

the brain that control muscle coordination. Muscles may be weak and atrophied and abnormalities of eye movement may be present. The patient may present as cachectic. Clinical tests should demonstrate low serum vitamin B_1 concentration and low erythrocyte transketolase activity but an increase in pyruvate. A magnetic resonance image or computed tomography scan of the brain (*Chapter 18*) of a Wernicke-Korsakoff syndrome patient can show changes in the thalamus or hypothalamus. If the case history is significant for chronic alcohol abuse, then serum or urine alcohol concentrations and liver enzyme activities may be increased above normal.

Wernicke-Korsakoff syndrome is a life-threatening condition with a mortality rate of 10 to 20%. Treatment is aimed at controlling the symptoms as much as possible and preventing any progression of the disorder although some symptoms, particularly the loss of memory and cognitive skills, may be permanent. Hospitalization is required for the initial control of symptoms. In lethargic, unconscious or comatose patients, appropriate monitoring and care is necessary, particularly to prevent obstruction of the airways. Carbohydrate loading, for example by glucose infusion, may precipitate Wernicke's encephalopathy in at-risk patients but can be prevented by supplements of vitamin B_1 prior to the glucose infusion. Injections or oral supplements of vitamin B_1 may improve some symptoms but do not generally lead to the recovery of memory and intellect. Total abstinence from alcohol is required to prevent progressive damage to the brain and peripheral nerves and a well-balanced, nourishing diet is recommended. Joining a support group whose members share common experiences and problems can often help in coping with the stresses of the illness. There may be a need for custodial care if the loss of cognitive skills is severe.

A deficiency of vitamin B_{12} causes megaloblastic anemia (*Chapter 13*) and degeneration of the spinal cord. However, deficiencies are generally uncommon, even in cases of severe malabsorption (*Chapter 11*), since considerable amounts of the vitamin are stored in the liver. Deficiencies can occur in strict vegetarians since sources are animal products. When a deficiency does occur, it is seen most commonly in pernicious anemia, an autoimmune disease characterized by lack of intrinsic factor required for absorption of the vitamin from the GIT (*Chapters 11* and *13*). Bacterial overgrowth in the GIT or diseases affecting the small intestine, such as Crohn's disease (*Chapter 11*), can also lead to a deficiency. Elderly people with atrophic gastritis absorb vitamin B_{12} poorly. However, the first sign of this is neuropathy because the anemia is hidden by folic acid intakes.

Folic acid deficiency is relatively common and occurs because of an inadequate dietary intake in alcoholics and the elderly or because of increased requirements, for example pregnancy and diseases associated with increased cell and nucleic acid turnover, such as leukemia. The deficiency can also arise because of malabsorption and because some drugs affect folic acid metabolism, for example anticonvulsant drugs interfere with its absorption. The major clinical feature of folic acid deficiency is megaloblastic anemia (*Chapter 13*). An increased intake of folic acid before and during pregnancy is associated with a decreased risk of the fetus developing neural tube defects. Taking supplements of folic acid before conception and in the first three months of pregnancy reduces the incidence of spina bifida by more than 20%. In women who have already had a pregnancy affected by a neural tube defect, taking a daily folic acid supplement reduces their chances of a similarly affected pregnancy by approximately 70%. Folic acid supplements are associated with decreased amounts of homocysteine in the plasma with a reduced risk of cardiovascular disease (*Chapter 14*).

Patients suffering a lack of only vitamin H (biotin) are extremely rare. They tend to be individuals who consume extremely large amounts of raw eggs, since the white contains the protein avidin, which binds tightly to biotin (*Figure 10.30*). The vitamin is not released unless the egg is cooked;

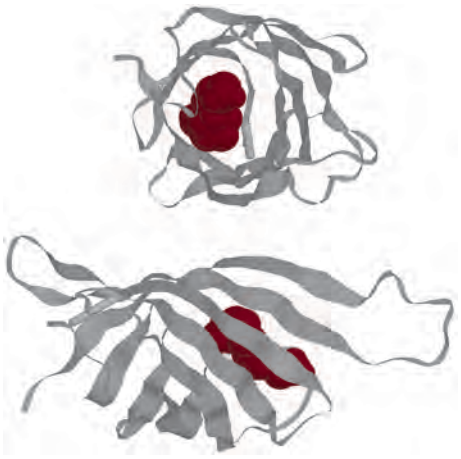


Figure 10.30 Molecular model of vitamin H (biotin), shown in red, bound to avidin. PDB file 1AVD.

Figure 10.31 Molecular model of serum retinol binding protein with a bound retinol form of vitamin A (red). PDB file 1BRP.

however, more than 20 raw eggs must be consumed daily for this to become a serious problem. Biotin deficiency occasionally occurs in hospital patients on parenteral nutrition and leads to anorexia, nausea, dermatitis and depression.

A lack of vitamin C causes scurvy. Inadequate dietary intake occurs in infants aged six to 12 months who receive processed milk without vitamin C supplements and in the elderly who have vitamin C deficient diets. The clinical features of scurvy include skin **papules**, **petechial** and muscle hemorrhages, poor wound healing, gum disease, anemia and osteoporosis. It has been suggested that vitamin C reduces the incidence, duration and severity of the common cold without any side effects, but there is no scientific evidence for these claims.

A deficiency of vitamin A is rare in the developed world; indeed, large amounts are stored in the liver and transported around the body bound to retinol-binding protein in the plasma (*Figure 10.31*). In contrast, deficiencies are major health issues in parts of Africa and South-East Asia. In pregnant women, vitamin A deficiency not only causes night blindness but may increase the risk of maternal mortality. Affected patients may present with anemia and disorders of ectodermal tissues and increased risk of disease and death from severe infections.

A deficiency of vitamin D impairs mineralization of bone matrix causing rickets in children (*Figure 10.32*) and osteomalacia in adults. Rickets results in deformities of the legs that bow due to the weight of the body, skull, rib cage and pelvis. During the 1950s, rickets was virtually eradicated in the UK by fortification of infant foods with vitamin D. Unfortunately, some susceptible children suffered vitamin D toxicity and developed hypercalcemia (*Chapter 8*). As a consequence, the amount of vitamin D added to foods was reduced and rickets reappeared. Overt rickets is now rare in the UK, although subclinical rickets affects about 10% of young children. Osteomalacia causes pain in the bones, especially of the pelvis and legs, and there is an increased susceptibility to fractures of the long bones following minor trauma. It is not uncommon in the UK, especially among women of some ethnic origins because of their lack of exposure to sunlight during purdah and the wearing of traditional clothes.

Vitamin E deficiency is rare. When it does occur, it is most likely in newborn children because transfer of vitamin E across the placenta is poor and these children also have less adipose tissue, where most of the vitamin is stored. Deficiencies of vitamin E can occur with long-term parenteral nutrition and in prolonged and severe steatorrhea (*Chapter 11*). Vitamin E deficiency in children causes irritability, edema, hemolytic anemia and neurological dysfunction. Decreased concentrations of plasma vitamin E have been associated with progression of atherosclerosis and growth of some tumors. Other symptoms such as ataxia, dysarthria, sensory loss and paresthesia have been described in adults.

The clinical effects of vitamin K deficiency include a prolonged clotting time and a bleeding tendency as described in *Chapter 13*. A maternal deficiency can lead to serious bone defects in the fetus. Vitamin K deficiency is most common in neonates because it cannot cross the placenta and milk is a poor dietary source so the baby is at risk of bleeding. Newly born babies lack bacteria in their GIT that can synthesize vitamin K, although the significance of intestinal synthesis by bacteria is debatable anyway. For this reason, it has been recommended that all neonates are given a single prophylactic dose of vitamin K. In adults, a deficiency may be seen in fat malabsorption or in people using antibiotics that reduce intestinal bacteria. An inadequate intake may reduce the density of bone and increase the risk of osteoporosis and associated fractures, particularly in postmenopausal women.

Margin Note 10.4 Skin papules and petechial hemorrhages

Papules are solid, limited raised areas of skin about 5 mm in diameter but their shape and color may vary. They may be transitional lesions, and can become vesicular or ulcerate. Larger lesions are called nodules. **Petechial hemorrhages** are small round dark red spots caused by bleeding under the skin.

Hypervitaminoses

Hypervitaminoses are relatively rare compared with deficiencies. An excess of vitamins B_6 and niacin can be toxic and is usually associated with excessive intake of vitamin supplements. Large doses of niacin are associated with a variety of clinical problems, including abnormalities of liver functions, hyperglycemia, an increase in plasma uric acid and vasodilation. Daily doses of vitamin B_6 greater than 500 mg over an extended period can cause a sensory neuropathy.

Most examples of hypervitaminoses are associated with vitamins A and D. Vitamin A is stored in the liver and excessive dietary intake over prolonged periods can lead to a toxic overload. Typical symptoms are pain in the bones, a scaly dermatitis, nausea and diarrhea with enlargements of the liver and spleen. Most cases of vitamin A toxicity are caused by patients overdosing with vitamin supplements. The only natural food known to contain dangerous levels of the vitamin is polar bear liver; not a common dietary item in most societies! Animal studies have shown that vitamin A can produce teratogenic effects when administered in high doses. The consumption of excessively large amounts of vitamin A during pregnancy may increase the risk of congenital malformations.

Excess of vitamin D is, again, largely associated with the overconsumption of vitamin supplements. Toxicity is due to overstimulation of calcium absorption from the gut and excessive resorption from bone which results in its demineralization. The weakening of the bone and hypercalcemia (*Chapter 8*) promote metastatic calcification and a tendency in the patient to form kidney stones.

Figure 10.32 A child with the characteristic bowed legs of rickets.

NUTRITIONAL DISORDERS OF MINERALS AND TRACE ELEMENTS

Minerals and trace elements are necessary for numerous and diverse metabolic activities. Clinical disorders arising from deficiencies in the dietary intakes of minerals are not uncommon and a number are described in *Chapter 8*. Conditions caused by excessive mineral ingestion are less common but several are also outlined in the same chapter.

The total quantity of any one trace element in the body is usually less than 5 g and these elements are often required in quantities of less than 20 mg per day, hence dietary deficiencies are uncommon. Chromium deficiency can occur in patients on parenteral nutrition without adequate supplementation and leads to glucose intolerance. An excess of chromium (II) has no known symptoms, although chromium (III) and especially chromium (VI) compounds are toxic. A deficiency of cobalt is rare and causes indigestion, diarrhea, weight loss and a loss of memory. An excess of cobalt is not associated with any known symptoms, although a high intake over a prolonged period may lead to infertility in men. In addition, there are occasional reports of cobalt cardiomyopathy following occupational exposure.

Copper deficiency is uncommon, except in patients on synthetic oral or on long-term parenteral nutrition. It can occur in infants because of malnutrition, malabsorption, chronic diarrhea or prolonged feeding with low copper milk diets. Premature infants are particularly susceptible because of their low copper stores in the liver. Copper deficiency causes neutropenia and hypochromic anemia in the early stages, both of which respond to dietary copper but not iron. This is followed by bone abnormalities such as osteoporosis, decreased pigmentation of the skin, pallor and neurological abnormalities in the later stages. A dietary excess of copper is rare but occasionally happens following food contamination and causes salivation, stomach pain, nausea, vomiting and diarrhea (*Box 10.1*).

Margin Note 10.5 Warfarin and vitamin K

Warfarin is often used therapeutically as an anticoagulant *(Chapter 13)*. However, because of the similarities in structures, it is a vitamin K antagonist (*Figure 10.33 (A)* and *(B)*). Patients on warfarin therapy require increased amounts of the vitamin.

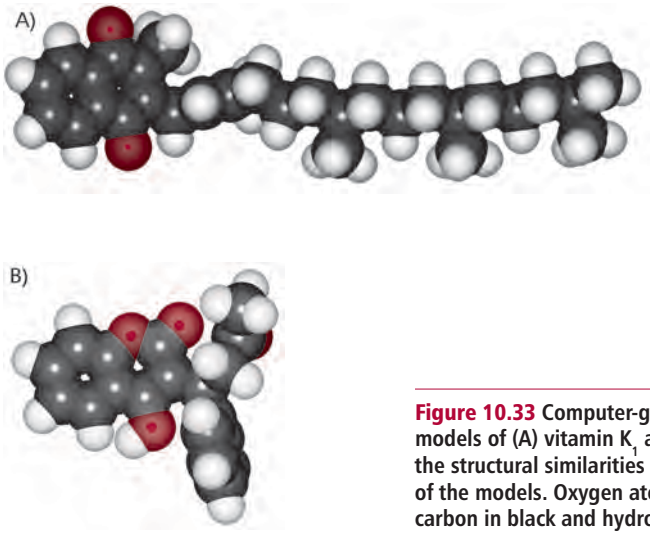


Figure 10.33 Computer-generated molecular models of (A) vitamin K_1 and (B) warfarin. Note the structural similarities in the 'left-hand' sides of the models. Oxygen atoms are shown in red, carbon in black and hydrogen in gray.

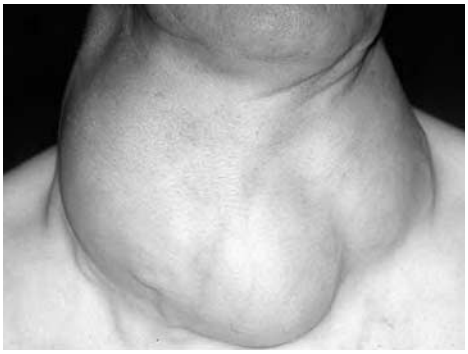


Figure 10.34 A well developed goiter. Courtesy of S.J. Nixon, Royal Infirmary of Edinburgh, Scotland.

Nearly half of dietary fluoride is taken up by bone and can influence its mechanical properties. The incorporation of fluoride in tooth enamel as fluorapatite makes teeth more resistant to dental caries as it resists breakdown by acids. Fluoride deficiency leads to impaired bone formation and dental defects (*Box 10.5*).

Iodine deficiency causes an enlargement of the thyroid gland called goiter (*Figure 10.34*), while a prolonged deficiency in children can lead to cretinism (*Chapter 7*). Iodine deficiency is commonest in upland areas with thin limestone soil because minerals, such as iodine are easily leached from these types of soils and plants in the area are iodine deficient. The situation is exacerbated if commercial iodized salt is not available. In some areas of Africa, Brazil and the Himalayas, more than 90% of the population may develop goiter due to iodine deficiency. Excessive intake of dietary iodide can also lead to goiter. This is most commonly seen in Japanese communities who have a high dietary intake of seaweed.

A lack of iron leads to anemia, which is described in *Chapter 13*. Increased intake of dietary, medicinal or transfused iron can cause hemosiderosis,

BOX 10.5 Dental caries and fluoride

The bulk of the tooth is composed of a hard tissue called dentine. The exposed part of the tooth or crown is covered with enamel. Dental caries or tooth decay is caused by bacteria in the plaque and is the commonest cause of toothache (*Chapter 3*). It is particularly common in children. Bacteria in the plaque catabolize sugars producing organic acids that can demineralize the enamel and the underlying dentine. The development of dental caries depends upon a balance between the plaque and bacteria and the ability of enamel to resist attack. The commonest cause of dental caries is poor dental hygiene and a frequent intake of dietary sugars. Regular brushing of the teeth can remove plaque and reduce acid production since it takes about 24 hours for the bacteria to reestablish themselves. Treatment of caries involves removing the decayed part of the teeth by drilling and replacing the decayed material with a filling.

Epidemiological studies have demonstrated the benefits of adding fluoride to drinking water (fluoridation) because as little as one part per million (ppm) can prevent dental caries. Studies in the UK showed that children living in areas with water fluoride concentrations of about 1 ppm had 50% fewer cases of dental

characterized by deposits of iron compounds in organs such as the liver and heart. Acute ingestion of large doses of ferrous salts can be fatal, particularly in children under the age of two. Manganese deficiency is rare but is believed to cause ataxia, hearing loss and dizziness. Inhalation of dust from mining and other industrial sources can lead to manganese toxicity and causes severe neurological dysfunction, similar to Parkinson's disease (*Chapter 18*). A dietary deficiency of molybdenum has not been reported. However, molybdenum deficiency was noted in a patient on parenteral nutrition who suffered from mental disturbances that progressed to coma. Supplementation of molybdenum improved the patient's clinical condition. Levels of manganese in food and water must exceed 100 mg kg^{-1} body weight to produce manganese toxicity. However, few data are available but the major signs include diarrhea and anemia. The high concentrations are thought to stimulate xanthine oxidase, leading to increased serum uric acid and gout (*Chapter 8*).

Selenium deficiency results from a low dietary intake in parts of the world with soils of low selenium content and has been reported in patients on long-term parenteral nutrition. A deficiency of selenium may lead to a cardiomyopathy. In China, this is called Keshan's disease and affects young women and children in selenium deficient regions and although selenium deficiency is a basic factor in Keshan's disease, its occurrence is seasonal and it is associated with viral infections that cause inflammation of the heart. Prophylactic selenium prevents the disease developing but selenium supplements do not reverse heart muscle damage. A large intake of selenium causes selenosis, a condition characterized by loss of hair, skin and nails.

Zinc deficiency is relatively common in populations in rural areas of the Middle East and subtropical and tropical areas where unleavened whole wheat bread can provide up to 75% of the energy intake. The little zinc in wheat is bound by the relatively large amounts of phytic acid and fiber present that inhibit its absorption. This is not a problem in leavened bread, as yeasts produce phytases that inactivate the phytic acid. Zinc deficiency also occurs during prolonged parenteral nutrition if inadequate amounts are provided. A deficiency is associated with a period of severe catabolism, as would occur in PEM. A severe deficiency occurs in the skin condition acrodermatitis enteropathica, where there is an inherited defect in GIT zinc absorption. A deficiency of zinc delays the onset of puberty. High doses of zinc reduce the amount of copper the body can absorb causing anemia and weakness of the bones.

caries than those in areas where the water fluoride was below 0.1 ppm. Indeed, removal of fluoride from the water increased the incidence of caries. These UK studies have been supported by others worldwide, where similar results have been obtained despite ethnic, social, climatic and dietary differences. Fluoride in toothpastes, mouthwashes or when consumed in a liquid or tablet form is also effective in preventing dental caries. The addition of fluoride to drinking water at concentrations greater than 12 ppm promotes dental **fluorosis**, a mottling of the teeth as they form in the jaws. Its effects are generally cosmetic and only cause functional problems when the disorder is severe. Other concerns of fluoridation include its possible association with cancer and arthritis. There is, however, a weak association between fluoridation and an increased susceptibility to bone fractures.

The addition of fluoride to drinking water has also raised ethical issues because it is seen by some as an infringement of personal liberty in that individuals have no choice but to drink water containing fluoride. The use of fluoridation requires careful consideration of the ethical issues and the balance between its beneficial and any potentially harmful effects.

Figure 10.35 Measuring arm circumference.

Figure 10.36 Measuring skin fold thickness.

10.4 INVESTIGATING NUTRITIONAL DISORDERS

The main objectives in investigating nutritional disorders are to detect malnutrition, determine the most appropriate treatment and to monitor the progress of the patient during treatment. A number of fairly general investigations are available for patients suspected of suffering from malnourishment, for example taking a medical history, physical examination and laboratory investigations. A patient's medical history may help to reveal the underlying basis of the complaint. A significant part is determining the dietary history, which usually involves dietary recall of the last one to seven days, or food frequency questionnaires where patients estimate how often a particular food on a list has been eaten. A medical history also includes specific questions concerning recent weight changes, dietary habits, for example alcohol consumption, appetite, GIT function, use of vitamin and mineral supplements and drug intake. A physical examination can include anthropometric measurements, such as weight, height, body mass index (*Margin Note 10.2*), arm circumference and skinfold thickness. Arm circumference is an indicator of muscle mass. The arm circumference is measured at the midarm point in millimeters (*Figure 10.35*) and values are typically 293 mm in males and 285 mm in females. Skinfold thickness indicates the extent of subcutaneous fat stores. It is commonly measured at the biceps, triceps, subscapular and suprailiac sites in both males and females. In, for example, the triceps measurement the arm is allowed to hang freely and a fold of skin above the midpoint of the arm is pulled from the underlying muscle and measured to the nearest millimeter using calipers (*Figure 10.36*). Values are typically 12.5 and 16.5 mm for males and females respectively. Measurements at the four sites should be made in duplicate and should not vary by more than 1 mm. If consecutive measurements become increasingly smaller the fat is being compressed and other sites should be assessed while the tissue recovers. However, the accuracy of the test depends upon selecting the sites correctly, an appropriate technique in taking the measurements and the experience of the tester; hence the trend is more important than the values at any one time. Values for arm circumference and skinfold thickness are compared with standard values for the same sex. Undernutrition is indicated if they are less than 90% of these values.

The appearance of the skin, hair, nails, eyes, bones, teeth and mucous membranes may reveal signs of malnutrition. A number of general laboratory-based investigations on blood and urine samples can aid in diagnosing malnutrition and are listed in *Table 10.8*. These tests are not reliable when

Test	Clinical value in assessment of malnutrition
Serum albumin	reduced values in kwashiorkor, poor protein intake and zinc deficiency
Total iron-binding capacity (*Chapter 13*)	reduced values in kwashiorkor and poor protein intake
Total lymphocyte count (*Chapter 13*)	reduced values in PEM especially kwashiorkor
Serum creatinine (*Chapters 1* and *8*)	reduced values in muscle wasting because of energy deficiency
Creatinine clearance (*Chapter 8*)	reduced values in muscle wasting because of energy deficiency
Hemoglobin (*Chapter 13*)	reduced values in anemia possibly due to nutritional deficiency
Prothrombin time (*Chapter 13*)	increased in vitamin K deficiency

Table 10.8 Laboratory tests for investigation of malnutrition

used in isolation, as their findings are also altered in some disease states. Hair and nail samples are of questionable clinical value and are not routinely taken.

PROTEIN-ENERGY MALNUTRITION

A diagnosis of PEM must identify the type present. Individuals affected by maramus present with decreased anthropometric measurements, loss of muscle mass and body weight. There is also a decline in body temperature, pulse and metabolic rate. Serum protein levels are often low but can be normal. Children suffering from PEM have reduced rates of growth and are shorter, particularly in marasmus, compared with their normal counterparts. This can be easily assessed using charts of growth rates (*Figure 10.37*). They also have an impaired immune system, because of reduced protein synthesis in particular of immunoglobulins, and, as a consequence, infections such as measles that a child would normally be expected to survive are common causes of death in severe cases. A diagnosis of kwashiorkor is made following a thorough physical examination together with a medical and dietary history. Patients affected with kwashiorkor have the characteristic swollen abdomen, show hypoalbuminemia and a reduced lymphocyte count or **lymphopenia**.

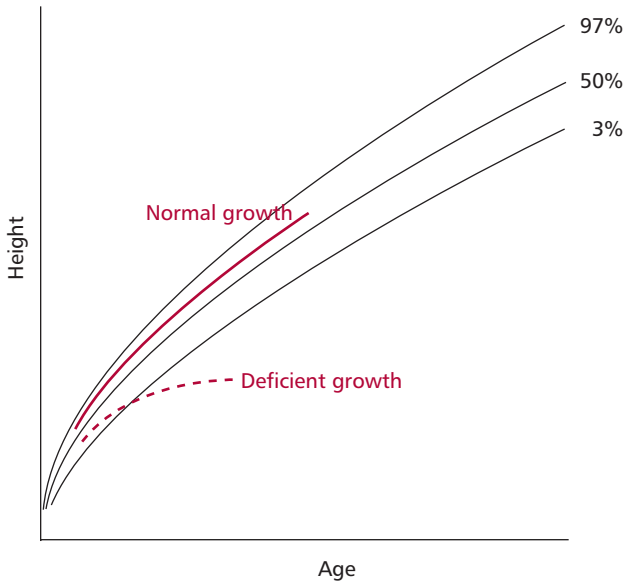


Figure 10.37 A generic growth chart. Charts are available for different sexes and ethnic groups.

OBESITY

In addition to arm circumference and skinfold thickness, the distribution of fat in obese patients can be assessed by determining the waist:hip ratio. The waist circumference is measured at its narrowest point and divided by that of the hip at its widest. Ratios greater than 0.80 for women and 0.95 for men increase the risk of developing clinical problems associated with obesity (*Table 10.7*). Ultrasonography can also be used on soft tissue adipose material. The technique reflects ultrasound waves from internal tissues or organs and the echo patterns are analyzed to form a picture of body tissues called a sonogram. The extent of fat deposition can be accurately determined but is more expensive than other methods and not widely used.

ANOREXIA NERVOSA AND BULIMIA NERVOSA

Anorexia nervosa and BN are difficult to identify, given that the patients often take extreme measures to hide the condition and, indeed, often refuse to admit to any problem. Diagnosis relies on a medical history, clinical investigation

supported by anthropometric measurements, coupled with a sympathetic psychological assessment.

VITAMINS

The majority of vitamin disorders encountered in clinical practice are deficiencies. The investigative procedures are varied and depend upon the vitamin in question. Chemical tests can help to confirm the diagnosis of overt vitamin deficiencies and may enable diagnosis to be made at a relatively early stage. The types of tests used include direct measurements of the concentration of the vitamin or one of its metabolites in plasma, serum, erythrocytes, urine or tissue biopsies. The concentration of vitamin in plasma does not necessarily reflect body vitamin status and a measurement of the concentration in blood cells may be a better indicator. Enzyme-based tests are available for some vitamins. Metabolites that accumulate in the blood or urine following the blockage of a metabolic pathway normally catalyzed by an enzyme that requires a vitamin as a cofactor or coenzyme may also be investigated.

Vitamin B_1 (thiamin) deficiency can be assessed by direct measurement of its concentration in plasma or indirectly by determining the increase in erythrocyte transketolase activity in the presence of added TPP. The increase in activity is called the activation coefficient. A coefficient less than 15% is considered normal; an increase of 15–25% indicates a marginal deficiency, while an increase greater than 25% with clinical signs is indicative of severe thiamin deficiency. Thiamin deficiency can also be assessed by the clinical response to administered thiamin, that is, an improvement in the condition after administering thiamin supplements. The nutritional status of vitamin B_2 (riboflavin) is investigated in a similar manner by determining the activation of glutathione reductase activity of erythrocytes in the presence of added FAD.

Assessing the nutritional status of niacin is more difficult. The usual method is to determine the concentrations of metabolites of niacin, for example 1-methylnicotinamide and 1-methyl-3-carboxamido-6-pyridone, in urine samples. Both are reasonably good measures of niacin status, as is the ratio of the concentrations of NAD^+ to $NADP^+$ in erythrocytes. A ratio of less than 1.0 may identify subjects at risk of developing a niacin deficiency. The nutritional status of vitamin B_5 (pantothenic acid) can also be assessed by determining its concentration in plasma or urine samples. In general, plasma pantothenic acid concentrations decrease in patients on a pantothenic acid deficient diet. However, the concentrations of pantothenic acid in blood respond less readily to intake than does the concentration in urine.

The status of vitamin B_6 can be investigated in a manner similar to those for thiamin and riboflavin by determining the activation coefficients of erythrocyte alanine and aspartate transaminase activities (ALT and AST respectively) in the presence of the cofactor pyridoxal phosphate. Alternatively, vitamin B_6 status may be assessed by the tryptophan loading test. Tryptophan is normally catabolized by the pathway shown in *Figure 10.38*. However, the activity of kynureninase decreases markedly in B_6 deficient patients. If such a patient is given an oral dose of 50 mg per kilogram body weight of tryptophan, then there is an increase in the amounts of kynurenic and xanthurenic acids formed and these appear in the urine. Generally less than 30 mg of xanthurenic acid is excreted daily; higher amounts are indicative of vitamin B_6 deficiency. However, some other disorders of tryptophan catabolism can also lead to an increase in xanthurenic acid production so abnormal results must be treated with caution.

A possible deficiency of vitamin H (biotin) can be investigated by measuring its concentration in whole blood, serum or urine. Determining plasma biotin

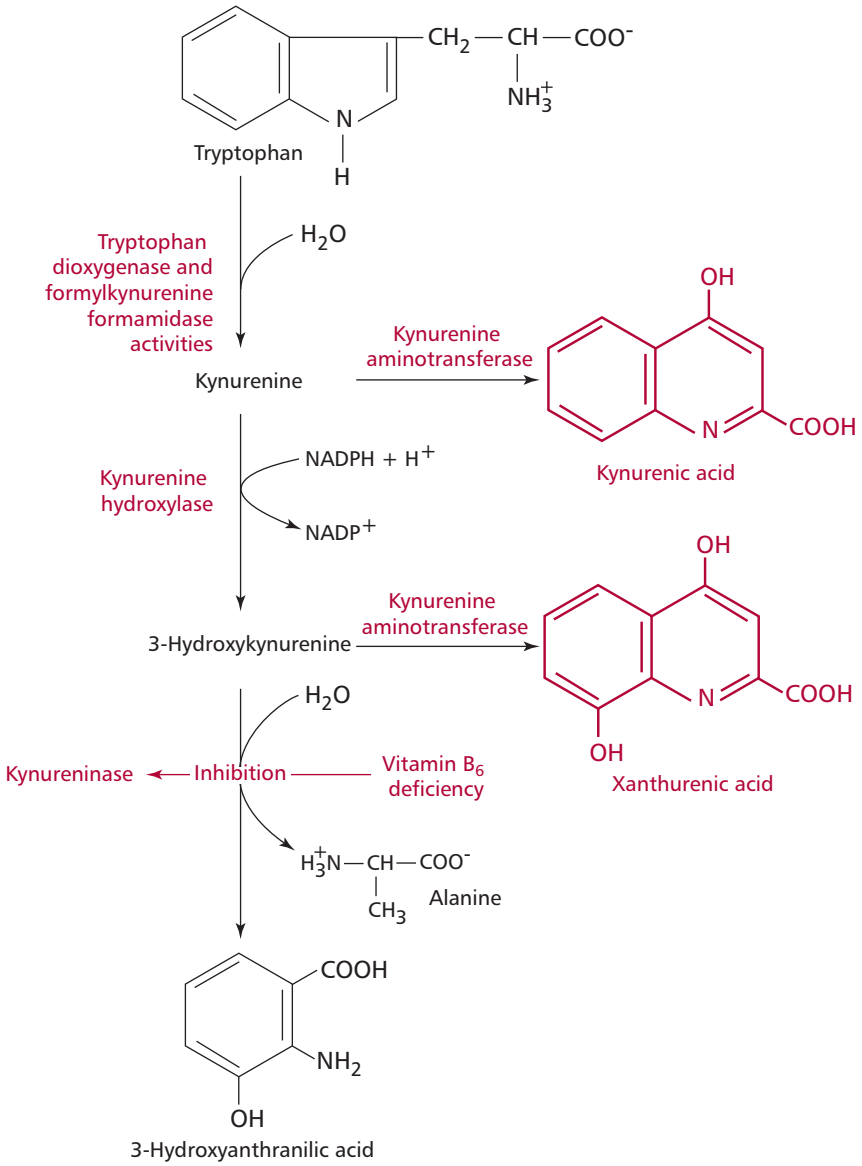


Figure 10.38 The catabolism of xanthurenic acid, which is the basis of the tryptophan load test for vitamin B_6 status. See text for details.

is not a reliable indicator of status. Changes in urinary excretion of biotin or of its metabolites are better indicators of biotin status.

Folic acid status may be investigated by directly measuring its concentration in serum or erythrocytes although these are associated with a number of problems. Serum folic acid tends to reflect dietary intake over the previous few weeks. Patients with both acquired and inherited folic acid deficiency may remain moderately deficient for months or years, taking in just enough folic acid to prevent low erythrocyte folic acid concentrations and frank anemia. Erythrocyte values are not sensitive to short-term variations; depletion occurs only in the later stages of deficiency and is usually accompanied by megaloblastic anemia. Both erythrocyte and serum folic acid studies must be performed. Severe folic acid deficiency is accompanied by a macrocytic anemia (*Chapter 13*) although the size of erythrocytes may be entirely normal in lesser degrees of depletion. Serum vitamin B_{12} concentrations should also be measured when evaluating folic acid deficiency since if either vitamin is deficient it can lead to a failure in absorption by megaloblastic intestinal cells resulting in a secondary deficiency of the other. Formiminoglutamic acid (FIGLU) is a substrate for the folic acid dependent enzyme, formimino-

glutamate formiminotransferase required for histidine catabolism. When the vitamin is deficient, FIGLU accumulates and is excreted into urine providing a sensitive test of deficiency. However, FIGLU also increases in vitamin B_{12} deficiency and liver disease, so a high FIGLU excretion is not specific for the diagnosis.

A deficiency of vitamin B_{12} (cobalamin) is investigated by measuring its serum concentration and by hematological examination of blood and bone marrow slides. Serum B_{12} can be measured in isolation or as part of a Schilling test to exclude intrinsic factor deficiency (pernicious anemia, *Chapter 13*). A Schilling test will assess whether vitamin B_{12} is being absorbed correctly by the body. The amount of vitamin B_{12} excreted in urine over a 24 h period is determined after giving the patient a known amount of radioactively labeled vitamin B_{12}. If the GIT is able to absorb vitamin B_{12} normally, then up to 25% of the vitamin will be present in the urine. If there is failure in absorption, then little or no vitamin B_{12} is detected in the urine. In the latter case, the test is repeated following an oral dose of intrinsic factor to determine whether the vitamin deficiency is due to lack of intrinsic factor or a GIT problem.

The concentration of vitamin C in the plasma is a poor indicator of deficiency. Measurements of cellular stores, especially in leukocytes are more useful. However, vitamin C concentrations in leukocytes should always be accompanied by a differential leukocyte count, given that different types of leukocytes vary in their capacity to accumulate the vitamin. A change in the proportion of polymorphonuclear leukocytes, which become saturated with vitamin C at lower concentrations than other leukocytes, would result in a change in total concentration of vitamin C per 10^6 cells, even if the nutritional status of the vitamin is unchanged.

The concentration of vitamin A in the plasma can be measured but this may be misleading as it only declines when tissue stores become severely depleted. Deficiency can also occur in severe protein deficiency which decreases the amount of its carrier protein. In such cases, the concentration of plasma vitamin A would increase once the protein deficiency was corrected. Clinical investigations of possible vitamin D deficiency involve determining serum calcium and phosphate concentrations and measuring serum alkaline phosphatase activity, since the enzyme is lost from cells during bone catabolism. The metabolite, 25-hydroxycholecalciferol in samples of plasma can be measured directly and is a good indicator of vitamin D status in the presence of normal renal function. Vitamin E status can also be assessed by direct measurement of its concentration in the plasma or serum, while vitamin K deficiency is investigated by assessing the prothrombin time of the patient (*Chapter 13*).

MINERALS AND TRACE ELEMENTS

A diagnosis of an overt mineral deficiency or excess can be confirmed by chemical tests that measure its concentration in the serum or, in some cases, urine. These measurements can give an indication of the amounts present in body tissues, although urine values tend to reflect dietary intake rather than the amounts stored in the body. The value of determining the serum concentrations of sodium, potassium, calcium and phosphate have been considered in *Chapter 8*. Investigations of chloride and sulfate are of little clinical relevance.

Measuring the concentrations of trace elements in clinical samples is complex and requires sensitive techniques because of their low values. Samples of plasma are often used but the determined values may not accurately reflect the concentration of the trace element at its site of action, which may be intracellular. However, for many trace elements, a low plasma concentration is indicative of a deficiency and adequate supplementation needs to be

provided, while a high value is an indicator of possible toxic levels. Copper deficiency is uncommon, except in patients on synthetic oral or intravenous diets. In these patients, serum copper is reduced to less than 12 μmol dm^{-3}. Low concentrations of plasma copper may indicate depleted stores but are a poor indicator of short-term copper status. Measuring Cu/Zn superoxide dismutase and cytochrome oxidase activities can also indicate copper status as the activities of these enzymes are reduced on a low copper diet. There is no satisfactory test for chromium deficiency and a diagnosis is usually made following improved glucose tolerance after chromium supplementation. Serum fluoride concentration can indicate fluoride exposure and can provide information on endemic fluorosis and allow preventative measures to be taken. Some, but not all studies, have reported a direct relationship between serum fluoride and the degree of fluorosis. Measurements of serum iodine may be a useful assessment of thyroid activity in adults. They may also be of use in investigating cretinism in infants, allowing a diagnosis to be made at an earlier age than is possible by other methods. Serum iodine measurements are also of value in assessing iodine toxicity. Methods to investigate the iron status of a patient are described in *Chapter 13*. Serum iron and total iron binding capacity can be investigated but serum ferritin is a better measure of total body iron stores. The amount of magnesium in serum is less than 1% of the total in the body and is therefore a relatively poor indicator of magnesium status. If hypomagnesemia is present (*Chapter 8*), then magnesium deficiency is likely but a normal serum value does not exclude a significant deficiency. Measurements of molybdenum in biological fluids are rarely required, which is perhaps fortunate since the methods used are inadequate due to the low concentrations involved. Selenium deficiency occurs with poor dietary intake and can be detected by its measurement in plasma or whole blood. However, determining erythrocyte activity of the selenium dependent enzyme, glutathione peroxidase can indirectly assess selenium status. Zinc concentrations less than 8 μmol dm^{-3} in the plasma may indicate zinc deficiency but low values may be associated with hypoalbuminemia, as most zinc is bound to albumin.

Chemical tests for mineral and trace element deficiencies must always be used to complement the medical history and physical examination since many of their findings may reflect underlying disease additional to the nutritional status of a patient. It is therefore necessary to understand these illnesses and how they influence the findings of physical and laboratory investigations.

10.5 GENERAL MANAGEMENT OF NUTRITIONAL DISORDERS

Patients who are malnourished or at risk of developing malnutrition require appropriate therapy, which ranges from simple dietary advice to long-term parenteral nutrition. The dietary needs of the patient must be carefully assessed to provide the correct amounts of energy, protein, vitamins, minerals and trace elements. Patients receive these diets by oral (*Figure 10.39*), tube and parenteral feeding; the last is most commonly administered by intravenous infusion. Oral supplementation should be used wherever possible and the common practice is to encourage consumption of specific foods or supplements that rectify the nutritional disorder in question. In cases where oral feeding is not possible, then liquid food is administered through a nasal tube to the stomach or small intestine. Tube feeding is particularly useful in patients with swallowing difficulties or anorexia. During tube feeding, liquid may be pumped continuously at a constant rate of 75 to 150 cm^3 per hour for 8–24 h. Liquid foods for tube feeding are available commercially as formulae that meet nearly all the patient needs. In some cases, food is administered as a bolus, that is, infusing a discrete volume of formula through the tube under gravity several

Figure 10.39 An example of a liquid food suitable for oral feeding.

times daily. It has the advantages of reducing the cost and allowing stable long-term patients more mobility. Parenteral feeding bypasses the GIT so nutrients are delivered directly into the blood. It is only used when oral or tube feeding have been deemed unsuitable; such as in patients who cannot eat or absorb food from the GIT. Total parenteral nutrition given via the peripheral veins or, in cases of long-term nutrition, through a central venous catheter can provide complete nutrition using preparations containing appropriate amounts of energy, amino acids, vitamins, minerals and trace elements. Like liquid foods for tube feeding, these preparations are available commercially but they are occasionally prepared individually to meet a patient's specific needs. Patients on long-term total parenteral nutrition require careful clinical and laboratory monitoring. Indeed, patients often have an increased risk of infection at the venous catheter site so care is necessary. Biochemical changes usually precede any clinical signs of nutrient deficiency and so regular laboratory monitoring is essential for early detection of any micronutrient deficiency.

Patients with PEM cannot immediately accept normal food because there are digestive enzyme deficiencies and often gastroenteritis. Rehydration is a priority and oral solutions (*Figure 10.40*) achieve this in some cases, while intravenous infusions may be necessary in severe cases. Diluted milk with added sugar may be given initially and as this becomes accepted the proportion of milk can be gradually increased. The cessation of diarrhea indicates that the health of the GIT mucosa is improving and normal foods can be gradually returned to the diet.

The management of obesity aims to reduce food intake, particularly total energy intake, and to encourage regular exercise. This is often achieved by cutting down on high energy foods, such as fats and alcohol. Education and psychological support can be helpful in cases of severe obesity. Orlistat, an inhibitor of pancreatic lipase, has been used to manage obesity since it reduces the digestion and absorption of dietary fats (*Chapter 11*) and sibutramine to suppress the appetite, in conjunction with an energy-controlled diet, has been used to control weight. Surgery is used in some cases of severe obesity. Jejuno-ileal bypass surgery for morbid obesity was first performed in 1952. In this process the end of the jejunum or the beginning of the ileum are removed and the remaining portions joined together. Most of the small intestine is removed leaving only a short length for digestion and absorption. Although jejuno-ileal bypass surgery results in a very good weight loss, severe side effects occur. The technique has been replaced with gastric bypass surgery where the upper part of the stomach is connected to the small intestine about one third of the way along its length. Thus only the lower part of the stomach and approximately two thirds of the small intestine are available for digestion and absorption, reducing energy intake and therefore weight, but dieting is still likely to be required. Again, this operation is not without the risk of developing serious postoperative complications. Liposuction may also be used to remove fat from under the skin though this is typically performed mainly for cosmetic rather than therapeutic reasons.

Eating disorders, such as AN and BN, are difficult to prevent and remain hard to treat. There are seemingly few effective treatments and no universally recognized plan of treatment. However, the goals of any therapy must be to establish normal eating patterns and to restore the patient's nutritional status and weight. Usually a multidisciplinary approach tailored to the individual is used. This will involve specialists in nutrition and mental health in addition to clinicians. Therapy generally involves the family, behavior modification and nutrition counseling, support groups and the use of antidepressants. Most patients with AN or BN are treated as outpatients although in severe cases hospitalization may be necessary. Given that compliance is often problematic, AN and BN are generally considered to be chronic disorders interrupted only by intermittent periods of short-lived remission.

A)

B)

Figure 10.40 Oral rehydrating solutions. (A) The informative cover of a UN approved sachet containing ingredients that form an oral rehydrating solution appropriate for children when dissolved in a suitable volume of water. (B) A commercially available oral rehydrating solution.

CASE STUDY 10.1

Andrew, a 51-year-old solicitor, had a health check. He was found to weigh 105 kg and his height was 1.82 m. Andrew is a smoker and does not exercise on a regular basis. He had a family history of heart disease. His blood pressure and plasma lipids were analyzed and the results are shown below (reference ranges are shown in parentheses):

Blood pressure	170/100 mmHg (120/80 mmHg)
Total cholesterol	6.3 mmol dm^{-3} (< 6.5 mmol dm^{-3} acceptable, < 5.2 mmol dm^{-3} is desirable)
Triacylglycerols	2.7 mmol dm^{-3} (0.45–1.80 mmol dm^{-3})
HDL cholesterol	0.7 mmol dm^{-3} (1.0–1.5 mmol dm^{-3})

Questions

(a) Calculate Andrew's BMI.

(b) Is Andrew obese?

(c) What risks are associated with obesity?

(d) What advice would you give Andrew?

CASE STUDY 10.2

Emily is a 17-year-old female. Over the past 18 months her periods have become increasingly irregular and intermittent and she consulted her doctor about this problem. During the consultation, Emily explained that she was studying for her preuniversity examinations and wishes to study law. Her parents and teachers expect her to do extremely well. She thought she was 'a bit overweight' and was dieting and about two years ago had started exercising more regularly. She was now jogging about 2 h a day and had recently taken up aerobic classes. A physical examination showed Emily to be 5′ 4″ tall and weigh 110 pounds. Body temperature, pulse rate and blood pressure were all normal. A urine ketostix gave a normal result.

Blood tests give the following results (reference ranges are shown in parentheses):

Glucose	4.3 mmol dm^{-3} (4.5–5.6 mmol dm^{-3})
Ketone bodies	110 μmol dm^{-3} (~70 μmol dm^{-3})

Questions

(a) Is Emily underweight?

(b) If so, by how much?

(c) Account for the clinical results.

(d) What treatment or advice would you give Emily?

CASE STUDY 10.3

John, a 74-year-old man residing in a nursing home, was seen by his doctor because he suffered from mental confusion and had difficulty walking because of paresthesiae and numbness in his legs. There was some general concern that the elderly residents at this nursing home were not being fed appropriately. A blood sample was taken and assessed and an erythrocyte transketolase activity test performed. Results are shown below.

Transketolase activity without added TPP	1.80 mmol h^{-1} per 10^9 erythrocytes
Transketolase activity with added TPP	2.21 mmol h^{-1} per 10^9 erythrocytes

Questions

(a) Does John suffer from deficiency of any vitamin?

(b) If so, how should he be treated?

10.6 SUMMARY

The body requires an adequate supply of proteins, carbohydrates, lipids, vitamins, minerals, trace elements and water for the maintenance of health, which between them provide energy and the raw materials for the synthesis

of biological molecules. The amount of each nutrient required to maintain health can be expressed as its dietary reference value (DRV). Nutritional disorders may arise from deficiencies or in some cases an excess of nutrients. Such disorders may be investigated, initially by taking a medical history, by the use of dietary questionnaires and by a physical examination, which may include taking anthropometric measurements. Laboratory tests may be used to confirm suspected diagnoses. Protein-energy malnutrition may lead to marasmus or kwashiorkor, while obesity, an increasing problem in developed countries, predisposes an individual to a variety of disorders including type 2 diabetes and coronary heart disease. Anorexia nervosa and bulimia nervosa are complex eating disorders with underlying psychological bases that require treatment, as well as help for the obvious nutritional deficits. The variety of disorders arising from vitamin deficits reflects the range of vitamins required for health and their diverse roles in the body. Hypervitaminoses are uncommon, although some B vitamins along with vitamin A and D toxicities have been observed when excessive amounts of vitamin supplements have been consumed. Disorders associated with mineral deficiencies are rare, though they do occur, for example is the development of thyroid goiter in diets deficient in iodine.

The management of nutritional disorders may require simple dietary advice, or, where severe, nutritional supplements. Medical interventions may require tube or parenteral feeding to restore a good nutritional status.

QUESTIONS

1. Blood copper binds to which plasma protein?
   a) thyroglobulin;
   b) ferritin;
   c) ceruloplasmin;
   d) hemoglobin;
   e) albumin.

2. Which of the following is **NOT** a complication of obesity?
   a) type 2 diabetes mellitus;
   b) vascular disease;
   c) hypertension;
   d) celiac disease;
   e) cholelithiasis.

3. Arrange the two following lists into their most appropriate pairings.

ATP7A	xanthine oxidase
bulimia nervosa	dental erosion
copper	acetyl CoA
iodide	dental caries
fluoride	Wilson's disease
folic acid	prothrombin time
leptin	Wernicke-Korsakoff syndrome
molybdenum	phytanic acid
edema	osteomalacia

pantothenic acid	heart disease
saturated fats	hemolytic anemia
thiamin	scurvy
vitamin B_1	green leafy vegetables
vitamin B_6	thiaminase
vitamin B_{12}	tryptophan
vitamin C	*OBESE/obese*
vitamin D	kwashiorkor
vitamin E	Crohn's disease
vitamin K	Menkes' disease
zinc	goiter

4. Your adolescent daughter tells you she is going to become a vegan (strict vegetarian). In the light of the accompanying table and your knowledge of protein nutrition, what advice would you give her?

Plant food	deficient in the following amino acids
Cereals, for example	
maize	lysine, methionine, tryptophan
rice	histidine, tryptophan
oats	methionine, tryptophan
wheat	lysine, threonine, tryptophan
Legumes	methionine, isoleucine, tryptophan
Nuts	lysine, threonine
Oil seeds	lysine, threonine
Other vegetable	methionine, isoleucine

5. A 72-year-old man who lived by himself was admitted to hospital following an accident. On admission, it was noted that he appeared emaciated, anemic and had widespread petechial hemorrhages. He also presented with gum disease. What types of nutritional deficiencies might be present?

6. *Figures 10.35* and *10.36* show the arm circumference and skinfold thickness being measured on two male patients, A and B respectively. The accompanying table gives some anthropometric data for them.

	A	B
Height	1.83 m	1.80 m
	6' 0''	5' 10''
Weight	77.5 kg	120 kg
	171 lb	266 lb
Triceps skin fold thickness/mm	12	15
Arm circumference/mm	270	320
Waist : hip ratio	0.90	0.98

What can be concluded from these data about the health risks to A and B?

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Useful web site:

http://www.foodstandards.gov.uk