THE PATHOPHYSIOLOGY OF FEVER. CHARACTERISTIC FEATURES OF CHILDREN

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https://doi.org/10.5281/zenodo.11094609

Abstract*. Fever plays an important role in fighting infections, and although it can be inconvenient, it does not require treatment in a child who does not have other diseases. Some studies even show that lowering the temperature can prolong some diseases. However, fever increases the metabolic rate and the load on the cardiopulmonary system. Thus, fever can be harmful to children with pulmonary or cardiac risks or neurological disorders. It can also be a catalyst for febrile seizures, which, as a rule, although benign, cause very great concern among parents and should also be differentiated from more serious diseases (for example, meningitis). In children, the ability to regulate the thermal balance of the body is relatively weak, so it is easier for them to overheat or hypothermia of the body than in adults. The main reason for this is the insufficient development of the nervous mechanisms of regulation of thermal balance and, first of all, vascular reactions. Premature infants are unable to maintain their temperature homeostasis and react to ambient temperature as poikilothermic.*

Keywords*: pathophysiology of fever, subfebrile fever, chills, endopyrogen.*

In children under the age of 3 months, a febrile reaction practically does not develop. An increase in temperature is observed in the severe course of the disease, especially with a fatal outcome. The reason for the temperature increases in these cases is not the development of fever, but a violation of the mechanisms of heat regulation of toxic origin: many pathogenic microorganisms, entering the body, cause metabolic disorders, separating the processes of oxidation and phosphorylation, which increases heat production. Thus, in this case we are dealing with hyperthermia, not fever. The pronounced ability to fever appears after the first year of life. With age, the height and duration of the temperature reaction increases. The reaction develops mainly due to the limitation of heat transfer and is an indicator of pronounced positive reactivity for the body. In emaciated children with pronounced signs of intoxication, the temperature rises gradually to a low level, or does not rise at all.

Fever goes through three stages of development:

Temperature rise (st. incrementi).

The temperature is at an elevated level (St. fastigii).

Temperature reduction (St. decrementi).

It is believed that secondary endopyrogens, penetrating into the brain, act directly on the cells of the thermoregulatory zone of the anterior hypothalamus. As a result, the setting point of temperature homeostasis is shifted to a new, higher level of regulation. The hypothalamus begins to perceive the normal blood temperature as low before that. The central cold receptors are excited and the person feels cold. As a result, reactions are triggered aimed at limiting heat transfer and increasing heat production. This is confirmed by experiments in which, after the introduction of endopyrogen, the hypothalamus was artificially warmed. In these cases, fever did not occur, and an increase in temperature was observed when warming was stopped. The effect of endopyrogene

(interleukin-1) on hypothalamic cells is mediated through an increase in the synthesis of prostaglandins of group E, in particular, an increase in the content of cyclic AMP and a restriction of calcium intake into the cytoplasm of the cell. Prostaglandin E inhibits phosphodiesterase, which leads to the accumulation of cyclic AMP in nerve cells and triggers a process leading to the blockade of calcium channels and, as a result, a change in the reactivity of the thermoregulation center. Blockade of the enzyme cyclooxygenase, involved in the synthesis of prostaglandins, leads to a decrease in fever temperature to the initial level. For example, acetylsalicylic acid (aspirin) has such an effect.

In the first stage, heat production always prevails over heat transfer, since the latter is sharply limited due to narrowing of peripheral vessels. The temperature rises faster if there is a chill. Chills are a feeling of cold, it causes muscle tremors. Shivering increases heat production (contractile thermogenesis), and the feeling of cold causes heat to hide, which additionally reduces heat transfer. At the same time, non-contractile thermogenesis increases, i.e., an increase in heat production in internal organs, primarily in the liver and adipose tissue. Sweating is sharply inhibited. The feeling of cold is associated not only with the excitation of the central cold thermoreceptors. After the destruction of the anterior hypothalamic region, the ability to fever is gradually restored. In this case, the leading role in the development of fever goes to the posterior hypothalamic region: it is through this region that the regulation of heat production and heat transfer is mediated. The feeling of cold may be associated with generalized narrowing of the skin vessels. There is a two-way connection between the center where information about vasoconstriction is received and the center where the feeling of cold is formed. Therefore, with a sharp narrowing of blood vessels, a person feels cold even if heat acts on the skin. A good illustration of this phenomenon may be the case when a person gets up under a hot shower. At the first moment, cold is felt, as the skin vessels constrict. In the future, the vessels expand and then the person feels warm. It is important to emphasize that the main reason for the temperature increase in the first stage is the limitation of heat transfer, which is not only a more efficient mechanism, but also more economical, since it does not require additional energy consumption from the body to generate heat. An increase in body temperature occurs until the blood temperature rises to a new setting point and the thermoreceptors of the hypothalamus begin to perceive it as normal. From this moment on, the processes of heat production and heat transfer are balanced. The second stage begins - the temperature is at a high level or the fever itself. In the second stage, heat production decreases, sometimes reaching the norm or falling below it. But there are cases when heat production remains elevated. This is usually due to the action of certain bacterial toxins that have the ability to separate oxidation and phosphorylation. As a result, the energy generated during oxidation is not accumulated in the macroergic bonds of ATP, but is released as heat. However, this does not significantly affect the temperature curve in fever, since the increase in heat production is compensated by an increase in heat transfer.

As a result of an increase in temperature, activation of phagocytosis, rearrangement of metabolism and functions of a number of organs, the destruction of exopyrogens accelerates, and consequently, the production of secondary pyrogens decreases. As a result, the reactivity of the thermoregulation center is restored to the initial level and it begins to perceive the elevated blood temperature as high. The excitation of the central heat receptors causes a feeling of heat in children. Reactions aimed at increasing heat transfer are activated. The third stage comes - a decrease in temperature. Peripheral skin vessels dilate, sweating increases. Breathing becomes more frequent

and shallower. As a result, evaporation in the upper respiratory tract increases. The temperature drop in the third stage of fever can occur gradually (lytic temperature drop) or very quickly, within a few hours (critical drop). In this case, there is a danger of developing acute cardiovascular insufficiency due to too sharp vasodilation. In stage III, heat production often increases slightly, which can be considered as a manifestation of anti-regulation, but heat transfer always increases even more.

It is known from clinical practice that a variety of pathological processes cause fever of varying intensity and duration. In addition to the specifics of the pyrogenic agent itself, the formation and severity of the febrile reaction depend on the individual characteristics of the child: age, nutrition and the state of the higher parts of the brain. Sometimes more severe, toxic forms of diseases occur almost without an increase in temperature: "cold" typhus, "cold" scarlet fever, diphtheria, etc. At the same time, diseases accompanied by damage to the nerve cells of the diencephalic region (encephalitis, brain injury, etc.) often leave long-term temperature "tails". In some forms of tuberculosis, sepsis, the daily rhythm of the temperature curve is distorted in the form of maximum temperature rises in the morning and sharp temperature drops to normal and below during the day. The reason for this is probably toxic damage to the central mechanisms of thermoregulation with a slight transition from functional stress during pyrogenic stimulation to depression and "breakdown" of the reaction, which is an unfavorable prognostic sign.

Fever is accompanied by an increase in the tone of the sympathetic-adrenal and vago-insulin systems with a predominance of adrenaline secretion. The endocrine system is also activated. Removal of the thyroid gland does not deprive the body of the ability to fever. However, with a decrease in thyroid function (hypothyroidism), a more sluggish course of fever is observed. On the contrary, with pronounced phenomena of hyperthyroidism, more abrupt temperature rises are observed. Simultaneous removal of the thyroid gland and pituitary gland, thyroid gland and adrenal glands disrupts thermoregulation and significantly reduces the ability to fever. Clinical observations also indicate a pronounced antipyrogenic effect of ACTH and glucocorticosteroids. Probably, by enhancing the processes of catabolism (protein breakdown), they inhibit the synthesis of endopyrogen.

According to the degree of temperature rise, fevers are distinguished:

subfebrile (no higher than 38 ° C),

moderate (up to 39 ° C),

high (from 39.1 to 40.9 ° C),

excessively high - hyperpyretic (41 ° C and above).

Due to the restructuring of the thermoregulation center and an increase in blood temperature, pronounced changes in the functions of other organs and systems occur. In case of infections, it is necessary to distinguish what is associated with the development of fever and what is associated with the occurrence of intoxication. When highly purified pyrogens are administered for therapeutic purposes or to volunteers, there are no pronounced disorders in the activity of internal organs or metabolism.

The introduction of highly purified pyrogens does not have a significant effect on this type of metabolism. Catabolic processes prevail in infectious diseases accompanied by lichoradism. A negative nitrogen balance appears. The content of creatine and urea in the urine increases. The appearance of these symptoms is primarily associated with starvation, intoxication, and catabolism of muscle proteins. In the first stage of fever, diuresis increases slightly in proportion to an increase

in blood pressure and increased renal blood flow. However, activation of the sympathetic-renal system and the release of mineralocorticoids in stages I and II leads to a delay in sodium chloride and, through the release of vasopressin, to a decrease in diuresis. In stage III, diuresis increases, fluid loss increases with sweat. Possible cause categories include localized or generalized infections, connective tissue diseases, and cancer. A variety of specific causes include inflammatory bowel diseases, diabetes insipidus with dehydration, and thermoregulation disorders. A false diagnosis of fever of unknown origin is likely to occur much more often than the true one, because often minor viral diseases are treated with exaggerated caution. In children, despite the variety of possible causes, true fevers of unknown origin are more likely to be an unusual manifestation of a common disease rather than a manifestation of a rare disease; respiratory infections account for almost half of infection-associated cases of fever of unknown origin.

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