General physiology
Lecture 39
Body Temperature Regulation
Mechanism of Fever

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Objectives

• Define core temperature and skin temperature comment on the differences in temperature in the hypothalamus, rectum, oral cavity, and skin.
• List and define the four mechanisms of heat transfer from the skin to the environment.
• Explain the feedback control of internal body temperature.
• Understand the short-term response to cold (to increase heat production and minimize heat loss) and heat (to decrease heat production and maximize heat loss).
• Describe the adaptations to cold and warm environments.
• Understand the mechanisms of fever.
Heat input and output.
Central core surrounded by an outer shell. Internal core temperature is homeostatically maintained.
Central core and outer shell temperature

- **Central core** The temperature within the central core, which consists of the abdominal and thoracic organs, the central nervous system, and the skeletal muscles, generally remains fairly constant.

- **Outer shell** The skin and subcutaneous fat constitute the In contrast to the constant high temperature in the core, the temperature within the shell is generally cooler and may vary substantially.

- Although core temperature varies daily with circadian rhythm and monthly in women, core body temperature of deep tissues is relatively constant, varying less than 1 degree F (+0.6 C).

- Skin Temperature - varies widely, depending on temperature of environment.
Core body temperature refers to the temperature of the internal environment of the body. This includes organs such as the heart and liver, and the blood.

Core Temperature - temperature of deep tissues is relatively constant, within ±1°F (±0.6°C) under normal conditions except when a person develops a febrile illness.

A nude person can be exposed to temperatures as low as 55°F (12.8°C) or as high as 130°F (55°C) in dry air and still maintain an almost constant core temperature.

Skin Temperature - varies widely, depending on temperature of environment.
Body temperature

• **Normal Core Temperature.** No single core temperature can be considered normal because measurements in many healthy people have shown a range of normal temperatures measured orally.

• Range of oral temp Lowest 97°F (36°C) to greater than 99.5°F (37.5°C).

• The average normal core temperature is generally considered to be between 98.0°F and 98.6°F when measured orally and about 1°F (0.6°C) higher when measured rectally.
Normal Body Temperature

• The rectal temperature is representative of the temperature at the core of the body and varies least with changes in environmental temperature.

• The oral temperature is normally 0.5°C lower than the rectal temperature, but it is affected by many factors, including ingestion of hot or cold fluids, gum chewing, smoking, and mouth breathing.

• Various parts of the body are at different temperatures, and the magnitude of the temperature difference between the parts varies with the environmental temperature. The extremities are generally cooler than the rest of the body.

• The temperature of the scrotum is carefully regulated at 32°C.
Estimated range of body “core” temperature in normal people

<table>
<thead>
<tr>
<th>Oral</th>
<th>Rectal</th>
</tr>
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<tbody>
<tr>
<td>96°F</td>
<td>36°C</td>
</tr>
<tr>
<td>98°F</td>
<td>37°C</td>
</tr>
<tr>
<td>100°F</td>
<td>38°C</td>
</tr>
<tr>
<td>102°F</td>
<td>39°C</td>
</tr>
<tr>
<td>104°F</td>
<td>40°C</td>
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- **Usual range of normal**
  - Oral: 98°F to 100°F
  - Rectal: 37°C to 38°C

- **Usual range of normal**
  - Oral: 96°F to 98°F
  - Rectal: 36°C to 37°C

- **Early morning**
  - Oral: 96°F
  - Rectal: 36°C

- **Early morning**
  - Oral: 98°F
  - Rectal: 37°C

- **Cold weather, etc.**
  - Oral: 98°F
  - Rectal: 37°C

- **A few normal adults**
  - Oral: 99°F to 100°F
  - Rectal: 38°C to 39°C

- **Many active children**
  - Oral: 98°F to 99°F
  - Rectal: 37°C to 38°C

- **A few normal adults**
  - Oral: 100°F to 101°F
  - Rectal: 38°C to 39°C

- **Many active children**
  - Oral: 99°F to 100°F
  - Rectal: 38°C to 39°C

- **Emotion or moderate exercise**
  - Oral: 100°F to 102°F
  - Rectal: 38°C to 39°C

- **Hard exercise**
  - Oral: 101°F to 104°F
  - Rectal: 39°C to 40°C

(Adapted from Dubois EF: Fever, Springfield, Ill: Charles C Thomas, 1949.)
Factors affecting body temp

- Food ingestion
- Emotion if there is increase in NE
- Thyroid hormone release
- Menstruation and Pregnancy: that core temperature averages 0.9°F (0.5°C) higher during the last half of the cycle from the time of ovulation to menstruation
- Time of the day
- Fasting.
- Sleep
- The extremities are generally cooler than the rest of the body.
- The temperature of the scrotum is regulated at 32°C
- Exercise
- Age: Older is colder The elderly naturally have lower temperatures with a midday average of 97.7°F (36.4°C).
- Temperature regulation is less precise in young children and they may normally have a temperature that is 0.5°C or so above the established norm for adults.
There is a diurnal variation in body temperature

Figure 14–21. Typical temperature chart of a hospitalized patient who does not have a febrile disease. Note the slight rise in temperature, due to excitement and apprehension, at the time of admission to the hospital, and the regular circadian temperature cycle.
Heat Production

1. Muscular activity including shivering
2. Basic metabolic processes
3. Food intake (specific dynamic action)
4. Thyroxine (and, to a less extent, other hormones, such as growth hormone and testosterone) on the cells
5. Epinephrine, norepinephrine, and sympathetic stimulation
Heat Loss

• Heat is transferred from the deeper organs and tissues to the skin, where it is lost to the air and surroundings.

• Rate at which heat is lost is determined almost entirely by two factors:
  • (1) how rapidly heat can be conducted from where it is produced in the body core to the skin
  • (2) how rapidly heat can then be transferred from the skin to the surroundings.
Mechanisms of heat loss from the Body to the surrounding

Body heat is dissipated by:
- Radiation
- Conduction and convection
- Evaporation of sweat
- Nonsensible evaporation
- Respiration
- With urine and feces
Mechanisms of heat loss From the Body to the surrounding

Direction of arrows denotes direction of heat transfer

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.
Mechanism of heat loss

• **Radiation** is the emission of heat to and from the skin by electromagnetic waves—the rate of the temperature transfer by radiation is proportional to the temperature difference between the body surface and the environment.

• **Conduction** is intermolecular thermal heat transfer and usually occurs between the skin and air. One loses heat more rapidly when immersed in water because conduction between the skin and water is faster than that between skin and air.

• **Convection** is the loss or gain of heat by the movement of air or water over the body. Because heat rises, air carries heat away from the body by convection.

• **Evaporation** of water from the skin and the respiratory tract can carry a large amount of heat generated by the body because of the amount of heat required to transform water from the liquid to the gas phase.
Cutaneous circulation and role of skin blood flow in temperature regulation

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,

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

8-fold difference in heat conduction between maximum dilation and maximum constriction
Summary of temperature-regulating mechanisms beginning with peripheral and central thermoreceptors
How Is Body Temperature Detected?
Role of the hypothalamus

• Hypothalamus temperature control center
  - Preoptic area of anterior hypothalamus
  - Heat sensitive and cold sensitive neurons

• Skin and deep body temperature receptors
  - Mainly detect cold and cool temperatures
  - Function to prevent hypothermia

• Role of posterior hypothalamus
  - Receives input from anterior hypothalamus and peripheral temp receptors to elicit mainly heat producing and heat conserving reactions
Temperature Decreasing Mechanisms when the body is too hot

- **Vasodilation** - transfers heat to skin
  - Inhibition of sympathetic centers in posterior hypothalamus that cause vasoconstriction

- **Sweating** - evaporative heat loss
  - Stimulation of preoptic area of hypothalamus stimulates sweating via sympathetic *cholinergic* fibers
  - Circulating Epi and NE specially during exercise

**Decreased heat production** The mechanisms that cause excess heat production, such as shivering and chemical thermogenesis, are strongly inhibited
Temperature Increasing Mechanisms When the Body Is Too Cold

- **Vasoconstriction** -
  - Impedes heat transfer to skin
  - Stimulation of sympathetic centers in posterior hypothalamus
- **Piloerection** - usually not important in humans
- **Increased heat production** -
  - Shivering Synchronous, rhythmic contractions of antagonistic muscles
  - None shivering thermogenesis
  - Sympathetic stimulation
  - Increase levels of NE and Epi
  - Increased level of Thyroxine specially during long term exposure to cold
Skin temperature

Peripheral thermoreceptors (In skin)

Core temperature

Central thermoreceptors (In hypothalamus, other areas of CNS, and abdominal organs)

Hypothalamic thermoregulatory integrating center

Behavioral adaptations

Motor neurons

Skeletal muscles

Muscle tone, shivering

Control of heat production or heat loss

Control of heat production

Sympathetic nervous system

Skin blood vessels

Skin vasoconstriction and vasodilation

Control of heat loss

Sympathetic nervous system

Sweat glands

Sweating

Control of heat loss
Concept of a “Set-Point” for Temperature Control

- A critical body core temperature of about 37.1°C (98.8°F)
- This crucial temperature level is called the “set-point” of the temperature control mechanism.
- All the temperature control mechanisms continually attempt to bring the body temperature back to this set-point level.
Pyrogens

• **Pyrogens** are circulating factors that cause fever.

• Although some bacteria release

• **exogenous pyrogens** such as **lipopolysaccharides (endotoxins)**, the unifying cause of fever during infection is the release of small proteins called **endogenous pyrogens** from macrophages and other immune cells. Macrophages activated during infection are an integral part of the immune response.

• Examples of endogenous pyrogens are **cytokines** such as the **interleukins** and **tumor necrosis factor**.

• These endogenous pyrogens can activate vagal afferents to the hypothalamus, and can also circulate to the brain to directly alter the hypothalamic set point for temperature.

• Since these pyrogens are peptides, they must be able to signal the hypothalamus despite the existence of the **blood–brain barrier**.
Fever - Resetting the Set-point

• **Pyrogens can directly reset set-point** -
  - Bacteria - lipopolysaccharides are pyrogens
  - Pyrogens from degenerating tissues

• **Pyrogens can indirectly reset set-point** -
  - Interleukin-1 released from phagocytes following phagocytosis of blood-borne pyrogens
  - IL-1 raises set-point by increasing prostaglandin production (mainly E$_2$)
Host-defense response and pathogenesis of fever.
Production of fever

Exogenous pyrogens such as lipopolysaccharides from infecting organisms

Endogenous pyrogens such as IL-1β, IL-6 and TNF are released by leukocytes

Local release of prostaglandin E₂ and thromboxanes

Temperature set-point

Hypothalamic “integrative center”

Cutaneous thermoreceptors

Ambient temperature

Facilitory motor pathways

Sympathetic adrenergics

Sympathetic cholinergics

↑ Shivering & metabolic heat production

↓ Cutaneous blood flow

↓ Sweat production

↑ Body heat content

FEVER

↓ Heat loss to environment

Environment around the body
Pathogenesis of Fever

Endotoxin
Inflammation
Other pyrogenic stimuli

Monocytes
Macrophages
Kupffer cells

Cytokines

Preoptic area of hypothalamus

Prostaglandin E2,

Prostaglandins

Raise temperature set point

FEVER
Time Course of Fever

Set-point suddenly raised to high value

Chills:
1. Vasoconstriction
2. Piloerection
3. Epinephrine secretion
4. Shivering

Crisis

Vasodilation Sweating

Set-point suddenly reduced to low value

Body temperature (°F)

Time in hours
Heat Acclimatization

• Improves response to heat in a few days, most gains within 10 days
  • ↑ plasma volume (Increase blood volume)
  • Increase stroke volume
  • Decrease resting heart rate
  • Decrease metabolic heat production
  • Sweat sooner, more, and with less sodium
• ↑ in the maximal rate of sweating (1.5L/h to 4L/h)
• ↓ loss of salt in the sweat and urine (↑ in Aldosterone)
• Skin vasodilates more quickly
Sweat gland innervated by an Acetylcholine – secreting Sympathetic nerve

• 1L of water evaporated from skin surface can lead to heat loss of 580 kcal

• Increase sweat production in non acclimatize person cause significant loss of Nacl when exposed to hot weather

• Rate of sweat production can vary from 0 to 1.5 L/h

• Acclimatization occurs after 1-6 weeks, sweating is increased but sodium loss is minimized due to the action of aldosterone which increase Na reabsorption by the ducts of sweat glands
Body temperature under different conditions

Temperature regulation seriously impaired

Temperature regulation efficient in febrile disease, health, and work

Temperature regulation impaired

Temperature regulation lost

°F
114
110
106
102
98
94
90
86
82
78
74
°F
44
42
40
38
36
34
32
30
28
26
24
°C
Upper limit of survival?
Heatstroke
Brain lesions
Fever therapy
Febrile disease and hard exercise
Usual range of normal
Lower limit of survival?

(Redrawn from DuBois EF: Fever. Springfield, Ill: Charles C Thomas, 1940.)
Heat Stroke

- Heat stroke occurs when body temperature rises above 106-108°F
  - Malfunction of preoptic temperature control center –
  - sweating ceases
  - Rising body temperature increases metabolism) which generates more heat (vicious cycle)
Heatstroke symptoms include

• **High body temperature.** A body temperature of 104 F (40 C) or higher is the main sign of heatstroke.

• **Altered mental state or behavior.** Confusion, agitation, slurred speech, irritability, delirium, seizures and coma can all result from heatstroke.

• **Alteration in sweating.** In heatstroke brought on by hot weather, your skin will feel hot and dry to the touch. However, in heatstroke brought on by strenuous exercise, your skin may feel moist.

• **Nausea and vomiting.** You may feel sick to your stomach or vomit.
Heatstroke

• **Flushed skin.** Your skin may turn red as your body temperature increases.

• **Rapid breathing.** Your breathing may become rapid and shallow.

• **Racing heart rate.** Your pulse may significantly increase because heat stress places a tremendous burden on your heart to help cool your body.

• **Headache.**
Heat Exhaustion

Due to circulatory problems:
- Excessive loss of salt and water due to severe sweating
- Heat cramps
- Vasodilation
- Venous return compromised
- Circulatory collapse
- **Body temperature may not be very high**
  (symptoms: weakness, vertigo, headache, vomiting)
- Common in Elderly
- Athletes and soldiers when doing heavy exercise in hot and humid environment
- Persons taking drugs that inhibit sweating and/or vasodilation e.g. atropine, scopolamine, phenothiazides, MAO inhibitors
Exposure of body to extreme cold

- If body temperature falls below 85°F temperature regulation is lost to depression of neurons in the hypothalamus.
- Frostbites exposure of body to very cold temperatures cause freezing of exposed surface areas.
- Circulatory impairment.
- Gangareen following thawing.
- Local vasodilatation may help to prevent frostbites, however is not far not well developed in humans compared to lower animals.