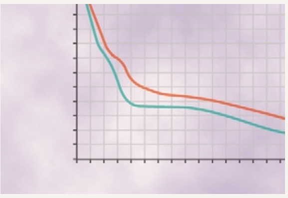
CHAPTER 72

Energetics and Metabolic Rate



Adenosine Triphosphate (ATP) Functions as an "Energy Currency" in Metabolism

In the past few chapters, we have pointed out that carbohydrates, fats, and proteins can all be used by cells to synthesize large quantities of adenosine triphosphate (ATP), which can be used as an energy source for almost all other cellular functions. For this reason, ATP has been called an energy "currency" in cell metabolism. Indeed, the transfer of energy from foodstuffs to most functional systems of the cells can be done only through this medium of ATP (or the similar nucleotide guanosine triphosphate, GTP). Many of the attributes of ATP are presented in Chapter 2.

An attribute of ATP that makes it highly valuable as an energy currency is the large quantity of free energy (about 7300 calories, or 7.3 Calories [kilocalories], per mole under standard conditions, but as much as 12,000 calories under physiologic conditions) vested in each of its two high-energy phosphate bonds. The amount of energy in each bond, when liberated by decomposition of ATP, is enough to cause almost any step of any chemical reaction in the body to take place if appropriate energy transfer is achieved. Some chemical reactions that require ATP energy use only a few hundred of the available 12,000 calories, and the remainder of this energy is lost in the form of heat.

ATP Is Generated by Combustion of Carbohydrates, Fats, and Proteins. In previous chapters, we discussed the transfer of energy from various foods to ATP. To summarize, ATP is produced from

1. *Combustion of carbohydrates*—mainly glucose, but also smaller amounts of other sugars such as fructose; this occurs in the cytoplasm of the cell through the anaerobic process of *glycolysis* and in the cell mitochondria through the aerobic *citric acid (Krebs) cycle.*
2. *Combustion of fatty acids* in the cell mitochondria by *beta-oxidation.*
3. *Combustion of proteins,* which requires hydrolysis to their component amino acids and degradation of the amino acids to intermediate compounds of the citric acid cycle and then to acetyl coenzyme A and carbon dioxide.

ATP Energizes the Synthesis of Most Important Cellular Components. Among the most important intracellular processes that require ATP energy is the formation of peptide linkages between amino acids during the synthesis of proteins. The different peptide linkages, depending on which types of amino acids are linked, require from 500 to 5000 calories of energy per mole. It will be recalled from the discussion of protein synthesis in Chapter 3 that four high-energy phosphate bonds are expended during the cascade of reactions required to form each peptide linkage. This provides a total of 48,000 calories of energy, which is far more than the 500 to 5000 calories eventually stored in each of the peptide linkages.

ATP energy is also used in the synthesis of glucose from lactic acid and in the synthesis of fatty acids from acetyl coenzyme A. In addition, ATP energy is used for the synthesis of cholesterol, phospholipids, the hormones, and almost all other substances of the body. Even the urea excreted by the kidneys requires ATP to cause its formation from ammonia. One might wonder about the advisability of expending energy to form urea, which is simply discarded by the body. However, remembering the extreme toxicity of ammonia in the body fluids, one can see the value of this reaction, which keeps the ammonia concentration of the body fluids at a low level.

ATP Energizes Muscle Contraction. Muscle contraction will not occur without energy from ATP. Myosin, one of the important contractile proteins of the muscle fiber, acts as an enzyme to cause breakdown of ATP into adenosine diphosphate (ADP), thus releasing the energy required to cause contraction. Only a small amount of ATP is normally degraded in muscles when muscle contraction is not occurring, but this rate of ATP usage can rise to at least 150 times the resting level during short bursts of maximal contraction. The postulated mechanism by which ATP energy is used to cause muscle contraction is discussed in Chapter 6.

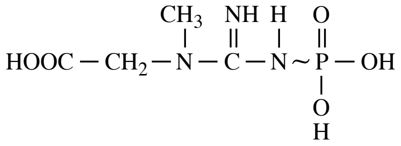
ATP Energizes Active Transport Across Membranes. In Chapters 4, 27, and 65, active transport of electrolytes and various nutrients across cell membranes and from the renal tubules and gastrointestinal tract into the blood is discussed. In each instance, we noted that active transport of most electrolytes and substances such as glucose, amino acids, and acetoacetate can occur against an electrochemical gradient, even though the natural diffusion of the substances would be in the opposite direction. To oppose the electrochemical gradient requires energy, which is provided by ATP.

ATP Energizes Glandular Secretion. The same principles apply to glandular secretion as to the absorption of substances against concentration gradients, because energy is required to concentrate substances as they are secreted by the glandular cells. In addition, energy is required to synthesize the organic compounds to be secreted.

ATP Energizes Nerve Conduction. The energy used during propagation of a nerve impulse is derived from the potential energy stored in the form of concentration differences of ions across the membranes. That is, a high concentration of potassium inside the fiber and a low concentration outside the fiber constitute a type of energy storage. Likewise, a high concentration of sodium on the outside of the membrane and a low concentration on the inside represent another store of energy. The energy needed to pass each action potential along the fiber membrane is derived from this energy storage, with small amounts of potassium transferring out of the cell and sodium into the cell during each of the action potentials. However, active transport systems energized by ATP then retransport the ions back through the membrane to their former positions.

Phosphocreatine Functions as an Accessory Storage Depot for Energy and as an "ATP Buffer"

Despite the paramount importance of ATP as a coupling agent for energy transfer, this substance is not the most abundant store of high-energy phosphate bonds in the cells. *Phosphocreatine,* which also contains high-energy phosphate bonds, is three to eight times as abundant. Also, the high-energy bond (~) of phosphocreatine contains about 8500 calories per mole under standard conditions and as much as 13,000 calories per mole under conditions in the body (37°C and low concentrations of the reactants). This is slightly greater than the 12,000 calories per mole in each of the two high-energy phosphate bonds of ATP. The formula for creatinine phosphate is the following:



$$\mathrm{HOOC-CH_2-\overset{\displaystyle CH_3}{\overset{|}{N}}-\overset{\displaystyle NH}{\overset{\|}{C}}-\overset{\displaystyle H}{\overset{|}{N}}\sim\underset{\underset{\displaystyle \overset{\displaystyle O}{H}}{|}}{\overset{\displaystyle O}{\overset{\|}{P}}}-OH}$$

Unlike ATP, phosphocreatine cannot act as a direct coupling agent for energy transfer between the foods and the functional cellular systems, but it can transfer energy interchangeably with ATP. When extra amounts of ATP are available in the cell, much of its energy is used to synthesize phosphocreatine, thus building up this storehouse of energy. Then, when the ATP begins to be used up, the energy in the phosphocreatine is transferred rapidly back to ATP and then to the functional systems of the cells. This reversible interrelation between ATP and phosphocreatine is demonstrated by the following equation:

$$\begin{array}{c}\text{Phosphocreatine + ADP}\\ \downarrow\uparrow\\ \text{ATP + Creatine}\end{array}$$

Note particularly that the higher energy level of the high-energy phosphate bond in phosphocreatine (1000 to 1500 calories per mole greater than that in ATP) causes the reaction between phosphocreatine and ADP to proceed rapidly toward the formation of new ATP every time even the slightest amount of ATP expends its energy elsewhere. Therefore, the slightest usage of ATP by the cells calls forth the energy from the phosphocreatine to synthesize new ATP. This effect keeps the concentration of ATP at an almost constant high level as long as any phosphocreatine remains. For this reason, we can call the ATP-phosphocreatine system an ATP "buffer" system. One can readily understand the importance of keeping the concentration of ATP nearly constant, because the rates of almost all the metabolic reactions in the body depend on this constancy.

Anaerobic Versus Aerobic Energy

Anaerobic energy means energy that can be derived from foods without the simultaneous utilization of oxygen; *aerobic energy* means energy that can be derived from foods only by oxidative metabolism. In the discussions in Chapters 67 through 69, it is noted that carbohydrates, fats, and proteins can all be oxidized to cause synthesis of ATP. However, *carbohydrates are the only significant foods that can be used to provide energy without the utilization of oxygen;* this energy release occurs during glycolytic breakdown of glucose or glycogen to pyruvic acid. For each mole of glucose that is split into pyruvic acid, 2 moles of ATP are formed. However, when stored glycogen in a cell is split to pyruvic acid, each mole of glucose in the glycogen gives rise to 3 moles of ATP. The reason for this difference is that free glucose entering the cell must be phosphorylated by using 1 mole of ATP before it can begin to be split; this is not true of glucose derived from glycogen because it comes from the glycogen already in the phosphorylated state, without the additional expenditure of ATP. *Thus, the best source of energy under anaerobic conditions is the stored glycogen of the cells.*

Anaerobic Energy Utilization During Hypoxia. One of the prime examples of anaerobic energy utilization occurs in acute hypoxia. When a person stops breathing, there is already a small amount of oxygen stored in the lungs and an additional amount stored in the hemoglobin of the blood. This oxygen is sufficient to keep the metabolic processes functioning for only about 2 minutes. Continued life beyond this time requires an additional source of energy. This can be derived for another minute or so from glycolysis—that is, the glycogen of the cells splitting into pyruvic acid, and the pyruvic acid becoming lactic acid, which diffuses out of the cells, as described in Chapter 67.

Anaerobic Energy Utilization During Strenuous Bursts of Activity Is Derived Mainly from Glycolysis. Skeletal muscles can perform extreme feats of strength for a few seconds but are much less capable during prolonged activity. Most of the extra energy required during these bursts of activity cannot come from the oxidative processes because they are too slow to respond. Instead, the extra energy comes from anaerobic sources: (1) ATP already present in the muscle cells, (2) phosphocreatine in the cells, and (3) anaerobic energy released by glycolytic breakdown of glycogen to lactic acid.

The maximum amount of ATP in muscle is only about 5 mmol/L of intracellular fluid, and this amount can maintain maximum muscle contraction for no more than a second or so. The amount of phosphocreatine in the cells is three to eight times this amount, but even by using all the phosphocreatine, maximum contraction can be maintained for only 5 to 10 seconds.

Release of energy by glycolysis can occur much more rapidly than can oxidative release of energy. Consequently, most of the extra energy required during strenuous activity that lasts for more than 5 to 10 seconds but less than 1 to 2 minutes is derived from anaerobic glycolysis. As a result, the glycogen content of muscles during strenuous bouts of exercise is reduced, whereas the lactic acid concentration of the blood rises. After the exercise is over, oxidative metabolism is used to reconvert about four fifths of the lactic acid into glucose; the remainder becomes pyruvic acid and is degraded and oxidized in the citric acid cycle. The reconversion to glucose occurs principally in the liver cells, and the glucose is then transported in the blood back to the muscles, where it is stored once more in the form of glycogen.

Oxygen Debt Is the Extra Consumption of Oxygen After Completion of Strenuous Exercise. After a period of strenuous exercise, a person continues to breathe hard and to consume large amounts of oxygen for at least a few minutes and sometimes for as long as 1 hour thereafter. This additional oxygen is used (1) to reconvert the lactic acid that has accumulated during exercise back into glucose, (2) to reconvert adenosine monophosphate and ADP to ATP, (3) to reconvert creatine and phosphate to phosphocreatine, (4) to re-establish normal concentrations of oxygen bound with hemoglobin and myoglobin, and (5) to raise the concentration of oxygen in the lungs to its normal level. This extra consumption of oxygen after exercise is over is called repaying the *oxygen debt.*

The principle of oxygen debt is discussed further in Chapter 84 in relation to sports physiology; the ability of a person to build up an oxygen debt is especially important in many types of athletics.

Summary of Energy Utilization by the Cells

With the background of the past few chapters and of the preceding discussion, we can now synthesize a composite picture of overall energy utilization by the cells, as shown in Figure 72–1. This figure demonstrates the anaerobic utilization of glycogen and glucose to form ATP and the aerobic utilization of compounds derived from carbohydrates, fats, proteins, and other substances to form additional ATP. In turn, ATP is in reversible equilibrium with phosphocreatine in the cells, and because larger quantities of phosphocreatine are present in the cells than ATP, much of the cells' stored energy is in this energy storehouse.

Energy from ATP can be used by the different functioning systems of the cells to provide for synthesis and growth, muscle contraction, glandular secretion, nerve impulse conduction, active absorption, and other cellular activities. If greater amounts of energy are demanded for cellular activities than can be provided by oxidative metabolism, the phosphocreatine storehouse is used first, and then anaerobic breakdown of glycogen follows rapidly. Thus, oxidative metabolism

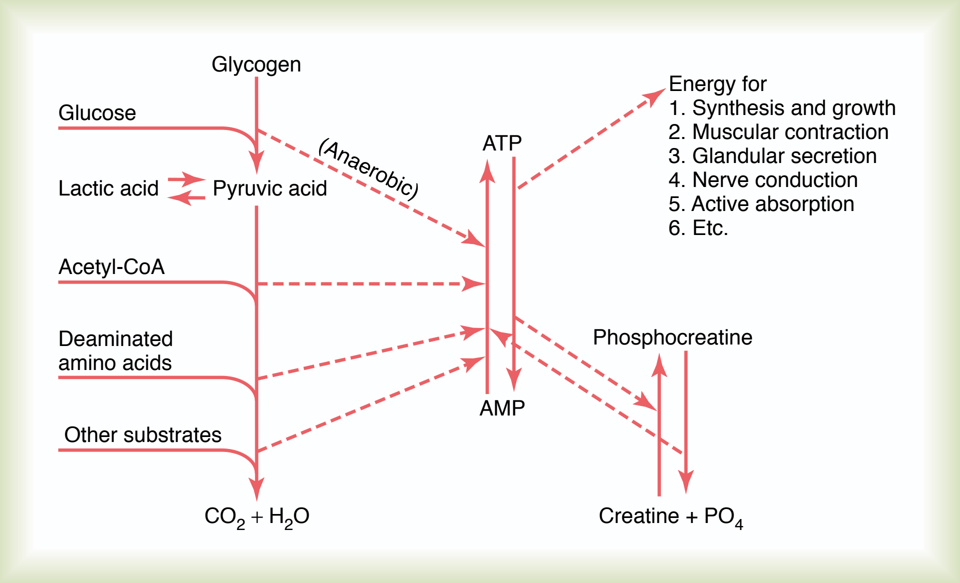


Figure 72–1

Overall schema of energy transfer from foods to the adenylic acid system and then to the functional elements of the cells. (Modified from Soskin S, Levine R: Carbohydrate Metabolism. Chicago: University of Chicago Press, 1946, 1952.)

cannot deliver bursts of extreme energy to the cells nearly as rapidly as the anaerobic processes can, but at slower rates of usage, the oxidative processes can continue as long as energy stores (mainly fat) exist.

Control of Energy Release in the Cell

Rate Control of Enzyme-Catalyzed Reactions. Before discussing the control of energy release in the cell, it is necessary to consider the basic principles of *rate control* of enzymatically catalyzed chemical reactions, which are the types of reactions that occur almost universally throughout the body.

The mechanism by which an enzyme catalyzes a chemical reaction is for the enzyme first to combine loosely with one of the substrates of the reaction. This alters the bonding forces on the substrate sufficiently so that it can react with other substances. Therefore, the rate of the overall chemical reaction is determined by both the concentration of the enzyme and the concentration of the substrate that binds with the enzyme. The basic equation expressing this concept is as follows:

$$\text{Rate of reaction} = \frac{K_1 \times [\text{Enzyme}] \times [\text{Substrate}]}{K_2 + [\text{Substrate}]}$$

This is called the *Michaelis-Menten equation.* Figure 72–2 shows the application of this equation.

Role of Enzyme Concentration in Regulation of Metabolic Reactions. Figure 72–2 shows that *when the substrate is present in high concentration,* as shown in the right half of the figure, the rate of a chemical reaction is determined almost entirely by the concentration of the enzyme. Thus, as the enzyme concentration increases from an arbitrary value of 1 up to 2, 4, or 8, the rate of the reaction increases proportionately, as demonstrated by the rising levels of the curves. As an example, when large quantities of glucose enter the renal tubules in a person with diabetes mellitus—that is, the substrate glucose is in great excess in the tubules—further increases in tubular glucose have little effect on glucose reabsorption, because the transport enzymes are saturated. Under these conditions, the rate of reabsorption of the glucose is limited by the concentration of the transport enzymes in the proximal tubular cells, not by the concentration of the glucose itself.

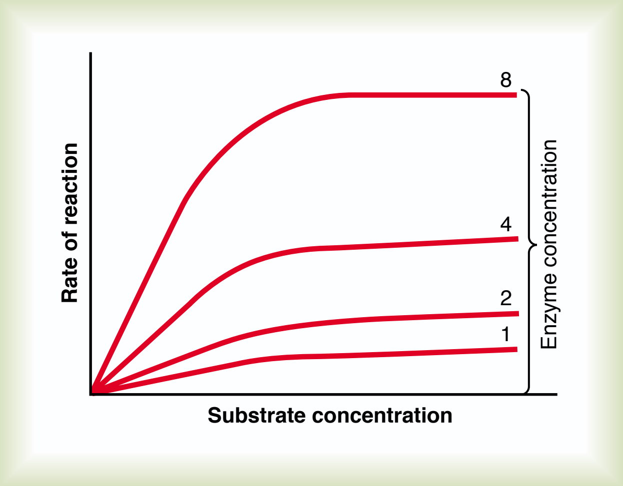


Figure 72–2

Effect of substrate and enzyme concentrations on the rate of enzyme-catalyzed reaction.

Role of Substrate Concentration in Regulation of Metabolic Reactions. Note also in Figure 72–2 that when the substrate concentration becomes low enough that only a small portion of the enzyme is required in the reaction, the rate of the reaction becomes directly proportional to the substrate concentration as well as the enzyme concentration. This is the relationship seen in the absorption of substances from the intestinal tract and renal tubules when their concentrations are low.

Rate Limitation in a Series of Reactions. Almost all chemical reactions of the body occur in series, with the product of one reaction acting as a substrate for the next reaction, and so on. Therefore, the overall rate of a complex series of chemical reactions is determined mainly by the rate of reaction of the slowest step in the series. This is called the *rate-limiting step* in the entire series.

ADP Concentration as a Rate-Controlling Factor in Energy Release. Under *resting* conditions, the concentration of ADP in the cells is extremely slight, so that the chemical reactions that depend on ADP as one of the substrates are quite slow. They include all the oxidative metabolic pathways that release energy from food, as well as essentially all other pathways for the release of energy in the body. Thus, *ADP is a major rate-limiting factor* for almost all energy metabolism of the body.

When the cells become active, regardless of the type of activity, ATP is converted into ADP, increasing the concentration of ADP in direct proportion to the degree of activity of the cell. This ADP then automatically increases the rates of all the reactions for the metabolic release of energy from food. Thus, by this simple process, the amount of energy released in the cell is controlled by the degree of activity of the cell. In the absence of cellular activity, the release of energy stops because all the ADP soon becomes ATP.

Metabolic Rate

The *metabolism* of the body simply means all the chemical reactions in all the cells of the body, and the *metabolic rate* is normally expressed in terms of the rate of heat liberation during chemical reactions.

Heat Is the End Product of Almost All the Energy Released in the Body. In discussing many of the metabolic reactions in the preceding chapters, we noted that not all the energy in foods is transferred to ATP; instead, a large portion of this energy becomes heat. On average, 35 per cent of the energy in foods becomes heat during ATP formation. Then, still more energy becomes heat as it is transferred from ATP to the functional systems of the cells, so that even under optimal conditions, no more than 27 per cent of all the energy from food is finally used by the functional systems.

Even when 27 per cent of the energy reaches the functional systems of the cells, most of this eventually becomes heat. For example, when proteins are synthesized, large portions of ATP are used to form the peptide linkages, and this stores energy in these linkages. But there is also continuous turnover of proteins—some being degraded while others are being formed. When proteins are degraded, the energy stored in the peptide linkages is released in the form of heat into the body.

Another example is the energy used for muscle activity. Much of this energy simply overcomes the viscosity of the muscles themselves or of the tissues so that the limbs can move. This viscous movement causes friction within the tissues, which generates heat.

Consider also the energy expended by the heart in pumping blood. The blood distends the arterial system, and this distention itself represents a reservoir of potential energy. As the blood flows through the peripheral vessels, the friction of the different layers of blood flowing over one another and the friction of the blood against the walls of the vessels turn all this energy into heat.

Essentially all the energy expended by the body is eventually converted into heat. The only significant exception occurs when the muscles are used to perform some form of work outside the body. For instance, when the muscles elevate an object to a height or propel the body up steps, a type of potential energy is created by raising a mass against gravity. But when external expenditure of energy is not taking place, all the energy released by the metabolic processes eventually becomes body heat.

The Calorie. To discuss the metabolic rate of the body and related subjects intelligently, it is necessary to use some unit for expressing the quantity of energy released from the different foods or expended by the different functional processes of the body. Most often, the *Calorie* is the unit used for this purpose. It will be recalled that 1 *calorie*—spelled with a small “c” and often called a *gram calorie*—is the quantity of heat required to raise the temperature of 1 gram of water 1°C. The calorie is much too small a unit when referring to energy in the body. Consequently, the Calorie—sometimes spelled with a capital “C” and often called a *kilocalorie,* which is equivalent to 1000 calories—is the unit ordinarily used in discussing energy metabolism.

Measurement of the Whole-Body Metabolic Rate

Direct Calorimetry Measures Heat Liberated from the Body. Because a person ordinarily is not performing any external work, the whole-body metabolic rate can be determined by simply measuring the total quantity of heat liberated from the body in a given time.

In determining the metabolic rate by direct calorimetry, one measures the quantity of heat liberated from the body in a large, specially constructed *calorimeter.* The subject is placed in an air chamber that is so well insulated that no heat can leak through the walls of the chamber. Heat formed by the subject’s body warms the air of the chamber. However, the air temperature within the chamber is maintained at a constant level by forcing the air through pipes in a cool water bath. The rate of heat gain by the water bath, which can be measured with an accurate thermometer, is equal to the rate at which heat is liberated by the subject’s body.

Direct calorimetry is physically difficult to perform and is used only for research purposes.

Indirect Calorimetry—The “Energy Equivalent” of Oxygen. Because more than 95 per cent of the energy expended in the body is derived from reactions of oxygen with the different foods, the whole-body metabolic rate can also be calculated with a high degree of accuracy from the rate of oxygen utilization. When 1 liter of oxygen is metabolized with glucose, 5.01 Calories of energy are released; when metabolized with starches, 5.06 Calories are released; with fat, 4.70 Calories; and with protein, 4.60 Calories.

Using these figures, it is striking how nearly equivalent are the quantities of energy liberated per liter of oxygen, regardless of the type of food being metabolized. For the average diet, the *quantity of energy liberated per liter of oxygen used in the body averages about 4.825 Calories.* This is called the *energy equivalent* of oxygen; using this energy equivalent, one can calculate with a high degree of precision the rate of heat liberation in the body from the quantity of oxygen used in a given period of time.

If a person metabolizes only carbohydrates during the period of the metabolic rate determination, the calculated quantity of energy liberated, based on the value for the average energy equivalent of oxygen (4.825 Calories/L), would be about 4 per cent too little. Conversely, if the person obtains most energy from fat, the calculated value would be about 4 per cent too great.

Energy Metabolism—Factors That Influence Energy Output

As discussed in Chapter 71, energy intake is balanced with energy output in healthy adults who maintain a stable body weight. About 45 per cent of daily energy intake is derived from carbohydrates, 40 per cent from fats, and 15 per cent from proteins in the average American diet. Energy output can also be partitioned into several measurable components, including energy used for (1) performing essential metabolic functions of the body (the “basal” metabolic rate); (2) performing various physical activities; (3) digesting, absorbing, and processing food; and (4) maintaining body temperature.

Overall Energy Requirements for Daily Activities

An average man who weighs 70 kilograms and lies in bed all day uses about 1650 Calories of energy. The process of eating and digesting food increases the amount of energy used each day by an additional 200 or more Calories, so that the same man lying in bed and eating a reasonable diet requires a dietary intake of about 1850 Calories per day. If he sits in a chair all day without exercising, his total energy requirement reaches 2000 to 2250 Calories. Therefore, the approximate daily energy requirement for a very sedentary man performing only essential functions is 2000 Calories.

The amount of energy used to perform daily physical activities is normally about 25 per cent of the total energy expenditure, but it can vary markedly in different individuals, depending on the type and amount of physical activity. For example, walking up stairs requires about 17 times as much energy as lying in bed asleep. In general, over a 24-hour period, a person performing heavy labor can achieve a maximal rate of energy utilization as great as 6000 to 7000 Calories, or as much as 3.5 times the energy used under conditions of no physical activity.

Basal Metabolic Rate (BMR)—The Minimum Energy Expenditure for the Body to Exist

Even when a person is at complete rest, considerable energy is required to perform all the chemical reactions of the body. This minimum level of energy required to exist is called the *basal metabolic rate* (BMR) and accounts for about 50 to 70 per cent of the daily energy expenditure in most sedentary individuals (Figure 72–3).

Because the level of physical activity is highly variable among different individuals, measurement of the BMR provides a useful means of comparing one person's metabolic rate with that of another. The usual method for determining BMR is to measure the rate of oxygen utilization over a given period of time under the following conditions:

1. The person must not have eaten food for at least 12 hours.
2. The BMR is determined after a night of restful sleep.
3. No strenuous activity is performed for at least 1 hour before the test.
4. All psychic and physical factors that cause excitement must be eliminated.
5. The temperature of the air must be comfortable and between 68° and 80°F.
6. No physical activity is permitted during the test.

The BMR normally averages about 65 to 70 Calories per hour in an average 70-kilogram man. Although much of the BMR is accounted for by essential activities of the central nervous system, heart, kidneys, and other organs, the *variations* in BMR among different individuals are related mainly to differences in the amount of skeletal muscle and body size.

Skeletal muscle, even under resting conditions, accounts for 20 to 30 per cent of the BMR. For this reason, BMR is usually corrected for differences in body size by expressing it as Calories per hour per square meter of body surface area, calculated from height and weight. The average values for males and females of different ages are shown in Figure 72–4.

Much of the decline in BMR with increasing age is probably related to loss of muscle mass and replacement of muscle with adipose tissue, which has a lower rate of metabolism. Likewise, slightly lower BMRs in women, compared with men, are due partly to their lower percentage of muscle mass and higher percentage of adipose tissue. However, there are other factors that can influence the BMR, as discussed next.

Thyroid Hormone Increases Metabolic Rate. When the thyroid gland secretes maximal amounts of thyroxine, the metabolic rate sometimes rises 50 to 100 per cent above normal. Conversely, total loss of thyroid secretion decreases the metabolic rate to 40 to 60 per cent of normal. As discussed in Chapter 76, thyroxine increases the rates of the chemical reactions of many cells in the body and therefore increases metabolic rate. Adaptation of the thyroid gland—with increased secretion in cold climates and decreased secretion in hot climates—contributes to the differences in BMRs among people living in different geographical zones; for example, people living in arctic regions have BMRs 10 to 20 per cent higher than those of persons living in tropical regions.

Male Sex Hormone Increases Metabolic Rate. The male sex hormone testosterone can increase the metabolic rate about 10 to 15 per cent. The female sex hormones may increase the BMR a small amount, but usually not enough to be significant. Much of this effect of the male sex hormone is related to its anabolic effect to increase skeletal muscle mass.

Growth Hormone Increases Metabolic Rate. Growth hormone can increase the metabolic rate 15 to 20 per cent as a result of direct stimulation of cellular metabolism.

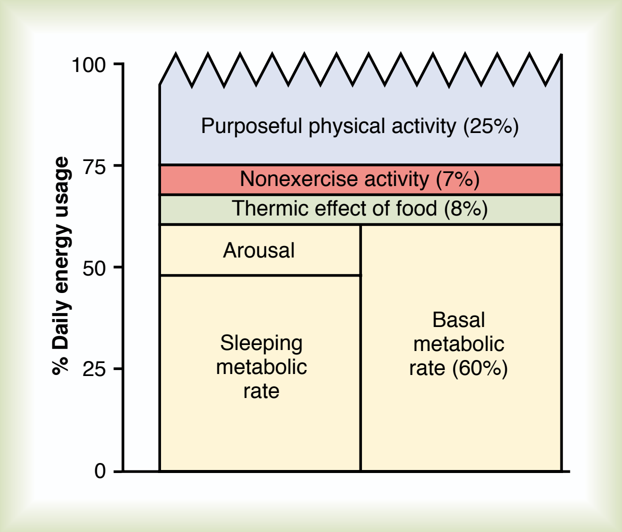


Figure 72–3

Components of energy expenditure.

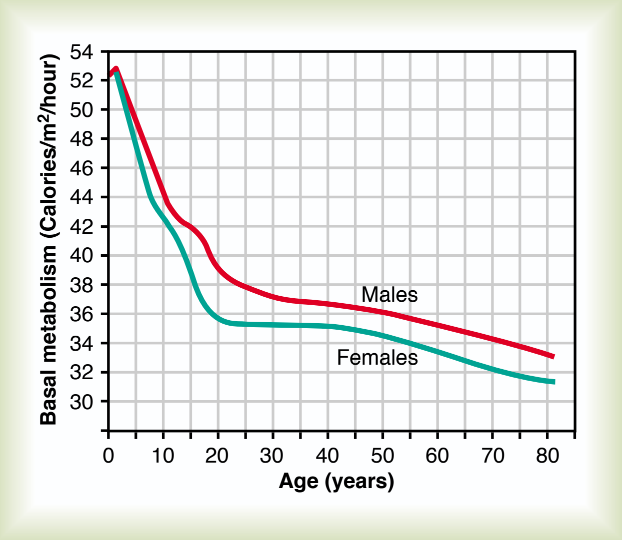


Figure 72–4

Normal basal metabolic rates at different ages for each sex.

Fever Increases Metabolic Rate. Fever, regardless of its cause, increases the chemical reactions of the body by an average of about 120 per cent for every 10°C rise in temperature. This is discussed in more detail in Chapter 73.

Sleep Decreases Metabolic Rate. The metabolic rate decreases 10 to 15 per cent below normal during sleep. This fall is due to two principal factors: (1) decreased tone of the skeletal musculature during sleep and (2) decreased activity of the central nervous system.

Malnutrition Decreases Metabolic Rate. Prolonged malnutrition can decrease the metabolic rate 20 to 30 per cent, presumably due to the paucity of food substances in the cells. In the final stages of many disease conditions, the inanition that accompanies the disease causes a marked decrease in metabolic rate, to the extent that the body temperature may fall several degrees shortly before death.

Energy Used for Physical Activities

The factor that most dramatically increases metabolic rate is strenuous exercise. Short bursts of maximal muscle contraction in a single muscle can liberate as much as 100 times its normal resting amount of heat for a few seconds. For the entire body, maximal muscle exercise can increase the overall heat production of the body for a few seconds to about 50 times normal, or to about 20 times normal for more sustained exercise in a well-trained individual.

Table 72–1 shows the energy expenditure during different types of physical activity for a 70-kilogram man. Because of the great variation in the amount of physical activity among individuals, this component of energy expenditure is the most important reason for the differences in caloric intake required to maintain energy balance. However, in industrialized countries where food supplies are plentiful, such as the United States, caloric intake periodically exceeds energy expenditure, and the excess energy is stored mainly as fat. This underscores the importance of maintaining a proper level of physical activity to prevent excess fat stores and obesity.

Table 72–1

Energy Expenditure During Different Types of Activity for a 70-Kilogram Man

Form of Activity	Calories per Hour
Sleeping	65
Awake lying still	77
Sitting at rest	100
Standing relaxed	105
Dressing and undressing	118
Typewriting rapidly	140
Walking slowly (2.6 miles per hour)	200
Carpentry, metalworking, industrial painting	240
Sawing wood	480
Swimming	500
Running (5.3 miles per hour)	570
Walking up stairs rapidly	1100

Extracted from data compiled by Professor M. S. Rose.

Even in sedentary individuals who perform little or no daily exercise or physical work, significant energy is spent on spontaneous physical activity required to maintain muscle tone and body posture and on other nonexercise activities such as "fidgeting." Together, these nonexercise activities account for about 7 per cent of a person's daily energy usage.

Energy Used for Processing Food—Thermogenic Effect of Food

After a meal is ingested, the metabolic rate increases as a result of the different chemical reactions associated with digestion, absorption, and storage of food in the body. This is called the *thermogenic effect of food,* because these processes require energy and generate heat.

After a meal that contains a large quantity of carbohydrates or fats, the metabolic rate usually increases about 4 per cent. However, after a high-protein meal, the metabolic rate usually begins rising within an hour, reaching a maximum of about 30 per cent above normal, and this lasts for 3 to 12 hours. This effect of protein on the metabolic rate is called the *specific dynamic action of protein.* The thermogenic effect of food accounts for about 8 per cent of the total daily energy expenditure in many persons.

Energy Used for Nonshivering Thermogenesis—Role of Sympathetic Stimulation

Although physical work and the thermogenic effect of food cause liberation of heat, these mechanisms are not aimed primarily at regulation of body temperature. Shivering provides a regulated means of producing heat by increasing muscle activity in response to cold stress, as discussed in Chapter 73. Another mechanism, *nonshivering thermogenesis,* can also produce heat in response to cold stress. This type of thermogenesis is stimulated by sympathetic nervous system activation, which releases norepinephrine and epinephrine, which in turn increase metabolic activity and heat generation.

In certain types of fat tissue, called *brown fat,* sympathetic nervous stimulation causes liberation of large amounts of heat. This type of fat contains large numbers of mitochondria and many small globules of fat instead of one large fat globule. In these cells, the process of oxidative phosphorylation in the mitochondria is mainly "uncoupled." That is, when the cells are stimulated by the sympathetic nerves, the mitochondria produce a large amount of heat but almost no ATP, so that almost all the released oxidative energy immediately becomes heat.

A neonate has a considerable number of brown fat cells, and maximal sympathetic stimulation can increase the child's metabolism more than 100 per cent. The magnitude of this type of thermogenesis in an adult human, who has virtually no brown fat, is probably less than 15 per cent, although this might increase significantly after cold adaptation.

Nonshivering thermogenesis may also serve as a buffer against obesity. Recent studies indicate that sympathetic nervous system activity is increased in obese persons who have a persistent excess caloric intake. The mechanism responsible for sympathetic activation in obese persons is uncertain, but it may be mediated partly through the effects of increased leptin, which activates pro-opiomelanocortin neurons in the hypothalamus. Sympathetic stimulation, by increasing thermogenesis, helps to limit excess weight gain.

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