Maintenance of Life and Control Mechanisms

MD 567712
Cells and Molecular Biology

https://www.freepik.com/free-photos-vectors/balance

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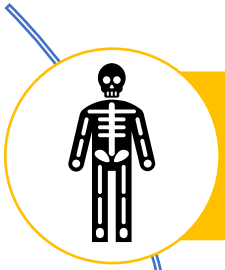
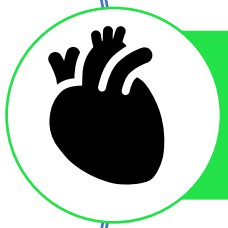
Scope



Body homeostasis and regulation



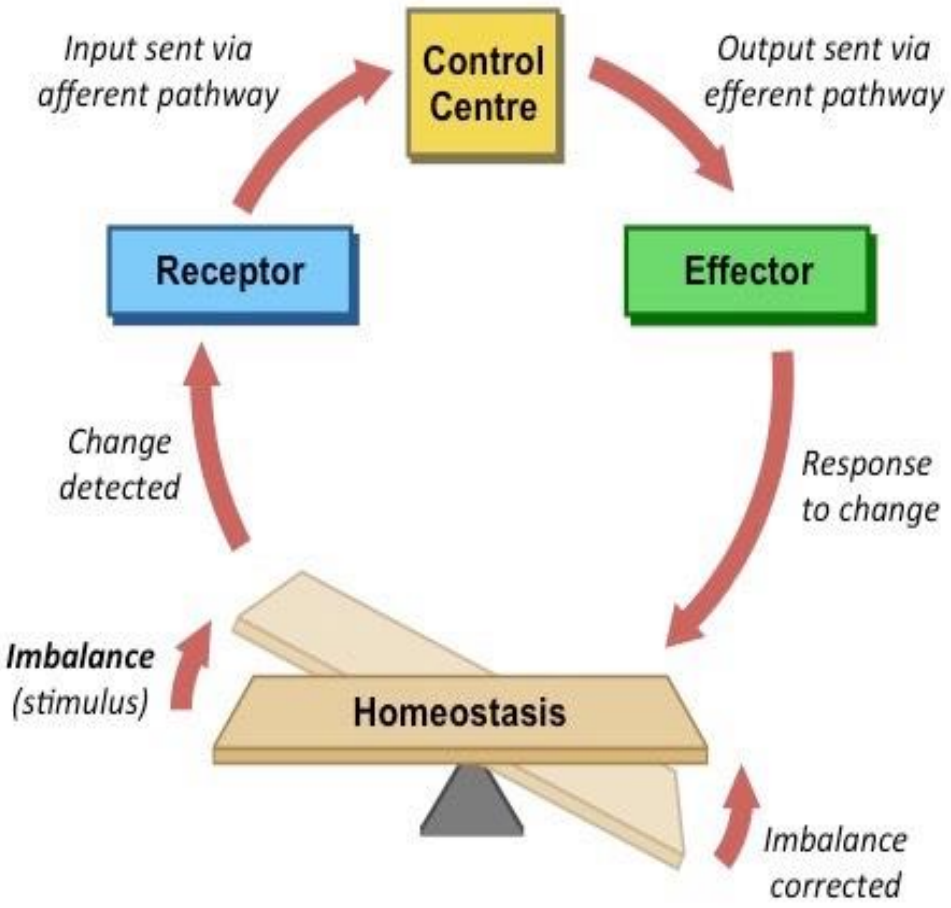
Controls of fluids and electrolytes balances

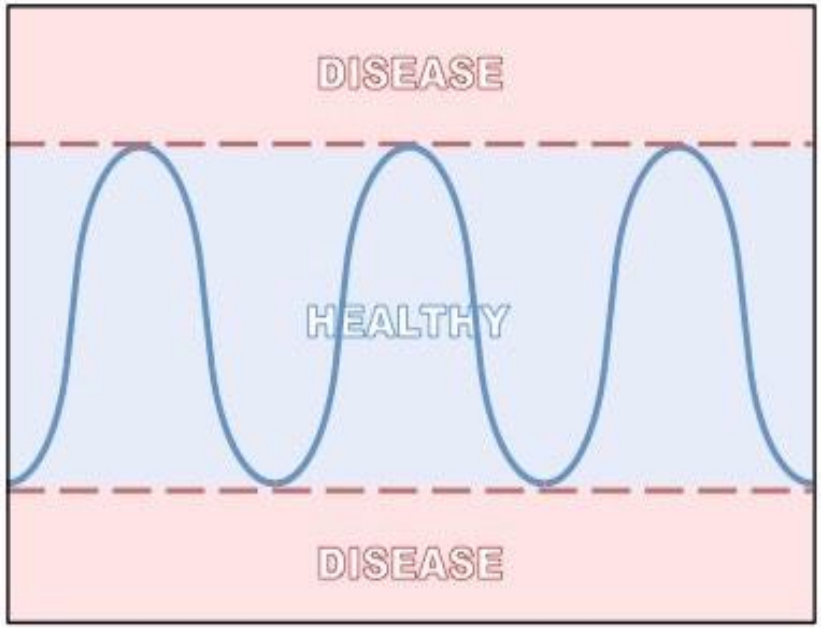
Regulation of body metabolisms and thermoregulation

Body Homeostasis

Homeostasis

Homeostasis is the maintenance of a stable internal environment and requires integration of organ system functions.





Homeostasis does **not** involve keeping conditions static

It involves keeping conditions within tightly regulated *physiological tolerance limits*

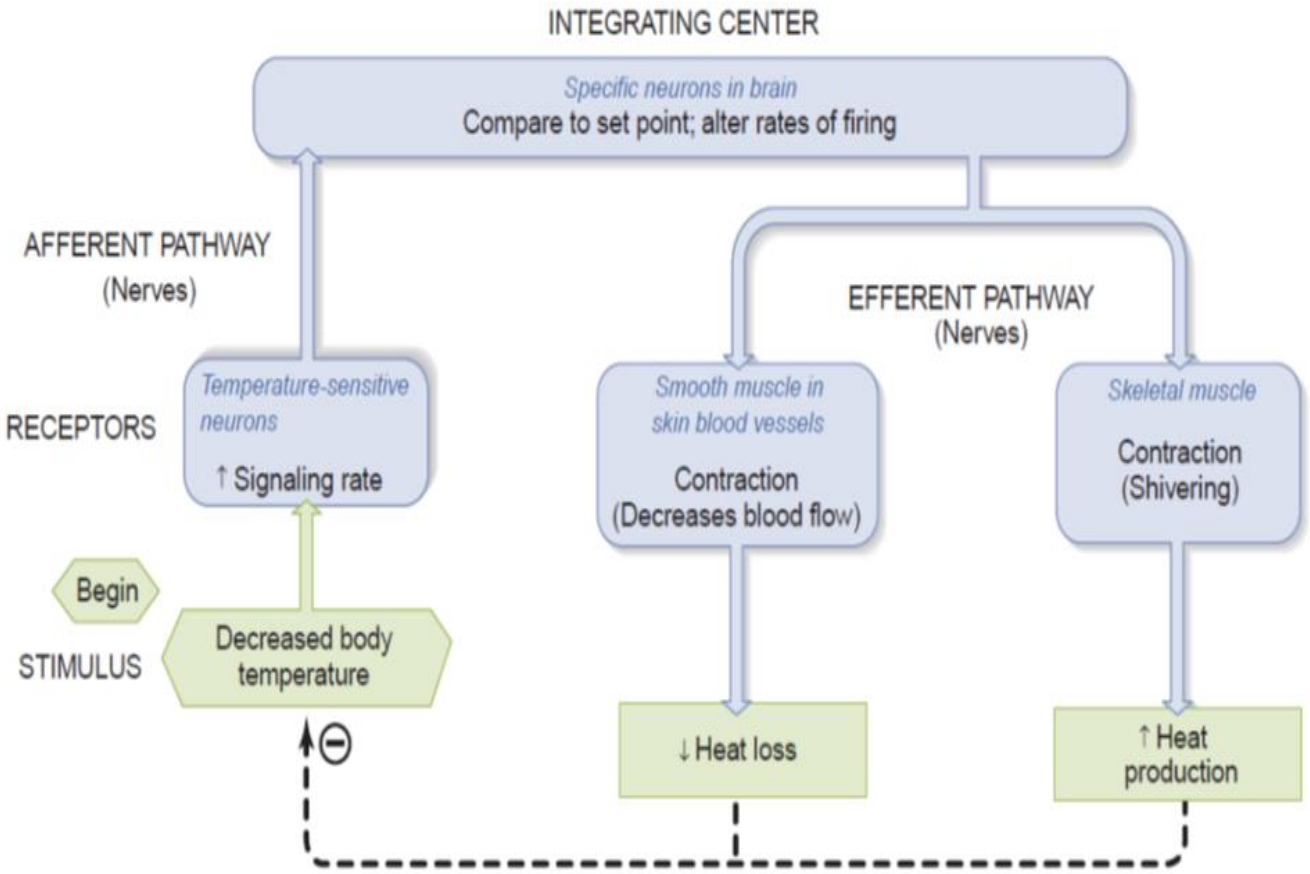
https://ib.bioninja.com.au/standard-level/topic-6-human-physiology/66-hormones-homeostasis-and/homeostasis.html

Homeostatic regulation : Feedback loops

Feedback loops

- **Negative feedback**
- **Positive feedback**

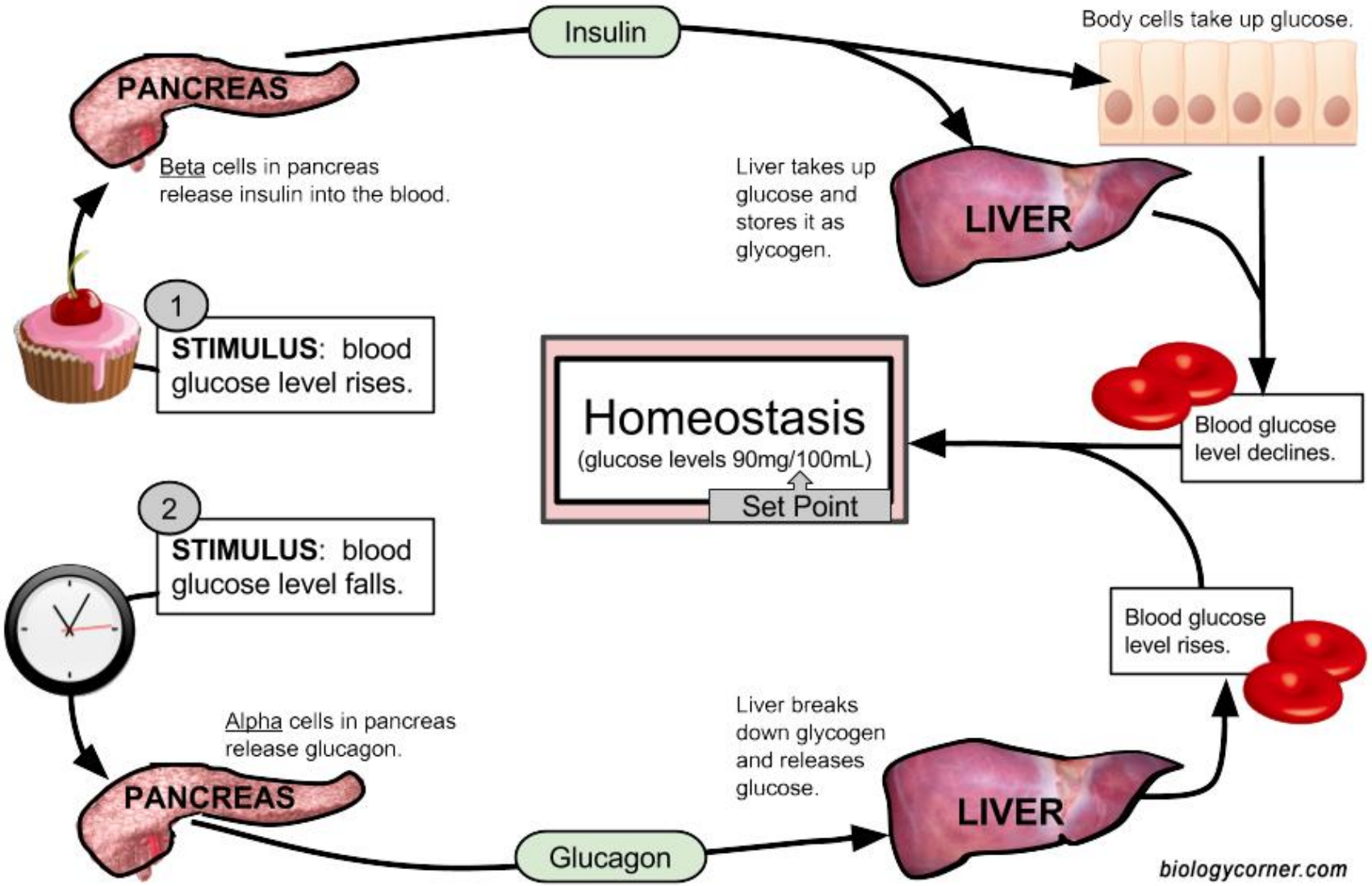
- **Receptor**
- **Control center**
- **Effector**



Negative feedback

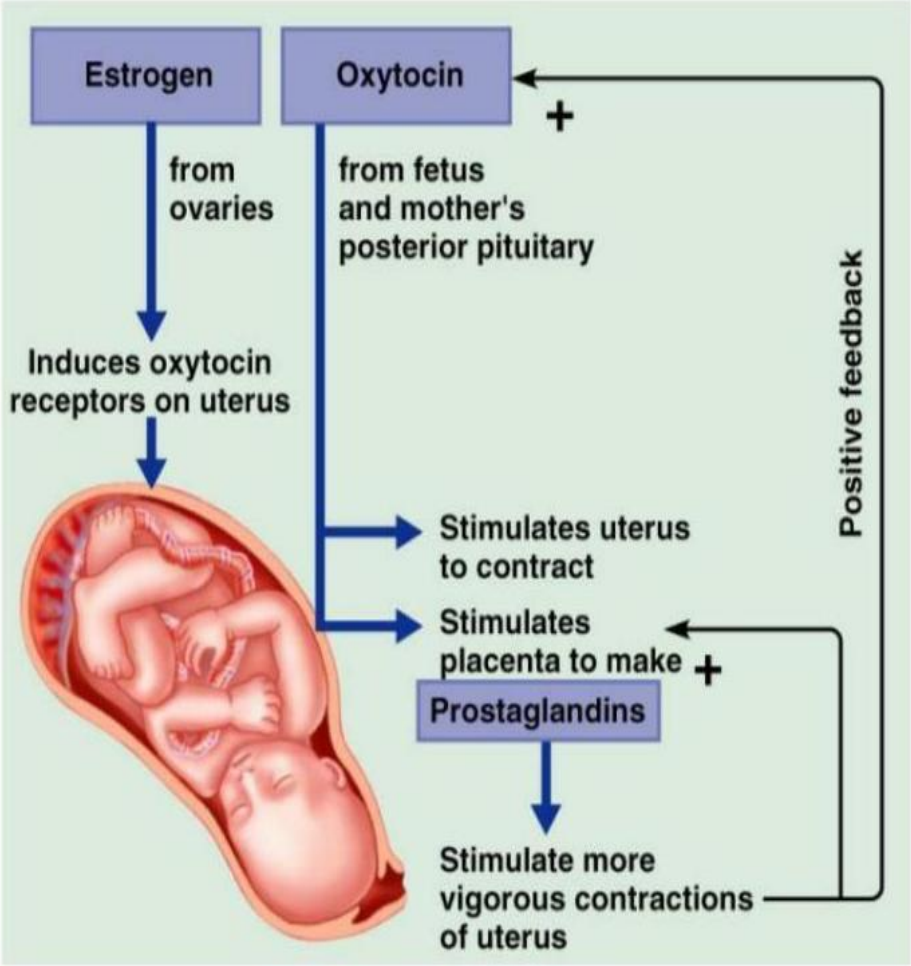
Negative feedback: a reaction in which the system responds in such a way as to reverse the direction of change.

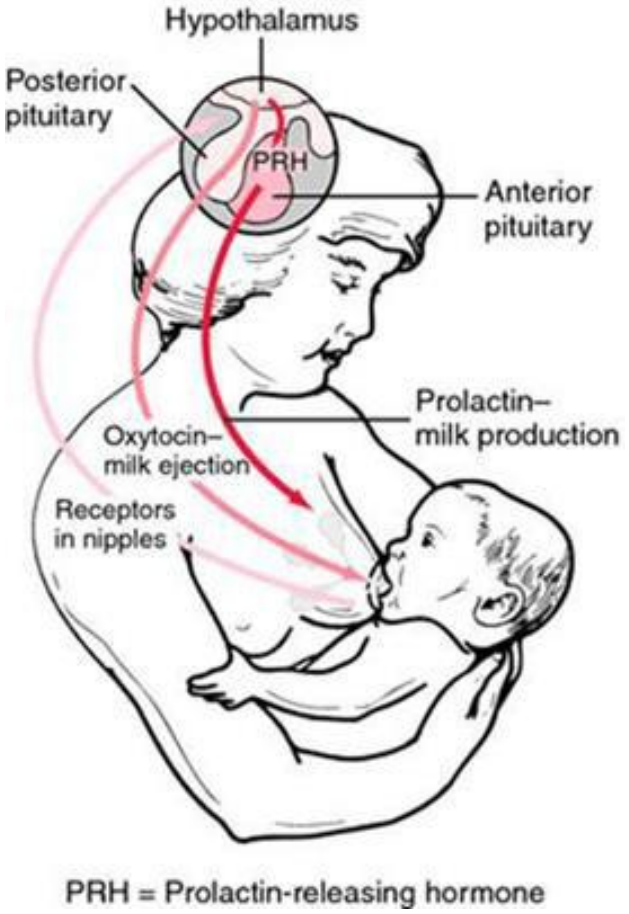
Glucose regulation



Positive feedback

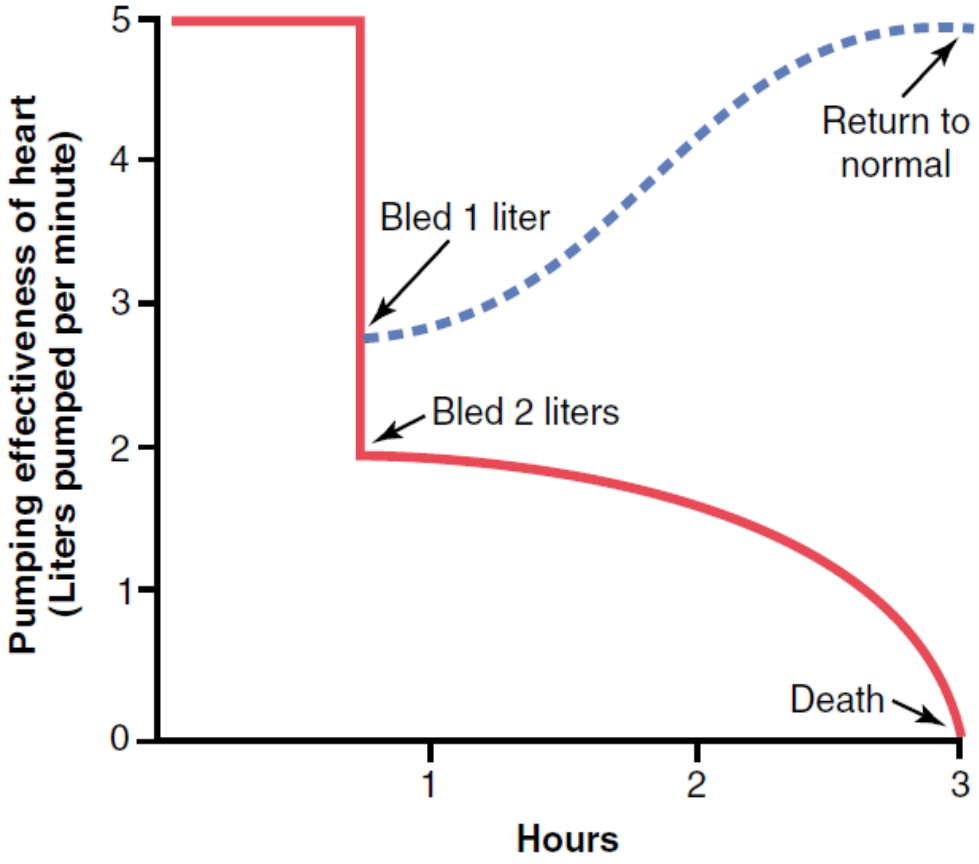
Positive feedback: a response is to amplify the change in the variable.





Stimuli for lactation. From Applegate, 2000.

Positive feedback can sometimes cause vicious cycles and death



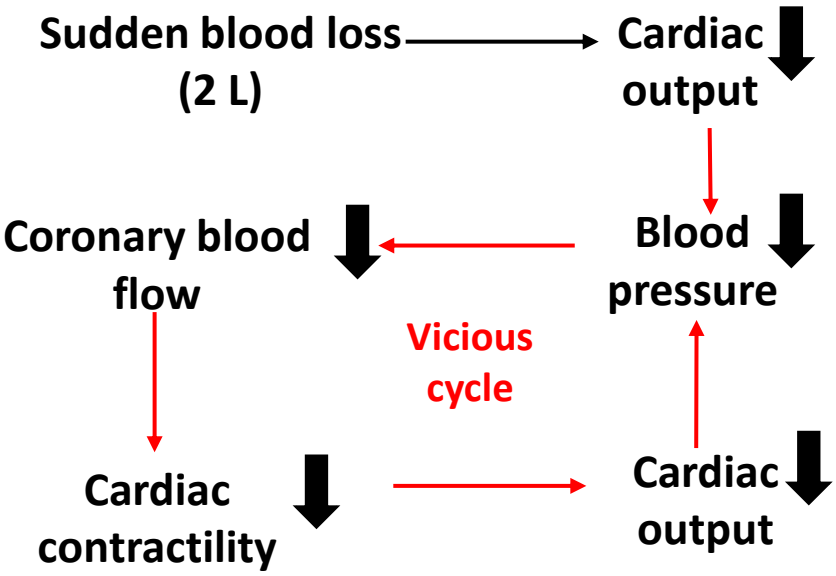
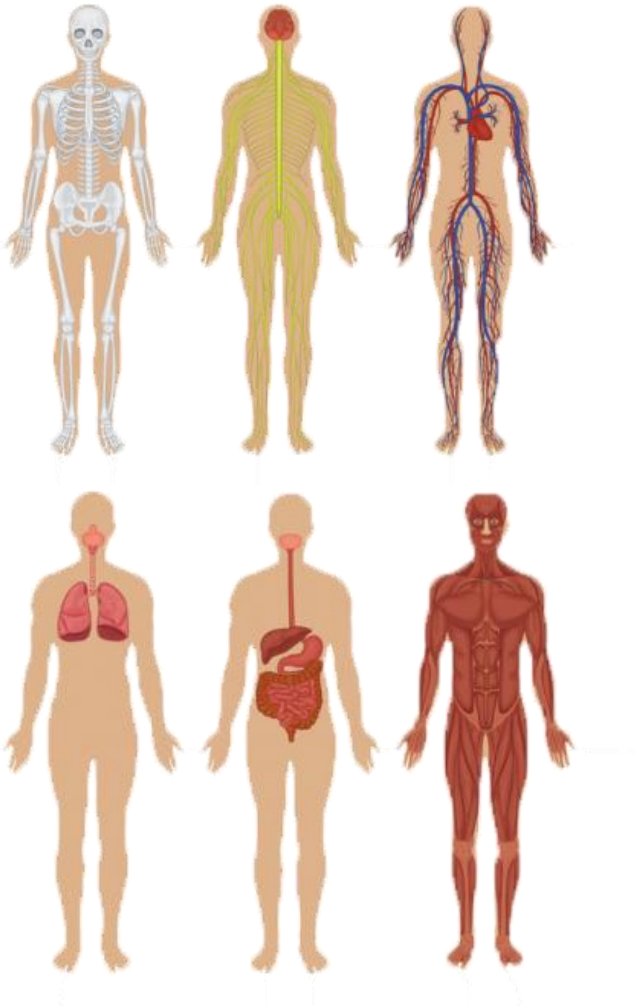


Figure 1-3 Recovery of heart pumping caused by *negative feedback* after 1 liter of blood is removed from the circulation. Death is caused by *positive feedback* when 2 liters of blood are removed.

Summary

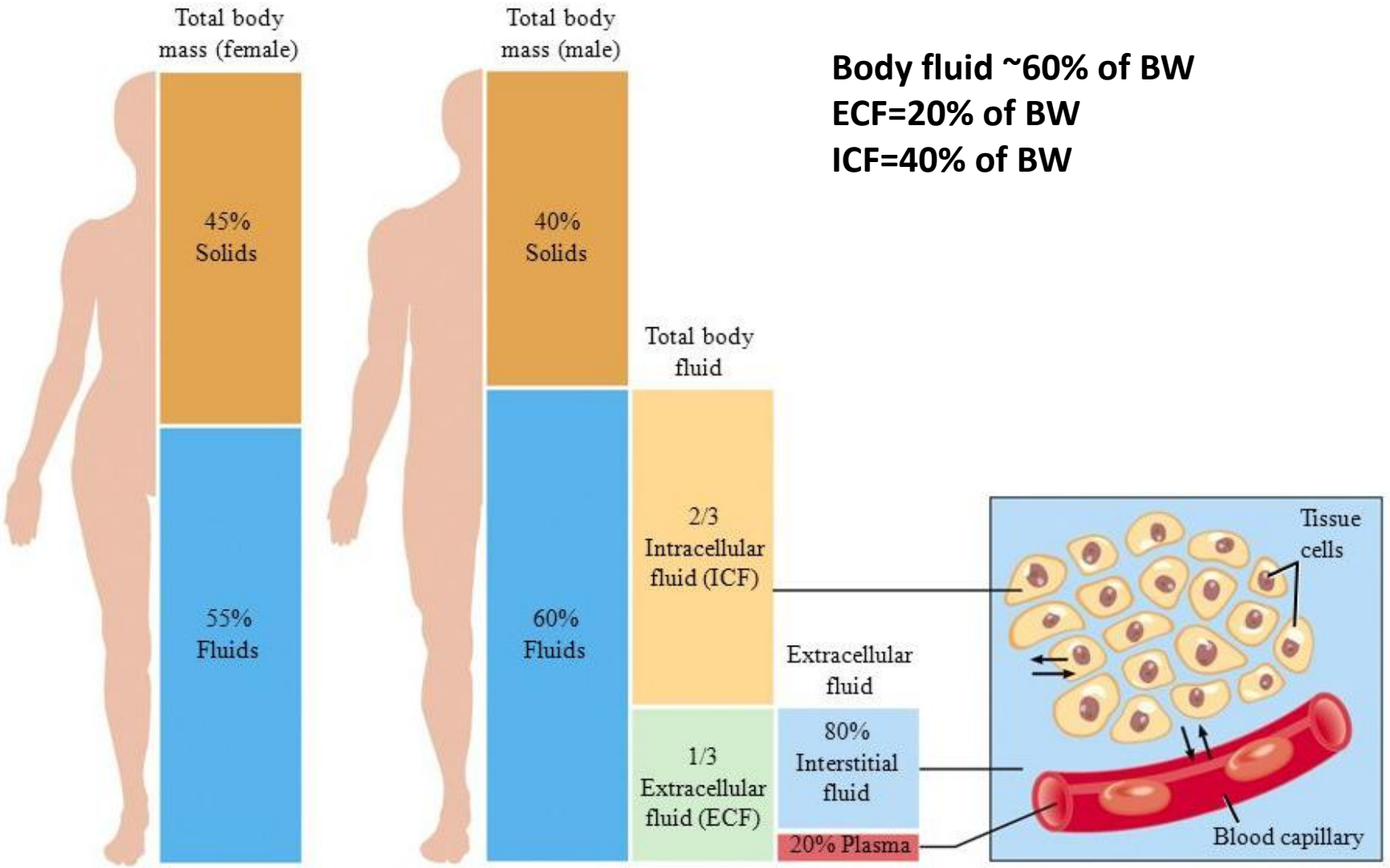
Body System	Components	Major Function(s)
Cardiovascular	Heart, blood vessels, blood	Transport of materials throughout the body
Digestive	Gastrointestinal tract, liver, pancreas	Assimilation of nutrients; elimination of some wastes
Endocrine	Endocrine glands	Coordination of body functions through release of regulatory molecules
Immune	Thymus, spleen, lymphatic system, white blood cells	Defense against pathogens
Integumentary	Skin	Protection against external environment
Musculoskeletal	Skeletal muscle and bones	Movement and support
Nervous	Brain, spinal cord, peripheral nerves	Coordination of body functions through electrical signals and release of regulatory molecules; cognition
Reproductive	Gonads, penis, vagina, uterus	Procreation
Respiratory	Lungs	Oxygen and carbon dioxide and exchange with external environment
Urinary	Kidneys, bladder	Homeostasis of ion concentrations in internal environment; elimination of wastes

Homeostasis Throughout the Body!!



Controls of fluids and electrolytes balances

Body fluids

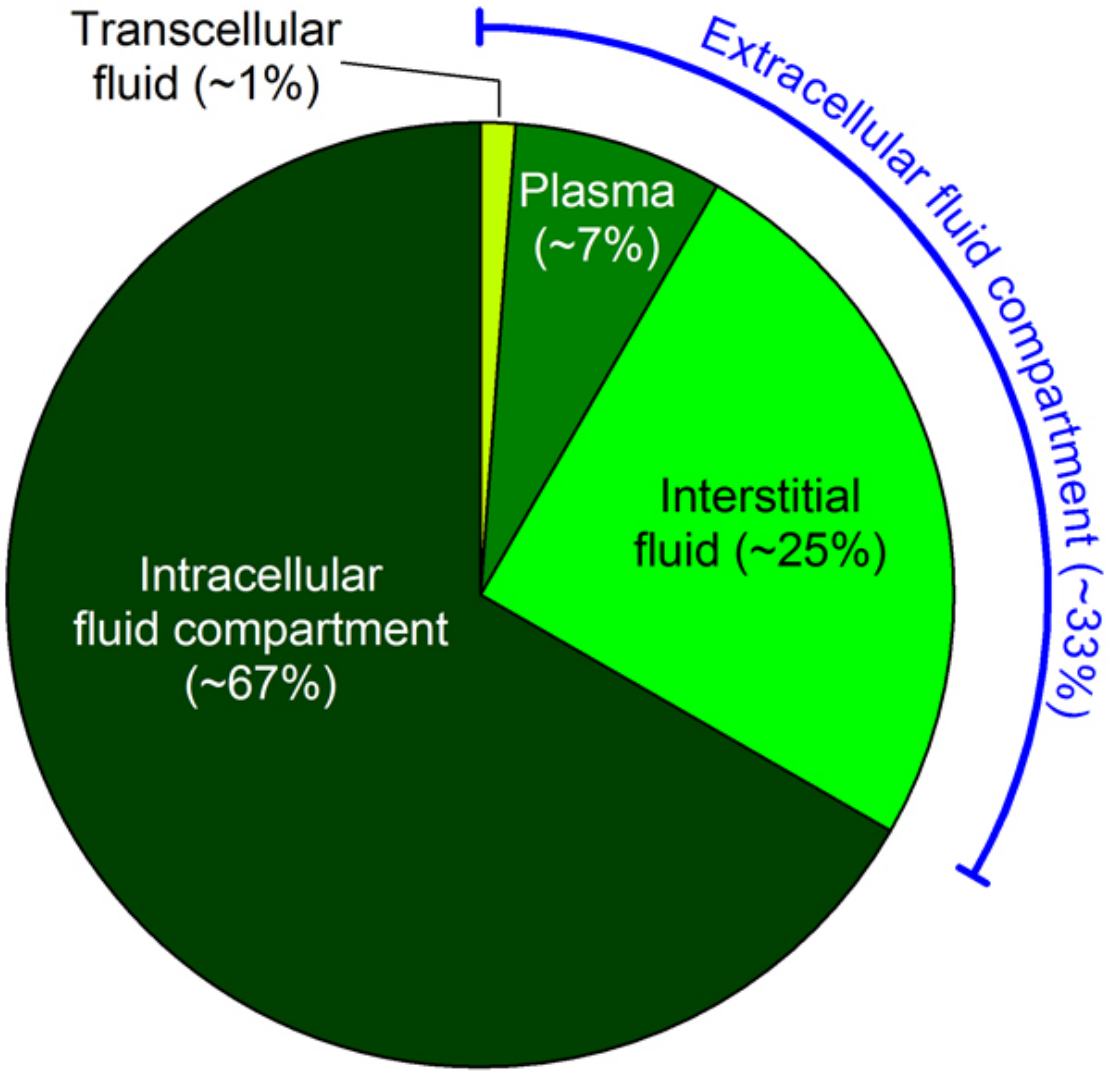


(a) Distribution of body solids and fluids in average lean, adult female and male

(b) Exchange of water among body fluid compartments

Body fluid ~60% of BW
ECF=20% of BW
ICF=40% of BW

Body fluids



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What fraction of total-body water is extracellular?

Assume that water constitutes 60% of a person's body weight.

What fraction of this person's body weight is due to extracellular body water?

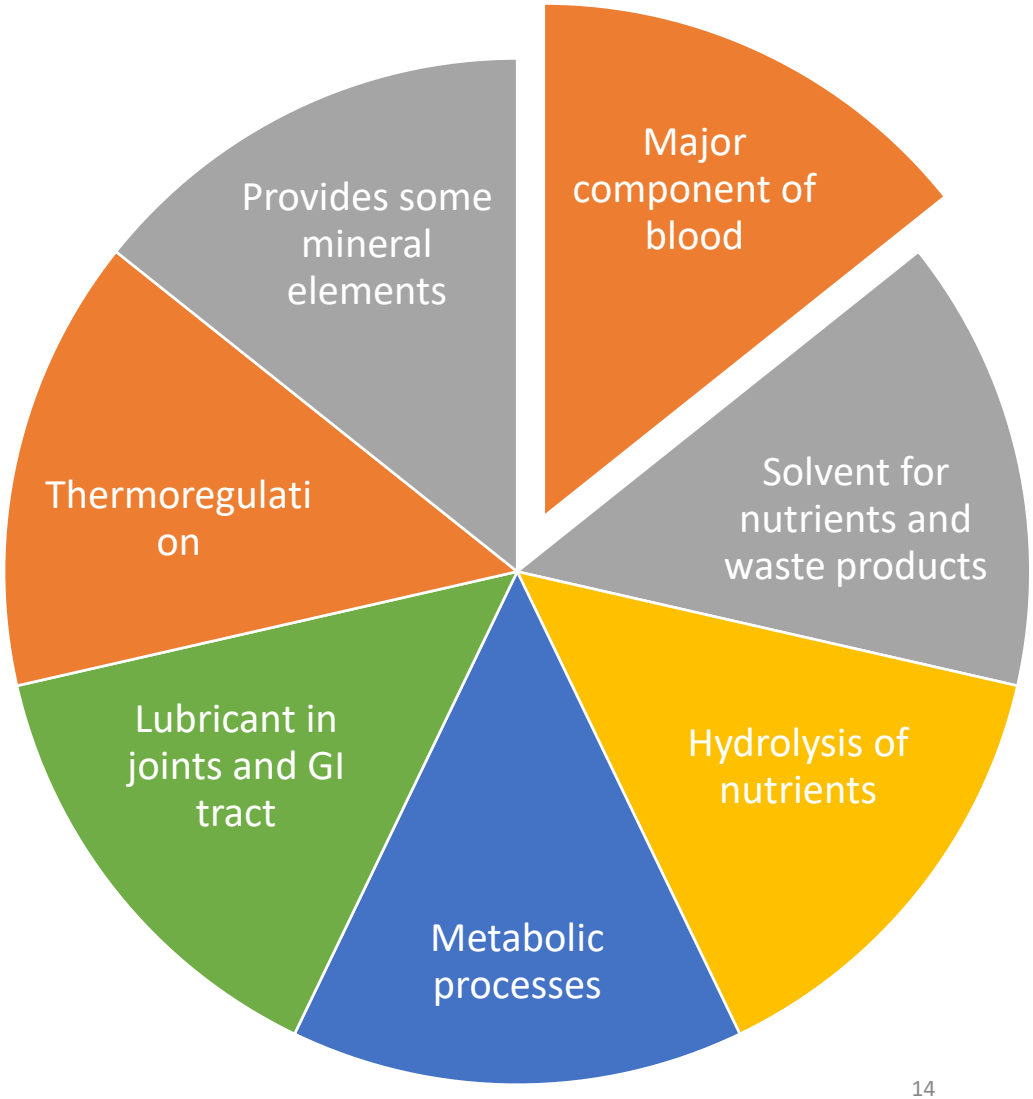
Composition and functions of body fluids

Organic substances

Glucose
Amino acids
Fatty acids
Hormones
Enzymes

Inorganic substances

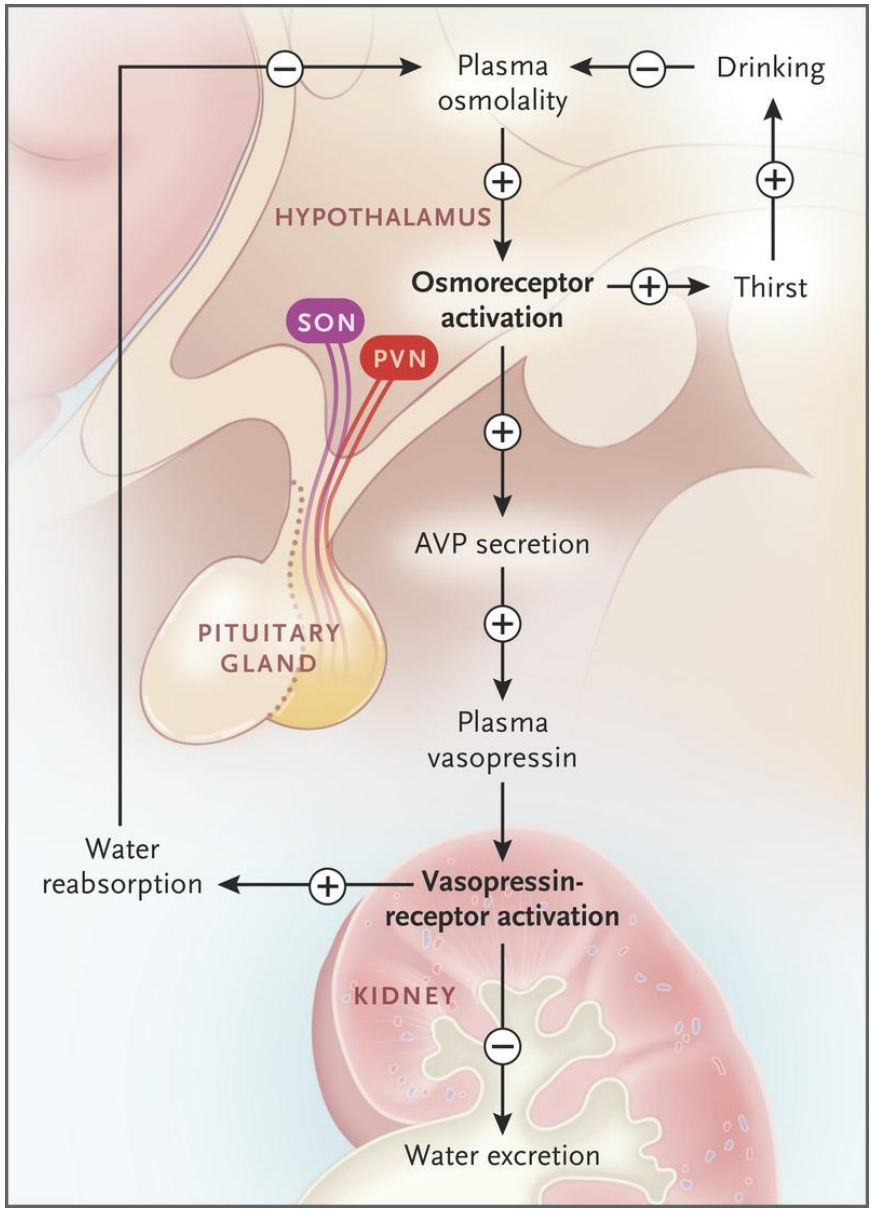
Sodium
Potassium
Calcium
Magnesium
Chloride
Phosphate
Sulphate



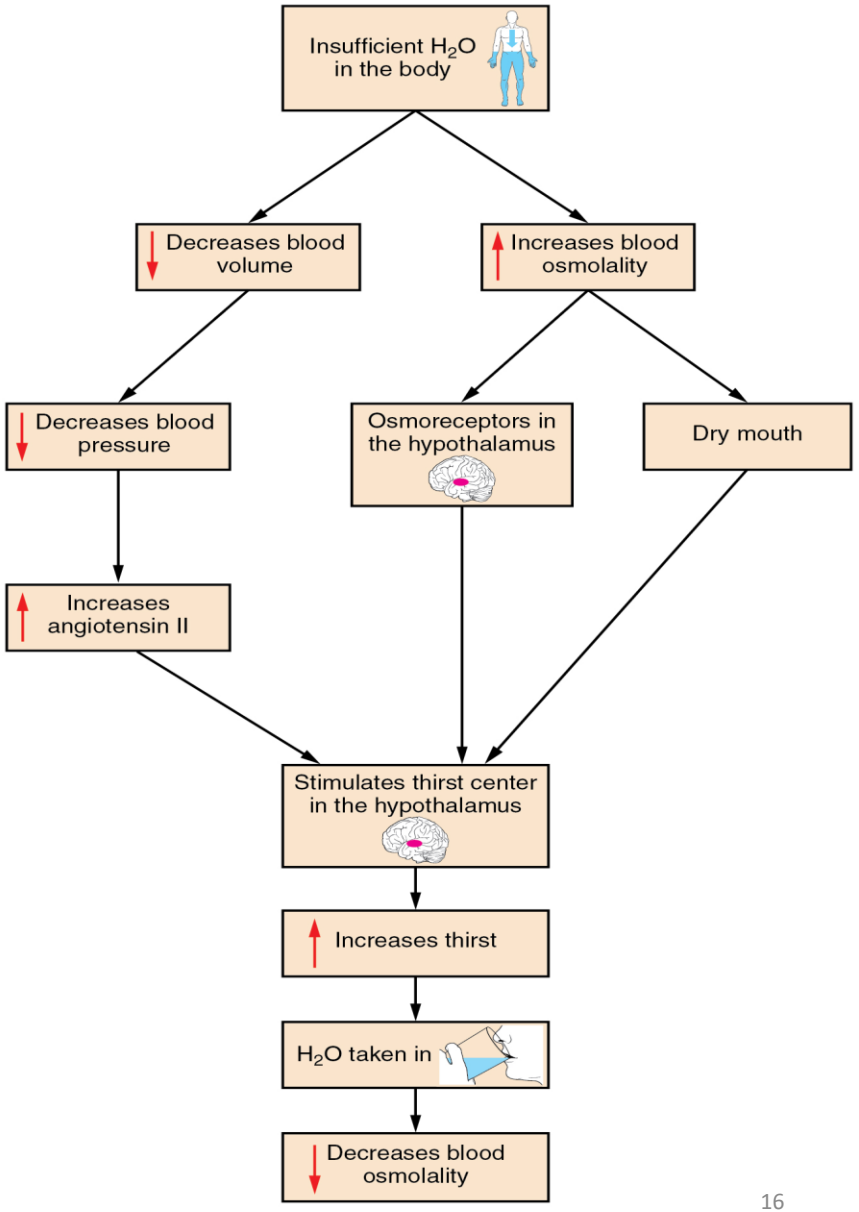
Body fluid balances

	Normal	Prolonged, Heavy Exercise
Intake		
Fluids ingested	2100	?
From metabolism	200	200
Total intake	2300	?
Output		
Insensible—skin	350	350
Insensible—lungs	350	650
Sweat	100	5000
Feces	100	100
Urine	1400	500
Total output	2300	6600

Regulation of water balance

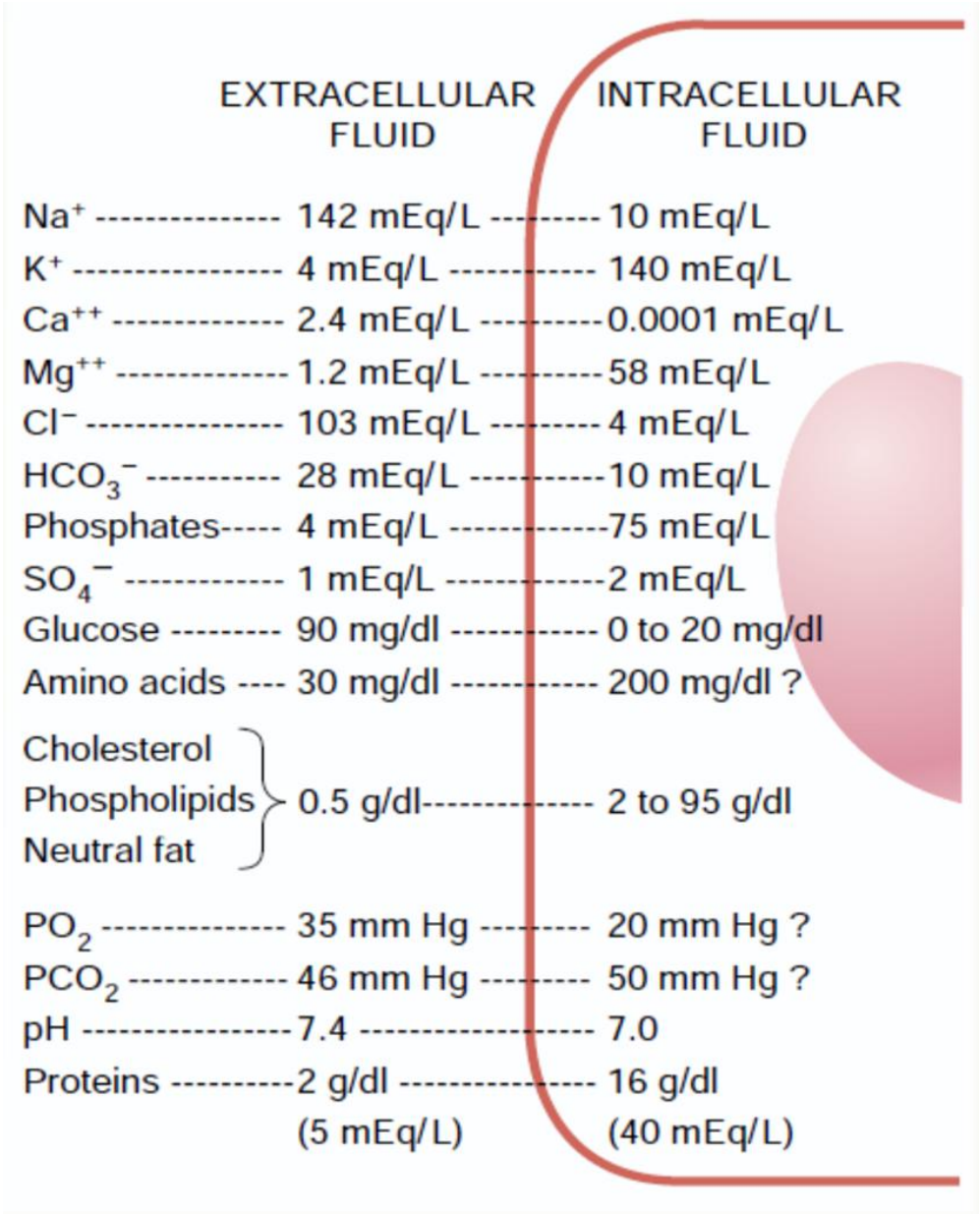


https://www.nejm.org/doi/full/10.1056/nejmra1404726



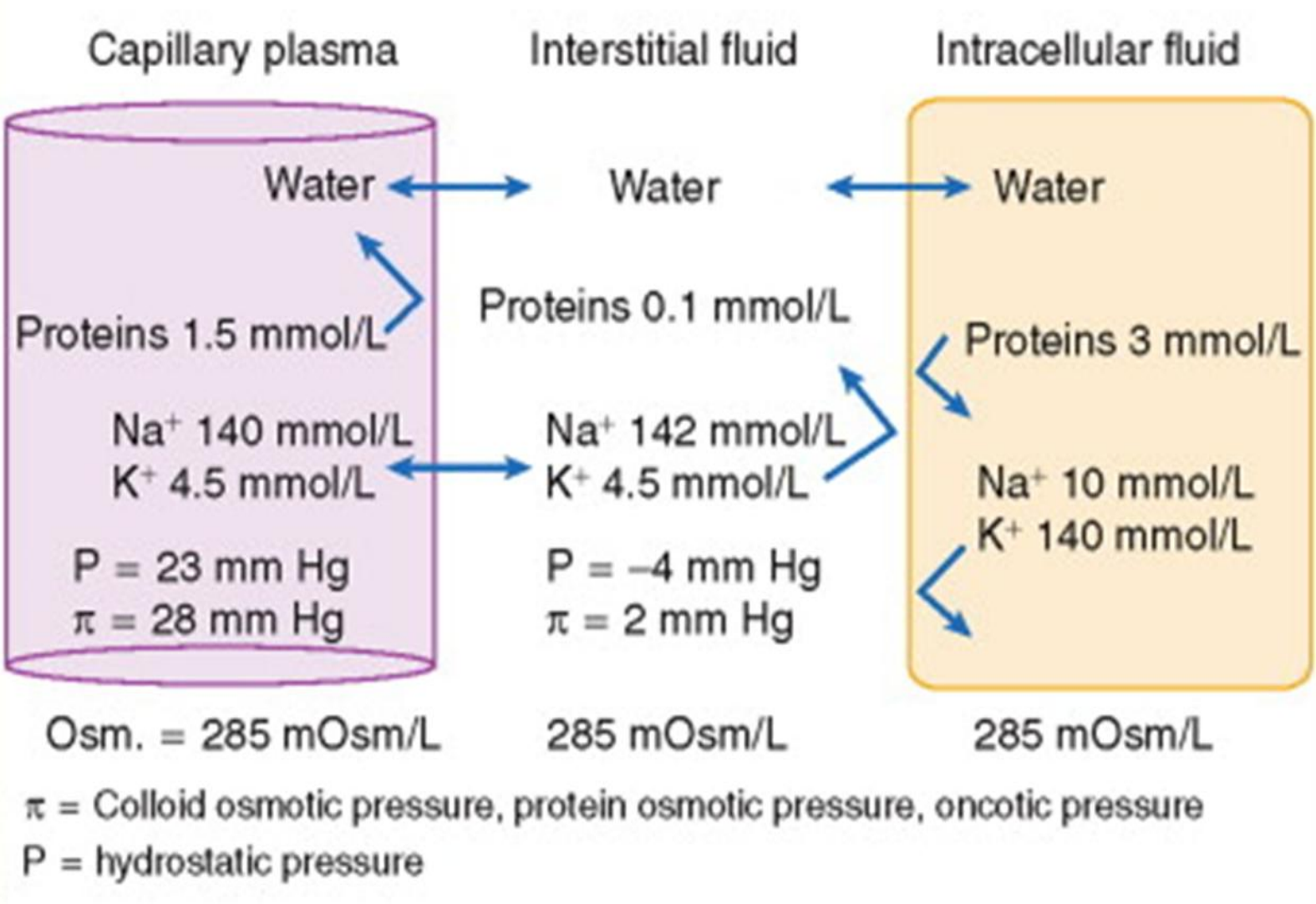
https://open.oregonstate.education/aandp/chapter/26-2-water-balance/

Electrolyte



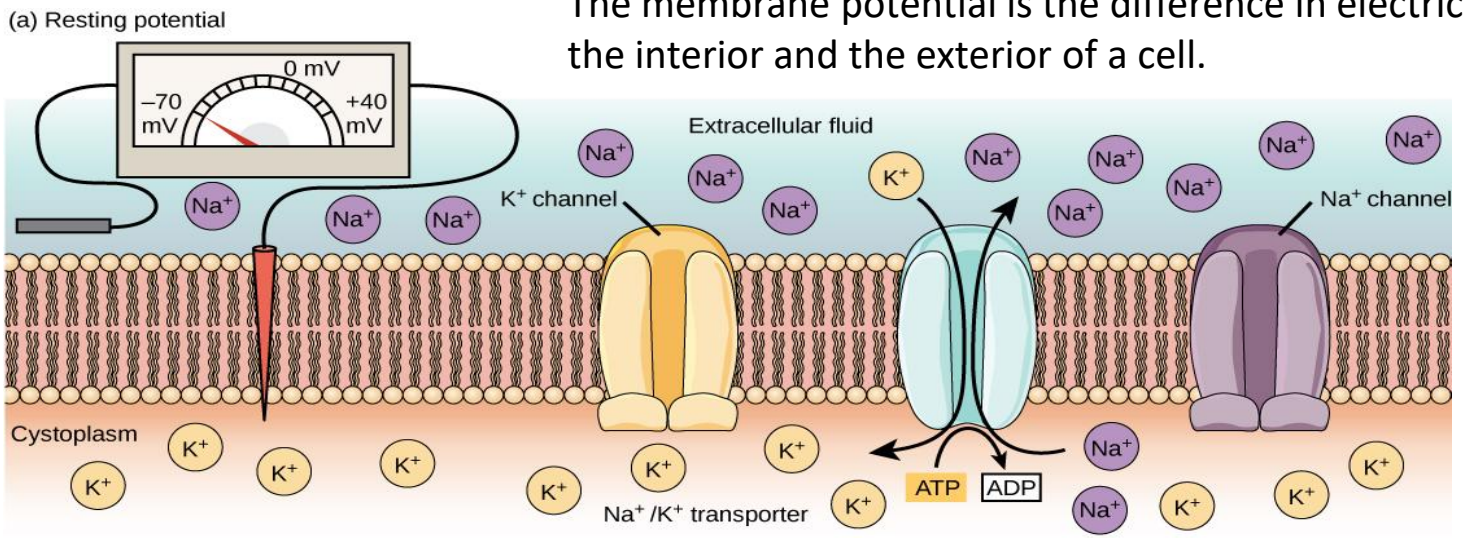
- Control osmosis
- Acid base balance
- Cell polarization
- Co-factors for enzymes

Electrolytes: ECF VS ICF

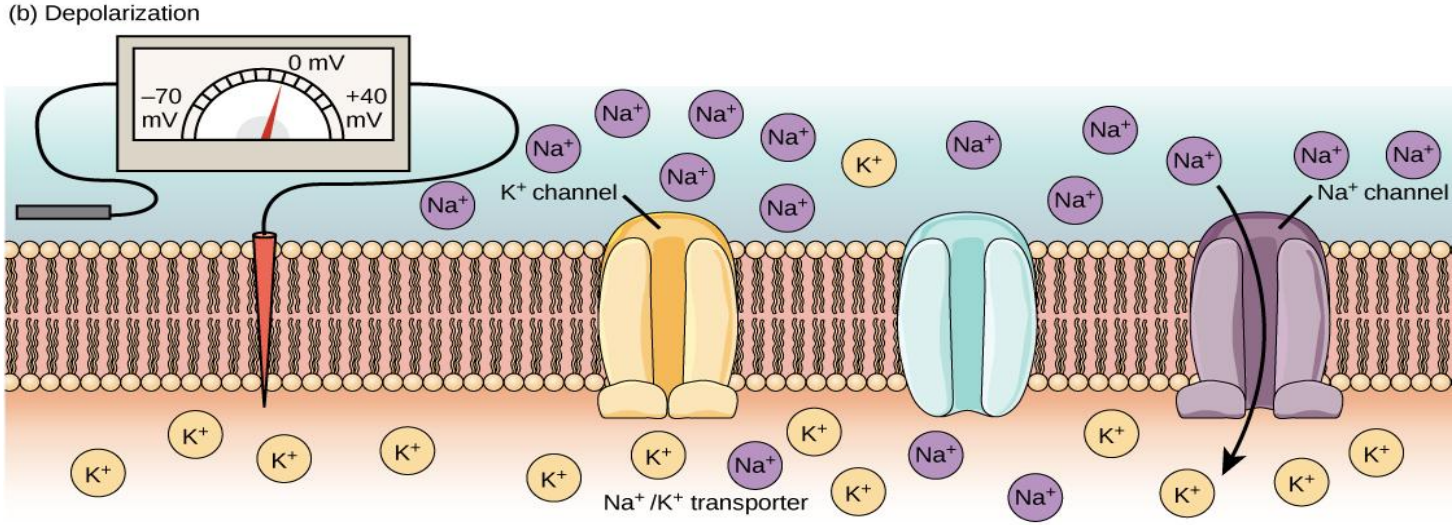


Membrane potential

The membrane potential is the difference in electric charge between the interior and the exterior of a cell.



At the resting potential, all voltage-gated Na^+ channels and most voltage-gated K^+ channels are closed. The Na^+/K^+ transporter pumps K^+ ions into the cell and Na^+ ions out.

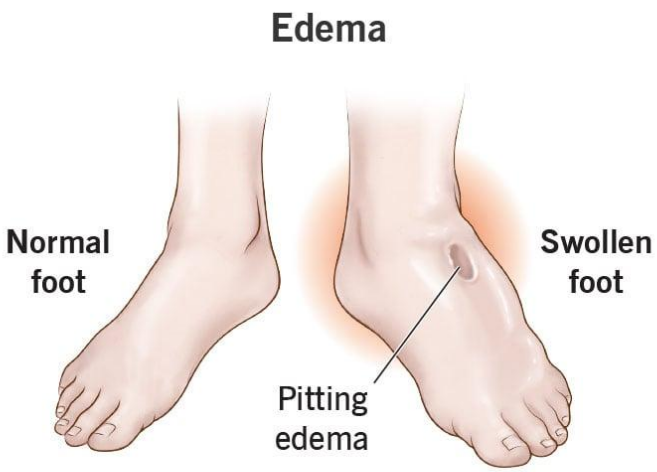


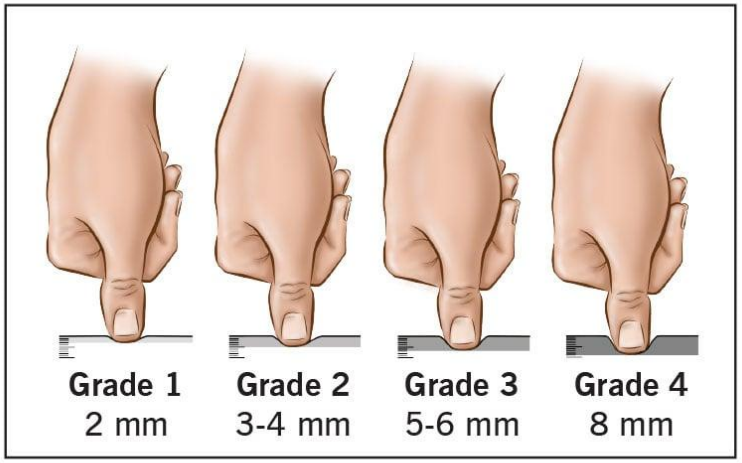
In response to a depolarization, some Na^+ channels open, allowing Na^+ ions to enter the cell. The membrane starts to depolarize (the charge across the membrane lessens). If the threshold of excitation is reached, all the Na^+ channels open.

https://www.lecturio.com/concepts/membrane-potential/

Fluid imbalance

Edema





Dehydration

THIRST

With the onset of thirst you've already lost approximately 2% of bodyweight in fluid.

FATIGUE

A critical symptom, it puts you at risk on site, affecting your ability to concentrate, stay focus & reduces reaction times

SWEATING

Fluid & electrolytes help retain fluids but are lost from sweat

– OTHER SYMPTOMS TO LOOK OUT FOR –

- Dry mouth
- Dry skin
- Irritability
- Light-headedness
- Decreased urination

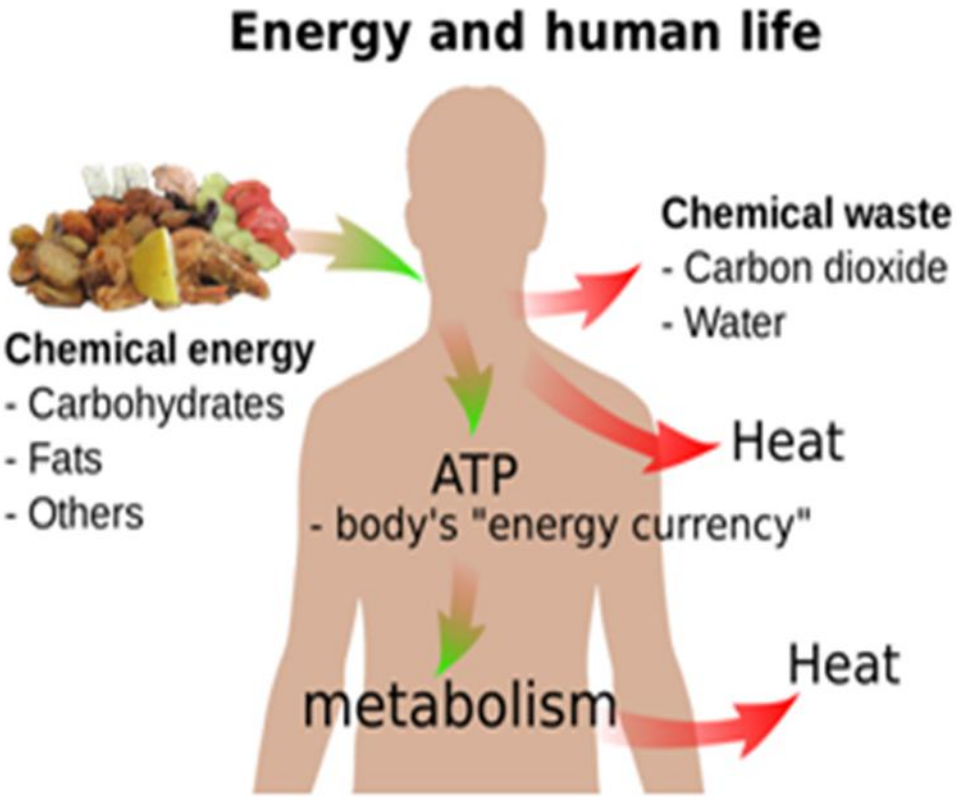
- Dark coloured urine
- Muscle cramps
- Headaches
- Nausea

- Speech confusion
- Poor concentration
- Lapses in memory
- Sleep impairment
- Fainting

Regulation of Body Metabolism and Body temperature

Metabolism

"Metabolism is the sum of all energy-requiring and energy-consuming processes of the body"



→ chemical reaction, biosynthesis

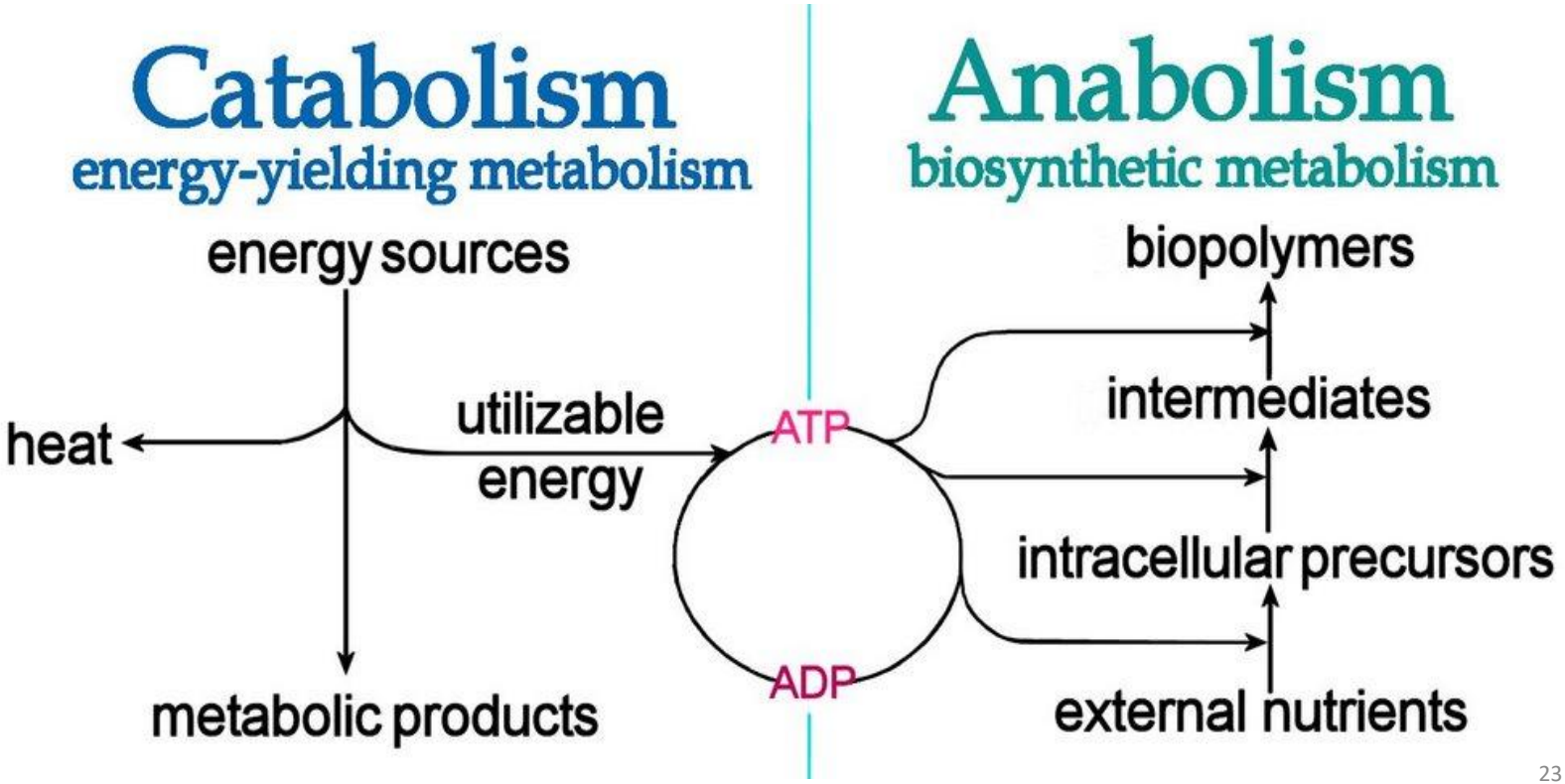
→ maintain body temperature

→ perform work

Main metabolism

Catabolic reactions break down large organic molecules into smaller molecules, releasing the energy contained in the chemical bonds

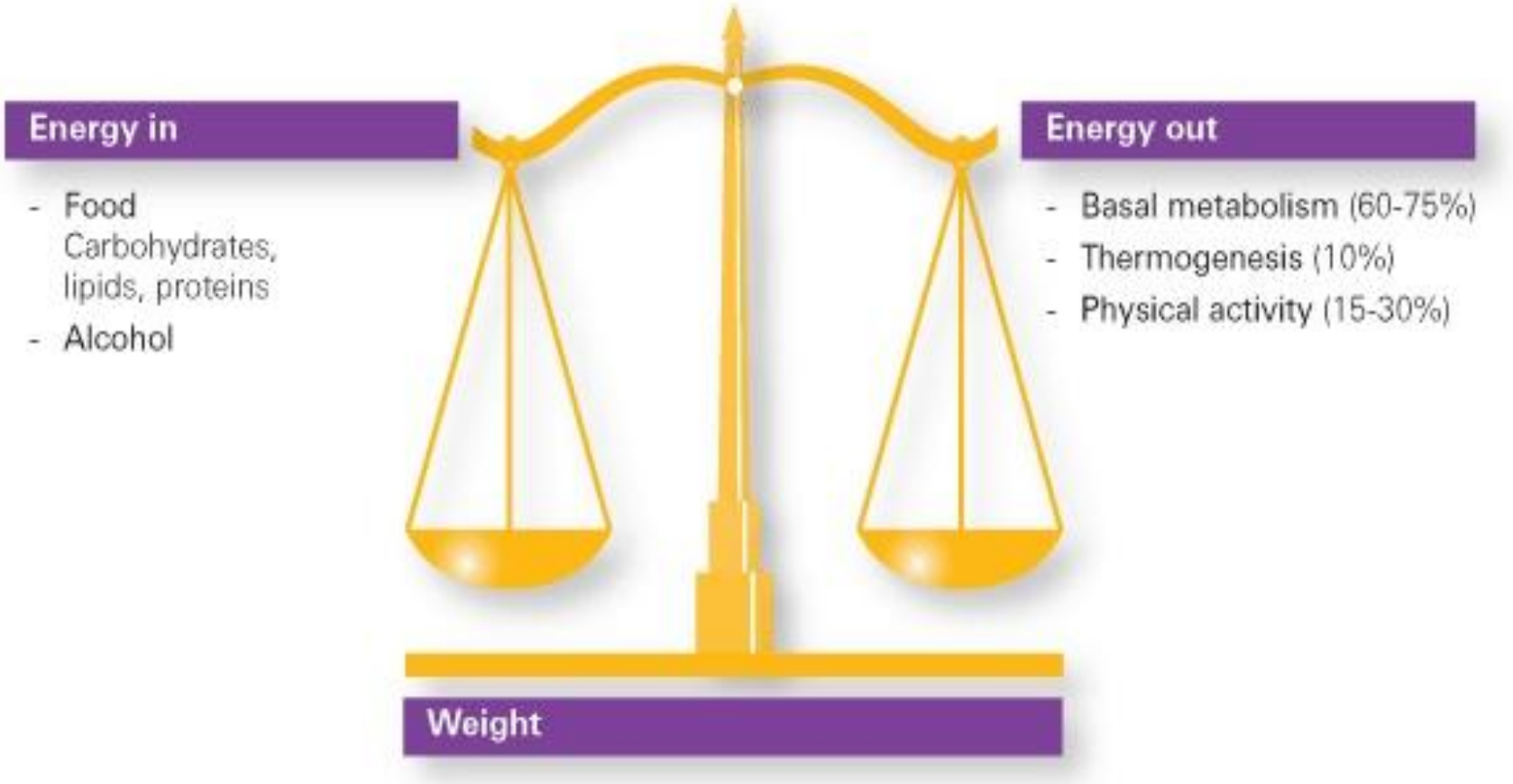
Anabolic reactions involve the joining of smaller molecules into larger ones



Energy balance :Law of thermodynamics

“Energy neither created nor destroyed when it is converted from one form to another”

Food intake = Energy output



Chemical energy of food = heat energy + work energy ± energy storage

Positive/ negative energy balance

Positive energy balance

Food intake > Energy output

Energy storage

Weight gain

Negative energy balance

Food intake < Energy output

Energy storage usage

Weight loss

Body mass index (BMI) = Weight (kg)/Height^2 (m)

International Obesity Taskforce (IOTF)-propose classification of BMI categories for Asia

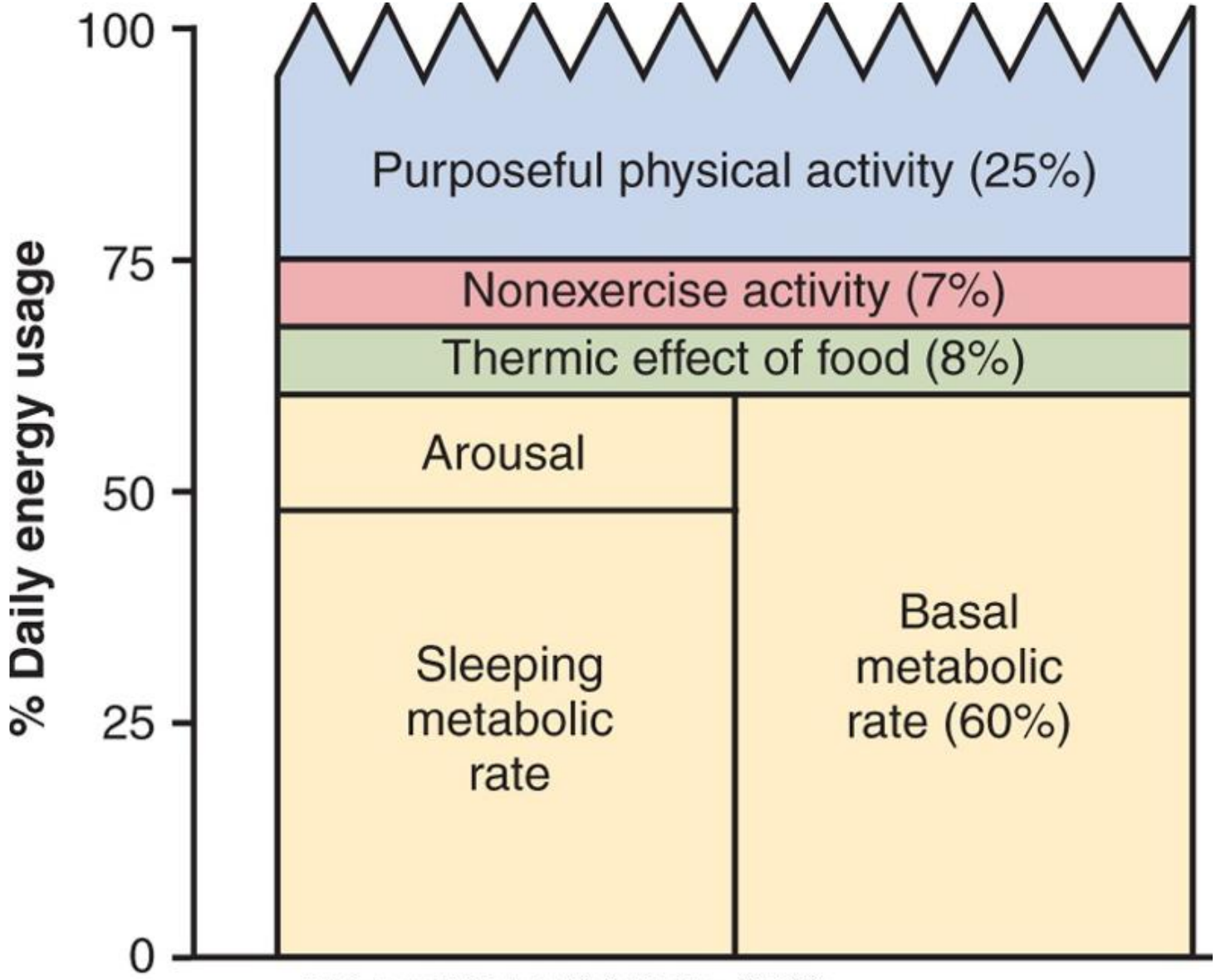
BMI (kg/m^2)	Classification
< 18.5	Underweight
18.5-22.9	Normal
23.0-24.9	Overweight
25.0-29.9	Obese I
≥ 30	Obese II

อ้างอิงจาก Robert C Weisell, 2002

Metabolic rate

"Metabolic rate = the energy expended by an organism at rest in order to maintain body functions "

Components of energy expenditure



BW=70 kg

BMR=60-70 kcal/hr

Guyton and Hall, 2011

Energy expenditure during different types of activity for 70-kg man

Form of Activity		Energy kcal/h
Sitting at rest		100
Walking on level ground at 4.3 km/h (2.6 mi/h)		200
Walking on 3% grade at 4.3 km/h (2.6 mi/h)		360
Weight lifting *(light workout)*		220
Bicycling on level ground at 9 km/h (5.3 mi/h)		300
Shoveling snow		480
Jogging at 9 km/h (5.3 mi/h)		570
Rowing at 20 strokes/ min		830

Basal metabolic rate (BMR)

BMR = the quantity of calories burned by the whole body per unit time at rest which depending on muscle mass and body size (calories/hr/m^2)

** BMR→ accounts for approximately 60–75% of total daily energy expenditure in individuals with a sedentary occupation.

Basal conditions

1. The person must not have eaten any food for at least 12 hrs.

2. After a night of restful sleep (8 hrs.)

3. No strenuous exercise is performed for at least 1 hr. before the test

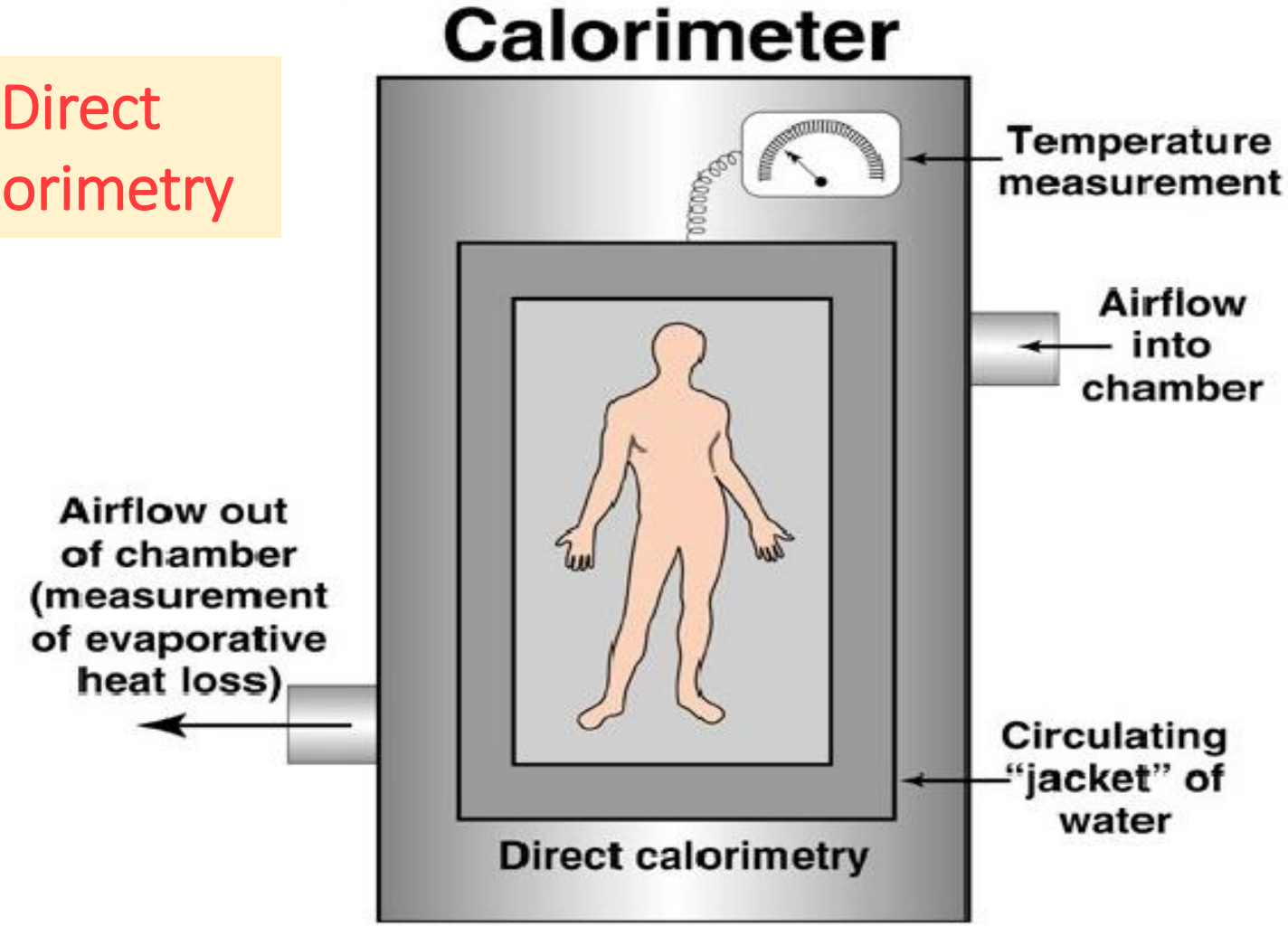
4. All psychic and physical factors that cause excitement must be eliminated

5. The temperature of the air must be comfortable and be somewhere between the limits of 68 and 80 F (20-27 C)

Measuring BMR Directly

- Rarely used due to time and expense
- Requires 12 hrs of fasting
- Requires an environmentally controlled room or chamber

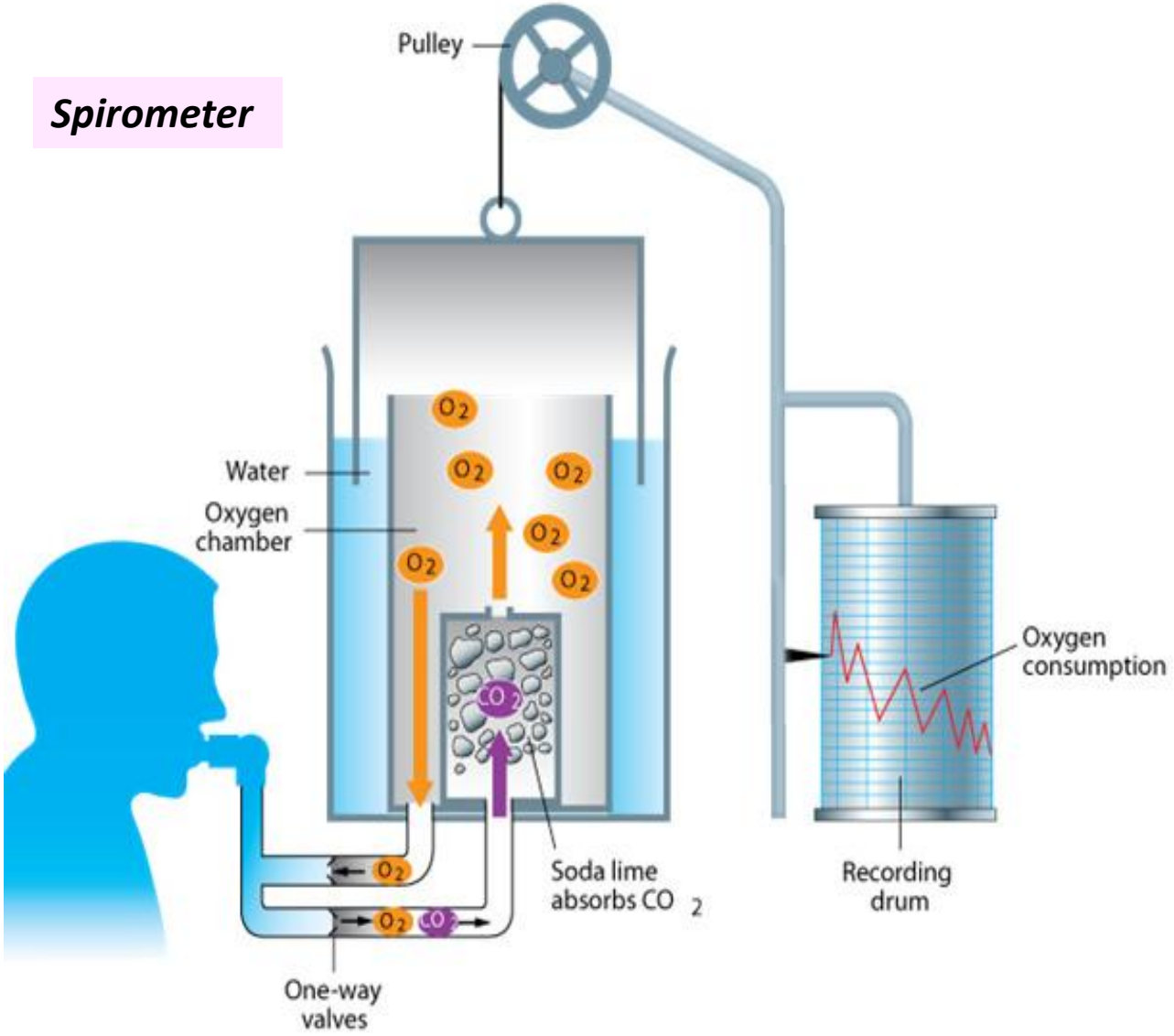
Direct calorimetry



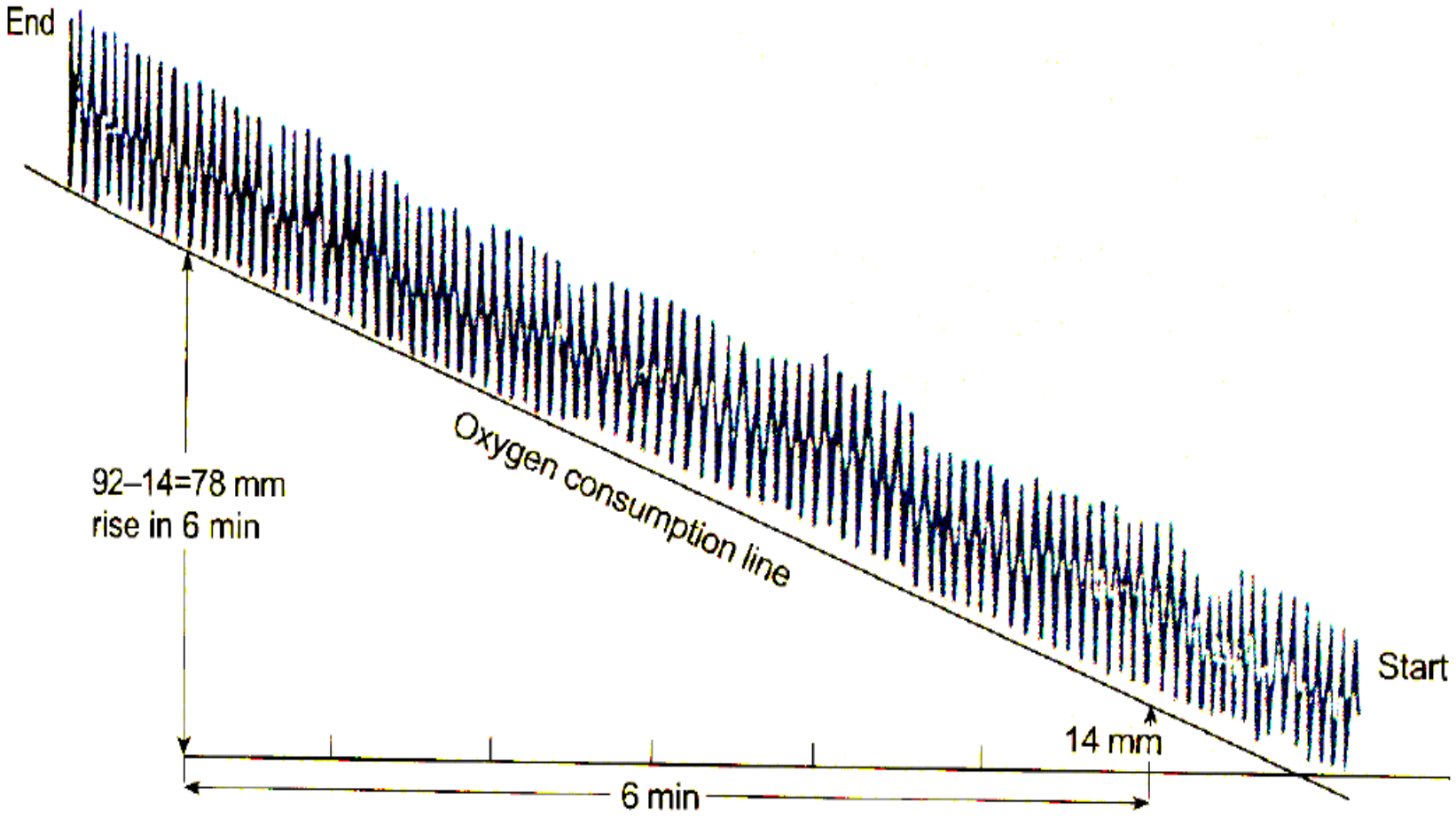
Indirect calorimetry

Indirect calorimeter used to measure metabolism by determining the amount of oxygen consumed and the carbon dioxide produced under laboratory conditions

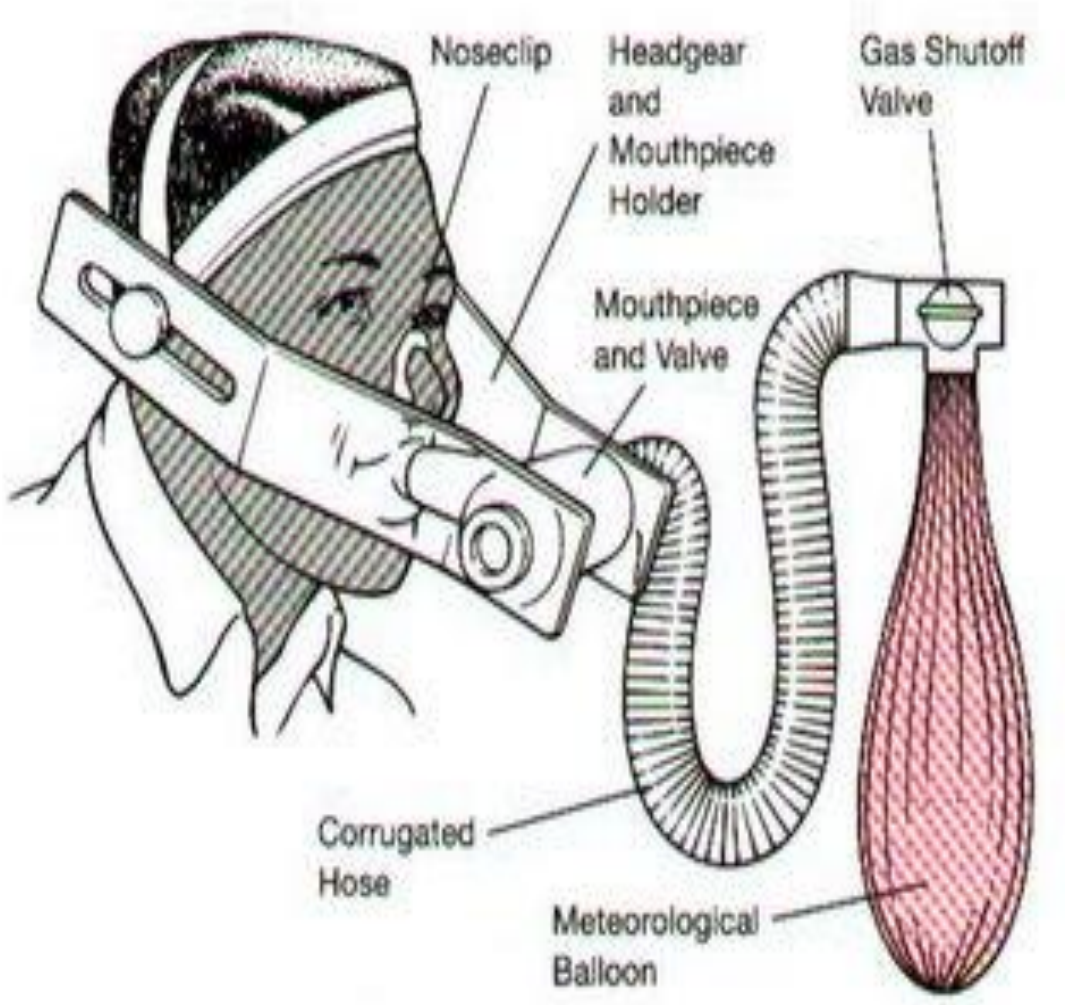
Spirometer



$$\text{Metabolic rate} = \frac{VO_2\ (L/hr) \times 4.825\ (kcal)}{\text{Body surface area}\ (m^2)}$$



Indirect calorimetry: Douglas bag



Douglas bag

Factors that affect the metabolic rate

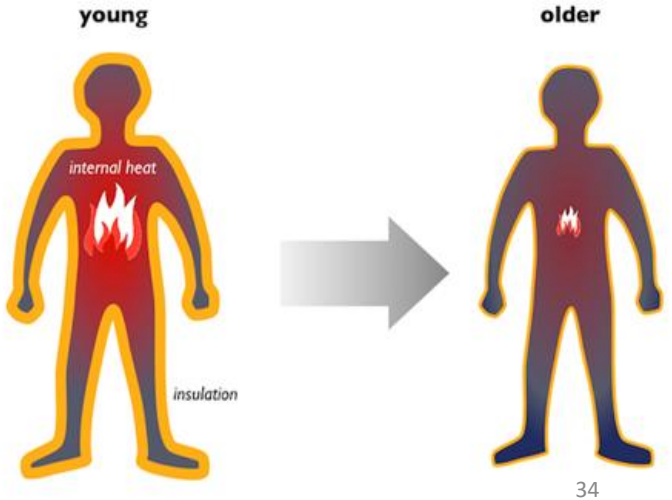
Age, Sex, Nation, Body size, Body temperature, Type of food intake, Pregnancy, Hormone, Emotion, Fever, Malnutrition

Increases Metabolic Rate

- Thyroid Hormone
- Male Sex Hormone
- Growth Hormone
- Fever
- Exercise

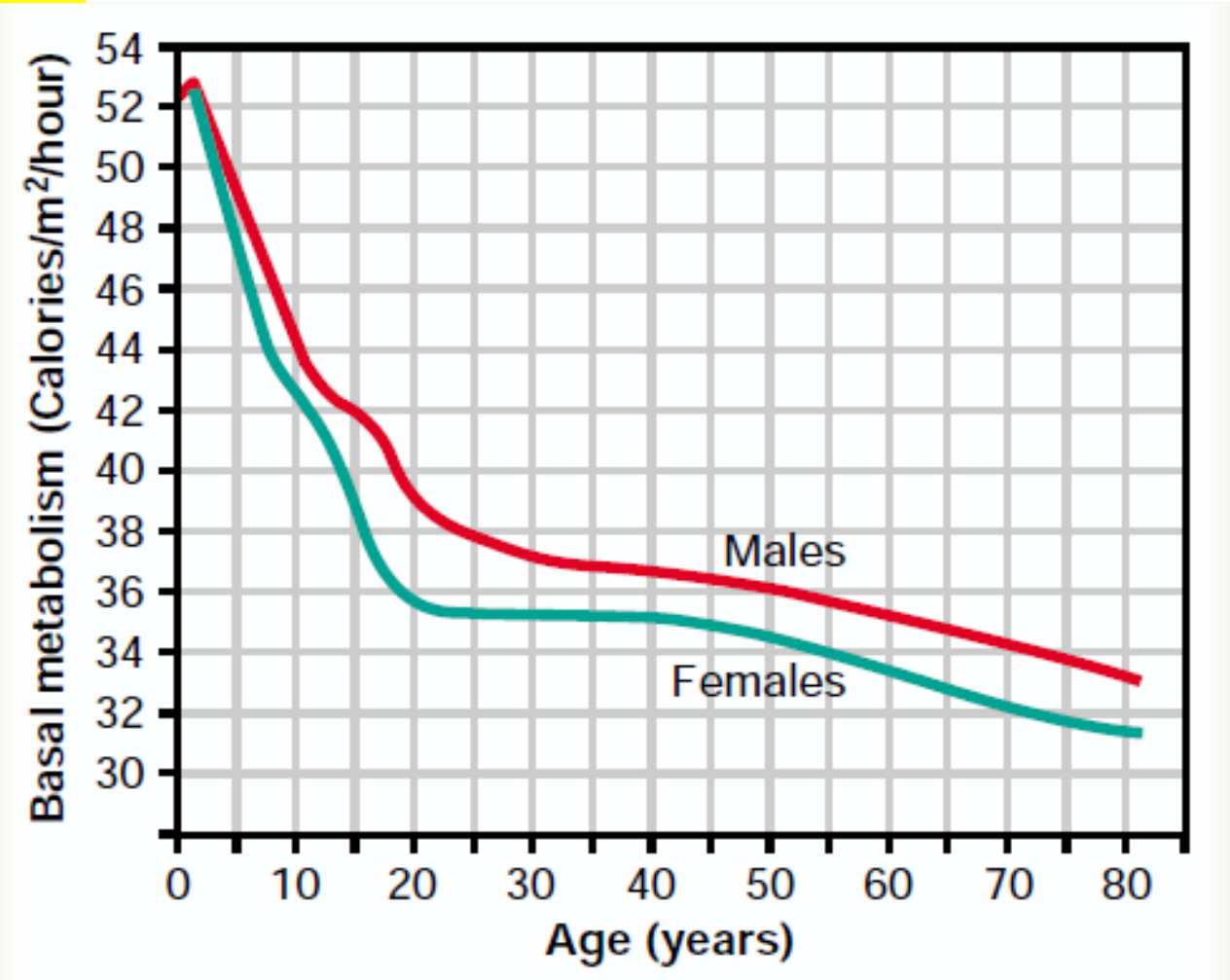
Decreases Metabolic Rate

- Sleep
- Malnutrition
- Aging



Factors that affect the metabolic rate

Age & sex



Normal basal metabolic rates at different ages for each sex.

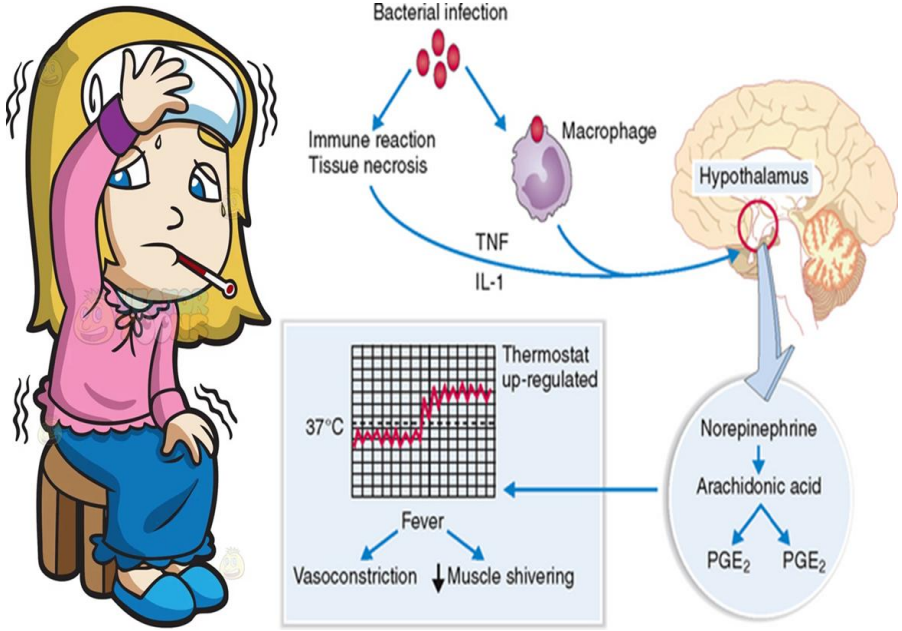
Guyton and Hall, 2011

Factors that affect the metabolic rate

Fever

- Increased metabolic rate

(All chemical reactions increase 120% for every 10 C rise in temperature)

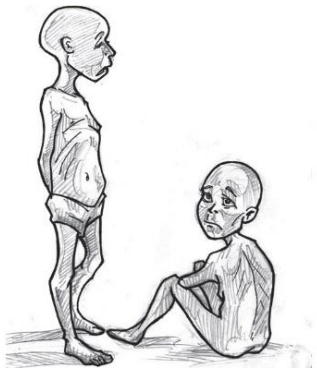


Sleep: decreases metabolic rate (10-15%)

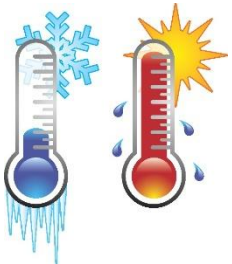
- decreased muscle tone
- decreased activity of central nervous system

Malnutrition

- Prolong poor nutrition decrease BMR 20-30 %



Environmental temperature



if temperature is very low or very high, the body has to work harder to maintain its normal body temperature, which increases the BMR.

METABOLIC FACTORS

nutritionwithjudy

KEY TAKEAWAY: IT'S NOT ONE THING.
These factors affect your metabolic rate.

Age: The older you get, the slower your metabolic rate.

https://pubmed.ncbi.nlm.nih.gov/2382714/

Body Size: The bigger the body, the more calories burned.

https://pubmed.ncbi.nlm.nih.gov/15855403/

Outside Temps: If body is exposed to cold, it burns more calories.

https://pubmed.ncbi.nlm.nih.gov/1437394/

Muscle Mass: The greater your muscle mass, the more calories you burn.

https://pubmed.ncbi.nlm.nih.gov/2243122/

Movement: The more active you are, the more calories you burn. Metabolism speeds up accordingly.

https://pubmed.ncbi.nlm.nih.gov/21311363/

Hormones: Hypothyroidism can slow down metabolic rate and increase your risk of weight gain.

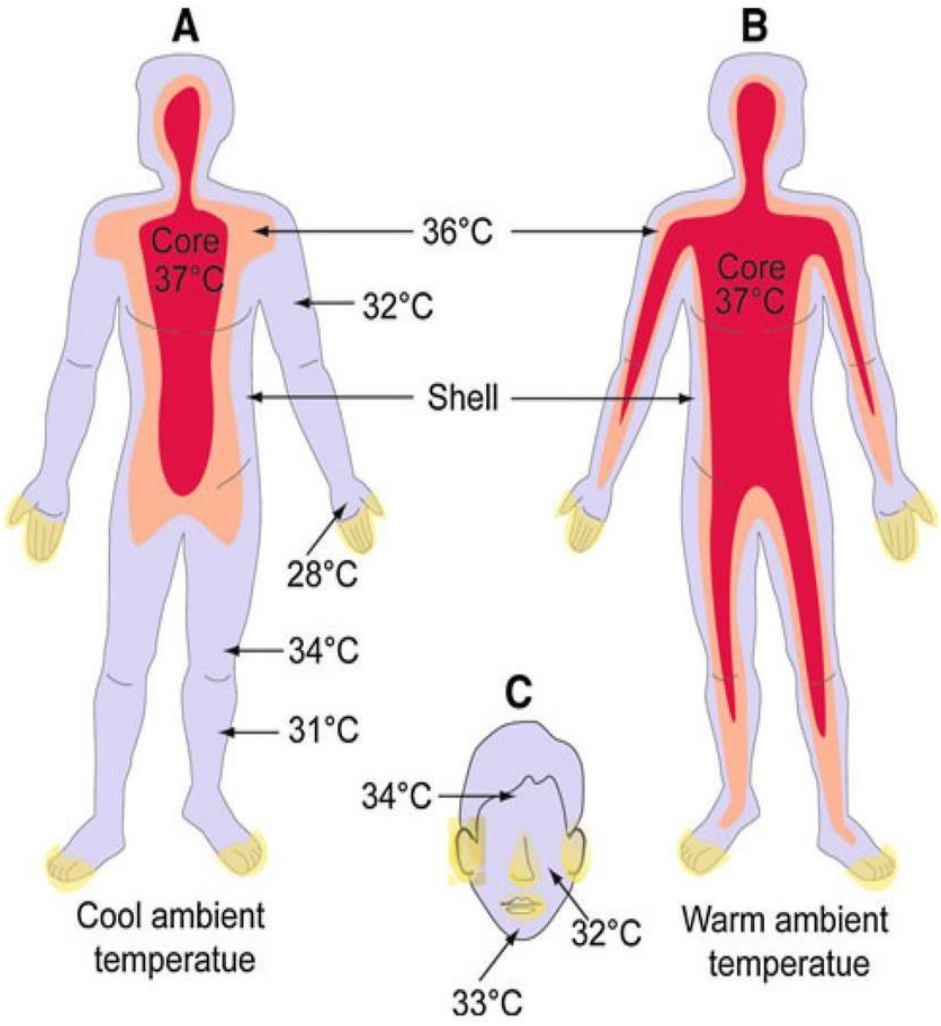
https://pubmed.ncbi.nlm.nih.gov/18230905/

Maintenance of life by thermoregulation

Normal Body temperatures

- Normal Body Temperature (NBT) – 98.8^{0}F (37.1^{0}C)
- Range of NBT (97^{0}F to 99^{0}F)

- Core temperature
- Skin temperature



Homeotermic Temperature = Core temp.
=37.1^{0}C

- Oral Temp (97^{0}F to 99^{0}F, 36-37.5^{0}C)
- Rectal Temp (0.5^{0}F to 1^{0}F) above the Oral
- Rectal Temp reflects the Core Body Temp
- Skin (Shell) Temp Variable

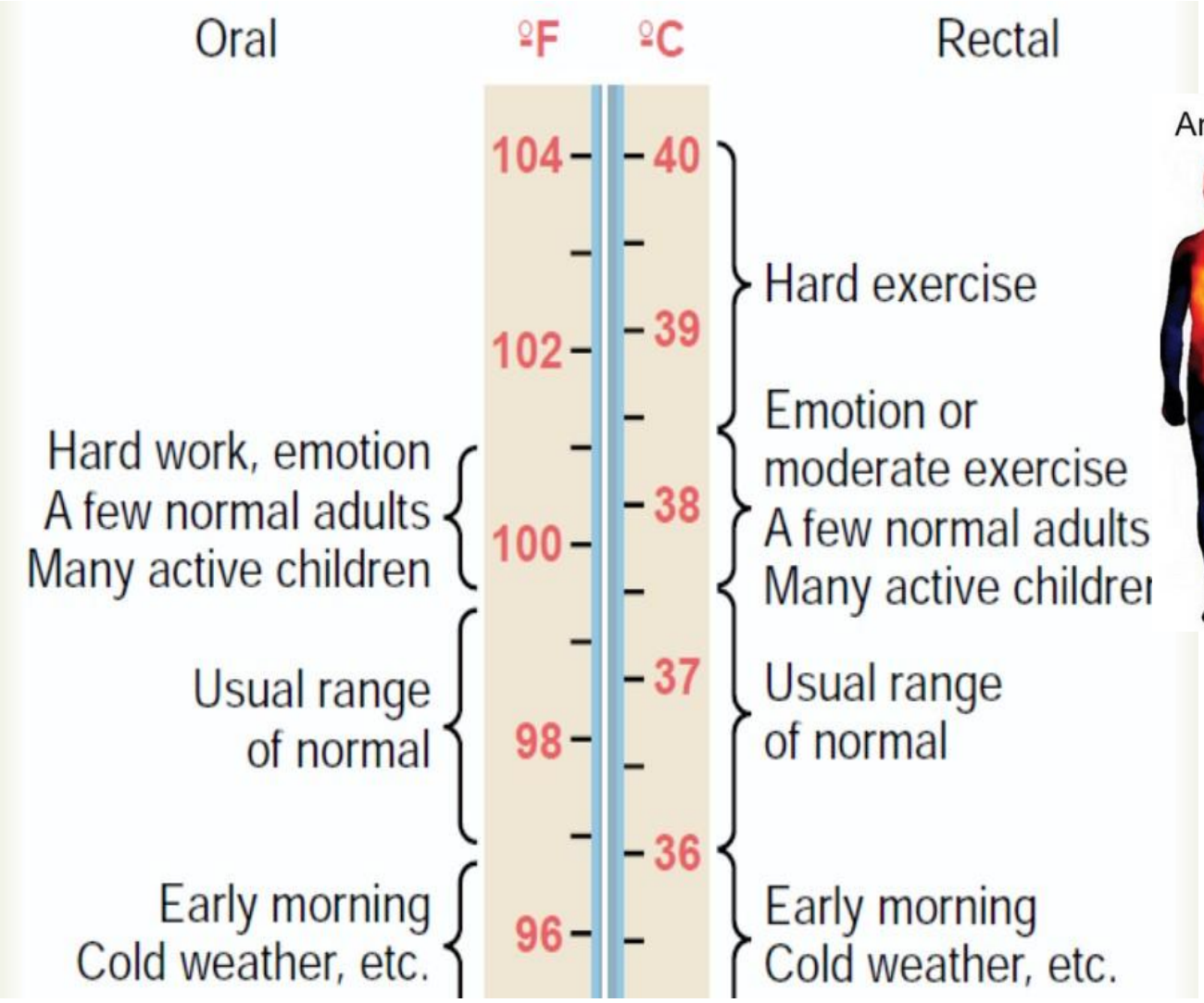
**Core Body Temp remain almost constant

Hypothalamus → ANS
Hypothalamus → Endocrine
Hypothalamus → Skeletomotor response

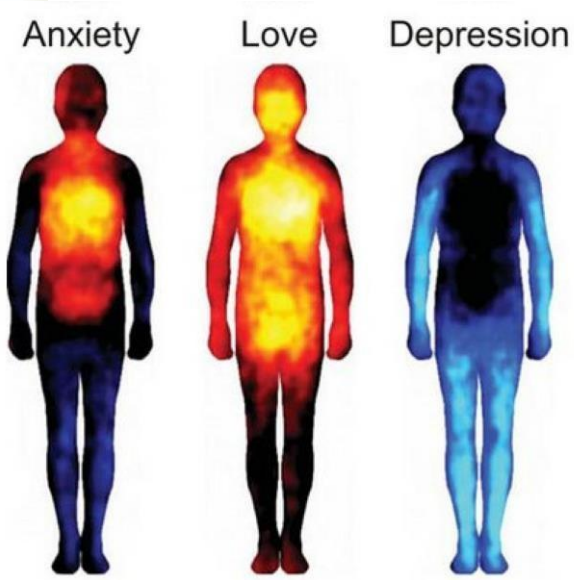
From: http://ceska-posta.info/body-temperature-diagram

Variation in core temperature

- Variation in core temp. ~ ±0.6 °C (1F)



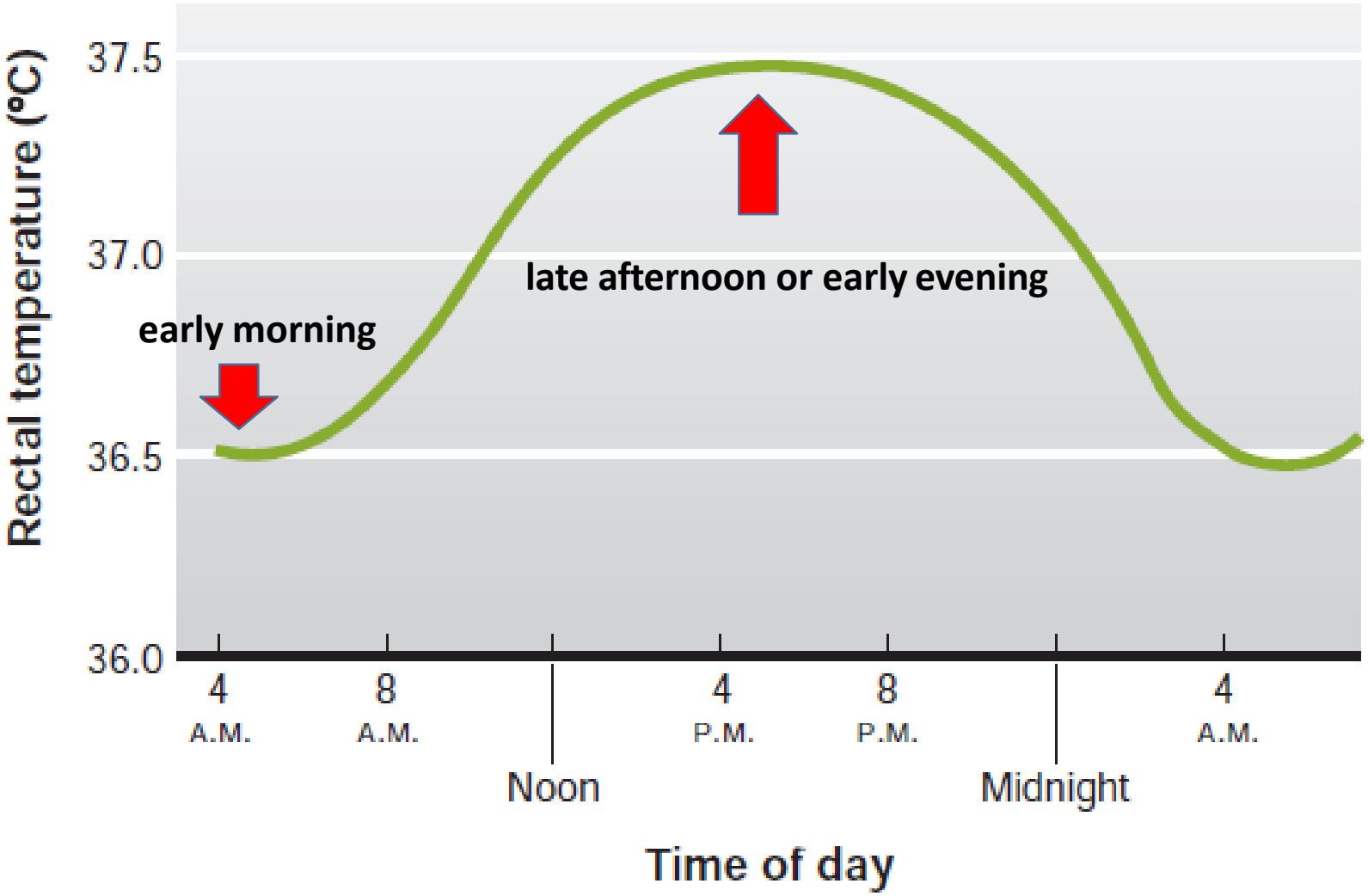
- **Emotion**



- **Age: young> old**
- **Physical activity**
  Activ>Inactive

Variation in core temp:Circadian rhythmicity

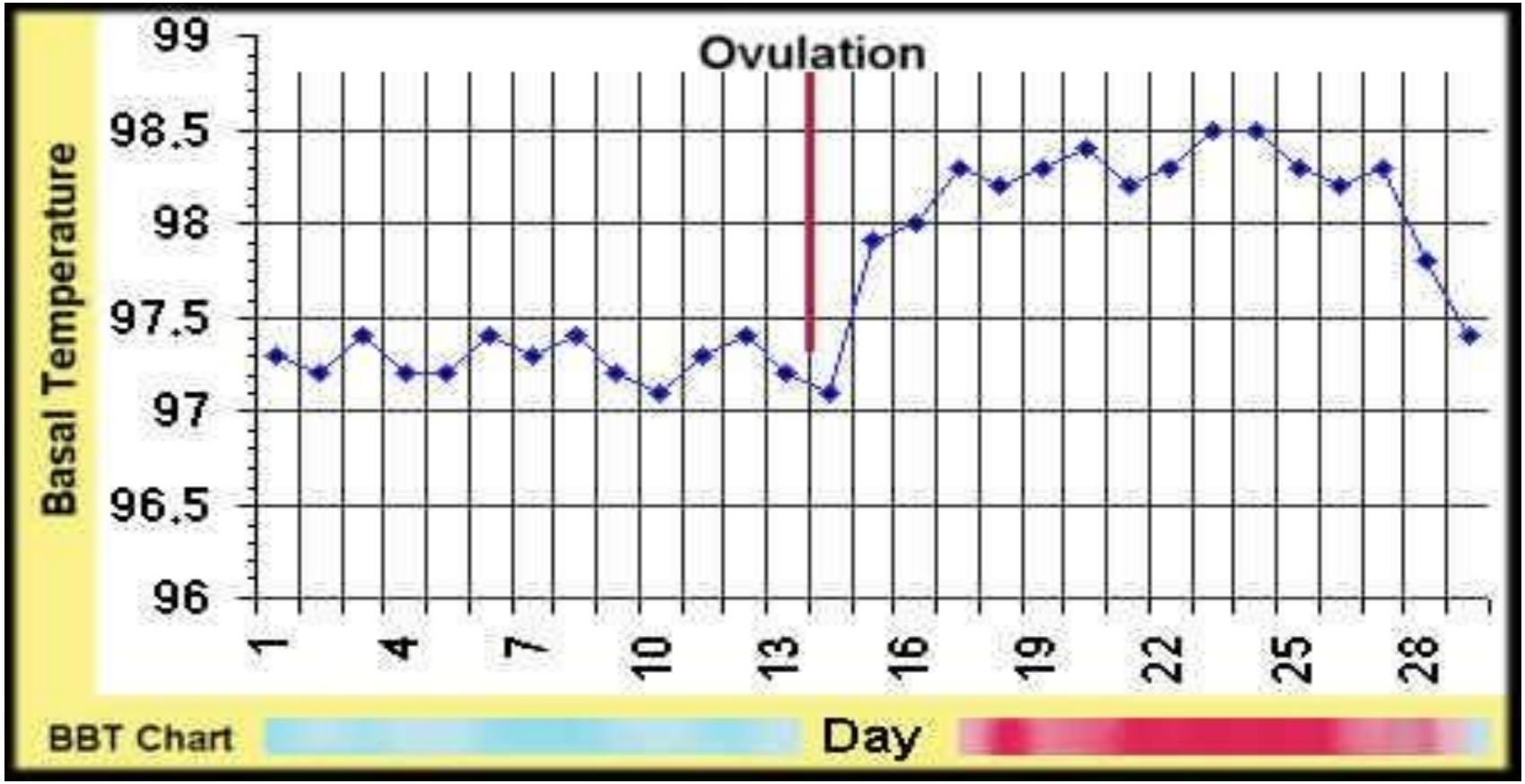
- **Associated with sleep-wake cycle**



Vander, A. J. et al (2014).

Variation in core temp: The menstrual cycle

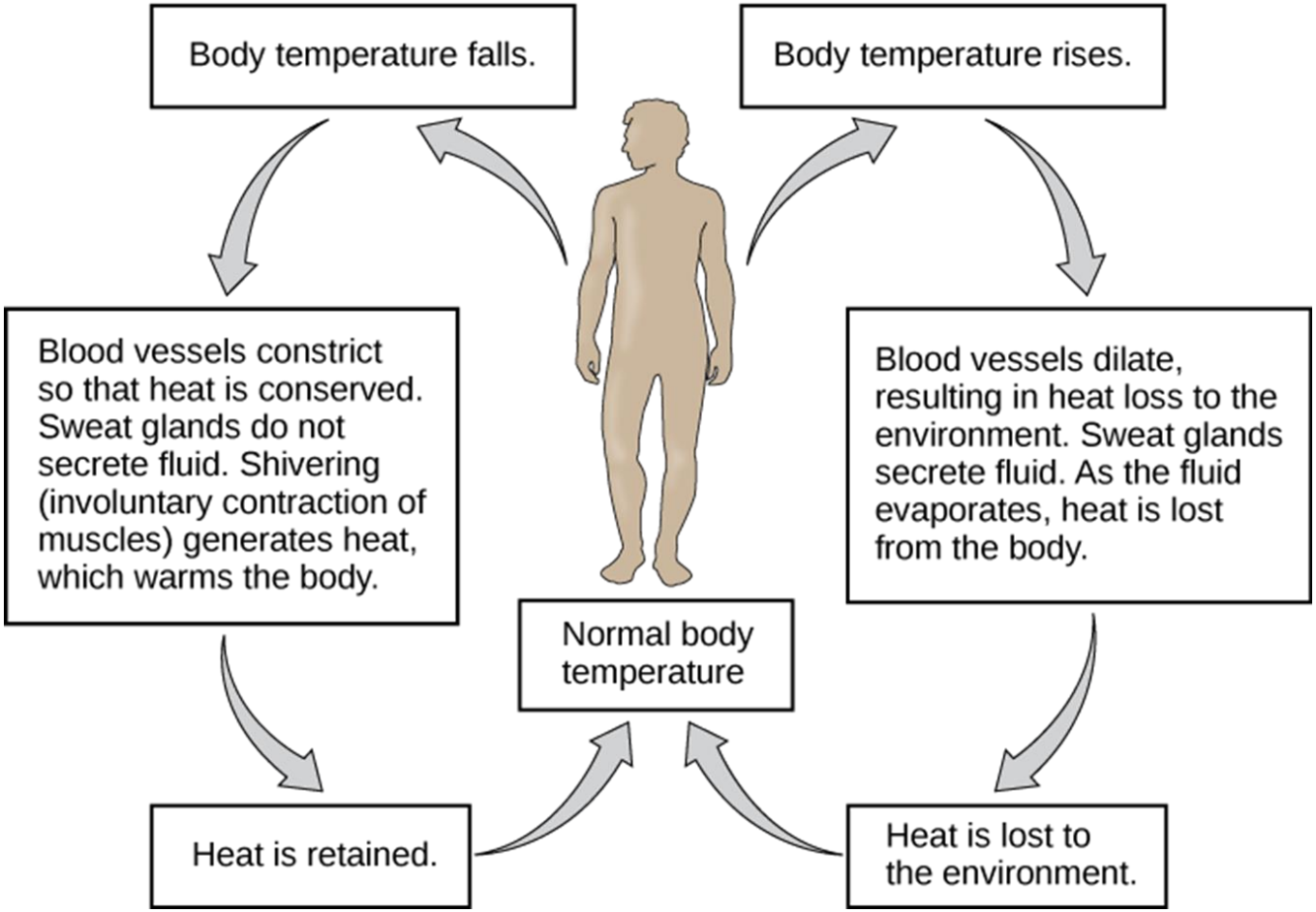
The ovulatory phase (ovulation day) → a temperature rise ~ **0.5 °C**



Hormone → Progesterone → thermosensitive neuron in hypothalamus → increase core temp.

Thermal Balance

- This homeothermy applies only to the core temperature (~37.1 ℃) of the body.
  - ➢ Higher than NBT → denature enzymes and block metabolic pathways
  - ➢ Lower than NBT → slow down metabolism and affect the brain



Body Temperature Is Controlled by Balancing Heat Production Against Heat Loss

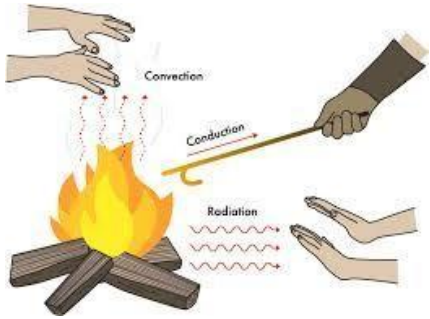
Heat Production

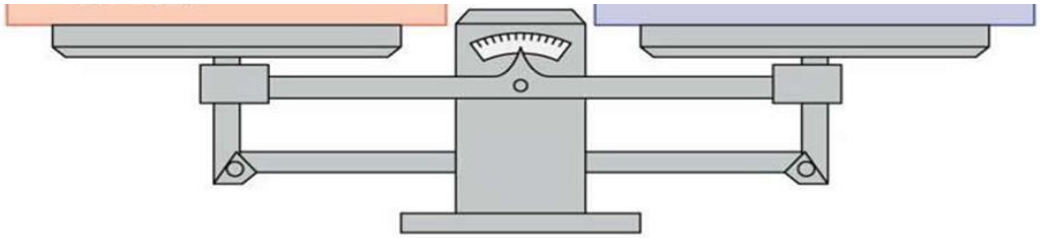
- Basal metabolic rate
- Muscle activity
- Shivering
- Vasomotor
- Sweating
- Piloerection
- Thyroxine and epinephrine

Skin

Heat Loss

- Conduction
- Convection
- Radiation
- Evaporation





Extra rate of metabolism caused by hormone

Non-shivering or chemical thermogenesis

- **Thyroxine**
- **Testosterone**
- **Growth hormone**

Thyroid hormone

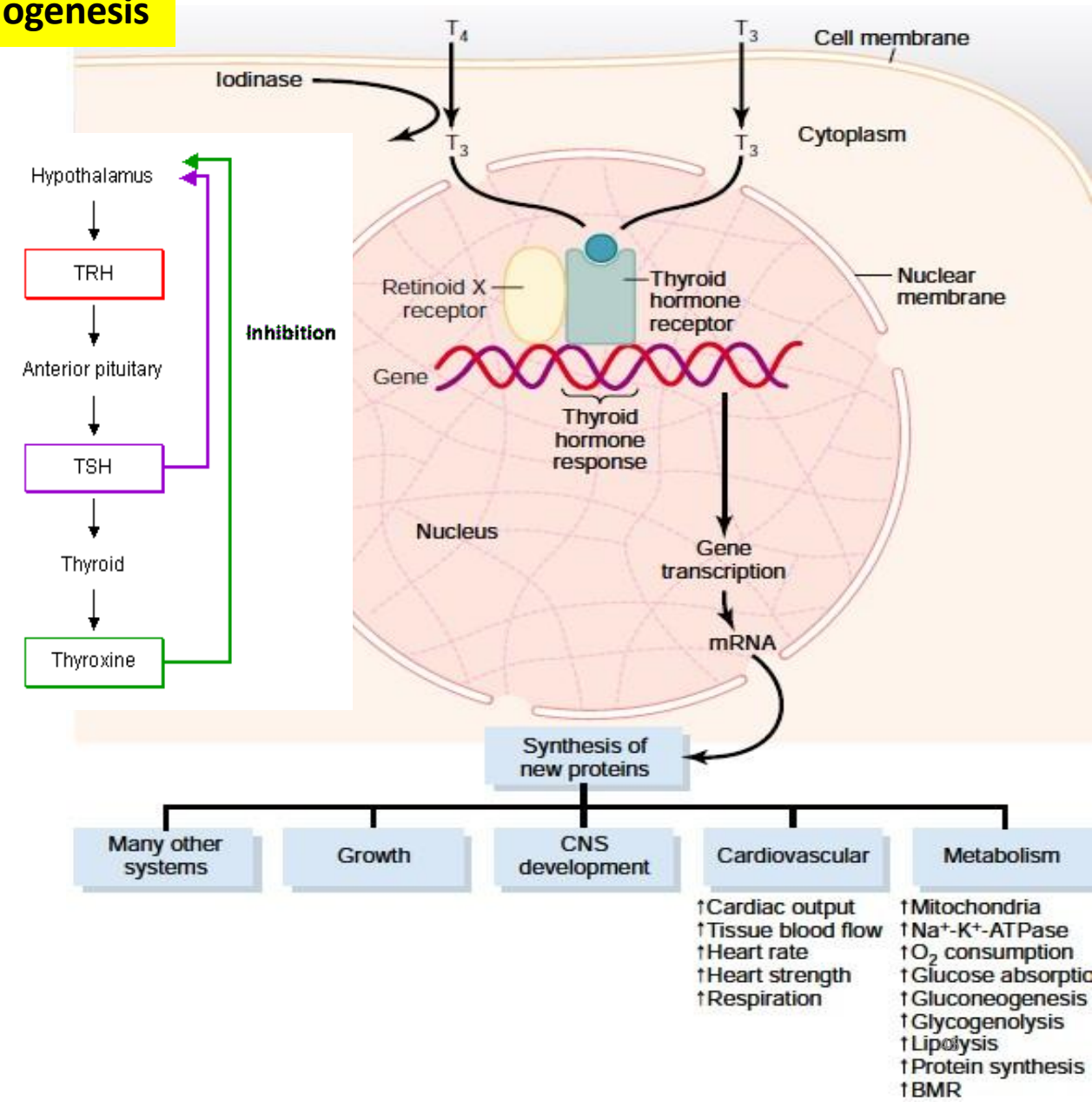
Increase metabolic rate ~50-100% above normal

Testosterone

Anabolic effect in increasing skeletal muscle mass

Growth hormone

Increasing skeletal muscle mass



Physical activity & Shivering

Muscle contraction

cold temperature

increase cell metabolism

Shivering center in posterior hypothalamus

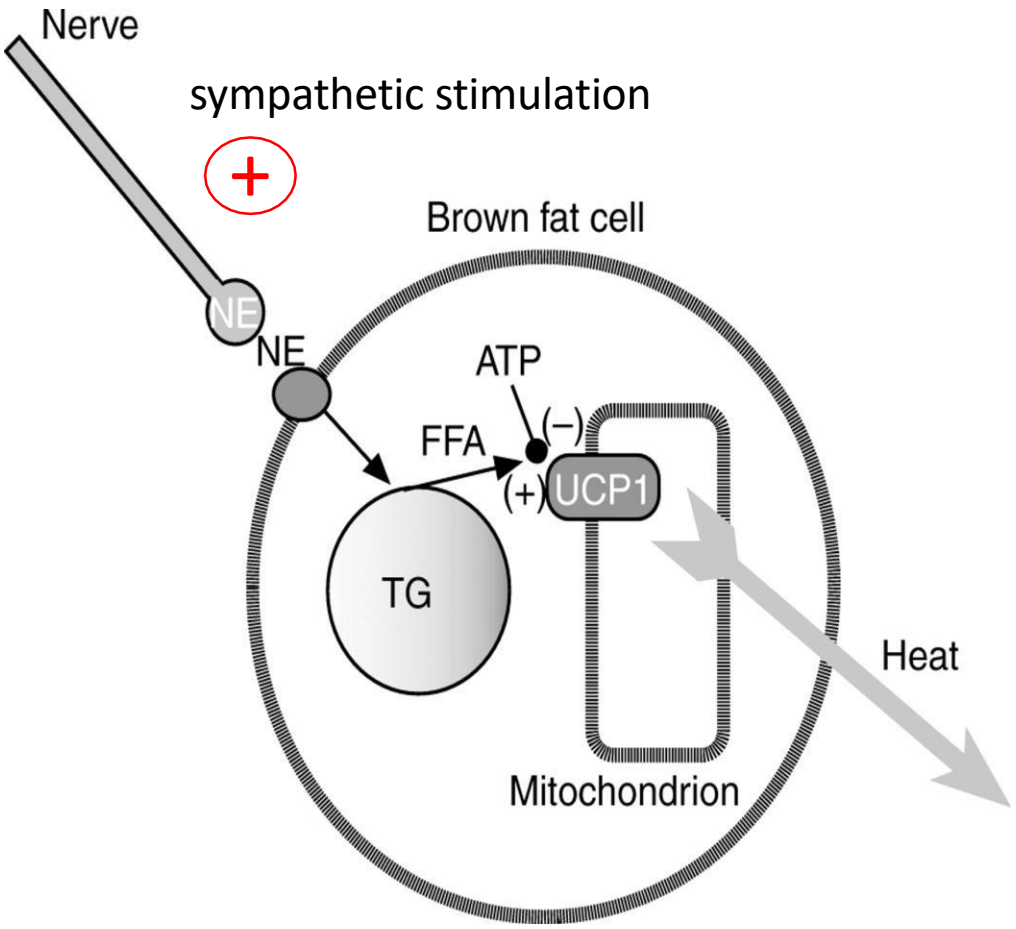
Spinal cord

increase heat production

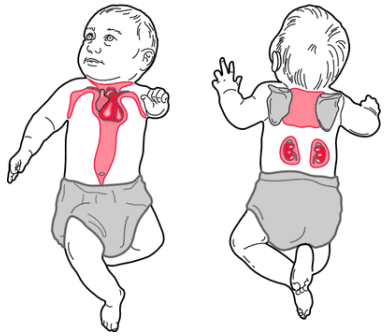
Muscle contraction 10-20 time/min

Sympathetic "Chemical" Excitation of HeatProduction

- Extra metabolism caused by the effect of epinephrine, norepinephrine, and sympathetic stimulation on the cells



Norepinephrine



Brown adipose tissue (BAT)

uncoupling protein-1 (UCP1)

+

Uncoupling oxidative phosphorylation

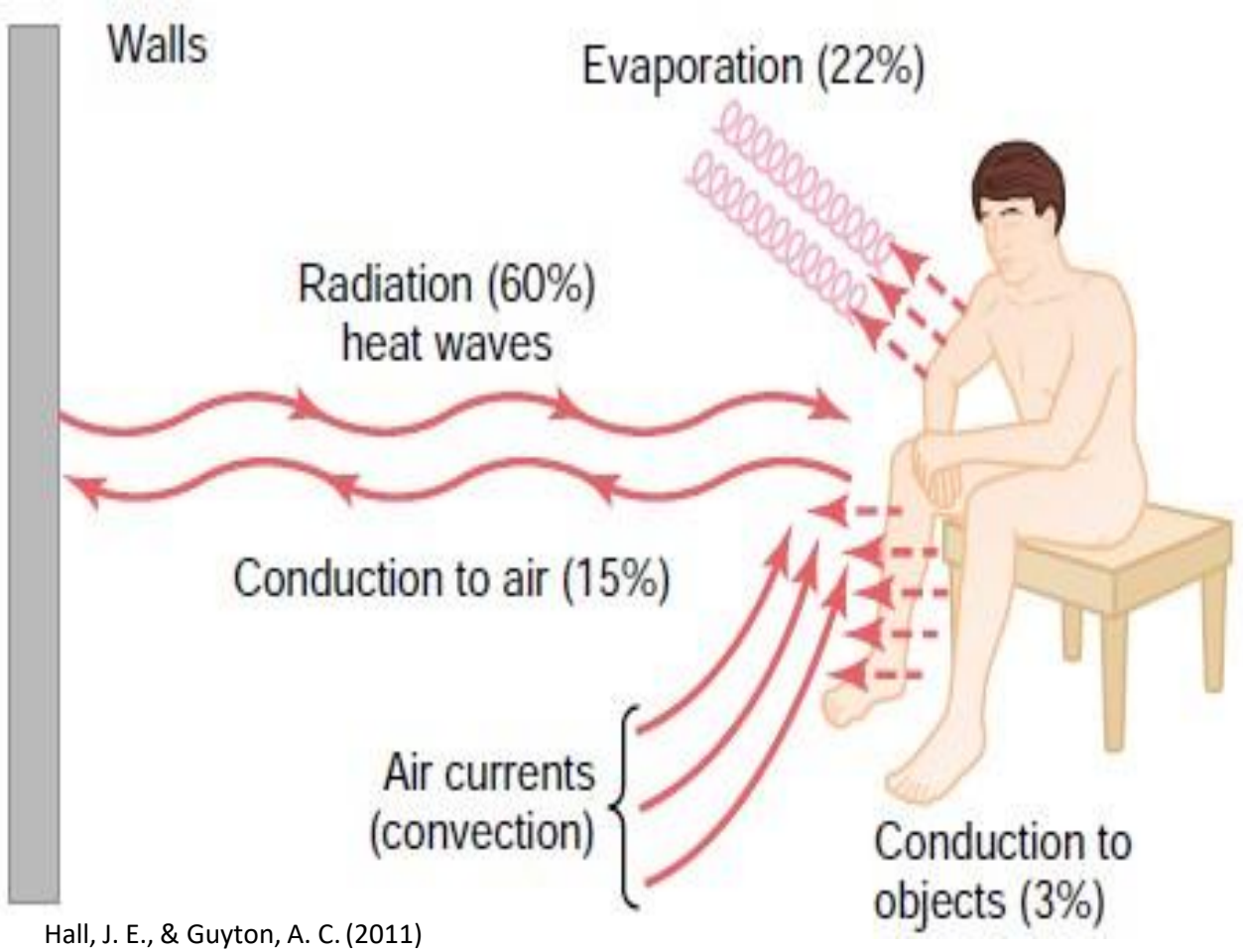
release

Energy in a form of Heat

Cannon B and Nedergaard J. The Journal of Experimental Biology 214, 242-253

Heat Loss or Thermolysis

- ❑ Radiation
- ❑ Conduction
- ❑ Convection
- ❑ Evaporation
- ❑ Respiration
- ❑ Loss through urine & feces



Rate of heat lost

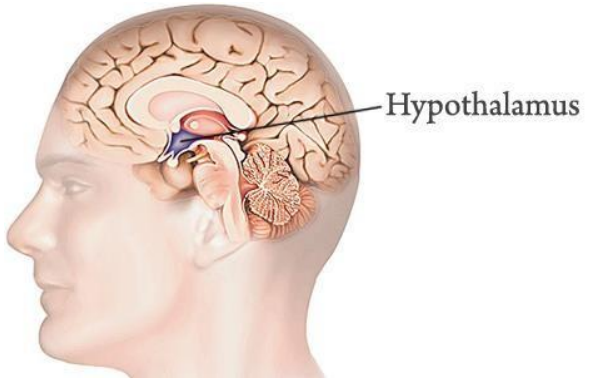
(1) How rapidly heat can be conducted from where it is produced in the body core to the skin

(2) how rapidly heat can then be transferred from the skin to the surroundings

Hall, J. E., & Guyton, A. C. (2011)

Thermoregulator System

- **Physiological Mechanism**
- **Behavioral Mechanism**



- Temperature is regulated by nervous feedback mechanisms
- Thermoregulatory center located in the **Hypothalamus**

Thermoregulator System

Center

Hypothalamus

Set point 37.1°C

Thermoreceptors

-Peripheral receptor

-Central receptor

-Deep body tissue receptor

-Warm receptor

-Cold receptor

Controllers

-Anterior hypothalamus

-Preoptic area

-Posterior hypothalamus

Effectors

-Skin arterioles

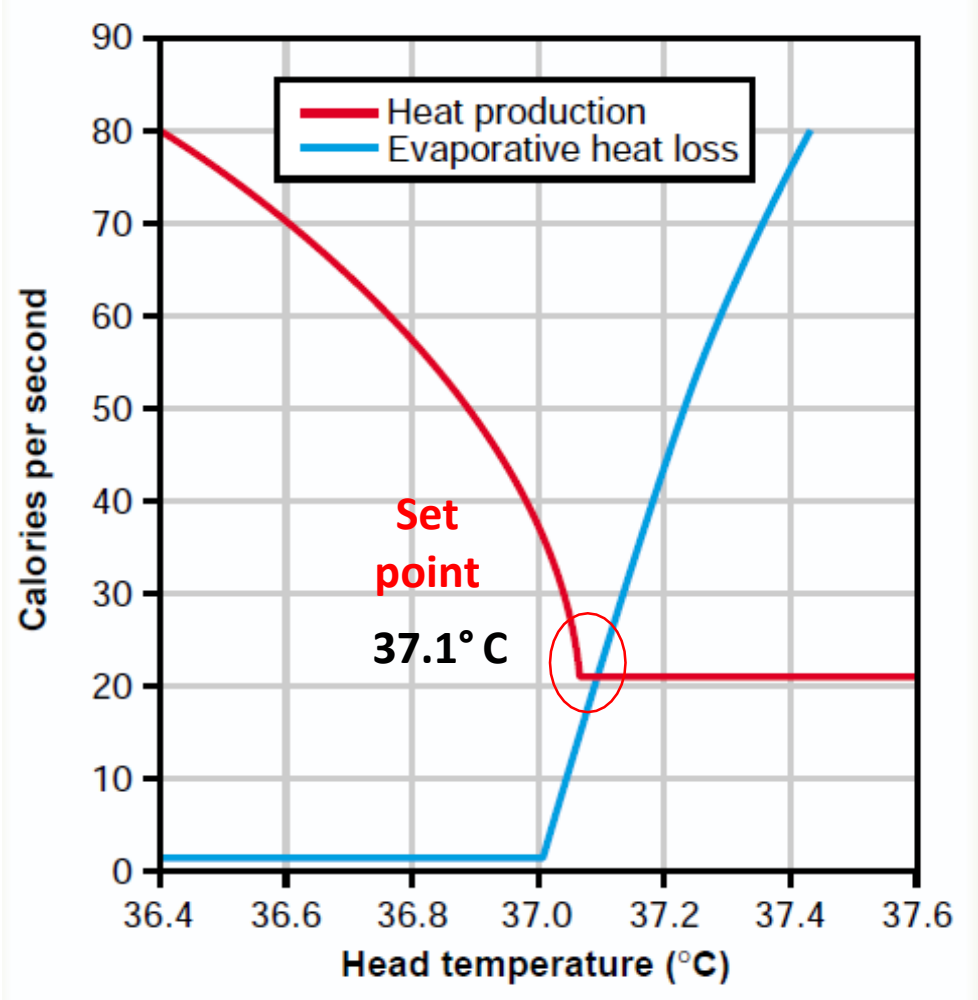
-Skeletal muscle

-BAT

-Sweat gland

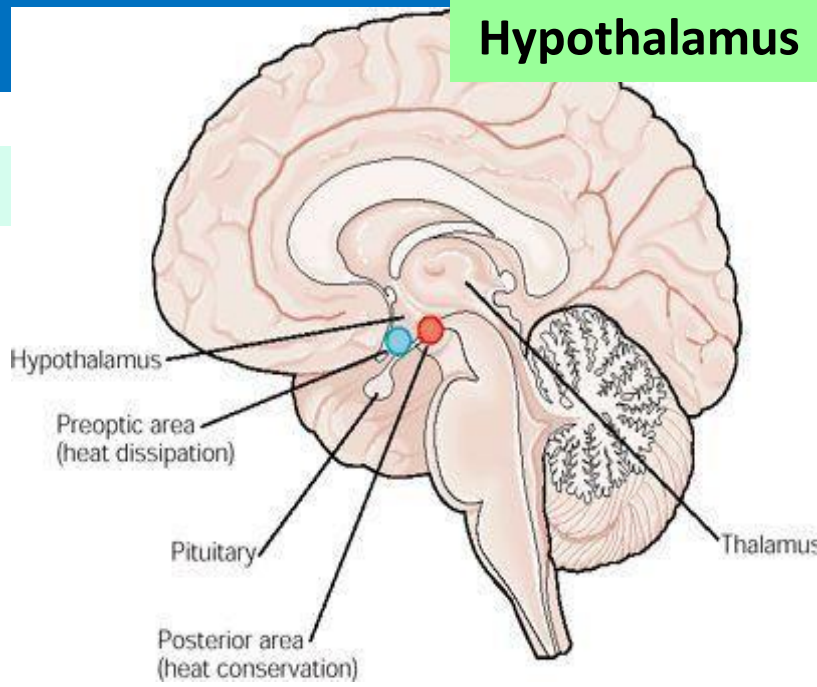
Role of the hypothalamus

Thermoregulatory center located in the Hypothalamus



Hall, J. E., & Guyton, A. C. (2011).

Hypothalamus



-Anterior hypothalamus
-Preoptic area
➡ Thermostat

-Posterior hypothalamus
➡ Integrated signal

Thermoregulatory regulatory responses

- Autonomic nervous system
- Somatic nervous system
- Endocrine system

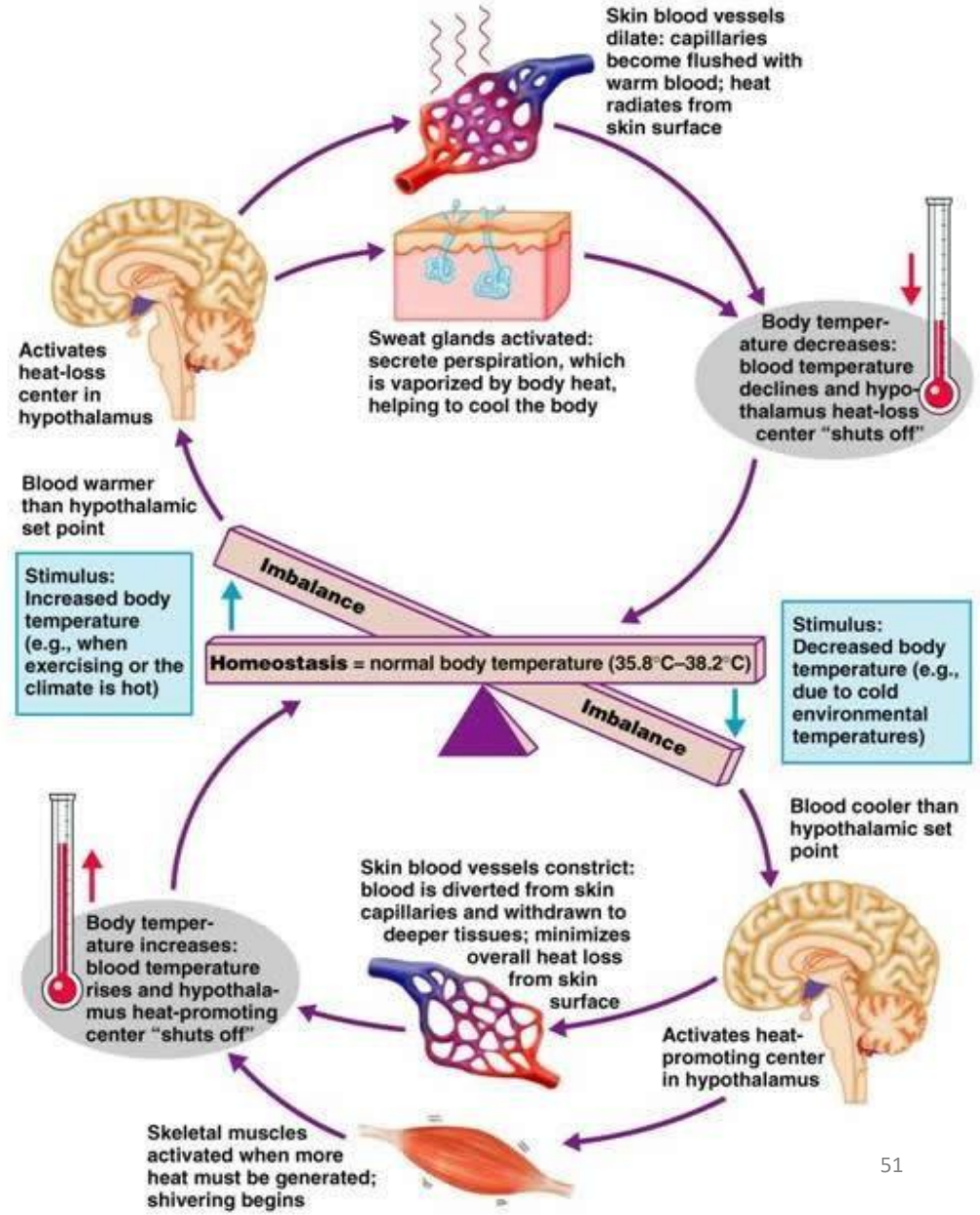
Feedback system

Feedback system

1. Receptor
-Sensor that responds to changes (stimuli)

2) Control Center
- Sets range of values
- Evaluates input and
- Sends output

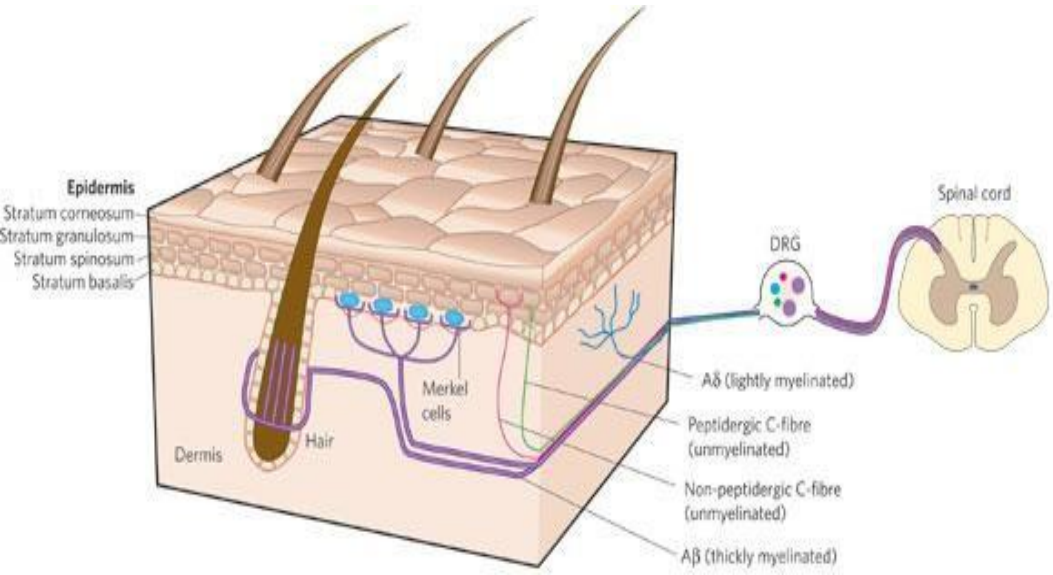
3) Effector
-Receives output from control center
- Produces a response



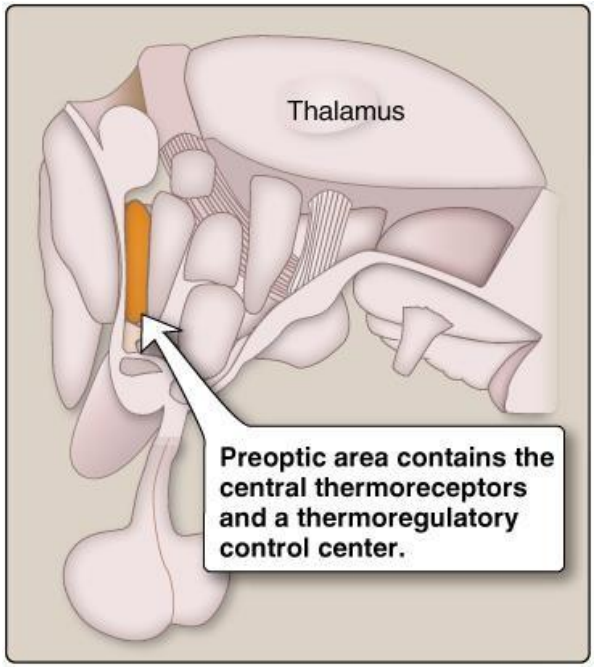
Thermoreceptor

Cold receptors & Warmth receptors

- **Peripheral thermorecptor**



- **Central thermoreceptor**



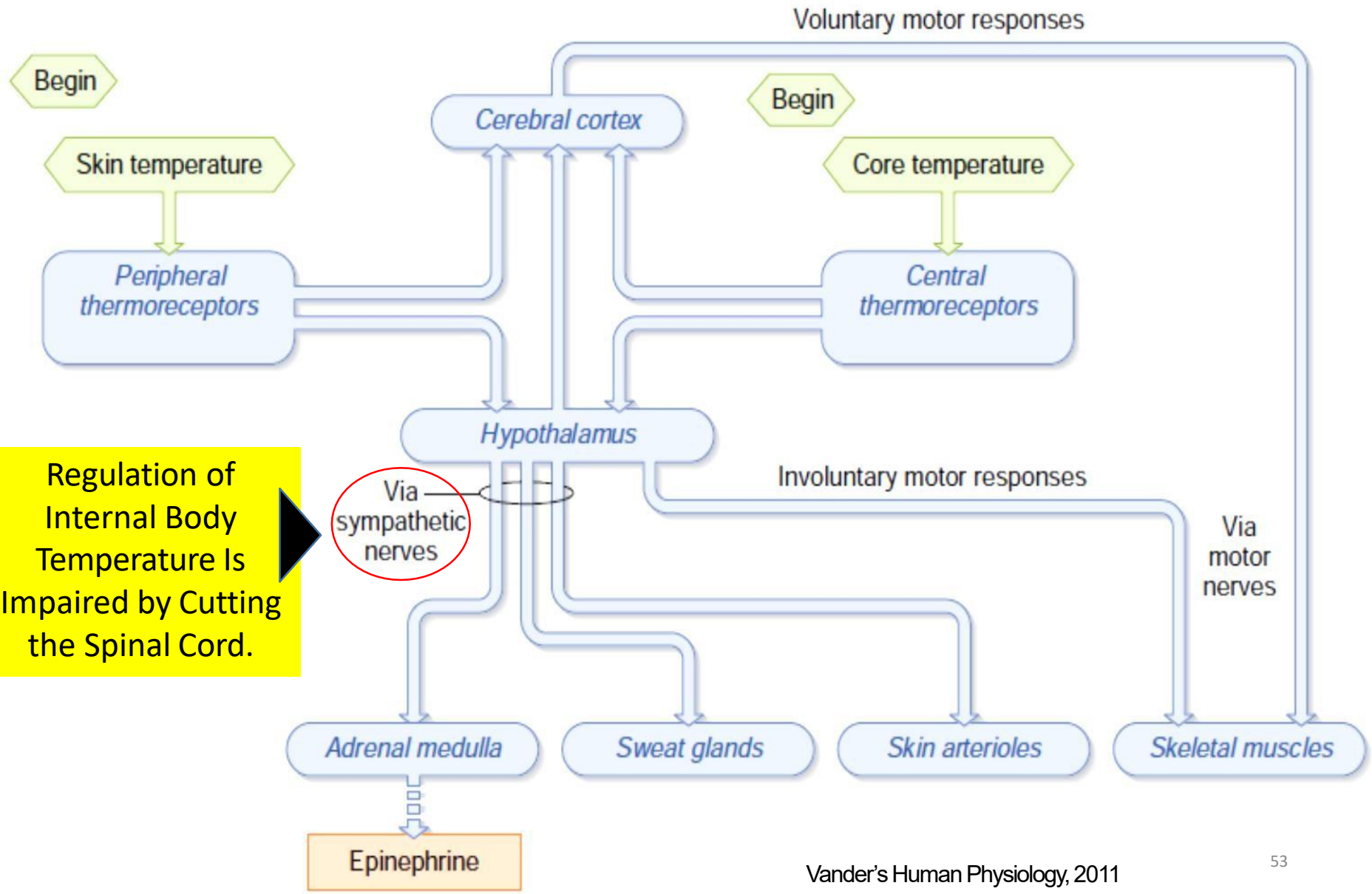
- **Deep organ receptor**
  - **Spinal cord**
  - **Abdominal viscera**
  - **Great veins**

Cold receptors > Warmth receptors

(-) ↓

Hypothermia

Summary of temperature-regulating mechanisms



Regulation of Internal Body Temperature Is Impaired by Cutting the Spinal Cord.

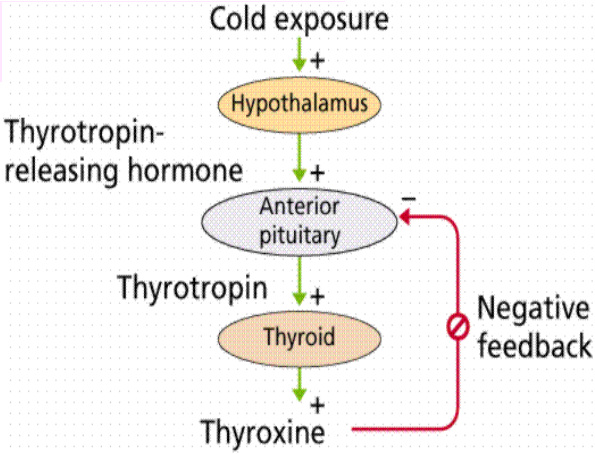
Vander's Human Physiology, 2011

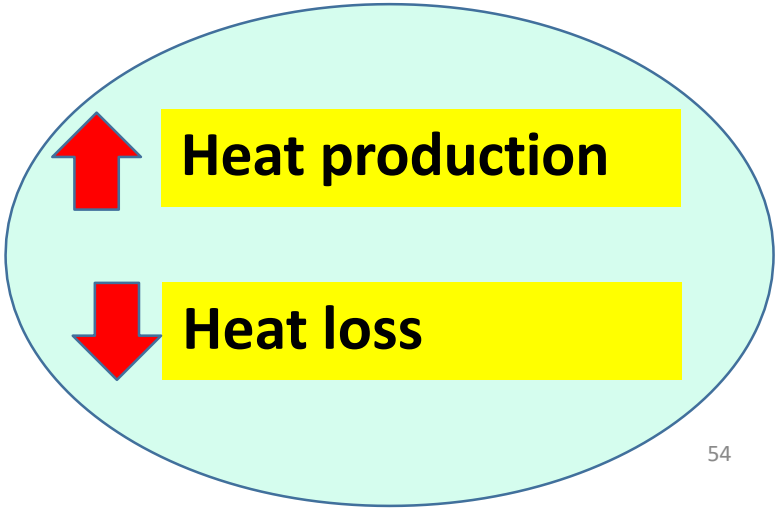
Thermoregulatory regulatory responses

Activated by Exposure to Cold

- Cutaneous vasoconstriction
- Increase thermogenesis
- Piloerection

- **Shivering**
- Increase voluntary activity
- Increase TSH secretion→ thyroxine ↑
- Increase Catecholamine
- **Vasoconstriction**
- Horripilation
- Curling up





Thermoregulatory regulatory responses

Activated by Exposure to heat

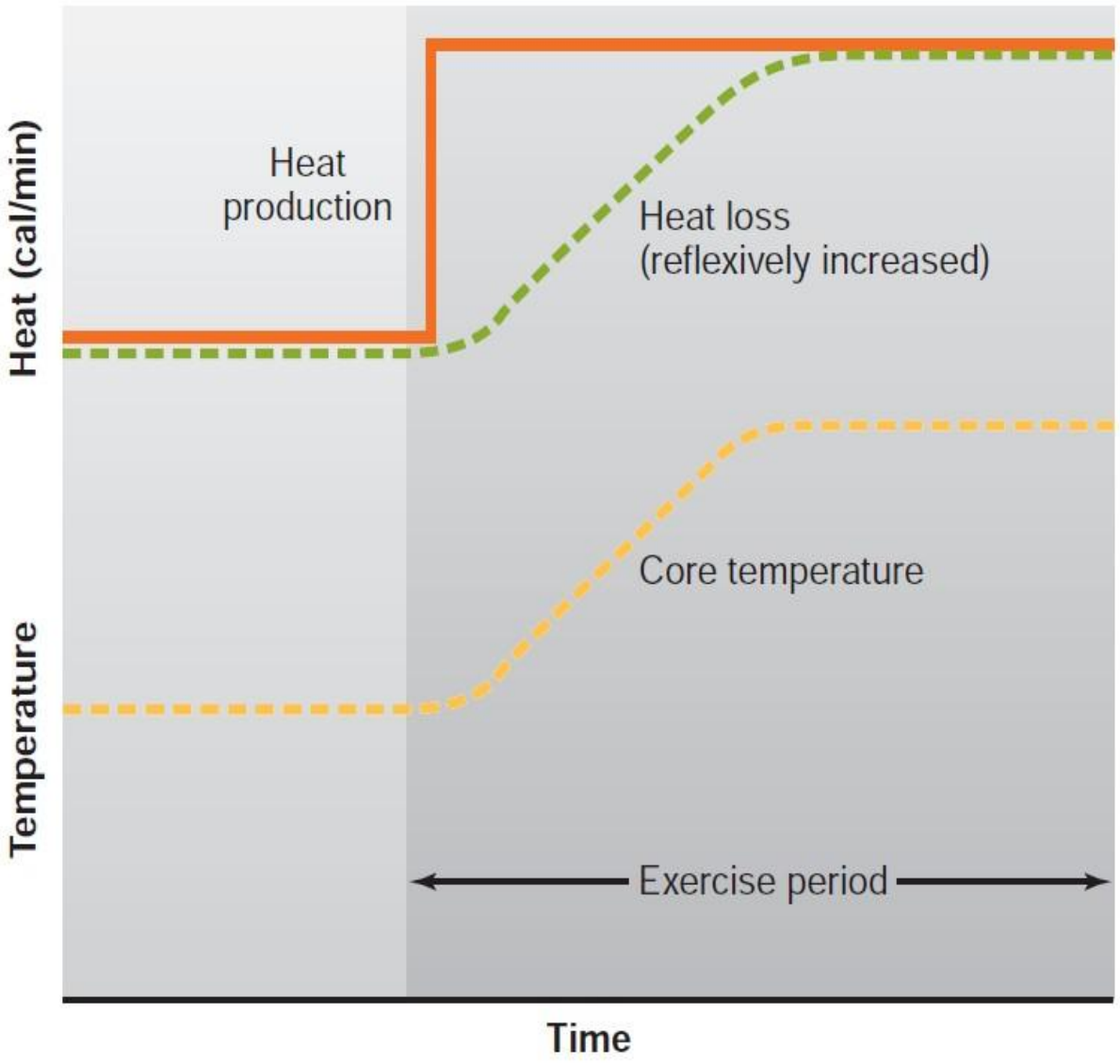
- Cutaneous vasodilation
- decrease thermogenesis
- Sweating

- **Vasodilatation**
- **Sweating**
- Increase in Respiration
- Anorexia
- Apathy
- Decrease TSH secretion

Heat production

Heat loss

Body temperature regulation during exercise



Heat production

↓

core temperature

↓ triggers reflexes

the central thermoreceptors

↓

Heat loss

↓

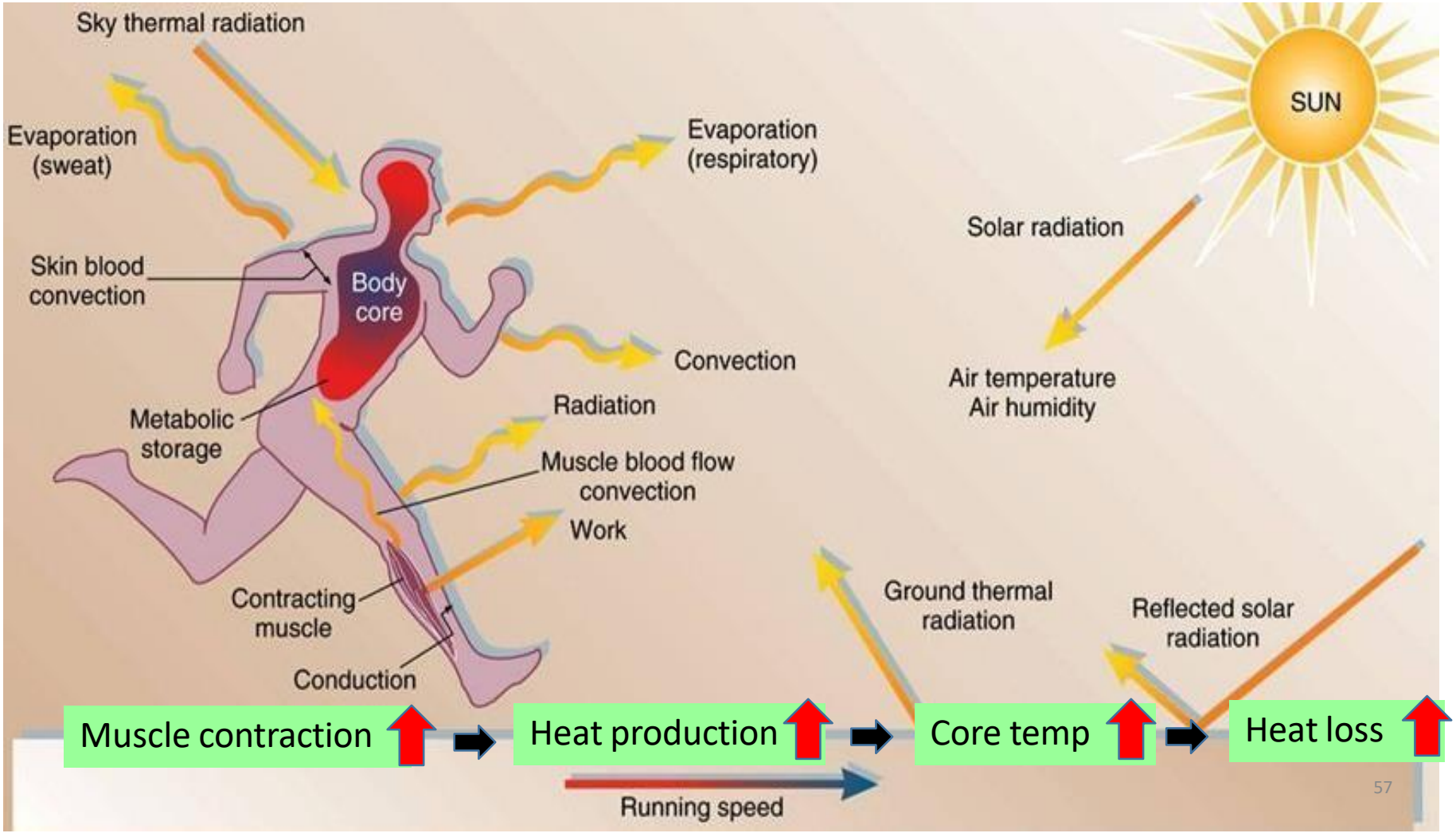
- skin blood flow
- **sweating**

Barrett, K. E., & Ganong, W. F. (2012).

Heat exchange mechanism during exercise

Mechanisms of heat loss during exercise

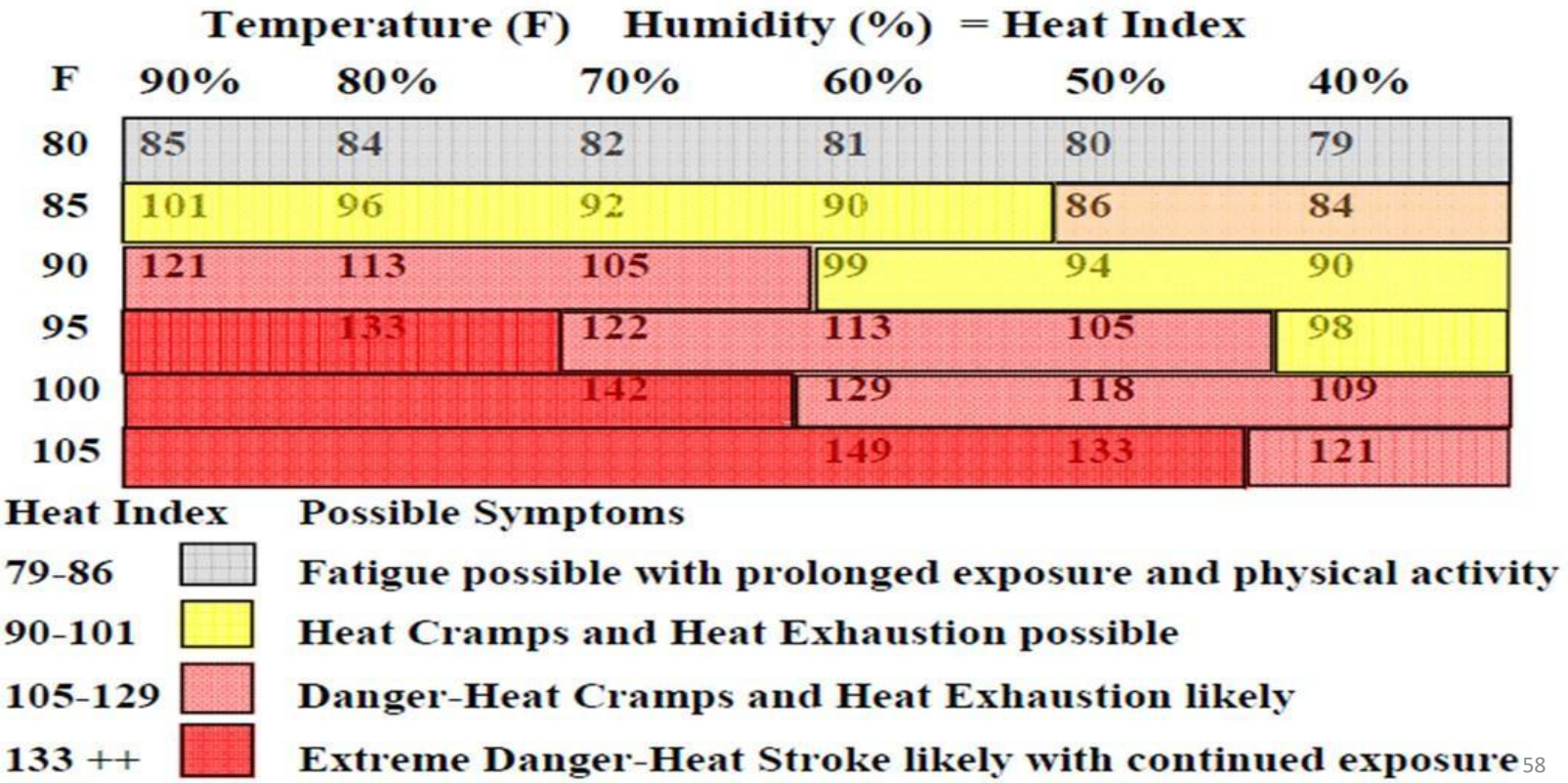
1. Evaporation→ Most important means of heat loss
2. Convection → Small contribution
3. Radiation → Small role in total heat loss



Exercise in the hot environment

Hot Environment

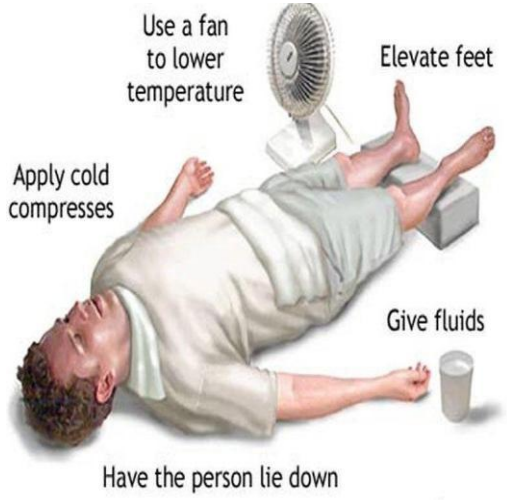
- muscle fatigue and impaired performance
- Reduced mental drive for motor performance
- Reduced muscle blood flow
- Accelerated glycogen metabolism
- Increased lactic acid production
- Increased free radical production



http://www.diabetesuniversitydmcp.com/exercise-in-the-heat.html

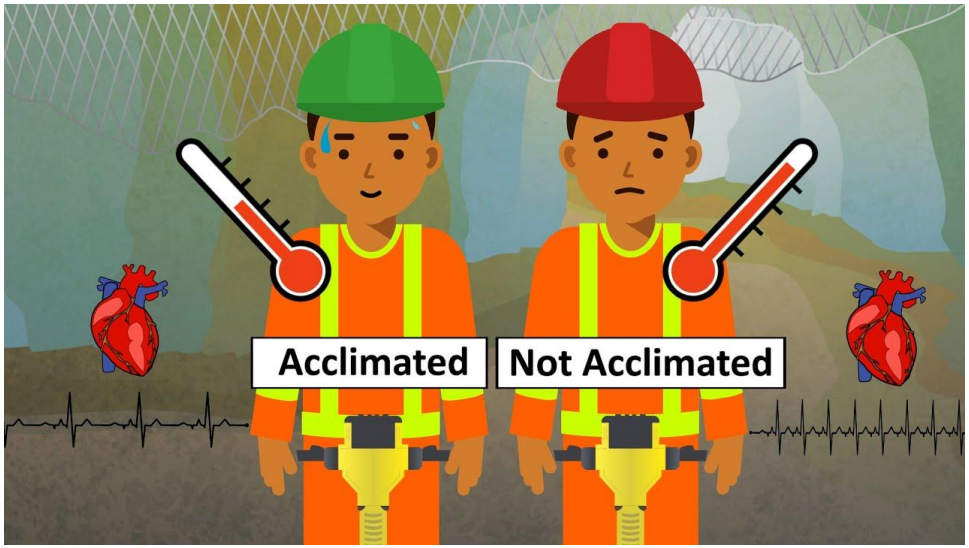
Prolonged exercise in a moderate environment

- Core temperature will increase gradually above the normal resting value (reach a plateau at ± 30 to 45 minutes).
- Exercise in a hot/humid environment, core temperature does not reach a plateau increases the risk of **heat injury.**

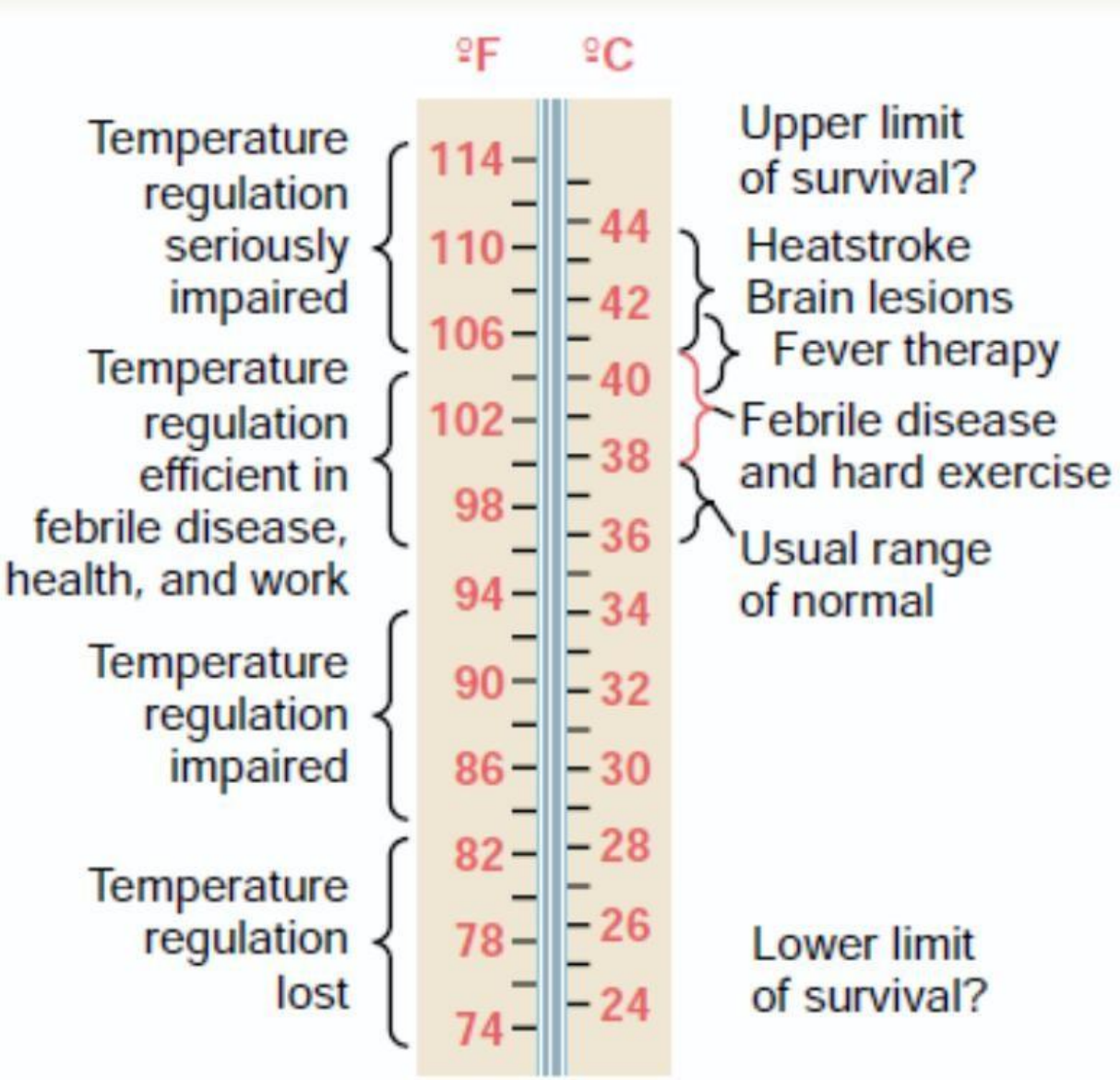


Heat acclimatization

- an increase in plasma volume
- an earlier onset of sweating
- a higher sweat rate
- a reduction in the amount of electrolytes lost in sweat
- a reduction in skin blood flow
- increased levels of heat shock protein in tissues



Abnormalities of Body Temperature Regulation



- **Hyperthermia**

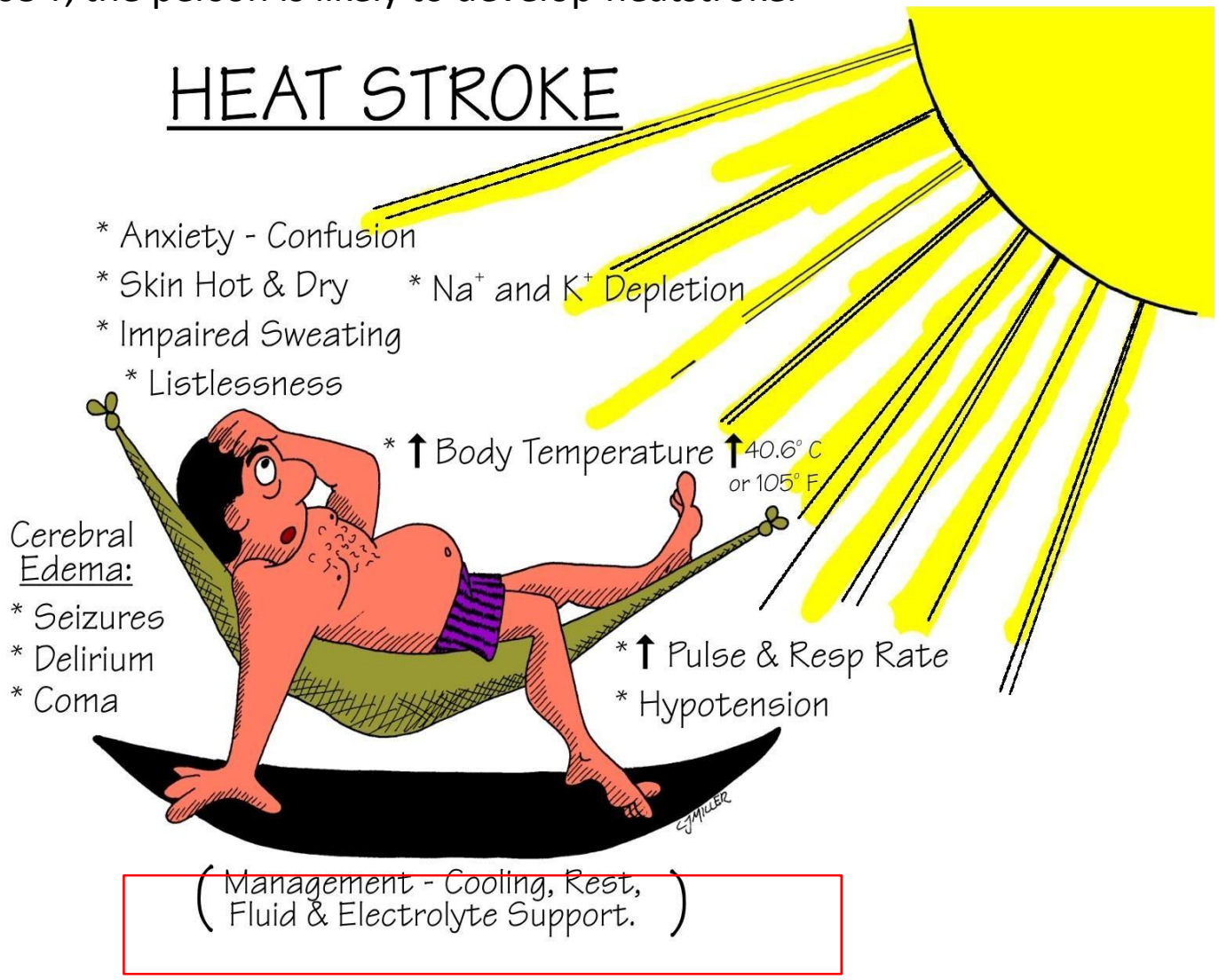
Heat production > Heat loss

- **Hypothermia**

Heat production < Heat loss

Hyperthermia: Heat Stroke

When the body temperature rises beyond a critical temperature, into the range of 105° to 108°F, the person is likely to develop heatstroke.



Cause

↑ Body temp >41 °C

↓ Sweating

↓ Heat loss

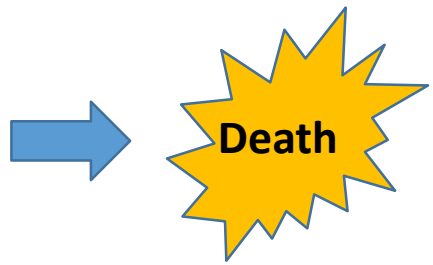
Heat stroke

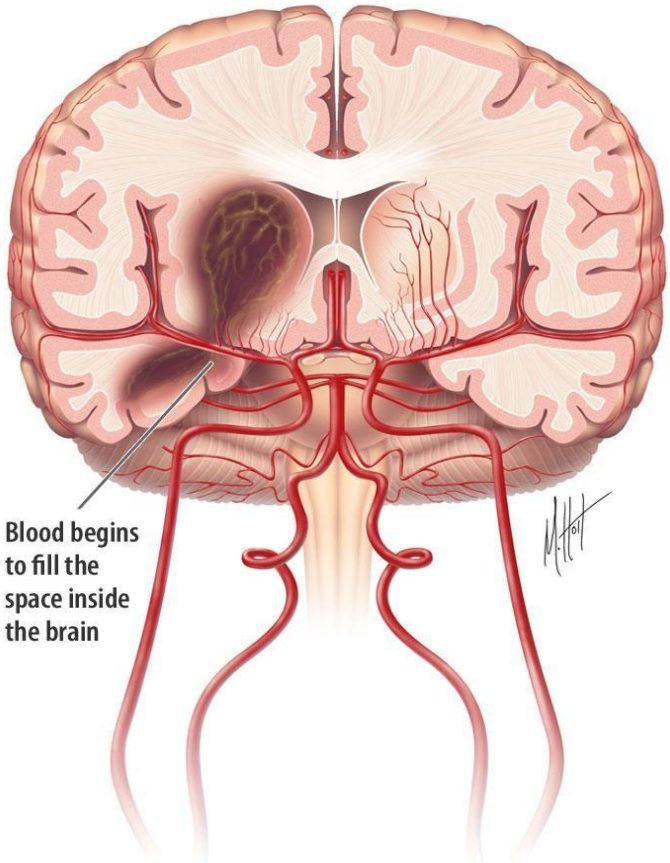
Circulatory shock

Hyperpyrexia (>41.6°C)

The pathological findings

- **Local hemorrhages**
- **parenchymatous degeneration of cells**
- **damage to the liver, kidneys, and other organs**

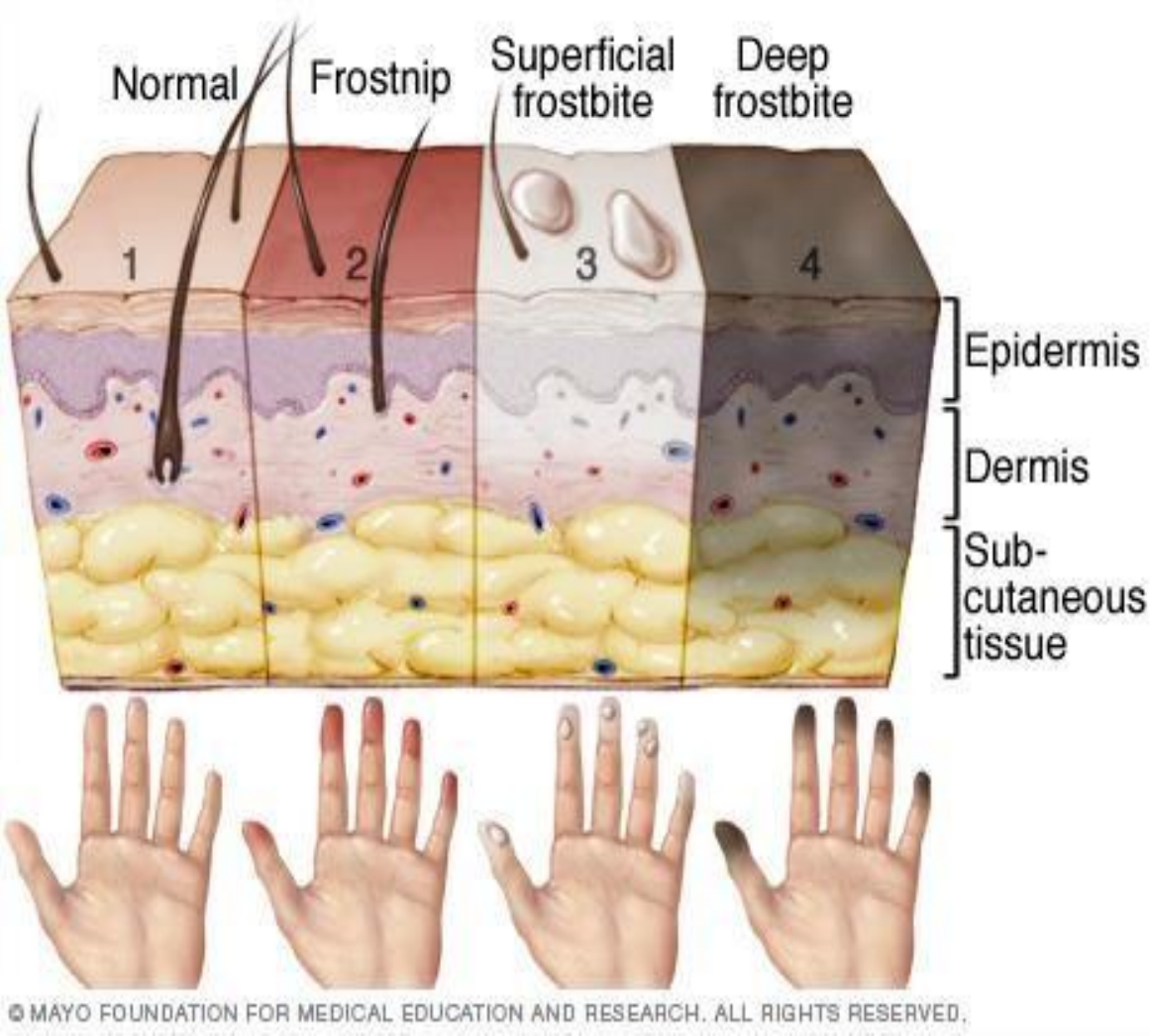




cold water bath

Hypothermia: Frostbite

- Loss of Temperature Regulation at Low Temperatures



Extremely low temperature

↓

Formation of ice crystals in cells

↓

Cells death

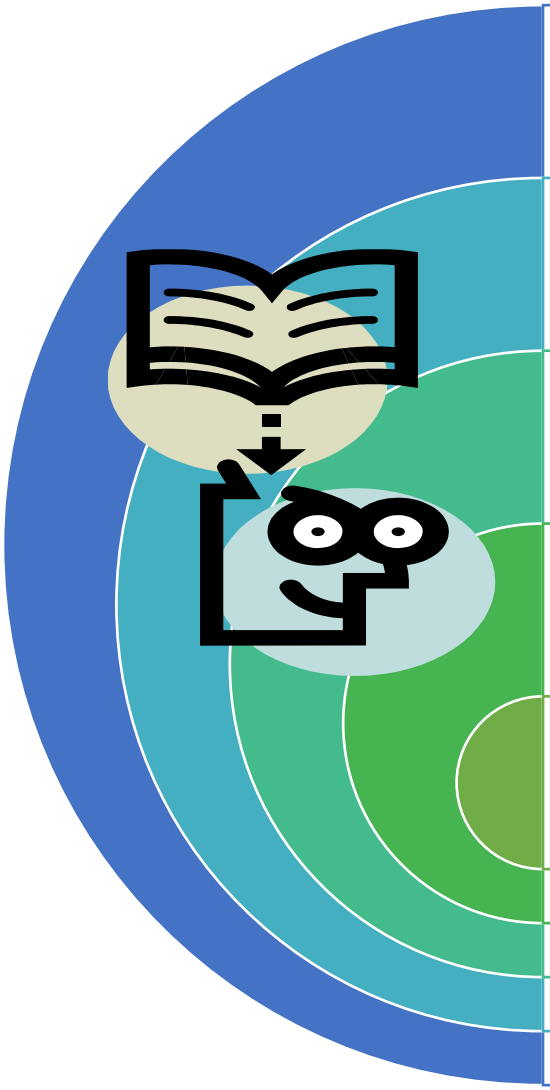
Artificial Hypothermia

Brain and Heart surgery

Add a strong sedative drug→ reduce hypothamamic temperature controller activity→ cooling the person with ice → ↓ HR, BMR

- the body's cells can survive 30 minutes to more than 1 hour without blood flow during the surgical procedure

Resources



Widmaier, E. P., Raff, H., Strang, K. T., & Vander, A. J. (2014). *Vander's Human Physiology: The Mechanisms Of Body Function*. Boston, Mcgraw-hill Higher Education.

Hall, J. E., & Guyton, A. C. (2011). *Guyton And Hall Textbook Of Medical Physiology*. Philadelphia, PA, Saunders Elsevier.

Barrett, K. E., & Ganong, W. F. (2012). *Ganong's Review Of Medical Physiology*. New York, Mcgraw-hill Medical.

Despopoulos, A. & Silbernagl, S. (2003). *Color Atlas of Physiology*. Berlin,Germany. Appl Druck GmbH & Co. KG

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