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Temperature Regulation in Human

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

Basic facts:

- The temperature of the deep tissues of the body—the "core" of the body—remains constant, within ±1°F (±0.6°C), between 98.0° and 98.6°F when measured orally and about 1°F higher when measured rectally.
- The *skin temperature,* in contrast to the *core temperature,* rises and falls with the temperature of the surroundings.
- No single core temperature can be considered normal; a *range* of normal temperatures measured orally, from less than 97 °F (36 °C) to over 99.5 °F (37.5 °C).
- When excessive heat is produced in the body by strenuous exercise, the temperature can rise temporarily to as high as 101°F to 104°F.
- Conversely, when the body is exposed to extreme cold, the temperature can often fall to values below 96°F (Figure 1).

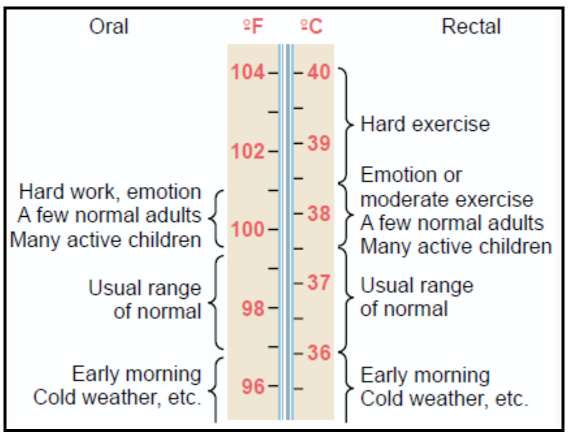


Figure 1: Average oral and rectal temperature of a normal average man during different phases of activity

Heat Production

Heat production is a principal by-product of metabolism. The different factors that determine the metabolic rate of the body are:

- basal rate of metabolism of all the cells of the body,
- extra rate of metabolism caused by muscle activity, including muscle contractions caused by shivering,
- extra metabolism caused by the effect of thyroxine, growth hormone and testosterone) on the cells,
- extra metabolism caused by the effect of epinephrine, norepinephrine and sympathetic stimulation on the cells,
- extra metabolism caused by increased chemical activity in the cells themselves, especially when the cell temperature increases,
- extra metabolism needed for digestion, absorption, and storage of food (thermogenic effect of food).

Temperature Regulation

Invertebrates generally cannot adjust their body temperatures and so are at the mercy of the environment. In vertebrates, mechanisms for maintaining body temperature by adjusting heat production and heat loss have evolved. In reptiles, amphibians, and fish, the adjusting mechanisms are relatively rudimentary, and these species are called "cold-blooded" **(poikilothermic)** because their body temperature fluctuates over a considerable range. In birds and mammals, the "warm-blooded" **(homeothermic)** animals, a group of reflex responses that are primarily integrated in the hypothalamus, operate to maintain body temperature within a narrow range in spite of wide fluctuations in environmental temperature. The hibernating mammals are a partial exception. While awake they are homeothermic, but during hibernation their body temperature falls.

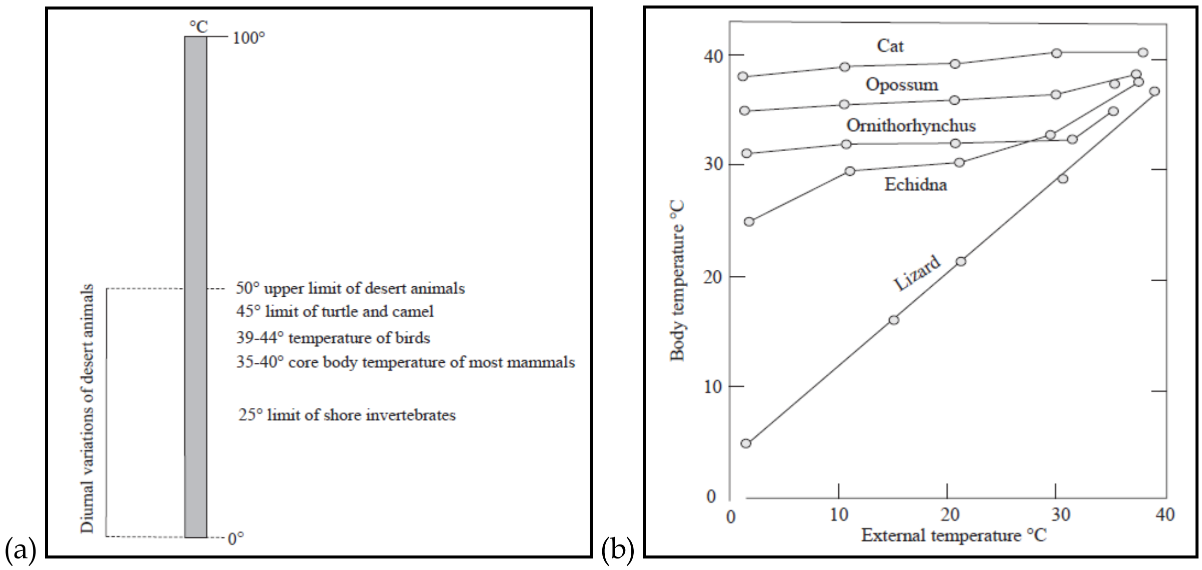


Figure 2: (a) Range of temperature in which animals survive (b) internal adjustments of body temperature among different animals under varying external temperatures

Blood vessels are distributed profusely beneath the skin. Especially important is a continuous venous plexus that is supplied by inflow of blood from the skin capillaries (Figure 3). In the most exposed areas of the body—the hands, feet, and ears—blood is also supplied to the plexus directly from the small arteries through highly muscular *arteriovenous anastomoses.* The rate of blood flow into the skin venous plexus can vary tremendously—from barely above zero to as great as 30 per cent of the total cardiac output. A high rate of skin flow causes heat to be conducted from the core of the body to the skin with great efficiency, whereas reduction in the rate of skin flow can decrease the heat conduction from the core to very little.

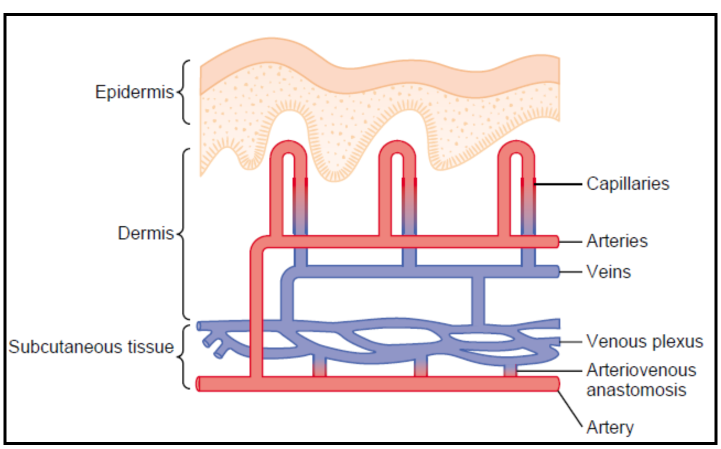


Figure 3: Distribution of artery, vein and capillaries in the epidermal layer of skin

Thermoregulatory adjustments involve local responses as well as more general reflex responses. When cutaneous blood vessels are cooled they become more sensitive to catecholamines and the arterioles and venules constrict. This local effect of cold directs blood away from the skin. Another heat-conserving mechanism that is important in animals living in cold water is heat transfer from arterial to venous blood in the limbs. The deep veins **(venae comitantes)** run alongside the arteries supplying the limbs and heat is transferred from the warm arterial blood going to the limbs to the cold venous blood coming from the extremities (**countercurrent exchange**). This keeps the tips of the extremities cold but conserves body heat.

Some common mechanism of regulation of loss of body heat are as discussed below:

- Curling up "in a ball" is a common reaction to cold in animals and has a counterpart in the position some people assume on climbing into a cold bed.
- Curling up decreases the body surface exposed to the environment.
- Shivering is an involuntary response of the skeletal muscles, but cold also causes a semiconscious general increase in motor activity.
- Examples include foot stamping and dancing up and down on a cold day.
- Increased catecholamine secretion is an important endocrine response to cold.

The reflex responses activated by cold are controlled from the posterior hypothalamus. Those activated by warmth are controlled primarily from the anterior hypothalamus. Stimulation of the anterior hypothalamus causes cutaneous vasodilation and sweating, and lesions in this region cause hyperthermia, with rectal temperatures sometimes reaching 43°C (109.4 °F). Posterior hypothalamic stimulation causes shivering, and the body temperature of animals with posterior hypothalamic lesions falls toward that of the environment.

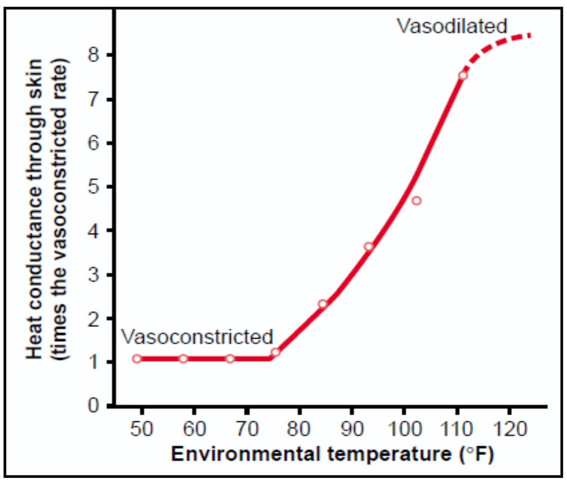


Figure 4: Effect of changes in the environmental temperature on heat conductance from the body core to the skin surface.

The hypothalamus is said to integrate body temperature information from sensory receptors (primarily cold receptors) in the skin, deep tissues, spinal cord, extrahypothalamic portions of the brain, and the hypothalamus itself. Each of these five inputs contributes about 20% of the information that is integrated. There are threshold core temperatures for each of the main temperature-regulating responses and when the threshold is reached the response begins. The threshold is 37 °C for sweating and vasodilation, 36.8 °C for vasoconstriction, 36 °C for non-shivering thermogenesis, and 35.5 °C for shivering. Humans tolerate body temperatures of 21–24 °C (70–75 °F) without permanent ill effects, and induced hypothermia has been used in surgery. On the other hand, accidental hypothermia due to prolonged exposure to cold air or cold water is a serious condition and requires careful monitoring and prompt re-warming.

Loss of heat:

The various methods by which heat is lost from the skin to the surroundings are shown in Figure 5. They include *radiation, conduction, convection* and *evaporation,* which are explained next.

A. **Radiation.**

- In a nude person sitting inside at normal room temperature, about 60 per cent of total heat loss is by radiation.
- Loss of heat by radiation means loss in the form of infrared heat rays, a type of electromagnetic wave.
- Most infrared heat rays that radiate from the body have wavelengths of 5 to 20 micrometers, 10 to 30 times the wavelengths of light rays.
- The human body radiates heat rays in all directions; if the temperature of the body is greater than the temperature of the surroundings, a greater quantity of heat is radiated from the body than is radiated to the body.

B. **Conduction.**

- Only minute quantities of heat, about 3 per cent, are normally lost from the body by direct conduction from the surface of the body to *solid objects,* such as a chair or a bed.
- Loss of heat by *conduction to air* represents a sizable proportion of the body's heat loss (about 15 per cent) even under normal conditions.
- Once the temperature of the air adjacent to the skin equals the temperature of the skin, no further loss of heat occurs in this way, because now an equal amount of heat is conducted from the air to the body.
- Therefore, conduction of heat from the body to the air is self-limited *unless the heated air moves away from the skin,* so that new, unheated air is continually brought in contact with the skin, a phenomenon called *air convection.*

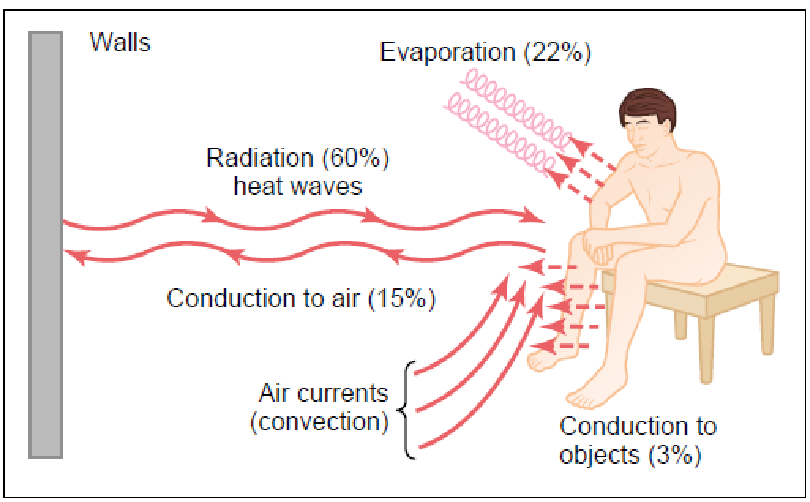


Figure 5: Different means of heat loss

C. **Convection.**

- The removal of heat from the body by convection air currents is commonly called *heat loss by convection.*
- The heat must first be *conducted* to the air and then carried away by the convection air currents.

- A small amount of convection almost always occurs around the body because of the tendency for air adjacent to the skin to rise as it becomes heated.
- In a nude person seated in a comfortable room without gross air movement, about 15 per cent of his or her total heat loss occurs by conduction to the air and then by air convection away from the body.

D. **Evaporation.**

- When water evaporates from the body surface, 0.58 Calorie (kilocalorie) of heat is lost for each gram of water that evaporates.
- Even when a person is not sweating, water still evaporates *insensibly* from the skin and lungs at a rate of about 600 to 700 ml/day.
- This causes continual heat loss at a rate of 16 to 19 Calories per hour; this insensible evaporation through the skin and lungs cannot be controlled for purposes of temperature regulation because it results from continual diffusion of water molecules through the skin and respiratory surfaces.
- As long as skin temperature is greater than the temperature of the surroundings, heat can be lost by radiation and conduction. But when the temperature of the surroundings becomes greater than that of the skin, instead of losing heat, the body gains heat by both radiation and conduction.
- Under these conditions, *the only means by which the body can rid itself of heat is by evaporation.* Therefore, anything that prevents adequate evaporation when the surrounding temperature is higher than the skin temperature will cause the internal body temperature to rise.
- Some mammals lose heat by **panting.** This rapid, shallow breathing greatly increases the amount of water vaporization in the mouth and respiratory passages and therefore the amount of heat lost. Because the breathing is shallow, it produces relatively little change in the composition of alveolar air

Remark: Occasionally, human beings are born with congenital absence of sweat glands. These people can stand cold temperatures as well as normal people can, but they are likely to die of heatstroke in tropical zones because without the evaporative refrigeration system, they cannot prevent a rise in body temperature when the air temperature is above that of the body.

Sweat Secretion:

The sweat gland is a tubular structure consisting of two parts:

(1) a deep subdermal *coiled portion* that secretes the sweat,

(2) a *duct portion* that passes outward through the dermis and epidermis of the skin.

As in many other glands, the secretory portion of the sweat gland secretes a fluid called the *primary secretion* or *precursor secretion;* the concentrations of constituents in the fluid are then modified as the fluid flows through the duct.

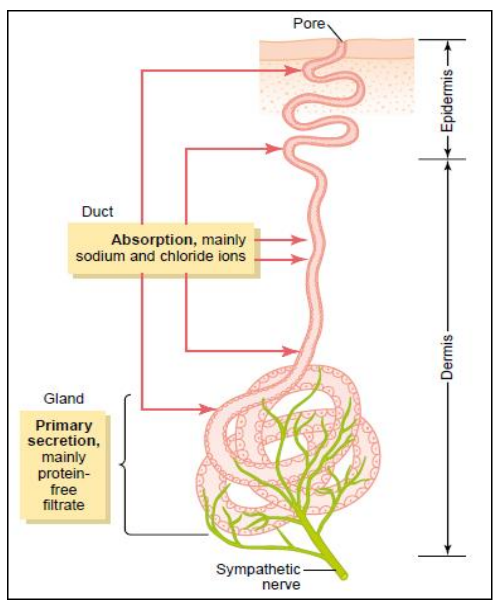
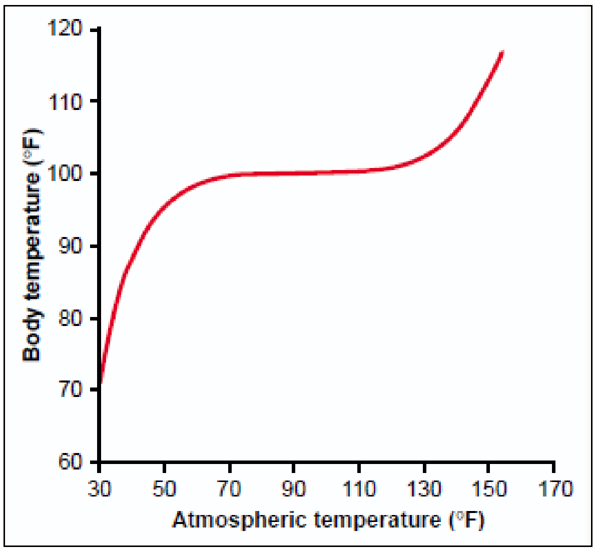


Figure 6: Structure of a sweat gland

Regulation of Body Temperature—Role of the Hypothalamus

In general, a nude person in dry air between 55° and 130°F is capable of maintaining a normal body core temperature somewhere between 97° and 100°F. The temperature of the body is regulated almost entirely by nervous feedback mechanisms, and almost all these operate through *temperature-regulating centers* located in the *hypothalamus.* For these feedback mechanisms to operate, there must also be temperature detectors to determine when the body temperature becomes either too high or too low. Figure7a depicts what happens to the body "core" temperature of a nude person after a few hours' exposure to *dry* air ranging from 30° to 160°F. The precise dimensions of this curve depend on the wind movement of the air, the amount of moisture in the air, and even the nature of the surroundings.

(a)


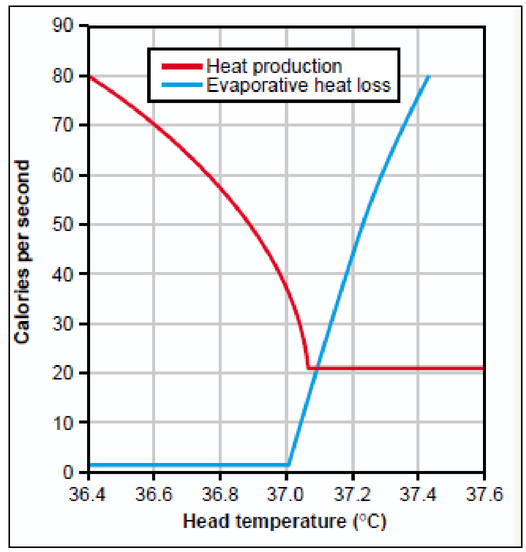
(b)


Figure 7: (a) Effect of high and low atmospheric temperatures of several hours' duration on the internal body "core" temperature; (b) the effect of hypothalamic temperature on evaporative heat loss from the body and on heat production caused primarily by muscle activity and shivering

Hypothalamic Stimulation of Shivering

Located in the dorsomedial portion of the posterior hypothalamus near the wall of the third ventricle is an area called the *primary motor center for shivering.* This area is normally inhibited by signals from the heat center in the anterior hypothalamic-preoptic area but is excited by cold signals from the skin and spinal cord.

- Therefore, as shown by the sudden increase in "heat production" (Figure 7b), this center becomes activated when the body temperature falls even a fraction of a degree below a critical temperature level.
- It then transmits signals that cause shivering through bilateral tracts down the brain stem, into the lateral columns of the spinal cord, and finally to the anterior motor neurons.
- These signals are non-rhythmical and do not cause the actual muscle shaking.
- Instead, they increase the tone of the skeletal muscles throughout the body by facilitating the activity of the anterior motor neurons.
- When the tone rises above a certain critical level, shivering begins. This probably results from feedback oscillation of the muscle spindle stretch reflex mechanism. During maximum shivering, body heat production can rise to four to five times normal.

Role of the Anterior Hypothalamic-Preoptic Area in Thermostatic Detection of Temperature

The anterior hypothalamic preoptic area has been found to contain large numbers of heat-sensitive neurons as well as about one third as many cold-sensitive neurons. These neurons are believed to function as temperature sensors for controlling body temperature.

- The heat-sensitive neurons increase their firing rate 2- to 10-fold in response to a 10°C increase in body temperature.
- The cold-sensitive neurons, by contrast, increase their firing rate when the body temperature falls.
- When the preoptic area is heated, the skin all over the body immediately breaks out in a profuse sweat, while the skin blood vessels over the entire body become greatly dilated.
- This is an immediate reaction to cause the body to lose heat, thereby helping to return the body temperature toward the normal level. In addition, any excess body heat production is inhibited.
- Therefore, it is clear that the hypothalamicpreoptic area has the capability to serve as a thermostatic body temperature control center.

Temperature-increasing mechanisms when the body is too cold

When the body is too cold, the temperature-control system device an opposite procedures:

- *Skin vasoconstriction throughout the body.* This is caused by stimulation of the posterior hypothalamic sympathetic centers.
- *Piloerection.* Piloerection means hairs “standing on end.” Sympathetic stimulation causes the arrector pili muscles attached to the hair follicles to contract, which brings the hairs to an upright stance. This is not important in human beings, but in lower animals, upright projection of the hairs allows them to entrap a thick layer of “insulator air” next to the skin, so that transfer of heat to the surroundings is greatly depressed.
- *Increase in thermogenesis (heat production).* Heat production by the metabolic systems is increased by promoting shivering, sympathetic excitation of heat production, and thyroxine secretion.

Temperature-decreasing Mechanisms when the body is too hot

The temperature control system uses three important mechanisms to reduce body heat when the body temperature becomes too great:

- *Vasodilation of skin blood vessels.* In almost all areas of the body, the skin blood vessels become intensely dilated. This is caused by inhibition of the sympathetic centers in the posterior hypothalamus that cause vasoconstriction. Full vasodilation can increase the rate of heat transfer to the skin as much as eightfold.
- *Sweating.* The effect of increased body temperature to cause sweating is demonstrated by the blue curve in Figure 8a, which shows a sharp increase in the rate of evaporative heat loss resulting from sweating when the body core temperature rises above the critical level of 37°C (98.6°F). An additional 1°C increase in body temperature causes enough sweating to remove 10 times the basal rate of body heat production.
- *Decrease in heat production.* The mechanisms that cause excess heat production, such as shivering and chemical thermogenesis, are strongly inhibited.

Set point:

At a critical body core temperature of about 37.1°C (98.8°F), drastic changes occur in the rates of both heat loss and heat production. At temperatures above this level, the rate of heat loss is greater than that of heat production, so the body temperature falls and approaches the 37.1°C level. At temperatures below this level, the rate of heat production is greater than that of heat loss, so the body temperature rises and again approaches the 37.1°C level. This crucial temperature level is called the “set-point” of the temperature control mechanism. That is, all the temperature control mechanisms continually attempt to bring the body temperature back to this set-point level.

Chemical thermogenesis

An increase in either sympathetic stimulation or circulating norepinephrine and epinephrine in the blood can cause an immediate increase in the rate of cellular metabolism. This effect is called *chemical thermogenesis.*

- It results at least partially from the ability of norepinephrine and epinephrine to *uncouple* oxidative phosphorylation, which means that excess foodstuffs are oxidized and thereby release energy in the form of heat but do not cause adenosine triphosphate to be formed.
- The degree of chemical thermogenesis that occurs in an animal is almost directly proportional to the amount of *brown fat* in the animal's tissues.
- This is a type of fat that contains large numbers of special mitochondria where uncoupled oxidation occurs; these cells are supplied with strong sympathetic innervation.

Role of thyroxin:

- Cooling the anterior hypothalamicpreoptic area also increases production of the neurosecretory hormone *thyrotropin-releasing hormone* by the hypothalamus.
- This hormone is carried by way of the hypothalamic portal veins to the anterior pituitary gland, where it stimulates secretion of *thyroid stimulating hormone.*
- Thyroid-stimulating hormone in turn stimulates increased output of *thyroxine* by the thyroid gland.
- The increased thyroxine increases the rate of cellular metabolism throughout the body (Figure 8), which is yet another mechanism of *chemical thermogenesis.*
- This increase in metabolism does not occur immediately but requires several weeks' exposure to cold to make the thyroid gland hypertrophy and reach its new level of thyroxine secretion.
- Exposure of animals to extreme cold for several weeks can cause their thyroid glands to increase in size 20 to 40 per cent.

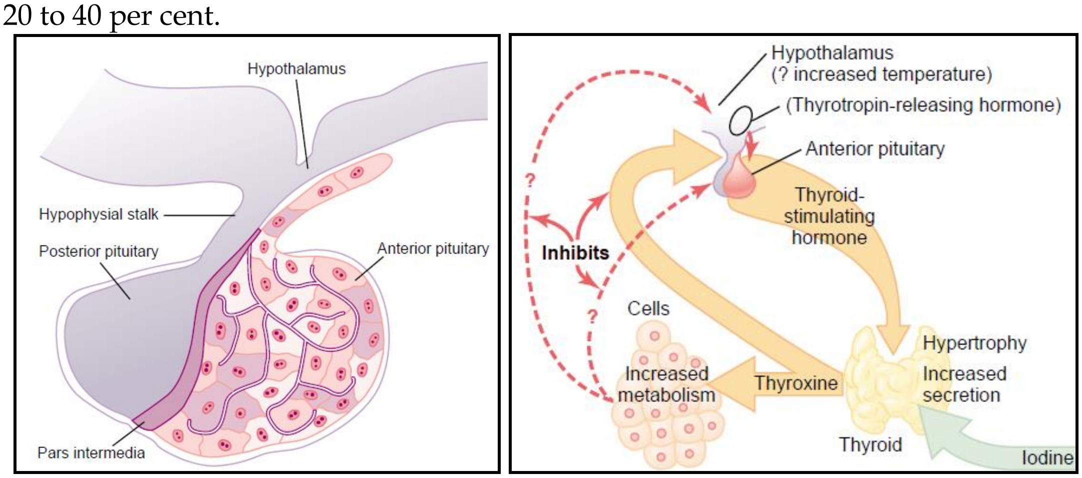


Figure 8 (a) Location of hypothalamus (b) mechanism of temperature regulation by thyroid-hypothalamus interaction

Behavioral control of temperature:

Aside from the subconscious mechanisms for body temperature control, the body has another temperature-control mechanism that is even more potent. This is *behavioral control of temperature,* which can be explained as follows:

- Whenever the internal body temperature becomes too high, signals from the temperature-controlling areas in the brain give the person a psychic sensation of being overheated.
- Conversely, whenever the body becomes too cold, signals from the skin and probably also from some deep body receptors elicit the feeling of cold discomfort.
- Therefore, the person makes appropriate environmental adjustments to re-establish comfort, such as moving into a heated room or wearing well-insulated clothing in freezing weather.

Effect of Pyrogens

Many proteins, breakdown products of proteins, and certain other substances, especially lipopolysaccharide toxins released from bacterial cell membranes, can cause the set-point of the hypothalamic thermostat to rise. Substances that cause this effect are called *pyrogens.*

- Pyrogens released from toxic bacteria or those released from degenerating body tissues cause fever during disease conditions.
- When the set-point of the hypothalamic temperature-regulating center becomes higher than normal, all the mechanisms for raising the body temperature are brought into play, including heat conservation and increased heat production.
- Within a few hours after the set-point has been increased, the body temperature also approaches this level, as shown in Figure 9.

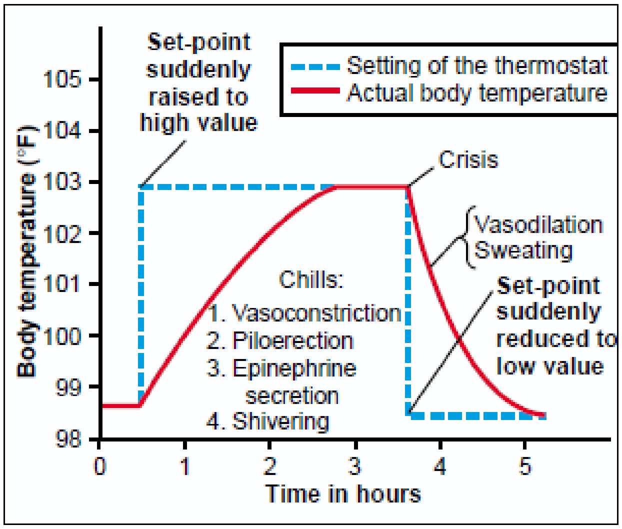


Figure 9: Effects of changing the set-point of the hypothalamic temperature controller

Role of Interleukin-1

Some pyrogens (e.g. *endotoxins* from gram-negative bacteria) function indirectly and may require several hours of latency before causing their effects.

- When bacteria or breakdown products of bacteria are present in the tissues or in the blood, they are phagocytized by the blood leukocytes, by tissue macrophages, and by large granular killer lymphocytes.
- All these cells digest the bacterial products and then release cytokine *interleukin-1*—also called *leukocyte pyrogen* or *endogenous pyrogen*—into the body fluids.
- The interleukin-1, on reaching the hypothalamus, immediately activates the processes to produce fever, sometimes increasing the body temperature a noticeable amount in only 8 to 10 minutes.
- As little as one ten-millionth of a gram of endotoxin lipopolysaccharide from bacteria, acting in concert with the blood leukocytes, tissue macrophages, and killer lymphocytes, can cause fever.
- It have suggested that interleukin- 1 cases fever by first inducing the formation of one of the prostaglandins, mainly prostaglandin E2, or a similar substance, which acts in the hypothalamus to elicit the fever reaction. When prostaglandin formation is blocked by drugs, the fever is either completely abrogated or at least reduced.
- This may be the explanation for the manner in which aspirin reduces fever, because aspirin impedes the formation of prostaglandins from arachidonic acid. Drugs such as aspirin that reduce fever are called *antipyretics.*

Reference:

1. Animal Physiology by Richard W. Hill, Gordon A. Wyse, Margaret Anderson
2. Eckert Animal Physiology
3. Guyton and Hall Textbook of Medical Physiology