PATHOPHYSIOLOGY OF HEAT EXCHANGE

FEVER is a universal typical protective and compensatory reaction to pyrogens developed in the course of evolution.

It is characterized by an increase in body temperature as a result of changes in the activity of thermoregulation centers under the influence of pyrogenic substances.

The occurrence of fever
does not depend on the ambient temperature,
there is no violation of thermoregulation processes,
but the activity of the thermoregulation center changes (the setting point of temperature homeostasis is shifted).

CLASSIFICATION OF OF FEVER‘S TYPES

By the degree of temperature rise:

1. subfebrile (up to 38°C),
2. febrile (38-39°C),
3. pyretic (39-41°C),
4. hyperpyretic (above 41°C).

According to the etiology:

1. infectious,
2. non-infectious.

Fever occurs under the influence of pyrogenic substances.

They are divided into two groups:

- exogenous pyrogens (primary),
- endogenous pyrogens (secondary, cell-tissue, fever mediators).

The cause of infectious fever

is exogenous pyrogens of microorganisms (pyrogenic substances that are released by microorganisms during their vital activity and destruction).

By their structure – lipopolysaccharides.

Exogenous pyrogens can't raise the temperature on their own. The formation of endogenous pyrogens is necessary.

Non – INFECTIOUS FEVERS-occur under the influence of the following factors:

- aseptic processes (damage, inflammation) – injuries, hemorrhages.
- introduction of protein solutions;
- introduction of salt solutions;
- introduction of oil emulsions;
- the introduction of a cleaned pyrogen-free (drug pirogenal).

The development of fever is associated with migration to the lesion of white blood cells and the formation of endogenous pyrogens.

Endogenous pyrogens are not contained in the body in the finished form.

They are formed in the human body under the influence of:

- exogenous pyrogens;
- immune complexes;
- mediators of inflammation;
- toxins;
- products of tissue necrosis, including tumors;
- hormones.

Sources of endogenous pyrogens are phagocytes, for example, white blood cells (granulocytes, monocytes, resident macrophages of internal organs), as well as glial cells.

By their structure, endogenous pyrogens are proteins that do not have species specificity and quickly cause an increase in body temperature.

REPRESENTATIVES OF ENDOGENOUS PYROGENS

1. Leukocyte pyrogen – released by neutrophils and monocytes.
2. Interferon-alpha is released by lymphoblasts stimulated by viruses. Immunomodulator, antitumor and antiviral effect.

3. Interleukin-1 is released by macrophages and lymphocytes. In addition to pyrogenic activity, it has the following properties:

- it stimulates protein synthesis in the liver;
- stimulates the processes of proliferation, regeneration;
- activates the hypothalamic-pituitary-adrenal system;
- activates the slow sleep phase;
- reduce appetite;
- participates in the mechanisms of muscle pain;
- stimulates the phagocytic activity of white blood cells;
- activates the immune system;
- it can destroy tumor cells.

PATHOGENESIS OF FEVER

EXOGENOUS PYROGENS

↓

PYROGENIC CYTOKINES

↓

PREOPTIC ZONE OF THE HYPOTHALAMUS

↓

ACTIVATION of phospholipase A2

aspirin → (inhibits)

↓

INCREASED ACTIVITY OF CYCLOOXYGENASE

↓

INCREASING PGE2

↓

ACTIVATION OF ADENYLATE CYCLASE

↓

Increasing cAMP

↓

increased activity of cAMP-dependent protein kinases

↓

REDUCING THE THRESHOLD OF EXCITABILITY OF COLD NEURONS

The TEMPERATURE INCREASE in fever is associated with the predominance of **heat production** processes

(increased muscle tone,

muscle tremors,

increased oxidative processes,

narrowing of peripheral blood vessels)

over heat transfer processes.

The course of the febrile reaction is also influenced by other biologically active substances – fever modulators (they do not cause fever themselves, but change the sensitivity of the hypothalamus to endogenous pyrogens):

- thyroxine, progesterone – increase the intensity of fever;
- glucocorticoids – reduce the intensity.

ANTIPYRETIC SYSTEM

Serves to prevent excessive temperature rise (above 41°C).

The activation of this system occurs under the influence of interleukin-1.

1. Activation of the renin – angiotensin system in the hypothalamus.
2. Hyperactivity of the a - adrenoreactive systems of the hypothalamus.
3. Glucocorticoids:

a) reduce the synthesis of endogenous pyrogens;

b) increase proteolytic destruction of endoperoxides;

c) reduce the formation of mediator protein in the hypothalamus;

d) reduce the formation of arachidonic acid;

4. Oxytocin, ACTH, alpha melanostimulating hormone:

a) inhibit the synthesis of interleukin-1

b) reduce the permeability of the blood-brain barrier to endogenous pyrogens.

Protective and compensatory value of fever

• fever increases the immune response of the body due to the activation of T - and B-lymphocytes, accelerating the conversion of the latter into plasma cells, which stimulates the formation of antibodies; interferon formation increases;

• a moderate rise in body temperature can activate the function of phagocytic cells and NK cells (natural killer cells);

• activates the enzymes that inhibit the reproduction of viruses;

• slows down the reproduction of many bacteria and reduces the resistance of microorganisms to drugs;

• increase barrier and antitoxic functions of the liver;

• hepatocytes intensively produce acute phase proteins; some of these proteins bind bivalent cations necessary for the reproduction of microorganisms;

• in addition, an increase in body temperature with fever is often the first and only sign of any disease, this is an alarm signal.

Negative effects of fever on the body

- stimulation of heart function, which can lead to the development of an overload form of heart failure, especially in the elderly and senile, as well as in patients who have previously had a particular heart disease.
- the possibility of collapse with a critical decrease in body temperature in the final stage of fever.
- in high-grade fever, immune responses may be suppressed. Moderate fever has been found to increase the survival rate of infected animals, while excessively high fever increases mortality.
- children with high fever may develop seizures, which are not always eliminated by taking antipyretic medications. At temperatures above 41 °C children may develop brain edema or acute circulatory failure due to lability of water-salt metabolism.
- long-term febrile patients (with tuberculosis, brucellosis, sepsis) are usually in a state of severe exhaustion and weakening of vital functions. Of course, in infectious diseases, disorders are caused not only by the action of high temperature, but also by microbial toxins.

HYPERTHERMIA is a pathological process characterized by an increase in body temperature without the participation of pyrogenic substances.

Classification of HYPERTHERMIA:

1. EXOGENOUS – overheating associated with the receipt of a large amount of heat from the environment.
2. ENDOGENOUS – an increase in temperature due to the body's own heat.

Exogenous hyperthermia is a pathological process in which an increase in body temperature is associated with an increase in heat input to the body from the environment and/or as a result of a delay in excess heat in the body due to difficulty in releasing it to the environment due to a violation of thermoregulation.

THE PATHOGENESIS OF OVERHEATING

Stage 1 – adaptations.

The mechanisms of thermoregulation are maximally strained (increased heat output to the environment) – sweating, peripheral vascular dilation, tachypnoe, tachycardia, acceleration of blood flow. BODY TEMPERATURE IS NOT ELEVATED.

Stage 2 – compensation.

The thermoregulation center is disrupted. The evaporation process is disrupted, blood thickens, blood pressure drops, electrolytes are lost, and tachypnea is pronounced. Heat transfer mechanisms become ineffective and turn from sanogenetic to pathogenetic. Hypoxia occurs. BODY TEMPERATURE RISES.

Stage 3 – inhibition (comatose state) – the respiratory and vasomotor centers are disrupted due to hypoxia and accumulation of toxic products.

Endogenous hyperthermia

- with damage to the thermoregulation center;
- with an increase in heat production – pathological contractile thermogenesis, dissociation of oxidation and phosphorylation;
- with a decrease in heat transfer processes – persistent vascular spasm with excessive production of catecholamines, reduced sweating with atropine poisoning.

DIFFERENCES BETWEEN FEVER AND OVERHEATING

FEVER

- is associated with the action of endogenous pyrogens
- the work of the thermoregulation center is not disturbed and is aimed at retaining heat in the body
- - antipyretics reduce body temperature
- carries mainly elements of protection
- formed by the end of 1 year of life
- begins with chills

OVERHEATING

- due to the action of excess heat
- , the work of the thermoregulation center is disrupted, aimed at removing heat from the body
- antipyretics do not reduce body temperature
- carries mainly elements of damage
- can occur at any age
- begins with hyperemia, increased sweating

QUESTIONS FOR SELF-KNOWLEDGE

1. Classification of hyperthermia.
2. The definition of overheating. The reasons and conditions of occurrence of overheating.
3. does the body temperature increase in the 1st stage of overheating?
4. What is the mechanism of thermoregulation disorders in the 2nd stage of overheating?
5. What is the difference between overheating from a fever?
6. How do you understand the role of the cold factor in the etiology of the disease?
7. Where is artificial hypothermia used and What is the essence of its use in medicine?
8. causes of non-infectious and infectious fevers?
9. Explain the mechanism of fever fever.

10. What type of fever is an increase in body temperature that Occurs after the introduction of purified pyrogenic substances?
11. does the temperature increase in fever depend on the ambient temperature?
12. Whether in febrile body's ability to regulate heat?
13. Do the pyrogenic activity of viruses?
14. do animals still have the ability to get feverish when the cortex is Removed?
15. What are exogenous pyrogens? Describe the mechanism of their action.
16. What mechanisms ensure a decrease in body temperature at the stage of temperature decline?
17. does fever always have a positive value?
18. What are the age-related features of the febrile reaction?
19. List the components of the antipyretic system, its role.
20. What is the essence of antipyretic therapy?

INDEPENDENT WORK OF STUDENTS IN THE CLASSROOM

Experiment.

objective: to evaluate the effect of anesthesia on the course of fever in rats.

Method: in two rats, measure the rectal temperature after fixing them to the table with their belly up. Then one of them intraperitoneally enter 1% solution of sodium ethaminal in an amount of 0.7 - 0.9 ml. After the onset of sleep in the animal, both rats should be injected intraperitoneally with 4 ml of pyrogenal. In the future, measure the temperature in both rats 15-30-45-60 minutes after the introduction of pyrogenal.

TASKS

1. an increase in body temperature in an experimental animal can be caused in various ways. What forms of heat transfer disorders develop when using the methods listed below? Explain the mechanisms of temperature increase in each case:

1) intramuscular administration of turpentine, 2) intravenous administration of broth culture of hemolytic Streptococcus, 3) subcutaneous administration of caffeine solution, 4) intramuscular administration of pyrogenal, 5) intravenous administration of dinitrophenol. 6) subcutaneous administration of a large dose of epinephrine, 7) intravenous administration of thyroxine.

2. two rabbits were subcutaneously injected with turpentine. Will there be differences in the intensity of the febrile reaction in rabbits if one of them is healthy and the other has severe granulocytopenia? Explain the answer.

3. an Intact rabbit and a rabbit with experimental thyrotoxicosis were injected with pyrogenal. Will there be differences in the feverish response in animals? Explain the answer.

4. two rabbits were injected with pyrogenal. Will the same intensity of fever occur in animals if one rabbit is intact, and the second one was previously repeatedly injected with glucocorticoids? Explain.

5. a 32-year-old Patient suddenly developed a severe headache, weakness, muscle pain, nasal congestion, and chills. Body temperature quickly rose to 39.20 C. The doctor who was called to the house diagnosed the flu. What is the mechanism of fever in this case? Name the types of fevers.

6. The patient with a chemical burn of the esophagus before planned operation was assigned parenteral nutrition. After intravenous administration of 10% albumin solution, the patient's body temperature temporarily increased (up to 37.60 C). Name the form of heat transfer disturbance. Explain the mechanism of temperature rise.

7. A hot shop worker working in an airtight suit has a sharp increase in body temperature. The examination revealed redness and abundant moisture of the skin, frequent shallow breathing, tachycardia, increased blood pressure. What is the name of this pathological process? Specify its stage. Identify the cause and conditions that contribute to the development of the process.