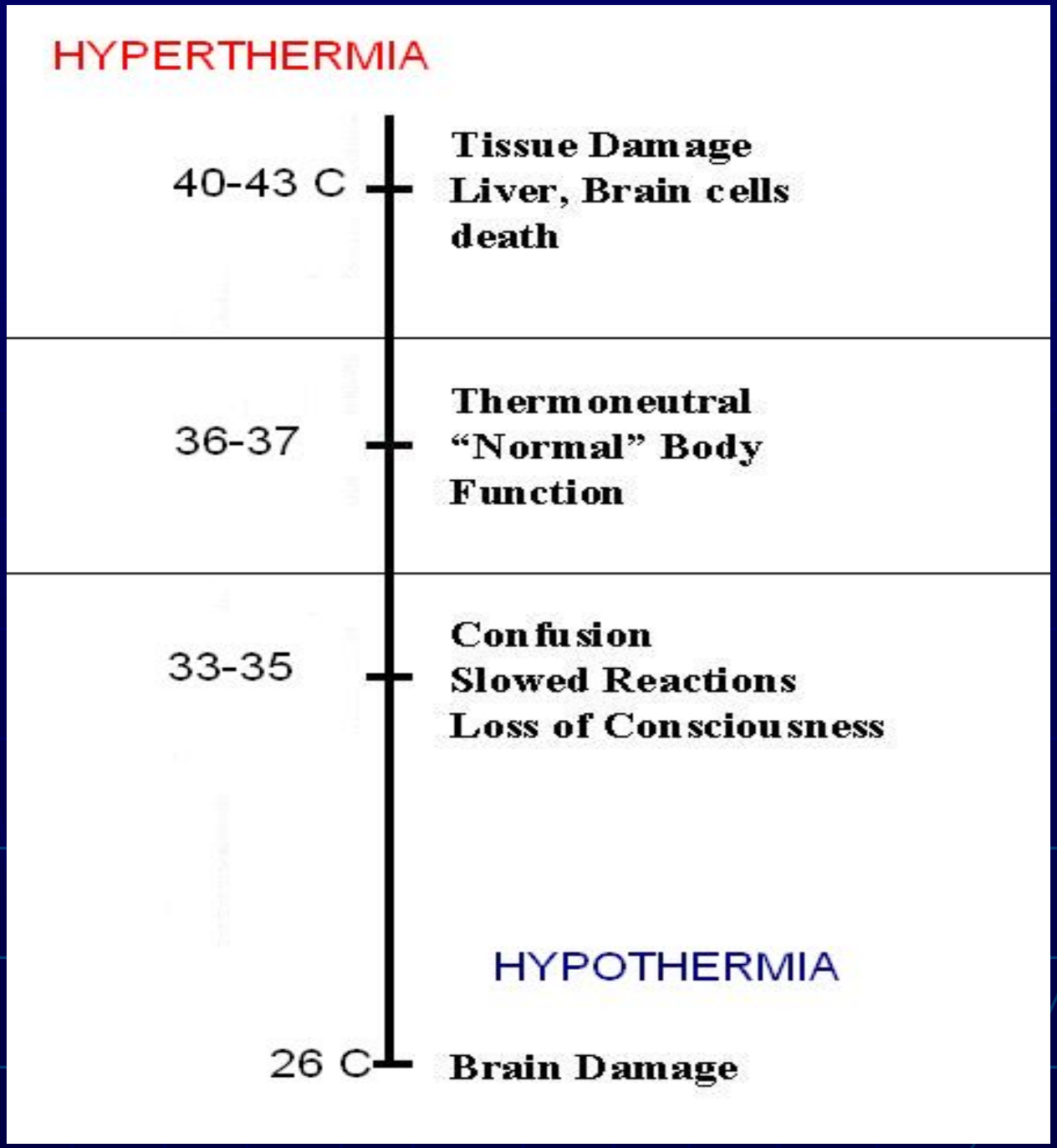
Thermoregulation pathology

Fever, hyperthermia, hypothermia

November 5th, 2013

Human thermoregulation



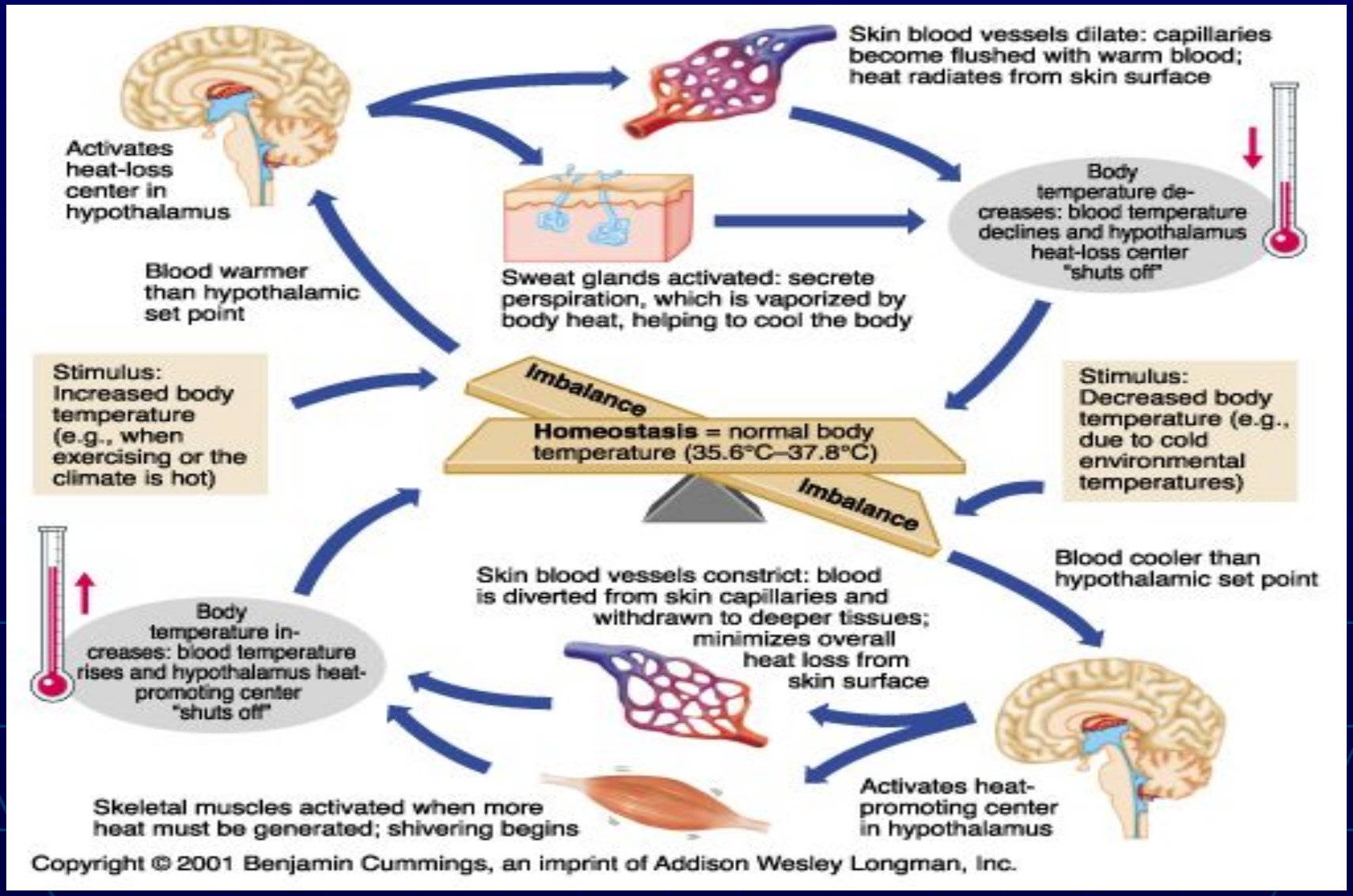
The sources of heat production

- Body BMR (Basal Metabolic Rate)
- Increased Metabolic Rate:
  - muscle activity (shivering);
  - effect of thyroxin on the cells;
  - effects of epinephrine, norepinephrine and sympathetic stimulation on the cells.

The ways of heat loss

- Heat conduction to the objects
- Heat conduction to the air (convection).
- Heat irradiation.
- Evaporation.

Thermoregulation mechanisms



The causes of fever

Primary pyrogens

- **Infectious pyrogens** (from bacteria, viruses, protozoa, fungi).
  - **polysaccharides and lipopolysaccharides of the microbial cell membrane.**

The causes of fever

Primary pyrogens

- **Non-infectious pyrogens**
  - **foreign** proteins, lipids or nuclear acids;
  - **products of tissue decay** (burns, mechanical traumas, surgical operations, internal hemorrhages, infarcts, allergic reactions, autoimmune processes, etc.)

The causes of fever

Secondary pyrogens

- **cytokines: IL-1, IL-6, TNF, gamma-interpherone (**produced and released by phagocytes)

Pyrogenic cytokines are synthesized in every case of primary pyrogens appearance.

Fever stages

- **Temperature increase stage**
  – stadium incrementi
- **High temperature standing stage**
  – stadium fastigii
- **Temperature descent stage**
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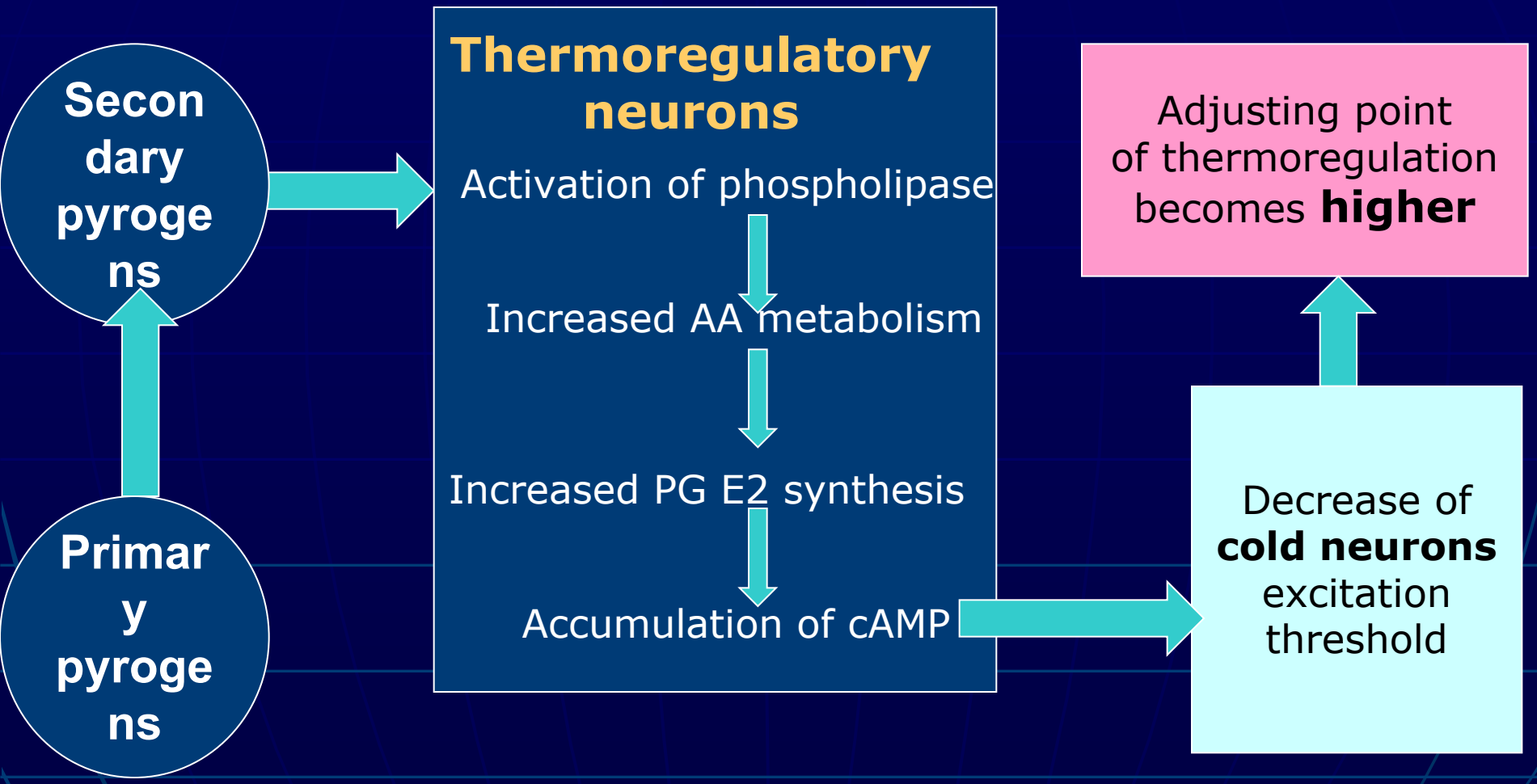
Temperature increase stage

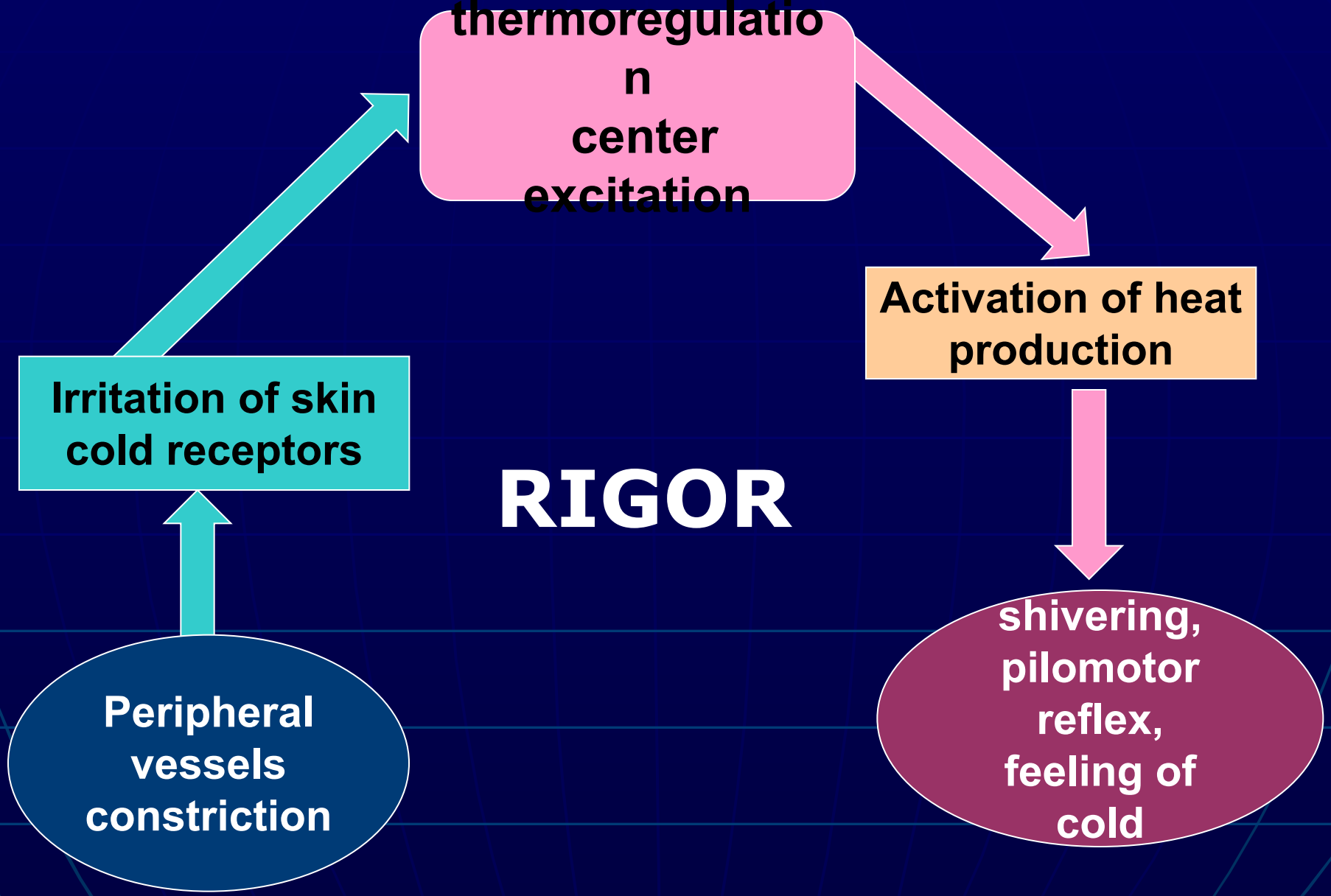


Temperature increase stage

Heat loss decreases due to:

- skin periphery vessels constriction
- sweat secretion inhibition
- decrease of evaporation.
- pilomotor reflex - “goose-flesh”

Temperature increase stage



Temperature increase stage

Heat production increases due to:

- contractive thermogenesis (increased tone of muscles and shivering).
- noncontractive thermogenesis (increased metabolism of inner organs).

High temperature standing stage

- no further temperature increase
- heat loss increases (in comparison with 1st stage)
- **thermoregulation is normal** (heat production and heat loss are in normal balance)

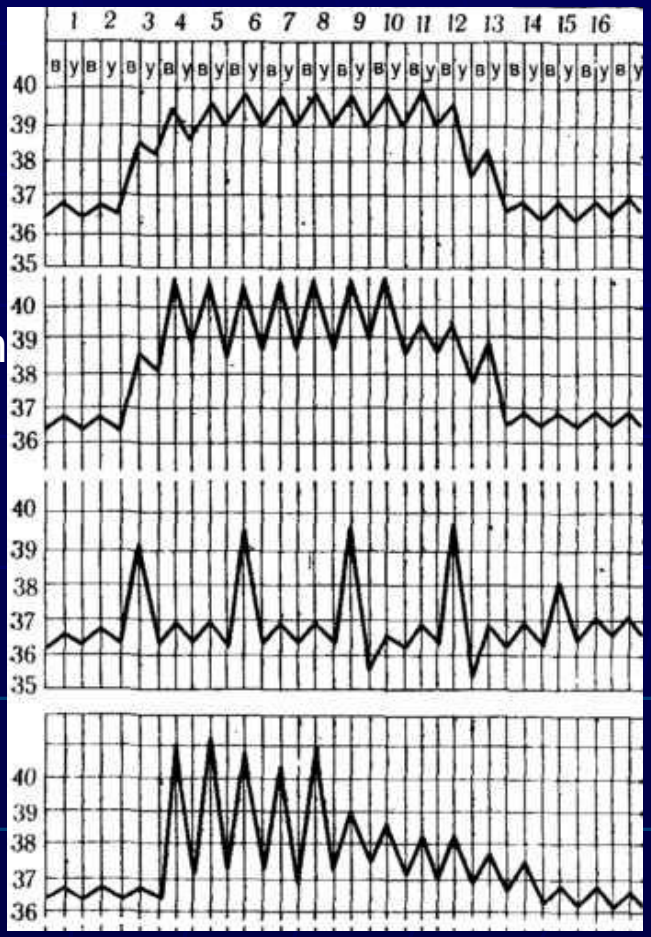
The types of temperature curves

Febris continua - temperature fluctuation within 1 C^0 range (abdominal typhus, croupous pneumonia).

Febris remittens - daily fluctuation exceeds the 1 C^0 range, temperature is high (exudative pleuritis).

Febris intermittens - daily fluctuation exceeds the 1 C^0 range, temperature may reverse to normal (malaria, infectious endocarditis).

Febris hectica - temperature fluctuation is 3 to 5 degrees (sepsis)



The level of temperarure increase

Subfebrile temperature up to 38 C

Febrile temperature – 38 - 39 C

Pyretic temperature –39 - 41C

Hyperpyretic – temperature is higher than 41C

Temperature descent stage

- Decrease of pyrogenic cytokines synthesis
- Adjusting point of heat regulation center returns to the normal physiological level
- Heat loss is prevailing
- The decrease of fever may be lytical (slow) or critical (fast).

Metabolic changes in fever

- BMR in the 1st and 2nd fever stage is increased. In the 3rd stage - decreases.
- Carbohydrate and lipids metabolism – prevalence of catabolic processes in the 1st and 2nd fever stage. In the 3rd stage – normal.
- Protein metabolism is disturbed in the case of long lasting fever – proteolysis will increase.

Metabolic changes in fever

Water metabolism

- 1st stage – increased water loss (due to increased diuresis).
- 2nd stage - accumulation of water in the organism.
- 3rd stage - increased water loss (increase of diuresis and sweating)

Changes in organs function in fever

- Nervous system – insomnia, high irritability, high sensitivity of skin and mucous covers.
- Endocrine system – increase of ACTH, catecholamines, TSH, thyroid hormones.
- Heart – tachycardia.
- Lungs – increased alveolar ventilation and gas diffusion.

Changes in organs function in fever

- GIT - loss of appetite, decrease of salivation, decreased secretion and motoric functions.
  - Liver and pancreas - decreased synthesis of digestive enzymes.
- Kidneys – increased diuresis in the 1 and 3 stage of fever and accumulation of water in the second stage.

The role of fever

POSITIVE

- **Bacteriostatic and bactericidal effects on microbes**
- **Activation of immune system (innate and specific immunity)**
- **Increased liver function (detoxication, protein and vitamins synthesis)**
- **Active excretion of toxins (due to increased sweating and diuresis).**

NEGATIVE

- **Functional overload of organs (lungs, heart, endocrine glands)**
- **Hypohydration (cholera) and blood hemolysis (malaria) may lead to disturbances of blood clotting**
- **Disturbances of GIT function due to increased level of toxic substances**

The causes of hyperthermia

- Exogenous – hot climate, hot workshops, heat-isolated cloth, air high humidity, insufficient ventilation.
- Endogenous disturbances of heat regulation, without pyrogens formation
  - heat regulation center violations (cerebral traumas, encephalitis, cerebral edema)
  - fever caused by psychical diseases, nervous excitation, stresses

The causes of hyperthermia

- Endogenous increase of heat production
  - intensive muscular loading
  - pathologic contractive thermogenesis – tetanus spasms.
  - disconnection of oxidation and phosphorylation processes which increases heat production (poisoning by 2,4-dinitrophenolum, hyperthyroidism).
- Endogenous decrease of heat loss
  - sweat secretion decrease under poisoning by cholinolytic medicines (Atropinum);
  - skin vessels spasms (adrenimimetic overdose and adrenali increased rejection).

Hyperthermia compensation stage

Increase of heat loss –dilating of skin arterioles, increase of skin temperature, increased perspiration.

Changes in organism's functions:

- increase of heart rate and BP;
- centralization of bloodflow;
- decrease of alveolar ventilation;
- decrease of working capacity, weakness, drowse, high irritability.

Changes in the organism due to body's temperature

- **38°C** - Sweating.
- **39°C** - Severe sweating, redness of the skin, fast heart rate and breathlessness.
- **40°C** - + Fainting, dehydration, weakness, vomiting, headache and dizziness, profuse sweating.

Compensation

- **41°C** - + hallucinations, delirium, drowsiness.
- **42°C** - + severe delirium and vomiting, coma, convulsions.
- **43°C** - + serious brain damage, continuous convulsions and shock, cardio-respiratory collapse will occur.
- **44°C or more** - almost certainly death will occur.

Decompensation

Hyperthermia decompensation stage

- cardiovascular disturbances – progressive tachycardia, decrease of heart stroke volume, microcirculation disorders, increased blood clotting.
- acidosis due to hypoxia.
- hypohydration (du to profound sweating) leads to increased blood viscosity
- metabolic violations

The biochemical effects of long exposure to high temperature

- Denaturation of proteins – blocking of all enzyme pathways
- Liquefaction of lipid membrane – destroying cell walls
- Damage of mitochondrial membranes - paralysis of energy production
- Increase of Na+ leak

The biochemical effects of long exposure to high temperature

- Increase of peroxidative oxidation of lipids – accumulation of high toxic suboxidized lipid metabolism products
- Carbohydrate metabolism and other energy pathways are disrupted.

The loss of energy in the cell reduces normal cellular functions and thermoregulation fails.

Heat stroke manifestation

- Body temperature >40 C
- CNS depression (the most important sign of heat stroke).
  - bizarre behavior
  - amnesia
  - collapse, delirium, stupor, and coma.
- The skin color may be ashen, implying circulatory collapse, or pink.
- Symptoms of autonomic nervous system dysfunction, miosis, decreased pain response, and dehydration symptoms

Thermotherapy (pyrotherapy)

General thermotherapy - injection of bacterial lipopolysaccride (primary pyrogens).

- Aims:
  - to increase adaptive and innate immunity in chronic infectious diseases (arthritis, syphilis)
  - to intensify reparative processes in bones and other tissues after their damage, trauma, surgical operations.

Thermotherapy (pyrotherapy)

- **Local thermotherapy** may be used in cancer treatment:
  - tumor cells have difficulty dissipating heat.
  - local increase of temperature brake mitoses in cancer cells, cause denaturation of cancer cell membrane proteins.
  - Even if the cancerous cells do not die, they become more susceptible to ionizing radiation treatments or to certain chemotherapies.

Differences between fever and hyperthermia

	Fever	Hyperthermia
Cause	Bacterial pyrogens, tissues decay products with secondary pyrogens synthesis	External and internal factors, which don't cause secondary pyrogens synthesis
Ontogenetic aspects	Is formed in the end of the first year of life	Is formed in any period of life

Differences between fever and hyperthermia

	Fever	Hyperthermia
Temperature adjusting point	Higher than normal	Normal
Thermoregulation	Normal	Impaired
Symptoms	Depends on the stage	Don’t depend on the stage but severity increases with time
The role for the organism	Both positive and negative	Only negative
Treatment	Antipyretic medicines	Physical cooling

When fever treatment is needed

- when fever is accompanied with high pyretic temperature (more than 38,5 C);
- when fever is observed in the patient with cardio-vascular failure, diabetes mellitus or other endocrine diseases;
- in newborns (0-2 months), infants (2 months till 1 year) and aged people.

The causes of hypothermia

- not effective thermoregulation (infants, babies and aged people);
- too long exposure to the cold surroundings;
- disturbances of nervous system function (drugs, alcohol, toxic substances, parkinson disease);
- disturbances of endocrine system function (hypothyroidism, hypopituitarism, adrenal insufficiency) that lead to decreased heat production.

Hypothermia compensation stage

- Behavioral thermoregulation
- Reduction of heat loss - peripheral blood vessels constriction.
- Increase of heat production - activation of bloodflow in inner organs, induction of contractive thermogenesis (shivering).
- Heart and lungs: tachycardia, increase of BP and heart stroke volume, increased ventilation of lungs.

Changes in the organism due to body's temperature

35°C - Intense shivering, numbness and bluish / greyness of the skin.

34°C - Severe shivering, loss of movement of fingers, blueness and confusion.

Compensation

33°C + sleepiness, depressed reflexes, progressive loss of shivering, slow heart beat, shallow breathing.

32°C + Hallucinations, delirium, comatose. Shivering and nervous reflexes are absent.

31°C + shallow breathing and slow heart rate. Possibility of serious heart rhythm problems.

28°C + Severe heart rhythm disturbances, problems with breathing.

24-26°C or less - Death due to irregular heart beat or respiratory arrest.

Decompensation

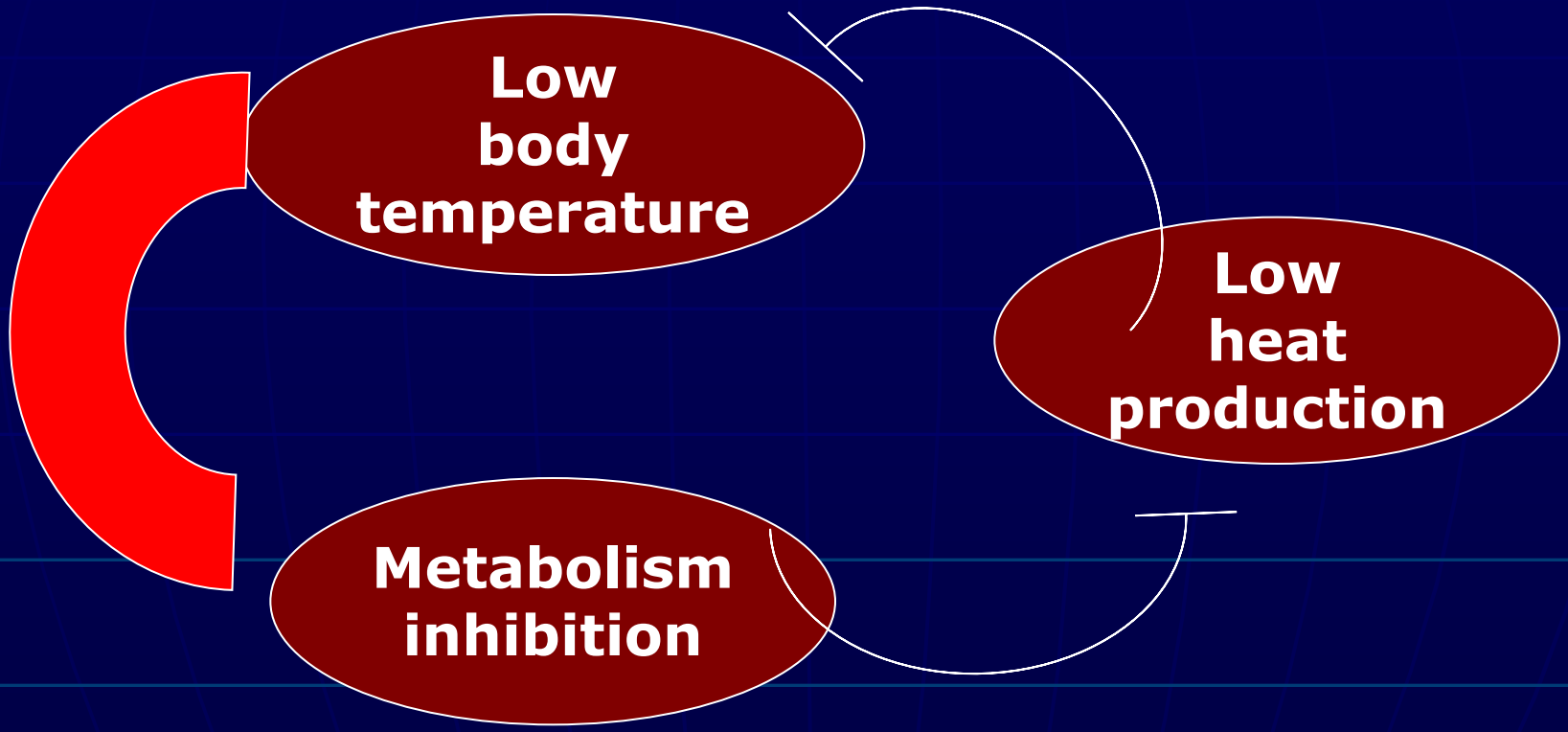
Hypothermia decompensation stage

- slowing of biochemical reactions (inhibition of metabolism);
- increase of blood viscosity, slowing of blood flow, increase of blood coagulation;
- development of tissue's hypoxia.

Cold core temperature (below 25^0C) causes the depression of brain respiratory, vascular and thermoregulation centers, the violation of heart contraction.

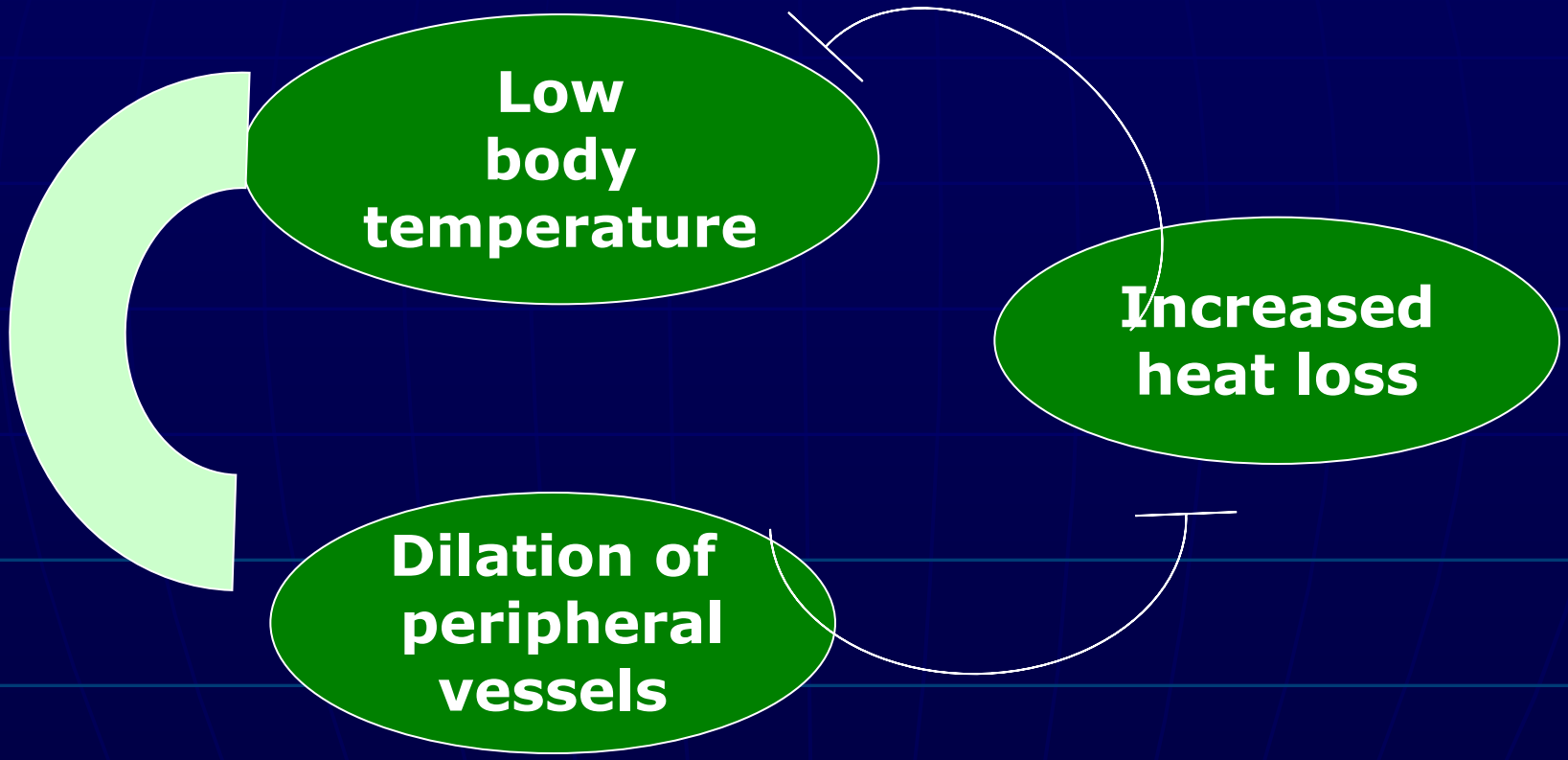
Vicious circles during hypothermia

Metabolic circle



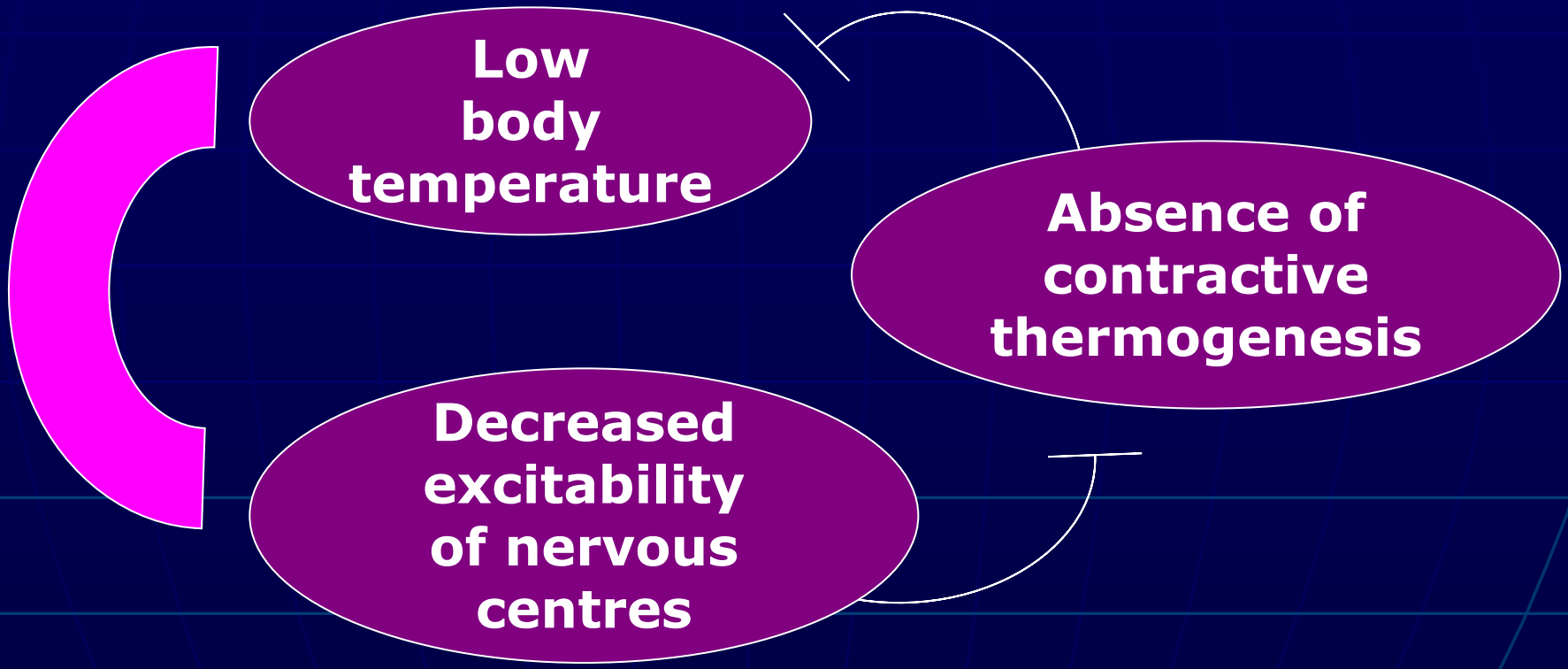
Vicious circles during hypothermia

Vascular circle



Vicious circles during hypothermia

Neuro-muscular circle



Controlled hypothermia

Systemic controlled hypothermia is used in surgical operations on the organs with stopped bloodflow – heart, brain, large vessels.

- Cells and tissues in the controlled hypothermia decrease their functional activity.
- It prevents disturbances of ABB, water and ion metabolism, increase tissue's resistance to hypoxia and other pathogenic stimuli.

Local induced hypothermia (brain, kidneys, liver, prostate etc.) is provided complex surgical operations.

The prospects of using medical hibernation

- **Organ preservation (for transplantation).**
- **Strokes treatment (prevention of brain death).**
- **Trauma (decrease of body's oxygen demand to survive bleedings).**