МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ

УЧРЕЖДЕНИЕ ОБРАЗОВАНИЯ
«ГОМЕЛЬСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ»

Кафедра патологической физиологии

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НАРУШЕНИЕ ТЕРМОРЕГУЛЯЦИИ. ЛИХОРАДКА

Учебно-методическое пособие по патологической физиологии
для иностранных студентов, обучающихся на английском языке

DISORDER OF THERMOTAX. FEVER

Educational grant for overseas students educates on English language

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THEME: INFRINGEMENTS OF THERMOTAX. FEVER

The motivational characteristic of the theme

The present methodical recommendations are developed with the purpose of optimization of educational process and recommended for preparation of students for practical class on the theme: «Infringements of thermoregulation. Fever».

In the manual questions on etiology and pathogenesis of fevers, hyperthermia, hypothermia are considered.

For self-checking mastering of the theme test questions, situational tasks, test tasks are applied. The presented information will be useful to students of foreign faculty with the purpose of better mastering of the material on the indicated theme.

The purpose of the class — to study the reasons of occurrence, mechanisms of development, the basic manifestations of various types of infringements of thermal exchange.

INFRINGEMENTS OF THERMOTAX

Fever, hyperthermy (overheating) an hypothermy (overcooling) are referred to impairment (infringement) of thermotax.

Fever

The Fever (febris — an armour, pyrexia — greek) is etiologic nonspecific and pathogenic uniform of typical pathological process, characterized by dynamic reorganization of function of the thermotax system in reply to action of pyrogenic substances and manifetating rise in temperature of the internal medium in the supreme homotherm animals and man.

The nature of fever interested researchers from time immemorial. Hippocrat specified universality of fever, as «a process of burning of pathogenic poisons». K. Galen treated essence of fever as «unnatural heat». T. Sidengam understood fever as «the natural machine for struggle against enemies». A. Zakuto established, that fever can exist without superfluous heat. Only in XIX century bases about etiology and pathgenesis of fever have been incorporated. L. Krel described the development of non temperature reactions in fever, S.P. Botkin established frustration of functions of the higher nervous system, in feverish conditions. Domestic and foreign scientists made their contribution in development of the doctrine about fever the contribution: V.V. Podvysotsky, Selie, A.V. Repreev, I. Dinarello, A.A. Lihachev, P.P. Avrorov, P.N. Vesyolkin, E.V. Majstrah, etc.

Fever is referred to late enough acquisitions of evolution. The development of fever in phylogeny is connected with a level of organization of the central nerous system and formation of thermotaxic mechanisms. Therefore fever occurs only in the supreme homotherm animals and man. For the first time the ability to be in has appeared in rodents and insectivorous. In homotherm organisms sensitivity to pyrogenic substances depends on the level of their development (expressiveness of fever increases in the line: the mouse — the rat — the rabbit — primates — the person).

During evolutionary development the fever was generated as nonspecific protective reaction of the organism in reply to occurrence of foreign material in its internal medium. Fastening of fever in phylogeny is the proof of its protectively-adaptive value. However, as any typical pathological process, fever can render pathogenic influence on the organism. Still P.N. Vesyolkin said, that «fever as genetically determined stereotype cannot be perfect». Therefore in each concrete case fever demands flexible medical tactics and an individual approach which is defined by the character of disease, age, features of disease and a number of other factors.

Etiology of fevers

The reason of fever are pyrogens (from Greek. pyros – fire, pyretos – heat).

Classification of pyrognes

Pyrogenic substances can be divided into two big groups:

- Primary.
- Secondary.

Primary (exogenous) pyrogenes can be of the infectious and non infectious nature.

Viruses, mushrooms, bacteria, rickettsia, uni- and multicellular parasites are referred to infectious primary pyrogenes.

Proteins and proteincontent substances, lipids and fat-containing substances, steroids, nucleoproteids are referred to noninfectious primary pyrogenes. Lipopolysaccharids (endotoxin) possess the greatest pyrogeny.

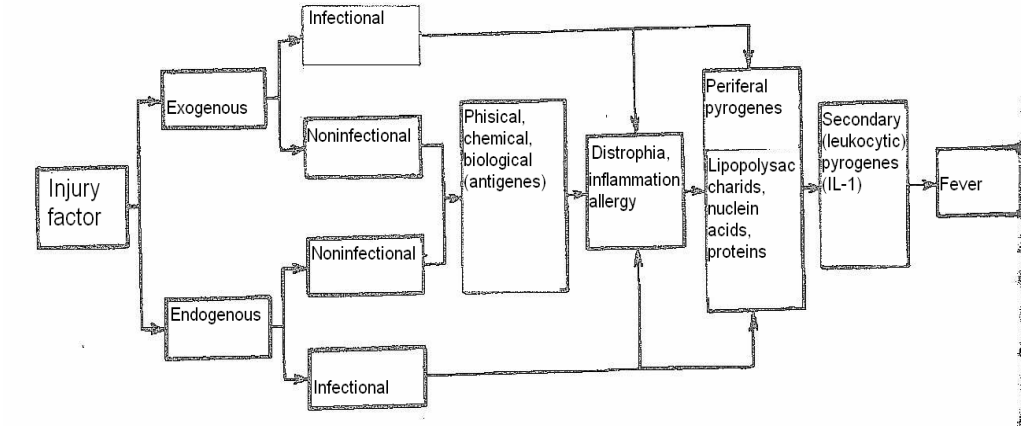


Figure 1 — An origin, types and character of pyrogenes

Properties of exopyrogenes

1. Do not cause fever independently.
2. Temperature-stable.
3. Nontoxical.
4. Nonallergenic.
5. Nonantigenic.
6. Hapten.
7. Tolerance develops at repeated usage.
8. Cause a number of protective effects.
9. There is no group specificity.

Primary pyrogenes do not cause a fever independently. Primary pyrogenes cause fever mediately, promoting formation of secondary pyrogenes in macroorganism. Secondary (leukocytic) pyrogenes, forming in the organism, cause the development of fever. Primary pyrogenes are etiologic factors, and secondary — pathogenetic.

Secondary (endogenous) pyrogenes are produced in a macroorganism as a result of influence of primary pyrogenes. They are formed mainly in phagocytic leukocytes (neutrophills, monocytes, macrophages), in lymphocytes — in a small amount. They are named true pyrogenes because of their ability to cause a fever.

Endogenous pyrogenes are referred to:

Interleukin 1 (IL-1), interleukin 8 (IL-8), interleukin 6 (IL-6), tumor necrosis factor - TNF, gamma-interferon (gamma-IFN).

Cytokines play a key role in signaling a fever. IL-1, IL-6, and TNF-α are produced by leukocytes (and other cell types) in response to infectious agents or immunologic and toxic reactions and are released into the circulation. IL-1 acts directly and also by inducing IL-6, which has essentially similar effects in producing the acute-phase reactions. Among the cytokines, IL-1, IL-6, TNF-α, and the interferons can cause fever, thus functioning as primary endogenous pyrogens. Peripheral cytokines signal the brain through four mechanisms to cause fever: They can enter the brain through regions lacking a bloodbrain barrier (specialized areas along the cerebral ventricular surface); they can cross the blood-brain barrier by specific transport mechanisms; they can transmit a signal to the brain via the vagus nerve; and they can activate brain vasculature stimulating release of mediators such as prosta-giandins (PGE), NO, or cytokines (IL-1/3), which act on brain parenchyma] cells. The specific mechanism employed may depend on the conditions. For example, in a mild inflammatory response, when peripheral cytokine levels are low. the cytokine signal may be transmitted by the vagus nerve. In contrast. during more significant sepsis, circulating cytokine levels are high, and the vascular route to brain activation becomes more prominent. Once generated, the signal is transmiaed from the anterior through the posterior hypothalamus to the vasomotor center to induct the responses.

Properties of endopyrogenes

1. Cause development of fever.
2. Basically are produced in micro- and macrophages of the organism.
3. Nontoxic.
4. Thermolabile.
5. Do not possess specific specificity.
6. Tolerance is not formed to them.
7. Increase protective properties of the organism.

- Strengthen phagocytosis.
- Strengthen development of glucocorticoids.
- Strengthen regeneration of tissues.
- Strengthen detoxicative function of the liver.
- Improve processes of microcirculation.
- Secretion of endogenous pyrogenes does not lead to phagocytes ruin.

It is necessary to note, that secondary pyrogenes except their pyrogenic activity have several specialized functions (see the Application № 1).

Conditions at which the causal factor is realized have the certain value in etiology of fever . It is known, that conditions themselves cannot cause diseases, but are capable to affect the etiologic agent. The condition of reactance of the organism, timeliness and adequacy of being carried on antibacterial therapy play an important role among these conditions, etc.

The factors determining the occurance of feverish process

(according to A.D. Ado, 1994 year)

1. Condition of reactance (excitability) of temperature thermal centers and peripheral thermoreceptors.
2. Activity of synthesis and transport mediators of fever (acetilcholine, serotonin, peptides, etc.).
3. Changes of amount and structure of leukocytes in blood of the patient during the disease.
4. Speed of formation and allocation of endopyrogenes.
5. Permeability of hematoencephalic and histohaematic barriers.
6. Specific immunologic and allergic stage of the patient organism, caused by the condition of immunocompetent system, including development of antibodies, activity of lymphocytes and macrophages.
7. Nonspecific reactance of endocrine and immunocompetent systems.

Besides the degree of rise in temperature in various diseases depends on introduction raising of the central nervous system substances: caffeine, phenamin, etc.

Pathogenesis of fevers

Development of fever begins with accumulation of secondary (endogenous) pyrogenes in blood. With the blood flow endogenous pyrogenes reach the hypotha-

lamic centers of thermoregulation and influence thermosensitive neurons of preoptic areas of front hypothalamus, activating enzyme phospholipase A_2. Activation of this enzyme leads to clearing of arachidonic acid from phospholipids of neurons. Then under the action of endogenous pyrogenes cycloxigenaise is activated. It directs the metabolism of arachidonic acid on the way of formation of prostoglandine E_2. Prostoglindines E_2 activate adenylate cyclase, that leads to accumulation of 3′-5′cAMP in cytoplasm of neurons. Accumulation of 3′-5′cAMP increases the activity of cAMP-dependent proteinkinase and some other enzymes. It leads to reorganization of the metabolism of neurons: excitability coldsensitive neurons increases, and of warmsensitive ones decreases.

Thus, the basic part of pathogenesis of fevers is a change of excitability of central hypothalamic receptors.

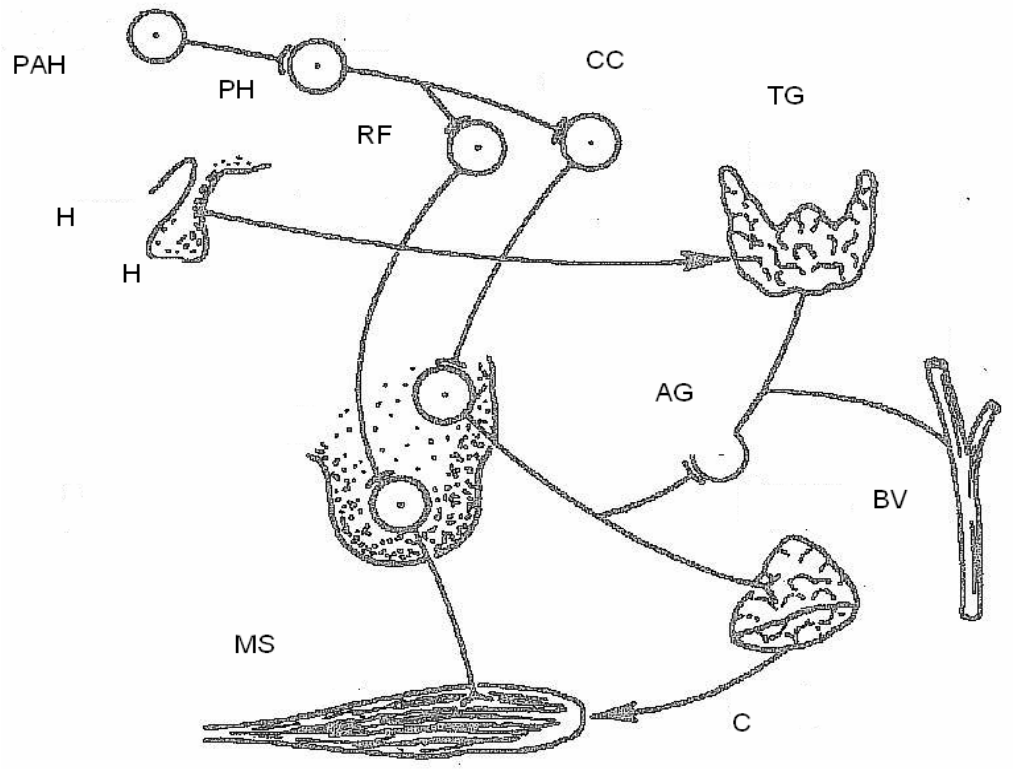


Figure 2 — The scheme illustrating mechanisms of rise in temperature of the body in 1 stage of fever. Designations: PAH — preoptic area of front hypothalamus; PH — posterior hypothalamus; CC — the cardiovascular center; the R F — a reticular formation; H — hypophysis; TH — thyrotropic hormone of a hypophysis; TG — thyroid gland; BV — blood vessel of the skin; AG — an adrenal gland; MS — muscular shiver; C — catecholamine

Decrease in a threshold of depolarization of cold sensitive neurons raises their excitability to action of cold factors, thus blood of usual normal temperature (37ºC) starts to excite them. It leads to the development of some efferent commands in the form of sympathetic adrergic influences. An activation a pressor

department of the cardiovascular center (strengthening of the cardiovascular activity, narrowing of a gleam of peripheral vessels, etc.) occurs.

Stages of fever

Three stages are distinguished according to the criterion of change of temperature in the development of feverish reaction.

1. Stage of rise of temperature (st. incrementi).
2. Stage of standing of temperature at a high level (st. fastigii).
3. Stage of decrease (reduction) in temperature (st. decrementi).

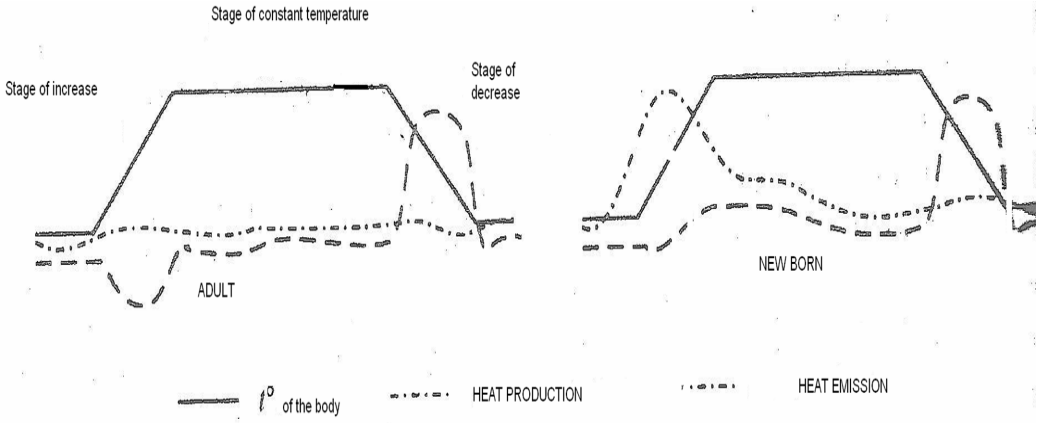


Figure 3 — Heat production, heat emission and body temperature in various stages of fever in adults and children

The characteristic of stages of fever

For the first stage of fever the positive thermal balance, i.e. prevalence of heat production over heat emission is characteristic. There is an accumulation of heat in an organism. The increased sensitivity of cold thermoneurons leads to the fact that the organism perceives normal ambient temperature as lowered one. It leads to a spasm of skin vessels, the termination of sweat, muscular shiver develops. The patient has fever. Rise of body temperature can be fast, and fever is very strong and on the contrary, gradual, with an insignificant fever or even without it.

In the second stage there is a formation of balance between heat production and heat emission. The balance between these processes is estalished at a new higher level is established (installed). The body temperature above norm, is supported at one level, but regulation of temperature is kept. Fever stops, arterial hyperemia develops. Duration of the second stage of fever depends on the character of pathological process.

The third stage of fever is characterized by negative thermal balance, i.e. processes of heat emission prevail over heat production. Abunolant sweating occurs due to expansion of skin vessels. Heat production decreases due to destruction of microorganisms and destruction of endogenous pyrogenes with fermental systems.

Temperature drop can be gradual (lysis) and fast (crisis). Critical decrease in temperature is connected with a sharp expansion of skin vessels and can be accompanied by collapse. Fast temperature drop can be dangerous, especially, in the persons of advanced age suffered myocardial infarction or having cardiosclerosis. In lytic decrease of temperature heat production and heat emission change gradually: heat production decreases inertly, and heat emission gradually comes back to norm.

The brief scheme of pathogenesis of fevers

Exogenous pyrogenes
↓
Interaction of exogenous pyrogenes with leukocytes
↓
Activation of phagocytosis
↓
Allocation of endogenous pyrogenes
↓
Neurons of the center of thermoregulation: formation of Pg E_2, cAMP
↓
Decrease in a threshold of excitability of cold receptors
↓
Increase of a level of «an adjusting point» of the center of thermoregulation
↓
Restriction of heat emission, increase of heat production
↓
Rise in temperature up to a new level of regulation

The characteristic of fever

Clinical interpretation of fever has an important diagnostic value. The doctor should pay attention to the following signs: the onset, expressiveness, duration of fever, type of a temperature curve, terms of occurrence and character of organ lesions.

I. The onset of fever can be:

1. *Acute* (during several hours) — for example, meningococcus meningitis, ornithosis, leptospirosis.

2. *Gradual* (during several days) — for example, typhoid fever, paratyphus.

II. On a degree of rise in body's temperature (expressiveness):

<u>subfebrile (up to 38°C):</u>

- low (up to 37,5°C);
- high (from 37,6°C up to 38°C);

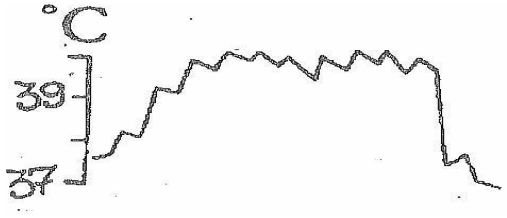
febrile (more 38°C):

- moderate (up to 39°C);
- high (up to 41°C);
- hyperpyrethic (from above 41°C).

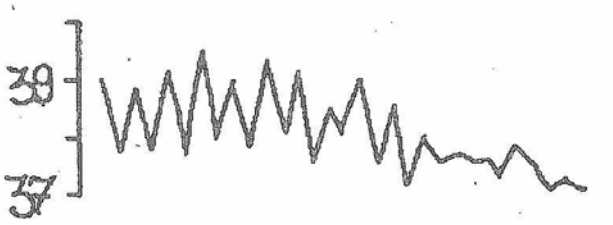
III. On the temperature curve:

Passing type (febris ephemera) — unitary short-term «candle» of temperature with the duration of some hours. This type is described, for example in a heavy current of pseudo-tuberculosis and in a delay of milk in nonfeeding puerpera.

Constant type (febris continua) — it is characterized by high temperature, without sharp daily fluctuations (no more than 1 degree). It is observed in lobar pneumonia, typhoid and epidemic fevers, fever of Q, pseudo-tuberculosis.

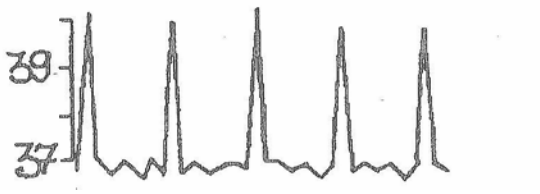


Aperient (febris remittens) — similar to a temperature curve of a constant type, but has a little more expressed range of daily fluctuations (1–3 degrees), and, the temperature does not fall



up to the norm. It occurs at the end of typhoid fever, and sometimes – the whole disease. In a similar way bronchus pneumonia, tuberculosis, exudative pleurisy, many virus infections and aseptic fevers can develop.

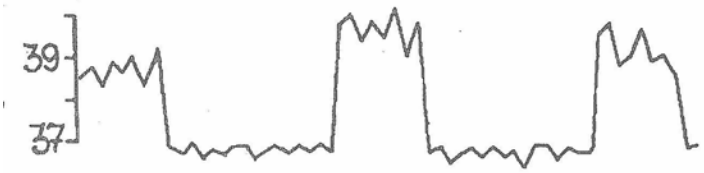
Alternating (febris intermittens) — a form having greater ranges with decrease of morning temperature up to norm and below, fluctuations 3–4 degrees. It occurs in acute hepatites,



tuberculosis and a sepsis. It is often characterized by separate short-term attacks of rise in temperature (paroxism, separated from each other the periods of apyrexy). In malaria the attacks can repeat every day (febris guotidiana), or oc-

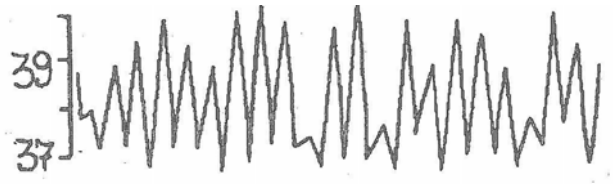
cure in a day on the third one (febris tertiana) — in infection PI.vivax, in two days on the fourth one (febris guartana) — in infection Pl. malariae.

Returnable type (febris recurrens) — a correct alternation of the periods of pyrexia and apyrexia lasts for some days. An example — a returnable typhus: in this case dependence of the temperature curve on the activator is well visible. Spirochete of Obermeyer is phagocyted by macrophages it also is makes multiple copies in them. In due course multiplied spirochetes break through a phagocytic barrier and flood the blood: corresponds the next attack of fever to it.

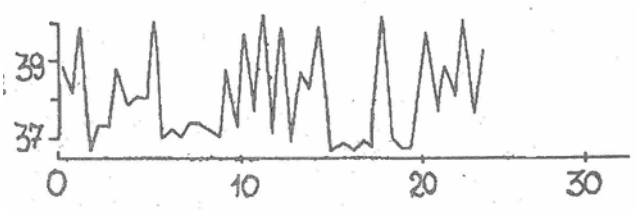


It lasts for 6–8 days then the temperature critically decreases and there comes the period of apyrexy which lasts for 6–8 days too. Returnable fevers accompany borreliosises. Aseptic returnable fever of Pel-Epshtein is observed in lymphogranulomatosis when the febrile and apyrexic periods alternate and last for 3–10 days. Periodic granulocytopenia is accompanied by episodes of fever every 3 weeks.

Exhausting, exhausting, hectic (febris hectica) — is characterized by a long current and greater daily fluctuations of temperature (up to 3–5 degrees). It occurs in sepsis, deep local and system infections**, for example,** heavy progressing tuberculosis, malignant tumours. Quite often in hectic fever there is a distortion of a daily rhythm with morning peaks and evening recession of temperature.



Wrong, atypic (febris irregularis seu atypica) — is characterized by infringement of a daily rhythm, there are rises in temperature in the mornings and recessions by the evening (febris inversa), or two-three rises and falling, or irregular fluctuations of temperature during of day. It occurs mainly in sepsis.



Wavy or undulating (febris undulans) — is characterized by gradual increase of body temperature up to high values and then gradual decrease up to subfebrile (sometimes normal). The cycle repeats in two-three weeks. It occurs

in infectious (brucellosis, visceral leishmaniasis) and non infectious (lymphogranulomatosis) diseases.

According to A.P. Kazantsev two more types of feverish curves are distinguished:

1. Sharp wavy fever (febris undulans acuta) — unlike undulating, it is characterized by rather short-term waves (3–5 day) and absence of remission between waves — in the form of of some fading waves. It occurs in ornithosis, typhoid fever, mononucleosis.

2. Reccurent (febris recidiva) — unlike returnable fever, it is usually characterized by one relapse developing at different terms (two days – some months). It is observed in leptospirosis, pseudo-tuberculosis.

Character of the temperature curve reflects the condition of the centers of thermotax:

- ***Constant fever* — is an evidence of steady excitation of the thermotaxic center.**
- ***The aprient fever* — characterizes unstable excitation of the thermotaxic center.**
- ***The alternating fever* — is characteristic of a septic condition.**
- ***The hectic fever* — characterizes the change of the periods of excitation and other-wordly braking of the thermotaxic center.**

The perverted character of fever is an evidence of a fast exhaustion of the thermotaxic center.

IV. Terms of occurrence of organic lesions in fever:

- Less than one day — scarlet fever, German measles, meningococcus infection.
- From one about up to three day — achicken pox, measles.
- More than three day — virus hepatites, typhoid fever.

V. Character of organic lesions in fever:

The most frequent organic lesions are:

- Skin rash — children's infections (measles, German measles, scarlet fever).
- Tonsillitis — quinsy, diphtheria, infectious mononucleosis.
- Diarrhea — shigellosis, salmonellosis.
- Lymphoadenopathy — toxoplasmosis, HIV, disease of the cat's scratch.

• Increase of the liver and the spleen — virus hepatites, typhoid fever.

• Changes in the entral nervous system — encephalites, meningitises.

VI. Dynamics of change of the temperature curve under the action of medical products.

1. Normalization of temperature — on administration of etiotropic preparation (except drug of steady forms).

2. Absence of decrease in temperature (for example, inefficiency of antibiotic therapy in virus diseases).

Because of administration of anti-infectious chemotherapy and antipyretics classical temperature curves occur less often and have ceased to possess the former differential-diagnostic value.

Value of fever for organism

Positive value of fever:

1. *Interfere duplication of microorganisms*. It is connected with the fact that in fever the amount of serum ionized iron (basically due to its combination with ferritin), ionized zinc decreases, and concentration of copper increases. Fever reduces stability of activators of diseases to antimicrobic preparations (at temperature of 40°C practically mycobacteriua tuberculosis, gonococcus, treponema, some pneumococus practically don't propagate themselves).

2. *The fever strengthens the immune answer*. There is an activation of specific immunity — development of antibodies; and the nonspecific mechanism of protection — stimulation of phagocytosis increases.

3. *The fever promotes development of some protective factors*, such as interferon, lyozyme (interferon — a unique organismic factor effectively influencing a virus of the flu). At higher, than norm temperature there is an activation of endocellular enzymes interfering the reproduction of viruses.

4. In a fever *the general adaptable syndrome develops*, mechanisms of hypothalamo-pituitary-adrenal protection begin.

5. *Fever is often the first and a unique sign of disease*, therefore supervision over its character is an important element of diagnostic tactics of the doctor.

6. In most cases fever provides physiologically justified patient's bed regime (children are an exeption).

7. *Artificially created fev*er (introduction of pyrogenes) forms conditions for more effective specific treatment of slow diseases (bone-articulate tuberculosis, syphilis, gonorrhoea, etc.).

Negative value of fever:

1. Increases loading on the cardiovascular system (especially, in persons with the lesion of this system).

2. At critical temperature drop undesirable manifestation of III stage of fever are possible.

3. Oppression of the nervous system.

4. The mediated frustration of functions, organs and systems.

5. Expressed 5–7 day time fever for 3–4 weeks switches off spermatogenesis.

Indications for febrifugal therapy:

Correction of a temperature mode demands the differentiated approach.

1. Hyperthermal fever.

2. Fever in persons with the lesion of the cardiovascular system.

3. Fever in children of younger age inclined to the development of a convulsive syndrome.

4. The separate clinical cases of diseases demanding a specialized estimation (pregnancy, treatment of bacterial shock, etc.).

Thermotax in newborns

The feature of reactance of newborn children, as well as cubs of other mammals, within the first weeks after the birth is a great intensity of untrembling thermogenesis in muscles and, especially, in cells of brown fat.

Brown fat settles down in the interscapular area, in mediastinum, along the aorta and large vessels, along the backbone and the sympathetic trunk, under the armpits, in the abdominal cavity, behind the brestbone, around kidneys and adrenal glands and in sucking pads — on cheeks of babies. Brown colour of this type of fatty tissue is caused by a lot of mitachondrias with their ferriferous coloured cytochromes. The brown fatty tissue is the most powerful generator of metabolic heat in the organism. Mitochondrias of brown adipocytes contain protein thermoginin (the activator of non phosphorylating oxidations), developed crists and contact with fine plural liposomes. The cells of brown fat are supplied by a lot of noradrenal receptors and contain sympathetic noradrenergic nerve endings.

In newborns paraoptic ganglia lie in brown fat along a backbone .The feature of adrenal glands of the fetus is the prevalence of noradrenaline in brain substance (it is kept during the first 3–4 months of extrauterine live). On the signal of hypothalamus sympathetic nerves and chromaffin tissue of adrenal glands through synapses and blood activate lipolysis and thermogenesis in brown lipocytes. Warming up of blood in large vessels and system effect of free fat acids promote rise in temperature. Blood from congestions of paravertabral brown fat flows through unique venous anastomoses of newborns in the spinal venous sine and warms up spinal thermoensors in segments C5-Th1. It also brakes trembling thermogenesis at newborns, allowing their muscles to continue tonic activity. The rest of brown fat make the contribution to mechanisms of temperature adaptation of children till 10–11 years of age.

Features of thermotax in newborns:

1. Newborns provide the needs in thermogenesis by means of the untrembling mechanism which cannot be found out without special measuring means.

Actually the development of heat in such children can, without participation of the mechanism of shiver, to raise on 100–200 % and more in comparison

with the level of development of heat at rest. Original mechanisms of temperature adaptation of newborns are very powerful, but the problems facing them, especially, in prematurity, essentially are more difficult, than in adults, therefore their homotherm is limited.

2. The small size of the newborn. From the point of view of technology of thermotax it is a disadvantage (the correlation between the surface and the volume of the body of prematurity newborn is approximately three times more, than the corresponding correlation in the adult).

3. The superficial layer of the body has no big thickness and the isolating layer of fat is rather thin (therefore even the maximal narrowing of vessels cannot limit carrying of heat from the organism in the environment up to such degree, as in adults). Shortage of brown and white fat in prematurity (and its maintenance in prematurity — no more than 2 % of body weight of a body whereas in mature — 8 %) creates especially great problems with thermotax and makes a temperature mode of nursery by the basis of an effective survival the prematurities. To solve similar problems, the organism of the mature newborns should 4–5 times increase the development of heat to unit of the body, and the organism of the prematurity child (at weight of 1–1,5 kg) should 10 times increase the heat development.

4. Maximal thermotaxic formation and narrowing of vessels in newborns arises at more high heat of a skin temperature, than in adults (about 23ºC).

5. Healthy newborns are rather persistent against overcooling (the limit of therectal temperature compatible to life is below in them than in adults — 22–23ºC).

6. Instability of newborns to overheating is defined by the limiting mechanisms connected with small resources of parameters of water-salt homeostasis.

7. Newborns allocate cytokine and answer them with a true fever, however, mechanisms of fever in the early childhood are characterized by originality.

Children are included in the group of risk on development of complications in feverish reactions:

1. At the age of from 2 months of life at presence of temperature 38ºC and more.

2. At the age of up to 2 years at temperature above 40ºC (an opportunity of the infectious process caused by Haemophilus influenzae, Streptococcus pneumoniae).

3. All age groups at temperature above 41 ºC (probability of sepsis, meningitis).

4. With hyperthermal conditions.

5. With a convulsive syndrome in the anamnesis.

6. With heart diseases and vessels.

Endogenous anti-pyrogenic system

In the organism of the person there is a system of endogenous anti-pyrogenesis which regulate the level of rise of temperature.

Arginine-vasopressin mechanism (AVP) and an alpha — intermedin hormone (α-MSH) are reffered to anti-pyrogenic system. AVP and α-MSH act on the centers of thermotax, not leaving for blood-flow, and cause restriction of fever. In the basis of AVP action there is a neuromodulative mechanism of influence on the thermotax centers, leading to elimination of effects of activation on the periphery due to decrease in excitability of coldsensitive neurons.

Anti-pyretic action α-MSH is caused by the structure the C — end of the molecule and it's 20000 times stronger than action of acetaminophenol.

A long fever of not clear origin

Under the term (a long fever of not clear origin) we understand a body temperature which is above 38,8 ºC, proceeding more than 3 weeks in a clear clinical picture.

Under diagnosis in 75–85 % of cases reveal an infection, is revealed in 25–30 % — malignant tumours and in 15 % — diffuse diseases of the connecting tissue.

Pyrotherapy

Pyrotherapy (greck.: pyr-fire + therapia – treatment) – a method of treatment by means of artificial rise in of body temperature of the patient.

Artificial hyperthermia in medicine has been applied for a long time.

History of pyrotherapy

A.S. Rozenbljum (1876 year) — infection with a returnable typhus 12 sick with progressive paralysis.

J. Wagner-Yaureggu (1887 year.) — infection with malaria of incurable patients.

T. Kuli (1893 .) — application of toxins of Hemolytic streptococcus for treatment of tumours of head and neck.

T. Klyuyev, N. Roskin — reception of pyrogenic preparation from Tripanosoma cruzai.

Effects of pyrotherapy

1. Stimulating action on the central nervous system, sympatho-adrenal systems.
2. Nonspecific, desensibilizative and anti-inflammatory action.
3. Bactericidal effect in diseases of the infectious nature.
4. Stimulation of plastic and reparative processes in bones, tissues and parenchimatous organs (in their destruction, damage, etc.).

Pyrotherapy is divided into general and local. General pyrotherapy is carried on by means of pyrogenal or substances stimulating synthesis of endogenous pyrogenes.

*Pyrogena*l is lipopolysacharidum, forming during microorganisms Psedomonas aeruginosa life. Activity of pyrogenal is expressed in minimal pyrogenous dozes. 1 minial pyrogenous dose – the amount of substance causing on introduction to rabbits causing rise in temperature of body on 0,6 ºC and more on introduction to rabbits.

Local therapy is carried on in a complex with other methods of treatment for stimulation of immune and not immune protective mechanisms.

Hyperthermy

Hyperthermy is a the typical form of frustration of the thermal exchange, developing in the organism of the person as a result of its sharp increase of heat content, not connected with fever that is manifested by rise in temperature of the kernel of the body above 38ºC and infringement of functions of organs and systems.

The reasons of hypethermy: the heat of the environment; the agents interfering realization of mechanisms of heat emission of the organism; isolatives of processes of oxidation and phosphorylation in mitochondrias.

Risk factors:

1. Significant humidity of air, air-and water-proof clothes (a combination of humidity and immovability).
2. Intensive muscular work.
3. Age (old men, children).
4. Diseases (cardiac insufficiency, arterial hypertensia, hyperthyrosis, adiposity, etc.).
5. Smoking, alcoholic intoxication.

Nosologic forms of thermal lesions (according to the CART, 1980 year)

1. Thermal and a sunstroke.
2. Thermal faint.
3. Thermal spasmes.
4. Thermal exhaustion owing to reduction of the contents of salts in an organism.
5. Not specified thermal exhaustion.
6. Thermal exhaustion passing.
7. Thermal hypostasis.
8. Other displays of thermal influence.
9. Nonspecified.

Pathogenesis of hyperthermy

Action on the organism of various types of heat is realized differently: radiating heat — warms up superficial and deep tissues simultaneously, convec-

tional and conductional heat cause superficial heating of tissues, and then-internal organs.

On the action of hyperthermal factors in the organism the triad of emergency reactions occures: behavioural, strengthening of processes of heat emission and decrease of heat production, stress-reaction. The significant pressure of thermotax mechanisms leads to increase in expenses of energy and to an additional rise in temperature of the body, i.e. the vicious circle (circulus vitiosus) is formed. Thus, in hyperthermy infringement of mechanisms of thermotax develops as a result of an overstrain and failure of thermotaxic systems (unlike fever).

Stages of overheating

There are 4 stages of overheating in conditions of relative rest depending the ambient temperature:

1. The first — t 40 ºC.
2. The second — t 50 ºC.
3. The third — t above 60 ºC.
4. The fourth — t in the armpit hollow above 40 ºC.

Differ between fever and hypothermal conditions and reactions

Criterion	Fever	Hyperthermy
Etiology	Pyrogenic substances	High temperature of environment, factors which preventing realization of heat emission mechanisms, disconnectors of oxidative phosphorylation in mitochondria
Master link of pathogenesis	Preservation of mechanisms of thermotax of organism	Breakdown mechanisms of thermoregulation
Change of thermoregulation	Controllable passage of thermotax system on more high level	Noncontrollable increase of body temperature
Biochemical processes	Process of oxidative phosphorylation activate, synthesis of ATP increases, protective reactions of organism mobilize	Blockade of ATP syntesis occurs, break up of ATP takes place. Exess production of heat takes place.
Manifestation on stage of temperature increasing	Shivering and moderate stimulation of functions (in case of body temperature increase on 1ºC – puls increases on 8–10 ictuses per minute and respiratory movements increase on 2–3 times per minute	Acute sweating, sense of heat, acute pulse and respiration increasing (on 10–15 movements) in case of body temperature increasing on 1ºC.
Surrounding temperature dependence	Level of body temperature doesn't depend on surrounding temperature	There is direct dependence between body temperature and surrounding temperature
Influence of warming	Body temperature does not change	Body temperature increases
Influence of cooling	Body temperature does not change	Body temperature decreases

Hypothermy

Hypothermy — a typical form of frustration of the thermal exchange, developing in the organism of the person as a result of significant reduction of heat content, that is manifested by decrease in temperature of the kernel of the body below 35 ºC and infringement of functions of organs and systems.

Also it is prolonged exposure to low ambient temperature leads to hyperthermia, a condition seen all too frequently in homeless persons. Lowering of body temperature is hastened by high humidity in cold, wet clothing and dilation of superficial blood vessels as a result: of the ingestion of alcohol. At about 90 ºF, loss of consciousness occurs, followed by bradycardia and atrial fibrillation at lower coreb.

The reasons of hypothermy: a low ambient temperature, extensive paralyses of muscles and reduction of their weight, infringement of metabolism, decrease of exothermic processes of metabolism, an extreme degree of exhaustion of the organism.

Risk factors of over cooling:

1. Raised humidity, increase in speed of movement of air.
2. Damp or wet clothes.
3. Getting into cold water.
4. Decrease in resistency of the organism.
5. Alcoholic intoxication.

We distinguish: actually hypothermy and hypothermia artificialis. Artificial hypothermy is applied in medicine in two versions: general and local.

Classification of hypothermic conditions

1. *Primary (spontaneous) hypothermy* — develops as a result of infringement of function of the hypothalamic centers of thermotax suffered infection of a brain in neonatal period, in a number of encephalopathies, in syndrome Shapiro (congenital hypoplasia of a calloused body).

2. *Secondary hypothermy* — results from sharp increase of heat emission, not compensated by growth of heat production (develops on getting hit into cold water, sometimes in the air, on giving residence of narcosis).

The periods of hypothermia

(on J.V. Lobzinu, A.T. Marjanovich, B.H. Tsygan)

1. The norm period — is characterized by continuation of independent pulmonary respiration.

- Phase of indemnification.

2. Proer hypothermy — it is characterized by overstrain and exhaustion of mechanisms of thermotax.

- Phase of decompensation (the phase includes three stages: adynamic, soporose, convulsive).

3. *The anoxic period* – begins with respiratory standstill.

The appendix 1

THE DIRECTORY OF SOME TERMS AND CONCEPTS ON THE THEME OF THE CLASS

Malignant hyperthermia. This syndrome, as a rule is observe as a complication of narcosis (especially on use of halothane). The body temperature quickly rises up to 42 ºC and above, general rabdomyolysis occures, expressed acidosis develops. Lethality reaches 70 %. **Frequency:** in children — 1 on 15 000, in adults 1 on 75 000 anesthesias. Half of patients were exposed earlier anesthesias without visible attributes of complication. **Other reasons:** physical work at heat, fever, intake of alcohol and neuroleptics. **Genetic aspects:** Types of genetic predisposition to development of malignant hyperthermy. Type 1 (# 145600, 19q13.1 - q 13.2, defects of genes RYRI, MHS, CCO {180901}) — a mutation of ryanodine receptor of musculoskeletal type. Manifestation – King-Denbro syndrome. Clinically: low height, lumbar lordosis, ptosis, crypthorchism is possible. Synonyms: King's syndrome, Evans myopathy.

Poikilotherm (from greek. poikilos — changeable and therme — heat) **animal** are haematocryal animals whose body temperature depends mainly on the ambient temperature (for example Cyclostomata fishes, amphibians, reptiles, etc.).

Homotherm (from greek. homoios — the same) **animals** are the warm-blooded animals, capable to maintain rather constant body temperature on significant changes of temperature conditions of dwelling (mammals, birds, man).

«Kernel» of a body — functional concept in thermophysiology, uniting internal organs (sometimes skeletal muscles) in which there is a formation of heat.

«Membrne» of the body — functional concept in thermophysiology, presented with the skin, subscutaneus fat (sometimes skeletal muscles) by means of which there is a dispersion of heat which has formed in «kernel» in an environment.

«A set point» (English set point) — in 60^{x} years of XIX century Libermeister put forward a hypothesis, that in hypothalamus there is a certain set point similar to that which there is in any thermostat with the center of thermotax compares with the information with real body temperature.

IFN-γ (from English interfere with — to the prevent (replication of viruses)) — is name an immune interferon as only it is produce by immune T-cells — subpopulations Th1, CD^{+}_{8}, cytotoxic lymphocytes in NK. The main biological effects: the strongest activator of macrophages, activates NK to realization of cytolysis of cells-targets, induces expression on cells of proteins of MHC-I and MHC-II, representing antigenes (including viral) for T-cells, participates in anti-virus action ofcytotoxic lymphocytes, is a local cofactor in the direction of differentiation of CD^{+}_{4} Th0 – cells in Th I, participates in switching of biosynthesis of isotypes of Ig.

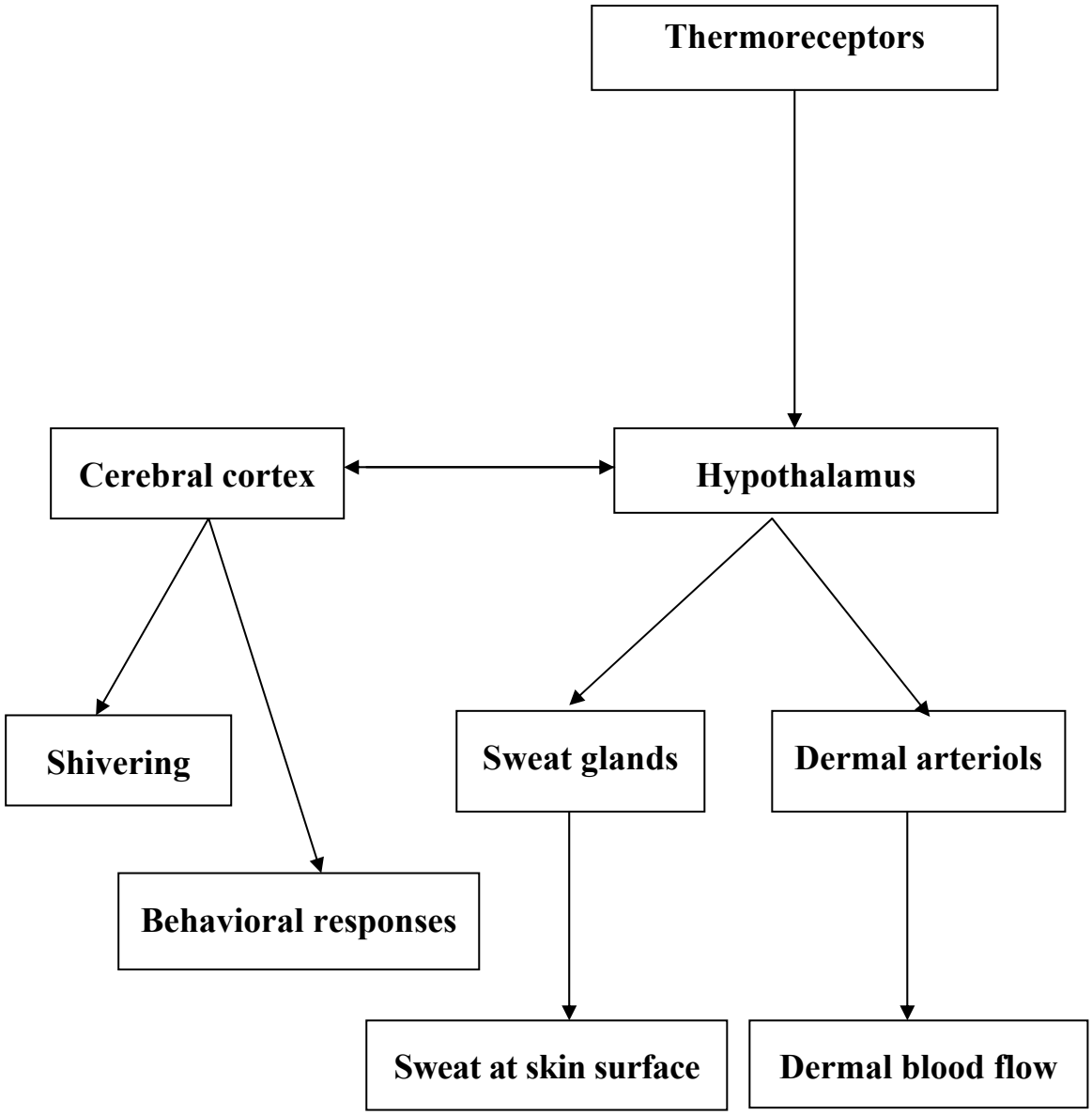
IL-1α – in molecule 159 the aminoacid rest, monomeasure. Receptors: CD 121a, CD 121b.

IL-1β – in molecule 153 the aminoacid rest, monomeasure. Receptors: CD 121a, CD121b. Basically is a secreted by a cell into extracellular space (and IL-1 mainly in a cell). Participates in development of reaction of a sharp phase.

TNF-α tumours necrosis factor. Cells producers: activated macrophages, neutrophills, NK and corpulent cells. Local effects **TNF-create** the center of local inflammation in barrier tissues on introduction pathogene in them. Activates endothelium. Participates in development of a system sharp phase (systemic vasodilation, the increased permeability of vessels, the DIC-syndrome, development of polyorganic insufficiency, loss of weight of a body). Earlier TNF-α were named cachectin as it causes increased catabolism of fats and proteins in fatty and muscular tissues. In septic shock it perfors a role of «inductor of apoptosis» at the level of the organism as a whole.

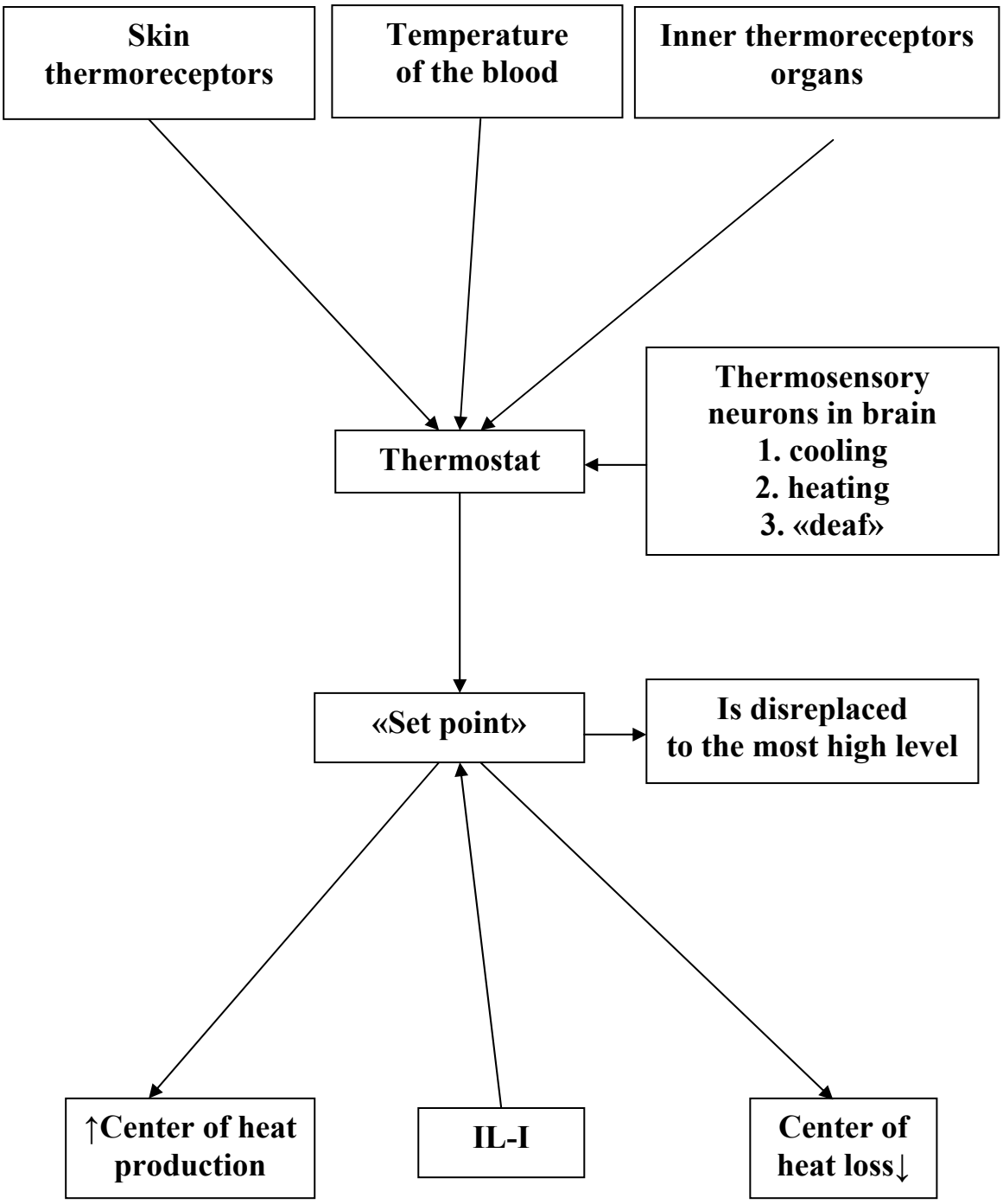
The appendix 2

PRINCIPAL MECHANISMS OF HUMAN THERMOREGULATION



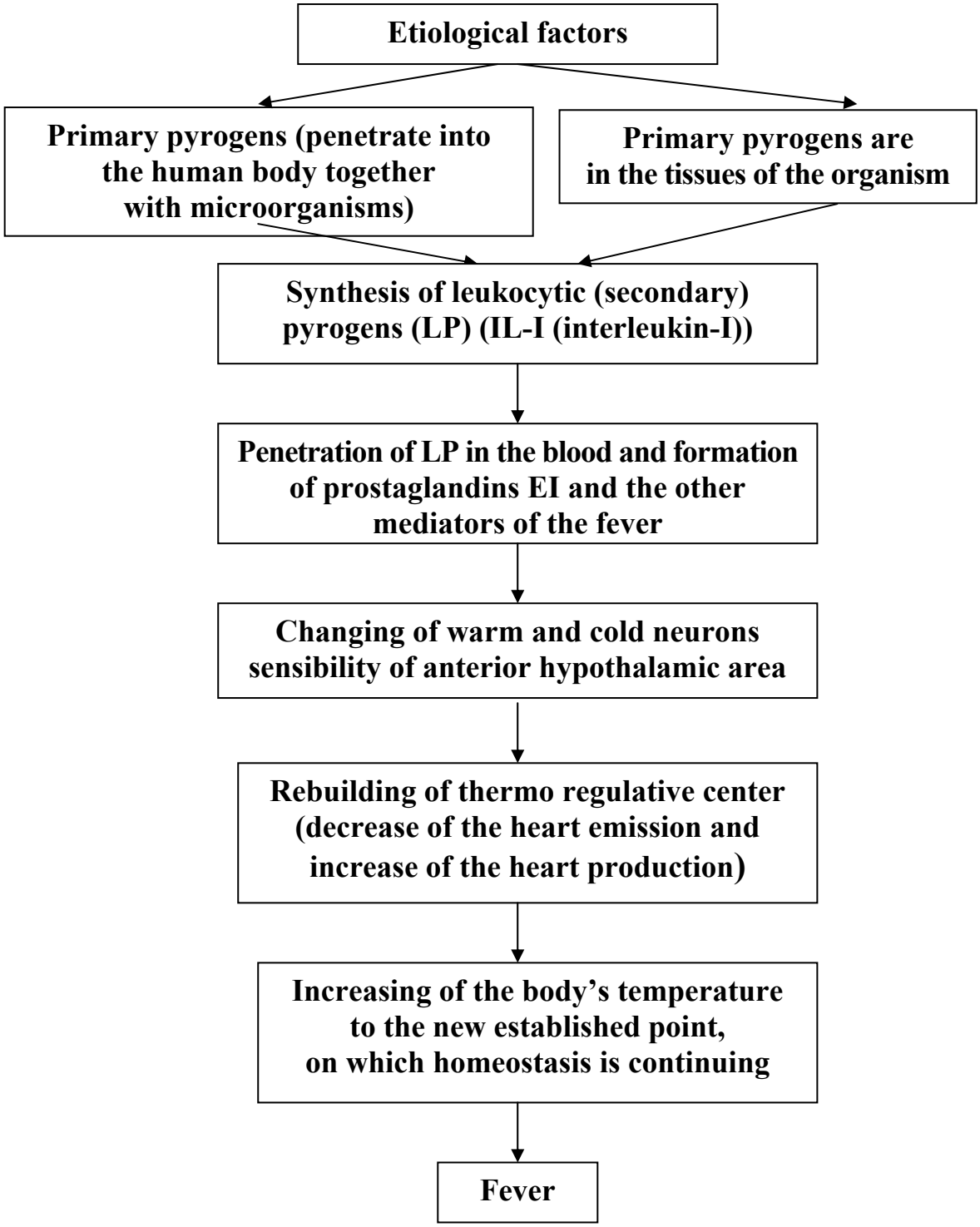
The appendix 3

THE MAIN MECHANISMS OF FEVER DEVELOPMENT



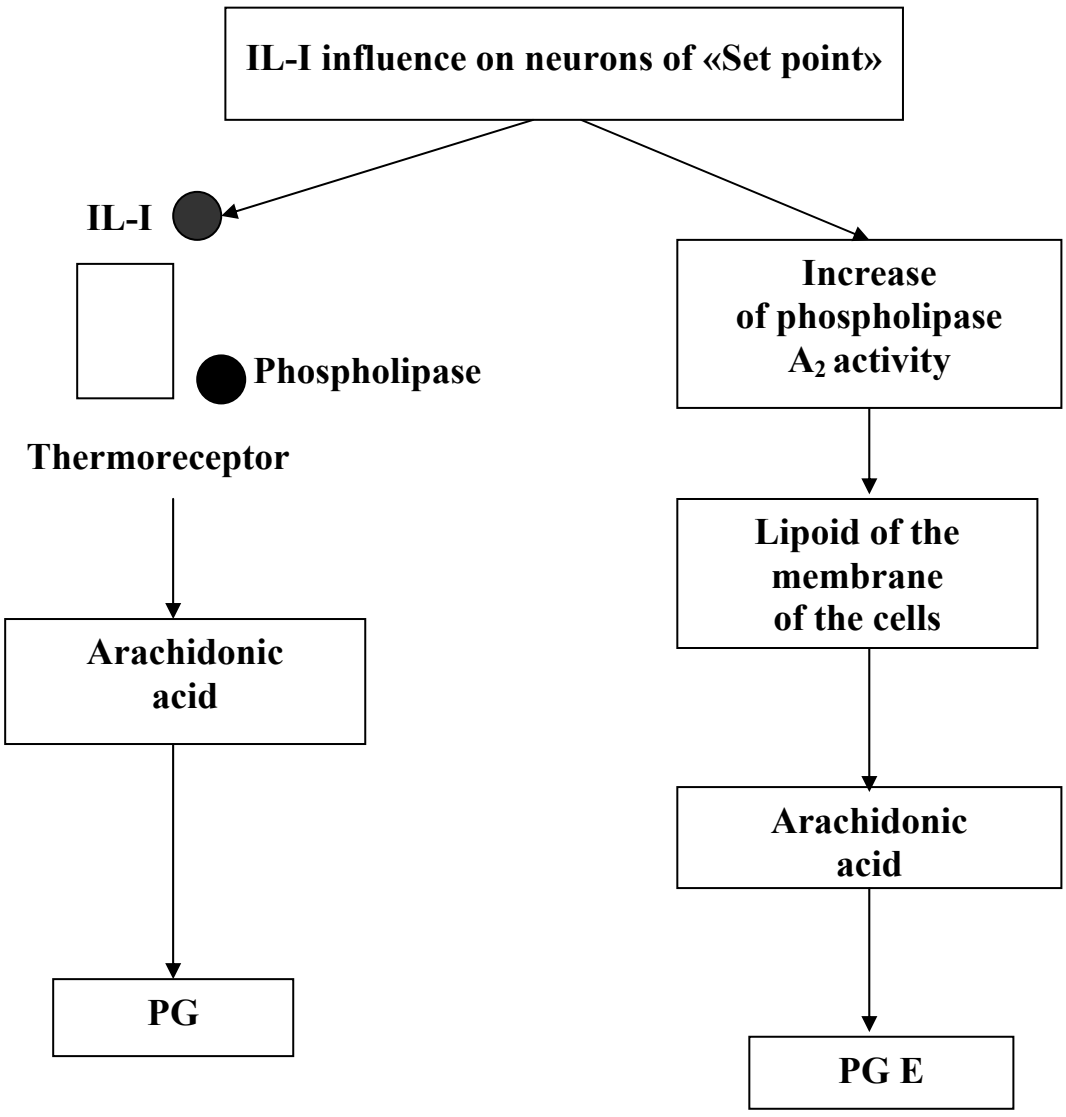
The appendix 4

PATHOGENESIS OF THE FEVER



The appendix 5

MECHANISM OF IL-1 ACTING



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