Body Temperature Regulation
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OBJECTIVES:

1. List the body temperatures, high and low, at which temperature regulation is lost.
2. Distinguish between Fever and Hyperthermia.
5. Describe how heat input and heat output are regulated.
6. Describe the anatomical location and sensitivities of the temperature sensors.
7. Describe how skin and hypothalamic temperatures are combined to make appropriate responses to changes in core and skin temperature.
8. Describe the Set-Point theory of Body Temperature Regulation.
9. Describe how infections produce fevers.

I. INTRODUCTION AND OVERVIEW

The Physician and the Thermometer.

The normal constancy of body temperature and its deviation from this value produced by disease makes the measurement of body temperature one of the most common, non-invasive clinical procedures. In this lecture, we will try to examine the mechanisms which ensure precise body temperature regulation and then examine the mechanisms by which disease increases body temperature. We will begin by looking at the range of temperatures the body might obtain and the definition and measurement of what we mean by body temperature. Next we will examine briefly the mechanisms by which the body can gain or lose heat and how these mechanisms may be regulated. Finally, we examine the Set-Point theory of temperature regulation and how this accounts for the increase in body temperature associated with many bacterial and viral infections.

TWO NEW TERMS:

Poikilotherm - Describes a creature that allows its body temperature to vary with the environmental temperature.

Homeotherm - Describes a creature that tries to keep its body temperature constant despite variations in the environmental temperature.

Although Man is considered a homeotherm, He is actually a hybrid of sorts. He allows his surface (skin) temperature to vary while trying to keep his body core temperature constant.
II. OPERATIONAL RANGE OF BODY TEMPERATURE

Figure 1. Effect of core temperature on ability to respond to abnormal temperature.

Failure of Temperature Regulation has severe consequences. Note that the body only survives in a fairly narrow range of body temperatures as compared to the temperature ranges found in our environment. Between 95°F and 105°F (34 to 40°C) temperature regulation is not in jeopardy. Above 106°F (40°C) and below 84°F (34°C) temperature regulation is lost. (See Fig. 1). Too hot is more acutely dangerous than too cold, but don’t tell that to Arctic explorers.

III. BODY CORE TEMPERATURE

The temperature of mixed venous blood reflects the thermal status of all of the body tissues and is therefore, the best representation of the body core temperature. Since very little heat transfer takes place in the lungs and venous blood is well mixed as it enters the pulmonary artery, pulmonary arterial blood temperature is close to mixed venous blood temperature. Pulmonary arterial blood temperature is estimated by taking esophageal temperature at the level of the heart. This approach is often used during surgery.

IV. PRACTICAL MEASUREMENT OF BODY CORE TEMPERATURE

The next best estimate of core temperature is obtained by measuring rectal temperature, which is usually a few tenths of a degree centigrade higher than arterial blood temperature. Vaginal temperature is virtually identical to rectal temperature. Tolerated in infants but often causes discomfort in adolescents and adults.
Oral temperature, which tends to be 0.5-1.5° C below the prevailing rectal temperature, is most frequently used because this approach is well tolerated by patients.

Modern technology has brought the technique of measuring temperature by infrared radiation detection to the textbook and bedside. Today there are such instruments for reading body temperature from the radiation of heat from the capillary blood flow in the ear. This technique has the advantage of not requiring the conscious participation by the patient.

V. THE PRECISION AND POWER OF TEMPERATURE REGULATION

Body temperature is maintained within very narrow limits in the face of very wide ranges in the rate of heat gain or loss. This power is shown in the figure below which shows core (rectal) temperature of a naked individual exposed to the indicated temperatures for 3 hours.

![Figure 2](image.png)

Figure 2. Core temperature of naked individual after exposure to indicated temperature for 3 hours.

The **thermal neutral zone** is the ambient temperature range over which normal body temperature is achieved without activation of metabolic and evaporative processes. For a nude adult this zone is between 27° C and 33° C. For adults clad in a more socially acceptable manner and slightly more active, such as listening to this lecture, that range is lowered to **21 to 28° C**.

VI. TEMPERATURE IS A MEASURE OF HEAT CONTENT

Heat content is determined by the kinetic energy of the molecules of a body. To raise or lower temperature, energy must be added or reduced respectively. The relation between heat and temperature is given by the equation:
\[ H = M \times SH \times X \times T \]
\[ (Heat) = (mass) \times (specific\ heat) \times (absolute\ temperature) \]

The heat content of a 70 Kg man with a body temperature of 98.6° F (37° C) is:

\[ H = 70 \text{ Kg} \times 0.85 \text{ Kcal} \times \frac{273° + 37°}{\text{Kg} \times °T} \]

\[ H = 18,445 \text{ Kcal} \]

The point is that to keep temperature constant a balance between mechanisms by which the body gains heat and the body loses heat must be maintained.

VII. SOURCES OF HEAT INPUT (H_i)

A. Environment, e.g., Ambient temperature above body temperature.

Obviously this mechanism is greatly dependent on the external environment.

B. Metabolism - The major and constant source of heat gain by the body.

To appreciate how much energy must be added to the body to change core temperature consider the following problem: How long would it take for resting metabolism, which consumes 250 ml O_2/min, to raise core temperature 1°C?

You will need to know that 5 Kcal of heat are produced per L 0_2, consumed.

Using the relationship: \( H = M \times SH \times T \) given in section 6:

Increasing the temperature 1°C in a human weighing 70 Kg requires:

\[ H = 70 \times 0.85 \times 1 = 59.5 \text{ Kcal} \]

Resting metabolism produces heat at the rate of:

\[ 0.25 \text{ L O}_2/\text{min} \times 5 \text{ Kcal/L O}_2 = 1.25 \text{ Kcal/min} \]

To produce 59.5 Kcal at 1.25 Kcal/min would require 47.6 min (59.5/1.25).

Note: During exercise, O_2 consumption can be as high as 2.5 L/min. Therefore, 4.76 minutes of exercise at this rate would raise core temperature 1°C assuming no compensation takes place.
The point is that metabolism is a constant source of heat gain even at rest. It can become critical during exercise particularly if heat loss mechanisms are compromised.

VIII. MECHANISMS OF HEAT LOSS ($H_o$)

A. Radiation ($H_r$)

Physicists refer to this as black body radiation. Biophysically it is expressed as:

$$H_r = K_r A_r (T_s - T_e)$$

- $K_r$ = proportionality constant for radiation loss
- $A_r$ = skin area involved in radiant energy exchange
- $T_s$ = skin temperature
- $T_e$ = environmental temperature

Simply put, the rate of heat loss by radiation is proportional to exposed skin area and the temperature difference between skin and environment. Note this could be a source of heat gain in the appropriate environment.

B. Convection/Conduction ($H_c$)

Conduction occurs by direct contact and exchange of thermal energy by molecular collision. Convection implies movement. The usual sequence is conduction between the body and the layer of air in immediate contact with the skin. Then this layer moves either by thermal stirring or general air movement (wind) causing convection. This is the usual route of heat loss (~60%) in the thermal neutral zone. Again biophysically:

$$H_c = K_c A_c (T_s - T_a)$$

- $T_a$ = air temperature next to the skin
- $A_c$ = skin area involved in convection
- $K_c$ = proportionality constant for convection/conduction

C. Evaporation ($H_e$)

This is the process of sweating. It is potentially the greatest mechanism for heat loss. It is routinely activated in exercise but usually makes a minimal contribution in resting conditions. Of course there is always a little evaporative heat loss due to evaporation from the oral cavity but this is generally referred to as insensible loss as it plays no role in normal temperature regulation. Biophysically the relationship is similar but the parameters are slightly different:
He = K_c. A_w (pH_{2O_s} - pH_{2O_a})

K_c = proportionality constant for evaporative loss
A_w = area of wet skin
pH_{2O_s} = vapor pressure of water at skin temperature
pH_{2O_a} = vapor pressure of water in the ambient air

**IX. ADJUSTMENTS IN HEAT GAIN**

A. **Thyroid hormone**

The thyroid hormones T_3 and T_4 can increase metabolic rate and heat production as much as 10-25 per cent. In man, variations in thyroid hormone levels and adjustments in basal metabolism (generally by changing basal Na^+-K^+ ATPase levels) are generally chronic or adaptive responses. Levels are low in heat acclimation and elevated in cold adaptation. Interestingly, the cardiac myosin isoform changes from fast to slow in heat acclimation, probably in response to changes in thyroid hormone levels.

B. **Sympathetic nervous system**

In man an important method for increasing tissue metabolic rate is activation of sympathetic neurons innervating the beta receptors of many tissues, especially the lipolysis of the brown fat of adipose tissue. This response to the cold in man is well documented and can increase metabolic rate by as much as 25 per cent.

C. **Shivering**

Shivering is the most potent mechanism for increasing heat production. (Metabolic rate can increase up to 500 percent). Shivering is the rhythmic contraction of skeletal muscle. It is produced by skeletal muscle contractions which are interrupted by stretch induced inhibition of contraction. The response is organized from the posterior hypothalamus and involves alpha and gamma motor neurons. This is a semiconscious mechanism. Higher levels of neural activity can suppress it.

D. **Exercise**

This is of course a voluntary process. Stomping your feet and clapping your hands when you are cold are obvious examples.
X. ADJUSTMENTS IN HEAT LOSS

A. Conduction/Convection

The rate of heat loss by radiation and conduction/convection is proportional to $T_s$, skin temperature and exposed surface area. The mechanisms regulating heat loss by these routes involve both conscious and reflex levels mechanisms to regulate skin temperature. Consciously skin surface area is regulated by adding or removing clothing as appropriate. Skin temperature is regulated by regulating skin blood flow. As with shivering this response is organized from the posterior hypothalamus. Skin blood flow is regulated by changes in sympathetic tone. Increases in sympathetic tone decrease blood flow, decreases in sympathetic tone increase blood flow. In discussing blood flow a distinction is made between apical skin (fingers, hands, toes, feet, ears, nose, and lips) and nonapical skin (skin over the rest of the body).

In the cutaneous vasculature, branches from subcutaneous arteries penetrate the dermis and form an arterial plexus in the deep dermis. The vessels within this plexus run parallel to the surface and give rise to arterioles that penetrate to the subpapillary region, where a subpapillary plexus is formed. Here, capillaries connect to the subpapillary venous plexus and single capillary loops ascend to each papilla. The descending portion of the capillary loop ascend to each papilla. The descending portion of capillary loop joins the subpapillary venous plexus, which drains into the deeper cutaneous venous plexus. In apical regions of skin muscular arteriovenous anastomoses form non-nutrient connections between arterioles and venules. Arterioles, arteriovenous anastomoses, and venues all are innervated by the sympathetic nervous system. Only alpha receptors are seen in these vessels. The venous plexi contain variable amounts of blood which can be significant under extreme conditions. The arteries and veins run in parallel and close together which allows for some heat exchange between warm arterial blood and cooled venous blood. Blood flow is regulated by sympathetic tone. A decrease in tone increases flow through arterioles and, more important for temperature regulation increases arteriovenous shunting of blood to venous plexi. With these venous plexi close to the surface of the skin there is a heating of skin and an increase in heat loss by radiation, conduction/convection, and an assistance in evaporative loss of heat. (Warm skin evaporates water more rapidly than cold skin.) These anatomical arrangements are shown in Figs. 3 & 4.
Figure 3. Functional arrangement of skin vasculature.

B. **Heat loss by evaporation.**

The most effective method for producing heat loss is to evaporate water from the surface of the skin. The rate of evaporative heat loss depends upon exposed surface area, skin temperature, skin wetness, and ambient air relative humidity. Skin temperature is regulated as described above. Skin wetness is dependent upon the activity of sweat glands (exocrine glands) controlled by the sympathetic nervous system. This portion of the sympathetic nervous system is unique because the transmitter is acetylcholine. The receptor is muscarinic. Sweat glands form a primary secretion from which salts are reabsorbed as the secretion travels along the tubule leading to a pore as shown in Fig. 4. The evaporation of one liter of water removes 580 Kcal from the body. Under optimal conditions the body can evaporate about 1.5 liters of sweat per hour, which is about 12 times the basal rate of heat production.
C. Radiation

Heat loss (or gain) by radiation is most potently controlled consciously, i.e., adding or removing clothing or other garments to control the exposed surface area.

XI. THERMAL RECEPTORS

To maintain normal core temperature requires error sensors and appropriate adjustments in the rate of heat production and heat loss.

Two major classes of sensors have been identified: skin temperature sensors, and hypothalamic (core temperature) sensors.
A. **Skin Temperature Receptors**

Skin receptors show 3 peaks of activity:

![Graph showing relative firing rates of skin temperature sensors.](image)

Figure 5. Relative firing rates of skin temperature sensors.

B. **The anterior hypothalamus receptors**

The hypothalamic receptors show 2 areas of activity. Notice how much narrower the response range is for hypothalamic receptors. Some feel there are also thermal receptors in the great veins and thoracic cavity. They probably contribute but the hypothalamic ones seem to predominate.

![Graph showing relative firing rates of hypothalamic temperature sensors.](image)

Figure 6. Relative firing rates of hypothalamic temperature sensors.
XII. THE NOTION OF SET POINT

The information received from skin and hypothalamic sensors are compared to a set-point temperature in the hypothalamus.

Responses to information received from temperature sensors are organized within the preoptic/anterior hypothalamus. The diagram below, Fig. 7, shows temperature information coming into the hypothalamus from the skin and hypothalamus and being compared to set point temperature. If that information shows the sum of core and skin temperature to be below some preset, desired level known as the set point temperature, heat loss mechanisms are inactivated and heat production mechanisms activated. Heat production → shivering and increases in metabolic rate. Heat loss → vasodilation and sweating. To decrease heat loss there is active vasoconstriction. The circle shows that the temperature and set point information are algebraically summed. If the sum is 0, there is no response. If the sum is positive, i.e., if the sum of input, except set-point temperature, is below set-point temperature; heat conservation and heat production are initiated. If the sum is negative, heat production is inhibited and heat loss mechanisms are activated.

Figure 7. Integration of temperature information.

Abbreviations: AH - anterior hypothalamus, PH - posterior hypothalamus, SW - sweat, SH - shiver, VC - vasoconstriction, M - metabolism, R - reference point = set point

XIII. SET POINT CAN BE CHANGED BY EITHER PERIPHERAL OR CENTRAL INFORMATION

A. Peripherally

Decreases in skin temperature shift the set point temperature upward. This resetting seems to anticipate the central response to the stimulus. The body will react as if it is cold already, i.e., the normal body temperature is below the new set point. Shivering and cutaneous vasoconstriction will result.
You will see this result in lab. It is the basis of the cold pressor test for normal sympathetic neural activity.

B. **Centrally**

The most important example of central resetting of set point is exercise. The set point in exercise is centrally elevated to at least 39°, presumably to accommodate the tremendous increase in heat production due to the increased metabolic activity of the exercising muscles. Other central resetting influences are hormonal such as the change in body temperature during the female ovulation cycle and also the circadian clock whereby body temperature is lowered at night.

**XIV. SET POINT CAN ALSO BE CHANGED BY EXOGENOUS SIGNALS (PYROGENS)**

Fever is the situation where the set point is elevated such that body temperature is maintained at a higher level than normal. Fever accompanies some trivial and some very serious clinical conditions. Whatever the etiology, the pathophysiology of fever appears to be the same whenever fever occurs. The sequence is outlined below:

The role of the immune system in fever. The response of the body to an invasion by any foreign body or organism is to activate the immune system. The stepwise responses are:

A. Macrophages or B-lymphocytes phagocytize foreign organisms, virally infected cells, or tissue debris. Activation of these cells includes activation of the gene for interleukin-1 (IL-1). Also, IL-6 and IL-8 have recently been shown to have similar properties.

B. IL-1 diffuses into the vascular space and is carried by blood to the anterior hypothalamus. It is important to note that IL-1 is lipid soluble enough to penetrate the blood-brain barrier.

C. At the anterior hypothalamus phospholipase A₂ is activated by IL-1 and arachidonic acid is released from plasma membranes.

D. Cellular cyclooxygenase initiates a series of reactions which produce prostaglandins. One of these prostaglandins, prostaglandin E₂, is believed to be the agent which shifts the temperature set-point, in the anterior hypothalamus, to a higher than normal value.

E. The response of the body to this increase in set-point is to initiate responses which decrease heat loss (e.g., vasoconstriction) and increase heat production (e.g., shivering). When body temperature reaches this new
set-point temperature the body will maintain this temperature until the set point is returned to normal.

XV. **RESETTING THE SET POINT**

One obvious method for returning the set-point to normal is to eliminate the infection. A second method for returning the set-point temperature to normal is to stop the production of prostaglandin $E_2$. This is done clinically by inactivating cyclooxygenase, which can be done either by prescribing antipyretics such as acetylsalicylic acid (aspirin) or acetaminophen (e.g., Tylenol). Note: these drugs do not produce hypothermia, they merely return the set-point to normal.

XVI. **OTHER CONDITIONS OF LOSS OF PRECISE BODY TEMPERATURE REGULATION**

A. **Fever vs. Hyperthermia**

Many people use the term fever to describe any rise in body temperature. There is a physiological difference between fever and other hyperthermias. In all hyperthermias, body core temperature rises. Only in fever, however, is there no tendency for compensatory mechanisms to restore body temperature to a normal level. In fever body temperature is actively defended at the febrile level; exposure of a febrile patient to a cold environment will excite vasoconstriction and shivering even though body temperature is elevated. Moreover, the febrile patient consciously prefers a high body temperature and so feels cold when exposed to a cold environment, even though the thermometer shows him clearly to be hot. Physical cooling is an appropriate therapy in hyperthermias other than fever, but during fever cooling will be resisted physiologically and will distress the patient.

B. **Heat Exhaustion**

Excess sweating produces dehydration and vasodilation, which reduces blood volume, decreases unstressed volume and decreases cardiac output. The subject will be light-headed and feeling weak and may even experience symptoms as severe as syncope. The skin will be pale and clammy. There is usually no significant hyperthermia although body temperature will generally be in the 38° to 40° range (remember they were probably exercising too strenuously or in a hot environment). Placing the subject in a cool environment and administering water or fluids orally is usually sufficient therapy.

C. **Heat Stroke**

When large inputs of heat; e.g., during exercise in a hot environment,
produce core temperatures in excess of 40°C there is a risk of heat stroke. At core temperatures of above 42°C heat stroke is almost certain to take place. These high core temperatures destroy the function of the brain, liver, and other organs and death ensues rapidly. The severity of pathology depends upon the temperature of the core and the duration of the high core temperature. Treatment consists of rapid cooling. This needs to be done under supervision to avoid producing hypothermia. If supervision is not immediately available then application of water to naked skin and increased evaporation of the water by movement of air can be quite successful in reducing core temperature.

D. **Hypothermia**

Hypothermia is defined as a condition in which the core temperature is less than 35°C. At core temperatures of about 27°C respiration stops and death ensues if there is no external intervention. Hypothermia is more commonplace because ambient temperature is often far below core temperature. It is more frequency seen in the elderly patient.

**XVII. RECOMMENDED READING**


SAMPLE PROBLEMS

Instructions: Identify the correct answers (more than one may be correct).

1. A patient is observed to have cold wet skin. Which actions of the autonomic nervous system best account for this condition?
   A. increased parasympathetic activation of vascular beta receptors and increased activation of parasympathetic innervation of sweat glands
   B. decreased sympathetic activation of sweat glands and increased sympathetic activation of vascular beta receptors
   C. decreased parasympathetic activation of sweat glands and increased parasympathetic activation of vascular alpha receptors
   D. increased sympathetic activation of sweat glands and increased sympathetic activation of vascular alpha receptors

2. Which set of changes, all taken individually, could increase (body) core temperature?
   A. ↑ muscle contraction, ↑pH_{2}O_{s}, ↓pH_{2}O_{a}
   B. ↑ muscle contraction, ↓pH_{2}O_{s}, ↑pH_{2}O_{a}
   C. ↑ muscle contraction, ↓pH_{2}O_{s}, ↓pH_{2}O_{a}
   D. ↓ muscle contraction, ↓pH_{2}O_{s}, ↓pH_{2}O_{a}
   E. ↓ muscle contraction, ↓pH_{2}O_{s}, ↑pH_{2}O_{a}

   Where pH_{2}O_{s} = partial pressure of water at the skin and pH_{2}O_{a} = partial pressure of water in ambient air.

3. An increase in skin temperature increases heat loss (either directly or indirectly) by?
   A. radiation
   B. convection
   C. evaporation
   D. pyrogens

4. A patient is observed to stop shivering. This could be due to which of the following changes?
   A. A decrease in air temperature
   B. An increase in hypothalamic temperature
   C. An increase in interleukin-1
   D. Administration of a cyclooxygenase inhibitor
ANSWERS

1. D (cold implies low skin blood flow, hence arteriolar vasoconstriction via α1-receptor activation and wet implies sweating, hence sympathetic cholinergic activation of the sweat glands)

2. B (↑ muscle contraction means ↑metabolism and hence heat, the other factors deal with evaporative heat loss which is to be minimized by ↓ in the gradient for heat loss, i.e., ↓pH₂Os, ↑pH₂0a)

3. A, B, C (hopefully obvious)

4. B, D (If a person is shivering, one should assume the body temperature is less than the set point. If the shivering stops, one assumes the body temperature has risen to the set point OR that the set point has fallen down to the body temperature. Options A and C raise the set point while option D lowers it albeit not below normal. Option B would activate the central thermoreceptors so that the body would think it is warm, not cold, and stop shivering.)