Fuel Metabolism

In order to survive, humans must meet two basic metabolic requirements: we must be able to synthesize everything our cells need that is not supplied by our diet, and we must be able to protect our internal environment from toxins and changing conditions in our external environment. In order to meet these requirements, we metabolize our dietary components through four basic types of pathways: fuel oxidative pathways, fuel storage and mobilization pathways, biosynthetic pathways, and detoxification or waste disposal pathways. Cooperation between tissues and responses to changes in our external environment are communicated though transport pathways and intercellular signaling pathways (Fig. I.1).

The foods in our diet are the fuels that supply us with energy in the form of calories. This energy is used for carrying out diverse functions such as moving, thinking, and reproducing. Thus, a number of our metabolic pathways are *fuel oxidative pathways* that convert fuels into energy that can be used for biosynthetic and mechanical work. But what is the source of energy when we are not eating—between meals, and while we sleep? How does the hunger striker in the morning headlines survive so long? We have other metabolic pathways that are *fuel storage pathways*. The fuels that we store can be molibized during periods when we are not eating or when we need increased energy for exercise.

Our diet also must contain the compounds we cannot synthesize, as well as all the basic building blocks for compounds we do synthesize in our *biosynthetic pathways*. For example we have dietary requirements for some amino acids, but we can synthesize other amino acids from our fuels and a dietary nitrogen precursor. The compounds required in our diet for biosynthetic pathways include certain amino acids, vitamins, and essential fatty acids.

Detoxification pathways and *waste disposal pathways* are metabolic pathways devoted to removing toxins that can be present in our diets or in the air we breathe, introduced into our bodies as drugs, or generated internally from the metabolism of dietary components. Dietary components that have no value to the body, and must be disposed of, are called xenobiotics.

In general, biosynthetic pathways (including fuel storage) are referred to as *anabolic pathways,* that is, pathways that synthesize larger molecules from smaller components. The synthesis of proteins from amino acids is an example of an anabolic pathway. *Catabolic* pathways are those pathways that break down larger molecules into smaller components. Fuel oxidative pathways are examples of catabolic pathways.

In the human, the need for different cells to carry out different functions has resulted in cell and tissue specialization in metabolism. For example, our adipose tissue is a specialized site for the storage of fat and contains the metabolic pathways that allow it to carry out this function. However, adipose tissue is lacking many of the pathways that synthesize required compounds from dietary precursors. To enable our cells to cooperate in meeting our metabolic needs during changing conditions of diet, sleep, activity, and health, we need *transport pathways* into the blood and between tissues and *intercellular signaling pathways*. One means of communication is for *hormones* to carry signals to tissues about our dietary state. For example, a message that we have just had a meal, carried by the hormone insulin, signals adipose tissue to store fat.

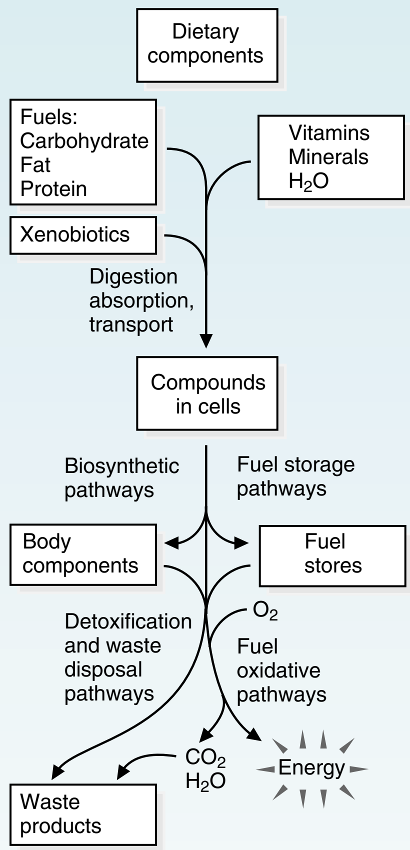

Fig. I.1. General metabolic routes for dietary components in the body. The types of Pathways are named in blue.

In the following section, we will provide an overview of various types of dietary components and examples of the pathways involved in utilizing these components. We will describe the fuels in our diet, the compounds produced by their digestion, and the basic patterns of fuel metabolism in the tissues of our bodies. We will describe how these patterns change when we eat, when we fast for a short time, and when we starve for prolonged periods. Patients with medical problems that involve an inability to deal normally with fuels will be introduced. These patients will appear repeatedly throughout the book and will be joined by other patients as we delve deeper into biochemistry.

1 Metabolic Fuels and Dietary Components

Fuel Metabolism. *We obtain our fuel primarily from* ***carbohydrates, fats****, and* ***proteins*** *in our diet. As we eat, our foodstuffs are* ***digested*** *and* ***absorbed****. The products of digestion circulate in the blood, enter various tissues, and are eventually taken up by cells and* ***oxidized*** *to produce* ***energy****. To completely convert our fuels to carbon dioxide (CO_2) and water (H_2O), molecular* ***oxygen*** *(O_2) is required. We breathe to obtain this oxygen and to eliminate the* ***carbon dioxide*** *(CO_2) that is produced by the oxidation of our foodstuffs.*

Fuel Stores. *Any dietary fuel that exceeds the body's immediate energy needs is stored, mainly as* ***triacylglycerol*** *(fat) in adipose tissue, as* ***glycogen*** *(a carbohydrate) in muscle, liver, and other cells, and, to some extent, as* ***protein*** *in muscle. When we are fasting, between meals and overnight while we sleep, fuel is drawn from these stores and is oxidized to provide energy (Fig. 1.1).*

Fuel Requirements. *We require enough energy each day to drive the* ***basic functions*** *of our bodies and to support our* ***physical activity****. If we do not consume enough food each day to supply that much energy, the body's fuel stores supply the remainder, and we lose weight. Conversely, if we consume more food than required for the energy we expend, our body's fuel stores enlarge, and we gain weight.*

Other Dietary Requirements. *In addition to providing energy, the diet provides* ***precursors*** *for the* ***biosynthesis*** *of compounds necessary for cellular and tissue structure, function, and survival. Among these precursors are the* ***essential fatty acids*** *and essential* ***amino acids*** *(those that the body needs but cannot synthesize). The diet must also supply* ***vitamins****,* ***minerals****, and* ***water****.*

Waste Disposal. *Dietary components that we can utilize are referred to as nutrients. However, both the diet and the air we breathe contain* ***xenobiotic compounds****, compounds that have no use or value in the human body and may be toxic. These compounds are excreted in the urine and feces together with metabolic waste products.*

Essential Nutrients
- Fuels
  - Carbohydrates
  - Fats
  - Proteins
- Required Components
  - Essential amino acids
  - Essential fatty acids
  - Vitamins
  - Minerals
  - Water

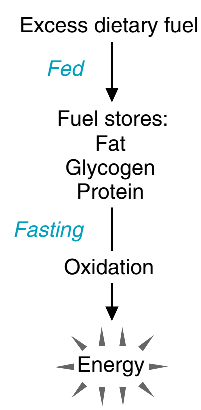

Fig. 1.1. Fate of excess dietary fuel in fed and fasting states.

THE WAITING ROOM

Percy Veere is a 59-year-old school teacher who was in good health until his wife died suddenly. Since that time, he has experienced an increasing degree of fatigue and has lost interest in many of the activities he previously enjoyed. Shortly after his wife's death, one of his married children moved far from home. Since then, Mr. Veere has had little appetite for food. When a

Percy Veere has a strong will. He is enduring a severe reactive depression after the loss of his wife. In addition, he must put up with the sometimes life-threatening antics of his hyperactive grandson, Dennis (the Menace) Veere. Yet through all of this, he will "persevere."

neighbor found Mr. Veere sleeping in his clothes, unkempt, and somewhat confused, she called an ambulance. Mr. Veere was admitted to the hospital psychiatry unit with a diagnosis of mental depression associated with dehydration and malnutrition.

Otto Shape is a 25-year-old medical student who was very athletic during high school and college, and is now "out-of-shape." Since he started medical school, he has been gaining weight (at 5 feet 10 inches tall, he currently weighs 187 lb). He has decided to consult a physician at the student health service before the problem gets worse.

Ivan Applebod is a 56-year-old accountant who has been morbidly obese for a number of years. He exhibits a pattern of central obesity, called an "apple shape," which is caused by excess adipose tissue deposited in the abdominal area. His major recreational activities are watching TV while drinking scotch and soda and doing occasional gardening. At a company picnic, he became very "winded" while playing baseball and decided it was time for a general physical examination. At the examination, he weighed 264 lb at 5 feet 10 inches tall. His blood pressure was slightly elevated, 155 mm Hg systolic (normal = 140 mm Hg or less) and 95 mm Hg diastolic (normal = 90 mm Hg or less).

Ann O'Rexia is a 23-year-old buyer for a woman's clothing store. Despite the fact that she is 5 feet 7 inches tall and weighs 99 lb, she is convinced she is overweight. Two months ago, she started a daily exercise program that consists of 1 hour of jogging every morning and 1 hour of walking every evening. She also decided to consult a physician about a weight reduction diet.

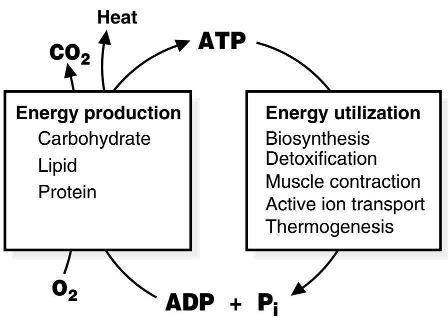

Fig. 1.2. The ATP–ADP cycle.

Oxidative pathways are catabolic; that is, they break molecules down. In contrast, anabolic pathways build molecules up from component pieces.

I. DIETARY FUELS

The major fuels we obtain from our diet are carbohydrates, proteins, and fats. When these fuels are oxidized to CO_2 and H_2O in our cells, energy is released by the transfer of electrons to O_2. The energy from this oxidation process generates heat and adenosine triphosphate (ATP) (Fig 1.2). Carbon dioxide travels in the blood to the lungs, where it is expired, and water is excreted in urine, sweat, and other secretions. Although the heat that is generated by fuel oxidation is used to maintain body temperature, the main purpose of fuel oxidation is to generate ATP. ATP provides the energy that drives most of the energy-consuming processes in the cell, including biosynthetic reactions, muscle contraction, and active transport across membranes. As these processes use energy, ATP is converted back to adenosine diphosphate (ADP) and inorganic phosphate (P_i). The generation and utilization of ATP is referred to as the ATP–ADP cycle.

The oxidation of fuels to generate ATP is called respiration (Fig. 1.3). Before oxidation, carbohydrates are converted principally to glucose, fat to fatty acids, and protein to amino acids. The pathways for oxidizing glucose, fatty acids, and amino acids have many features in common. They first oxidize the fuels to acetyl CoA, a precursor of the tricarboxylic acid (TCA) cycle. The TCA cycle is a series of reactions that completes the oxidation of fuels to CO_2 (see Chapter 19). Electrons lost from the fuels during oxidative reactions are transferred to O_2 by a series of proteins in the electron transport chain (see Chapter 20). The energy of electron transfer is used to convert ADP and P_i to ATP by a process known as oxidative phosphorylation.

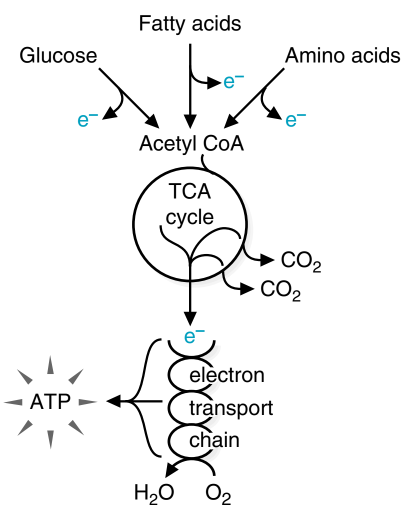

Fig. 1.3. Generation of ATP from fuel components during respiration. Glucose, fatty acids, and amino acids are oxidized to acetyl CoA, a substrate for the TCA cycle. In the TCA cycle, they are completely oxidized to CO_2. As fuels are oxidized, electrons (e^-) are transferred to O_2 by the electron transport chain, and the energy is used to generate ATP.

In discussions of metabolism and nutrition, energy is often expressed in units of calories. "Calorie" in this context really means kilocalorie (kcal). Energy is also expressed in joules. One kilocalorie equals 4.18 kilojoules (kJ). Physicians tend to use units of calories, in part because that is what their patients use and understand.

The food "calories" used in everyday speech are really "Calories," which = kilocalories. "Calorie," meaning kilocalorie, was originally spelled with a capital C, but the capitalization was dropped as the term became popular. Thus, a 1-calorie soft drink actually has 1 Cal (1 kcal) of energy.

A. Carbohydrates

The major carbohydrates in the human diet are starch, sucrose, lactose, fructose, and glucose. The polysaccharide starch is the storage form of carbohydrates in plants. Sucrose (table sugar) and lactose (milk sugar) are disaccharides, and fructose and glucose are monosaccharides. Digestion converts the larger carbohydrates to monosaccharides, which can be absorbed into the bloodstream. Glucose, a monosaccharide, is the predominant sugar in human blood (Fig. 1.4).

Oxidation of carbohydrates to CO_2 and H_2O in the body produces approximately 4 kcal/g (Table 1.1). In other words, every gram of carbohydrate we eat yields approximately 4 kcal of energy. Note that carbohydrate molecules contain a significant amount of oxygen and are already partially oxidized before they enter our bodies (see Fig. 1.4).

Table 1.1. Caloric Content of Fuels

	kcal/g
Carbohydrate	4
Fat	9
Protein	4
Alcohol	7

B. Proteins

Proteins are composed of amino acids that are joined to form linear chains (Fig. 1.5). In addition to carbon, hydrogen, and oxygen, proteins contain approximately 16% nitrogen by weight. The digestive process breaks down proteins to their constituent amino acids, which enter the blood. The complete oxidation of proteins to CO_2, H_2O, and NH_4^+ in the body yields approximately 4 kcal/g.

C. Fats

Fats are lipids composed of triacylglycerols (also called triglycerides). A triacylglycerol molecule contains 3 fatty acids esterified to one glycerol moiety (Fig. 1.6).

Fats contain much less oxygen than is contained in carbohydrates or proteins. Therefore, fats are more reduced and yield more energy when oxidized. The complete oxidation of triacylglycerols to CO_2 and H_2O in the body releases approximately 9 kcal/g, more than twice the energy yield from an equivalent amount of carbohydrate or protein.

Q: An analysis of **Ann O'Rexia's** diet showed she ate 100 g carbohydrate, 20 g protein, and 15 g fat each day. Approximately how many calories did she consume per day?

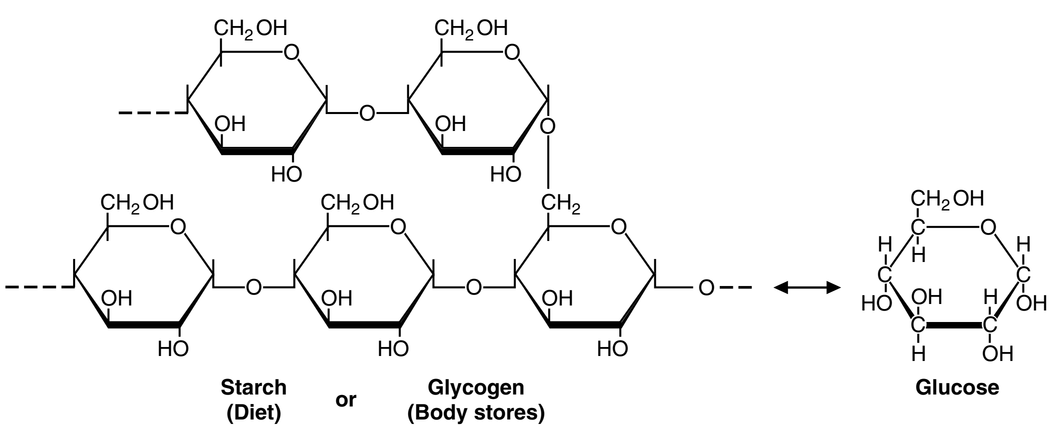

Fig. 1.4. Structure of starch and glycogen. Starch, our major dietary carbohydrate, and glycogen, the body's storage form of glucose, have similar structures. They are polysaccharides (many sugar units) composed of glucose, which is a monosaccharide (one sugar unit). Dietary disaccharides are composed of two sugar units.

A: **Miss O'Rexia** consumed
100 × 4 = 400 kcal as carbohydrate
20 × 4 = 80 kcal as protein
15 × 9 = 135 kcal as fat
for a total of 615 kcal/day.

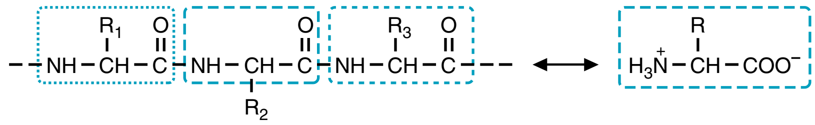

Fig. 1.5. General structure of proteins and amino acids. R = side chain. Different amino acids have different side chains. For example, R_1 might be $-CH_3$; R_2, -⊚ ; R_3, $-CH_2-COO^-$.

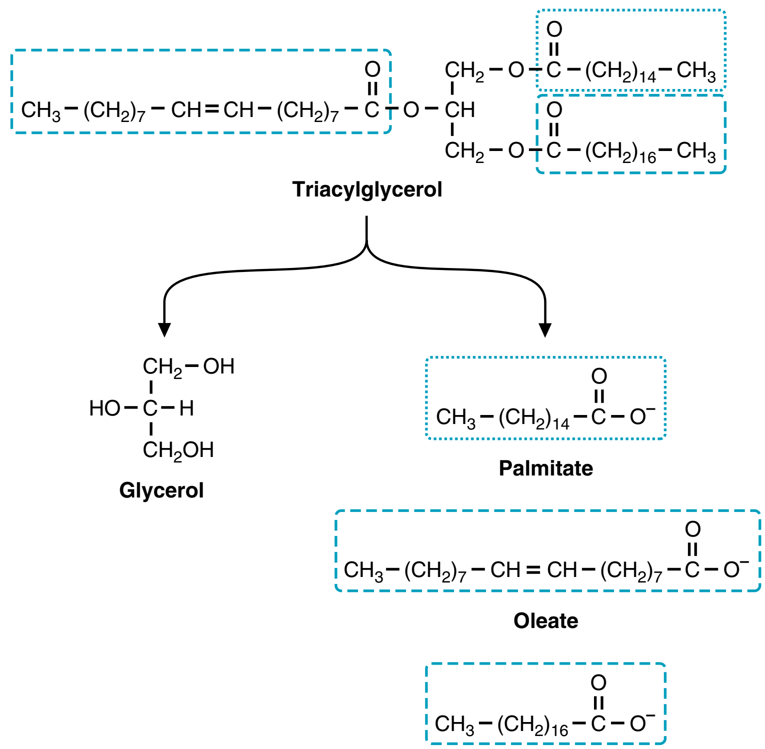

Fig. 1.6. Structure of a triacylglycerol. Palmitate and stearate are saturated fatty acids, i.e., they have no double bonds. Oleate is monounsaturated (one double bond). Polyunsaturated fatty acids have more than one double bond.

Q: **Ivan Applebod** ate 585 g carbohydrate, 150 g protein, and 95 g fat each day. In addition, he drank 45 g alcohol. How many calories did he consume per day?

D. Alcohol

Many people used to believe that alcohol (ethanol, in the context of the diet) has no caloric content. In fact, ethanol (CH_3CH_2OH) is oxidized to CO_2 and H_2O in the body and yields approximately 7 kcal/g—that is, more than carbohydrate but less than fat.

II. BODY FUEL STORES

It is not surprising that our body fuel stores consist of the same kinds of compounds found in our diet, because the plants and animals we eat also store fuels in the form of starch or glycogen, triacylglycerols, and proteins.

Although some of us may try, it is virtually impossible to eat constantly. Fortunately, we carry supplies of fuel within our bodies (Fig. 1.7). These fuel stores are light in weight, large in quantity, and readily converted into oxidizable substances. Most of us are familiar with fat, our major fuel store, which is located in adipose tissue. Although fat is distributed throughout our bodies, it tends to increase in quantity in our hips and thighs and in our abdomens as we advance into middle age. In addition to our fat stores, we also have important, although much smaller, stores of carbohydrate in the form of glycogen located primarily in our liver and muscles. Glycogen

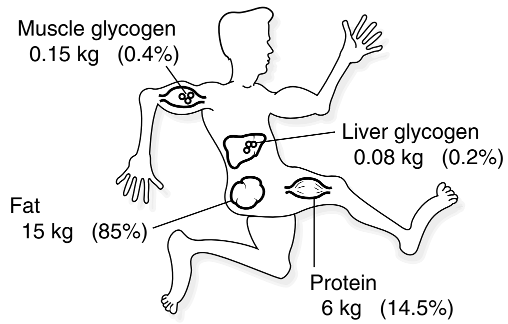

Fig. 1.7. Fuel composition of the average 70-kg man after an overnight fast (in kilograms and as percentage of total stored calories).

A: **Mr. Applebod** consumed
585 × 4 = 2,340 kcal as carbohydrate
150 × 4 = 600 kcal as protein
95 × 9 = 855 kcal as fat
45 × 7 = 315 kcal as alcohol

for a total of 4,110 kcal/day.

consists of glucose residues joined together to form a large, branched polysaccharide (see Fig. 1.4). Body protein, particularly the protein of our large muscle masses, also serves to some extent as a fuel store, and we draw on it for energy when we fast.

A. Fat

Our major fuel store is adipose triacylglycerol (triglyceride), a lipid more commonly known as fat. The average 70-kg man has approximately 15 kg stored triacylglycerol, which accounts for approximately 85% of his total stored calories (see Fig. 1.7).

Two characteristics make adipose triacylglycerol a very efficient fuel store: the fact that triacylglycerol contains more calories per gram than carbohydrate or protein (9 kcal/g versus 4 kcal/g) and the fact that adipose tissue does not contain much water. Adipose tissue contains only about 15% water, compared to tissues such as muscle that contain about 80%. Thus, the 70-kg man with 15 kg stored triacylglycerol has only about 18 kg adipose tissue.

In biochemistry and nutrition, the standard reference is often the 70-kg (154-lb) man. This standard probably was chosen because in the first half of the 20th century, when many nutritional studies were performed, young healthy medical and graduate students (who were mostly men) volunteered to serve as subjects for these experiments.

B. Glycogen

Our stores of glycogen in liver, muscle, and other cells are relatively small in quantity but are nevertheless important. Liver glycogen is used to maintain blood glucose levels between meals. Thus, the size of this glycogen store fluctuates during the day; an average 70-kg man might have 200 g or more of liver glycogen after a meal but only 80 g after an overnight fast. Muscle glycogen supplies energy for muscle contraction during exercise. At rest, the 70-kg man has approximately 150 g of muscle glycogen. Almost all cells, including neurons, maintain a small emergency supply of glucose as glycogen.

What would happen to a 70-kg man if the 135,000 kcal stored as triacylglycerols in his 18 kg of adipose tissue were stored instead as skeletal muscle glycogen? It would take approximately 34 kg glycogen to store as many calories. Glycogen, because it is a polar molecule with –OH groups, binds approximately 4 times its weight in water, or 136 kg. Thus, his fuel stores would weigh 170 kg.

C. Protein

Protein serves many important roles in the body; unlike fat and glycogen, it is not solely a fuel store. Muscle protein is essential for body movement. Other proteins serve as enzymes (catalysts of biochemical reactions) or as structural components of cells and tissues. Only a limited amount of body protein can be degraded, approximately 6 kg in the average 70-kg man, before our body functions are compromised.

III. DAILY ENERGY EXPENDITURE

If we want to stay in energy balance, neither gaining nor losing weight, we must, on average, consume an amount of food equal to our daily energy expenditure. The daily energy expenditure (DEE) includes the energy to support our basal metabolism (basal metabolic rate or resting metabolic rate) and our physical activity, plus the energy required to process the food we eat (diet-induced thermogenesis).

Daily energy expenditure = RMR + Physical Activity + DIT where RMR is the resting metabolic rate and DIT is diet-induced thermogenesis. BMR (basal metabolic rate) is used interchangeably with RMR in this equation.

A. Resting Metabolic Rate

The resting metabolic rate (RMR) is a measure of the energy required to maintain life: the functioning of the lungs, kidneys and brain, the pumping of the heart, the maintenance of ionic gradients across membranes, the reactions of biochemical pathways, and so forth. Another term used to describe basal metabolism is the basal metabolic rate (BMR). The BMR was originally defined as the energy expenditure of a person mentally and bodily at rest in a thermoneutral environment 12 to18 hours after a meal. However, when a person is awakened and their heat production or oxygen consumption is measured, they are no longer sleeping or totally at mental rest, and their metabolic rate is called the resting metabolic rate (RMR). It is also sometimes called the resting energy expenditure (REE). The RMR and BMR differ very little in value.

The BMR, which is usually expressed in kcal/day, is affected by body size, age, sex, and other factors (Table 1.2). It is proportional to the amount of metabolically active tissue (including the major organs) and to the lean (or fat-free) body mass. Obviously, the amount of energy required for basal functions in a large person is greater than the amount required in a small person. However, the BMR is usually lower for women than for men of the same weight because women usually have more metabolically inactive adipose tissue. Body temperature also affects the BMR, which increases by 12% with each degree centigrade increase in body temperature (i.e., "feed a fever; starve a cold"). The ambient temperature affects the BMR, which increases slightly in colder climates as thermogenesis is activated. Excessive secretion of thyroid hormone (hyperthyroidism) causes the BMR to increase, whereas diminished secretion (hypothyroidism) causes it to decrease. The BMR increases during pregnancy and lactation. Growing children have a higher BMR per kilogram body weight than adults, because a greater proportion of their bodies is composed of brain, muscle, and other more metabolically active tissues. The BMR declines in aging individuals because their metabolically active tissue is shrinking and body fat is increasing. In addition, large variations exist in BMR from one adult to another, determined by genetic factors.

A rough estimate of the BMR may be obtained by assuming it is 24 kcal/day/kg body weight and multiplying by the body weight. An easy way to remember this is 1 kcal/kg/hr. This estimate works best for young individuals who are near their ideal weight. More accurate methods for calculating the BMR use empirically derived equations for different gender and age groups (Table 1.3). Even these calculations do not take into account variation among individuals.

Table 1.2. Factors Affecting BMR Expressed per kg Body Weight

Gender (males higher than females)
Body temperature (increased with fever)
Environmental temperature (increased in cold)
Thyroid status (increased in hyperthyroidism)
Pregnancy and lactation (increased)
Age (decreases with age)

Q: What are **Ivan Applebod's** and **Ann O'Rexia's** RMR? (Compare the method for a rough estimate to values obtained with equations in Table 1.3.)

Registered dieticians use extensive tables for calculating energy requirements, based on height, weight, age, and activity level. A more accurate calculation is based on the fat-free mass (FFM), which is equal to the total body mass minus the mass of the person's adipose tissue. With FFM, the BMR is calculated using the equation $BMR = 186 + FFM \times 23.6$ kcal/kg per day. This formula eliminates differences between sexes and between aged versus young individuals that are attributable to differences in relative adiposity. However, determining FFM is relatively cumbersome—it requires weighing the patient underwater and measuring the residual lung volume.

Indirect calorimetry, a technique that measures O_2 consumption and CO_2 production, can be used when more accurate determinations are required for hospitalized patients. A portable indirect calorimeter is used to measure oxygen consumption and the respiratory quotient (RQ), which is the ratio of O_2 consumed to CO_2 produced. The RQ is 1.00 for individuals oxidizing carbohydrates, 0.83 for protein, and 0.71 for fat. From these values, the daily energy expenditure (DEE) can be determined.

B. Physical Activity

In addition to the RMR, the energy required for physical activity contributes to the DEE. The difference in physical activity between a student and a lumberjack is enormous, and a student who is relatively sedentary during the week may be much

Table 1.3. Equation for Predicting BMR from Body Weight (W) in kg

Males		Females	
Age Range (years)	BMR kcal/day	Age Range (years)	BMR kcal/day
0–3	60.9W − 54	0–3	61.0W − 51
3–10	22.7W + 495	3–10	22.5W + 499
10–18	17.5W + 651	10–18	12.2W + 746
18–30	15.3W + 679	18–30	14.7W + 496
30–60	11.6W + 879	30–60	8.7W + 829
>60	13.5W + 487	>60	10.5W + 596

From Energy and protein requirements: report of a Joint FAO/WHO/UNU Expert Consultation. Technical report series no. 724. Geneva World Health Organization, 1987:71. See also Schofield et al. Hum Nutr Clin Nutr 1985;39 (suppl).

Table 1.4. Typical Activities with Corresponding Hourly Activity Factors

ACTIVITY CATEGORY	Hourly Activity Factor (for Time in Activity)
Resting: sleeping, reclining	1.0
Very light: seated and standing activities, driving, laboratory work, typing, sewing, ironing, cooking, playing cards, playing a musical instrument	1.5
Light: walking on a level surface at 2.5–3 mph, garage work, electrical trades, carpentry, restaurant trades, house cleaning, golf, sailing, table tennis	2.5
Moderate: walking 3.5–4 mph, weeding and hoeing, carrying loads, cycling, skiing, tennis, dancing	5.0
Heavy: walking uphill with a load, tree felling, heavy manual digging, mountain climbing, basketball, football, soccer	7.0

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The hourly activity factor is multiplied by the BMR (RMR) per hour times the number of hours engaged in the activity to give the caloric expenditure for that activity. If this is done for all of the hours in a day, the sum over 24 hours will approximately equal the daily energy expenditure.

A: Mr. **Applebod** weighs 264 lb or 120 kg (264 lb divided by 2.2 lb/kg). His estimated RMR = 24 kcal/kg/day × 120 = 2,880 kcal/day. His RMR calculated from Table 1.3 is only 2,271 kcal (11.6 W + 879 = (11.6 × 120) + 879). **Miss O'Rexia** weighs 99 lb or 45 kg (99/2.2 lb/kg). Her estimated RMR = (24 kcal/kg/day) × (45 kg) = 1,080 kcal/day. Her RMR from Table 1.3 is very close to this value (14.7 W + 496 = 1,157 kcal/day). Thus, the rough estimate does not work well for obese patients because a disproportionately larger proportion of their body weight is metabolically inactive adipose tissue.

more active during the weekend. Table 1.4 gives factors for calculating the approximate energy expenditures associated with typical activities.

A rough estimate of the energy required per day for physical activity can be made by using a value of 30% of the RMR (per day) for a very sedentary person (such as a medical student who does little but study) and a value of 60 to 70% of the RMR (per day) for a person who engages in about 2 hours of moderate exercise per day (see Table 1.4). A value of 100% or more of the RMR is used for a person who does several hours of heavy exercise per day.

Based on the activities listed in Table 1.4, the average U.S. citizen is rather sedentary. Sedentary habits correlate strongly with risk for cardiovascular disease, so it is not surprising that cardiovascular disease is the major cause of death in this country.

C. Diet-Induced Thermogenesis

Our DEE includes a component related to the intake of food known as diet-induced thermogenesis (DIT) or the thermic effect of food (TEF). DIT was formerly called the specific dynamic action (SDA). After the ingestion of food, our metabolic rate increases because energy is required to digest, absorb, distribute, and store nutrients.

The energy required to process the types and quantities of food in the typical American diet is probably equal to approximately 10% of the kilocalories ingested. This amount is roughly equivalent to the error involved in rounding off the caloric content of carbohydrate, fat, and protein to 4, 9, and 4, respectively. Therefore, DIT is often ignored and calculations are based simply on the RMR and the energy required for physical activity.

D. Calculations of Daily Energy Expenditure

The total daily energy expenditure is usually calculated as the sum of the RMR (in kcal/day) plus the energy required for the amount of time spent in each of the various types of physical activity (see Table 1.4). An approximate value for the daily energy expenditure can be determined from the RMR and the appropriate percentage of the RMR required for physical activity (given above). For example, a very sedentary medical student would have a DEE equal to the RMR plus 30% of the RMR (or 1.3 × RMR) and an active person's daily expenditure could be 2 times the RMR.

Q: What are reasonable estimates for **Ivan Applebod's** and **Ann O'Rexia's** daily energy expenditure?

E. Healthy Body Weight

Ideally, we should strive to maintain a weight consistent with good health. Overweight people are frequently defined as more than 20% above their ideal weight. But what is the ideal weight? The body mass index (BMI), calculated as

BMI equals:

$$\text{Weight/height}^2\ (\text{kg/m}^2)$$

or

$$\frac{\text{Weight (lbs)} \times 704}{\text{height}^2\ (\text{in}^2)}$$

Where the height is measured without shoes and the weight is measured with minimal clothing.

BMI values of:

18.5 − 24.9 = desirable
<18.5 = underweight
25 − 29.9 = overweight
≥30 = obese

Q: Are **Ivan Applebod** and **Ann O'Rexia** in a healthy weight range?

A: **Mr. Applebod's** BMR is 2,271 kcal/day. He is sedentary, so he only requires approximately 30% more calories for his physical activity. Therefore, his daily expenditure is approximately 2,271 + (0.3 × 2,271) or 1.3 × 2,271 or 2,952 kcal/day. **Miss O'Rexia's** BMR is 1,157 kcal/day. She performs 2 hours of moderate exercise per day (jogging and walking), so she requires approximately 65% more calories for her physical activity. Therefore, her daily expenditure is approximately 1,157 + (0.65 × 1157) or 1.65 × 1,157 or 1,909 kcal/day.

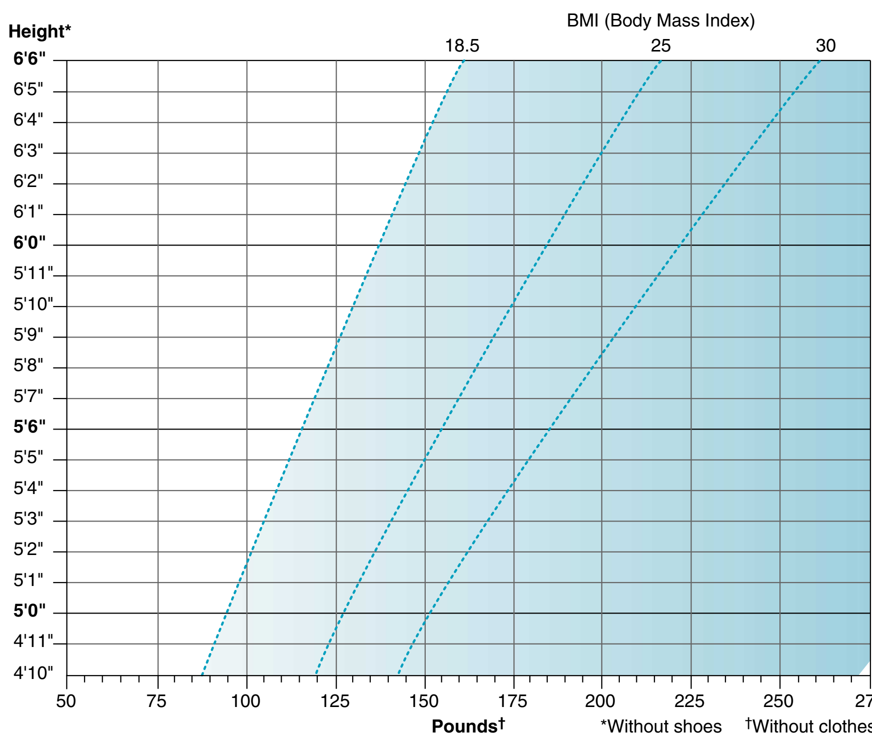
weight/height^2 (kg/m^2), is currently the preferred method for determining whether a person's weight is in the healthy range.

In general, adults with BMI values below 18.5 are considered underweight. Those with BMIs between 18.5 and 24.9 are considered to be in the healthy weight range, between 25 and 29.9 are in the overweight or preobese range, and above 30 are in the obese range.

F. Weight Gain and Loss

To maintain our body weight, we must stay in caloric balance. We are in caloric balance if the kilocalories in the food we eat equal our DEE. If we eat less food than we require for our DEE, our body fuel stores supply the additional calories,

To evaluate a patient's weight, physicians need standards of obesity applicable in a genetically heterogeneous population. Life insurance industry statistics have been used to develop tables giving the weight ranges, based on gender, height, and body frame size, that are associated with the greatest longevity, such as the Metropolitan Height and Weight Tables. However, these tables are considered inadequate for a number of reasons (e.g., they reflect data from upper-middle-class white groups). The BMI is the classification that is currently used clinically. It is based on two simple measurements, height without shoes and weight with minimal clothing. Patients can be shown their BMI in a nomogram and need not use calculations. The healthy weight range coincides with the mortality data derived from life insurance tables. The BMI also shows a good correlation with independent measures of body fat. The major weakness of the use of the BMI is that some very muscular individuals may be classified as obese when they are not. Other measurements to estimate body fat and other body compartments, such as weighing individuals underwater, are more difficult, expensive, and time consuming and have generally been confined to research purposes.



If patients are above or below ideal weight (such as **Ivan Applebod** or **Ann O'Rexia**), the physician, often in consultation with a registered dietician, prescribes a diet designed to bring the weight into the ideal range.

and we lose weight. Conversely, if we eat more food than we require for our energy needs, the excess fuel is stored (mainly in our adipose tissue), and we gain weight (Fig. 1.8).

When we draw on our adipose tissue to meet our energy needs, we lose approximately 1 lb whenever we expend approximately 3,500 calories more than we consume. In other words, if we eat 1,000 calories less than we expend per day, we will lose about 2 lb/week. Because the average individual's food intake is only about 2,000 to 3,000 calories/day, eating one-third to one-half the normal amount will cause a person to lose weight rather slowly. Fad diets that promise a loss of weight much more rapid than this have no scientific merit. In fact, the rapid initial weight loss the fad dieter typically experiences is attributable largely to loss of body water. This loss of water occurs in part because muscle tissue protein and liver glycogen are degraded rapidly to supply energy during the early phase of the diet. When muscle tissue (which is approximately 80% water) and glycogen (approximately 70% water) are broken down, this water is excreted from the body.

IV. DIETARY REQUIREMENTS

In addition to supplying us with fuel and with general-purpose building blocks for biosynthesis, our diet also provides us with specific nutrients that we need to remain healthy. We must have a regular supply of vitamins and minerals and of the essential fatty acids and essential amino acids. "Essential" means that they are essential in the diet; the body cannot synthesize these compounds from other molecules and therefore must obtain them from the diet. Nutrients that the body requires in the diet only under certain conditions are called "conditionally essential."

The Recommended Dietary Allowance (RDA) and the Adequate Intake (AI) provide quantitative estimates of nutrient requirements. The RDA for a nutrient is the average daily dietary intake level necessary to meet the requirement of nearly all (97–98%) healthy individuals in a particular gender and life stage group. Life stage group is a certain age range or physiologic status (i.e., pregnancy or lactation). The RDA is intended to serve as a goal for intake by individuals. The AI is a recommended intake value that is used when not enough data are available to establish an RDA.

A. Carbohydrates

No specific carbohydrates have been identified as dietary requirements. Carbohydrates can be synthesized from amino acids, and we can convert one type

Malnutrition, the absence of an adequate intake of nutrients, occurs in the United States principally among children of families with incomes below the poverty level, the elderly, individuals whose diet is influenced by alcohol and drug usage, and those who make poor food choices. More than 13 million children in the United States live in families with incomes below the poverty level. Of these, approximately 10% have clinical malnutrition, most often anemia resulting from inadequate iron intake. A larger percentage have mild protein and energy malnutrition and exhibit growth retardation, sometimes as a result of parental neglect. Childhood malnutrition may also lead to learning failure and chronic illness later in life. A weight for age measurement is one of the best indicators of childhood malnourishment because it is easy to measure, and weight is one of the first parameters to change during malnutrition.

The term *kwashiorkor* refers to a disease originally seen in African children suffering from a protein deficiency. It is characterized by marked hypoalbuminemia, anemia, edema, pot belly, loss of hair, and other signs of tissue injury. The term *marasmus* is used for prolonged protein–calorie malnutrition, particularly in young children.

Q: Are **Ivan Applebod** and **Ann O'Rexia** gaining or losing weight?

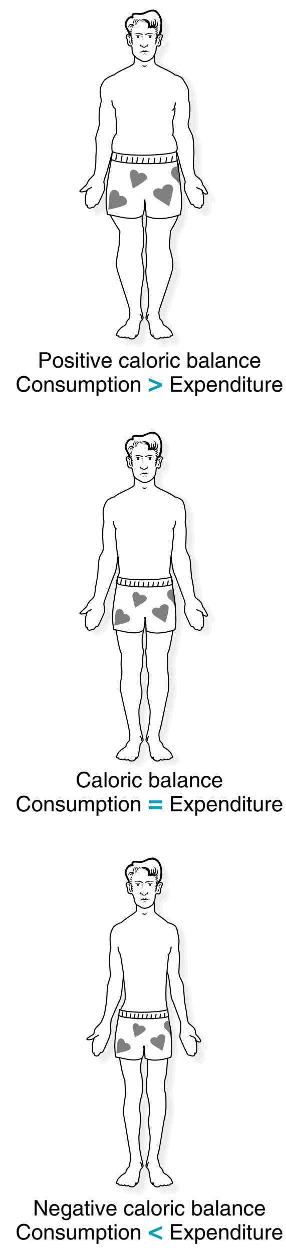


Fig. 1.8. Caloric balance.

A: **Ivan Applebod**'s weight is classified as obese. His BMI is 264 lb × 704/70 in^2 = 37.9. **Ann O'Rexia** is underweight. Her BMI is 99 lb × 704/67 in^2 = 15.5.

A: **Mr. Applebod** expends about 2,952 kcal/day and consumes 4,110. By this calculation, he consumes 1,158 more kcal than he expends each day and is gaining weight. **Miss O'Rexia** expends 1,909 kcal/day while she consumes only 615. Therefore, she expends 1,294 more kcal/day than she consumes, so she is losing weight.

of carbohydrate to another. However, health problems are associated with the complete elimination of carbohydrate from the diet, partly because a low-carbohydrate diet must contain higher amounts of fat to provide us with the energy we need. High-fat diets are associated with obesity, atherosclerosis, and other health problems.

B. Essential Fatty Acids

Although most lipids required for cell structure, fuel storage, or hormone synthesis can be synthesized from carbohydrates or proteins, we need a minimal level of certain dietary lipids for optimal health. These lipids, known as essential fatty acids, are required in our diet because we cannot synthesize fatty acids with these particular arrangements of double bonds. The essential fatty acids α-linoleic and α-linolenic acid are supplied by dietary plant oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are supplied in fish oils. They are the precursors of the eicosanoids (a set of hormone-like molecules that are secreted by cells in small quantities and have numerous important effects on neighboring cells). The eicosanoids include the prostaglandins, thromboxanes, leukotrienes, and other related compounds.

C. Protein

The RDA for protein is approximately 0.8 g high-quality protein per kilogram of ideal body weight, or approximately 60 g/day for men and 50 g/day for women. "High-quality" protein contains all of the essential amino acids in adequate amounts. Proteins of animal origin (milk, egg, and meat proteins) are high quality. The proteins in plant foods are generally of lower quality, which means they are low in one or more of the essential amino acids. Vegetarians may obtain adequate amounts of the essential amino acids by eating mixtures of vegetables that complement each other in terms of their amino acid composition.

1. ESSENTIAL AMINO ACIDS

Different amino acids are used in the body as precursors for the synthesis of proteins and other nitrogen-containing compounds. Of the 20 amino acids commonly required in the body for synthesis of protein and other compounds, nine amino acids are essential in the diet of an adult human because they cannot be synthesized in the body. These are lysine, isoleucine, leucine, threonine, valine, tryptophan, phenylalanine, methionine, and histidine.

Students often use mnemonics to remember the essential amino acids. One common mnemonic is "Little TV tonight. Ha!" or **LIL** (**l**ysine-**i**soleucine-**l**eucine) **TV** (**t**hreonine-**v**aline) **T**o (**t**ryptophan) **PM** (**p**henyl- alanine-**m**ethionine). **(HA)** (**h**istidine-**a**rginine)!

Certain amino acids are conditionally essential, that is, required in the diet only under certain conditions. Children and pregnant women have a high rate of protein synthesis to support growth, and require some arginine in the diet, although it can be synthesized in the body. Histidine is essential in the diet of the adult in very small quantities because adults efficiently recycle histidine. The increased requirement of children and pregnant women for histidine is therefore much larger than their increased requirement of other essential amino acids. Tyrosine and cysteine are considered conditionally essential. Tyrosine is synthesized from phenylalanine, and it is required in the diet if phenylalanine intake is inadequate, or if an individual is congenitally deficient in an enzyme required to convert phenylalanine to tyrosine (the congenital disease phenylketonuria). Cysteine is synthesized by using sulfur from methionine, and it also may be required in the diet under certain conditions.

2. NITROGEN BALANCE

The proteins in the body undergo constant turnover; that is, they are constantly being degraded to amino acids and resynthesized. When a protein is degraded, its amino acids are released into the pool of free amino acids in the body. The amino acids from dietary proteins also enter this pool. Free amino acids can have one of three fates: they are used to make proteins, they serve as precursors for synthesis of essential nitrogen-containing compounds (e.g., heme, DNA, RNA), or they are oxidized as fuel to yield energy. When amino acids are oxidized, their nitrogen atoms are excreted in the urine principally in the form of urea. The urine also contains smaller amounts of other nitrogenous excretory products (uric acid, creatinine, and NH_4^+) derived from the degradation of amino acids and compounds synthesized from amino acids (Table 1.5). Some nitrogen is also lost in sweat, feces, and cells that slough off.

Nitrogen balance is the difference between the amount of nitrogen taken into the body each day (mainly in the form of dietary protein) and the amount of nitrogen in compounds lost (Table 1.6). If more nitrogen is ingested than excreted, a person is said to be in positive nitrogen balance. Positive nitrogen balance occurs in growing individuals (e.g., children, adolescents, and pregnant women), who are synthesizing more protein than they are breaking down. Conversely, if less nitrogen is ingested than excreted, a person is said to be in negative nitrogen balance. A negative nitrogen balance develops in a person who is eating either too little protein or protein that is deficient in one or more of the essential amino acids. Amino acids are continuously being mobilized from body proteins. If the diet is lacking an essential amino acid or if the intake of protein is too low, new protein cannot be synthesized, and the unused amino acids will be degraded, with the nitrogen appearing in the urine. If a negative nitrogen balance persists for too long, bodily function will be impaired by the net loss of critical proteins. In contrast, healthy adults are in nitrogen balance (neither positive nor negative), and the amount of nitrogen consumed in the diet equals its loss in urine, sweat, feces, and other excretions.

D. Vitamins

Vitamins are a diverse group of organic molecules required in very small quantities in the diet for health, growth, and survival (Latin *vita*, life). The absence of a vitamin from the diet or an inadequate intake results in characteristic deficiency signs and, ultimately, death. Table 1.7 lists the signs or symptoms of deficiency for each vitamin, its RDA or AI for young adults, and common food sources. The amount of each vitamin required in the diet is small (in the microgram or milligram range), compared with essential amino acid requirements (in the gram range). The vitamins are often divided into two classes, water-soluble vitamins and fat-soluble vitamins. This classification has little relationship to their function but is related to the absorption and transport of fat-soluble vitamins with lipids.

Most vitamins are used for the synthesis of coenzymes, complex organic molecules that assist enzymes in catalyzing biochemical reactions, and the deficiency symptoms reflect an inability of cells to carry out certain reactions. However, some vitamins also act as hormones. We will consider the roles played by individual vitamins as we progress through the subsequent chapters of this text.

Although the RDA or AI for each vitamin varies with age and sex, the difference is usually not very large once adolescence is reached. For example, the RDA for

Table 1.6. Nitrogen Balance

Positive Nitrogen Balance	Growth (e.g., childhood, pregnancy)	Dietary N > Excreted N
Nitrogen Balance	Normal healthy adult	Dietary N = Excreted N
Negative Nitrogen Balance	Dietary deficiency of total protein or amino acids; catabolic stress	Dietary N < Excreted N

Table 1.5. Major Nitrogenous Excretion Products

Urea
Creatinine
Uric acid
NH_4^+

Multiple vitamin deficiencies accompanying malnutrition are far more common in the United States than the characteristic deficiency diseases associated with diets lacking just one vitamin, because we generally eat a variety of foods. The characteristic deficiency diseases arising from single vitamin deficiencies were often identified and described in humans through observations of populations consuming a restricted diet because that was all that was available. For example, thiamine deficiency was discovered by a physician in Java, who related the symptoms of beri-beri to diets composed principally of polished rice. Today, single vitamin deficiencies usually occur as a result of conditions that interfere with the uptake or utilization of a vitamin or as a result of poor food choices or a lack of variety in the diet. For example, peripheral neuropathy associated with vitamin E deficiency can occur in children with fat malabsorption, and alcohol consumption can result in beri-beri. Vegans, individuals who consume diets lacking all animal products, can develop deficiencies in vitamin B_{12}.

In the hospital, it was learned that **Mr. Percy Veere** had lost 32 lb in the 8 months since his last visit to his family physician. On admission, his hemoglobin (the iron-containing compound in the blood, which carries O_2 from the lungs to the tissues) was 10.7 g/dL (reference range, males = 12 – 15.5), his serum iron was 38 μg/dL (reference range, males = 42 – 135), and other hematologic indices were also abnormal. These values are indicative of an iron deficiency anemia. His serum folic acid level was 0.9 ng/mL (reference range = 3 – 20), indicating a low intake of this vitamin. His vitamin B_{12} level was 190 pg/mL (reference range = 180 – 914). A low blood vitamin B_{12} level can be caused by decreased intake, absorption, or transport, but it takes a long time to develop. His serum albumin was 3.2 g/dL (reference range = 3.5 – 5.0), which is an indicator of protein malnutrition or liver disease.

Table 1.7. VITAMINS [a]

Vitamin	Dietary Reference Intakes (DRI) Females (F) Males (M) (18–30 yrs old)	Some Common Food Sources	Consequences of Deficiency (Names of deficiency diseases are in bold)
Water-soluble vitamins			
Vitamin C	**RDA** F: 75 mg M: 90 mg **UL:** 2 g	Citrus fruits; potatoes; peppers, broccoli, spinach; strawberries	**Scurvy:** defective collagen formation leading to subcutaneous hemorrhage, aching bones, joints, and muscle in adults, rigid position and pain in infants.
Thiamin	**RDA** F: 1.1 mg M: 1.2 mg	Enriched cereals and breads; unrefined grains; pork; legumes, seeds, nuts	**Beri-beri:** (wet) Edema; anorexia, weight loss; apathy, decrease in short-term memory, confusion; irritability; muscle weakness; an enlarged heart
Riboflavin	**RDA** F: 1.1 mg M: 1.3 mg	Dairy products; fortified cereals; meats, poultry, fish; legumes	**Ariboflavinosis:** Sore throat, hyperemia, edema of oral mucusal membranes; cheilosis, angular stomatis; glossitis, magenta tongue; seborrheic dermatitis; normochromic normocylic anemia
Niacin[b]	**RDA** F: 14 mg NEQ M: 16 mg NEQ **UL:** 35 mg	Meat: chicken, beef, fish; enriched cereals or whole grains; most foods	**Pellagra:** Pigmented rash in areas exposed to sunlight; vomiting; constipation or diarrhea; bright red tongue; neurologic symptoms
Vitamin B_6 (pyridoxine)	**RDA** F: 1.3 mg M: 1.3 mg **UL:** 100 mg	Chicken, fish, pork; eggs; fortified cereals, unmilled rice, oats; starchy vegetables; noncitrus fruits; peanuts, walnuts	Seborrheic dermatitis; microcytic anemia; epileptiform convulsions; depression and confusion
Folate	**RDA** F: 400 µg M: 400 µg	Citrus fruits; dark green vegetables; fortified cereals and breads; legumes	Impaired cell division and growth; **megaloblastic anemia**; neural tube defects
Vitamin B_{12}	**RDA** F: 2.4 µg M: 2.4 µg	Animal products[c]	**Megaloblastic anemia** Neurologic symptoms
Biotin	**AI** F: 30 µg M: 30 µg	Liver Egg yolk	Conjunctivitis; central nervous system abnormalities; glossitis; alopecia; dry, scaly dermatitis
Pantothenic acid	**AI** F: 5 mg M: 5 mg	Wide distribution in foods, especially animal tissues; whole grain cereals; legumes	Irritability and restlessness; fatigue, apathy, malaise; gastiointestinal symptoms; neurological symptoms
Choline	**AI** F: 550 mg M: 425 mg **UL**: 3.5 g	Milk; liver; eggs; peanuts	Liver damage
Fat-soluble vitamins			
Vitamin A	**RDA** F: 700 µg M: 900 µg **UL**: 3000 µg	Carrots; Dark green and leafy vegetables; sweet potatoes and squash; broccoli	Night blindness; **xerophthalmia;** keratinization of epithelium in GI, respiratory and genitourinary tract, skin becomes dry and scaly
Vitamin K	**RDA** F: 90 µg M: 120 µg	Green leafy vegetables; cabbage family (brassica); Bacterial flora of intestine	Defective blood coagulation; hemorrhagic anemia of the newborn
Vitamin D	**AI[d]** F: 5 µg M: 5 µg **UL:** 50 µg	Fortified milk; Exposure of skin to sunlight	**Rickets** (in children); inadequate bone mineralization (osteomalacia)
Vitamin E	**RDA** F: 15 mg M: 15 mg **UL:** 1 g	Vegetable oils, margarine; wheat germ; nuts; green leafy vegetables	Muscular dystrophy, neurologic abnormalities.

Dietary Reference Intakes (DRI): Recommended Dietary Allowance (RDA); Adequate Intake (AI); Tolerable Upper Intake Level (UL)

[a]Information for this table is from Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline (1998); Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000); Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (1997), Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2001). Washington, DC: Food and Nutrition Board, Institute of Medicine, National Academy Press.

[b]neq = niacin equivalents. Niacin can be synthesized in the human from tryptophan, and this term takes into account a conversion factor for dietary tryptophan.

[c]Vitamin B_{12} is found only in animal products.

[d]Dietary requirement assumes the absence of sunlight.

riboflavin is 0.9 mg/day for males between 9 and 13 years of age, 1.3 mg/day for males 19 to 30 years of age, still 1.3 mg/day for males older than 70 years, and 1.1 mg/day for females aged 19 to 30 years. The largest requirements occur during lactation (1.6 mg/day).

Vitamins, by definition, cannot be synthesized in the body, or are synthesized from a very specific dietary precursor in insufficient amounts. For example, we can synthesize the vitamin niacin from the essential amino acid tryptophan, but not in sufficient quantities to meet our needs. Niacin is therefore still classified as a vitamin.

Excessive intake of many vitamins, both fat-soluble and water-soluble, may cause deleterious effects. For example, high doses of vitamin A, a fat-soluble vitamin, can cause desquamation of the skin and birth defects. High doses of vitamin C cause diarrhea and gastrointestinal disturbances. One of the Reference Dietary Intakes is the Tolerable Upper Intake Level (UL), which is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects to almost all individuals in the general population. As intake increases above the UL, the risk of adverse effects increases. Table 1.7 includes the UL for vitamins known to pose a risk at high levels. Intake above the UL occurs most often with dietary or pharmacologic supplements of single vitamins, and not from foods.

E. Minerals

Many minerals are required in the diet. They are generally divided into the classifications of electrolytes (inorganic ions that are dissolved in the fluid compartments of the body), minerals (required in relatively large quantities), trace minerals (required in smaller quantities), and ultratrace minerals (Table 1.8).

Sodium (Na^+), potassium (K^+), and chloride (Cl^-) are the major electrolytes (ions) in the body. They establish ion gradients across membranes, maintain water balance, and neutralize positive and negative charges on proteins and other molecules.

Calcium and phosphorus serve as structural components of bones and teeth and are thus required in relatively large quantities. Calcium (Ca^{2+}) plays many other roles in the body; for example, it is involved in hormone action and blood clotting. Phosphorus is required for the formation of ATP and of phosphorylated intermediates in metabolism. Magnesium activates many enzymes and also forms a complex with ATP. Iron is a particularly important mineral because it functions as a component of hemoglobin (the oxygen-carrying protein in the blood) and is part of many enzymes. Other minerals, such as zinc or molybdenum, are required in very small quantities (trace or ultra-trace amounts).

Sulfur is ingested principally in the amino acids cysteine and methionine. It is found in connective tissue, particularly in cartilage and skin. It has important functions in metabolism, which we will describe when we consider the action of coenzyme A, a compound used to activate carboxylic acids. Sulfur is excreted in the urine as sulfate.

A dietary deficiency of calcium can lead to osteoporosis, a disease in which bones are insufficiently mineralized and consequently are fragile and easily fractured. Osteoporosis is a particularly common problem among elderly women. Deficiency of phosphorus results in bone loss along with weakness, anorexia, malaise, and pain. Iron deficiencies lead to anemia, a decrease in the concentration of hemoglobin in the blood.

Which foods would provide Percy Veere with good sources of folate and vitamin B_{12}?

Table 1.8. Minerals Required in the Diet

Electrolytes	Minerals	Trace Minerals	Ultratrace or Trace Minerals[a]
Sodium	Calcium	Iodine	Manganese
Potassium	Phosphorus	Selenium	Fluoride
Chloride	Magnesium	Copper	Chromium
	Iron	Zinc	Molybdenum
	Sulfur		Others?

[a] These minerals are classified as trace or as ultratrace.

A: Folate is found in fruits and vegetables: citrus fruits (e.g., oranges), green leafy vegetables (e.g., spinach and broccoli), fortified cereals, and legumes (e.g., peas) (see Table 1.7). Conversely, vitamin B_{12} is found only in foods of animal origin, including meats, eggs, and milk.

Minerals, like vitamins, have adverse effects if ingested in excessive amounts. Problems associated with dietary excesses or deficiencies of minerals are described in subsequent chapters in conjunction with their normal metabolic functions.

F. Water

Water constitutes one half to four fifths of the weight of the human body. The intake of water required per day depends on the balance between the amount produced by body metabolism and the amount lost through the skin, through expired air, and in the urine and feces.

V. DIETARY GUIDELINES

Dietary guidelines or goals are recommendations for food choices that can reduce the risk of developing chronic or degenerative diseases while maintaining an adequate intake of nutrients. Many studies have shown an association between diet and exercise and decreased risk of certain diseases, including hypertension, atherosclerosis, stroke, diabetes, certain types of cancer, and osteoarthritis. Thus, the American Heart Institute and the American Cancer Institute, as well as several other groups, have developed dietary and exercise recommendations to decrease the risk of these diseases. The "Dietary Guidelines for Americans (2000)", prepared under the joint authority of the US Department of Agriculture and the US Department of Health and Human Services, merges many of these recommendations. Recommended servings of different food groups are displayed as the food pyramid (Fig. 1.9). Issues of special concern for physicians who advise patients include the following:

A. General Recommendations

- Aim for a healthy weight and be physically active each day. For maintenance of a healthy weight, caloric intake should balance caloric expenditure. Accumulate at least 30 minutes of moderate physical activity (such as walking 2 miles) daily. A regular exercise program helps in achieving and maintaining ideal weight, cardiovascular fitness, and strength.
- Choose foods in the proportions recommended in the food pyramid, including a variety of grains and a variety of fruits and vegetables daily.
- Keep food safe to eat. For example, refrigerate leftovers promptly.

B. Vegetables, Fruits, and Grains

- Diets rich in vegetables, fruits, and grain products should be chosen. Five or more servings of vegetables and fruits should be eaten each day, particularly green and yellow vegetables and citrus fruits. Six or more daily servings of grains should be eaten (starches and other complex carbohydrates, in the form of breads, fortified cereals, rice, and pasta). In addition to energy, vegetables, fruits, and grains supply vitamins, minerals, protective substances (such as carotenoids), and fiber. Fiber, the indigestible part of plant food, has various beneficial effects, including relief of constipation.
- The consumption of refined sugar in foods and beverages should be reduced to below the American norm. Refined sugar has no nutritional value other than its caloric content, and it promotes tooth decay.

C. Fats

- Fat intake should be reduced. For those at risk of heart attacks or strokes, fat should account for no more than 30% of total dietary calories, and saturated fatty acids

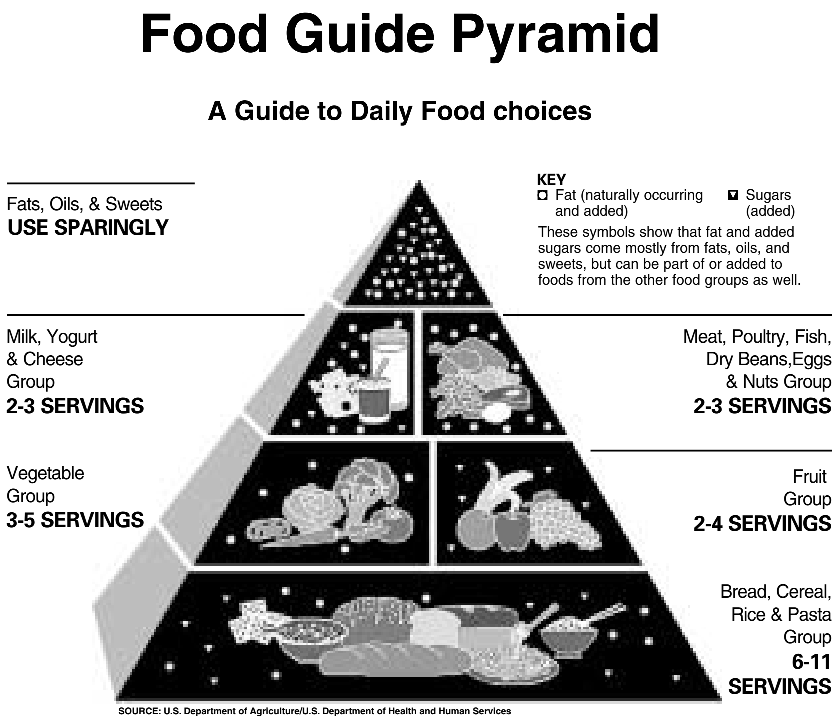


Fig. 1.9. The Food Guide Pyramid. The pyramid shows the number of servings that should be eaten each day from each food group. Within each group, a variety of foods should be eaten. Some examples of serving size: Grain products—1 slice of white bread or ½ cup of cooked rice; Vegetable group—½ cup cooked vegetables; Fruit group—1 apple or banana; Milk Group—1 cup of milk or 2 oz processed cheese; Meat and Beans Group—2–3 oz cooked lean meat or fish or 1 egg or 2 tbsp peanut butter. Nutrition and Your Health: Dietary Guidelines for Americans, 2000. Washington, DC: Dietary Guidelines Committee: The U.S. Department of Agriculture and the U.S. Department of Health and Human Services.

should account for 10% or less. Foods high in saturated fat include cheese, whole milk, butter, regular ice cream, and many cuts of beef. Trans fatty acids, such as the partially hydrogenated vegetable oils used in margarine, should also be avoided.

- Cholesterol intake should be less than 300 mg/day in subjects without atherosclerotic disease and less than 200 mg/day in those with established atherosclerosis.

Cholesterol is obtained from the diet and synthesized in most cells of the body. It is a component of cell membranes and the precursor of steroid hormones and of the bile salts used for fat absorption. High concentrations of cholesterol in the blood, particularly the cholesterol in lipoprotein particles called low density lipoproteins (LDL), contribute to the formation of atherosclerotic plaques. These plaques (fatty deposits on arterial walls) are associated with heart attacks and strokes. A high content of saturated fat in the diet tends to increase circulatory levels of LDL cholesterol and contributes to the development of atherosclerosis.

D. Proteins

- Protein intake for adults should be approximately 0.8 g/kg ideal body weight per day. The protein should be of high quality and should be obtained from sources low in saturated fat (e.g., fish, lean poultry, and dry beans). Vegetarians should eat a mixture of vegetable proteins that ensures the intake of adequate amounts of the essential amino acids.

E. Alcohol

- Alcohol consumption should not exceed moderate drinking. Moderation is defined as no more than one drink per day for women and no more than two drinks per day for men. A drink is defined as 1 regular beer, 5 ounces of wine (a little over ½ cup), or 1.5 ounces of an 80-proof liquor, such as whiskey. Pregnant women should drink no alcohol.

The ingestion of alcohol by pregnant women can result in fetal alcohol syndrome (FAS), which is marked by prenatal and postnatal growth deficiency, developmental delay, and craniofacial, limb, and cardiovascular defects.

F. Vitamins and Minerals

- Sodium intake should be decreased in most individuals. Sodium is usually consumed as salt, NaCl. Individuals prone to salt-sensitive hypertension should eat less than 3 g sodium per day (approximately 6 g NaCl).
- Many of the required vitamins and minerals can be obtained from eating a variety of fruits, vegetables, and grains (particularly whole grains). However, calcium and iron are required in relatively high amounts. Low-fat or nonfat dairy products and dark green leafy vegetables provide good sources of calcium. Lean meats, shellfish, poultry, dark meat, cooked dry beans, and some leafy green vegetables provide good sources of iron. Vitamin B_{12} is found only in animal sources.
- Dietary supplementation in excess of the recommended amounts (for example, megavitamin regimens) should be avoided.
- Fluoride should be present in the diet, at least during the years of tooth formation, as a protection against dental caries.

The high intake of sodium and chloride (in table salt) of the average American diet appears to be related to the development of hypertension (high blood pressure) in individuals who are genetically predisposed to this disorder.

VI. XENOBIOTICS

In addition to nutrients, our diet also contains a large number of chemicals called xenobiotics, which have no nutritional value, are of no use in the body, and can be harmful if consumed in excessive amounts. These compounds occur naturally in foods, can enter the food chain as contaminants, or can be deliberately introduced as food additives.

Dietary guidelines of the American Cancer Society and the American Institute for Cancer Research make recommendations relevant to the ingestion of xenobiotic compounds, particularly carcinogens. The dietary advice that we eat a variety of food helps to protect us against the ingestion of a toxic level of any one xenobiotic compound. It is also suggested that we reduce consumption of salt-cured, smoked, and charred foods, which contain chemicals that can contribute to the development of cancer. Other guidelines encourage the ingestion of fruits and vegetables that contain protective chemicals called antioxidants.

CLINICAL COMMENTS

Physicians have an average lifespan that is longer than the general population, and generally practice healthier behaviors, especially with regard to fat consumption, exercise, alcohol consumption, and smoking. Physicians who practice healthy behaviors are more likely to counsel patients with respect to these behaviors and are better able to motivate their patients.

Otto Shape. Otto Shape sought help in reducing his weight of 187 lb (BMI of 27) to his previous level of 154 lb (BMI of 22, in the middle of the healthy range). Otto Shape was 5 feet 10 inches tall, and he calculated that his maximum healthy weight was 173 lbs. He planned on becoming a family physician, and he knew that he would be better able to counsel patients in healthy behaviors involving diet and exercise if he practiced them himself. With this information and assurances from the physician that he was otherwise in good health, Otto embarked on a weight loss program. One of his strategies involved recording all the food he ate and the portions. To analyze his diet for calories, saturated fat, and nutrients, he used the Interactive Healthy Eating Index, available online from the USDA Food and Nutrition Information Center.

Ivan Applebod. Ivan Applebod weighed 264 lb and was 70 inches tall with a heavy skeletal frame. For a male of these proportions, a BMI of 18.5 to 24.9 would correspond to a weight between 129 and 173 lb. He is currently almost 100 lb overweight, and his BMI of 37.9 is in the obese range.

Mr. Applebod's physician cautioned him that exogenous obesity (caused by overeating) represents a risk factor for atherosclerotic vascular disease, particularly when the distribution of fat is primarily "central" or in the abdominal region (apple shape, in contrast to the pear shape, which results from adipose tissue deposited in the buttocks and hips). In addition, obesity may lead to other cardiovascular risk factors such as hypertension (high blood pressure), hyperlipidemia (high blood lipid levels), and type 2 diabetes mellitus (characterized by hyperglycemia). He already has a mild elevation in both systolic and diastolic blood pressure. Furthermore, his total serum cholesterol level was 296 mg/dL, well above the desired normal value (200 mg/dL).

Mr. Applebod was referred to the hospital's weight reduction center, where a team of physicians, dieticians, and psychologists could assist him in reaching his ideal weight range.

Ann O'Rexia. Because of her history and physical examination, Ann O'Rexia was diagnosed as having early anorexia nervosa, a behavioral disorder that involves both emotional and nutritional disturbances. Miss O'Rexia was referred to a psychiatrist with special interest in anorexia nervosa, and a program of psychotherapy and behavior modification was initiated.

Percy Veere. Percy Veere weighed 125 lb and was 71 inches tall (without shoes) with a medium frame. His BMI was 17.5, which is significantly underweight. At the time his wife died, he weighed 147 lbs. For his height, a BMI in the healthy weight range corresponds to weights between 132 and 178 lb.

Mr. Veere's malnourished state was reflected in his admission laboratory profile. The results of hematologic studies were consistent with an iron deficiency anemia complicated by low levels of folic acid and vitamin B_{12}, two vitamins that can affect the development of normal red blood cells. His low serum albumin level was caused by insufficient protein intake and a shortage of essential amino acids, which result in a reduced ability to synthesize body proteins. The psychiatrist requested a consultation with a hospital dietician to evaluate the extent of Mr. Veere's marasmus (malnutrition caused by a deficiency of both protein and total calories) as well as his vitamin and mineral deficiencies.

The prevalence of obesity in the U.S. population is increasing. In 1962, 12.8% of the population had a BMI equal to or greater than 30 and therefore were clinically obese. That number increased to 14.5% by 1980 and to 22.5% by 1998. An additional 30% were pre-obese in 1998 (BMI = 25.0 – 29.9). Therefore, more than 50% of the population is currently overweight, that is, obese or pre-obese.

Increased weight increases cardiovascular risk factors, including hypertension, diabetes, and alterations in blood lipid levels. It also increases the risk for respiratory problems, gallbladder disease, and certain types of cancer.

BIOCHEMICAL COMMENTS

Dietary Reference Intakes. Dietary Reference Intakes (DRIs) are quantitative estimates of nutrient intakes that can be used in evaluating and planning diets for healthy people. They are prepared by the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (DRI) of the Food and Nutrition Board, Institute of Medicine, and the National Academy of Science, with active input of Health Canada. The four reference intake values are the Recommended Dietary Allowance (RDA), the Estimated Average Requirement (EAR), the Adequate Intake (AI), and the Tolerable Upper Intake Level (UL). For each vitamin, the Committee has reviewed available literature on studies with humans and established criteria for adequate intake, such as prevention of certain deficiency symptoms, prevention of developmental abnormalities, or decreased risk of chronic degenerative disease. The criteria are not always the same for each life stage group. A requirement is defined as the lowest continuing intake level of a nutrient able to satisfy these criteria. The EAR is the daily intake value that is estimated to meet the requirement in half of the apparently healthy individuals in a life stage or gender group. The RDA is the EAR plus 2 standard deviations of the mean, which is the amount that should satisfy the requirement in 97 to 98% of the population. The AI level instead of an RDA is set for nutrients when there is not enough data to determine the EAR.

The Tolerable Upper Intake Level (UL) refers to the highest level of daily nutrient intake consumed over time that is likely to pose no risks of adverse effects for almost all healthy individuals in the general population. Adverse effects are defined as any significant alteration in the structure or function of the human organism. The

An example of the difference between the AI and the EAR is provided by riboflavin. Very few data exist on the nutrient requirements of very young infants. However, human milk is the sole recommended food for the first 4 to 6 months, so the AI of the vitamin riboflavin for this life stage group is based on the amount in breast milk consumed by healthy full-term infants. Conversely, the riboflavin EAR for adults is based on a number of studies in humans relating dietary intake of riboflavin to biochemical markers of riboflavin status and development of clinical deficiency symptoms.

UL does not mean that most individuals who consume more than the UL will suffer adverse health effects, but that the risk of adverse effects increases as intake increases above the UL.

Suggested References

A good, comprehensive textbook on nutrition is Shils ME, Olson JA, Shike M, Ross, AC. Modern nutrition in health and disease. Baltimore: Williams & Wilkins, 1999. Extensive nutrition tables, including Metropolitan Height and Weight Tables, are available in the appendices.

Recent Dietary References Intakes prepared by the Food and Nutrition Board of the National Academy of Science (1997–2001) are available in several volumes published by the National Academy Press (see Table 1.7) and may be consulted online at http://books.nap.edu/.

To analyze diets for calories and nutrient contents, consult food databases and resource lists made available by the USDA. The site www.nal.usda.gov/fnic provides lists of resources on food composition, such as the database U.S. Department of Agriculture, Agricultural Research Service. 2001. USDA Nutrient Database for Standard Reference, Release 14. Nutrient Data Laboratory Homepage, http://www.nal.usda.gov/fnic/foodcomp. This site also provides lists of resources for diet analysis, and links to the Interactive Healthy Eating Index, which is a program students can use to analyze their diets (http://147.208.9.133). A useful computer program for evaluating the diet of individuals, the MSU Nutriguide, can be obtained from Department of Nutrition, Michigan State University.

Dietary recommendations change frequently as new data become available. Current Dietary Recommendations are available from the following sources: Food and Nutrition Information Center, National Agricultural Library, USDA (www.fns.usda.gov); National Heart, Lung, and Blood Institute Information Center (www.nhlbi.nih.gov); American Heart Association (www.Americanheart.org); American Institute for Cancer Research (www.aicr.org); and the American Diabetes Association (www.diabetes.org). Another reliable source for nutrition information on the internet is www.navigator.tufts.edu.

A number of medical schools in the United States have received Nutrition Academic Awards from the National Institute of Heart, Blood and Lung, National Institutes of Health (www.nhlbi.nih.gov/funding/naa). These schools are developing products for medical nutrition education.

REVIEW QUESTIONS—CHAPTER 1

Directions: For each question below, select the single best answer.

1. In the process of respiration, fuels

   (A) are stored as triacylglycerols.
   (B) are oxidized to generate ATP.
   (C) release energy principally as heat.
   (D) combine with CO_2 and H_2O.
   (E) combine with other dietary components in anabolic pathways.

2. The caloric content per gram of fuel

   (A) is higher for carbohydrates than triacylglycerols.
   (B) is higher for protein than for fat.
   (C) is proportionate to the amount of oxygen in a fuel.
   (D) is the amount of energy that can be obtained from oxidation of the fuel.
   (E) is higher for children than adults.

3. The resting metabolic rate is

   (A) equivalent to the caloric requirement of our major organs and resting muscle.
   (B) generally higher per kilogram body weight in women than in men.
   (C) generally lower per kilogram body weight in children than adults.
   (D) decreased in a cold environment.
   (E) approximately equivalent to the daily energy expenditure.

4. The RDA is

   (A) the average amount of a nutrient required each day to maintain normal function in 50% of the U.S. population.
   (B) the average amount of a nutrient ingested daily by 50% of the U.S. population.
   (C) the minimum amount of a nutrient ingested daily that prevents deficiency symptoms.
   (D) a reasonable dietary goal for the intake of a nutrient by a healthy individual.
   (E) based principally on data obtained with laboratory animals.

5. A 35-year old sedentary male patient weighing 120 kg was experiencing angina (chest pain) and other signs of coronary artery disease. His physician, in consultation with a registered dietician, conducted a 3-day dietary recall. The patient consumed an average of 585 g carbohydrate, 150 g protein, and 95 g fat each day. In addition, he drank 45 g alcohol. The patient

   (A) consumed between 2,500 and 3,000 kcal per day.
   (B) had a fat intake within the range recommended in current dietary guidelines (i.e., year 2000).
   (C) consumed 50% of his calories as alcohol.
   (D) was deficient in protein intake.
   (E) was in negative caloric balance.