A butterfly basks in the sun to heat its flight muscles before takeoff. Butterflies are partly ectotherms, dependent on the environment for their internal temperature. However, during flight, the butterfly becomes partly endothermic as its muscles generate heat.

Paul Yancey

15

Energy Balance and Thermal Physiology

15.1 Introduction: Thermodynamics and Life

Each cell needs energy to perform the functions essential for its own survival and to carry out its specialized contribution toward maintaining homeostasis. All energy used by animal cells is ultimately provided by food (exogenous energy-rich nutrients), intake of which is regulated to maintain **energy balance,** the internal homeostasis of nutrients available for the cells. In this chapter, we show how this balance occurs. We also consider temperature, one of the key components of energy equations. Temperature profoundly affects the rate of chemical reactions within cells, and animals have evolved various strategies to cope with these effects. Compare, for example, the butterfly above with the hummingbird on the next page. Moreover, solid evidence shows that Earth's atmosphere and oceans have been warming at least in part due to anthropogenic CO_2, and effects of this rise on organisms are already being documented. Before we examine energy balance and temperature, however, let us set the stage by examining the key energy equations.

Life follows the laws of thermodynamics

Perhaps the most distinctive characteristic of life that delineates it from nonliving systems is the way it uses energy. Whereas nonliving energetic processes—volcanoes, earthquakes, storms, and so forth—create disorder, living systems somehow produce their own order unique to each individual. Yet all these processes (indeed, all known processes in the universe) obey fundamental laws regarding energy—the **laws of thermodynamics.** There are three of these laws, with two that are relevant to physiology:

- The *First Law of Thermodynamics* is that energy can be neither created nor destroyed. Therefore, energy is subject to the same kind of input–output balance as are the chemical components of life such as H_2O and salt (see p. 612). The First Law of Thermodynamics suggests that life might operate forever on its internal energy content, simply converting one form to another as necessary. However, the Second Law says this is not possible.
- The *Second Law of Thermodynamics* is that the **entropy** (a measure of disorder or randomness) of a system *plus its surroundings* increases over time as the energy content degrades to unusable heat. This is expressed in the following equation, where Δ indicates change and S is entropy:

$$\Delta S_{net} = \Delta S_{surroundings} + \Delta S_{system} > 0 \text{ for spontaneous reactions}$$

The Second Law of Thermodynamics is in many ways the most important physical law regarding life in the universe. Most people are aware that the universe seems to run down over time, and only by expending energy can we reverse this trend. But life itself seems to defy this decay (until death, at least), and indeed some people have suggested that life violates the Second Law. However, they are forgetting that the law covers a system *plus its surroundings*, not just a system

Paul Yancey

A hummingbird is endothermic: It regulates its internal body temperature primarily by internal metabolism. However, it is also heterothermic: At night, its metabolism and body temperature may decrease by many degrees to save energy.

by itself. The system called "life" does *not* violate the law, because the order it creates can arise only at the expense of its environment. That is, as life becomes more organized, the surrounding environment becomes even more disorganized. The net result—increased order in an organism, increased disorder in the surroundings—is *always* an increase in net disorder (entropy). Plants, for example, create order at the expense of the sun, which is creating enormous disorder as it radiates out light and particles. Animals create order at the expense of the local environment: They eat ordered molecules (food such as glucose) and release less ordered waste molecules (such as CO_2) and—perhaps most importantly—heat, which directly increases disorder. Thus, life must continuously extract energy from the environment to maintain itself, whereas the rest of the universe degrades even faster than it would on its own. In short, the "metabolic cost of living" is a constant struggle against entropy (a struggle that is ultimately lost through aging and death).

To compensate for entropy, animals require input of food energy, most of which is ultimately converted to heat output

Since energy cannot be created or destroyed, it is subject to the same kind of *input–output balance* we described for other body components such as water and salt (p. 612).

Energy Input *Input* energy is that in ingested foodstuffs for most animals. As you have just seen, nondormant organisms need ongoing energy input from the environment. Each cell in an animal needs energy to perform functions essential for its own survival (for example, reversing the effects of entropy by restoring ion gradients and repairing damaged structures) and to carry out its specialized contributions toward maintenance of the whole animal. This requires food (from the environment, or in some animals, from internal symbionts). Chemical energy locked in the bonds that hold atoms together in food molecules is released when these molecules are broken down in the body. However (as a consequence of the Second Law of Thermodynamics), 100% of the food energy cannot be used usefully, because some energy is always lost to entropy.

Energy Output Energy *output* or *expenditure* falls into two categories (Figure 15-1). **External work** is the energy expended when skeletal muscles are contracted to move external objects or to move the body in relation to the environment. **Internal work** constitutes all other forms of biological energy expenditure that do not accomplish mechanical work outside the body. That is, it encompasses all the internal energy-expending activities that must go on all the time just to sustain life, such as skeletal muscle contractions associated with postural maintenance and shivering, the work of pumping blood and breathing, the energy required for active transport of critical materials across plasma membranes, and the energy used during synthetic reactions essential for the maintenance, repair, and growth of cell structures.

Although energy cannot be created or destroyed, it can be converted from one form to another. For example, **chemical energy** in ATP is converted into **kinetic energy** of locomotion by muscle contractile proteins. But not all energy in nutrient molecules can be harnessed to perform useful biological work like this (in accordance with the Second Law). The energy in nutrient molecules that is not used for work is transformed into **thermal energy,** or **heat.** During biochemical processing, only about 50% of the energy in nutrient molecules is transferred to ATP; the other 50% of nutrient energy is immediately lost as heat. During ATP expenditure by the cells, another 25% of the energy derived from ingested food becomes heat. Because animal bodies are not heat engines, they cannot convert heat into work. Therefore, not more than 25% of nutrient energy is available to accomplish work, whether external or internal. The remaining 75% is lost as heat during the sequential transfer of energy from nutrient molecules to ATP to cellular systems.

Furthermore, of the energy actually captured for use by animals, *almost all expended energy eventually becomes heat.* To exemplify, energy expended by a heart to pump blood is gradually changed into heat by friction as blood flows through vessels. Likewise, energy used in the synthesis of cellular structural protein initially reduces entropy, but it eventually appears as heat when that protein is degraded during the normal course of turnover of bodily constituents. Even in the performance of external work, skeletal muscles convert chemical energy inefficiently, with as much as 75% of the expended energy being lost as heat, and the 25% converted into kinetic energy being dissipated as heat when an animal stops moving. Thus, all energy that is liberated from ingested food but not used for net growth eventually becomes heat. This heat is not necessarily wasted energy, however, because it is used to maintain body temperature in some animals (which affects the rate at which chemical reactions can proceed), but not to do work.

Because most animal energy expenditure eventually appears as heat, energy is normally expressed in terms heat energy, the basic units of which are as follows:

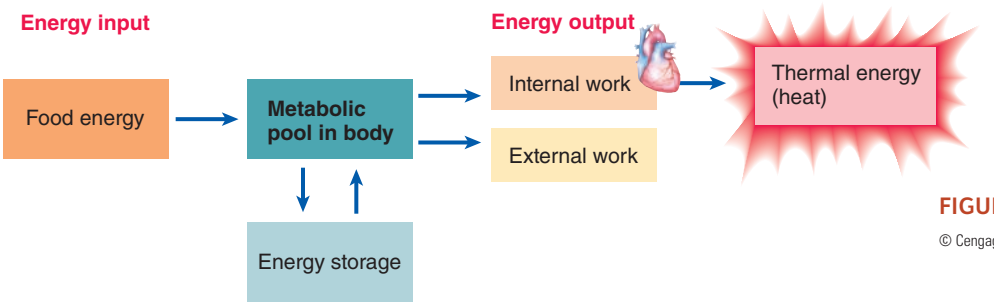


FIGURE 15-1 **Energy input and output.**

1. The **calorie** is the amount of heat required to raise the temperature of 1 g of H_2O by 1°C (specifically, from 14.5 to 15.5°C). This unit is too small to be convenient when discussing animals because of the magnitude of heat involved, so the **kilocalorie (kcal)** or **Calorie,** equal to 1,000 calories, is used. When nutritionists speak of "calories" in quantifying the energy content of food, they are actually referring to kilocalories or Calories.
2. The **joule,** the international unit for energy of any kind, is equal to 0.239 calories. The term **kilojoule (kJ)** (1,000 joules) is commonly used, again because of the magnitude of animal energies. *Most scientific research now uses the joule or kilojoule rather than the calorie,* but in the United States the Calorie is still used in human nutrition.

As a common example, 4.1 kcal or 17.1 kJ of heat energy are released when 1 g of glucose is oxidized or "burned," whether the oxidation takes place inside or outside a body.

check your understanding 15.1

Describe the laws of thermodynamics and how they apply to life.

Define *internal* and *external work* in an animal and why heat is the primary output.

15.2 Energy Balance: General Principles

Now let's examine how animals achieve energy balance as limited by thermodynamics.

Energy input must equal energy output, which is measured as metabolic rates of basal metabolism, activity, diet-induced thermogenesis, and production

Because energy cannot be created or destroyed, energy input *must* equal energy output (heat plus storage), as represented by the following equation (where E = energy):

$$E_{input} = E_{output}$$

Metabolic Rate and the "Animal Energy Equation" In the balance equation above, *output* energy (expenditures used for external and internal work) is generally measured as the *rate* at which energy is expended. This is broadly termed the **metabolic rate:**

$$\text{Metabolic rate} = \frac{\text{energy expenditure}}{\text{unit of time}}$$

Rather than simply using internal and external work, physiologists break this rate into specific major expenditures, in what might be called "*the animal energy equation*":

$$E_{input} - E_{loss} = E_{SMR/BMR} + E_{activity} + E_{DIT} + E_{production}$$

where *input* is the total food energy obtained and *loss* is that portion lost per unit time via feces, urine, skin sloughing, and so forth. Thus. the left side of the equation is *net energy intake*. The other four right-side components—the output expenditures—are as follows:

1. ***SMR and BMR*** are **standard** and **basal metabolic rates.** These internal-work expenditures are the "idling speed": *the minimal amount of energy needed per unit time to sustain waking (nonsleep) life under optimal conditions.*
2. *Activity* energy is the cost per unit time of neuromuscular efforts above the SMR or BMR level. This involves both internal and external work.
3. ***DIT*** is **diet-induced thermogenesis** (*thermo-*, "heat"; *genesis*, "production"), also called **specific dynamic action (SDA),** is an increase in metabolic rate above the SMR or BMR level that occurs as a consequence of food intake (internal work).
4. *Production* refers to the rate of energy storage, such as adipose deposition, net growth during development, and reproduction (all internal work). This is the only component that does not rapidly become heat (increasing entropy), but rather decreases entropy as an increase in body mass. However, it can also be negative when a fasting animal taps into its reserves for energy, and so this component effectively becomes energy input for the animal.

We will examine each of these expenditure components in detail, but first, let's see how metabolic rates are measured.

Methodology The rate of energy use can be measured directly or indirectly.

1. **Direct calorimetry** assumes all energy ends up as heat and involves the cumbersome procedure of placing the subject in an insulated chamber with H_2O circulating through the walls. The difference in the temperature of the H_2O entering and leaving the chamber reflects the amount of heat liberated by the subject and picked up

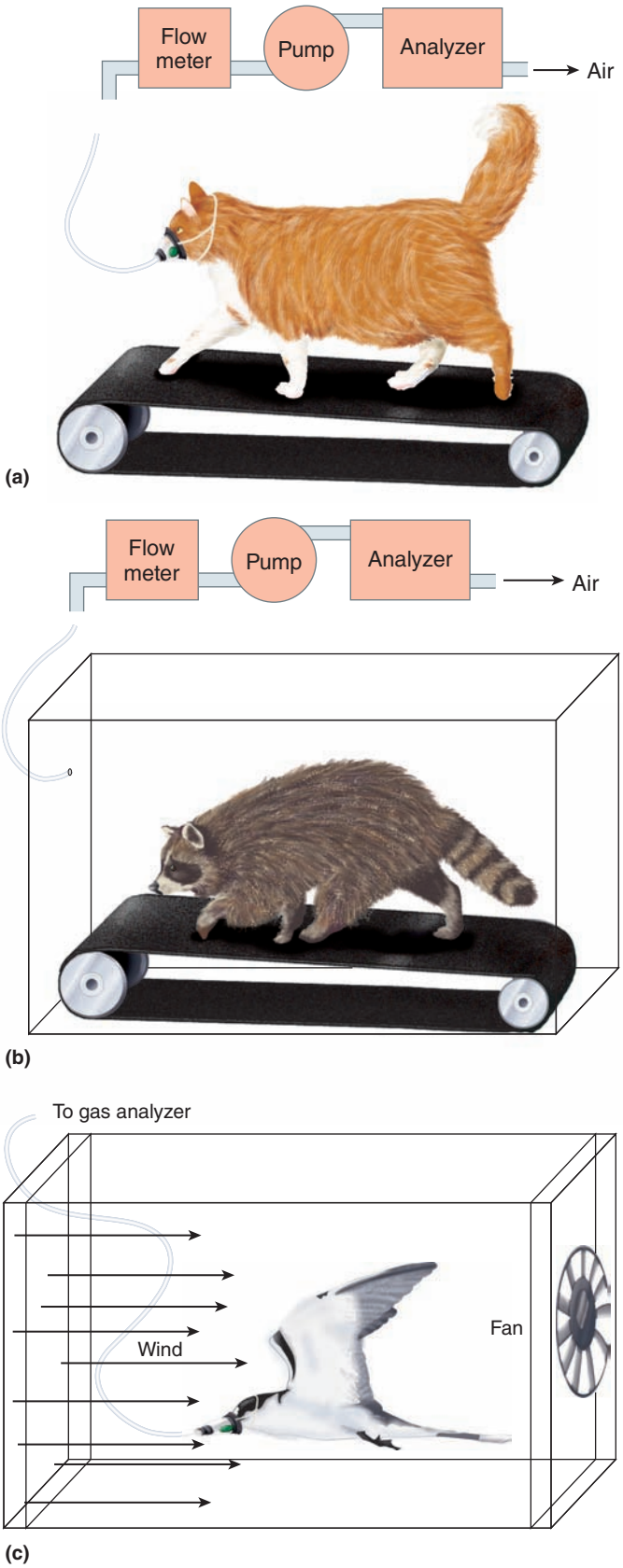


FIGURE 15-2 Measuring oxygen consumption by animals.
(a, b) Animals on treadmills, which force an animal to run at controlled speeds. The animal may be fitted with a mask for measuring gases in exhaled breath, or may be in an enclosed chamber from which gases are sampled. (c) A bird flying in a wind tunnel, which forces the animal to fly at controlled speeds. A face mask samples gases in exhaled breath.

by the H_2O as it passes through the chamber. Even though this method provides a direct measurement of heat production, it is not practical, because a calorimeter chamber can be costly, particularly for large animals. Therefore, other more practical methods of **indirect calorimetry** for determining metabolic rates were developed for widespread use.

2. In the indirect **respirometry method,** only the subject's O_2 uptake per unit of time (called the $\dot{V}_{O_2}$) is measured, which is a straightforward task in most cases (Figure 15-2). Recall that food energy is liberated with the use of oxygen during aerobic metabolism. Accordingly, a direct relationship exists between the volume of O_2 used and the quantity of heat produced. This relationship also depends on the type of food being oxidized, with the following average values, known as the *physiological fuel values:*

   Carbohydrates: 4.1 kcal/g = 17.1 kJ
   Proteins: 4.3 kcal/g = 17.9 kJ
   Fats: 9.3 kcal/g = 38.9 kJ

   An estimate, the **energy equivalent of O_2,** can be made of the quantity of heat produced per liter of O_2 consumed, using the animal's typical diet. For a typical human in North America, for example, the average is 4.8 kcal (20.0 kJ) per liter of O_2 consumed. Thus, in determining metabolic rate, a simple measurement of O_2 consumption can be used to reasonably approximate heat production by multiplying by this factor. However, for nonhuman animals the composition of the diet may not be easily obtained; thus, (1) metabolic rates may be reported simply as liters of oxygen consumed per unit time, or (2) an estimate may be made using the **respiratory quotient (*RQ*),** the ratio of CO_2 produced to O_2 consumed. This requires measurements of carbon dioxide production ($\dot{V}_{CO_2}$), an increasingly common technique. The *RQ* varies depending on the foodstuff consumed. When carbohydrate is being used, the *RQ* is 1; that is, for every molecule of O_2 consumed, one molecule of CO_2 is produced:

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + 30\text{–}32\ ATP + heat$$

   For fat use, the *RQ* is 0.7; for protein, it is 0.8. Using the *RQ* and the physiological fuel values, an energy equivalent of O_2 can be closely estimated. (Note that a slight correction is necessary to convert gas volumes to moles: 1 mole of O_2 = 22.39 L, whereas 1 mole of CO_2 = 22.26 L.)

   On a diet consisting of a mixture of these three nutrients, resting O_2 consumption in a human averages about 250 mL/min, and CO_2 production averages about 200 mL/min, for an average *RQ* of 0.8:

$$RQ = \frac{CO_2\ \text{produced}}{O_2\ \text{consumed}} = \frac{200\ \text{mL/min}}{250\ \text{mL/min}} = 0.8$$

   Measurement of *RQ* in a newly hatched or migrating bird or in a diving seal reveals a value closer to 0.7, indicating their reliance on fats during these energy-

intensive activities. Conversely, because carbohydrates yield more energy per O_2 consumed, it is thought that high-altitude animals rely more on carbohydrate that fat compared to low-altitude relatives. Marie-Pierre Schippers and colleagues recently verified this for the Andean leaf-eared mouse.

3. The **doubly labeled water** method is another form of indirect calorimetry, in which animals (often captured in the wild) are given $D_2{}^{18}O$, water made from heavy hydrogen (deuterium D) and the oxygen isotope ^{18}O. Deuterium is eliminated from the body as water (D_2O), but ^{18}O is eliminated as both water ($D_2{}^{18}O$) and $C^{18}O_2$. Researchers measure the difference between the elimination rates of each, calculate CO_2 production rate, and convert it into energy expenditure using the *RQ*. This is the method used to measure **field metabolic rate** (**FMR**), an average metabolic expenditure over the time of the analysis.

Now let's see how respirometry is used to measure minimal metabolic rates. An animal's metabolic rate varies, depending on a variety of factors, such as genetics, external temperature, exercise, food intake, shivering, and anxiety. To determine the minimal energy requirements for survival, metabolic rate must be measured under standardized conditions established to control the variables that can alter rate. It is measured under the following specified conditions:

1. To eliminate any nonresting muscular exertion, the animal should be quiescent and should have refrained from muscular activity for some time. (Note that metabolic rate during sleep is lower than the minimal rate as defined here.)
2. The animal should have minimal anxiety or stress levels. Stress usually increases metabolic rates in vertebrates; this is due to secretion of epinephrine, which increases heart rate (p. 416). For many animals this necessitates an acclimation period to laboratory conditions prior to the actual measurement. This factor has not been well studied.
3. The animal should not have eaten any food within an appropriate amount of time before the rate determination, to avoid diet-induced thermogenesis (DIT).
4. There should be no elevated energy costs of reproduction, such as pregnancy, egg brooding, lactation, or seasonal gamete production.
5. The measurement should be performed at an optimal temperature for that organism.

Regarding point 5, recall that animals fall into two broad categories of thermal adaptation: **ectotherms** (such as amphibians), which depend on external heat for their body temperatures, and **endotherms** (such as mammals), which use internal heat to regulate body temperatures (these are discussed in detail later in this chapter). Because of this difference, there are two types of this minimal metabolic rate:

- **Standard metabolic rate** (**SMR**) is an ectotherm's resting metabolic rate at a particular temperature, which may be the average temperature experienced naturally, the temperature the animal prefers if given a choice, or any temperature within its normal range. SMR values usually change dramatically with temperature, and thus the temperature of the test conditions must be reported.
- **Basal metabolic rate** (**BMR**) is an endotherm's resting metabolic rate in its **thermal neutral zone** (**TNZ**), a range of external temperatures that do not induce thermoregulatory processes by the animal. For example, the TNZ for lightly clothed humans lies around so-called room temperature. In the TNZ, there is no shivering, significant sweating, or other thermoregulatory processes that would raise the metabolic rate. (See TNZ later, p. 748.)

Measurements of BMR/SMR are difficult to make, and any exceptions to the conditions just listed must be reported. Another term is used if measurements are made under less-controlled conditions: the **resting metabolic rate** (**RMR**), the rate of a quiescent animal in which all the strict conditions are not met. RMR values are typically 10 to 25% higher than the BMR but are often used because measurements in a controlled laboratory with all of the strict conditions are not always practical.

Let's know look at the four expenditure components in detail, beginning with $E_{production}$.

Energy of production determines net energy balance

The production component ($E_{production}$) leads to the concept of energy balance, the factor that determines whether an animal will be at a stable weight, losing weight, or gaining weight, and whether that individual is maintaining a mass* that is optimal or is over- or underweight. For example, gaining significant mass is normal in juvenile growth and in hibernators laying down internal stores for the winter, but in other cases it leads to **obesity**, defined as having a body mass that is high enough to impair health. Conversely, starvation in famines, as may occur in overpopulated deer, may lead to health-threatening low body mass. Thus, understanding of energy balance is of great importance not only for human health but also for health of all animals, domestic or wild. There are three possible states of balance:

- *Neutral energy balance*. If the net amount of energy in food intake (input minus losses) exactly equals the amount of energy expended (output) other than production, then body mass remains constant ($E_{production} = 0$).
- *Positive energy balance*. If the net energy intake exceeds the amount of nonproduction energy expended, and the extra energy taken in is not used immediately, but is stored (a for example, fat stored in adipose tissue or a growing fetus), then body mass increases ($E_{production}$ is positive).
- *Negative energy balance*. Conversely, if the net energy intake is less than the body's immediate nonproduction energy requirements, the animal must use its stored energy to supply energy needs, and, accordingly, body mass decreases ($E_{production}$ is negative).

Thus, the other expenditures—BMR/SMR, activity, and DIT—determine whether there is sufficient energy left over from net intake for production. Let's look at BMR/SMR next.

*Note that *mass* is a measure of the amount of material in an object, with units in grams. *Weight* is popularly used in the same way, but actually, it is the gravitational force acting on a mass, in units of newtons. We will generally use *mass* except for terms like *overweight*.

BMR and SMR are regulated in part by thyroid hormones

The BMR or SMR is not a constant for a species; for example, it can vary between individuals, life stages, and sexes. We do not know all of the factors that regulate the rate of BMR and SMR, but in vertebrates, thyroid hormones (p. 301) are the primary (though not sole) determinant: As thyroid hormones increase, the SMR or BMR increases correspondingly. For example, in an experiment on Western fence lizards (*Sceloporus occidentalis*), SMR fell 31% in animals with their thyroids removed, and SMR was restored to normal by injections of thyroid hormone (T_4) (p. 298). Other factors include stress production of epinephrine, which also increases metabolic rate.

Recent research has found that *bile acids,* which are released during fat digestion (p. 686), bind to receptors on adipose cells in mice and skeletal muscle in humans. The receptors activate a gene for an enzyme (deiodinase) that converts the inactive T_4 into the biologically active T_3 (p. 301). In this way, consuming excess fat may temporarily lead to increased basal metabolic rates.

BMR and SMR scale with body mass

BMR and SMR can also differ considerably among species; in particular, endotherms have much higher BMRs than the SMRs of ectotherms. We will examine this later in the section titled Thermal Physiology. Here we examine the phenomenon of *scaling*. As discussed in previous chapters (e.g., pp. 10, 155, 414, 505, and 601), some physiological features depend on the size of organisms because of scaled factors such as surface area and volume. Perhaps the most consistent, yet controversial, scaling relationship is that between BMR or SMR and body mass. Numerous studies have found that although larger animals certainly consume more energy than smaller animals (Figure 15-3a), they have lower metabolic rates *per unit mass* than smaller ones (Figure 15-3b). Basically, a gram of elephant costs much less energy to maintain than a gram of shrew!

The actual scaling factor (the rate at which metabolism changes with body size) is found by plotting the BMR values for whole animals against their body masses on a log–log plot (Figure 15-3a). A straight line with a positive slope is obtained, with the following formula:

$$M = aW^b$$

where M is metabolic rate, a is the metabolic rate per unit mass (usually rate per kg), W is the body mass, and b is the slope. Again, this plot shows that larger animals do use more energy. But the slope (b) is always less than 1, which signifies the lower metabolic rates (per unit mass) of larger animals (if b were 1, then all animals would use energy at the same rate per unit mass). In fact, for mammals, *a consistent slope (b) of about 0.75 (3/4)* has been obtained in numerous studies. Similar scaling is found for birds, again with a slope between 0.7 and 0.8. Other physiologic and anatomic features also scale to body mass with slopes of about 0.75, such as alveolar surface area (see p. 509).

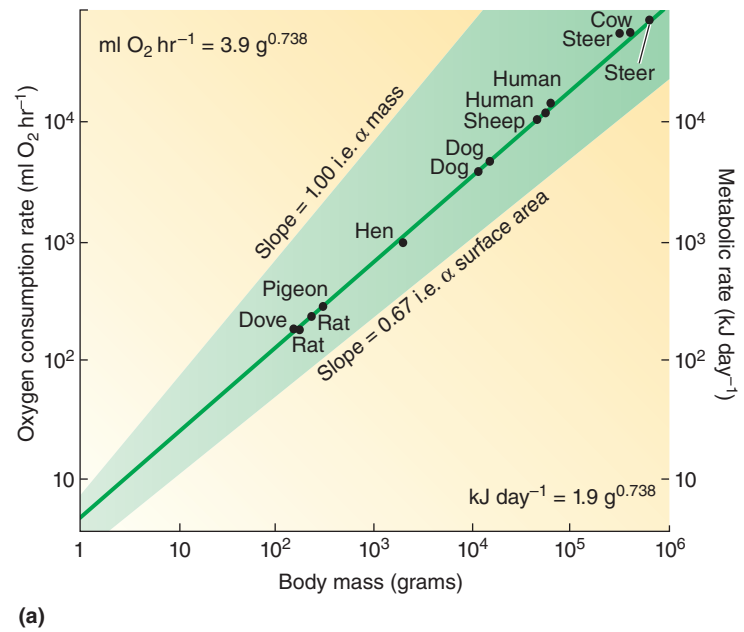
Scaling and Thermoregulation Following the discovery of the 0.75 scaling by Max Kleiber in 1932, a widely accepted hypothesis was generated: Scaling reflects properties of the ratio between surface area and volume with respect to temperature regulation by endotherms. The argument goes as follows: (1) Surface area increases as the square of the radius, whereas volume increases as the cube; therefore, smaller organisms have a higher ratio of surface area to volume (see Figure 1-4). Due to the square-cube difference, area/volume ratio scales by a power of 2/3 (0.67), at least for spheres. (2) Endotherms produce heat by their volumes (mass) and lose it from their surface areas. (3) Therefore, a smaller endotherm must have a higher metabolic rate per unit mass to compensate for its higher rate of heat loss (via surface area). In fact, as this hypothesis predicts, metabolic rates within a single mammalian species do often scale with size by a factor of 0.67.

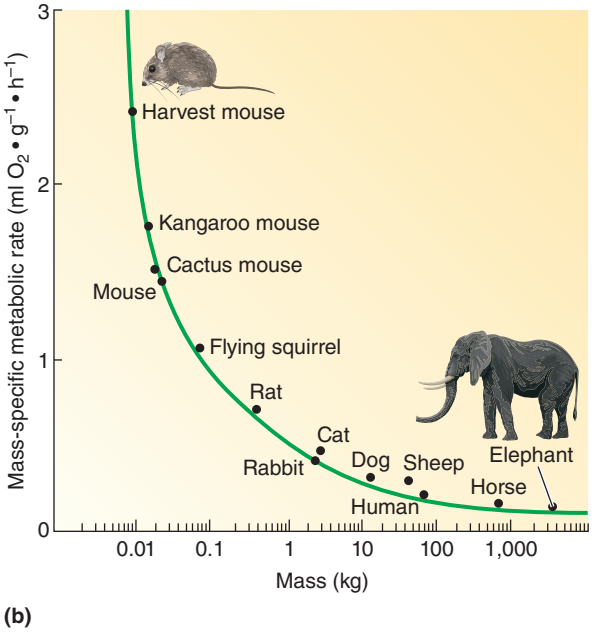
This hypothesis makes perfect physical sense, but it has two major flaws. First, the hypothesis predicts that BMR will scale with a slope of about 0.67, but instead a slope of 0.75 has been repeatedly found among species. Second, other studies have reported that ectotherms such as nonavian reptiles and fishes (and even unicellular organisms) have SMRs that scale by factors less than 1.0 (see Figure 15-3c for insects, showing a slope of 0.825). The hypothesis is irrelevant to most of these organisms, because most do not generate (and retain) body heat for the purposes of thermoregulation. So why does metabolism scale with an apparent 3/4 factor among endotherms, and by slopes of less than 1 in animals in general? Neither of these flaws has been satisfactorily explained. See *Challenges and Controversies: A Universal Scale of Life?* (p. 722) for recent hypotheses.

Increased muscle activity is the factor that can most increase metabolic rate, as indicated by metabolic scope

The next expenditure category is neuromuscular *activity*. Expressed primarily as locomotion powered by skeletal muscles (external work) and breathing by respiratory muscles and circulatory flow from the heart (internal work), this is potentially the greatest energy usage for an animal, at least for short periods of time. Even slight increases in muscle tone notably elevate metabolic rate, and metabolic rates can increase manyfold during extreme activity. Table 15-1 shows examples for a human and a hummingbird. Note that the rates for the bird are much smaller than for the human, as befitting the bird's much smaller size. However, if we compare these animals on a per-kg basis, a very different perspective is found. The human marathon runner expends about 77 kJ/hr per unit kg, but the hovering hummingbird expends about 870! This is thought to be the maximum possible for vertebrate muscle (see the Suggested Reading by Suarez). And yet, the metabolic rate of a flying honeybee can be at least three times that of the hummingbird.

Metabolic Scope A convenient indicator of an animal's activity capacity is the ratio of metabolic rate at its highest level to the BMR or SMR—the **metabolic scope.** For example, the ratio for a human marathoner is about 17 (1,300/77 in kcal/hr, Table 15-1). **Aerobic scope** values are derived from activity measured using oxygen consumption. This has been done for many animals, using laboratory devices such as treadmills, wind tunnels, and water flumes (Figure 15-2). Aerobic scope values for terrestrial vertebrates (including





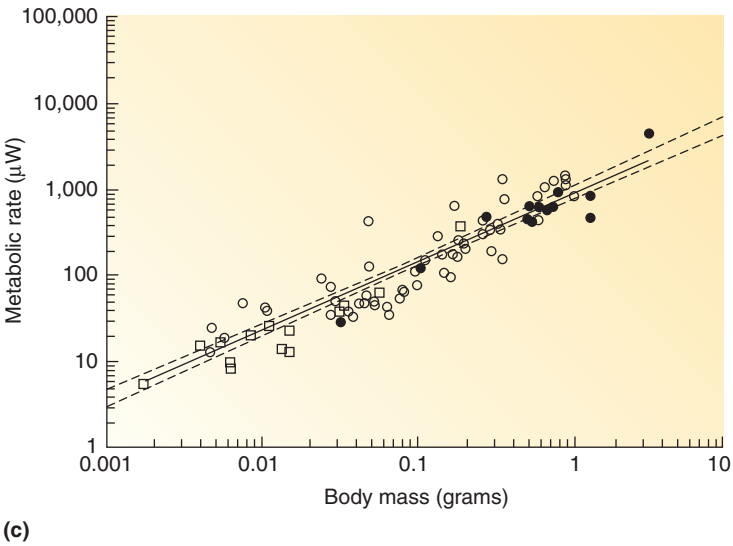


FIGURE 15-3 Scaling: Metabolic rate as a function of body mass in mammals and arthropods. (a) Relationship between the log of metabolic rate (expressed as oxygen consumption, volume per hour) and the log of body mass in mammals. The equation in the upper left corner shows that metabolic rate scales to a power of 0.738. (b) Similar to (a), but with the metabolic rate (*y*-axis) calculated on the basis of unit mass (volume per hour per kg) and plotted on an arithmetic scale. (c) Relationship between the log of metabolic rate (expressed in μW) and the log of body mass in ants (*open squares*), beetles (*closed circles*) and spiders (*open circles*). The metabolic rate here scales to a power of 0.825.

Sources: (a) From P. C. Withers. (1992). *Comparative Animal Physiology*. Fort Worth, TX: Saunders, using data from M. Kleiber. (1932). Body size and animal metabolism. *Hilgardia* 6:315–353. (b) From K. Schmidt-Nielsen. (1960). *Animal Physiology*. Englewood Cliffs, NJ: Prentice-Hall, p. 193, Figure 5.9. (c) Lighton, J. R. B. and L. J. Fielden, (1995), Mass scaling of standard metabolism in ticks: A valid case of low metabolic rates in sit-and-wait strategists, 'Physiological Zoology', 68:43-62. Copyright © 1995 University of Chicago Press.

both ectotherms and endotherms) fall in the range of about 5 to 40, following a scaling pattern. That is, whole-animal aerobic metabolic rate can be elevated above the basal level by a factor of about 5 to 10 for a small vertebrate like a hummingbird, up to 24-fold in human medium-distance runners and cross-country skiers, and 40 or more in large mammalian runners like horses. In contrast, for some flying insects, the aerobic scope factor can be over 100!

Why is aerobic scope limited to the 5 to 40 range for so many vertebrates? The limit appears to be the delivery of oxygen by the circulatory system. There seems to be a strict limit to the rate of pumping through a network of narrow vessels. The values for some insects show that the insect respiratory system, with trachea that carry oxygen directly to muscles, may be much more effective (although limited by body size; see p. 505).

Locomotory Costs and Speed Metabolism during locomotion generally increases with speed, as you would expect, but there are some interesting exceptions. For running mammals, the increase in metabolism is roughly linear with velocity (Figure 15-4a). For a swimming fish, the cost increases exponentially as drag from the environment begins to have more and more effect (Figure 15-4b) because water is so much more dense than air. Flight energetics show varying patterns: In some species, metabolic rate is independent of speed at medium to high levels, whereas in others metabolism actually *decreases* at medium speeds (Figure 15-4c). This is because at low speeds much energy is needed to overcome gravity when a bird is first ascending from a perch. Once airborne at medium speeds, a bird can save energy by *gliding*, using its forward momentum to generate lift with its wings to stay aloft. (Bird wings have an *aerofoil* shape: flat or slightly concave on the bottom and curved on the top so that air moving over the wing must travel a greater distance across the top than it does across the bottom. This creates negative pressure (lift) on the top relative to the bottom, drawing the wing up.)

Challenges and Controversies

A Universal Scale of Life?

Why is metabolism not linearly proportional to body mass? As discussed in the main text, the primary hypothesis has focused on heat and ratios of surface area to volume. But these do not explain why a relationship scaled to a 3/4 power rather than a 2/3 power is found among many forms of life. Indeed, some scientists have claimed that the 3/4 power applies to all life from microbes to trees, and in some sense must represent a universal phenomenon of life. Because the heat loss hypothesis (see main text) cannot apply to ectothermic organisms, several other hypotheses have been generated. One of these might be called the *four-dimensional* or *fractal transport* hypothesis. Three researchers (Brian Enquist, James Brown, and Geoffrey West) noted that all organisms require a means of transporting and distributing internal nutrients, gases, and wastes. In multicellular organisms, this usually involves networks of increasingly finer branching tubes, such as blood vessels, tracheae, and xylem (in plants). The researchers showed that any network that maximizes the packing of two-dimensional tubular surface areas in a three-dimensional space scales to a 3/4 power. After joining the team, Jamie Gillooly showed that factoring in temperature could account for the fact that colder organisms have scaling lines that fall below the lines of warmer organisms. These ideas lead to their Metabolic Theory of Ecology, which states that temperature and metabolic rate govern most interactions and patterns in ecosystems.

This is the first hypothesis that seems to apply to many different kinds of organisms, and is thus attractive. But critics have pointed out that BMR is not limited by transport systems, because those systems are only pushed to their limits at maximal metabolism. Also, some researchers are not convinced that all life forms follow the 3/4 scaling pattern; for example, some ectotherms show scaling slopes considerably different from 0.75 (see Figure 15-3c). Moreover, recent studies have found that the slope varies among taxonomic groups from 0.4 to 1.0; the slope tends to be near 0.6 for smaller vertebrates and 0.87 for larger ones. Another study suggested that the true slope for mammals is actually close to 0.67, with the 0.75 value arising from large herbivores whose prolonged digestive processes (DIT) yield laboratory measurements of MR that are not true BMRs. Regardless, it does appear that larger organisms are more efficient than smaller ones. But the causes are likely to remain controversial for many years.

Finally, changes in **gait** (modes of limb use during locomotion) can alter the linear pattern. As you learned in Chapter 8, most terrestrial vertebrates have elastic tendons in their legs that can store energy each time a leg hits the ground. This energy can be released on the next step, so that much of the energy required to lift the limbs is not wasted. Horses also have tendons in their backs, which come into play during a gallop gait. The ultimate example is found in hopping kangaroos and wallabies, which have been found to have no increase in metabolism as they increase hopping velocity (although they do show the expected linear increase while walking). See Figure 15-4d, and p. 358 for details.

Actual metabolic rates during locomotion (as well as scope) are scaled with body size, so that larger animals use less energy per unit body mass to cover a given distance than do smaller animals (Figures 15-4a and b). That is, it costs much less to move a gram of dog than a gram of mouse the same distance. This appears to be true of insects as well as vertebrates. It is not readily apparent why this should be, although one of the current hypotheses to explain scaling suggests that it may reflect the scaling of oxygen delivery (see *Challenges and Controversies: A Universal Scale of Life?*).

Diet-induced thermogenesis occurs after eating in most animals

The third energy-expenditure category is *diet-induced thermogenesis* (DIT; or *specific dynamic action*, SDA), which manifests as a rise in metabolism and heat production for several hours after eating. DIT has two components.

1. **Obligatory DIT** is the result of the increased metabolic activity associated with the costs of obtaining and processing food, that is, gut motility, production of gut secretions, nutrient uptake, biosynthesis of proteins, glycogen stores, and lipids, and excretion of wastes.
2. **Regulatory DIT** is increased heat production after a meal, largely for the purpose of removing excess nutrients, for example, "burning off" excess calories ingested (p. 729).

Obligatory DIT has been found in all phyla of animals tested; regulatory DIT has historically been studied in endotherms but may also occur in many types of animals. We examine the role of regulatory DIT in body mass control shortly.

Although the exact costs involved with DIT are not all certain, there are clear patterns. Within an individual, large and/or hard-to-digest meals induce a greater DIT than small and/or readily digested meals. Species differences are diverse; for example, DIT reaches a peak within a few hours in most endotherms, but it takes up to several days in sluggish ectotherms such as seastars. The extent of DIT also varies; for instance, humans show an increase of up to 50% in metabolism after a large meal, whereas other mammals, ectothermic vertebrates, and insects may exhibit 100% to 800% increases or more. The record may be held by the Burmese python, which shows a 4,400% increase in metabolism after swallowing a rodent! This animal (and other snakes that eat large, infrequent meals) actually undergoes *atrophy* of its digestive organs in between meals, presumably to save energy. This down-regulation is manifested as lower liver and intestinal masses and lower density of nutrient transporters in the intestine (see p. 692). Then, on ingesting its large but infrequent prey item, the snake restores all these atrophied features in concert with the movement of the load through the respective regions of the digestive tract. This up-regulation accounts for the enormous DIT.

Now that we have examined the details of energy balance and its components, we turn to its regulation.

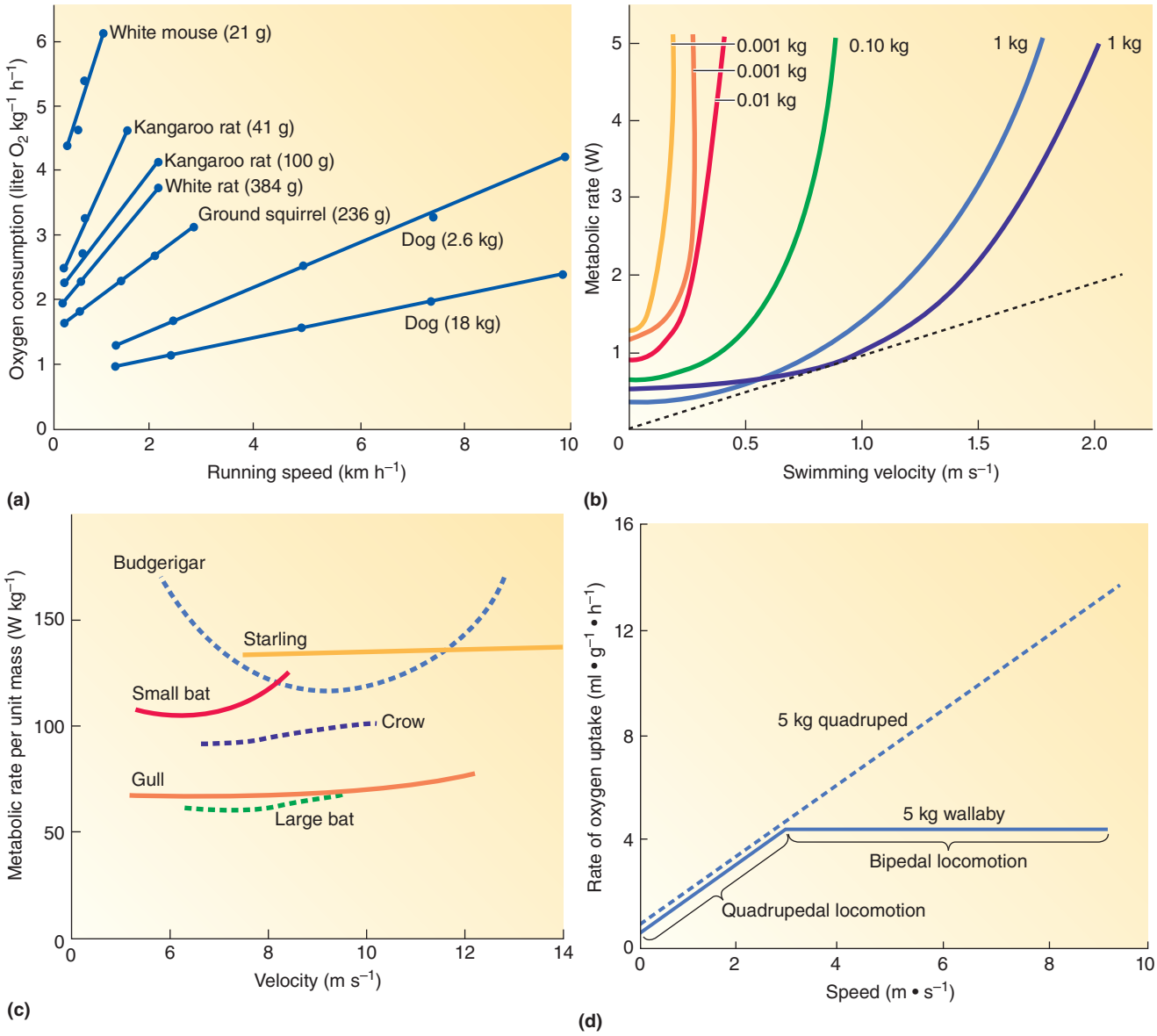


FIGURE 15-4 Metabolic rates (measured as oxygen consumption) as a function of animal locomotory speed. (a) Metabolic rates (per body mass) for running terrestrial mammals. Rate increases linearly with speed, with costs being higher in smaller mammals. (b) Metabolic rate (per whole animal) for a swimming fish. Rate tends to increase exponentially with speed. (c) Metabolic rate (per body mass) for flying birds and bats. A decrease in rate is seen at intermediate speeds due to gliding in some species. (d) Metabolic rate (per body mass) for a wallaby. When the animal uses all four limbs (quadrapedal locomotion), the rate increases linearly, as in part (a). But after the animal switches to bipedal hopping at higher speeds, rate becomes independent of speed.

Sources: (a) From P. Willmer, G. Stone, & I. Johnston. (2000). *Environmental Physiology of Animals.* Oxford, UK: Blackwell Science, as modified from C. R. Taylor, K. Schmidt-Nielsen, & J. L. Raab. (1970). Scaling of the energetic cost of running to body size in mammals. *American Journal of Physiology* 219:1104–1107. (b) From P. Willmer, G. Stone, & I. Johnston. (2000). *Environmental Physiology of Animals.* Oxford, UK: Blackwell Science, as modified from R. H. Peters. (1983). *The Ecological Implications of Body Size.* Cambridge UK: Cambridge University Press. (c) P. Willmer, G. Stone, & I. Johnston. (2000). *Environmental Physiology of Animals.* Oxford, UK: Blackwell Science, as modified from R. M. Alexander. (1999). *Energy for Animal Life.* Oxford, UK: Oxford University Press. (d) Modified from R. V. Baudinette, G. K. Snyder, & P. B. Frappell. (1992). Energetic cost of locomotion in the tammar wallaby. *American Journal of Physiology* 262:R771–R778.

check your understanding 15.2

Define *metabolic rate, standard* and *basal metabolic rate (SMR/BMR),* and *dietary-induced thermogenesis (DIT).* Explain how these are measured by indirect calorimetry.

Discuss scaling features and hypotheses regarding BMR/SMR.

Describe the three states of energy balance.

Discuss aerobic scope and the costs of different modes of locomotion.

TABLE 15-1 Rate of Energy Expenditure for a 70-kg Human and a 10-g Hummingbird during Different Types of Activity

	ENERGY EXPENDITURE*	
Form of Activity—Human	**(kcal/hour)**	**kJ/hour**
Sleeping	65	272
Awake, lying still (BMR or RMR)	77	322
Sitting at rest	100	418
Standing relaxed	105	439
Walking on level (4.3 km/hr)	200	836
Sexual intercourse	280	1,170
Bicycling on level (9 km/hr)	304	1,271
Shoveling snow, sawing wood	480	2,006
Swimming	500	2,090
Jogging (8.7 km/hr)	570	2,383
Walking up stairs	1,100	4,600
Running a marathon (winning pace)	1,300	5,400
Form of Activity—Hummingbird†	**(kcal/hour)**	**kJ/hour**
Resting (RMR)	0.3	1.25
Hovering	2.1	8.7

*kcal = kilocalories; kJ = kilojoules
†For *Eulampis jugularis* (purple-throated carib) from L. L. Wolf & F. W. Hainsworth. (1971). Time and energy budgets of territorial hummingbirds. *Ecology* 52:980–988.

15.3 Energy Balance: Regulation

Some adult animals maintain long-term neutral energy balance, while others undergo regulated periods of positive or negative energy balance

Physiologists have observed that many adult mammals, including humans, maintain a fairly constant mass (weight) over long periods of time. This implies that homeostatic mechanisms (with a set point) exist to maintain a long-term balance between energy intake and energy expenditure. Moreover, individuals may have different set points for body masses (you may have noticed that some humans stay lean no matter how much they eat, whereas other, overweight humans have great difficulty losing weight).

Conversely, periodic changes in body mass are adaptive in some animals. For example, hibernators (such as a marmot, Figure 15-5a) typically increase their body mass greatly during active (feeding) seasons and decrease during hibernation as they live off of their internal energy stores. Migratory birds may similarly gain and lose mass during premigration feeding and the migration itself, respectively. Reproductive periods such as pregnancy also include periods of mass increases followed by decreases. Finally, long-term balance is not maintained in some adult animals; for example, many adult fish indefinitely grow larger if food supplies permit (see Chapter 7, pp. 291–292).

To achieve either a constant body mass (with the exception of minor fluctuations caused by changes in H_2O content) or adaptive changes in mass as in a hibernator, there must be regulatory mechanisms to control some or all components of the animal energy equation. How does this occur? There must be *sensors* to detect energy status, an *integrator* to receive and process energy information, *effectors* to make adjustments, and appropriate *signal mechanisms* among these components. Energy regulation has been most thoroughly studied in mammals, on which we focus this discussion. We begin with the integrator component.

Food intake in mammals is controlled primarily by the hypothalamus in response to numerous inputs

In mammals, control of food intake—the input side of the animal energy equation—has been found to be a function of a pair of **feeding,** or **appetite, centers** and another pair of **satiety centers.** These integrators are located in the **arcuate nucleus** of the hypothalamus, an arc-shaped collection of neurons located adjacent to the floor of the third ventricle. The functions of these areas have been elucidated by a series of experiments that involve either destruction or stimulation of these specific regions in laboratory rats. Stimulation of the clusters of nerve cells designated appetite centers makes the animal hungry, driving it to eat voraciously, whereas selective destruction of these areas suppresses eating behavior to the point that the animal starves itself to death. (Note that eating is a behavioral effector, a point we'll return to later on p. 728.) In contrast, stimulation of the satiety centers signals satiety, or the feeling of having had enough to eat. Consequently, the stimulated animal refuses to eat, even if previously deprived of food. As expected, destruction of this area produces the opposite effect—profound overeating and obesity—because the animal never achieves a feeling of being full (Figure 15-5b). Thus, the feeding centers tell animals when to eat, whereas the satiety centers tell them when they have had enough.

Although it is convenient to consider these specific areas as direct regulators of feeding behavior, this approach is too simplistic. Physiologists now know that complex systems and numerous signals provide information about the body's energy status. Recent studies have uncovered multiple, highly integrated, redundant pathways, crisscrossing into and out of the hypothalamus, that are involved in controlling food intake and maintaining energy balance. Integration of multiple molecular signals ensures that effector feeding behavior is synchronized with the body's immediate and long-term energy needs. Let's examine these, beginning with a closer look at the hypothalamic integrator.

Arcuate Nucleus: The Integrator The arcuate nucleus has two subsets of neurons that function in an opposing manner. One subset releases *neuropeptide Y,* and the other releases *melanocyte-stimulating hormones* (*MSHs*) derived from *pro-opiomelanocortin* (*POMC*), a precursor molecule

(a)

(b)

(a) Paul Yancey; (b) Wilbert E. Gladfelter, Ph.D., Department of Physiology, School of Medicine, West Virginia University

FIGURE 15-5 "Fat" mammals. (a) The hoary marmot (*Marmota caligata*) of western North America. This heterotherm must build up large deposits of fat before winter, when it hibernates. (b) Comparison of a normal rat with a rat whose satiety center (in the hypothalamus) has been destroyed. Several months after destruction of the classical satiety center in the ventromedial area of the hypothalamus, the rat on the right had gained considerable mass as a result of overeating compared to its normal littermate on the left. Rats sustaining lesions in this area also display less grooming behavior, accounting for the soiled appearance of the fat rat.

that can be cleaved in different ways to produce several different hormones (see p. 271). **Neuropeptide Y (NPY),** one of the most potent appetite stimulators ever found, leads to increased food intake, thus promoting mass gain. MSHs, a group of hormones known to be important in regulating skin color in some species (see p. 284), have been shown to exert an unexpected role in energy homeostasis in mammals. Most notably **α melanocyte-stimulating hormone (α-MSH)** suppresses appetite, thus leading to reduced food intake and mass loss.

Beyond the Arcuate Nucleus: Orexins and Others NPY and α-MSH are not the final signals in appetite control. These arcuate-nucleus chemical messengers, in turn, influence the release of neuropeptides in other parts of the brain that exert more direct control over food intake. Scientists are currently trying to unravel the other factors and regions that act upstream and downstream from arcuate nucleus to regulate appetite. Two such regions in the hypothalamus have been found to be richly supplied by axons from the NPY- and MSH-secreting neurons of the arcuate nucleus. These areas are the **lateral hypothalamic area (LHA)** and **paraventricular nucleus (PVN).** In a recently proposed model, the LHA and PVN release chemical messengers in response to input from the arcuate nucleus neurons. These messengers act downstream from the NPY and α-MSH signals to regulate appetite. The LHA produces two closely related neuropeptides known as **orexins** A and B, which are potent stimulators of food intake (*orexis* means "appetite"). NPY stimulates and α-MSH inhibit the release of orexins, thus regulating appetite and food intake. However, orexins (which are produced in a circadian rhythm) also increase wakefulness and physical activity, so are not committed to mass gain. By contrast, the PVN releases neuromodulators, for example, **corticotropin-releasing hormone (CRH),** that decrease appetite and food intake. (As its name implies, CRH is better known for its role as a hormone; see p. 289.)

The release of all of these brain regulators requires sensory input that "informs" the hypothalamus of the body's energy status for both long-term maintenance of energy balance and the short-term control of food intake. Let's next look at the key input signals based on current research (Figure 15-6).

Leptin and insulin are signals of long-term energy balance

Scientists' notion of fat cells (**adipocytes**) in adipose tissue as merely storage space for triglyceride fat underwent a dramatic change late in the last century with the discovery of their active role in energy homeostasis. Adipocytes secrete several hormones, collectively termed **adipokines,** that play important roles in energy balance and metabolism. Thus, adipose tissue is now considered an endocrine gland. For example, **adiponectin** increases sensitivity to insulin (which helps protect against Type II diabetes mellitus), decreases body mass, and exerts anti-inflammatory actions. Unfortunately, obesity suppresses adiponectin secretion. Here we

Molecular Biology and Genomics
Discovering the Obesity Gene

The discovery and characterization of the leptin gene in 1994 by Jeffrey Friedman illustrates the importance of genetics to physiology. Physiologists had known for decades that obesity has a genetic component because different animal individuals on the same diets could have very different—and stable—body masses, with an apparent set point that could vary widely among individuals. Furthermore, the propensity for obesity could be passed from one generation to the next. Manipulations of the hypothalamus showed appetite was controlled in that brain region. Researchers widely suspected that mammalian bodies must have feedback signals that would tell the hypothalamus about the energy status of the body.

But physiologists had no luck finding such a signal. Enter the geneticists in the 1980s. By then, several strains of obese mice were established, including the *ob* strain, weighing about three times more than other mice. After eight years of genetic breeding and cloning experiments, Friedman and his colleagues showed that obesity was due to the functional absence of a single gene, dubbed the *ob* gene. They isolated and cloned the normal *ob* gene (in non-*ob* mice), and subsequent work showed that it codes for the protein hormone leptin, which has turned out to be one of the key energy signals in mammals. Without modern genetic methods, this might never have been discovered.

Using genome analysis and antibody detection, researchers have found leptin in most other vertebrates (reptiles including birds, and fishes). Leptin in broiler chickens is produced not only by adipose but also by liver tissue. The discovery of chicken leptin is being used to investigate methods for obesity control in these animals! Broiler chickens, as a source of human food, have been bred for maximal growth, but this has produced obese parent birds with low reproductive rates. For this reason, these birds are placed on restricted diets from an early age: Even so, both egg production and fertility dramatically decline with age. Researchers hope to manipulate leptin concentrations to reduce adipose stores while enhancing lean meat production.

Leptin-related genes and proteins have been studied in a reptile (the fence lizard *Scoleporus undulatus*) and a fish (the green sunfish *Lepomis cyanellus*). As in mammals, fasting sunfish have lower levels of plasma leptin than fed sunfish. Injecting mouse leptin into these animals induced effects similar to that seen in mammals: The injected lizard raised its body temperature slightly and its RMR by 250%, and showed a reduced appetite, whereas the injected sunfish began to metabolize its adipose stores. Thus, leptin is an ancient vertebrate signal of energy balance.

will focus on **leptin** (*leptin,* "thin"), an adipocyte hormone essential for normal body-mass regulation in mammals. As a sensory process, the amount of leptin in the blood informs the brain of the total amount of triglyceride fat stored in adipose tissue: That is, the larger the fat stores, the more leptin released into the blood. This bloodborne signal, discovered in the mid-1990s by genetic analysis of obese laboratory mice, was the first molecular satiety signal found by genetics (see *Molecular Biology and Genomics: Discovering the Obesity Gene*).

The arcuate nucleus is the major site for leptin action. Acting in negative-feedback fashion, increased leptin from burgeoning fat stores serves as a "trim-down" signal. Leptin suppresses appetite, thus decreasing food consumption and promoting mass loss, by inhibiting hypothalamic output of appetite-stimulating NPY and stimulating output of appetite-suppressing α-MSH. Conversely, a decrease in fat stores and the resultant decline in leptin secretion bring about an increase in appetite, leading to mass gain. The leptin signal is generally considered the dominant factor responsible for the long-term matching of food intake to energy expenditure so that total body energy content remains balanced and body mass remains constant.

Interestingly, leptin has recently been shown to also be important in reproduction, for example, as one of the triggers for the onset of puberty through its effects on *kisspeptin* neurons (see p. 798). The importance of its role in energy balance, and how that affects survival, was shown in recent experiments on Siberian hamsters. Susannah French and colleagues used a pump to infuse leptin into pregnant hamsters to keep the hormone artificially high. These mothers had significantly more offspring than mothers with a placebo treatment. Apparently, the treatment tricked the hypothalamus into "thinking" that energy was in excess, so the mother's body diverted more energy to the growing embryos. But, following the principles of energy balance, this came at a cost: The treated mothers had weakened immune responses and were more prone to bacterial infections.

Leptin may also be involved in the annual cycle of hibernating mammals such as Arctic ground squirrels, animals that do not maintain constant mass year-round because they must store up large adipose deposits in the productive seasons and survive on them in the winter. Some studies suggest that the brain ignores leptin signals in the autumn, allowing the animals to gain mass, whereas during the winter hibernation, the high leptin output of the stored fat effectively suppresses appetite.

Another bloodborne signal besides leptin that plays an important role in long-term control of body mass is **insulin,** a hormone secreted by the pancreas in response to a rise in the concentration of glucose and other nutrients in the blood following a meal (p. 316). It stimulates cellular uptake, use, and storage of these nutrients. Thus, the increase in insulin secretion that accompanies nutrient abundance, use, and storage appropriately inhibits the NPY-secreting cells of the arcuate nucleus, thus suppressing further food intake.

Gastrointestinal Hormones: Signals of Short-Term Energy Balance In addition to insulin's and leptin's importance in the long-term regulation of body energy and mass, other factors are believed to play a role in controlling the timing and size of meals. Early proposals suggested that cues of

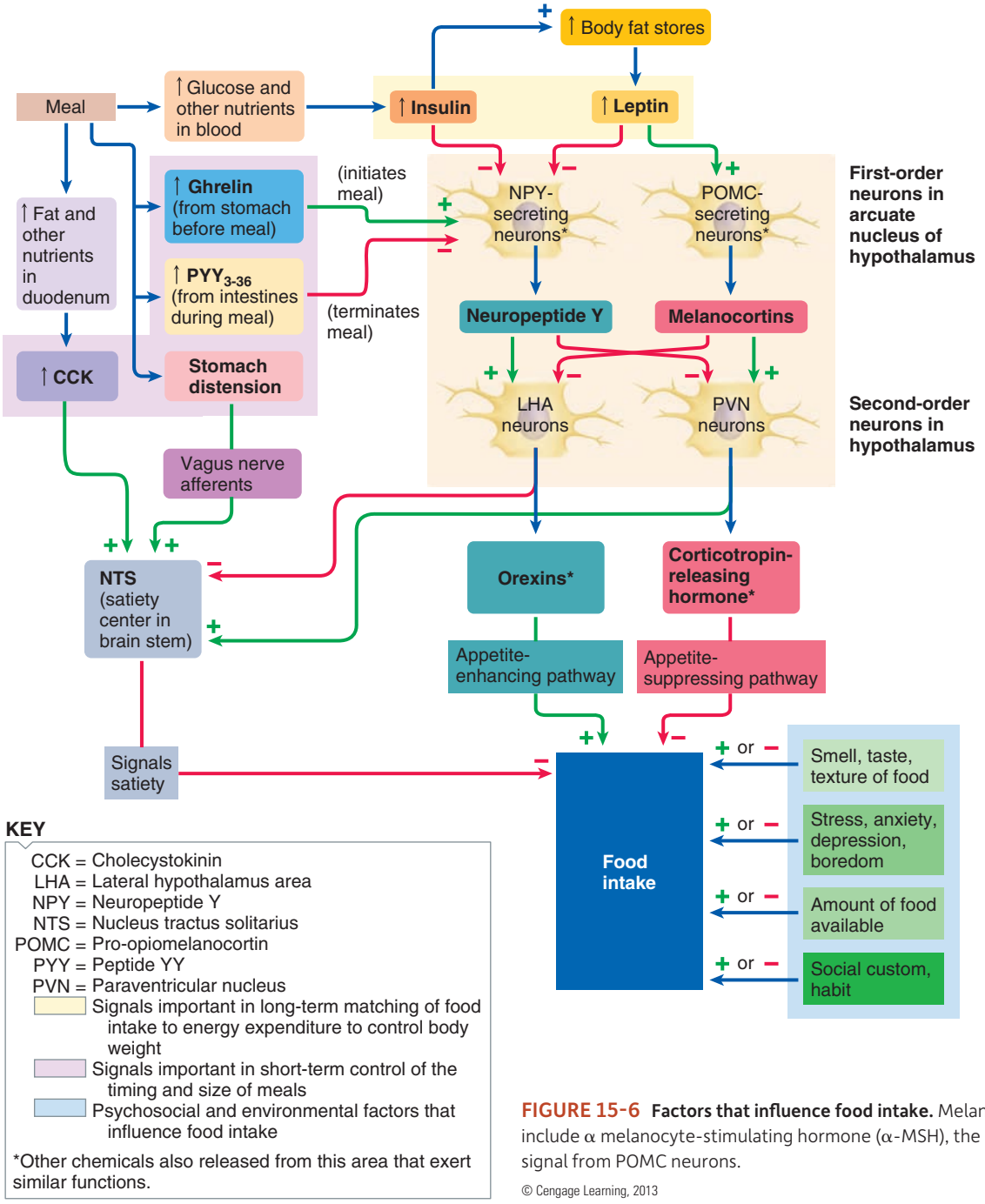


FIGURE 15-6 Factors that influence food intake. Melanocortins include α melanocyte-stimulating hormone (α-MSH), the primary signal from POMC neurons.

emptiness or fullness of the digestive tract signaled hunger or satiety, respectively. For example, stimulation of gastric stretch receptors has been shown to suppress food intake. However, neural input arising from stomach distension plays a more important role in controlling the rate of gastric emptying than in signaling satiety (see p. 672). Recent studies have found that the digestive tract has food-sensing receptors similar or identical to those in the tongue's taste buds. There is now good evidence that the following internal bloodborne signals reflecting the depletion or availability of energy-producing substances, sensed by the gut, are important in the initiation and cessation of eating.

- **Cholecystokinin (CCK):** One of the gastrointestinal hormones released from the duodenal mucosa during digestion of a meal, CCK is an important satiety signal for regulating the size of meals. CCK is secreted in response to the presence of nutrients in the small intestine. Through multiple effects on the digestive system, CCK facilitates the digestion and absorption of these nutrients (see p. 684). It is appropriate that this bloodborne signal, whose rate of secretion is correlated with the amount of nutrients ingested, also contributes to the sense of being filled after a meal has been consumed but before it has actually been digested and absorbed.

- **Ghrelin, Obestatin, and PYY_{3-36}:** Three peptides involved in the short-term control of food intake have recently been identified: *ghrelin*, *obestatin*, and *peptide YY_{3-36} (PYY_{3-36})*. All are secreted by the digestive tract; moreover, ghrelin and obestatin are arise from the same gene and its encoded protein, which breaks in half to form them. **Ghrelin** (Hindu for growth), the so-called hunger hormone (p. 712), is a potent appetite stimulator produced by the stomach and regulated by the feeding status. Secretion of this mealtime stimulator rises before and at the onset of meals and stimulates appetite behavior, then falls once food is eaten. Ghrelin stimulates appetite by activating the hypothalamic NPY-secreting neurons. Recent research suggests that ghrelin secretion can be activated indirectly by dietary fats entering the stomach. It may be that ghrelin informs the brain that fat-rich food is entering the gut and so appetite should be increased to take advantage of that food. **Obestatin,** conversely, has been called the "satiety hormone" as it appears to have effects opposite those of ghrelin. However its role in appetite regulation is still unsettled.

  PYY_{3-36} appears to be the main antagonist to ghrelin rather than obestatin. The secretion of PYY_{3-36}, which is produced by the small and large intestines, is at its lowest level before a meal but rises during meals and signals satiety. This peptide acts by inhibiting the appetite-stimulating NPY-secreting neurons in the arcuate nucleus. By thwarting appetite, PYY_{3-36} is believed to be an important mealtime terminator.

Table 15-2 summarizes the effects of these gastrointestinal signals. These could explain why animals stop eating before the ingested food is actually digested, absorbed, and made available to meet the body's energy needs. An animal may feel satisfied when adequate food to replenish the stores is in the digestive tract, even though the body's energy stores are still low. This would help prevent the overshoot phenomenon (in this case, overeating) that characterizes simple negative-feedback systems (p. 16).

TABLE 15-2 Effect of Involuntary Regulatory Signals on Appetite

Regulatory Signal	Source of Signal	Effect of Signal on Appetite
Neuropeptide Y	Arcuate nucleus of hypothalamus	Increases
α-MSH	Arcuate nucleus of hypothalamus	Decreases
Leptin	Adipose tissue	Decreases
Insulin	Endocrine pancreas	Decreases
Ghrelin	Stomach	Increases
PPY_{3-36}	Small and large intestines	Decreases
Orexins	Lateral hypothalamus	Increases*
Corticotropin-Releasing Hormone	Paraventricular nucleus of hypothalamus	Decreases
Cholecystokinin	Small intestine	Decreases
Stomach Distension	Stomach	Decreases

*Also increases in energy expenditures and wakefulness.

Effectors for energy balance are mechanisms to regulate eating and expenditures

The final components of a regulatory system are its effectors. Potentially any or all of the components of the animal energy equation could be regulated. Much remains to be learned about this, but a number of regulatory mechanisms are known. Let's examine some of these.

Regulation of Food Intake (Eating) On the input side of the equations, you have already seen how eating, the behavioral effector controlled in part by the hypothalamus, is affected by sensory signals such as leptin and ghrelin. Over a 24-hour period the energy in ingested food rarely matches energy expenditure for that day. The correlation between total caloric intake and total nonproduction energy output is strong, however, over long periods of time for animals with long-term neutral energy balance.

However, that balance can be disrupted by psychosocial and other environmental influences. For example, the amount of pleasure derived from eating can reinforce feeding behavior. This has been demonstrated in an experiment in which rats were offered their choice of highly palatable human foods. They overate by as much as 70 to 80% and became obese. When the rats returned to eating their regular monotonous but nutritionally balanced rat chow, their obesity was rapidly reversed as their food intake was controlled once again by physiological drives rather than by urges for the apparently tastier offerings. Stress, anxiety, depression, and apparent boredom have also been shown to alter feeding behavior in ways that are unrelated to energy needs in experimental animals as well as humans. Some types of stress, particularly involving *cortisol* (p. 286), lead to overeating (as if the hypothalamus "thinks" it needs to prepare for future starvation), while other types lead to undereating.

There is no question that regulation of eating is the most important factor in the long-term maintenance of energy balance and body mass. However, in laboratory studies on different strains of rats, genetically lean mice eat as much or more than genetically obese mice while remaining much leaner. Thus, regulation of expenditures (output) must also be important.

Compensatory Changes in Expenditures in Response to Underfeeding Some studies suggest that after several weeks of eating less than normal (e.g., as a result of starvation, or deliberate "dieting" in a human), a mammal may initiate small counteracting decreases in BMR, possibly by reductions in thyroid hormones (p. 301), and/or decreases in muscular activity by uncertain mechanisms. This energy-saving effect partially explains why some humans or laboratory animals on a diet become stuck at a plateau after having shed the first grams easily.

Chronic underfeeding can also lead to suppression or even reversal of production output. For example, starvation (as well as some other stresses) in mammals can lead to lower gonadotropin output and thus reduced spermatogenesis and oogenesis. This may occur in part because declining leptin levels in starvation cause a decrease in the release of *kisspeptin,* a regulator of reproductive hormones (p. 798). Many vertebrates such as rodents and ovoviparous fishes actually reabsorb their internal embryos or fetuses. Some vertebrates will even eat developing eggs (oviparous animal) or newborns. Nonvertebrates also exhibit similar energy-saving reproductive adjustments. Starving aphids, for example, reabsorb their developing oocytes, while starving great pond snails (*Lymnaea stagnalis*) stop producing egg-laying hormone due to reduced neurosecretory output from the brain.

Compensatory Increases in Expenditures in Response to Overfeeding Conversely, physiological processes that "burn off" excess calories account in part for the inability of some mammals (including some humans) to gain much mass despite excessive food intake. These involve regulatory DIT and muscular activity.

1. *Increased regulatory DIT: Uncoupling proteins and brown adipose tissue.* Humans and laboratory mammals have been found to release "unwanted" calories by activating **uncoupling proteins (UCP)** in some tissues. UCPs are channels for protons (H^+) that let the H^+ gradients generated from food energy in mitochondria dissipate, with no ATP synthesis. A major site of UCPs is **brown adipose tissue (BAT),** which probably evolved as a thermoregulatory organ in small and newborn mammals (as we will discuss later; p. 746). However, BAT can also be activated after a large meal (as regulatory DIT). BAT does not store fats but rather converts available energy in lipids into heat using **UCP-1,** and is now recognized as a major contributor to energy balance. Larger mammals were thought to lose their BAT as they aged, but new research shows that some lean humans have some BAT, while obese humans have little or none. White adipose tissue and skeletal muscle, containing UCP-2 and UCP-3, respectively, appear to be similarly used, and again, lean humans have higher densities of both UCPs than do obese individuals.

   BAT is activated by the sympathetic nervous system. Interestingly, the ghrelin system may suppress BAT. Yuxiang Sun and colleagues created two groups of knock-out mice, one lacking ghrelin and the other missing the ghrelin receptor. The latter group, in contrast to the ghrelin knock-out or control animals, did not gain weight on a high-fat diet. The researchers found that BAT, lacking the ghrelin receptor, increased its levels of UCP-1 and thus its ability to "burn off" excess fat. Thus, the normal ghrelin receptor may favor fat storage.

2. *Increased exercise and non-exercise activity thermogenesis.* Muscular activity levels may also be regulated for disposal of excess energy. In humans, involuntary movements called "fidgeting," like foot tapping, have been found to be more frequent in lean than in heavy individual humans. Lean rodents on a high-fat diet also exhibit purposeless repetitive movements. Such behavior is called **non-exercise activity thermogenesis (NEAT)** and is regulated by the hypothalamus. Laboratory rodents injected with leptin into blood, or orexin-A into the PVN, show a spontaneous increase in muscular (including NEAT) activity, and either lose more mass or gain less than control animals. In humans, voluntary activities such as exercise are of course well known to contribute to energy balance.

Different energy-balance set points among species result from evolutionary adaptations to different food supplies

Clearly, even though many mammals maintain a relatively constant body mass, species and individuals vary greatly in the mass they actually maintain (as we noted earlier). This has led to the proposal that the hypothalamic centers determining long-term satiety can evolve different *set points* for energy balance, possibly for adipose storage in particular. The two extreme set points are often termed "lean" and "obese" (or "heavy"). Although humans in modern Western societies tend to attach positive and negative connotations to lean and obese states, respectively, physiologists view these in a different light. Both extremes (and set points in between) can be evolutionarily advantageous depending on the environment:

- Lean animals do better in habitats where food is plentiful year-round so that storing a high amount of body fat is unnecessary. The advantage here is that such animals are more agile than heavy ones, better able to avoid predators and (in some species) to obtain food in the first place. Thus, carnivores in the tropics (such as tigers) are lean. (Although the leanness may be attributed to high activity levels, many carnivores in fact are sedentary for much of the time.) The trade-off between storage and agility was revealed in zebra finches by researchers in Scotland, who videotaped and weighed numerous birds on a daily basis. Some finches had access to excessive calories from human sources. A mere 7% gain in body mass led to a 33% loss in speed and maneuverability, making these overfed birds easier prey for cats and sparrow hawks. Thus, an obese or heavy set point has negative consequences in a food-plentiful habitat, including increased cardiovascular and oxidative stresses causing internal health problems, as well as reduced maneuverability. Household pets, as well as humans themselves, often suffer from the consequences of obesity.
- Conversely, a high adipose set point has very clear advantages in "feast or famine" habitats, where food is only abundant at limited times of the year. A clear example is the mammalian hibernator (see Figure 15-5a). An Arctic ground squirrel must reach an "obese" state (up to 50% body fat) before winter sets in or it will not survive the eight months during which it hibernates in its burrow. Desert habitats that have abundant food only during short rainy seasons also select for this adaptation. Overall, it is now recognized that having a propensity toward being "overweight" is not necessarily an abnormal physiological state but may be an evolutionary adaptation for a particular environment.

Researchers do not yet fully understand what determines these different set points in the neurological structure

of the brain. But, as discussed earlier in this chapter, fat storage levels and the associated set point may be closely tied to leptin and how the hypothalamus reacts to it. The hypothalamus of a lean-adapted mammal reacts strongly to a modest rise in leptin, shutting off appetite and acting as if it had a low set point. The hypothalamus of "obese" mammals, conversely, reacts only to very high levels of leptin. Also, humans and laboratory animals appear to differ in the thermogenic activity of tissues with uncoupling proteins, correlating with lean or obese set points. Research is continuing on these numerous fronts.

check your understanding 15.3

- Describe the role of the hypothalamus in energy balance regulation.
- Describe the source and role of the following in regulation of energy balance: leptin, insulin, ghrelin, $PYY_{3\text{-}36}$, and cholecystokinin (CCK).
- Describe the effectors that regulate energy input and energy expenditures.
- Discuss evolutionary differences in body-mass "set points."

15.4 Thermal Physiology: General Principles

We now turn to a major habitat factor intimately involved with energy. When physiological ecologists examine the distribution of species around the planet, noting that most species live in rather restricted ranges, they ask what factors are responsible for these restrictions. One of the most pervasive factors is temperature, which has direct and profound effects on biological functions.

Temperature alters rates of chemical reactions and denatures macromolecules

Temperature is a measure of heat energy, which in turn is manifested primarily in kinetic energy (movement) of molecules. The primary effects of this are shown in Figure 15-7, which shows a typical optimal curve of biological function and temperature. Basically, two different temperature effects create this curve:

1. *Kinetic energy of reactants:* On the left (up-trending) side of the plot, reaction rates increase with temperature simply from the increased kinetic energy of molecules. Reacting molecules (such as substrates and enzymes, for example) encounter each other more frequently. It has become customary to characterize this temperature response with a value called the Q_{10}, which is the ratio of a reaction rate (or metabolic process) at one temperature to the rate at 10°C cooler:

$$Q_{10} = \frac{\text{rate at temperature } T}{\text{rate at temperature } T_{-10}}$$

Q_{10} values are useful measures of the temperature sensitivity of a biological process (from single reactions to a whole organism's metabolism). In general, researchers have found that many reactions tend to double or triple for each 10°C rise, at least over a moderate range. However, at some point with rising temperature, the curve begins to flatten, reaches an optimum, and then declines.

2. *Denaturation of macromolecules.* Above the optimum (right side of the plot), rates of biological processes begin to decrease with temperature for one basic reason: The macromolecules (such as enzymes) responsible for the process begin to denature (that is, lose their tertiary levels of structure). As we discussed in Chapter 2 (p. 27), weak bonds stabilize many of these structures so that they can be flexible, but this makes them susceptible to loss of function at higher kinetic energies.

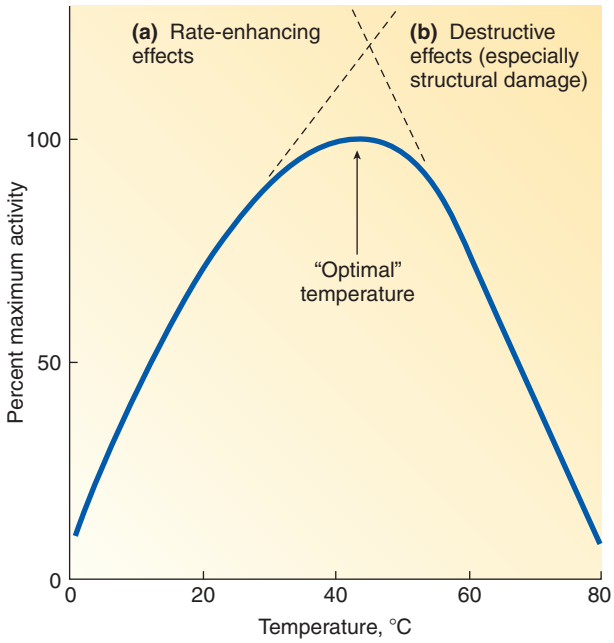


FIGURE 15-7 The relative activity of an enzymatic reaction as a function of temperature. The decrease in activity below 30°C is primarily due to reduced kinetic energy, while the decrease in activity above 50°C is due to disturbed protein structures, including denaturation.

Source: Modified from M. K. Campbell & S. Farrell. (2003). *Biochemistry*, 4th ed. Belmont, CA: Thomson, p. 137, Figure 5.2.

In general, this curve means that organisms cannot operate over a wide range of body temperatures. For animals, active metabolism seems to be restricted to a range from about –2°C (the freezing point of seawater) to 55 to 60°C. (A penguin living actively at –50°C air temperature in Antarctica does not violate this restriction, because its cells are warmed to about 40°C from internal heat production and retention.) This is a relatively narrow range, given that a temperature of –89.2°C (–128.5°F) has been recorded (in Antarctica) and hydrothermal vent temperatures may reach about 400°C (750°F)! Some animals have evolved ways to cope with body temperatures colder than freezing (as you will see), but metabolism in these animals is generally in a dormant state. At the other extreme, there is no convincing evidence of any animal tolerating over 55°C for anything but very brief periods (on some desert sands and at some

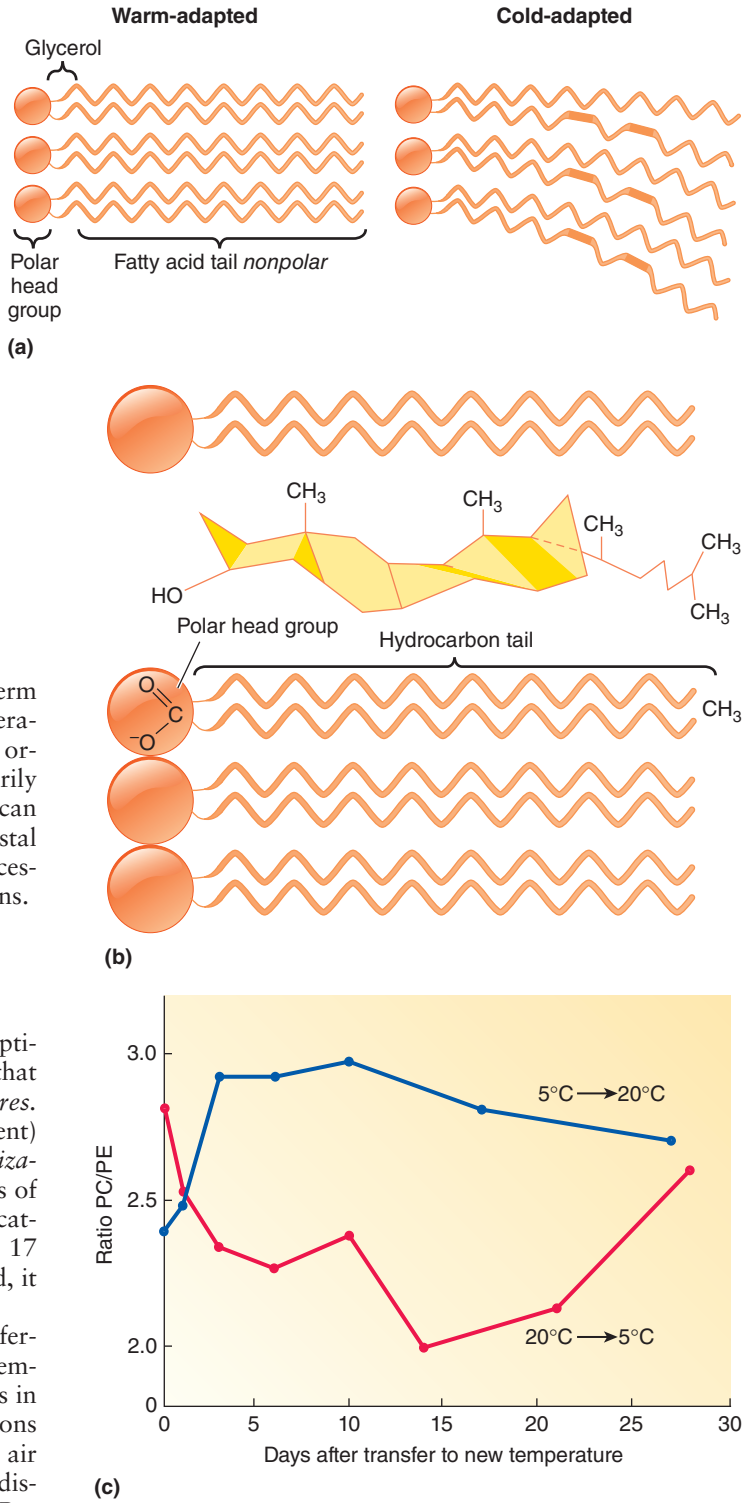


FIGURE 15-8 Schematic diagrams of membrane structures and their relationship to temperature. (a) Saturation level of membrane phospholipids changes with temperature adaptation. The *left* figure represents a warm-adapted membrane: The fatty-acid "tails" are highly saturated, allowing for close stacking of neighboring tails. This enhances thermostability at higher temperatures. The *right* figure represents a cold-adapted membrane: The fatty-acid "tails" are more unsaturated, creating double bonds that interfere with stacking of neighboring tails. This enhances flexibility at colder temperatures. (b) Stiffening of the membrane with cholesterol. Cholesterol reduces fluidity by stabilizing extended forms of the phospholipid tails. (c) The relationship between adaptation temperature and ratio of unsaturated phospholipid tails (phosphatidylethanolamine, PE) to saturated ones (phosphatidylcholine, PC) in gill membranes of rainbow trout transferred to different temperatures as shown.

Sources: (a) © Cengage Learning, 2013 (b) Modified from M. K. Campbell & S. O. Farrell. (2003). *Biochemistry,* 4th ed. Thompson, p. 202, Figure 7.14. (c) Hochachka, P. W. and G. N. Somero, (2002), Biochemical Adaptation, Oxford: Oxford University Press, as modified from J. A. Logue, A. L. DeVries, E. Fodor, & A. R. Cossins, (2000), Lipid compositional correlates of temperature-adaptive interspecific differences in membrane physical structure, 'Journal of Experimental Biology', 203:2105-2115. Reproduced with permission via Copyright Clearance Center.

marine hydrothermal vents; see p. 741). Ignoring long-term acclimatization for the moment, excessively high temperatures are usually more dangerous than cold ones. Many organisms can survive lower body temperatures temporarily because reactions merely slow down (although freezing can set a lower limit because of the lysis of cells from ice crystal formation in organisms that cannot prevent that), but excessive heat can irreversibly damage membranes and proteins.

Biomolecules can be altered to work optimally at different temperatures

For the most part, biological systems are subject to the optimal curve of Figure 15-7, but it is important to realize that *the optimum itself can change with different temperatures.* Changes can occur over two possible (and very different) time courses: within an organism's lifetime in *acclimatization* processes, and over many generations by the process of mutation and natural selection, that is, *evolution.* Both categories are sometimes loosely called "adaptation" (see p. 17 for more details on terminology). If "adaptation" is used, it is crucial to carefully explain the time course.

Not all organisms can successfully acclimatize to different temperatures, nor can all species evolve to survive temperatures outside of their normal ranges. Indeed, changes in habitat temperatures may be a major cause of extinctions over geological time; moreover, the current rise in global air and water temperatures is already affecting organismal distributions and physiologies (as we will discuss later). Regardless, optima clearly differ among species and within some species experiencing different thermal habitats, in part because of changes in two critical classes of biomolecules—membranes and proteins.

Membranes and the Homeoviscous Adaptation Biological membranes are held weakly together by hydrophobic interactions between the fatty acid chains of its phospholipids (p. 71), giving them a certain *viscosity* or fluidity that is vital to functions such as transport and diffusion. However, the weak structure makes them very susceptible to temperature changes. At low temperatures, viscosity increases and the membrane becomes too rigid for optimal function. At higher temperatures, membranes lose viscosity and become too fluid. If you have used butter from a refrigerator and also from a kitchen counter on a hot day, you are aware of these effects. As you saw in Chapter 3 (p. 72), a membrane can be changed to counter these effects by the length of the fatty acids and by the degree of *saturation* of its fatty acids (and, to some extent, by altering its cholesterol content). A hypothetical example is shown in Figures 15-8a and b, with a real

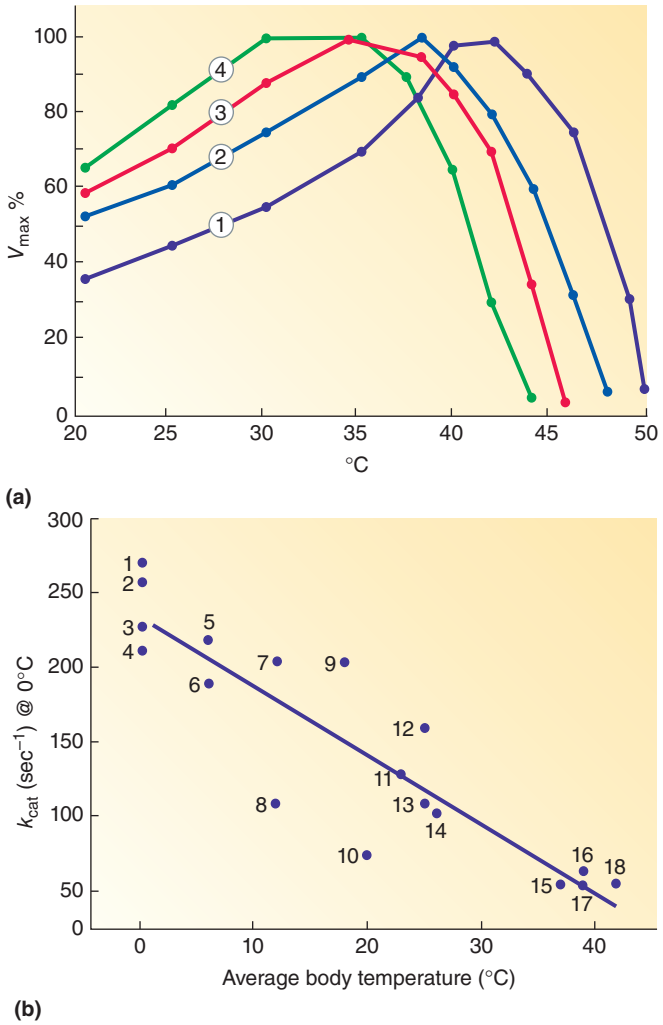


FIGURE 15-9 Relationship between enzyme activity and temperature in animals adapted to different temperatures. (a) The relative activity max (V_{max}) of myosin ATPase of four lizards, showing that animals adapted to higher temperatures have enzymes with higher thermal optima. 1. *Dipsosaurus dorsalis,* which has a preferred body temperature of 38.8°C; 2. *Uma notata,* preferred body temperature of 37.5°C; 3. *Scleroporus undulatus,* preferred body temperature of 36.3°C; 4. *Gerrhonotus multicarinatus,* preferred body temperature of 30.0°C. (b) The enzyme catalytic rate constant (k_{cat}) for *lactate dehydrogenases* (LDH, A_4 type) from various vertebrates adapted to different temperatures, showing that, in general, animals adapted to higher temperatures have enzymes with lower catalytic rates. Antarctic notothenioid fishes are 1. *Lepidonotothen nudifrons;* 2. *Parachaenichthys charcoti;* 3. *Champsocephalus gunnari;* 4. *Harpagifer antarcticus.* South American notothenioid fishes are 5. *Patagonotothen tessellata;* 6. *Eleginops maclovinus.* Temperate and subtropical fishes are 7. *Sebastes argentea* (rockfish); 8. *Hippoglossus stenolepis* (halibut); 9. *Sphyraena argentea* (barracuda); 10. *Squalus acanthias* (dogfish shark); 11. *Sphyraena lucasana* (barracuda); 12. *Gillichthys mirabilis* (goby); 13. *Thunnus thynnus* (bluefin tuna). A tropical fish is 14. *Sphyraena ensis* (barracuda). Terrestrial animals are 15. *Bos taurus* (cow); 16. *Gallus gallus* (chicken); 17. *Meleagris gallapavo* (turkey); and 18. *Dipsosaurus dorsalis* (desert iguana).

Sources: (a) Modified from P. Licht. (1967). Thermal adaptation in the enzymes of lizards in relation to preferred body temperature. In *Molecular Mechanisms of Temperature Adaptation,* ed. C. L. Prosser. Washington: American Association for the Advancement of Science. (b) P. W. Hochachka & G. N. Somero. (2002). *Biochemical Adaptation.* Oxford, UK: Oxford University Press; as modified from P. A. Fields & G. N. Somero. (1998). Hot spots in cold adaptation: Localized increases in conformational flexibility in lactate dehydrogenases A_4 orthologs of Antarctic notothenioid fishes. *Proceedings of the National Academy of Sciences USA* 95:11476–11481.

example in Figure 15-8c. First, consider a warm-adapted organism. Its membranes typically consist of *saturated fatty acids* (SFAs), in which the carbons in the "tails" are fully hydrogenated. This allows the tails to stack together tightly, giving the whole membrane enough viscosity to work properly at warm temperatures (Figure 15-8a, left). Cholesterol may be high as well, to further reduce fluidity (Figure 15-8b). However, these membranes become too rigid to work in the cold (as butter does in a refrigerator). Conversely, a cold-adapted organism typically has a higher proportion of *polyunsaturated fatty acids* (PUFAs), in which some carbons have fewer hydrogens and thus form double bonds with neighbor carbons. This puts "kinks" in the tails, making tight stacking impossible (Figure 15-8a, right). This makes the whole membrane less viscous and thus more fluid in the cold. But these membranes become too fluid to work in warm conditions. Thus, there is a trade-off between thermal stability and fluidity. Both membranes have approximately the same viscosity *when they are each measured at their adaptational temperatures*. Hence, the term **homeoviscous adaptation** was coined to refer to these saturation changes that preserve an optimal viscosity of the cell membrane.

Saturation levels are catalyzed by enzymes called **desaturases** (used in the cold to remove hydrogens) and **saturases** (used in warm conditions to add hydrogens). As noted, the time course of changes is critical when discussing this adaptation. In general, organisms from different thermal habitats have lipid compositions that follow the saturation principles just described. However, only some organisms can acclimatize (from winter to summer, for example) by regulating the saturases and desaturases and thus their membranes. In addition to the fish described in Chapter 3 (p. 72), an example is shown in Figure 15-8c.

Proteins and the "Homeoflexibility Adaptation" A similar type of change can occur with proteins, although generally only over evolutionary time. In this case, the trade-off is between *thermostability and protein flexibility* rather than fluidity. Recall from Chapter 2 (e.g., Figure 2-1) that many proteins need to be flexible to "do their job." As you saw earlier, increased temperature can cause these flexible structures to denature (Figure 15-7), but lower temperatures can make an enzyme too rigid to function well. As shown in Figure 15-9a for myosin (the "motor" protein of muscle; see Chapter 8), optimal temperatures for functionality do vary among species. How does this occur? A major clue was found in studies of *catalytic rate constants* (k_{cat}) for some enzymes. These values indicate how fast an enzyme can catalyze a particular reaction. The studies revealed an initially surprising result: Enzymes of animals with warm bodies, such as mammals, have relatively inefficient (low k_{cat}) enzymes, whereas cold-bodied animals have faster (high k_{cat}) enzymes. As with membranes, there appears to be a trade-off between the flexibility needed for fast catalysis and the thermostability needed to resist heat.

One particular enzyme, **lactate dehydrogenase (LDH)**, has been analyzed in some detail. LDH is the final enzyme of anaerobic glycolysis, catalyzing the conversion of pyruvate and NADH to lactate and NAD^+ (p. 55), and its action is paramount to survival in anaerobic burst activity, such as pouncing on food or escaping a predator. As shown in Figure 15-9b, k_{cat} of LDHs is inversely related to an animal's average body temperature. In its tertiary structure LDH has

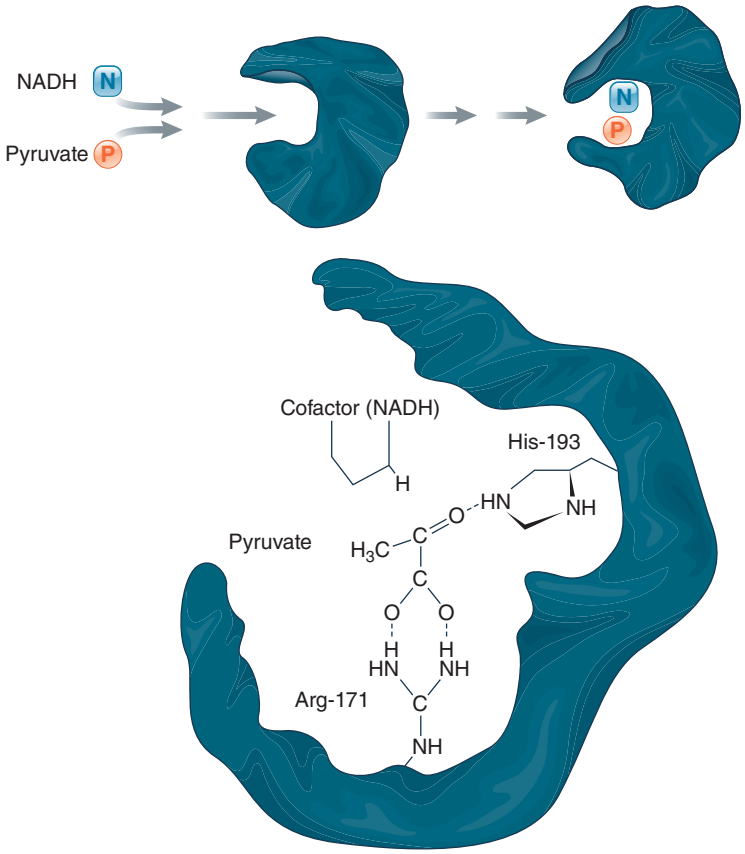


FIGURE 15-10 Schematic diagram of the enzyme lactate dehydrogenase (LDH), which binds NADH and pyruvate and catalyzes their conversion into NAD^+ and lactate. The *upper* diagram shows the conformational changes that occur upon binding, as a flexible loop of the enzyme closes over the active site. The flexibility of this loop evolves to match a species' thermal habitat (greater flexibility in the cold). The *lower* diagram shows the active site itself and the amino acids (Histidine-193 and Arginine-171) that bind pyruvate. The binding ability of the histidine may be protected from thermal disturbances by an animal decreasing its fluid pH with rising temperature (see main text, p. 738).

Source: P. W. Hochachka & G. N. Somero. (2002). *Biochemical Adaptation.* Oxford, UK: Oxford University Press; as modified from P. A. Fields & and G. N. Somero. (1998). Hot spots in cold adaptation: Localized increases in conformational flexibility in lactate dehydrogenases A_4 orthologs of Antarctic notothenioid fishes. *Proceedings of the National Academy of Sciences USA* 95:11476–11481.

a flexible loop, which opens and closes during its reaction (Figure 15-10). Warm-adapted LDHs have relatively stiff loops, rigid enough to resist denaturation at higher temperatures. But they are too inflexible to work at cold temperatures. Conversely, cold-adapted LDHs have relatively loose loops, able to open and close well in the cold. But they lose their structure more easily at higher temperatures.

Such differences in thermostability may evolve fairly straightforwardly, as revealed in recent studies on malate dehydrogenases (MDH, an enzyme of the citric-acid cycle, p. 50) in intertidal limpets of the western United States. Yunwei Dong and George Somero compared MDHs from *Lottia digitalis* of northern habitats and its close relative *L. austrodigitalis* of southern habitats. The MDH from the southern *L. austrodigitalis* is considerably more thermostable and can bind substrate more effectively at higher temperatures than the MDH of *L. digitalis* (northern). The differences are the result just one amino acid substitution. In the active site, MDH of *L. austrodigitalis* has a serine where *L. digitalis* MDH has a glycine. Importantly, serine allows for additional hydrogen bonding, improving binding at higher temperatures. Knowing such differences in thermal adaptation are critical to understanding the effects of global warming on species' distribution and survival.

The thermal adaptation strategies of animals depend on their primary source of heat

Let's now turn to the ways in which animals cope with environmental temperature changes that threaten their biomolecules. Recall that physiologists generally classify animals into two broad categories: **ectotherms** (*ecto,* "external")—those dependent on external sources for body heat—and **endotherms** (*endo,* "internal")—those more dependent on internal sources. Physiologists still frequently use a pair of older terms: **poikilotherms** (*poikilos,* "changeable")—animals whose body temperatures vary with the environment—and **homeotherms**—animals with narrowly varying body temperatures (recall that *homeo* means "similar," not "constant"). These terms often lead to confusion. Because we humans are mammals (endotherms) with fairly constant body temperatures (homeotherms), some people mistakenly believe the two terms are synonymous. But they are not, as we show in detail later. For now, consider an ectothermic lizard that can use sun and shade to keep its body temperature fairly constant (that is, it is homeothermic some of the time). Also consider a hibernating endotherm such as a marmot (p. 725): It is not homeothermic when considered on an annual basis. Rather it is an example of a **heterotherm,** an animal that has endothermy but is not fully homeothermic.

Note that there is no clear dividing line between a heterotherm and a homeotherm. For example, a camel in the desert absorbs a large heat load during the day, increasing its body temperature by several degrees (for example, from as low as 34°C to as high as 41°C) to avoid losing water by evaporative cooling. At night, it releases the heat and its body temperature drops. Does this level of change constitute homeothermy, or heterothermy? Some physiologists suggest that homeothermy be defined as internal temperature variations of no more than plus or minus 2°C, but in some ways the definitions do not matter. Rather, it is important to realize that there is a continuum of temperature regulation ranges and abilities, and that no endotherm has an absolutely constant internal temperature (hence the prefix *homeo* for "similar" rather than *homo* for "same"). Even your body temperature drops when you sleep and increases with heavy exercise and fever.

The internal body temperatures of both ectotherms and endotherms depend simply on the difference between heat input and heat output (Figure 15-11). *Heat input* occurs by gain from the external environment (which dominates in ectotherms) and from internal heat production (the most important source for endotherms). Conversely, *heat output* occurs by way of heat loss from exposed body surfaces to the external environment (in both ectotherms and endotherms). Let's first examine the inputs and outputs involving the environment.

Heat exchange between the body and the environment takes place by radiation, conduction, convection, and evaporation

Endotherms as well as ectotherms are influenced by heat exchanges with their environments, so it is important to understand how such exchanges occur. All heat loss or heat gain between the body and the external environment must take place between the body surface and its surroundings. The same physical laws of nature that govern heat transfer between inanimate objects also control the transfer of heat between the body surface and the environment. The temperature of an object may be thought of as a measure of the concentration of heat within the object. Accordingly, heat always moves down its "concentration" gradient, that is, down a **thermal gradient** from a warmer to a cooler region.

Organisms are subject to, and make use of, four mechanisms of heat transfer: *radiation, conduction, convection,* and *evaporation.*

1. **Radiation** refers to light energy, which exists as electromagnetic waves (and photons) that travel through space (Figure 15-12, step 1). Objects can both emit (source of heat loss) and absorb (source of heat gain) radiant energy. Heat is emitted from all objects (if not at absolute zero, –273°C) in the form of **infrared radiation** (wavelengths longer than red light). In the reverse direction, when radiant energy (especially infrared, but also visible light) strikes an object and is absorbed, the energy of the wave motion is transformed into heat within the object (manifested as increased vibrational energy within molecules). Whether a body loses or gains heat by radiation depends on the difference in temperature between the skin surface and the surfaces of various other objects in the body's environment, and on the amount of direct sunlight striking the skin. Because net transfer of heat by radiation is always from warmer objects to cooler ones, a body gains heat by radiation from objects warmer than the skin surface, such as the sun, rocks, or soil in the sun, or burning wood. In contrast, an animal loses heat by radiation to objects in its environment whose surfaces are cooler than the surface of the skin, such as trees, soil in the shade, and so forth.
2. **Conduction** is the transfer of heat between objects of differing temperatures that are in direct contact with each other (Figure 15-12, step 2). Heat moves down its thermal gradient from the warmer to the cooler object by being transferred from molecule to molecule. Except at absolute zero, all molecules are constantly vibrating, with warmer molecules moving faster than cooler ones. When molecules of differing heat content touch each other, the faster-moving, warmer molecule agitates the cooler molecule into more rapid motion, "warming up" the cooler molecule. During this process, the original warmer molecule loses some of its thermal energy as it slows down and cools off a bit. Therefore, given enough time, the temperature of the two touching objects eventually equalizes. The rate of heat transfer by conduction depends on the *temperature difference* between the touching objects and the *thermal conductivity* of the substances involved (that is, how easily heat is conducted by the molecules of the substances).

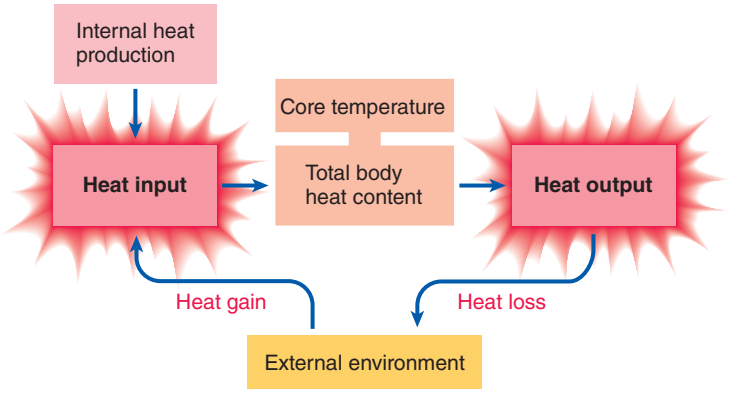
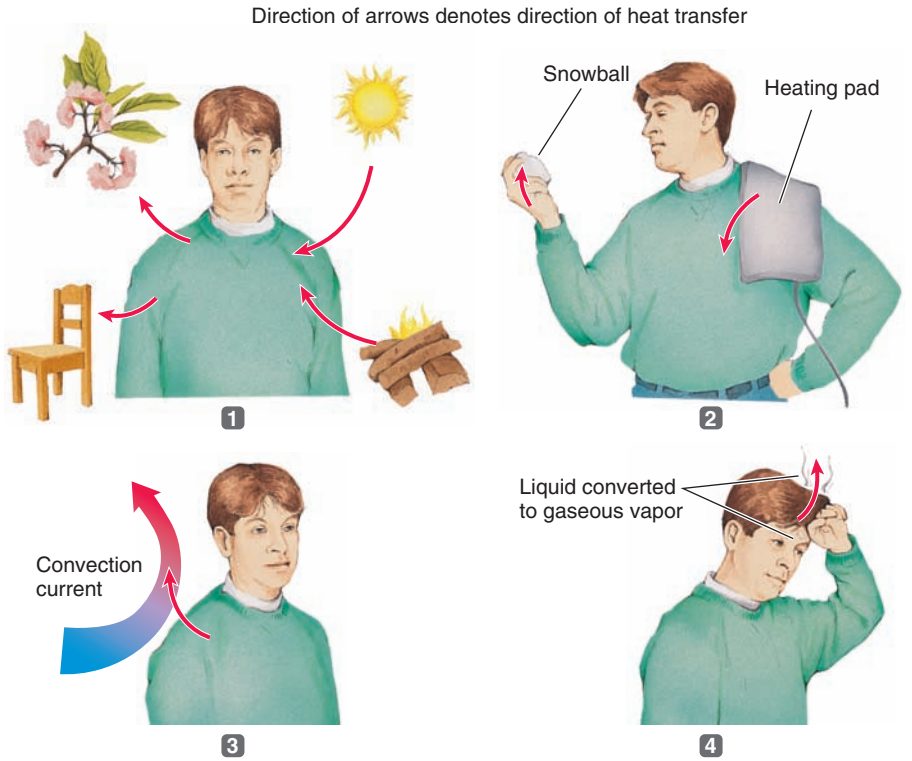


FIGURE 15-11 **Heat input and output.**

Heat can be lost or gained by conduction when the skin is in contact with a good conductor. When standing on snow, for example, an animal's foot becomes cold because heat conducts from the foot to the snow. Conversely, when an animal sits on a rock warmed by the sun, heat is transferred directly from the rock to its body. Similarly, bodies lose or gain heat by conduction to the layer of air in direct contact with the body. Only a small percentage of total heat exchange between the skin and air takes place by conduction alone because air is not a very good conductor of heat. Heat is conducted much more rapidly between a body surface and water, a better conductor than air.

3. **Convection** refers to the transfer of heat energy by *currents* of air or water (the medium). Let's follow an example for air next to skin, air that is warming from body heat. Because warm air is lighter (less dense) than cool air, the warmed air rises, and cooler air moves in next to the skin to replace the vacating warm air. The process is then repeated (Figure 15-12, step 3). Such movements in the external medium, known as *convection currents,* can carry heat away from a body. If it were not for convection currents, no further heat could be dissipated from the skin by conduction once the temperature of the layer of the medium immediately around the body equilibrated with skin temperature. The combined conduction–convection process of removing heat from a body is enhanced by forced movement of the medium across the body surface, either by external movements, such as those caused by wind and water currents, or by movement of the body through the medium, such as during locomotion.
4. **Evaporation** is the final method of heat transfer used by a body, but only in air. When water evaporates from the skin surface, such as that of a frog in air, the heat required to transform water from a liquid to a gaseous state is absorbed from the skin, thereby cooling the animal (Figure 15-12, step 4). Evaporative heat loss can occur from the linings of the respiratory airways as well as from the skin (*cutaneous* loss). Evaporation is particularly important for regulation if the air temperature rises above the temperature of skin. In that situation, the temperature gradient reverses itself so that heat is gained from the environment. Evaporation is the only means of heat loss under these conditions, and the pro-



1 **Radiation**—the transfer of heat energy from a warmer object to a cooler object in the form of electromagnetic waves ("heat waves"), which travel through space.

2 **Conduction**—the transfer of heat from a warmer to a cooler object that is in direct contact with the warmer one. The heat is transferred through the movement of thermal energy from molecule to adjacent molecule.

3 **Convection**—the transfer of heat energy by air currents. Cool air warmed by the body through conduction rises and is replaced by more cool air. This process is enhanced by the forced movement of air across the body surface.

4 **Evaporation**—conversion of a liquid such as sweat into a gaseous vapor, a process that requires heat (the heat of vaporization), which is absorbed from the skin.

FIGURE 15-12 **Mechanisms of heat transfer.**

cess can be understood in terms of the fundamental entropy equation given earlier. Recall that

$$\Delta S_{net} = \Delta S_{surroundings} + \Delta S_{system}$$
$$>0 \text{ for spontaneous reactions}$$

Here the system is the water droplet on the skin, and the surroundings are the body being cooled. When the air is hotter than the body, and yet the latter is being cooled, the $\Delta S_{surroundings}$ is thermodynamically unfavorable because entropy is actually decreasing during cooling against a heat gradient. However, the unfavorable factor is more than "paid for" by a **change of state** in water. During evaporation, water molecules go from a moderately ordered liquid state to a highly disordered vapor state, giving an enormously favorable ΔS_{system}. Essentially, the heat energy of the body is absorbed in the breaking of hydrogen bonds between water molecules as water vaporizes. This change of state, which is very effective, is exactly the process used in refrigerators and air conditioners, where liquid refrigerants vaporize in cooling coils, removing heat from the desired space. Energy in the form of a compressor motor must be used to reliquefy the refrigerant, recycling this costly resource, whereas in organisms, the cooling fluid—water—is lost and must be replaced.

Evaporation cannot succeed, however, if the air is saturated with water vapor, that is, at 100% relative humidity (RH). At that point, the rate of water vapor reforming hydrogen bonds and thus condensing into liquid is equal to the reverse process. *If the air is hotter than an animal's body at 100% RH, then there is no physiological means for cooling off.* Animals must allow their body temperatures to rise or must use behavioral mechanisms to avoid the situation.

Evaporation often occurs in a maladaptive way, that is, not for thermoregulation. A frog in a warm, dry area is in danger of dying from dehydration because it cannot stop cutaneous water loss. Inadvertent respiratory losses of water can also be dangerous; for example, exercising in cold, dry winter air can cause serious dehydration in humans.

Heat gain versus heat loss determines core body temperature, with mechanisms to gain external heat, retain internal heat, generate more internal heat, and lose excess heat

From a thermoregulatory viewpoint, an animal body may conveniently be viewed as a *central core* surrounded by an *outer shell*. The temperature within the inner core, which in a vertebrate consists of the abdominal and thoracic organs, the central nervous system, and the skeletal muscles, is the subject of regulation in animals that can thermoregulate, ectotherm and endotherm alike. That is, this internal **core temperature** remains fairly constant in homeotherms and may also vary less than environmental temperature in poikilotherms. The skin and subcutaneous fat constitute the outer shell. Temperatures within the shell may vary considerably more than in the core and are most often cooler than the core in endotherms.

The core temperature is a result of the difference between heat input and heat output (Figure 15-11). The means by which heat gains and heat losses can be balanced to regulate core body temperature generally fall into four broad

categories—in short, *gain, retain, generate,* and *lose* heat:

- *Gain external heat/avoid loss to cold environs* by using solar radiation, conduction from a warm surface or other source of environmental heat, and by avoiding cold areas. The heat gains are **ectothermic sources,** made use of primarily through specific thermoregulatory *behaviors* (such as solar basking), aided by *anatomic* features such as dark surfaces to absorb solar radiation effectively.
- *Retain internal heat.* Because of entropy, all metabolism produces some heat. This and any externally gained heat can be retained using *behavior* (such as entering an insulated burrow), *insulation* (such as hair), *reduced blood flow* to the integument to reduce losses, *countercurrent exchangers* in circulation that retain core heat, and *larger body sizes*. All these reduce heat loss via conduction, radiation, and sometimes convection and evaporation.
- *Generate more internal heat.* This is the definitive feature of **endothermy,** requiring significant heat-generating tissues.
- *Lose excess internal heat/avoid gains from hot environs* by *behavior* (such as seeking shade), *anatomy* (such as reflective white layers on the shell of an intertidal snail, and long, thin legs of desert insects which hold their bodies well above the hot ground), enhancing transfer via the integument through *increased blood flow,* and increasing *evaporation* (panting, sweating, cutaneous loss).

This list is only a brief overview; we now turn to the details for ectotherms.

check your understanding 15.4

Describe the basic effects of temperature on biological systems.

Discuss the evolutionary and functional aspects of homeoviscous adaptations of membranes and stability versus flexibility of proteins.

Define *endothermy, ectothermy, poikilothermy,* and *homeothermy.*

Discuss the features of the four heat transfer mechanisms: radiation, conduction, convection, and evaporation.

Discuss body heat balance and key features of "gain, retain, generate, and lose heat."

15.5 Ectothermy

Body temperatures of ectotherms may follow the environment, or may be regulated by heat gains, retention, and losses

What happens to an ectotherm when the environmental temperature is not near the optimum for its molecular structures? There are two broad categories of response: *poikilothermy* and *ectothermic regulation.*

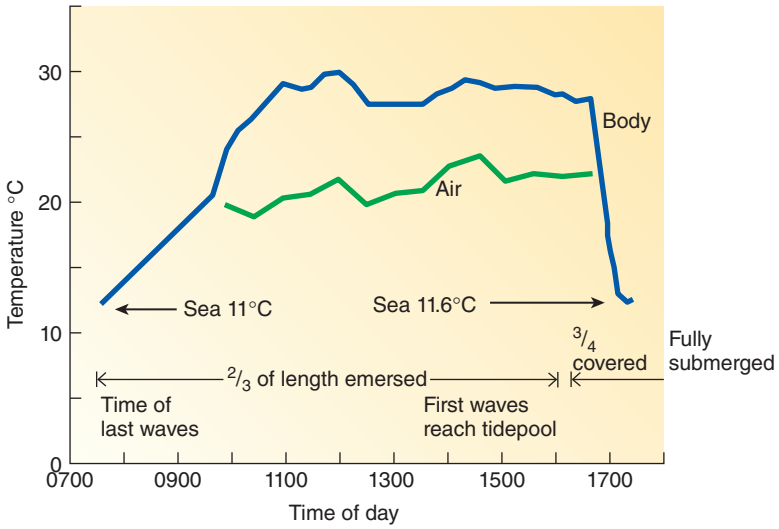


FIGURE 15-13 The body temperature of an intertidal mussel (*Mytilus californianus*) when the tide is out. The temperature is measured with a thermistor inserted inside the shell (*blue* line). As the tide goes out, the body temperature soars more than the air temperature (*green* line). Upon reemersion, the temperature drops rapidly.

Source: Modified from T. Carefoot. (1977). *Pacific Seashores.* Seattle, WA: University of Washington Press by arrangement with J. J. Douglas, Vancouver Canada. p. 68, Figure 67.

Poikilothermy Poikilothermic ectotherms that live in thermally variable environments undergo variations in body temperatures as well. Metabolic rates in such animals typically decrease in the cold (thus saving energy) and speed up as the environment warms (thus becoming better able to obtain food, up to a point). Survival may depend on using behavior to avoid extreme temperatures and/or limited physiological heat-loss mechanisms such as evaporation. If extreme temperatures cannot be avoided, poikilotherms may enter dormancy during the extremes or compensate through changes in internal biochemical optima (as you will see later). Some poikilotherms have body temperatures essentially identical to that of the environment—especially aquatic animals, because of the high heat conductivity and specific heat of water. These animals are sometimes called pure *thermoconformers.* But some have body temperatures that, although not nearly constant, vary less than the environment. This is particularly true of many ectotherms in terrestrial habitats because air transfers heat much less effectively than water.

Most life on this planet is poikilothermic. An extreme example is given in Figure 15-13, showing a mussel on an intertidal rock on the West Coast of North America. When the tide is in, its body temperature will be the same as the ocean, which is usually cold (about 11°C in this case). When the tide is out on a hot summer day, the mussel's body temperature soars and may reach 30°C or more. Some evaporative cooling may keep its temperature lower than it would be otherwise, but nevertheless it undergoes a large change in internal temperature.

Ectothermic Regulation An ectotherm in a constant environment, such as the cold deep sea or some polar ocean regions, is even more homeothermic (almost "homothermic") than any mammal. However, these animals typically cannot cope with any significant temperature changes. For example,

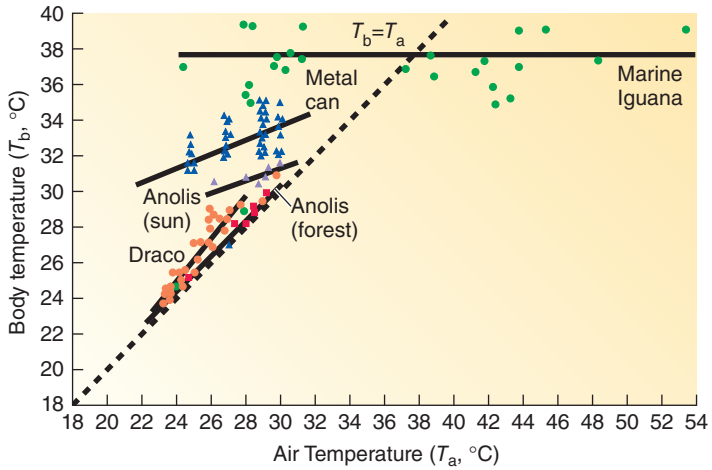


FIGURE 15-14 Relationship between body temperature and air temperature for lizards. The dotted black line is the relationship for pure poikilothermy (equal body [T_b] and air [T_a] temperature). Thermoconforming lizards *Draco* and *Anolis* in shaded forest habitat show a similar pattern (*red squares, orange circles,* respectively), while thermoregulating lizards marine iguana and *Anolis* in open sun have flatter lines (*green circles, purples triangles,* respectively). Also shown is the relationship for a water-filled metal can in the sun (*blue triangles*).

Source: From P. C. Withers. (1992). *Comparative Animal Physiology*. Fort Worth, TX: Saunders, p. 140, Figure 5-13.

Antarctic fishes can suffer heat-associated mortality at 5°C! Of more interest are ectotherms that actively use external heat exchanges to maintain their body temperatures at or near an optimum. Well-studied examples include lizards and butterflies (see opening photograph of this chapter). Let's examine the four strategies of heat regulation in a lizard to illustrate (see Figure 15-14):

- *Gain external heat/avoid loss to cold environs*. On cold mornings, the lizard basks in sunlight, soaking up infrared radiation and heat via conduction from warmed surfaces. (It also basks for the purpose of vitamin D production; see p. 329.) Once warmed up to an optimal level, it becomes active, seeking food while using both behavioral and physiological mechanisms to maintain a consistent body temperature.
- *Retain internal heat*. The lizard may *vasoconstrict* blood vessels going to its skin to reduce heat loss. In very large ectotherms, a phenomenon called **gigantothermy** may occur, in which an animal like a large turtle may absorb heat and then easily retain it for some time in a cooler environment due to their comparatively low surface-area-to-volume ratio.
- *Generate more internal heat*. This does not occur significantly in pure ectotherms. However, some very large (varanid) lizards, such as the Komodo dragon, warm up temporarily from high locomotory activity, retaining heat again because of their low surface area to volume ratio.
- *Lose excess internal heat/avoid gains from hot environs*. Blood vessels in the lizard's skin may dilate to increase heat loss. Evaporation from the mouth also provides cooling (one lizard, the Gila monster of southwestern United States, evaporates water from its cloaca rather than its mouth). When it gets too hot, the animal seeks shade. As another example, Sylvain Pincebourde and colleagues have recently shown that the intertidal ochre seastar (*Pisaster ochraceus* of the North American Pacific Northwest), instead of being a strict poikilotherm as long thought, can pump cold seawater into its coelom to lower its body temperature when overheating due to exposure to the sun at low tide. In order for certain animals to go outdoors during the colder winter temperatures, some zoos heat up the animal during the night so that they have sufficient heat to radiate during the daylight hours.

Using such mechanisms, some ectotherms can regulate body temperature as effectively as a mammal can, at least for some periods.

On a seasonal basis, some ectotherms can *migrate* to help minimize changes in body temperature. The monarch butterfly (p. 14), for example, spends summers in northern North America (such as Alaska and Canada) but joins a massive migration in the autumn to specific southern sites in California and Mexico for the winter months (as you will see later, such migrations are being altered by global warming). Some migratory fishes have similar behaviors; for example, the dogfish shark of the western Atlantic migrates between Florida in the winter and Maine in the summer.

Although these two categories of poikilothermy and ectothermic regulation are convenient, it is important to note that there is no distinct boundary between them. All ectothermic regulators that live in thermally variable habitats are also poikilotherms part of the time. For example, when there is no sun, warm burrow, or other heat source, a lizard cannot regulate its body temperature. At night, it usually cools off to approximately the air temperature. During this period, it is purely poikilothermic.

Some ectotherms can compensate biochemically for changes in body temperatures

Ectotherms in many habitats are subject to temperature changes that impair metabolism because they cannot behaviorally or physiologically adjust body temperature. The onset of winter and of summer are the most common examples. When it is too cold, a poikilotherm's metabolism may slow down to the point that it cannot obtain any food. Freezing may also kill it. If it is too hot, its membranes, proteins, and nucleic acids may suffer irreversible damage. To avoid problems, many poikilotherms undergo adaptive physiological or biochemical changes when exposed to temperature changes. Some of these changes occur on a daily basis, whereas others are seasonally induced. Some involve dormancy, whereas other changes allow for continued activity even with no mechanism for regulating body temperature.

In some cases, acclimatization to temperature changes allows an animal to maintain a useful level activity in a process called **metabolic compensation.** In this form of homeostasis, an animal's metabolic reactions in cold temperatures are increased to a level that is closer to that of warm-acclimated animals *even though their body temperatures are that of the environment's*. The reverse occurs with warm acclimatization. How is metabolic compensation achieved? In many cases, the mechanisms are not known, but several have been revealed in various animals, all involving specific biochemical changes:

1. *Enzyme concentration changes.* In cold acclimation and acclimatization (see definitions, p. 17), many ectotherms such as some fishes, frogs, and reptiles will increase their levels of metabolic enzymes, particularly those involved in aerobic pathways. An example is shown in Figure 15-15 for alligators, comparing animals acclimatized to winter and summer seasons. This particular study examined the activity levels of key enzymes in muscle tissue. Note that for LDH (structure in Figure 15-10), measured in the laboratory at 15, 22.5, and 30°C, the winter-acclimated animals have considerably higher enzyme activities at all measurement temperatures. This biochemical adjustment allows the cold-acclimated alligator to move better in the cold. Note also that the LDH level of the winter animals at 15°C is about the same as the level of the summer animals at 30°C, so this is a form of homeostasis. However, a cold-acclimated alligator will die of heat-related problems at warm temperatures at which the warm-acclimated animals will thrive. Thus, there appears to be a trade-off between metabolic rate and heat tolerance. Moreover, it takes energy to produce more enzymes, and because energy input is usually reduced in the cold, this strategy has limits.
2. *Homeoviscous membrane adaptation.* As we discussed previously, restructuring of membranes to maintain proper fluidity is a common strategy. The common carp, for example, uses this adaptation.
3. *pH regulation.* Most ectotherms in the cold have higher internal pH values than do warmer animals; that is, warmer animals are more acidic. To some extent, pH changes with temperature automatically because the neutral pH of water and the acid constants (pK_a) of protein buffers (p. 641) decrease with heating and increase with cooling. However, some buffer systems such as phosphate and bicarbonate do not have this property, so apparently animals must actively regulate pH to some extent. The primary hypothesis to explain this observation focuses on the amino acid *histidine*. Of the 20 amino acids used to build proteins, histidine is the most important in acting as a buffer (p. 641), because its pK_a is close to physiological pH, so it is nearly ideal for releasing or binding hydrogen ions over the normal physiological pH range. Binding and release of hydrogen ions by histidines are also crucial in many enzyme active sites for catalyzing reactions, as seen in LDH in Figure 15-10, where histidine with a bound H^+ binds to pyruvate, then donates that H^+ to pyruvate. Importantly, histidine's affinity for H^+ decreases with increasing temperature, so it binds H^+ too weakly to serve effectively as a buffer or catalyst if fluid pH is constant:

$$\text{Histidine} - H^+ \underset{\text{colder}}{\overset{\text{warmer}}{\rightleftharpoons}} \text{histidine} + H^+$$

Indeed, studies on LDHs from a variety of animals show that binding of pyruvate weakens greatly as temperature rises. The converse is also true: Binding becomes too tight in the cold. This problem can be offset if $[H^+]$ in body fluids is regulated. Take the case of increasing heat. If an animal regulates its body fluids to become more acidic, the higher $[H^+]$ via mass action increases the concentration of histidines in the charged form (histidine-H^+) to the level found at colder temperatures, and so restores binding affinity.

4. *Isoform regulation.* A final strategy requires that different forms of the same protein—called *isoforms*—be used at different temperatures. That is, there may be a set of winter proteins and another set of summer proteins, with the genes for these being activated only under appropriate environmental conditions. For example, the common carp expresses distinctly different forms of its myosin and myosin light-chain protein (MLC) in the summer and in the winter. Myosin is the main contractile protein of muscle (p. 337), whereas MLC binds to myosin and modifies its activity. Together, the isoforms expressed in the cold give the fish greater speed and force in the cold. However, the cold-adapted muscle then does not work well at higher temperatures.

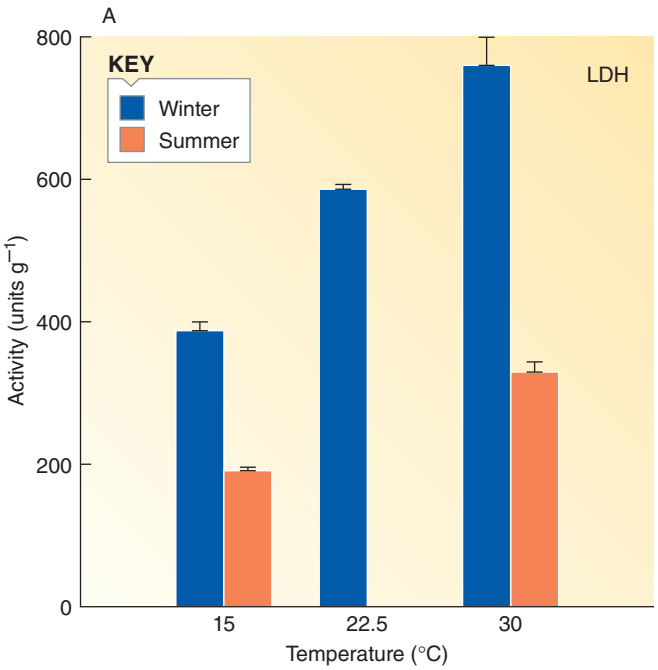


FIGURE 15-15 Activity of lactate dehydrogenase in muscle from alligators acclimatized to winter and summer conditions. Activity increases in the winter to make up for lower thermal energy. The *x*-axis indicates temperatures at which the activities were measured in the laboratory.

Source: From F. Seebacher, H. Guderley, R. M. Elsey, & P. L. Trosclair III. (2003). Seasonal acclimatization of muscle metabolic enzymes in a reptile (*Alligator mississippiensis*). *Journal of Experimental Biology* 206:1193–1200.

Isoform regulation appears to be uncommon, and many of the mechanisms of metabolic compensation are still unknown. Currently, DNA microarrays (p. 35) are being used to look for major changes in gene expression that occur during acclimation. A study by Andrew Gracey and colleagues of the common carp, which acclimatizes annually to winter temperatures, found that about 252 genes (out of 13,400 measured on a microarray) exhibit significantly upregulated expression in all tissues during cold exposure. The genes are involved in RNA processing and translation, mitochondrial metabolism, proteasome function, and restructuring of lipid membranes. Such studies are revealing previously unsuspected mechanisms of temperature acclimatization.

Ectotherms survive extreme cold by metabolic dormancy and by either freeze avoidance or freeze tolerance

Ectotherms generally cannot stay active in extreme cold. Many can survive low temperatures by dramatically lowering their metabolic rates, thereby reducing the rate at which ATP is consumed. Although they may be technically starving, they have sufficient reserves to survive the season. Frequently, metabolic rate can be reduced to as low as 1 to 10% of the normal resting rate: A 10-fold reduction in energy expenditure gains the animal a 10-fold extension of the time that fuel reserves will last. For example, in the Crucian carp the glycogen level that supports brain function for 16 hours in the anoxic winter ponds when energy demand is low, would support the fish for only eight minutes in the summer with the same amount of oxygen. Some species of insects completely arrest their development in a state of *diapause*. Turtles hibernate at depths below the frost line along the banks of streams and at the bottom of ponds. These reptiles survive the entire winter without breathing (p. 641) and with a heart rate of only one beat per minute.

Special adaptations are needed for ectothermic animals whose body temperatures drop below freezing. There are two broad categories of these adaptations: *freeze tolerance* and *freeze avoidance*.

Freeze Tolerance Some ectotherms actually survive freezing of some body fluids (with up to 80% of body water being frozen in such animals). Woolly bear caterpillars spend up to 10 months frozen in the high Arctic, barnacles and mussels freeze when exposed to subfreezing temperatures at low tide, and even some reptiles and amphibians freeze for variable periods of time. For example, spring peeper frogs (*Pseudacris crucifer*) and wood frogs (*Rana sylvatica*) can revive after having as much as 65% of body water converted to ice. During the frozen state, ATP use virtually ceases and neurological activity is minimally detectable. Energy needs of a tissue are normally supplied by nutrients delivered by the circulatory system. However, in a thawing animal the tissues are completely reliant on immediately available energy sources.

What happens to the tissues that actually freeze? Consider a key problem of freezing—the osmotic stress placed on an animal cell as it enters the frozen state. Formation of ice crystals in the ECF (extracellular fluid) immediately changes the osmotic balance with the ICF (intracellular fluid). Because ice excludes solutes from its structure, during the freezing process the composition of the ECF becomes progressively more concentrated as the concentration of water declines. In response, water moves out of the cell. Only when the concentration of solute is great enough can the transformation of water into ice be retarded. The majority of freeze-tolerant animals reach the critical minimum cell volume when approximately 65% of the total body water is converted into the frozen state.

To understand how some animals survive the stresses of freezing on metabolism and cell volume, let's look at what happens to a peeper or wood frog, starting when it is initially exposed to freezing temperatures. When water freezes on the frog's outer skin, a signal sent to the liver triggers a massive breakdown of glycogen in the liver. Consequently, a flood of *glucose* molecules enters the circulatory system, raising blood sugar concentrations over 450-fold (over 10-fold greater than a diabetic human with moderately uncontrolled blood-sugar concentrations). This serves as an *antifreeze* by lowering the freezing point through simple colligative properties (p. 79). In less than eight hours, the frog's organs become loaded with this nutrient, which has now assumed an additional role as a **compatible cryoprotectant.** The cryoprotectant acts as an *osmolyte* (p. 617) to help keep the cells in osmotic balance with the increasing osmotic pressure in the ECF. Cryoprotectants must also be *compatible* with macromolecules (p. 617). Thus, inorganic ions cannot be used: They are just as effective in lowering freezing points by colligative mechanisms (and that is why humans dump salt on icy roads in many wintry locales), but unlike the compatible solutes such as glucose, they disrupt macromolecules. (Compatibility is the reason humans use small carbohydrates such as ethylene glycol rather than corrosion-promoting salts in automobile radiators.) Wood frogs, at least, also accumulate *urea,* which at modest levels appears to reduce freezing damage to cells and may also help suppress metabolism. In addition, during thawing—the time when cells have no delivery of oxygen—glucose is immediately available as a fuel to generate ATP. Studies have shown that a frozen frog ventricle regains its ability to contract if it is thawed in the presence of glucose but not in the presence of other cryoprotectants such as glycerol. Using this strategy, the frog is ready to resume its active life.

Other animals are also freeze tolerant. For example, Arctic earthworms accumulate glucose in the winter, which serves as both a cellular antifreeze and fuel source. Many insects employ similar mechanisms, often using other carbohydrates such as *trehalose* (p. 614) as compatible cryoprotectants and antifreezes. In addition, many of these animals actually enhance the freezing of their ECFs with **ice-nucleating agents,** small proteins that trigger the formation of small ice crystals. Apparently these agents ensure that ice only forms in the ECF and that ice forms in an ordered fashion rather than in the "normal" way, which would create large crystals that could rupture membranes.

Freeze Avoidance Most overwintering animals are considered intolerant of internal freezing yet may still have body temperatures well below the freezing point. Again, many such animals have antifreeze compounds, but they are used somewhat differently. First, some overwintering animals use compatible cryoprotectants such as sorbitol and glycerol, but throughout the ECF and ICF rather than just the latter. Thus, the ECF is also protected from freezing. Examples include many insects, arachnids, and some Arctic fishes such as the rainbow smelt. However, other insects and polar fishes have special **antifreeze proteins,** which do not work by classic colligative mechanisms. These proteins are effective at much lower concentrations than the compatible cryoprotectants. They generally contain very hydrophilic amino acids and sugar side chains that are thought to bind to growing ice crystals and thus prevent their growth.

In addition to, or instead of using antifreezes, some overwintering animals appear to use the phenomenon of **supercooling.** This is a state of water in which the temperature is well below the freezing point but there is no

trigger or nucleation site to begin ice formation. Some polar fishes and arachnids, such as the Antarctic mite, employ this strategy. Painted turtles (*Chrysemys picta,* common in wetlands across eastern North America) also supercool in the winter, as does at least one mammal, the Arctic ground squirrel (see p. 751). Supercooling is a dangerous strategy, however, because any encounter with external ice can trigger a catastrophically rapid crystallization of body fluids.

Finally, some polar animals such as the Arctic springtail (*Megaphorura arctica*) avoid freezing through *cryoprotective dehydration.* While supercooling, these small insects lose water from their bodies to the point that they cannot freeze. At the same time, they build up *trehalose,* the protective solute we described in Chapter 13 (p. 614) that builds up in many dehydrated organisms in nonfreezing situations.

Ectotherms may survive temporary extreme heat with the heat shock response

Finally, let's examine what ectotherms do when exposed to excess heat. Given enough time, ectotherms may evolve (over many generations) thermostable proteins and membranes. These adaptations appear to have a thermal limit in eukaryotes well below that for prokaryotes; see *Challenges and Controversies: What Is the Maximum Temperature for Life?*

But what happens in the short term? If an organism is exposed to a sudden jump of about 5°C or more in cell temperature, an ancient mechanism is induced: the *heat shock response*. This occurs in all types of organisms from archaea to humans, and involves the activation of genes for **heat shock proteins (HSPs),** also known as **stress proteins** because other stresses (such as osmotic and chemical shocks) can induce them as well. As shown in Figure 15-16a, these small, thermostable, hydrophobic proteins bind to larger, unfolded proteins and assist their folding into functional conformations. They are attracted to hydrophobic amino acids that are normally in the interior of folded proteins but become exposed on denaturation (unfolding). Some HSPs are always present in cells, where they assist in the folding of newly formed polypeptides coming off ribosomes (hence HSPs are also called *molecular chaperones*). But during heat shock, other HSPs are rapidly induced at the gene transcription level, protecting the cell from heat death. This occurs as follows: In an unstressed cell, there are small amounts of HSPs such as **hsp70,** the most common form (whose weight is about 70,000 daltons). The hsp70s are bound in an inactive state to a protein called **HSF-1** (heat-shock factor 1). Under a sudden heat stress, the hsp70s detach from HSF-1 and bind to and stabilize unfolded proteins. The release also activates HSF-1, which is a *transcription factor* (p. 31). When active, HSF-1 binds to two other HSF-1 proteins to form a trimer (protein complex made of three separate proteins). The trimer enters the nucleus and binds to a *response element* in the DNA (p. 31) called **HSE (heat shock element);** this action in turn activates the transcription of genes for heat shock proteins. (This mechanism of transcription factors and response elements is a typical process of gene regulation in eukaryotes, as we discussed in Chapter 2.)

As noted, HSPs have been found in all forms of life. Mammals, for example, make them during a fever. An example for a poikilotherm is shown in Figure 15-16b, focusing on hsp70. Two different species of limpets (*Collisella* spp.) live at different levels on a rocky intertidal habitat. The species that lives higher up—and thus is more exposed to excessive heat from the sun when the tide is out—has higher levels of hsp70 and can make more hsp70 than can species living lower in the intertidal zone.

Although HSPs are thought to be universal, heat shock induction can apparently be lost in some species over evolutionary time. Notothenid fishes, for example, appear to have no heat shock response whatsoever. These Antarctic fish live in a nearly constant temperature environment, about –2°C year-round. In the laboratory, they begin to die of heat stress at 5°C and above! Yet even at 12°C, they cannot make additional HSPs above the basal levels.

check your understanding 15.5

- Describe the different responses in pure poikilothermy and ectothermic regulation.
- Discuss the biochemical adjustments that account for metabolic compensation in ectotherms.
- Discuss the differences in freeze tolerance and avoidance, with examples.
- Discuss how heat shock proteins aid survival at extreme temperatures.

15.6 Endothermy and Homeothermy

Endothermy has several benefits. The ectotherm's problem of either finding external heat sources or suffering a slowing metabolism from cooling, can be avoided. Since endotherms usually have body temperatures warmer than their habitats, they have consistently faster biochemical processes than do most ectotherms in the same habitat. This can provide a competitive advantage**:** expansion of daily activity into nighttime, higher digestion rates, sustained locomotion, habitat expansion, and regulated incubation temperature. Moreover, some endotherms achieve homeothermy—a consistently warm body temperature that allows proteins and membranes to always be at their optima.

But there is a large metabolic cost: Endotherms must generate heat internally to raise body temperature and must do so continuously if they are homeothermic. Heat production ultimately depends on the oxidation of metabolic fuel derived from food, and thus endotherms consume much more energy (5 to 20 times) than do ectotherms of the same mass. Conversely, a high metabolism increases the risk of overheating. So endotherms must also have mechanisms to remove excess heat that are more effective than those of ectotherms. In light of these advantages and disadvantages, we still do not fully understand the evolution of endothermy (see *Unanswered Questions: How, when, and why did endothermy evolve?*).

Challenges and Controversies

What Is the Maximum Temperature for Life?

Although hydrothermal vents can reach 400°C, no life has been found that can tolerate anything close to that level. In 2003, the highest temperature for life yet recorded was demonstrated to be 130°C (266°F), achieved by a hydrothermal vent archaean. What about animals at the vents? A polychaete annelid, *Alvinella,* which lives at deep-sea hydrothermal vents, has been reported to live at temperatures as high as 80°C. However, many researchers believe the body temperature measurements were flawed (they are difficult to make using a submersible vehicle on an animal that retreats inside a small hard calcium-carbonate tube). Nevertheless, one worm wrapped around the submersible's temperature probe reportedly survived a brief exposure to 105˚C! In the laboratory, however, *Alvinella*'s proteins do not work above about the 40 to 45°C range and its collagen (a major connective-tissue protein; p. 65) is stable up to 65°C, suggesting the field data are misleading. In work on a related species, *Paralvinella sulfincola,* Peter Girguis and Raymond Lee placed worms in high-pressure chambers with a regulated temperature gradient ranging from 20°C at one end to 61°C at the other. When kept at their natural habitat pressure, the worms crawled about and settled around the area at 50°C, where they appeared to behave normally. In other experiments, Lee and Christian Rinke found that some individuals could survive short periods at 60°C, and that the species has key enzymes stable up to 50 to 60°C.

On land, two animals rival the vent worm. Saharan desert ants (*Cataglyphis*) and Namibian desert pseudoscorpions (*Eremogarypus perfectus*) have been found to tolerate 55°C body temperatures for a few minutes, and the pseudoscorpion can tolerate up to 65˚C in the laboratory! The ant experiences 55˚C while running across hot sand to forage at midday. (This behavior gives them a competitive advantage because other animals are hiding in burrows to avoid the midday heat.) The ants survive in part by loading up on heat shock proteins before foraging. What actually sets the upper limit for these African ants, hydrothermal vent worms, arthropods, and other eukaryotes is not known, but it is suspected to be fundamental features of mitochondrial respiration and membrane stability, gene transcription, and/or translation that cannot be stabilized beyond a certain temperature.

Paul Yancey

Paralvinella sulfincola.

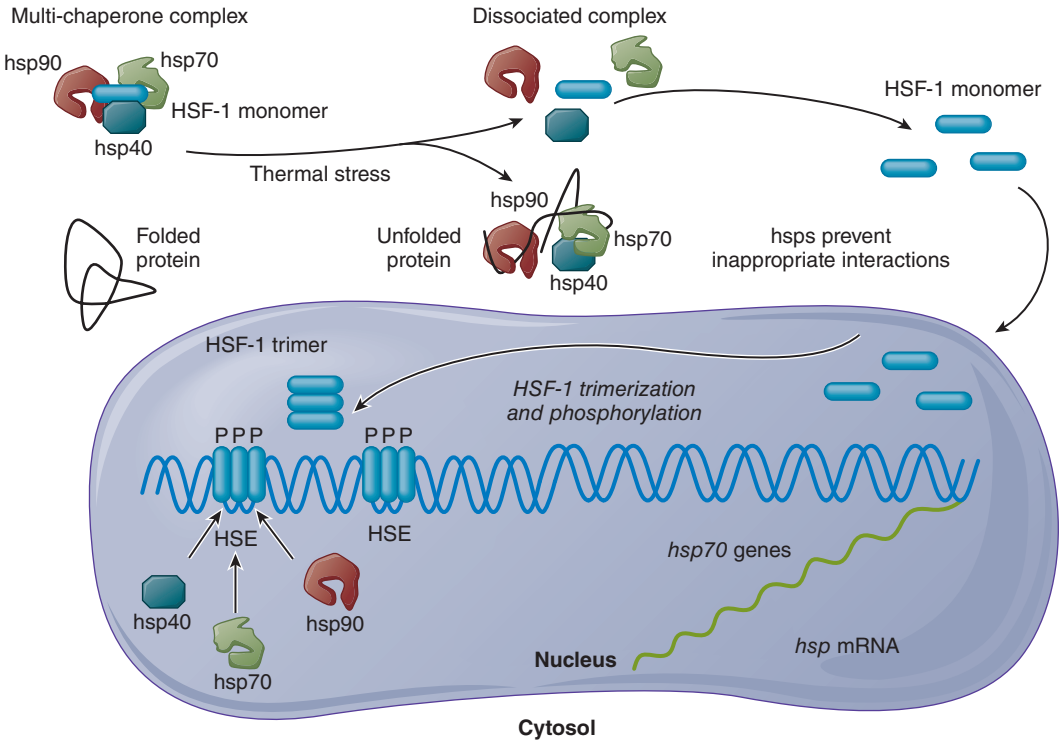
unanswered Questions | How, when, and why did endothermy evolve?

Despite the common view that endothermy and homeothermy have great advantages, scientists are not certain how, when, or even why they evolved. Consider the "when" question: While birds are endothermic, we are still not sure if their dinosaur ancestors were also. Because of their enormous sizes, some dinosaur species would have exhibited gigantothermy (p. 736) but not necessarily true endothermy. But what about smaller dinosaurs? Some fossil evidence suggests that at least some were endothermic—for example, some dinosaur bones have capillary densities similar to those of mammals and higher than in modern (non-avian) reptiles. Recent fossil discoveries of *theropod* dinosaurs (the direct ancestors of birds) have found remnants of feathers and birdlike air sacs (p. 513), consistent with endothermy, as are the birdlike bipedal stances of theropods like *Velociraptor.* Moreover, some fossil embryos and juveniles reveal a rapid growth rate as found in today's endotherms but not ectotherms. However, no dinosaur fossils show evidence of maxilloturbinals, the nasal heat exchangers (p. 745) found in living endotherms. Such exchangers do appear in the late Permian era in some fossils of therapsids, advanced reptiles that are the ancestors of mammals.

The "how" and "why" questions are also perplexing. In shivering mammals, flying insects, and swimming tunas, aerobic locomotory muscles are a major or sole source of extra heat. Thus, some biologists have proposed that enhanced aerobic locomotion evolved first and that only later was the heat output used for thermoregulation. Others propose the converse: that heat generation evolved first and that later benefited locomotory ability. Another hypothesis is that high body temperature initially arose because it greatly restricts infections by fungi. Yet other researchers suggest that the ability to keep embryos at an optimal developmental temperature was the first selective advantage of endothermy in land animals. Finally, the latest hypothesis is that endothermy began in herbivores. Eating plant matter yields a lot of carbon but very little nitrogen. Endothermy allows not only a way to eat more food to obtain that nitrogen but also the ability to "burn off" the excess carbon. Definitive evidence to distinguish among these competing ideas is still lacking. <<

Birds and mammals maintain a consistent internal core temperature (homeothermy)

Many organisms have evolved endothermy: birds, mammals, some fishes and non-avian reptiles, some insects, and even some plants! In all cases, these organisms rely on high levels of *aerobic metabolism* for sustainable heat production. High aerobic ability has another function: Most endotherms rely on aerobic metabolism for locomotion more than do ectotherms (with few exceptions) (see *Unanswered*



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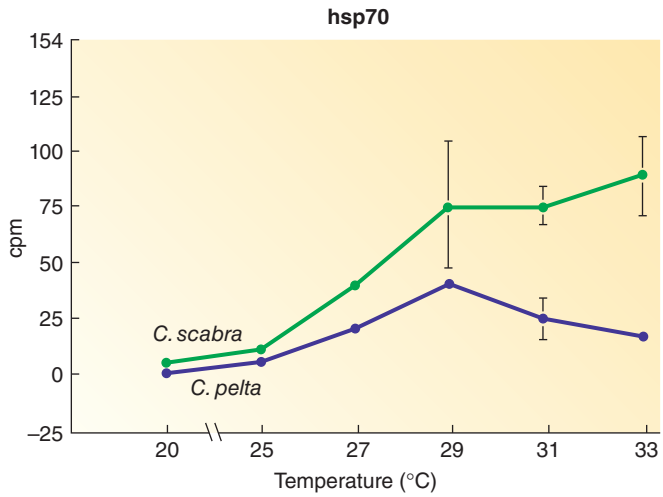

(b)

FIGURE 15-16 Role and regulation of heat shock proteins. (a) Model for regulation of hsp70, a major heat shock protein whose activity is activated by sudden temperature increases and other stresses. Under nonstress conditions, hsp70 (along with hsp40 and 90) is bound in an inactive state to heat-shock factor 1 (HSF-1) in the cytoplasm. Under temperature stress, this complex dissociates, and the hsp proteins bind to other, unfolded cell proteins, preventing aggregations and assisting in their refolding. The unbound HSF-1 moves to the nucleus, forms a trimer (three HSF-1 proteins), and binds to a promoter element in the DNA called the heat shock enhancer (HSE). This in turn activates the gene for hsp70, leading to synthesis of hsp70 mRNA and thus more hsp70 proteins to aid in the stress response. (b) *Collisella* limpets and their production of hsp70 at various temperatures. *C. scabra* lives higher in the rocky intertidal zone than *C. pelta,* and thus is exposed to higher temperatures more often. Hsp70 production is quantified by the incorporation of radioactive amino acids, determined by radioactive counts per minute (cpm).

Sources: (a) From Hochachka, P. W., and G. N. Somero, (2002), "Biochemical Adaptation", Oxford: Oxford University Press, Fig. 7.14, as modified from R. I. Morimoto and M. G. Santoro, (1998), Stress-inducible responses and heat shock proteins: New pharmacologic targets for cytoprotection, 'Nature Biotechnology', 16:833–838. Reproduced with permission of Nature Publishing Group via Copyright Clearance Center. (b) From B. M. Sanders, C. Hope, V. M. Pascoe, & L. S. Martin. (1991). Characterization of the stress protein response in two species of *Collisella* limpets with different temperature tolerances. *Physiological Zoology* 64:1471–1489.

Questions: How, when, and why did endothermy evolve?). Thus, a lizard (ectotherm) may have tremendous burst (anaerobic) capacity that allows it to outrun a mammal of the same size over short distances. However, in a long-distance chase the mammal's aerobic capacity allows it to outrun the lizard, which fatigues quickly.

Among all the different groups of endotherms, only birds and mammals exhibit homeothermy in all of their core organs. We consider these first. The other animals, which are more variable, are discussed later as *heterotherms.*

It is important to recognize that core body temperatures vary among species of birds and mammals (Table 15-3). Monotreme mammals (platypuses, echidnas), have lower set points than most placental mammals, which in turn have lower set points than most birds. Why these different set points have evolved is not clear. However, one consideration is that it is physiologically easier to warm up than to cool off. Heat is produced by metabolism (following the Second Law of Thermodynamics). But cooling off in an environment hotter than an animal's body requires evaporation of water—often a precious resource, and one that works poorly or not at all at high humidity (p. 735). Thus, it has been proposed that endotherms have evolved optima that are slightly above the average high environmental temperature of their ancestral habitats.

TABLE 15-3 Core Body Temperatures (T_b) Characteristic of Endothermic Vertebrates

Taxon	Common Names	T_b (°C)
Mammals		
Monotremes	Echidna, platypus	30
Edentates	Anteaters, etc.	33–34
Marsupials	Possums, kangaroos, etc.	36
Insectivores	Hedgehogs, moles, etc.	36
	Shrews	37–38
Chiropterans	Bats	37
Cetaceans	Whales, etc.	37–38
Pinnipeds	Seals, etc.	
Rodents	Mice, rats, etc.	
Perissodactyls	Tapir, rhinoceros, horses	
Primates	Monkeys, humans, etc.	38–39
Carnivora	Dogs, cats, etc.	
Artiodactyls	Cows, camels, pigs, etc.	
Lagomorphs	Rabbits	
Birds		
	Penguins	38
	Ostrich, petrels, etc.	39–40
	Pelicans, parrots, ducks, gamebirds	41–42
	Passerine songbirds	42

Source: Willmer, P., G. Stone and I. Johnston, (2000), "Environmental Physiology of Animals", p. 223, Table 8.11. Copyright © 2000 Blackwell Publishing. Reproduced with permission of Blackwell Publishing Ltd.

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A roadrunner ruffles it feathers to expose its dark skin, which absorbs sunlight to help heat the animal's blood.

Body temperatures also vary among individuals, and vary throughout the day within individuals. For diurnal mammals (including humans), body temperatures typically fall 1 to 2° C at night in response to a biological clock (p. 276). (This is one reason why most humans feel particularly sluggish if awakened before dawn.) The camel, which we described earlier (p. 733), varies even more. Furthermore, there is no one body temperature, because temperature can vary from organ to organ, even in the core; for example, active skeletal muscles are warmer than most other organs.

To maintain a stable core temperature, heat gains must balance heat loss, with mechanisms to gain, retain, generate, and lose excess heat

To maintain a constant total heat content and thus a stable core temperature, an animal body must balance heat input and output (Figure 15-11). We now elaborate on the means by which birds and mammals can adjust heat gains and losses to regulate core body temperature. Recall that the mechanisms fall into broad categories of *gain, retain, generate,* and *lose* (p. 736).

Gaining External Heat/Avoiding Loss to Cold Environs Birds and mammals evolved from ectothermic ancestors and thus have inherited many of the thermoregulatory behaviors and physiology of ectotherms. These include the following:

1. *Ectothermic behavior.* A cold bird or mammal may seek out sunshine or a warm surface, whereas a warm endotherm avoids excessive environmental cold, just as a lizard does. Thus, basking behaviors (serving as effectors) are common in many birds and mammals, especially smaller ones with their high ratios of surface area to volume, and especially in cold weather. House cats, for example, are well known to bask in patches of sunlight. Larger mammals may also exhibit such behaviors: A human basking on the beach or soaking in a hot tub is behaving like a lizard! Long-distance migrations may also serve in part as a thermoregulatory adaptation. For example, one reason why humpback and gray whales migrate from polar feeding waters in the summer to tropical birthing areas in the winter may be to provide a warm habitat for newborns.
2. *Anatomic features such as dark skin that help absorb solar radiation.* Insulation, such as feathers, actually interferes with this absorption. For this reason hummingbirds and roadrunners, which undergo *torpor* (reduced metabolism and body temperatures, p. 750) at night and bask in the sun in the morning to warm up, erect the feathers of their upper backs. Unlike other skin (which is pink), their skin here is black, to more efficiently absorb the solar radiation.

Retaining Internal Heat Retaining internal heat is accomplished by several mechanisms. Some of these also occur in some ectotherms, but in general these mechanisms are more prominent in endotherms:

1. *Vasoconstriction.* The insulative capacity of skin can be varied by controlling the amount of blood flowing through it. Blood flow to the skin serves two functions. First, it provides a nutritive blood supply to the skin. Second, because blood has been heated in the central core, it carries this heat to the skin. But an animal

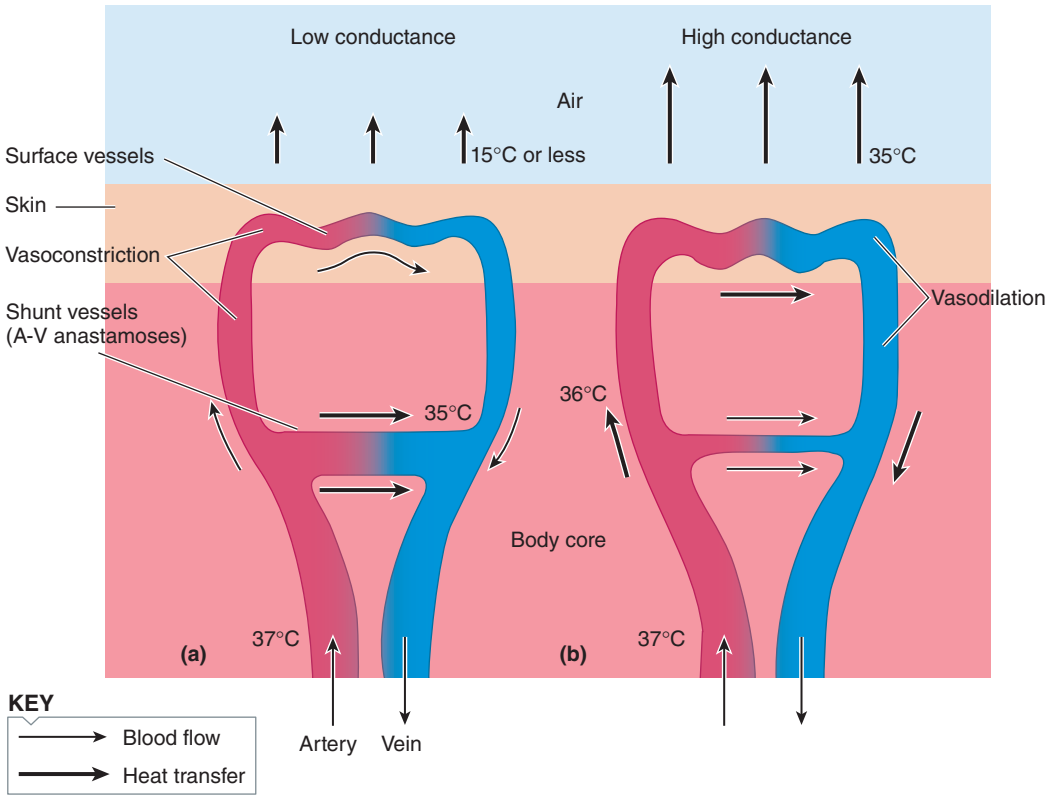


FIGURE 15-17 Changes in blood flow to the skin for thermoregulation. (a) In a cold environment, blood can be diverted through shunts (anastomoses) deep under the skin to reduce heat loss. (b) If body heat needs to be released to the environment, or if external heat needs to be absorbed from a warm environment, vessels just under the skin surface can be opened.

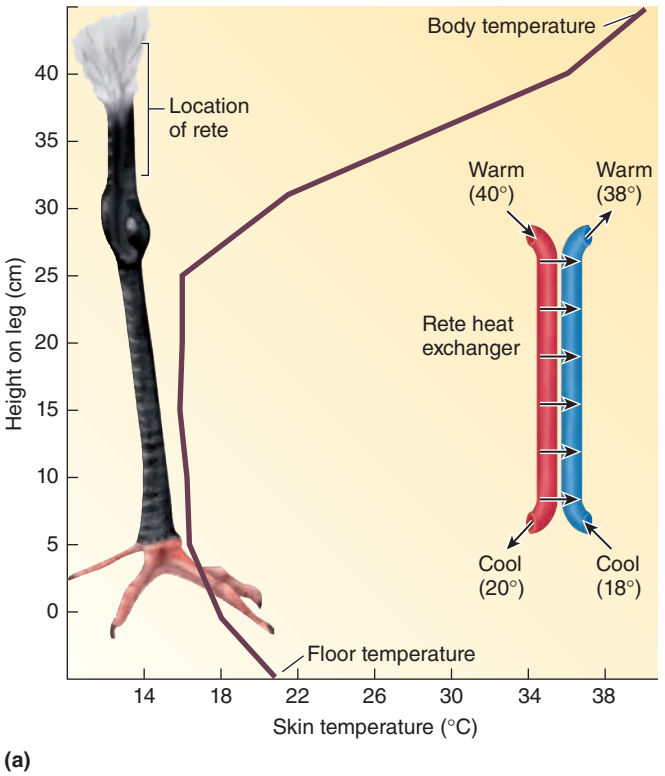
suffering excessive heat loss can vasoconstrict the skin vessels (Figure 15-17a). This reduces blood flow through the skin, decreasing heat loss by keeping the warm blood closer to the core and thus more insulated from the external environment. As you will see later, the hypothalamus regulates this blood flow in vertebrates. Some ectotherms, such as lizards, can use this process to some extent.

2. *Anatomic insulation.* Birds and mammals have evolved integumentary structures that help trap heat in their bodies. These *insulating* (low-heat-conducting) structures include feathers, hair, and subcutaneous adipose layers (including blubber). Such insulation may appear to be static anatomy, but there are some forms of regulation. Many mammals grow more hair and/or adipose tissue in the autumn. For example, the fur of white-tailed deer is thin in the summer and thick and long in the winter. Furthermore, the winter hairs are hollow, allowing them to trap heat inside the shaft. Birds such as goldfinches increase their feather masses up to 50% by wintertime. In animals with dense fur or feathers, contracting the tiny muscles at the base of the hair or feather shafts lifts the hair or feathers off the skin surface (the *piloerection* reflex, which humans retain vestigially). This puffing up traps a layer of poorly conductive air between the skin surface and the environment, increasing the insulating barrier between the core and the cold air and thus reducing heat loss.
3. *Behavioral insulation.* Additional insulation may result from behaviors such as nest building, postural changes, burrowing, and huddling. Certain postural changes, such as a cat curling up in a ball, reduce the exposed surface area from which heat can escape. Emperor penguins on the Antarctic ice often huddle in the thousands, a behavior estimated to save 25 to 50% energy. Another thermoregulatory behavior in many birds is perching on one leg, tucking the other leg against the body feathers (the leg is a major site of heat loss in birds.) Consider also the sea otter, which grooms its hair and coats it with an oily secretion to help trap a layer of insulating air.
4. *Larger body size in colder climates.* A trend in avian and mammalian species is the evolution of larger average body sizes (such as penguins) in cold-climate species compared to warm-climate relatives. This trend, known as *Bergman's rule*, is predictable based on the properties of ratios between surface area and volume that we discussed earlier (p. 720).
5. *Countercurrent exchangers.* Blood flow can be used to retain core heat in another way known as a **countercurrent exchanger,** found between the core body and many exposed peripheral organs that could lose heat rapidly. (Recall examples of countercurrent flow in fish gills, fish swimbladder systems, and mammalian nephrons.) The exchanger consists of a set of veins and arteries (or venules and arterioles) placed closely together in a dense array known as a **rete mirabile** (Figure 15-18a). Because the vessels are so closely packed, they are nearly in thermal equilibrium. Crucial to the rete's function is that blood flows in opposite directions (countercurrent) in the two types of vessels. Heat moves in the following way: Warm core blood moves out the arteries toward the cold peripheral tissue. In the rete, it encounters cold blood from that periphery. By conduction, the heat moves into

the cold vein and thus returns to the core. The venous blood leaving the rete is thus nearly at the temperature of the periphery so that little core heat is lost.

Retes are found in many endotherms and heterotherms (Figures 15-18b, c, and d). In mammals, they are often in the limbs, such as a dolphin's fluke and flippers. In birds, they are often in the legs to limit heat loss from the feet. You will see later how heterotherms such as tunas use retes.

A different type of countercurrent exchange is found in the nasal passages of birds and mammals. One drawback of endothermy is the potential for high water loss, and not just from thermoregulatory evaporation. Because the lungs must be kept moist for respiratory gases to dissolve into the cells lining the capillaries, lung air in endotherms is always warm and at 100% relative humidity. There is a danger of losing this body water and its heat content to the external environment. Instead, some of the moisture contained in the air from the lungs condenses onto the comparatively cool surface of the **maxilloturbinals** (folds in the nasal cavity; see p. 508), which can be very elaborate. For example, the camel's nose has an enormous surface area in these folds. The subsequent inhalation of drier air from the external environment evaporates this water and cools the surface of the maxilloturbinals in preparation for the next cycle. This type of countercurrent process is called a *temporal countercurrent exchanger*, where the opposing flows of a fluid are separated in time (using one tube) rather than in space (using two separate tubes). Mammals on average reclaim as much as 45% of the water (and its heat content) from the exhaled air, whereas kangaroo rats recycle up to 88% of their body water in this fashion. Birds also have such structures. However, ectothermic vertebrates, including non-avian reptiles, do not.



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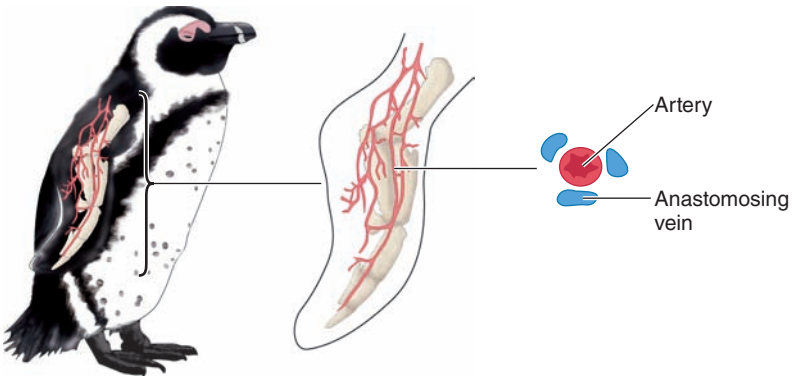
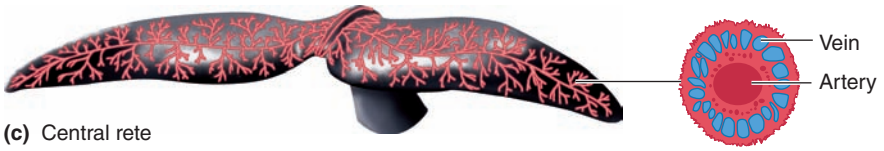
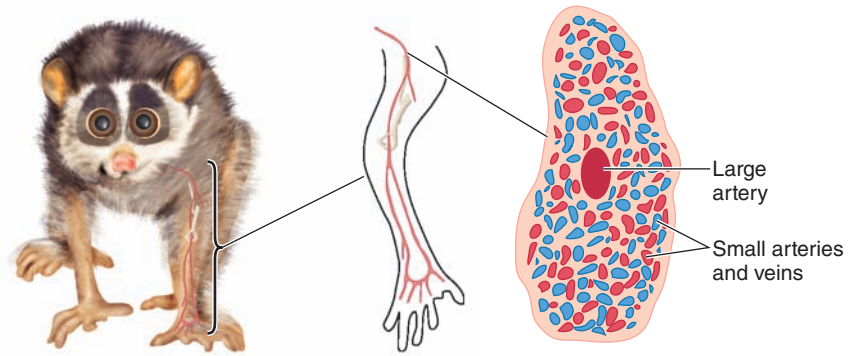


(b) Venae comitantes



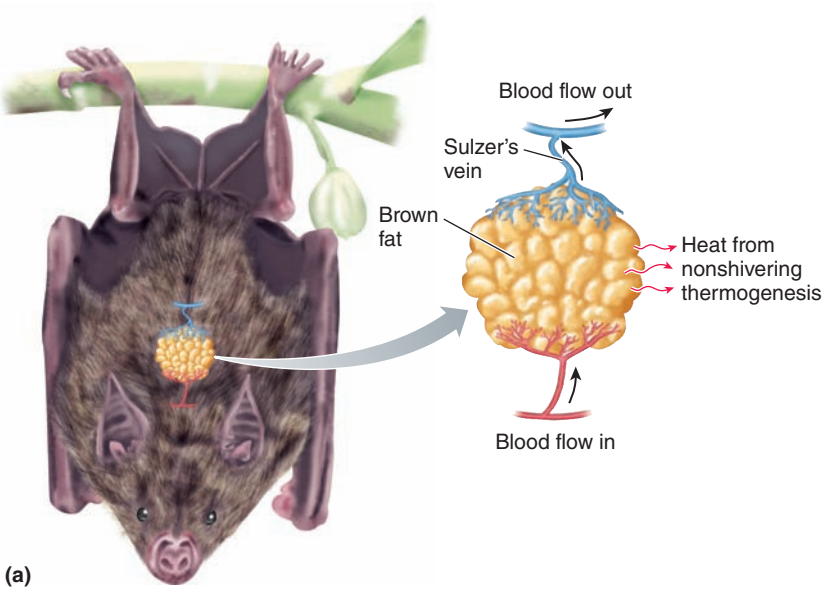
(c) Central rete



(d) Artery vein rete

FIGURE 15-18 Countercurrent heat exchangers (retes) in endotherms. (a) A rete exchanger in the leg of a stork at an air temperature of 12°C and floor temperature of 20°C, showing body temperature (*plotted line*) along the leg. The inset shows the principle of countercurrent exchange in a rete. (b) A *venae comitantes* rete, with two or more anastomosing veins surrounding a central artery (shown for a penguin flipper). (c) A centralized rete, with one central large artery surrounded by many separate, small veins (shown for fluke of a whale). (d) An artery–vein network rete, with many small arteries and veins together (shown for the limb of a loris).

Source: (a) From P. C. Withers. (1992). *Comparative Animal Physiology.* Fort Worth, TX: Saunders, as modified from M. P. Kahl. (1963). Thermoregulation in the wood stork, with special reference to the role of the legs. *Physiological Zoology* 36:141–151; (b) P. G. H. Frost, W. R. Siegfried, & P. J. Greenwood. (1975). Arterio-venous heat exchange systems in the jackass penguin *Spheniscus demersus*. *Journal of Zoology* 175:231–241; (c) P. F. Scholander & W. E. Schevill. (1955). Countercurrent vascular heat exchange in the fins of whales. *Journal of Applied Physiology* 8:279–282; (d) P. F. Scholander. (1957). The wonderful net. *Scientific American* 196:96–107.



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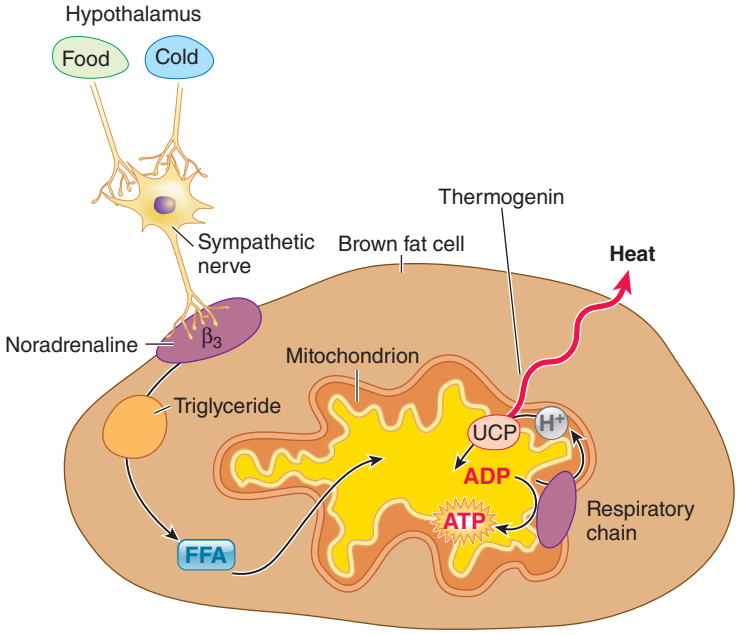

(b)

FIGURE 15-19 Brown adipose tissue (BAT) in endotherms. (a) BAT deposits in bats and other mammals are found between the shoulder blades and other locations not shown. (b) Schematic diagram illustrating how BAT generates heat. When activated by cold or diet via a nerve that releases norepinephrine, the uncoupling protein (UCP) called thermogenin in the BAT cells opens and allows protons (H^+) to pass through the inner mitochondrial membrane. This dissipates the proton gradient as heat without making ATP.

Source: (a) Modified from D. Randall, W. Burggren, & K. French. (2002). *Eckert Animal Physiology*. New York: W. H. Freeman and Company, Figure 17-22. (b) Modified from A. G. Dulloo. (1999). UCP2 and UCP3: genes for thermogenesis or lipid handling? *Obesity Matters* 2:5–8.

Generating More Internal Heat The hallmark of endotherms is their ability to produce internal heat for the purpose of thermoregulation, as follows:

1. *BMR.* One key adaptation was a large increase in birds' and mammals' overall BMR ("idling speed"). Indeed, the BMR of a bird or mammal is typically 5 to 20 times greater than the SMR of an ectotherm of the same mass. This appears to be due to "leaky" cell membranes. In one study comparing the liver, kidney, and brain of a mammal (laboratory rat) and a reptile (bearded dragon) of the same mass and body temperature, the endotherm (rat) tissues consumed O_2 two to four times faster, in part because the rat Na^+/K^+ ATPase pump used ATP three to six times faster. The pump runs faster because the rat's membranes are leakier to these ions, so the pump must work harder to restore the gradients.

   Thyroid hormones (p. 301) regulate the number of active Na^+/K^+ ATPase pump units in vertebrate cell membranes, with basal levels of these hormones being considerably higher in endothermic than in ectothermic vertebrates. In a resting mammal, most body heat is produced by the thoracic and abdominal organs.

2. *Shivering and other muscular activity.* The rate of heat production can be variably increased above the "idling" BMR level in the cold through skeletal muscle activity. Muscles constitute the largest organ system in the avian and mammalian body and are a ready source of heat from the contractile process. Any type of increased muscular activity (such as exercise and NEAT, p. 729) will increase heat production, but there are also specific thermoregulatory mechanisms. In response to a fall in core temperature caused by exposure to cold, skeletal muscle *tone* gradually increases. (Muscle tone is the constant level of tension within the muscles.) This produces some heat. Soon shivering begins. **Shivering** consists of rhythmic, oscillating skeletal-muscle contractions that occur at a rapid rate of 10 to 20 per second. This mechanism is very effective in increasing heat production; all the energy liberated during these muscle tremors is converted to heat because no external work is accomplished. Within a matter of seconds to minutes, internal heat production may increase two- to fivefold as a result of shivering.

3. *Nonshivering (chemical) thermogenesis.* There is one other way to boost heat production above the BMR level. In most experimental mammals, chronic cold exposure brings about an increase in metabolic heat production that is independent of muscle contraction, appearing instead to involve changes in heat-generating chemical activity. This **nonshivering thermogenesis** is mediated by the hormones epinephrine and thyroid hormone and by sympathetic nerves (which use the neurotransmitter norepinephrine). The cellular mechanisms triggered to produce heat are still not fully understood. One mechanism that has been delineated is found in newborn mammals and most small mammals (especially hibernators). These have deposits of *brown adipose tissue* (BAT) (Figure 15-19a), which (as you saw earlier) is especially capable of converting chemical energy into heat. BAT cells, which are devel-

opmentally derived from muscle rather than adipose cells, contain deposits of triglycerides packed with specialized mitochondria (the combination of fat and mitochondria gives this tissue its color). In their inner membranes, these mitochondria contain the *uncoupling protein* UCP-1 (p. 729), a gated proton (H^+) channel also called **thermogenin** (Figure 15-19b). Recall that normal mitochondria generate ATP by using a proton gradient (see Figure 2-20, p. 52). Normally, the protons move down their gradient through an ATP-synthesizing enzyme complex. But when thermogenin channels open, the two processes (H^+ flow and ATP synthesis) become uncoupled and the protons simply flow down their gradient (through thermogenin) without generating ATP, with the energy from this H^+ flow being completely dissipated as heat.

BAT is particularly important in newborn mammals, which have a higher ratio of surface area to volume than do adults, and in hibernators, where it is used to warm the mammal up rapidly as hibernation ends. Also, as we mentioned earlier (p. 729), there is some evidence that BAT may help lean animals "burn off" excess calories.

Losing Excess Heat/Avoiding Gains from Hot Environs A rise in core body temperature is potentially more dangerous than a decline, because of irreversible denaturation of proteins. Thus, several mechanisms exist to remove excess body heat, which can occur not only from hot weather but also from high muscular activity. These mechanisms are as follows:

1. *Reduced insulation.* Desert endotherms may have inherently low insulation; for example, the camel has virtually no subcutaneous fat, storing its adipose instead in its characteristic hump. As we noted earlier, layers of insulation may be regulated. The shedding of hair by a house cat or dog in the springtime is a familiar example. A bird in hot weather may loosely ruffle its feathers to convect heat from the skin.
2. *Enhanced radiation and vasodilation.* In the process of thermoregulation, skin blood flow can vary tremendously. The more blood that reaches the skin from the warm core, the closer the skin's temperature is to the core temperature. The skin's blood vessels diminish the effectiveness of the skin as an insulator by carrying heat to the surface, where it can be lost from the body by radiation, conduction, and convection. Accordingly, vasodilation of the skin vessels (Figure 15-17b), which permits increased flow of heated blood through the skin, increases heat loss. Some external structures with large surface areas help with heat removal from the blood, such as elephant ears and the large beak of the toucan.
3. *Enhanced evaporation.* As you saw earlier, evaporation is the only way to cool off if the environment is hotter than the skin. Recall the importance of the relative humidity (RH, p. 735) of the surrounding air. When the RH is high, the air is nearly or fully saturated with H_2O, so it has limited or no ability to take up additional moisture from the animal. Thus, little or no heat loss can occur on hot, humid days.

   Endotherms have at least two evaporation mechanisms specifically adapted for thermoregulation: **respiratory panting** and **"insensible" cutaneous loss** through the skin (see p. 631). Cutaneous loss is an important route, especially in smaller endotherms. For example, it accounts for well over half of evaporative loss in the desert kangaroo rat (p. 630). Panting involves a shallow, rapid, breathing pattern that permits large volumes of air to move over the hot, moist tongue and respiratory airways. The resultant increase in evaporative heat loss from the respiratory tract provides a cooling effect. Numerous species of birds supplement panting with a rapid fluttering of the well-vascularized esophageal region. This rhythmic inflation of the hyoid apparatus is termed **gular fluttering.** Because air movement in panting and gular fluttering is associated with surfaces that do not participate in gas exchange, problems with imbalances in the blood concentration of O_2 and CO_2 (hypocapnia and alkalosis; see pp. 542 and 647) are avoided. In many bird species, cutaneous evaporation accounts for about half of water loss at moderate temperatures, whereas at high temperatures most birds rely on respiratory evaporation. For example, the desert verdin (*Auriparus flaviceps*) at 50°C uses respiratory evaporation for 85% of total water loss. For unknown reasons the response of some species differs; for example, Spinifex pigeons increase their rate of cutaneous evaporation as temperatures rise.

   A few mammals have a third mechanism: **Sweating** is an active evaporative heat-loss process from specialized integumentary glands under sympathetic nervous control. Sweat is a dilute salt solution actively extruded to the surface of the skin by the glands and dispersed. For heat loss to occur, sweat must be evaporated from the skin. Humans and horses sweat over much of their bodies, but most mammals either lack or have limited distribution of sweat glands; for example, dogs have sweat glands only on their paw pads.
4. *Countercurrent exchange.* The rete mechanism discussed earlier for heat retention can also be used to prevent overheating of certain organs. In particular, some fast-running animals such as gazelles have a rete between their brains and the core body, in which warm blood in the carotid artery passes by cool venous blood from the nose, sinuses, and facial skin. This protects the brain from the high heat produced from the skeletal muscles when the animal is running from, say, an attacking cheetah (which also has a similar rete). Horses may protect their brains from overheating in a different way: In addition to cooling sinuses, they have unusual **guttural pouches** (sacs extending from the auditory tubes) surrounding the carotid arteries, which may also help cool the blood.
5. *Avoidance behavior.* Again, like their ectothermic ancestors, birds and mammals seek cooler environs when overheating. This can be a local change, such as moving under a shady tree, or a long-distance process, such as a seasonal migration.
6. *Anatomic reduction of heat gain.* Light-colored surfaces, such as skin, fur, or feathers, reflect sunlight. Camels, for example, have wool in the winter and shiny, reflecting hair in the summer (tropical camels maintain this reflecting hair year-round).

As we noted earlier, evaporative cooling must be balanced with the body's need for water; the camel is an excellent example of this trade-off in a hot climate (p. 733). Some desert birds use the same strategy; that is, they let their body temperatures rise during the day to reduce evaporative cooling, thus saving up to 50% of body water. Another

mechanism involves physiological regulation of the skin barrier. For example, zebra finches deprived of water add layers of lipids to their skin, reducing cutaneous water loss by 75% or more.

The hypothalamus and/or spine integrates a multitude of thermosensory inputs from both the core and the surface of the body

In vertebrates, the hypothalamus controls most mechanisms of thermoregulation. In birds, the hypothalamus appears to control metabolic rate, panting, vasodilation, and shivering, but a reflex integrator in the spine has also been identified that regulates vasodilation and constriction, panting, shivering, and erection of plumage. The hypothalamus (plus the spinal integrator in birds) acts like a "thermostat" in negative-feedback fashion. As we discussed in Chapter 1 (Figure 1-8), a house thermostat keeps track of the temperature in a room and triggers a heating mechanism (the furnace) or a cooling mechanism (the air conditioner) as necessary to maintain the room temperature at the indicated setting. Similarly, the hypothalamus receives afferent information about body temperature from various regions of the body and (particularly in mammals) initiates coordinated adjustments in heat gain and heat loss mechanisms as necessary to correct any deviations in core temperature from the set point. The hypothalamic thermostat is far more sensitive than your house thermostat. The hypothalamus in endotherms can respond to changes in blood temperature as small as 0.01°C.

To make the appropriate adjustments in the delicate balance between the heat loss mechanisms and the opposing heat-producing and heat-conserving mechanisms, the hypothalamus must be continuously appraised of both the skin temperature and the core temperature by means of specialized temperature-sensitive *thermoreceptors.* The core temperature is monitored by *central thermoreceptors,* which are located in the hypothalamus itself as well as elsewhere in the central nervous system and the abdominal organs. These sensors monitor the core temperature that is actually being defended homeostatically. *Peripheral thermoreceptors* monitor skin temperature throughout the body and transmit information about changes in surface temperature to the hypothalamus. To some extent, these sensors serve in *anticipation* fashion. That is, changes in skin temperature give advance warning of potential environmental threats to the core temperature, allowing corrections to be initiated before the core temperature is actually disturbed.

Two centers for temperature regulation are in the hypothalamus. The *posterior region,* activated by cold, triggers reflexes that mediate heat production and heat conservation. The *anterior region,* activated by warmth, initiates reflexes that mediate heat loss. Together, these work to maintain a remarkably consistent core temperature (which, however, oscillates slightly because of feedback delays; see p. 16). Let's see how.

To regulate core temperature homeostatically, the hypothalamus simultaneously coordinates heat production, heat loss, and heat conservation mechanisms

Let's now pull together the coordinated adjustments in heat production as well as heat loss and heat conservation in response to exposure to either a cold or a hot environment for a mammal (Figure 15-20). In response to cold exposure, the posterior region of the hypothalamus directs increased heat production, such as increased muscle tone and shivering and BAT activity, while simultaneously decreasing heat loss (that is, conserving heat) by skin vasoconstriction and other measures. Because there is a limit to the ability to reduce skin temperature through vasoconstriction, when the external temperature falls too low, even maximum vasoconstriction is not sufficient to prevent excessive heat loss. Accordingly, other measures must be instituted to further reduce heat loss, such as puffing up of hair. After maximum skin adjustments have been achieved physiologically, further heat loss can be prevented only by behavioral adaptations (as we described on p. 736).

Under the opposite circumstance—heat exposure—the anterior part of the hypothalamus reduces heat production by decreasing skeletal muscle activity and promoting increased heat loss by inducing skin vasodilation. When even maximal skin vasodilation is inadequate to rid the body of excess heat, sweating or panting is brought into play to accomplish further heat loss through evaporation.

Thermal Neutral Zone The consequences of thermoregulatory actions on metabolism are illustrated in Figure 15-21, which shows the metabolic rate as a function of environmental temperature. In the middle of this diagram lies the **thermal neutral zone (TNZ),** a range of environmental temperatures in which the animal does not need to expend significant energy for thermoregulation. In this zone, mechanisms involving insulation, blood vessels, and low-energy behaviors are sufficient. Below the neutral zone, at a point called the **lower critical temperature,** metabolic rate increases as the special heat-generating mechanisms are activated. If these mechanisms are insufficient, the animal may suffer from **hypothermia** (dangerously low body temperature). Above the neutral zone, at a point called the **upper critical temperature,** metabolism increases because of panting (which uses rapid muscle activity) or heavy sweating (which uses ion transport processes). These activities counterproductively but unavoidably generate even more heat to deal with, leading to the potential for **hyperthermia** (dangerously high body temperatures).

The width of the TNZ and the critical temperatures depend on the effectiveness of the thermoregulatory adaptations that do not require significant energy. Insulation is often the major factor. For example, the lower critical temperature for the lightly insulated cardinal (*Cardinal cardinalis*) is 18°C, whereas for the heavily insulated emperor penguin (*Aptenodytes forsteri*) it is –10°C. In tropical hummingbirds (such as *Colibri delphinae*), there are no critical temperatures; metabolic rate decreases linearly with environmental temperature as the latter is increased from 4 to 40°C. Seasonal acclimatization can alter the TNZ. For example, with a summer hair coat the critical lower temperature for a beef cow averages 15°C (59°F), whereas with a heavy winter coat wind chills of –8°C (18°F) are comfortably tolerated. Fermentation in rumens also produces heat as a by-product, contributing to the comparatively low critical lower temperatures observed in ruminants.

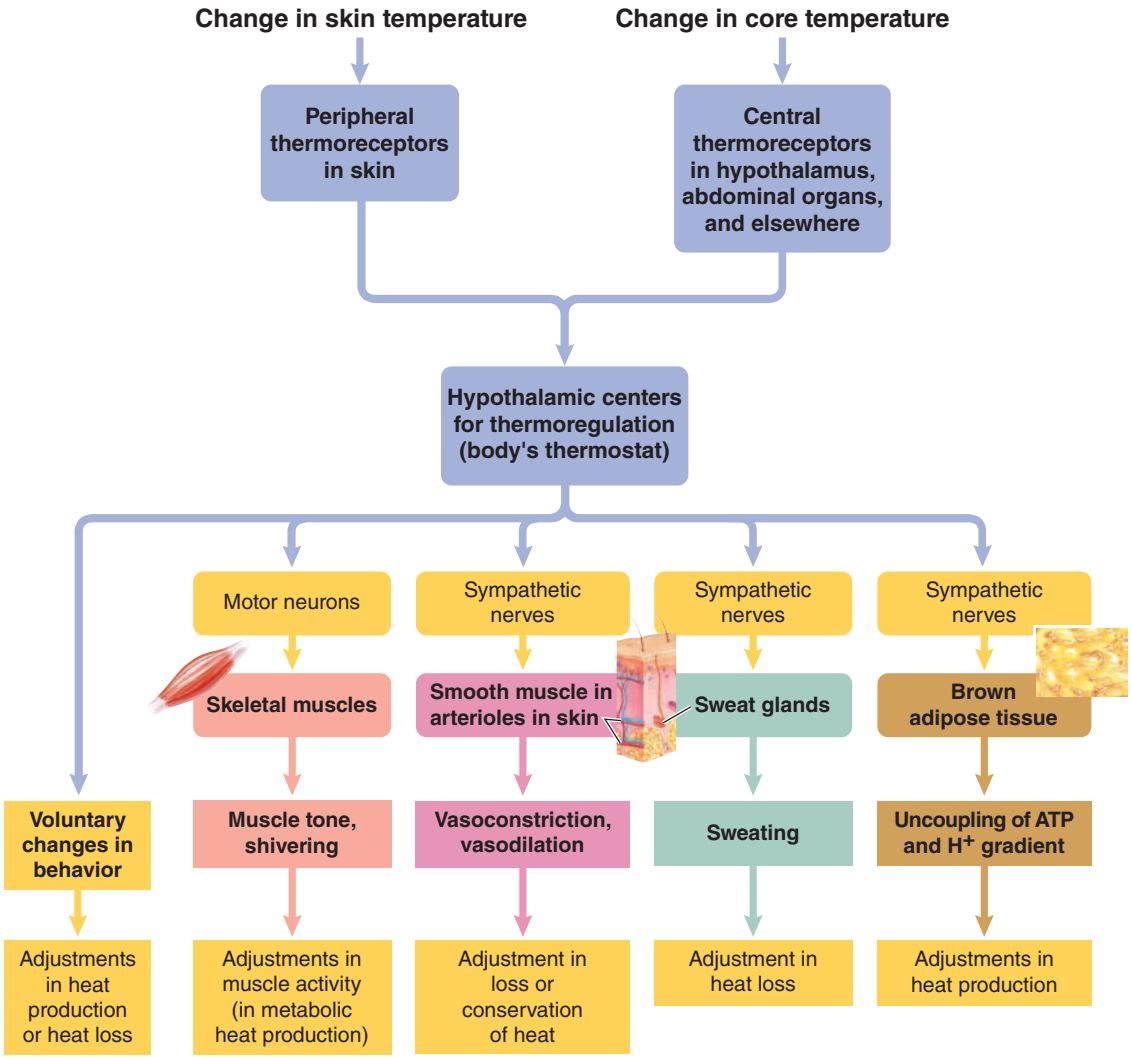

FIGURE 15-20 **Major thermoregulatory pathways in a mammal.**

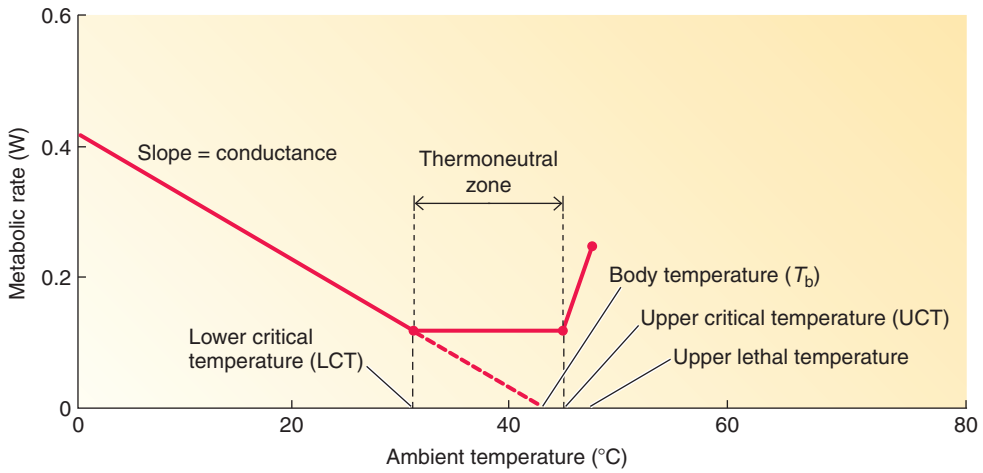

FIGURE 15-21 **The influence of ambient temperature on the metabolic rate (MR) of a small temperate endotherm, showing the thermoneutral zone where MR is constant.**

Source: Willmer, P., G. Stone and I. Johnston, (2000), "Environmental Physiology of Animals", Fig. 8.33. Copyright © 2000 Blackwell Publishing. Reproduced with permission of Blackwell Publishing Ltd.

During a fever, the hypothalamic thermostat is "reset" to an elevated temperature, which can be beneficial

Fever is an elevation in body temperature as a result of infection or inflammation. In mammals, in response to microbial invasion, certain white blood cells release a **pyrogen** (especially *interleukin-1, IL-1*), which among its many infection-fighting effects, acts on the hypothalamic thermoregulatory center to raise the setting of the thermostat (see p. 469). The hypothalamus now maintains the temperature at the new set level instead of maintaining normal body temperature. Shivering is initiated to rapidly increase heat production, while skin vasoconstriction is brought about to reduce heat loss, both of which drive the temperature upward. Thus, fever production in response to an infection is a "deliberate" mechanism, not a pathological one.

Although the overall physiological significance of a fever is still unclear, many medical and veterinary experts believe that a rise in body temperature has a beneficial role in fighting infection in mammals, including humans. A fever augments the inflammatory response and may interfere with bacterial multiplication (see p. 469). Experiments with ectotherms have demonstrated that this is an ancient defense mechanism. Infected lizards and fish seek out warmer habitat areas to raise their body temperatures above their normal optimum. This aids survival because ectotherms prevented from elevating their body temperatures in this way do not survive the infection as well. Medical experiments with humans also show that subjects treated with antifever drugs suffer more than untreated subjects from diseases like pneumonia.

check your understanding 15.6

Describe mechanisms of "gain, retain, generate, lose" heat in achieving homeothermy in birds and mammals.

Discuss how the hypothalamus maintains homeothermy with respect to temperatures out of the thermal neutral zone, and when and why it elevates temperature to create a fever.

15.7 Heterothermy

In addition to birds and mammals, many other animals (and even some fungi and plants) exhibit some form of endothermy, but unlike birds and mammals, they do not heat all their cores. Furthermore, some animals including many small birds and mammals cannot maintain high core temperatures continuously, because of their high ratios of surface area to volume, coupled with insufficient food supply. Such animals are called **heterotherms,** falling into two broad categories: *regional* and *temporal*.

Regional heterotherms heat only some parts of their bodies

Regional heterothermy occurs in endothermic animals that heat only certain organs or body regions, not their entire bodies. For example, flying insects such as bees and moths heat their thoraxes by the activity of flight muscles. As a preflight warm-up, some species shiver their flight muscles before takeoff. During flight they can keep their thoraxes at relatively constant and high temperatures by controlling hemolymph flow between the thorax and abdomen, which are connected by countercurrent flow channels (Figure 15-22a). The abdomen has a thin ventral surface, the *thermal window,* through which excessive heat can be lost.

In the marine realm, two groups of fishes—the *lamnid sharks* (such as the great white) and many *scombroid teleosts* (tunas and billfishes)—have evolved endothermy, primarily in their red or aerobic swimming muscles. These animals migrate over long distances, swimming continuously with these muscles and generating constant heat output. But it is not enough to heat the entire body, because too much heat is lost at the gills. A countercurrent rete system between the aerobic muscle and the gills prevents most of the loss (Figure 15-22b). Presumably, these warm, thermally regulated muscles give these fishes the ability to move between warm and cold waters more easily than ectotherms can. Remarkably, some of these fishes such as the swordfish have special heater organs behind their eyes to heat their retinas and brains. These organs evolved out of eye muscles and have become dedicated to heat production only! Presumably, this allows the fish to see prey better in cold, dark waters.

Temporal heterotherms maintain high body temperatures only for certain time periods

Temporal heterothermy is manifested in endotherms that regularly shift from a regulated high body temperature to a low body temperature, most commonly in daily *torpor* and seasonal *hibernation.*

Torpor Many small endotherms with high metabolic demands, such as shrews and birds, enter a short-term dormant state called **torpor** on a daily basis. At night, for example, a deer mouse's body temperature (Figure 15-23a) drops from around 35°C to as low as 15 to 20°C (depending on environmental temperatures), saving a large amount of energy. (Note that these animals usually do not let body temperatures drop close to freezing, possibly because the energy cost of rewarming on a daily basis would be prohibitive). This is important because this mouse needs almost constant food input to sustain its metabolism in the active state. Of particular interest is the Australian marsupial called the fat-tailed antechinus. This small mammal goes through nightly torpor, with core body temperatures dropping to 16 to 27°C, and it basks in the sun each morning to reheat its body to 33 to 37°C. Unlike other mammals, however, it does not simultaneously use endothermic mechanisms in the initial phases of rewarming. Thus, it uses lizard-like behavior in a fashion that suggests how thermoregulation first started in mammalian ancestors.

In addition, animals that employ daily torpor tend to have longer life spans. Hummingbirds, for example, typically undergo daily torpor and can live up to 10 years. In contrast, Norwegian shrews (six species, all about the same size as hummingbirds) live only 16 to 20 months and do not undergo regular torpor. The so-called southern African elephant shrew (*Elephantus myurus*), which is not a true shrew but is of similar size, does undergo torpor, and it lives four to six years. Thus, reductions in metabolism on a regular

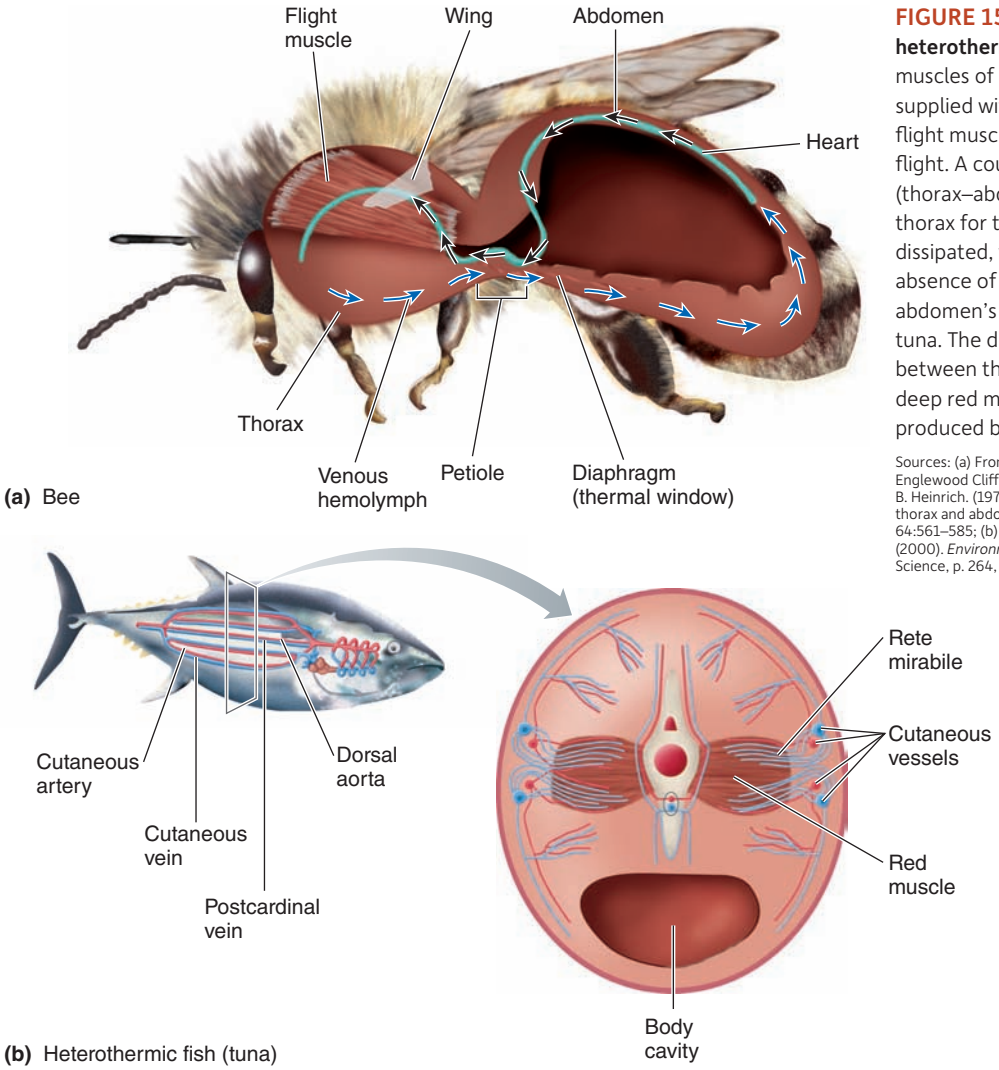

FIGURE 15-22 Countercurrent exchangers in heterotherms. (a) A bumblebee. The flight muscles of honeybees and bumblebees are supplied with blood from the heart, while the flight muscles produce heat at a high rate during flight. A countercurrent flow in the petiole (thorax–abdomen junction) retains heat in the thorax for the flight muscles. If heat needs to be dissipated, venous blood can be pumped in the absence of arterial flow, taking heat to the abdomen's thermal window for removal. (b) A tuna. The diagram shows the rete located between the outer (cutaneous) vessels and the deep red muscle. The rete traps the heat produced by those muscles.

Sources: (a) From K. Schmidt-Nielsen. (1960). *Animal Physiology.* Englewood Cliffs, NJ: Prentice-Hall, Figure 7.39, as modified from B. Heinrich. (1976). Heat exchange in relation to blood flow between thorax and abdomen in bumblebees. *Journal of Experimental Biology* 64:561–585; (b) Modified from P. Willmer, G. Stone, & I. Johnston. (2000). *Environmental Physiology of Animals.* Oxford, UK: Blackwell Science, p. 264, Figure 9.10.

basis may slow the manifestation of aging, much of which is thought to be caused by reactive oxygen species (ROS, p. 53) generated in proportion to metabolic rate.

Hibernation Many small endotherms become nearly or fully poikilothermic as winter approaches, entering a long-term dormant state called **hibernation,** in which body temperatures may drop to near ambient (Figure 15-23b). Remarkably, the Arctic ground squirrel even supercools slightly, with body temperatures of –3°C. Hibernators must store up large amounts of unsaturated fats (which do not turn hard like butter at cold body temperatures) to serve as energy reserves. However, these animals are usually not fully ectothermic. Mammalian hibernators still have a functioning hypothalamic thermostat, but with a greatly lowered set point. The hypothalamus has been shown to regulate a lowering of body temperature and also to regulate heating tissues such as BAT to prevent internal freezing. Many also go through periodic "bouts" of rewarming (Figure 15-23b) and then recooling every few days or weeks. It is not known why they do this, but one hypothesis is that they must warm up in order to void wastes and sometimes to eat cached food, with the latter serving in particular to restore glycogen stores in their brains. Another hypothesis is that they do this periodic awakening to reactivate their immune systems temporarily in case they have been infected.

Contrary to popular belief, only mammals about marmot size (3 kg) or smaller can truly hibernate, because of the principles of ratios between surface area and volume, discussed earlier. A bear is simply too large to cool off greatly and then reheat in a reasonable time in the springtime, so it essentially sleeps through much of the winter with a body temperature only about 5°C lower than normal. This may be more properly called *winter sleep,* although the term *hibernation* is still often used.

Though hibernation is usually associated with high latitudes, at least one tropical mammal, the Madagascan fat-tailed dwarf lemur (*Cheirogaleus medius*), hibernates. Its body temperature can be purely ectothermic at times, fluctuating by up to 20°C in a day.

Regulation of hibernation is still incompletely understood. In a startling discovery, Mark Roth and colleagues reported in 2005 that mice breathing moderate concentrations of H_2S (the "rotten-egg" gas that is toxic at high levels) went into a reversible, deep hibernation-like state. This is remarkable since mice do not hibernate naturally. How H_2S does

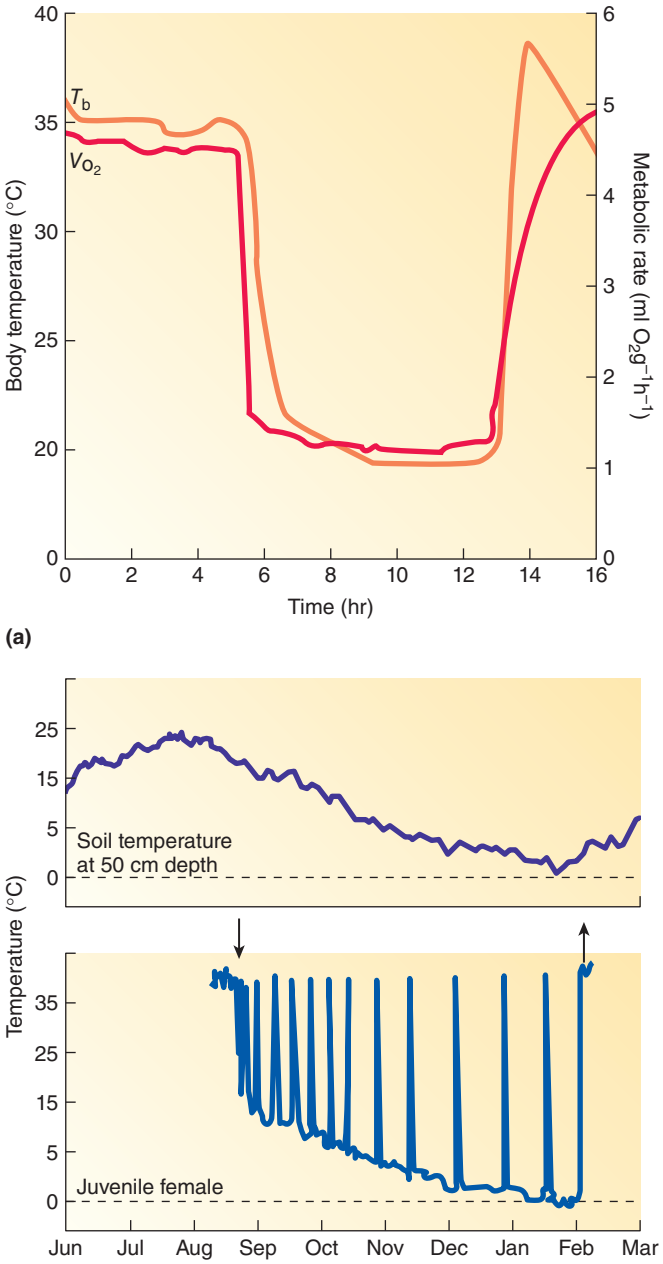

FIGURE 15-23 Temperatures of mammals in torpor and hibernation. (a) Metabolic rate (V_{O_2}) and body temperature (T_b) of a deer mouse during daily torpor. (b) Soil temperature and body temperature in a Richardson's ground squirrel (*Spermophilus richardsonii*) hibernating through the winter, showing periodic "bouts" of rewarming.

Sources: (a) From P. C. Withers. (1992). *Comparative Animal Physiology*. Fort Worth, TX: Saunders, using data from J. R. Nestler. (1990). Relationships between respiratory quotient and metabolic rate during entry to and arousal from daily torpor in deer mice (*Peromyscus maniculatus*). Physiological Zoology 63:504–515; (b) From G. R. Michener. (1998). Sexual differences in reproductive effort of Richardson's ground squirrels. *Journal of Mammalogy*, 79:1–19.

this, and whether natural hibernators use this gas, is not certain. Some evidence shows that the gas inhibits mitochondrial respiration, but it is also known to be a body regulatory signal (much like NO; p. 93) at minute concentrations.

Some colonial heterotherms create homeothermic "superorganisms"

Finally, spectacular examples of homeothermy can be found in certain animal colonies in which the individual animals are heterothermic or poikilothermic. Several social insects form large colonies that are thermoregulated by the collective behavior of the group. These "superorganisms" include many beehives and termite mounds, in which groups of animals construct ventilation tubes and use their wing beats to heat up or convectively cool the colony. Honeybees also carry water into their hives for evaporative cooling. Thus, beehives can maintain temperatures that are much less variable than the environment. In tropical habitats where the environmental temperature does not vary extensively, some termite mounds are homeothermic all year round.

Thermoregulated hives have recently been shown to be crucial to larval bee development. Pupated larvae were raised at 32, 34, and 36°C in the laboratory. Those raised at the lower temperatures had abnormal neural development. Amazingly, when the colony is infected with a pathogenic fungus, the bees can even create a feverlike state. The fungus, which can kill bee larvae, is greatly inhibited by the elevated temperature. Swarms of honeybees have also been documented using rapid wing beats to create heat intense enough (over 50°C) to kill parasitic wasps attempting to invade the hive.

One amazing group of mammals, the naked mole rats, has evolved a hivelike system that resembles these insect colonies. See *A Closer Look at Adaptation: The Naked Mole Rat—Mammalian Hive Ectotherm.*

check your understanding 15.7

Discuss regional heterothermy and the mechanisms involved in a tuna and a bee.

Discuss the features and adaptive value of hibernation and torpor.

15.8 Thermal Physiology and Climate Change

By the first decade of the 21st century, science had firmly established that the atmosphere and oceans are warming up. Indeed, the years 2005 and 2010 were the hottest years on record. Average ocean surface temperature in July 2009 was the warmest ever recorded. This **global warming** is clearly due, at least in part, to anthropogenic (man-made) "greenhouse" gases, mainly CO_2 from fossil-fuel burning and methane from cattle (p. 669), rice paddies, and other sources. (Recall from Chapter 13 that CO_2 is also acidifying the oceans.) These gases, which prevent infrared (heat) radiation from leaving the Earth, have increased dramatically in the last century or so in parallel with temperature increases.

Arctic regions have warmed the most, and climate is becoming more extreme

The warming trend is not by any means uniform. In particular, in the last 30 years, southern temperate regions have not experienced net warming, while the Arctic has experienced

A Closer Look at Adaptation

The Naked Mole Rat—Mammalian Hive Ectotherm

Although traditional physiology states that all mammals are endotherms, there is at least one remarkable exception: the naked mole rat. Twelve known species of naked mole rats live in underground tunnel complexes underneath savanna and grasslands of equatorial Africa. *Heterocephalus glaber* has been the most studied species. These mole rats have almost no body fur (although they do have fine hairs) and no subcutaneous fat, and thus have no effective insulation. Most amazingly, they cannot individually regulate their body temperatures via endothermy. Thus, their body temperatures do fluctuate somewhat. But a degree of homeothermy around 31°C is still achieved using mechanisms like those of social insects. First, they occasionally bask in the sun at their tunnel entrances. Second, the animals do produce some heat, and by huddling together while sleeping (along with some insulation provided by the soil around the tunnel), they can trap much of this heat. Altogether, their thermoregulatory mechanisms are very similar to those of termites in their mounds.

Thermoregulatory physiology of these mammals is not the only parallel to insect physiology. Both species have a social structure (termed *eusocial*) that is very much like the hive societies of social insects. There is a single queen mole rat, for example, that mates with a few dominant males; there are many workers that dig the tunnels and gather food; and there are a few soldiers that do not work but protect the colony from predators such as snakes. Thus, cooperation within the colony is essential to survival because a pair of mole rats on their own would not be able to perform all the functions needed to cope with environmental challenges.

A naked mole rat.

These animals are becoming laboratory models for medical research because they have other amazing physiological features relating to many other chapters in this book. For example, they have no functional nociceptors for noxious chemicals (Chapter 6, p. 260), allowing them to tolerate the buildup of ammonia in their burrows. They are incredibly tolerant of hypoxia (their brains surviving after 30 minutes without O_2), an obvious adaptation to burrow life (Chapter 11, p. 542). Their two large teeth evolved from fixed chewing structures (Chapter 14, p. 663) into independently moveable digging and manipulating devices, with about 30% of the animal's somatosensory cortex (Chapter 5, p. 192) devoted to those teeth. Perhaps most remarkably, their lifespan is about 30 years, compared to 3 years or less for a similar sized rat (lifespan normally scales inversely with body size; Chapter 1, p. 10). They do not get osteoporosis (Chapter 7, p. 328) and appear to avoid cancer as well, perhaps due to better immune-surveillance mechanisms (Chapter 10, p. 486), and they have proteins highly resistant to reactive oxygen species (ROS; Chapter 2, p. 53).

the greatest warming (Figure 15-24a) including increasing loss of the Arctic ice cap. Climate appears to be getting more chaotic, and the term **climate change** is increasingly used more often than global warming. Earth's climate has many (poorly understood) feedback components ("geophysiology," p. 14) and may exhibit the "flaws" inherent in feedback systems (p. 16) such as oscillating under- and overshoots (e.g., hotter summers but colder winters). Uncertain is whether climate change is subject to negative or positive feedbacks or both. For example, warmer oceans lead to more evaporation, which has increased rainfall and (in winter) snowfall in some areas; likewise, evaporation along with more DMS (p. 14) may also trigger more cloud formation that would block sunlight, thus cooling the planet (negative feedback). Conversely, increased melting of sea ice and snow (which reflect sunlight) exposes more water and dark land to the rays of the sun. The water and land in turn absorb more solar energy, which could accelerate global warming and melting, and so on (positive feedback).

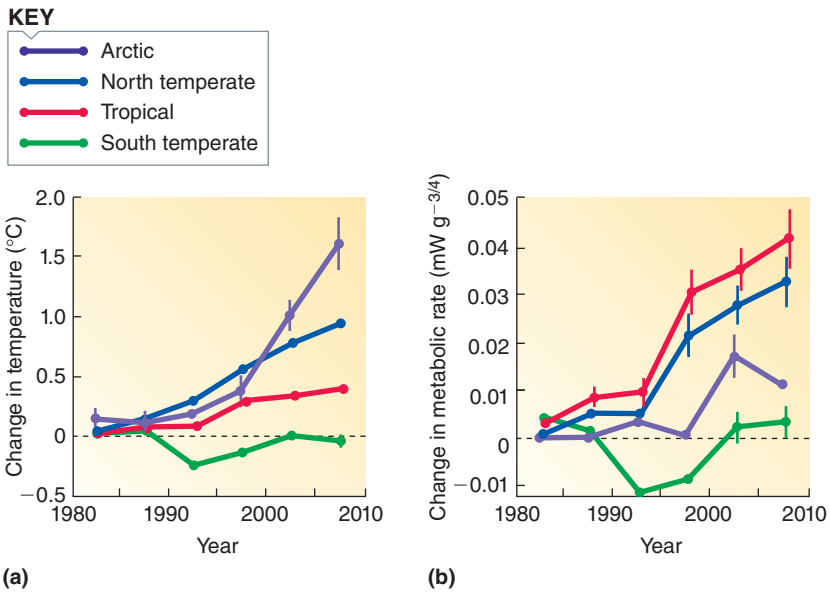

FIGURE 15-24 Global temperature changes and their effects on animal metabolic rates. (a) Recent changes in average temperatures for various geographical regions; (b) Predicted effects of those changes on mass-specific metabolic rates for ectotherms in those regions.

Source: M. E. Dillon, G. Wang & R. B. Huey, (2010), Global metabolic impacts of recent climate warming, 'Nature', 467:704–706. Used by permission from Macmillan Publishers Ltd, copyright 2010.

Animal physiology, behavior, and genes are already being affected by warming trends

As you might expect, due to the pervasive importance of temperature, habitat temperature changes are expected to impact all types of organisms. Animal physiologists are increasingly studying such impacts, at the theoretical level using physiological principles, in the laboratory to test potential effects, and in the natural world to test for effects already occurring. At the theoretical level, a study by Michael Dillon, George Wang, and Raymond Huey in 2010 yielded a perhaps unexpected prediction. While the Arctic is warming faster than the tropics (Figure 15-24a), metabolic rates (MR) of tropical ectotherms will likely rise faster than those of Arctic ectotherms (Figure 15-24b). This is because of the Q_{10} effect we described earlier (p. 730), in which MR doubles (or more) with each 10°C rise in temperature. This is an exponentially rather than linear effect. For example, an MR of 1 kJ/hr at 0°C might rise to 2 at 10°C, but an MR of 6 kJ/hr at 25°C could rise to 12 at 35°C. Thus, the absolute change is much greater in the tropics.

Laboratory studies are also revealing. For example, Hans Pörtner and colleagues have shown that, in fish at least, both cooling and warming reduce an animal's *aerobic scope* (p. 720) and that this might be the first major effect of climate change.

What about real-world effects? Considerable evidence has accumulated showing they are already occurring. Let's look at some of the studies.

Heat Shock Although global averages have risen only a few degrees, temporary but severe heat waves have greatly increased. For example, 30,000 flying foxes died of heat stress in Australia between 1994 and 2010 during unprecedented heat waves reaching 43°C or more. Tropical species are predicted to be hardest hit, not only because of the Q_{10} effect, but also because their physiologies are adapted to fairly consistent temperatures rather than seasonally changing ones.

Energy Balance Effects Habitat warming is affecting the "animal energy equation" for many animals, such as the following:

- *Tropical corals* that build reefs rely heavily on symbiotic algae for sugars and amino acids. Under heat stress, corals will "bleach"—that is, they expel their symbionts (with their photosynthetic pigments). Unless the coral can obtain more symbionts, they eventually die. Indeed, large-scale deaths of bleached coral have occurred during unprecedented temperatures. For example, in 2010, 50% of coral colonies died in many reefs of Southeast Asian and Indian Ocean after water temperature increased by 4°C above normal.
- *Tropical lizards* of Mexico are suffering: 12% of 200 populations of *Sceloporus serrifer* (blue spiny lizards) have died out in recent decades. Studies show that those lost populations were in areas where springtime temperatures have increased to the point that the animals probably had to reduce foraging time, staying in burrows to avoid overheating.
- *Yellow-bellied marmots* in Europe are getting fatter (and perhaps more successful) with warming due to longer foraging seasons, but *Arctic foxes* in Iceland have shrunk in size, perhaps as an adaptive way to cool off more easily, or due to decreased food supply.

Habitat Change Some animals have shifted habitats; for example, in 2003 Terry Root and colleagues gathered data from 143 studies and showed that hundreds of Northern Hemisphere species including mollusks, amphibians, birds, and mammals, as well as plants, have shifted north in correlation with warming. Other shifts include these:

- The two *limpet* species we discussed earlier (p. 733) have shifted ranges, with the southern species displacing the northern species in Monterey Bay, which has warmed up.
- The number of continental *butterfly* species in Britain has increased as they are now migrating north, presumably to find cooler temperatures.
- *Birds* in the University of California's Deep Canyon Reserve have moved upslope by 117 m in the last 30 years, correlating with an increase of 5°C in average temperature in the breeding season and a decline in rainfall by 44%.

Reproduction Finally, reproductive effects are also occurring, some of them genetic.

- The *grapevine moth* of Spain now breeds 12 days earlier than a century ago. The change correlates with a 3°C rise in springtime temperatures between 1984 and 2006. This pest, which eats grapevines, may increase its damage to vineyards.
- *Red squirrels* of the Yukon are breeding 18 days earlier than in the past, as springtime temperatures and food supply are increasing. This appears to be a genetic, evolved change.
- *Pitcher-plant mosquitoes* go into winter dormancy based on photoperiod, with northern populations entering dormancy earlier than southern ones. Now, in concert with warming, the northern groups are entering dormancy later, a change that is genetic (evolved).

As you can see, some species may be adapting to warming effects (some behaviorally, some by evolutionary genetic changes), while some are affected negatively and others positively. The long-term effects on ecological interactions are still uncertain. Only time will tell.

check your understanding 15.8

Discuss four findings that show effects of recent global warming on animal physiology.

making connections

How Energy Balance and Thermal Adaptations Contribute to the Body as a Whole

Because energy can be neither created nor destroyed, for body mass and body temperature, respectively, to remain constant, input must equal output in both an endotherm's total energy balance and its heat–energy balance. If total energy input exceeds total energy output, the extra energy is stored in the body, and body mass increases. Similarly, if the input of heat energy exceeds its output, body temperature increases. Conversely, if output exceeds input, body mass decreases or body temperature falls. The hypothalamus is

the major integrating center in mammals for maintaining both a constant total energy balance (and thus a constant body mass) and a constant heat–energy balance (and thus a constant body temperature). However, the effectors for temperature and energy regulation include components of many other systems covered in previous chapters. Energy balance, for example, obviously requires the digestive system and endocrine as well as hormonal regulation (such as insulin) and neural regulation (including behaviors such as eating). Temperature regulation involves (among other things) the skin and its blood vessels (and sweat glands in some mammals), respiration (panting), and skeletal muscles (shivering, or behavioral avoidance or seeking).

Body temperature is one of the most pervasive influences on body functions, which slow down if too cold, and suffer from denaturing macromolecules if too warm. Some ectotherms achieve partial homeostasis by controlling external heat exchanges (mainly through behavior), whereas others are not homeostatic but must adapt through dormancy or internal biochemical adjustments. Endotherms achieve homeostasis (homeothermy) much more consistently with physiological mechanisms.

Chapter Summary

- Life follows the laws of thermodynamics. Energy cannot be created or destroyed (First Law), and useful energy is continually lost to entropy (Second Law). To compensate for entropy, animals require input of food energy, most of which is converted to heat output.
- Energy input must equal energy output, which is measured as metabolic rates in the form of basal metabolism, activity, diet-induced thermogenesis (DIT), and production. Indirect calorimetry through respirometry of O_2 consumption is a common measurement method.
- Energy of production determines net energy balance, which can be positive, negative, or neutral. Basal and standard metabolic rates (BMR, SMR) are the "idling costs" for life, regulated in part by thyroid hormones. BMR and SMR are scaled to body mass: Smaller animals need more energy per unit mass than larger ones, for unclear reasons. Increased muscle activity is the factor that can most increase metabolic rate, as indicated by metabolic scope (ratio of maximal activity to BMR or SMR). DIT occurs after eating in most animals, and involves the costs of processing food.
- Some adult animals maintain long-term neutral energy balance, while others undergo regulated periods of positive or negative energy balance. Food intake in mammals is controlled primarily by the hypothalamus in response to numerous inputs, with internal signals such as orexins. Leptin from adipose and insulin from the pancreas are signals of long-term energy balance, while others such as ghrelin from the stomach and CCK from the intestine signal short-term energy deficiency or sufficiency. Effectors for energy balance are mechanisms to regulate eating and expenditures via regulated changes in BMR, DIT, activity, and production. Brown adipose tissue (BAT), for example, can burn off excess food energy.
- Different energy-balance set points among species result from evolutionary adaptations to different food supplies. Plentiful food favors "lean" set points to maintain agility, while intermittent food favors "heavy" set points for storing up reserves for famine periods.
- Temperature alters rates of chemical reactions and denatures macromolecules. Biomolecules can be altered to work optimally at different temperatures: Membrane fluidity is kept optimal by changes in saturation (homeoviscous adaptation), while proteins evolve to balance thermostability with flexibility needed for activity.
- The thermal adaptation strategies of animals depend on their primary source of heat: Endotherms rely on internal heat, ectotherms on external heat; poikilotherms have variable body temperatures, homeotherms have nearly constant body temperatures.
- Heat exchange between the body and the environment takes place by radiation, conduction, convection, and evaporation. Heat gain versus heat loss determines core body temperature. Animals gain heat from the environment while avoiding losses, retain body heat, generate more body heat, and lose excess heat.
- Body temperatures of ectotherms may follow the environment (poikilothermy), or may be regulated by external exchanges such as solar basking, shade seeking (ectothermic regulation via gain, retain, lose). Some ectotherms can compensate biochemically for changes in body temperatures with internal adjustments in enzyme concentration, pH, membrane saturation, and protein isoforms.
- Ectotherms survive extreme cold by metabolic dormancy and by either freeze tolerance (often with antifreeze carbohydrates in cells to prevent ICF but not ECF freezing), or freeze avoidance with antifreeze proteins, supercooling, or dehydration. Ectotherms may survive temporary extreme heat with heat shock proteins that protect other proteins.
- Birds and mammals maintain a consistent internal core temperature (homeothermy). To do so, heat gain must balance heat loss, using numerous mechanisms to gain (e.g., ectothermic behavior), retain (e.g., insulation, vasoconstriction, countercurrent exchangers), generate (e.g., high BMR, shivering, BAT), and lose excess (e.g., sweating, panting, vasodilation) heat.
- The hypothalamus and/or spine integrates a multitude of thermosensory inputs from both the core and the surface of the body. To regulate core temperature homeostatically, the hypothalamus simultaneously coordinates heat production, heat loss, and heat conservation mechanisms. During a fever, the hypothalamic thermostat is "reset" to an elevated temperature, which can be beneficial.
- Regional heterotherms heat only some parts of their bodies. Temporal heterotherms maintain high body temperatures only for certain time periods. Some colonial heterotherms create homeothermic "superorganisms" such as termite mounds and beehives.
- Climate change, particularly warming, is having documented effects on animal migration, metabolism, habitat location, and reproduction.

Review, Synthesize, and Analyze

1. If more food energy is consumed than is expended, explain the possible fates of the excess energy.
2. Explain how drugs that selectively block key appetite signals would affect feeding behavior.

3. The basal metabolic rate (BMR) is about 72 kcal/hr (301 kJ/hr) in an average human, with nearly all the energy converted to heat. If we could not lose this heat, our temperature would rise until we boiled (although we would die long before reaching that temperature). How long would that take? If an amount of energy ΔU is put into a liquid of mass m, the temperature change ΔT (in °C) is given by the following formula:

$$\Delta T = \Delta U/m \times C$$

Here, C is the specific heat of the liquid. For water, C = 1.0 kcal/kg-°C. Calculate how long it would take for BMR heat to boil your body fluids (assume 42 liters of water in your body and a starting body temperature at 37°C).

4. Why is it dangerous to engage in heavy exercise on a hot, humid day?
5. Discuss the advantages and disadvantages of ectothermy and endothermy, and why the latter might have evolved in some groups.
6. Different groups of homeotherms have different body temperatures. Why might that be?
7. Do you think fish run a fever when they have a systemic infection? Why or why not?
8. Compare the role of BAT in body-mass regulation and body-temperature regulation.
9. Small endotherms such as hummingbirds are temporal heterotherms, saving energy at night by undergoing torpor. Why don't large animals such as humans do this as well?
10. The discovery that H_2S triggers hibernation in a nonhibernating rodent has led to proposals for human applications. What might those be, and why?

Suggested Readings

Alexander, R. M. (1982). *Locomotion of Animals.* Glasgow, UK: Blackie. A classic text on mechanisms and energetics of animal locomotion.

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Burton, R. F. (2002). Temperature and acid–base balance in ectothermic vertebrates: The imidazole alphastat hypotheses and beyond. *Journal of Experimental Biology* 205:3587–3600. A review of the hypothesis on pH regulation as an adaptation to temperature.

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Heinrich, B. (1996). *The Thermal Warriors. Strategies of Insect Survival.* Cambridge, MA: Harvard University Press.

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Schmidt-Nielsen, K. (1998). *The Camel's Nose, Memoirs of a Curious Scientist.* Washington, DC: Shearwater Books. A lively, engaging discussion of a prominent comparative physiologist's pioneering research.

Secor, S. M., & J. M. Diamond. (2000). Evolution of regulatory responses to feeding in snakes. *Physiological and Biochemical Zoology* 73:123–141.

Storey, K. B. (1997). Organic solutes in freezing tolerance. *Comparative Biochemistry and Physiology* 117A:319–326.

Suarez, R. K. (1992). Hummingbird flight: Sustaining the highest mass-specific metabolic rates among vertebrates. *Experientia* 48:565–570.

Watanabe, M. E. (2005). Generating heat: New twists in the evolution of endothermy. *BioScience* 55:470–475. Another hypothesis on how endothermy evolved.

Wehner, R., A. C. Marsh, & S. Wehner. (1992). Desert ants on a thermal tightrope. *Nature* 357:586–587. About an ant that may be the most thermotolerant animal.

Weibel, E. R. (2002). The pitfalls of power laws. *Nature* 417:131–132.

West, G. B., J. H. Brown, & B. J. Enquist. (1999). The fourth dimension of life: Fractal geometry and allometric scaling of organisms. *Science* 284:1677–1679.