General patho-physiology: stress, neural and other control, autonomous nervous system, hormonal control, system approach…

Petr Maršálek

https://dec52.lf1.cuni.cz/~pmar/ftp/PPT-PATF/

Seminar circa 50 slides,
Topic code SY

Stress

Stress

Stress, stress syndrome

= neurohumoral defense reaction

= universal response to different external or internal changes and stimuli – stressors

Definition:
The state of threatened homeostasis or disharmony that is counteracted by a complex of physiologic and behavioral responses that reestablish homeostasis

Stress

Stressor

= factor, any adverse change of outer or inner conditions

-physical
-chemical
-biological
-psychosocial

(trauma, surgery, infection, intoxication, pain, working overload, intensive emotion ...)

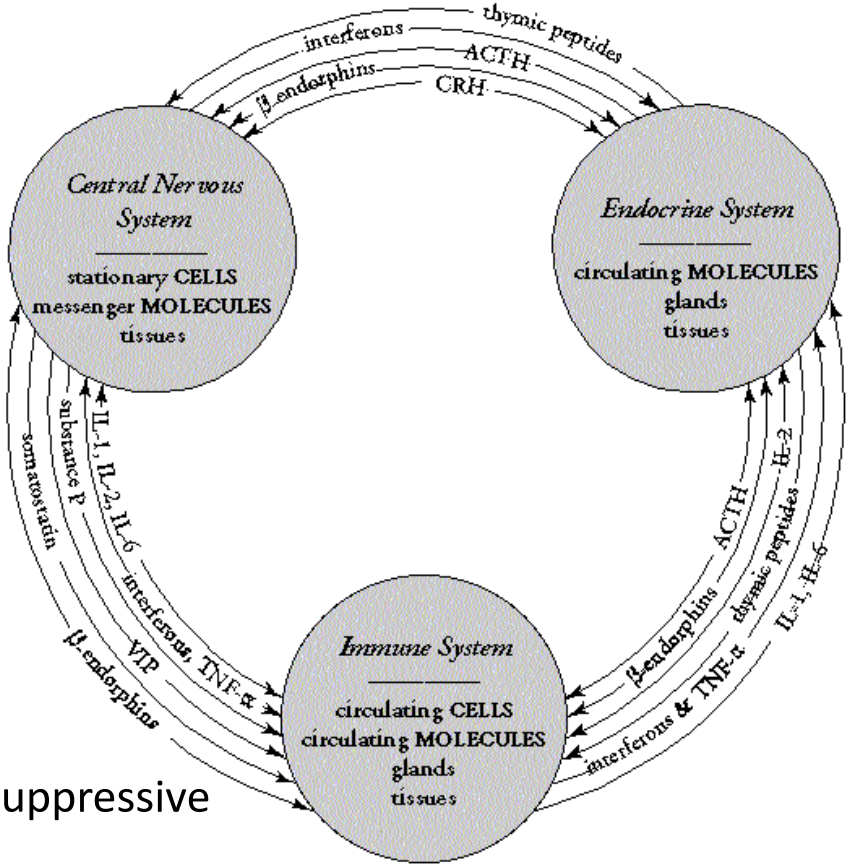
Stress

”Common adaptive syndrome”

= Neurohumoral reaction, response to stressor

mechanisms of stress activation

Stress and Inflammation



Stress with cortisol acts against
immune reaction, it is immuno=suppressive

Stress and Inflammation

Stress reaction

- Generalized reaction
- Activation and coordination from CNS (hypothalamus)
- Universal (non-specific) character

Inflammation

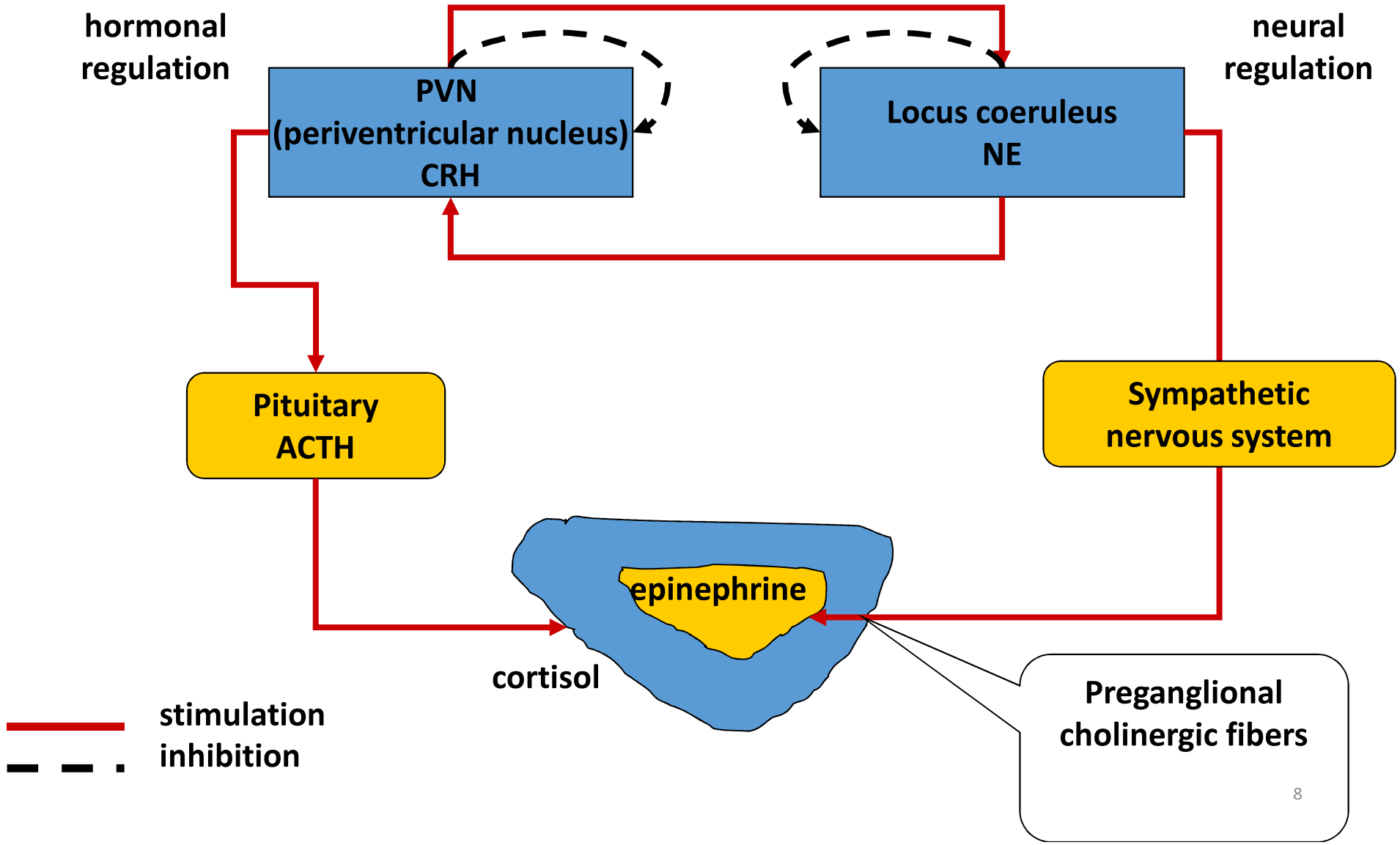
- Primarily local reaction ($\rightarrow$ generalization)
- Reaction of vascularized tissues
- Specific response – targeting against initial stimulus

Stress reaction - phases

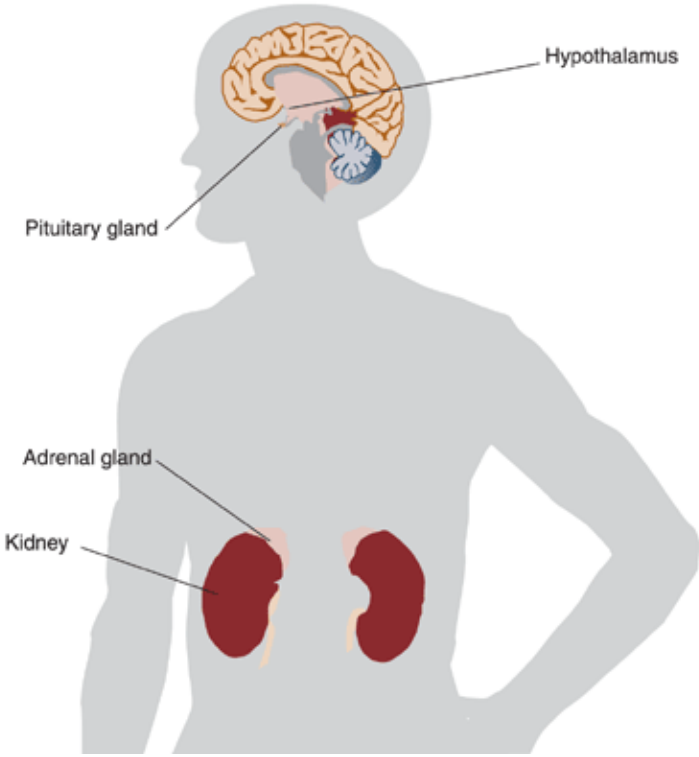
(Hans (Janos) Selye, 1907 - 1982)

Phase	Mediators	Dominant changes
Alarm	catecholamines	CNS activation
	gluco-corticoids (=gcc), growth hormone, melano-cortin (=gcc+acth)	hypothalamus
		cardiovascular effects
		glycogenosysis
		proteocatabolism
Resistance	gcc	gluconeogenesis
		proteocatabolism
		anti-inflammat. effects
		↓ Lymphocytes
		Na + water retention
Exhaustion	gcc	energetic depletion
		↓Glc
		metabolic acidosis

Stress axes


hormonal regulation
neural regulation
PVN (periventricular nucleus) CRH
Locus coeruleus NE
Pituitary ACTH
Sympathetic nervous system
epinephrine
cortisol
Preganglional cholinergic fibers
stimulation
inhibition

Stress system



Mechanisms of stress activation:

1. Activation of cerebral cortex

2. Activation of hypothalamus

3. Neuro-humoral response
   (sympatho - adrenal axis, pituitary - adrenal axis)

4. Peripheral actions
   (metabolic, cardiovascular, immune system...)

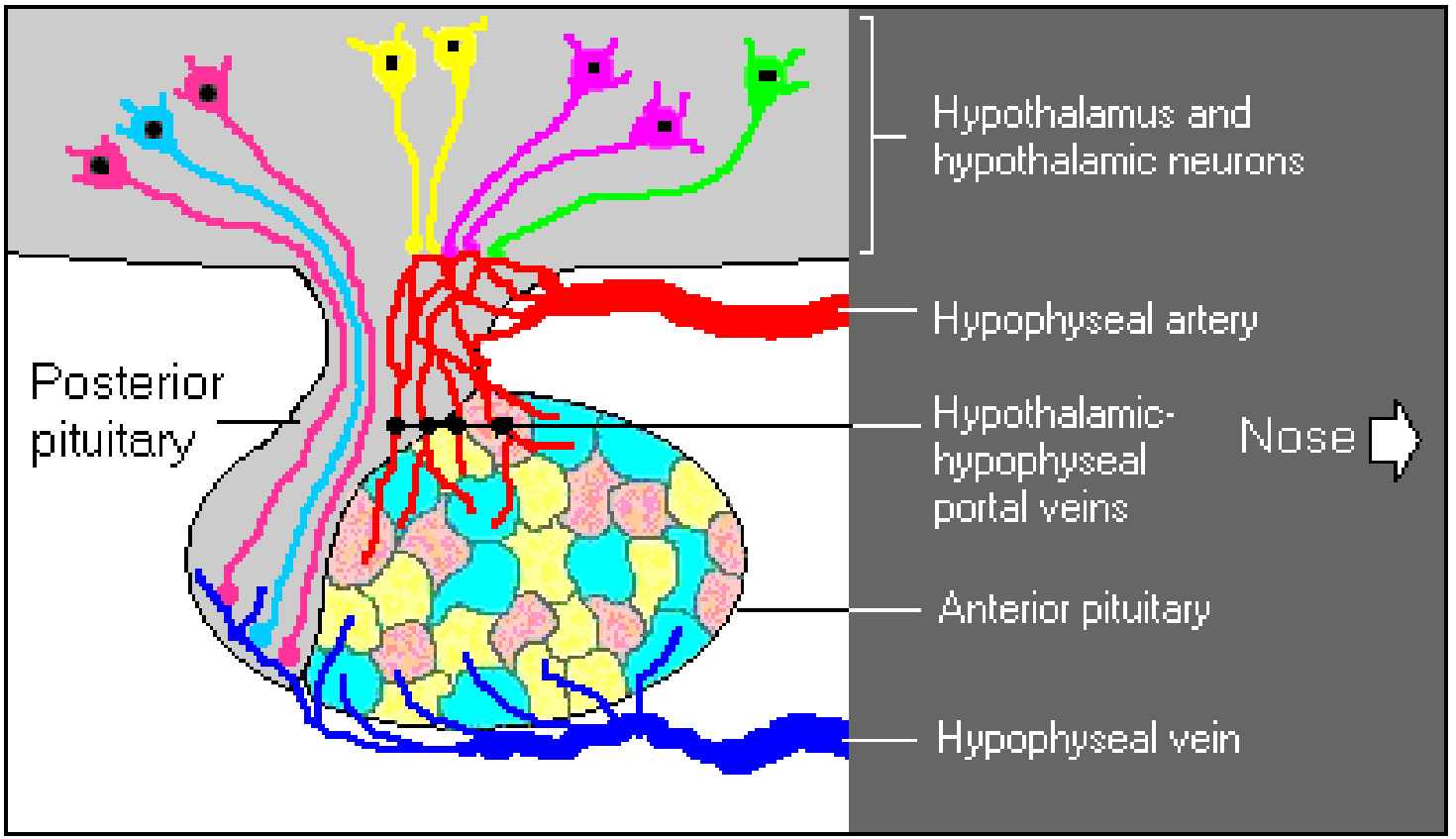
Hypothalamus

↑ epinephrine
↓ norepinephrine
(↑ ratio E / NE)

↑ CRH production in mediobasal centers
↑ ADH production in preoptical part of hypothalamus
↓ inhibition of TRH release
activation of sympathetic - adrenal axis

Pituitary gland

Hypothalamo - hypophyseal axis



Pituitary gland

↑ CRH + ↑ ADH	→	↑ POMC ↑ GH	
↓ TRH	→	↓ TSH	→ ↓T4, T3
↓ GnRH	→	↓ LH	
↑ACTH			

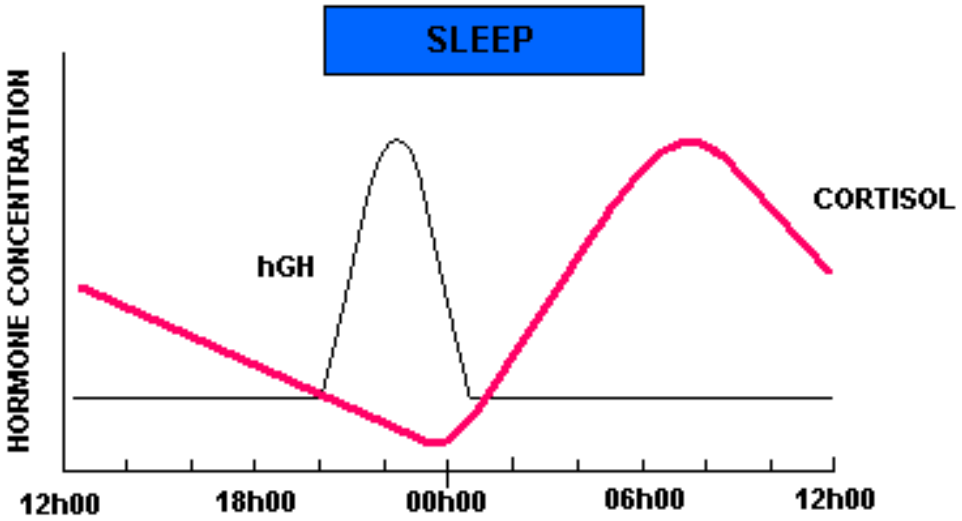
Pituitary - adrenal axis

↑CRH → stimulator of POMC in adenohypophysis
↑ACTH → activation of adrenal cortex
(↑cortisol, ↑ aldost.)

↓ role of negative feedback of corticoids

Pituitary - adrenal axis

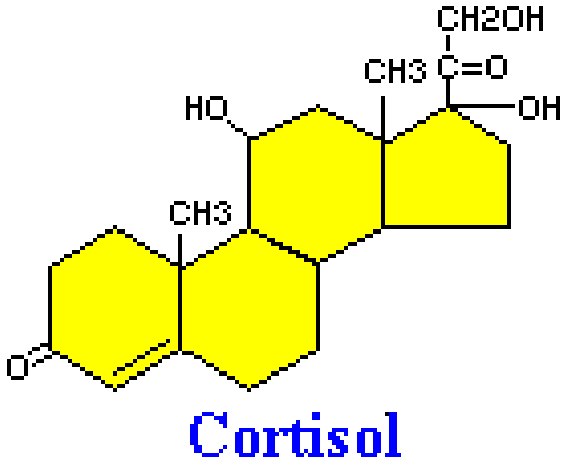
Secretion



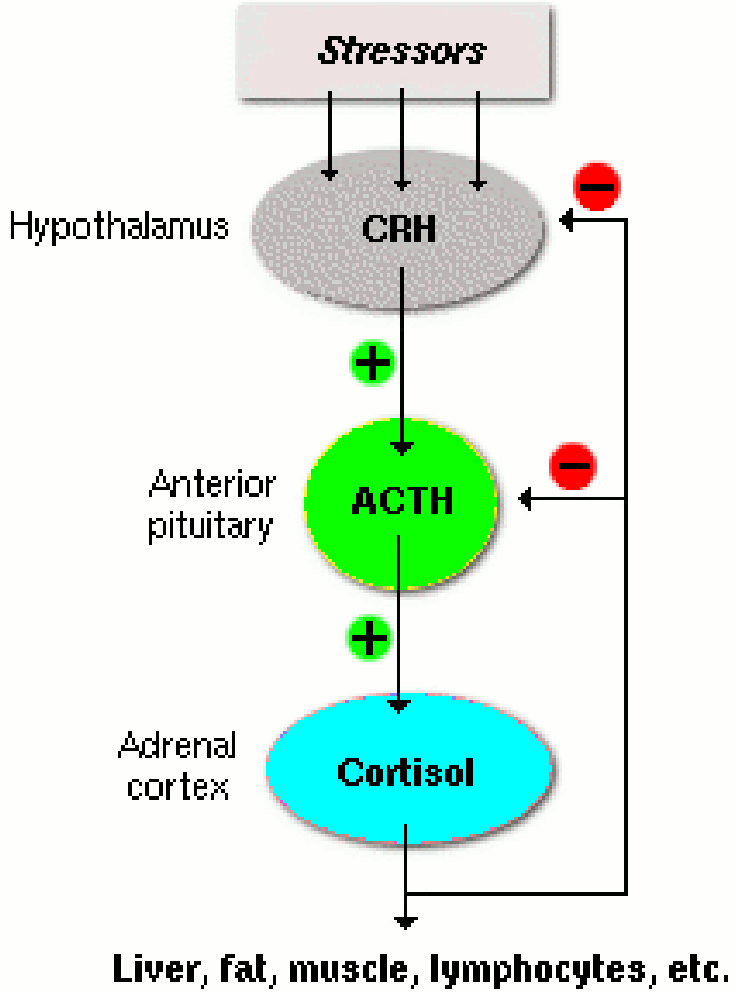
- **Ultradian rhythm** (short periods, episodic, pulsatile)

- **Circadian rhythm** (24 h periods)
  maximal secretion at 8-10 a.m.
  minimal secretion at 11 p.m.

Pituitary - adrenal axis

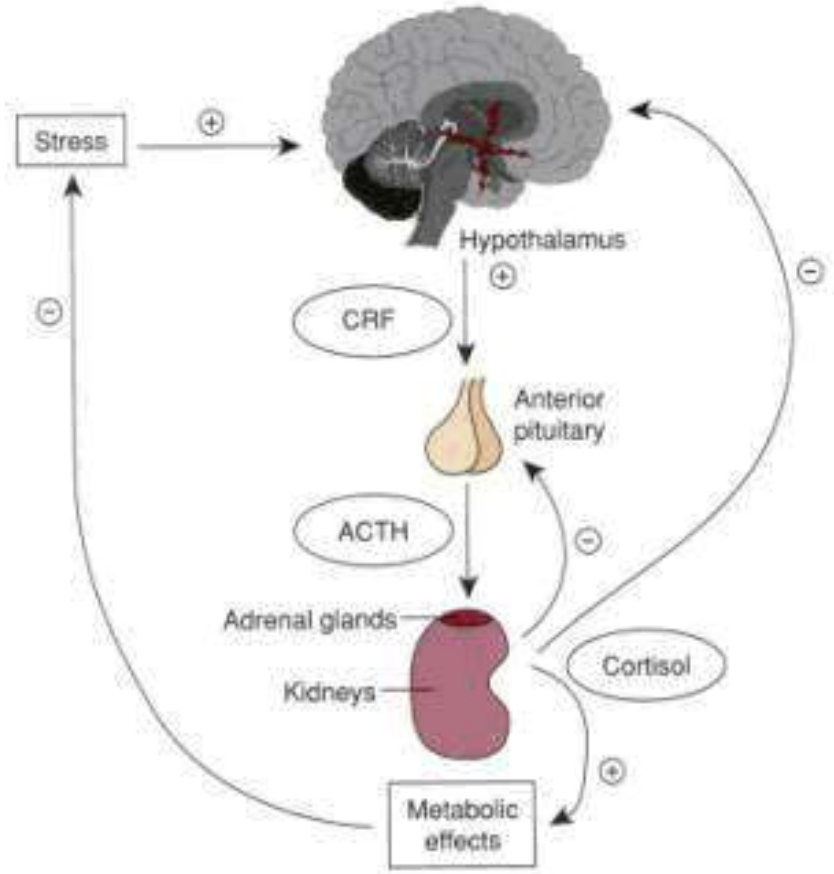


Cortisol



Cortisol secretion control

Negative feedback regulation



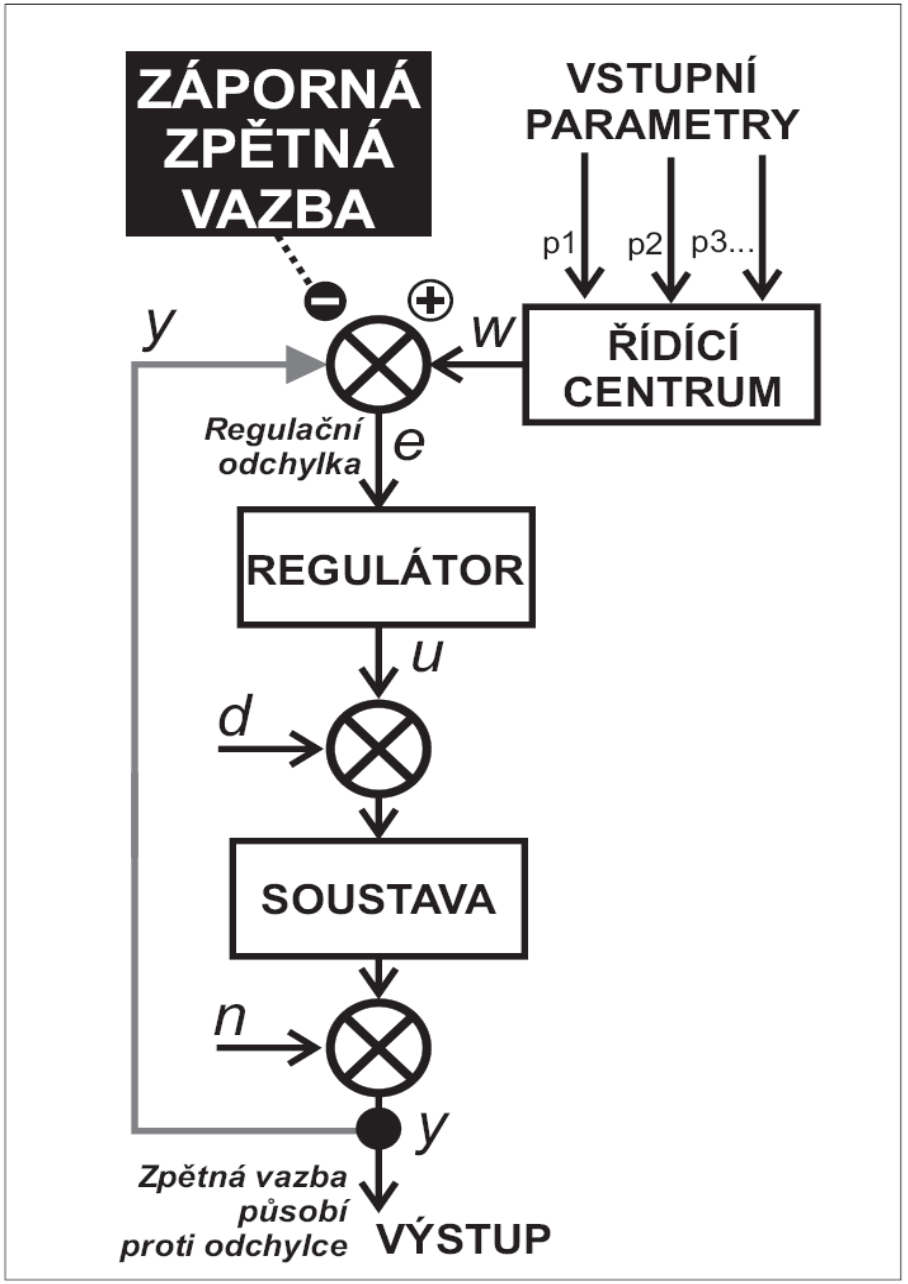
General control concepts, control theory

In contrast to description of cellular and molecular response stands a systemic description of homeostasis and its disturbances as interplay of control (sub)systems.

Control system: Negative feed-back

y…controlled variable, I/O
w…pre-set value
e…error signal
u…actuating variable
d,n…disturbance variables

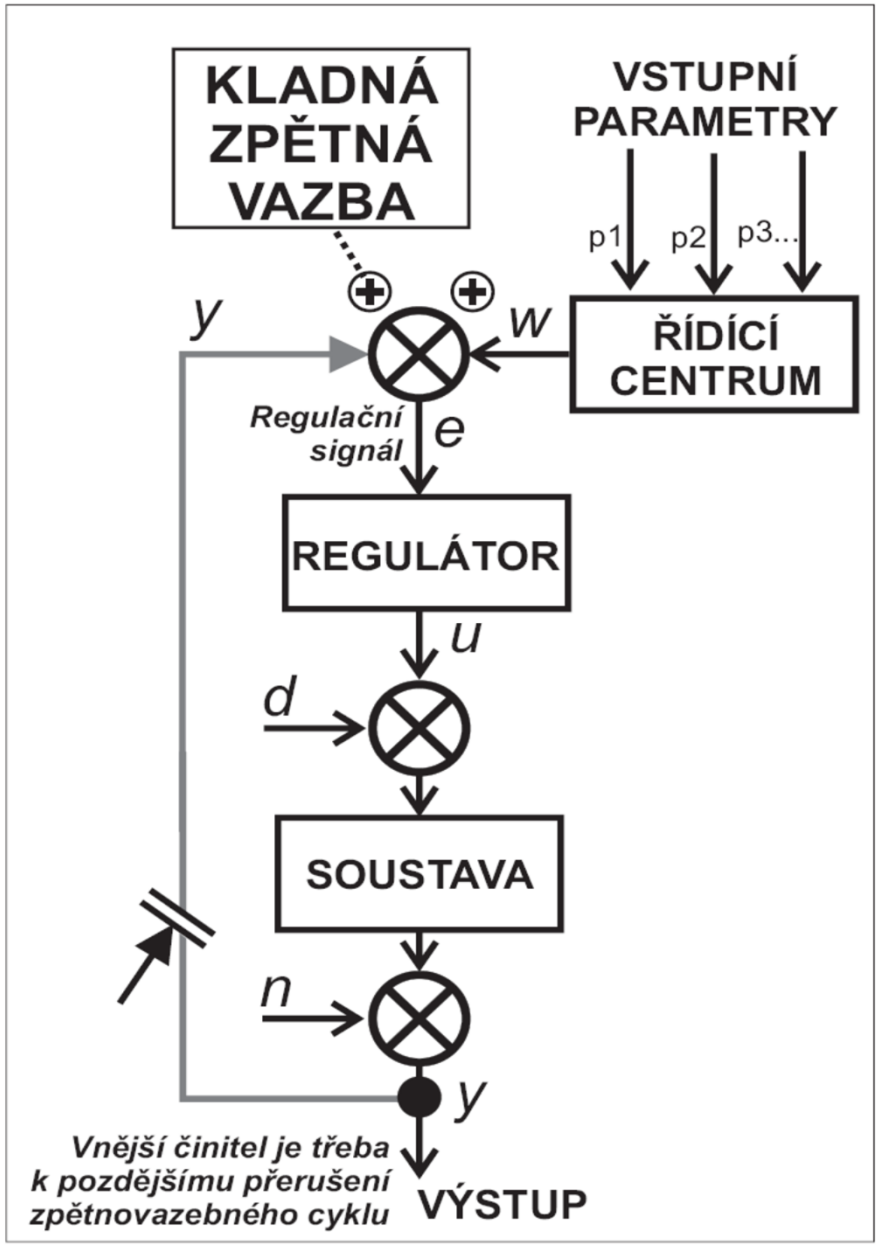
In **negative** feed-back, error signal *e* used for control is obtained by **subtraction** of the controlled variable (-*y*) from the pre-set value (+*w*), $e = w - y$.



Control system: Positive feed-back

y…controlled variable, i/o
w…pre-set value
e…error signal
u…actuating variable
d,n…disturbance variables

In **positive** feed-back, error signal *e* used for control results from **addition** of the controlled variable (+*y*) to the pre-set value (+*w*),
e = *w* + *y*.
Outer factor is needed to disconnect feedback cycle at the point from output back



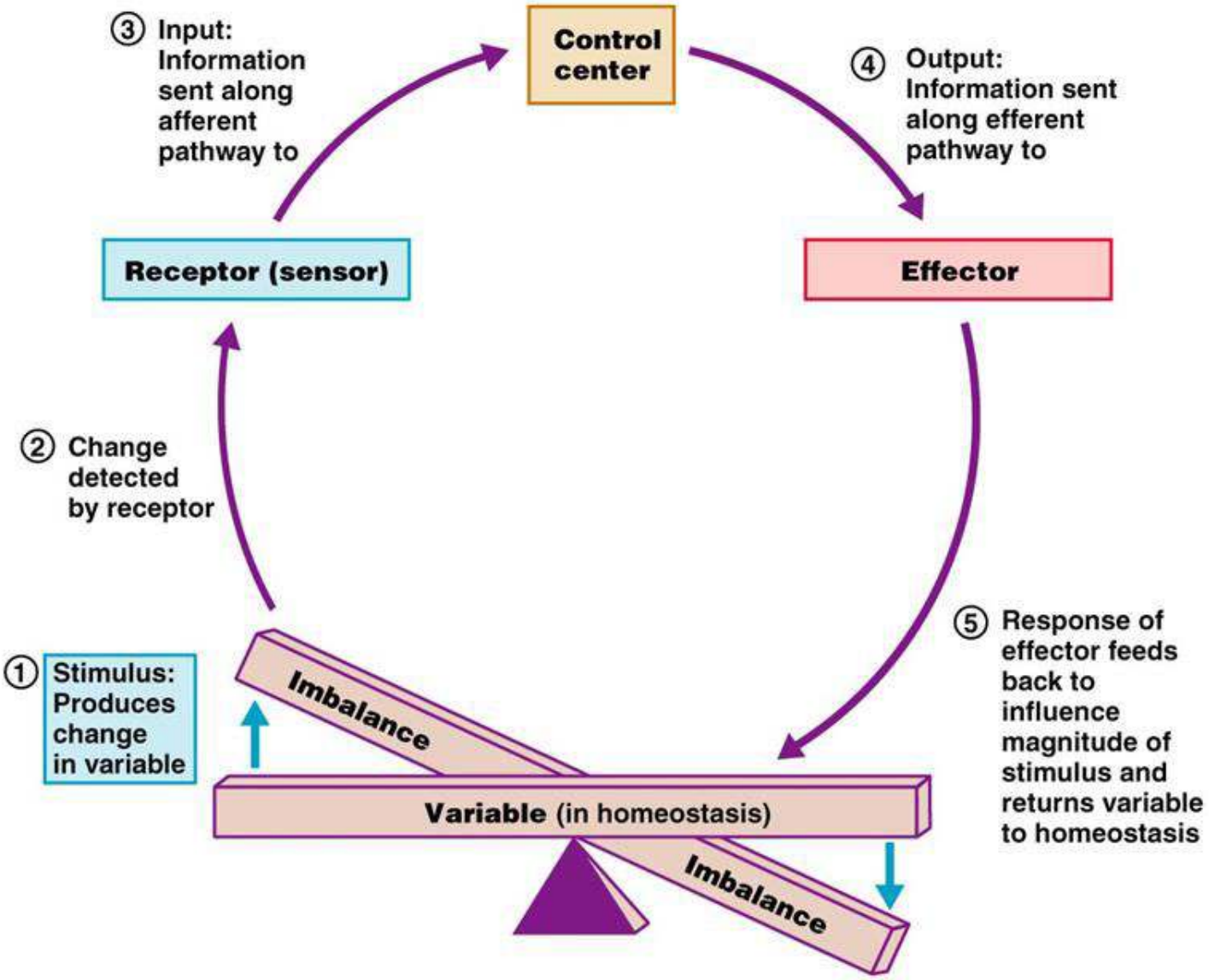
Examples – negative and positive feed-back

Negative feed-back – easy, almost everything is controlled this way:
blood pressure, temperature, glycemia, …
in general – homeostasis…

positive feedback – fewer examples, more difficult:
1) in physiology/ pato-physiology:
Fever onset, ovulation, production of sex hormones in large,
„avalanche-like“ trigger reactions:
hemocoagulation, division of lymfocytes
during the immune reaction (e.g the pneumonia crisis)

2) Pathology (pathologic values of variables, vicious circles, failures).
Building up of a new, pathologic equilibrium, example: adaptation to the lower PO2
failure of blood pressure control -> shock, hypo-perfusion, hypoxia…

Homeostasis, control circuit simplified



Adrenal glands

Glucocorticoids

- essential for an adequate course of stress reaction
- permissive effect on catecholamine action
- domination in 2nd phase of stress response (st. of resistance)

Effects:

- glycids ... gluconeogenesis
- proteins ... proteocatabolism (neg. N balance)
- lipids
- hematopoiesis (↑Neu, ↓Eos, ↓Ly, ↑Plt)
- anti-inflammatory effects ... cytokines, APP
- circulatory changes (↑BP, Na and water retention)

Adrenal glands

Glucocorticoids

Glucose

1. Gluconeogenesis stimulation in liver (6-10x)
2. Activity of enzymes for AA conversion to Glc
3. Mobilization of AA from tissues (x liver)
4. Elevation of hepatic glycogen
5. Decrease of Glc utilization in cells

Adrenal glands

Glucocorticoids

Proteins

1. Proteocatabolic effect in all tisues excepting liver
2. Low protein synthesis
3. Low AA transport into cells (muscles, lymphoid t.)
4. Proteoanabolic effect in liver (APP)

Adrenal glands

Glucocorticoids

Lipids

1. Mobilization of fatty acids from adipose t.
2. High oxidation of fatty acids (low utilization of Glc
- energy from fatty acids)

Adrenal glands

Glucocorticoids

Anti / inflammatory effects

1. The release of proteolytic enzymes, histamin, bradykinin
   x cortisol - stabilisation lysosomal membrane
2. Vasodilation in inflammatory tissue
   x cortisol - vasoconstrictory effect
3. High permeability
   x cortisol - decreased capillary permeability
4. Leucocyte infiltration
   x cortisol - inhibition of Leu migration
5. Cortisol - immunosuppresive effect (decrease of T Ly)
6. APP synthesis

Sympathetic - adrenal axis

Hypothalamus

→ Medulla oblongata
→ Medulla spinalis
→ Adrenal medulla + sympathetic ganglia

Metabolic and cardiovascular responses

Adrenal medulla

Catecholamine synthesis

Norepinephrine	**20%**	**1.2 - 3.4 nmol/l**

5-6 x elevation ... biological effects

Epinephrine	**80%**	**0.1 - 0.8 nmol/l**

2 x elevation ... biological effects

Adrenal medulla

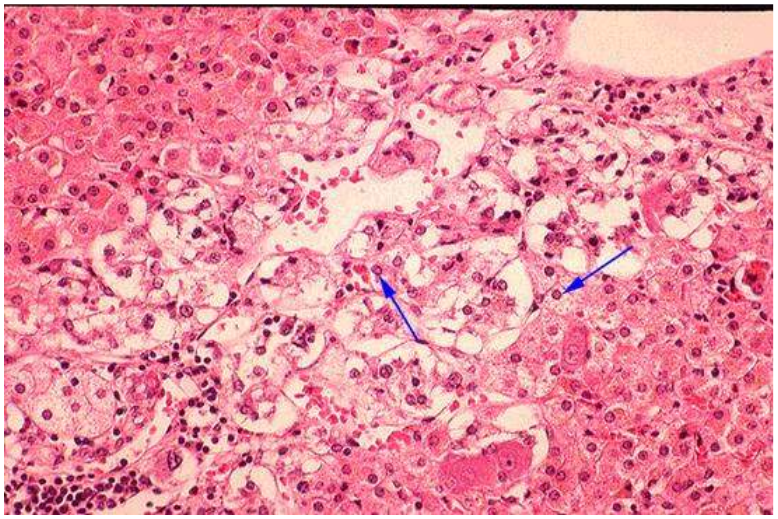
Catecholamines (adrenomedular system)

- rapid activation (sec...min.), rapid degradation
- crucial in an initial (alarm) phase of stress response

Effects

- cardiovascular (chrono, ino, bathmo, dromo-tropic) ↑CO, ↑BP
- metabolic ... hepatic glycogenolysis
  - ↑ intestinal resorption of glc.
  - ↓ insulin production
  - lipolysis, ↑FFA

Adrenal medulla



Chromaffine cells = pheochromocytes
Axons of preganglionic sympathetic nerves

Catecholamines:

- **Norepinephrine … adrenal medulla + CNS + PNS**
- **Epinephrine … adrenal medulla**
- **Dopamine … precursor of NE, adrenal medulla + noradrenergic neurons**

Receptors:

α … vasoconstriction, sweating, GIT
β … vasodilatation, GIT, catabolism, bronchodilation

Psycho - social stress

= Emotional activation of stress response

The role of paleocortical region (limbic cortex, neocortical region)

Activating (stressogenic) pathway
nc. amygdalae → mediobasal hypothalamus

Inhibiting (anti-stressogenic) pathway
fornix, gyrus hippocampi → corpora mamillaria of posterior hypothalamus

... protracted activation of sympathoadrenal + adrenocortical axis without psychiological benefit

... risk factor of psycho-somatic disorders

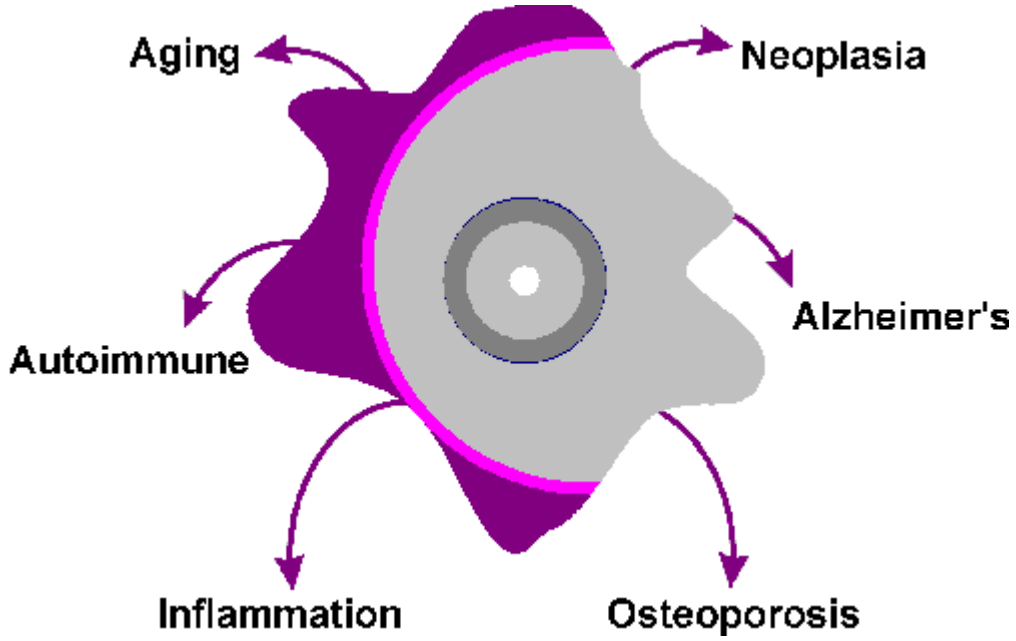
Stress and somatic disorders

Alterations of the ability to respond to stressors, as for example inadequate, excessive and/ or prolonged reactions, may lead to disease.

Moreover, excessive and/ or chronically imposed stressors may have adverse impact on a variety of physiologic functions, such as growth, reproduction, metabolism and the immunity, as well as on development and behavior.

Prenatal life, infancy, childhood and adolescence are critical periods characterized by increased vulnerability to stressors.

Stress and somatic disorders



Stress and somatic disorders

Atherosclerosis
Hemoconcentration
Heart ischemic dis.
Myocardial infarction
Stroke
Metabolic (Reaven) syndrome (insulinoresistance, hyperinsulinaemia, hypertension, hyperlipidaemia, hyperurikaemia...)
↑ sensitivity to infection
Malignancies ?
Gastric ulcer (Cushing syndrome ulcer)
Graves-Basedow disease
Psoriasis

... Psychosomatic medicine

Autonomous nervous system

This is a major control system. Often, in pathological physiology studies of nervous system it is forgotten. Because of: central nervous system,
humoral control (hormones), immune system, etc.

Neurotransmitter examples

Autonomic/ Vegetative nervous system

- sympathetic and parasympathetic,

-receptors (alpha- and beta- adrenergic, nicotinic and muscarinic cholinergic)

- mediators (adrenaline, noradrenaline (norepinephrine), acetylcholine)
- mediator synthesis (= biogenic amines)
- cleavage (choline-esterase, mono-amino-oxidase, and re-uptake)
- anatomic connections (segmental, versus head a torso, pre- and post- ganglionic fibers), urination, defecation, erection, ejaculation,

eye focusing = accomodation, pupil sphincter = adaptation,

- balancing sympathetic and parasympathetic effects

Plants and mushrooms with effect on the cholinergic synapse

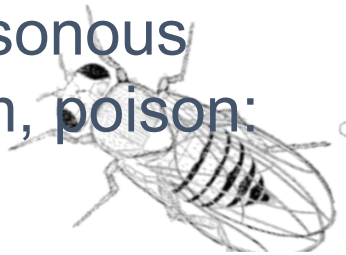
nicotinic and muscarinic cholinergic receptors

Clitocybe dealbata,
or sweating mushroom
Deadly poisonous mushroom,
poison: muscarine,
antidotum: atropine

Clitocybe odora,
Edible mushroom

Nicotiana tabacum,
Tobacco plant,
Deadly poisonous plant

Amanita muscaria,
or fly agaric
Mildly poisonous
mushroom, poison:
muscimol



Neural pathways/ neural control

CZ

Hledání účelnosti ve fyziologických reakcích. (Imunosupresivní léčba některých nemocí občas ukazuje, že patologenetický proces vůbec neprobíhá účelně.)

Nervový signál přenáší jen reprezentaci veličiny
s kladným znaménkem, proto se často vyskytuje
dualita současného řízení excitačními a inhibičními neurony

V případě vegetativního NS je to také dualita sympatiku a parasympatiku

Thermoregulation:

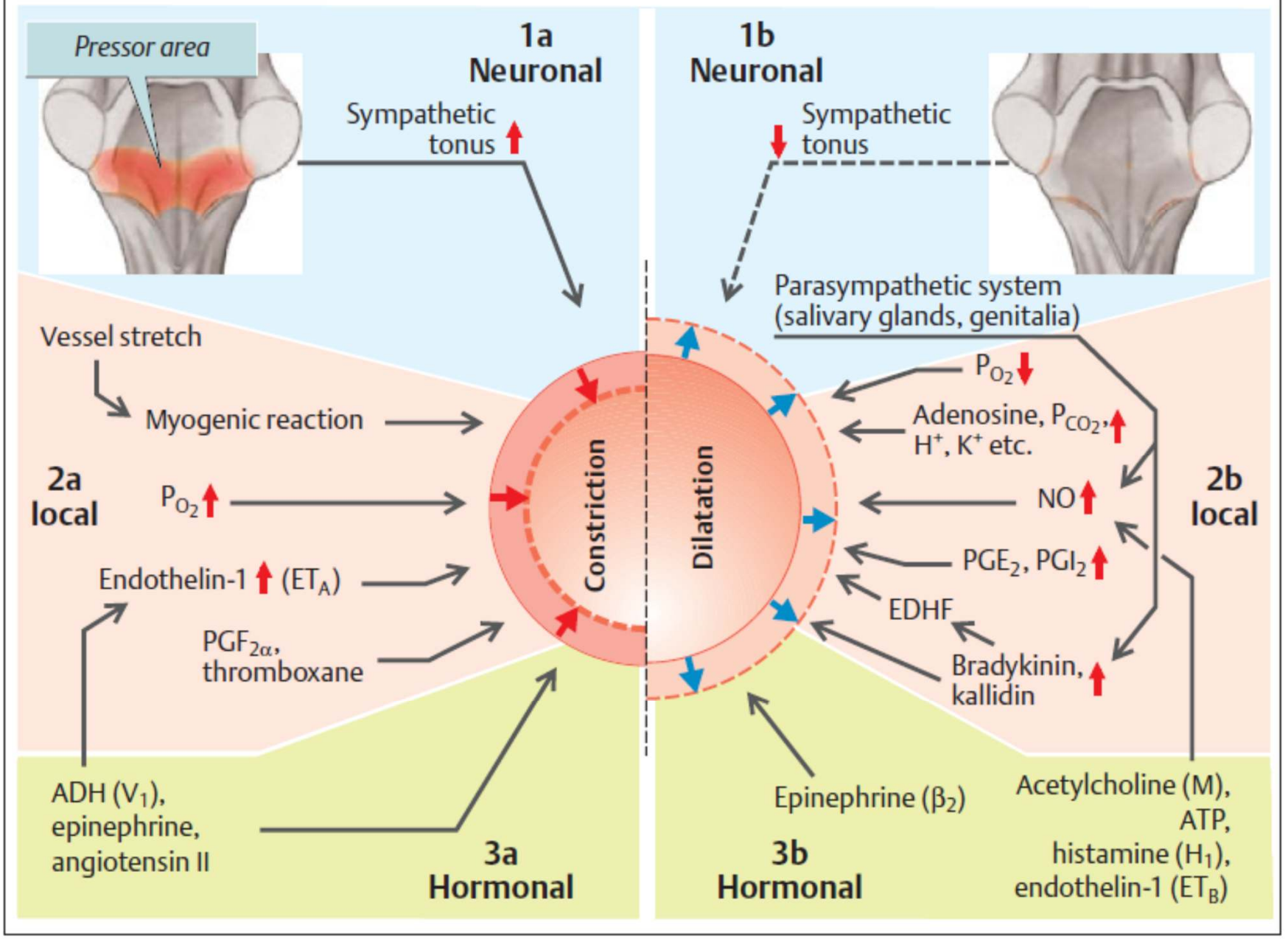
kožní vasokonstrikce/ vasodilatace
potní žlázy - sympatikus
výjimka v inervaci: cholinergní

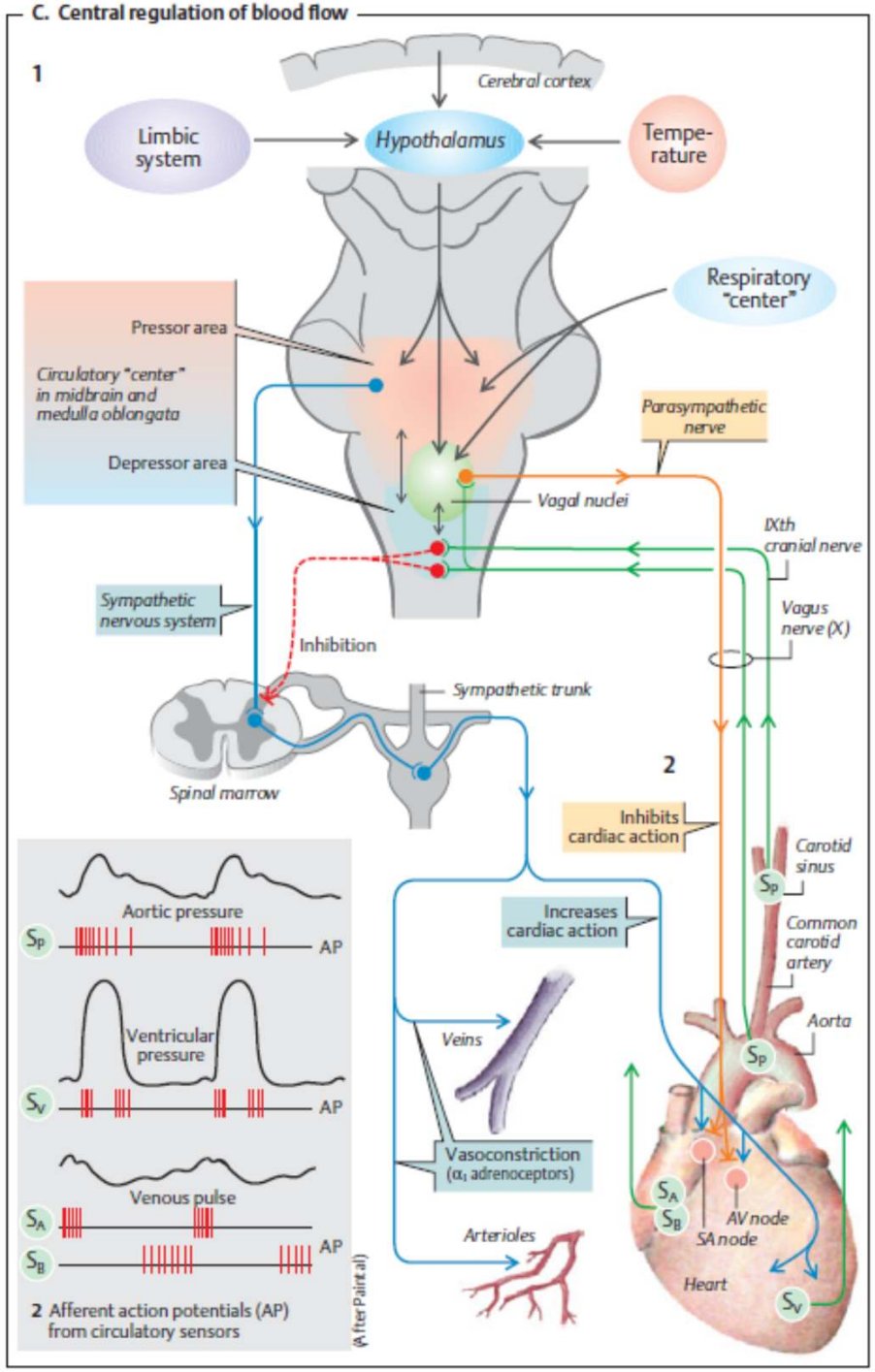
Baroreflex:
vybalancování
účinků sympatiku a parasympatiku
Zvýšení a snížení krevního tlaku:
(-press.=> +symp.-parasymp.
mimo jiné např.: orthostatický reflex)
(+press.=> -symp.+parasymp.)

Circulation and vaso-motor control

Failure of circulatory control
is manifested as shock
(defined as) such a drop of the systemic blood pressure, which cannot sustain oxygenation reserve in functioning of organs with vital importance
(heart, brain, respiratory muscles)

B. Vasoconstriction and vasodilatation



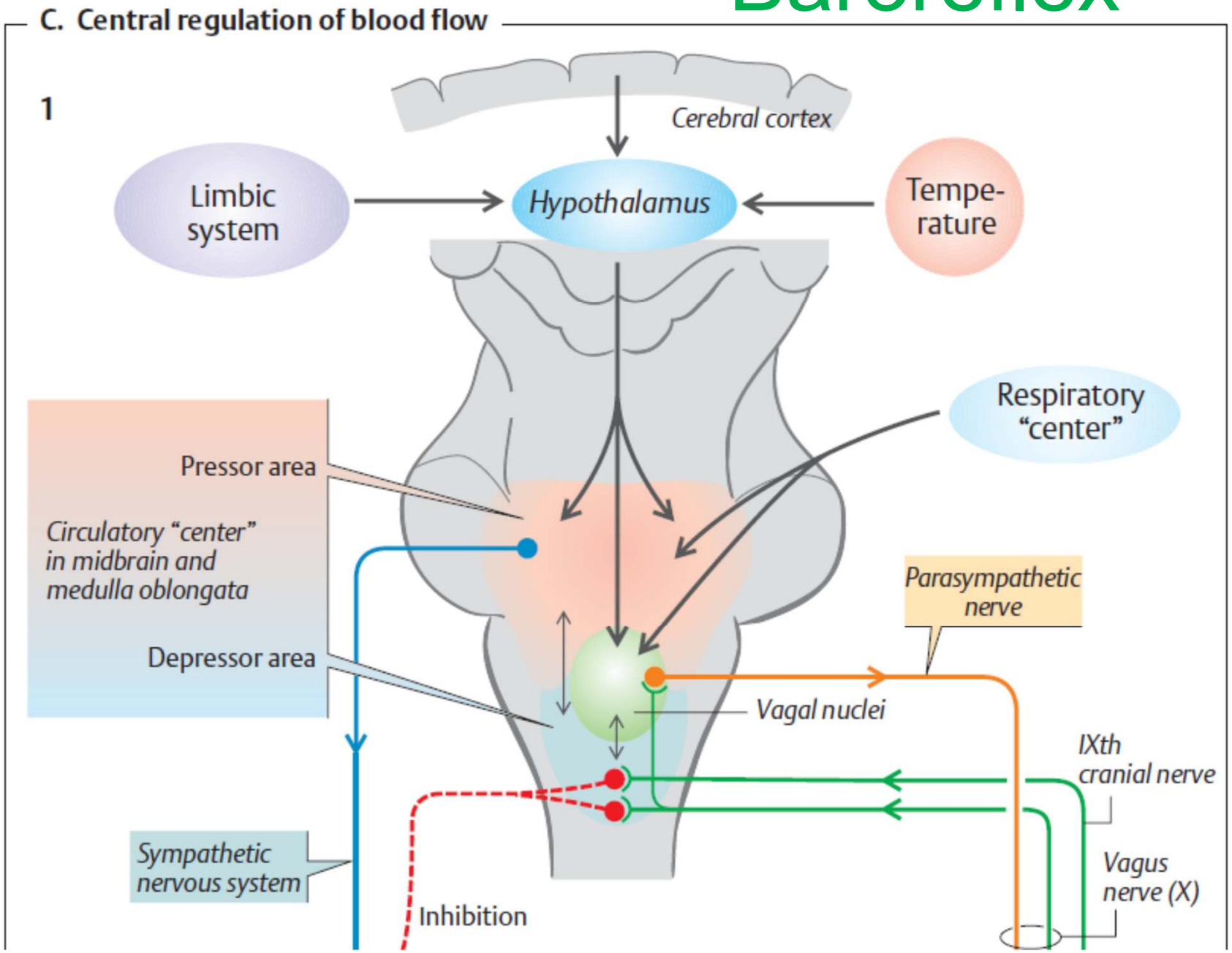


Baroreflex

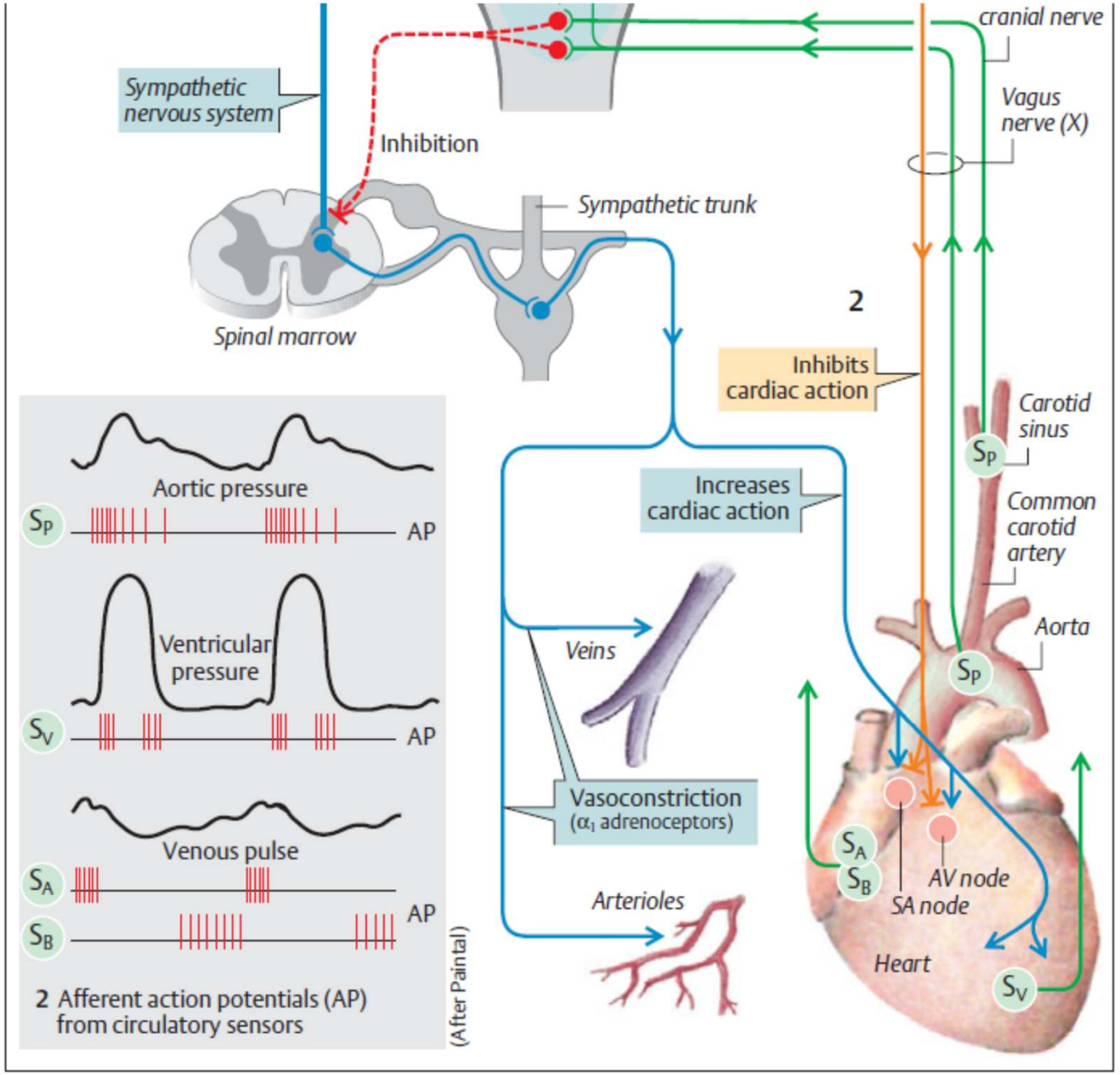
CZ

Baroreflex:
vybalancování
účinků sympatiku a parasympatiku
Zvýšení a snížení krevního tlaku:
(-press.=> +symp.-parasymp.
mimo jiné: orthostatický reflex)
(+press.=> -symp.+parasymp.)

Baroreflex


C. Central regulation of blood flow
1
Cerebral cortex
Limbic system
Hypothalamus
Tempe-rature
Respiratory "center"
Pressor area
Circulatory "center" in midbrain and medulla oblongata
Depressor area
Parasympathetic nerve
Vagal nuclei
IXth cranial nerve
Vagus nerve (X)
Sympathetic nervous system
Inhibition

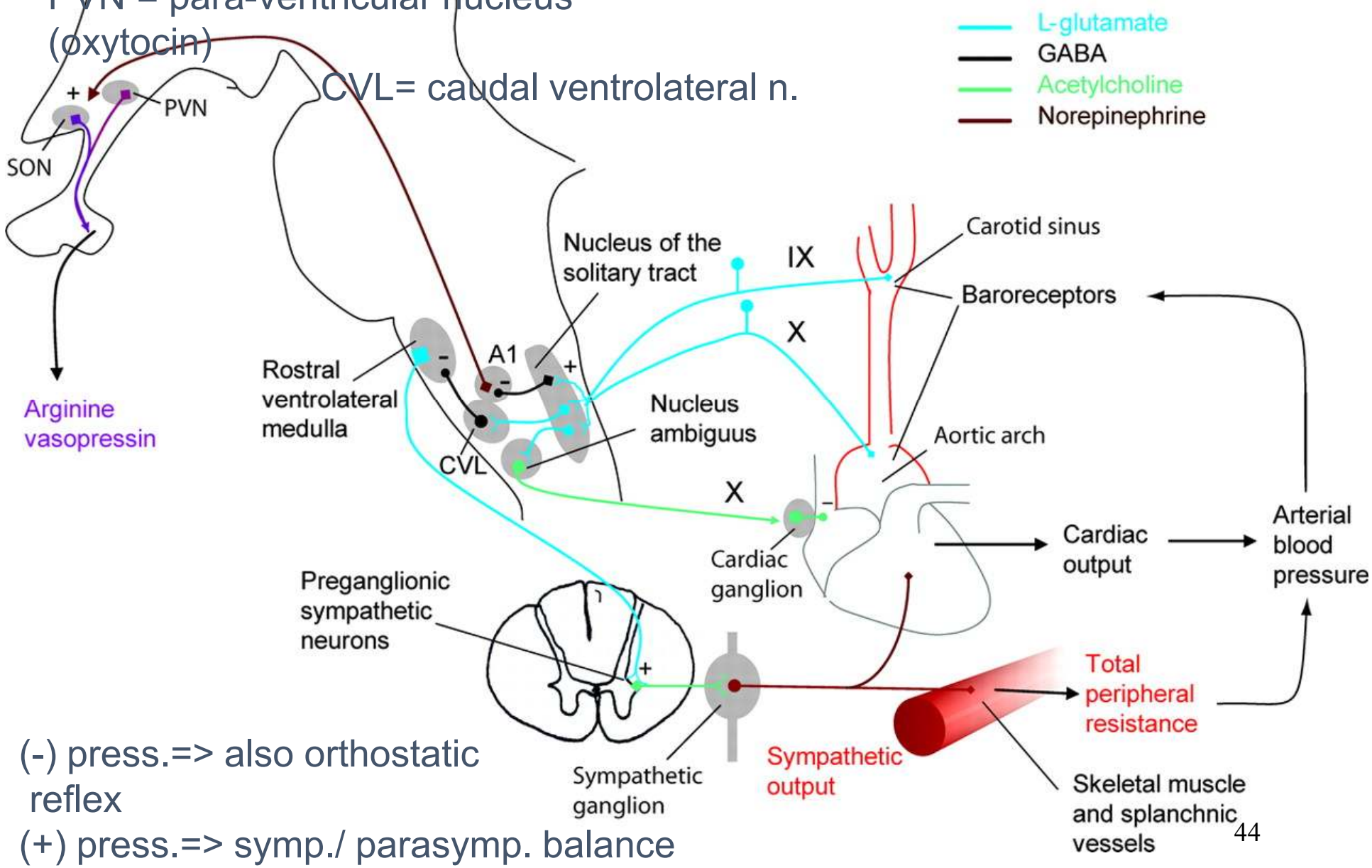
Baroreflex


cranial nerve
Vagus nerve (X)
Sympathetic nervous system
Inhibition
Sympathetic trunk
Spinal marrow
2
Inhibits cardiac action
Carotid sinus
Sp
Increases cardiac action
Common carotid artery
Aorta
Veins
Vasoconstriction
(α1 adrenoceptors)
Arterioles
SA
SB
AV node
SA node
Heart
SV
Aortic pressure
Sp
AP
Ventricular pressure
SV
AP
Venous pulse
SA
SB
AP
2 Afferent action potentials (AP) from circulatory sensors
(After Paintal)

Baroreflex

SON = supra-optic nucleus
(ADH, or vasopressin)
PVN = para-ventricular nucleus
(oxytocin)

CVL= caudal ventrolateral n.



(-) press.=> also orthostatic reflex

(+) press.=> symp./ parasymp. balance

Autonomous nervous system,

And its polarity, (or duality):

Parasympathetic versus sympathetic.

Fight and/ or flight versus relaxation/ regeneration

Sometimes more than 2 alternatives: vasomotor control can be:

1 alpha and 2 beta adrenergic and 3 cholinergic

Cholinoceptors

Nicotinic receptors:
- All postganglionic, autonomic ganglia cells and dendrites
- Adrenal medulla

Muscarinic receptors:
- All target organs innervated by postganglionic parasympathetic nerve fibers (and sweat glands innervated by sympathetic fibers)

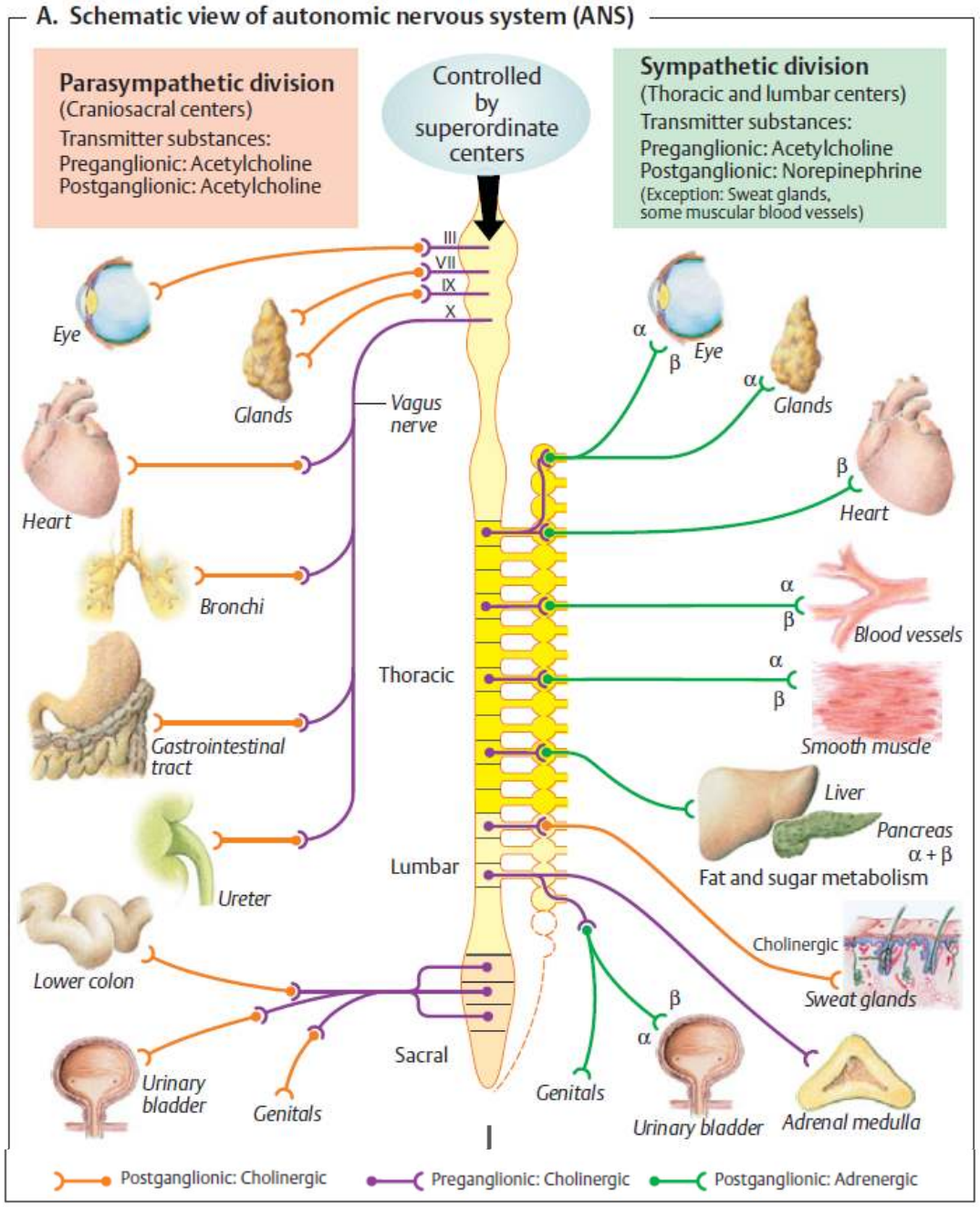
Adrenoceptors:

α Usually excitatory (except in GI tract, where they are indirect relaxants)

β Usually inhibitory (except in heart, where they are excitatory)

β_1 mainly in heart

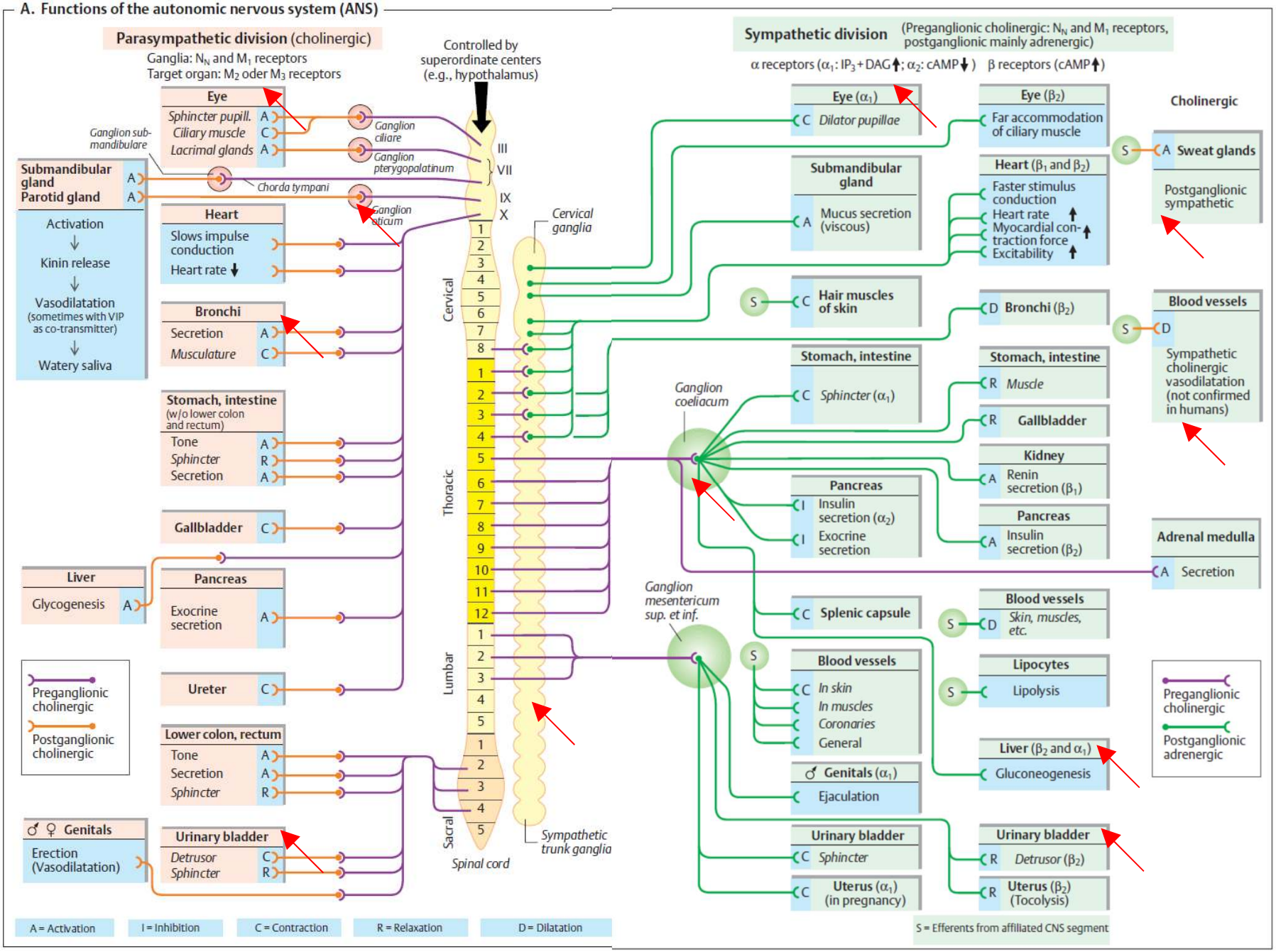
β_2 in bronchi, urinary bladder, uterus, gastrointestinal tract, etc.



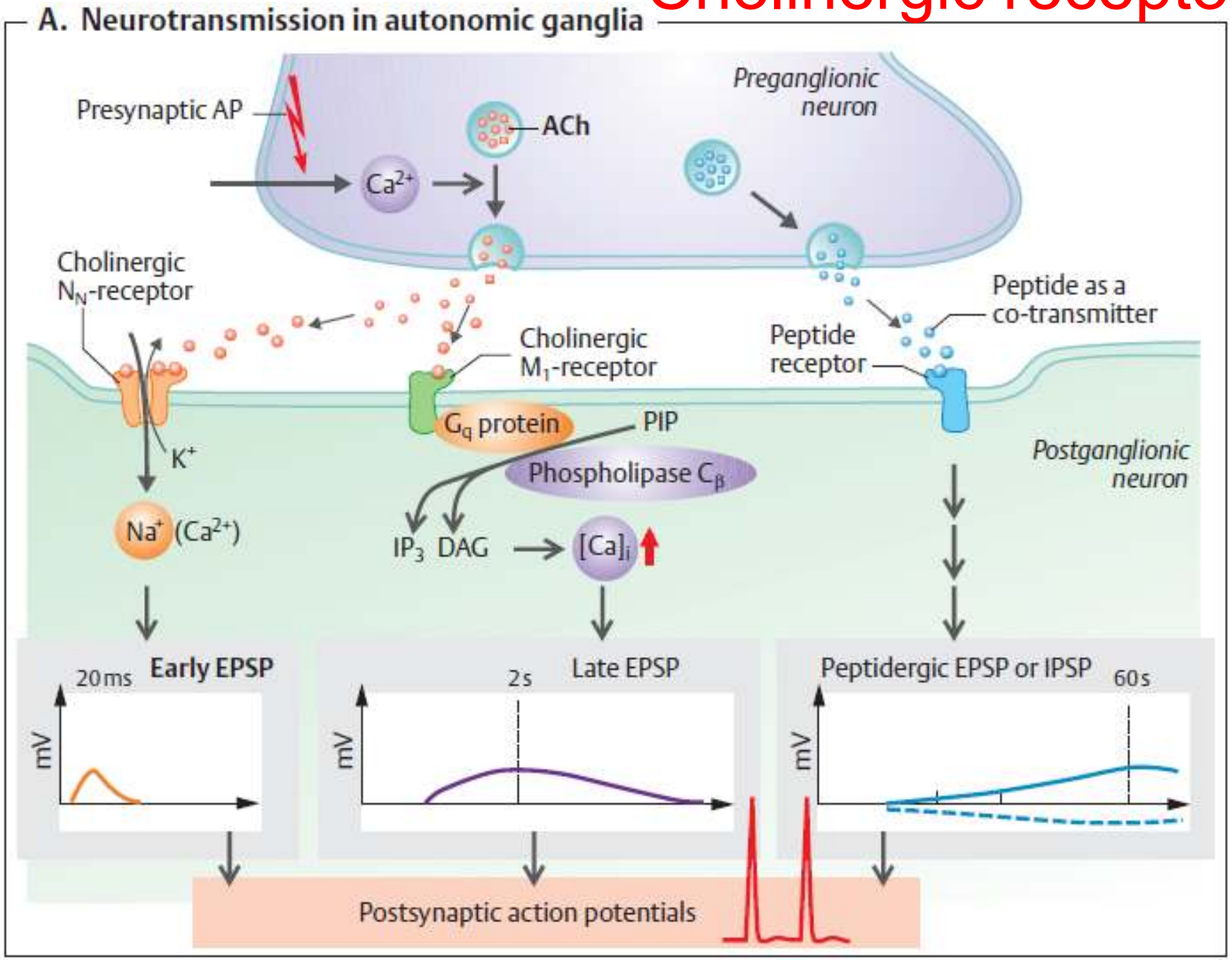
CZ

Oko a vegetativní systém

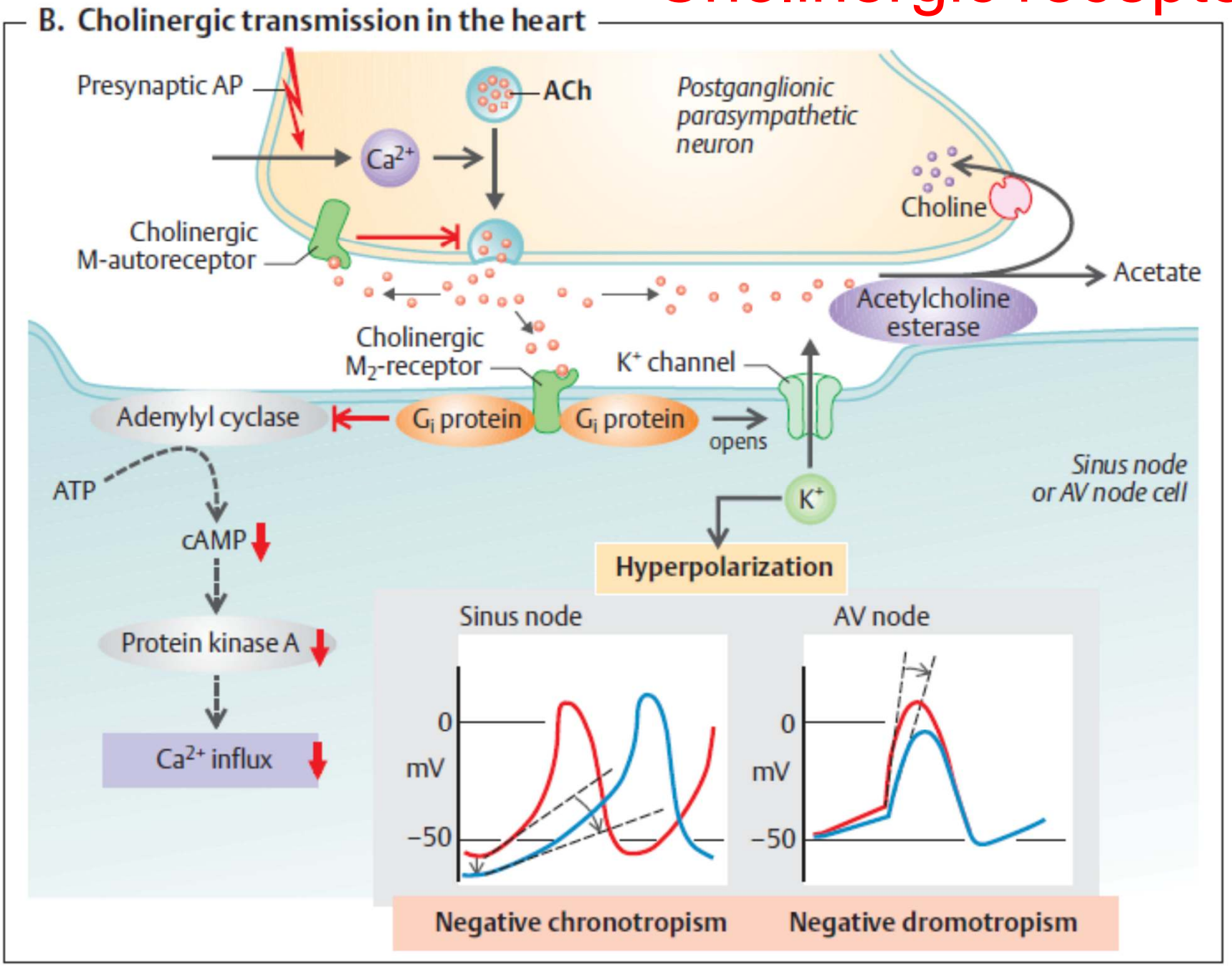
uvnitř jsou jen hladké svaly,
mióza – paras., cholinergní,
mydriáza – symp., alfa1 adren;
akomodace, m. ciliaris,
do dálky – symp. beta2,
na blízko – paras.;
slzné žlázy - paras.;


A. Functions of the autonomic nervous system (ANS)
Parasympathetic division (cholinergic)
Ganglia: N_N and M_1 receptors
Target organ: M_2 oder M_3 receptors
Controlled by superordinate centers (e.g., hypothalamus)
Eye
Sphincter pupill. A
Ciliary muscle C
Lacrimal glands A
Ganglion sub-mandibulare
Ganglion ciliare
Ganglion pterygopalatinum
Ganglion oticum
Chorda tympani
Submandibular gland A
Parotid gland A
Activation
Kinin release
Vasodilatation (sometimes with VIP as co-transmitter)
Watery saliva
Heart
Slows impulse conduction
Heart rate
Bronchi
Secretion A
Musculature C
Stomach, intestine (w/o lower colon and rectum)
Tone A
Sphincter R
Secretion A
Gallbladder C
Liver
Glycogenesis A
Pancreas
Exocrine secretion A
Ureter C
Lower colon, rectum
Tone A
Secretion A
Sphincter R
Genitals
Erection (Vasodilatation)
Urinary bladder
Detrusor C
Sphincter R
Preganglionic cholinergic
Postganglionic cholinergic
III
VII
IX
X
Cervical
Thoracic
Lumbar
Sacral
Cervical ganglia
Sympathetic trunk ganglia
Spinal cord
Sympathetic division (Preganglionic cholinergic: N_N and M_1 receptors, postganglionic mainly adrenergic)
α receptors (α1: IP3 + DAG ↑; α2: cAMP ↓) β receptors (cAMP ↑)
Eye (α1)
C Dilator pupillae
Submandibular gland
A Mucus secretion (viscous)
S C Hair muscles of skin
Stomach, intestine
C Sphincter (α1)
Ganglion coeliacum
Pancreas
I Insulin secretion (α2)
I Exocrine secretion
Ganglion mesentericum sup. et inf.
C Splenic capsule
Blood vessels
S C In skin
In muscles
Coronaries
General
Genitals (α1)
Ejaculation
Urinary bladder
C Sphincter
Uterus (α1) (in pregnancy)
Eye (β2)
Far accommodation of ciliary muscle
Heart (β1 and β2)
Faster stimulus conduction
Heart rate
Myocardial contraction force
Excitability
D Bronchi (β2)
Stomach, intestine
R Muscle
R Gallbladder
Kidney
A Renin secretion (β1)
Pancreas
A Insulin secretion (β2)
Blood vessels
S D Skin, muscles, etc.
Lipocytes
S Lipolysis
Liver (β2 and α1)
Gluconeogenesis
Urinary bladder
R Detrusor (β2)
Uterus (β2) (Tocolysis)
Cholinergic
S A Sweat glands
Postganglionic sympathetic
Blood vessels
S D Sympathetic cholinergic vasodilatation (not confirmed in humans)
Adrenal medulla
A Secretion
Preganglionic cholinergic
Postganglionic adrenergic
A = Activation
I = Inhibition
C = Contraction
R = Relaxation
D = Dilatation
S = Efferents from affiliated CNS segment

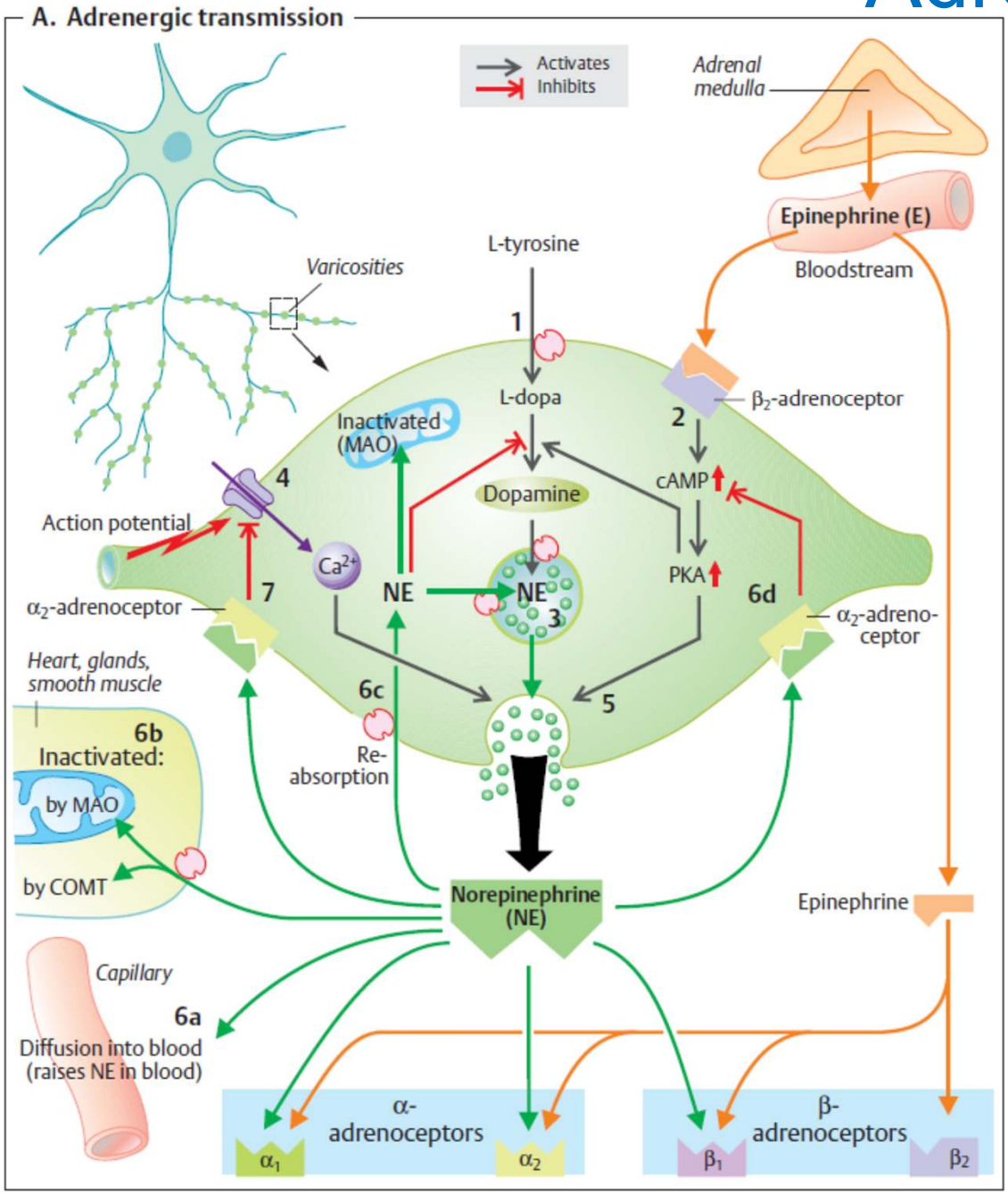
Cholinergic receptors

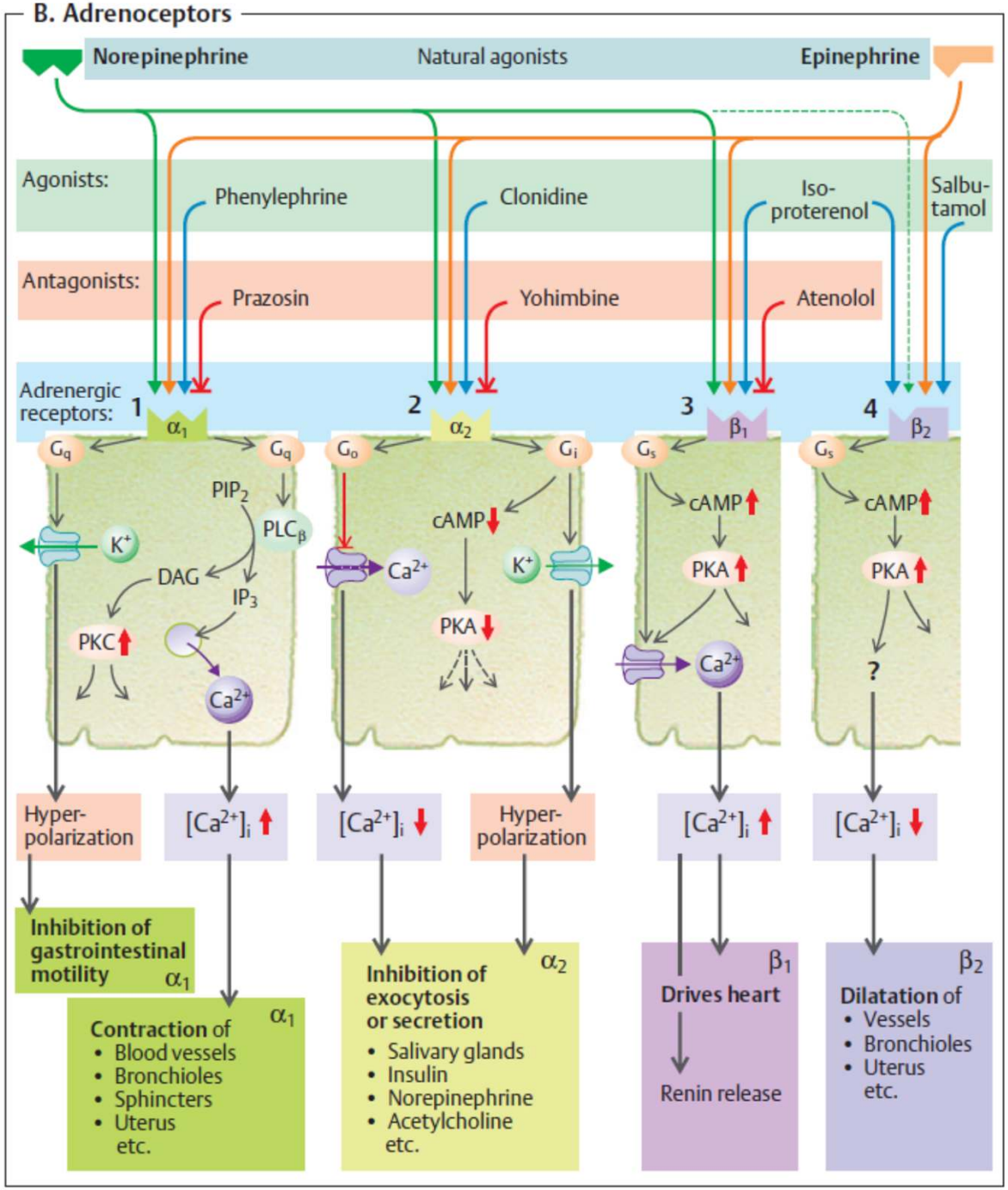


Cholinergic receptors

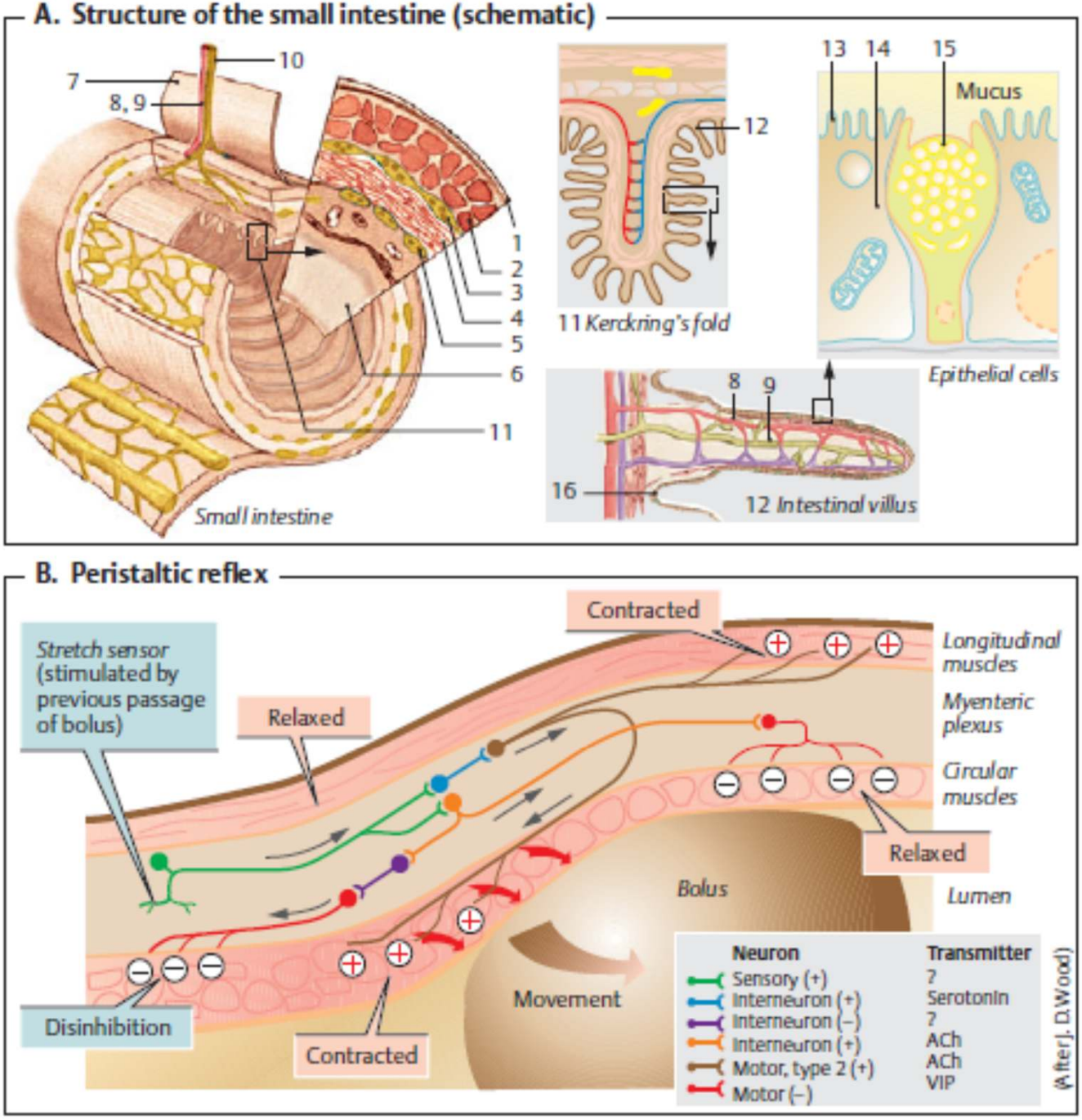


Adrenergic receptors





Adrenergic receptors

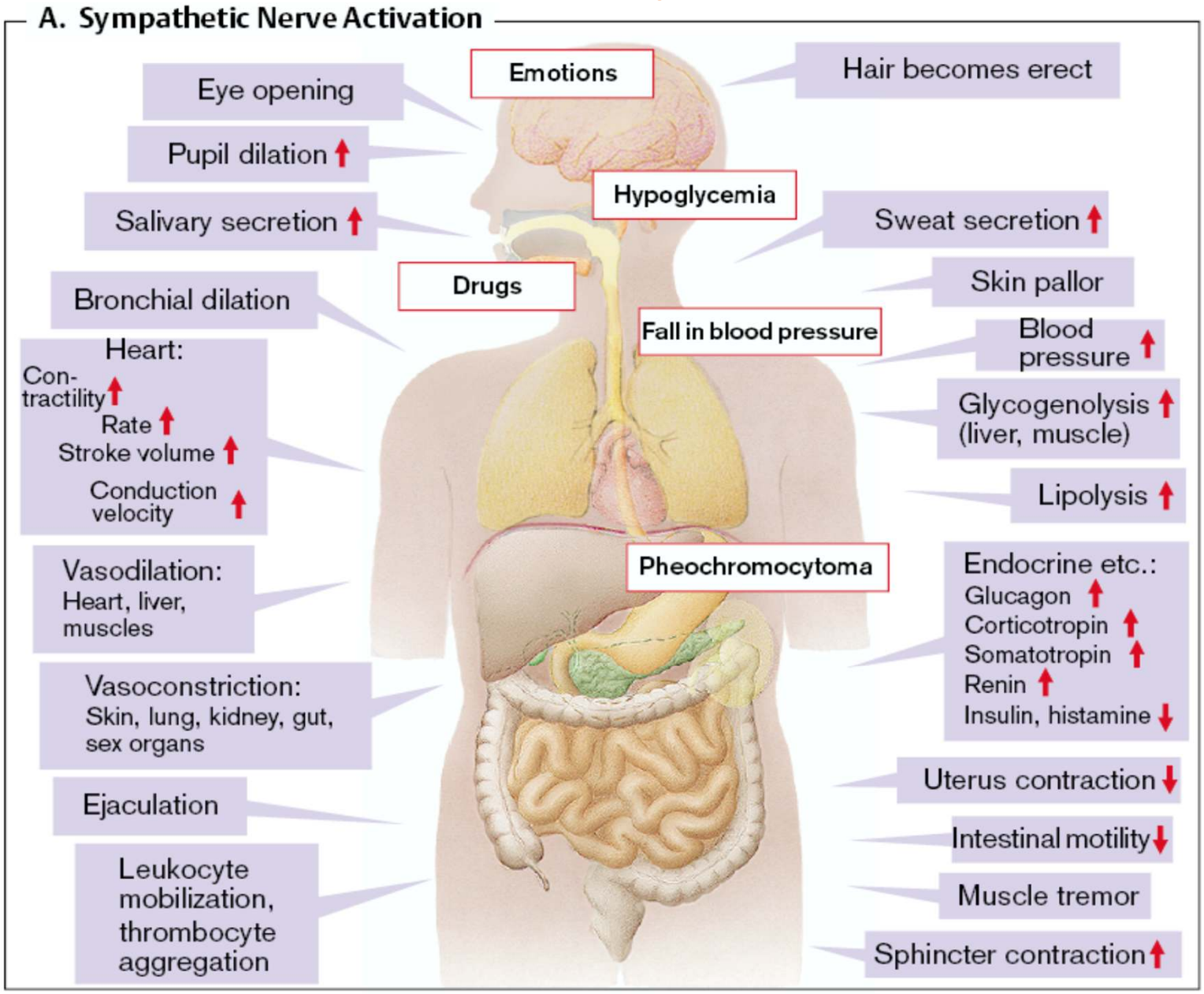


Další N.S.: Enterický nervový systém, myenterický a submukósní plexus, atd, atd

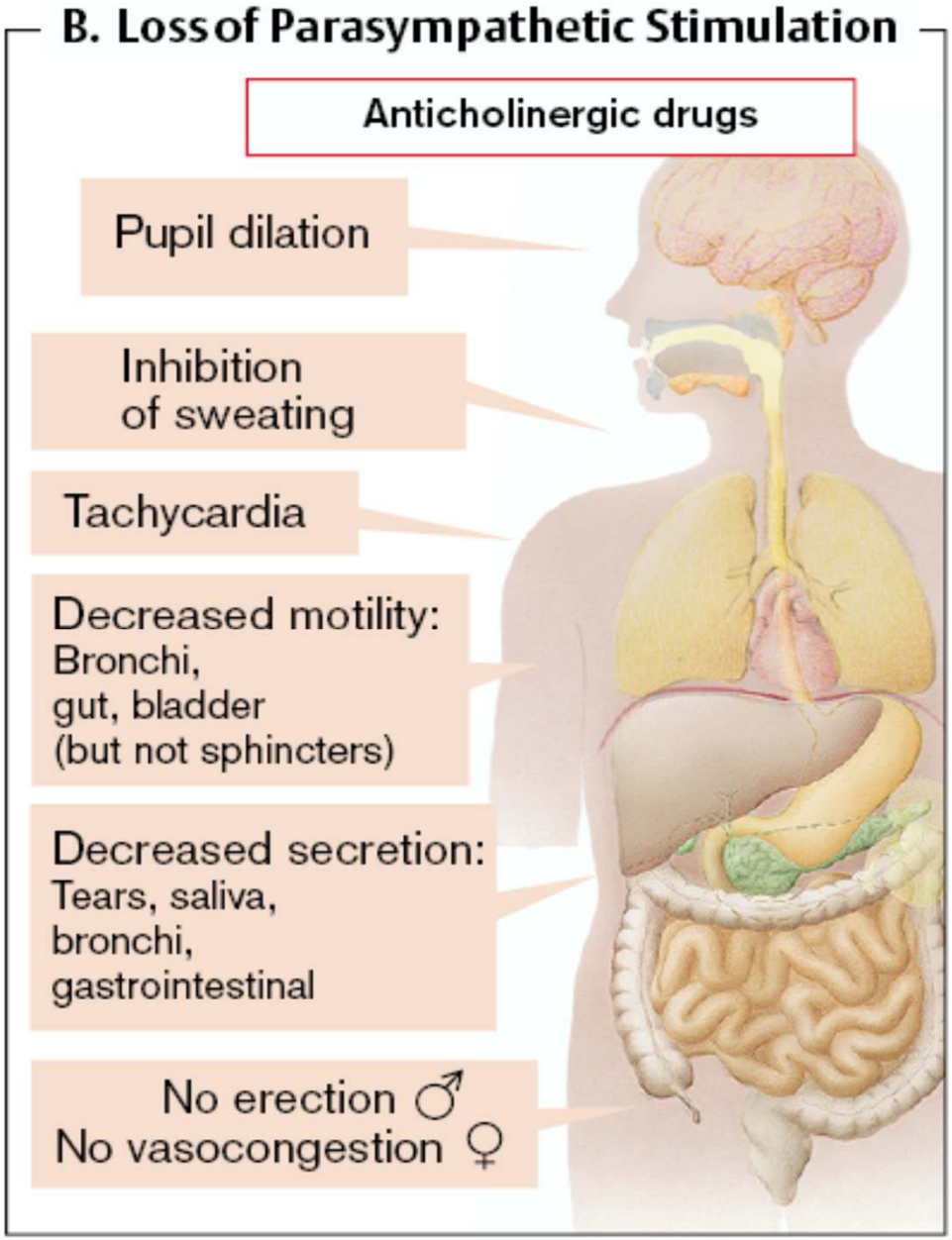
CZ

Je modulován hormony i vegetativním NS, ale peristaltika může probíhat i nezávisle na obou vlivech. Po laparotomii, či jiném inzultu nastává většinou přechodná paralýza, potom se opět restartuje.

Autonomous nervous system disorders



Influenced by various drugs

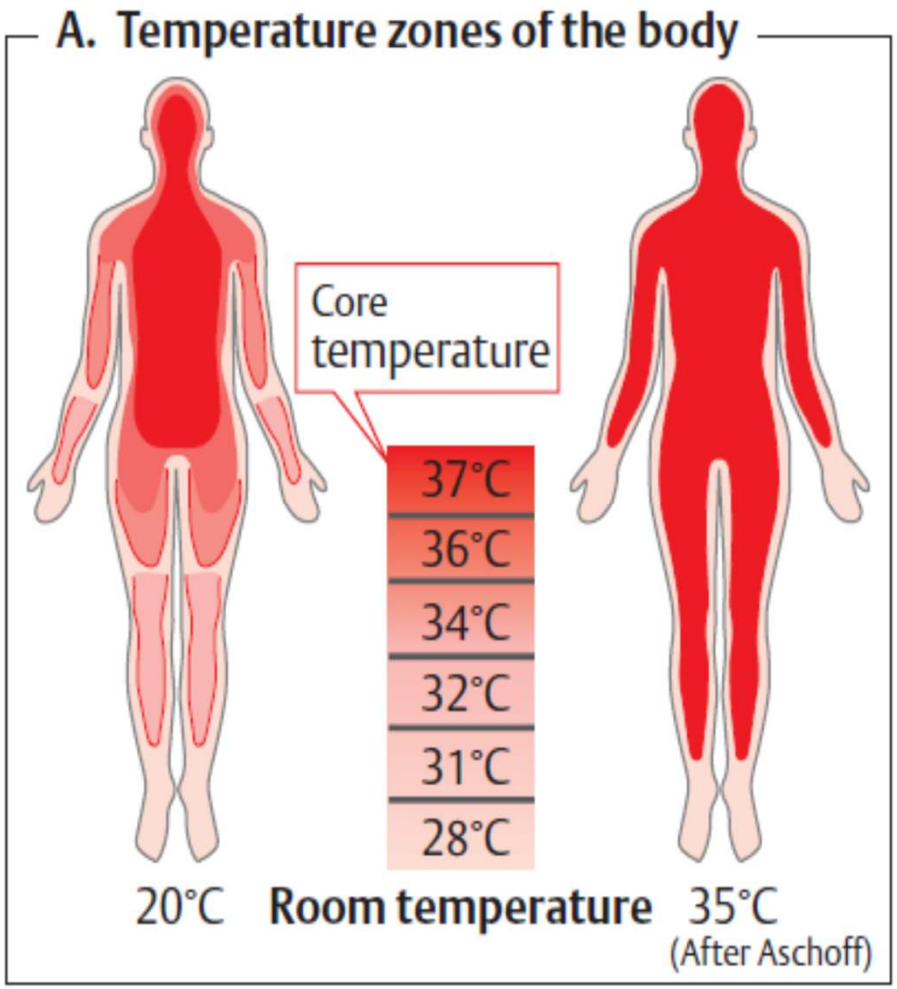


Influenced by various drugs

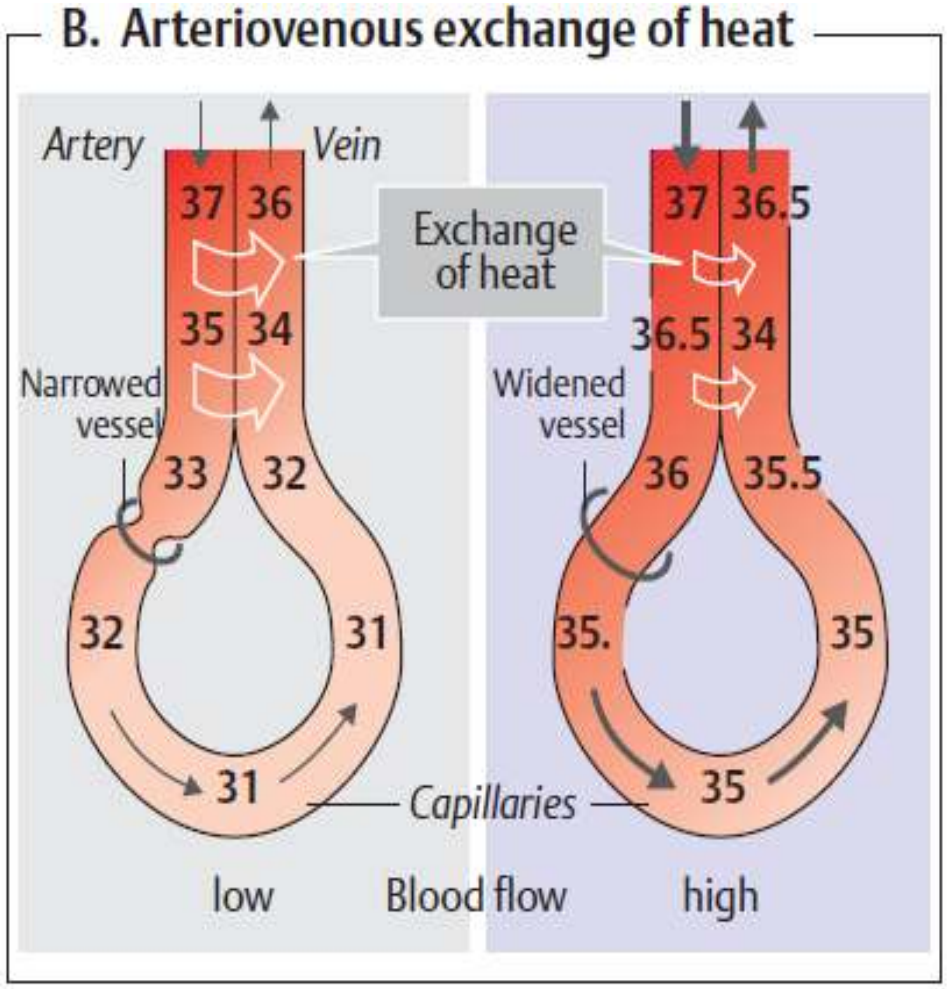
Temperature control, fever, hypothermia

- homeostasis
- processes to save heat
- processes to eliminate heat

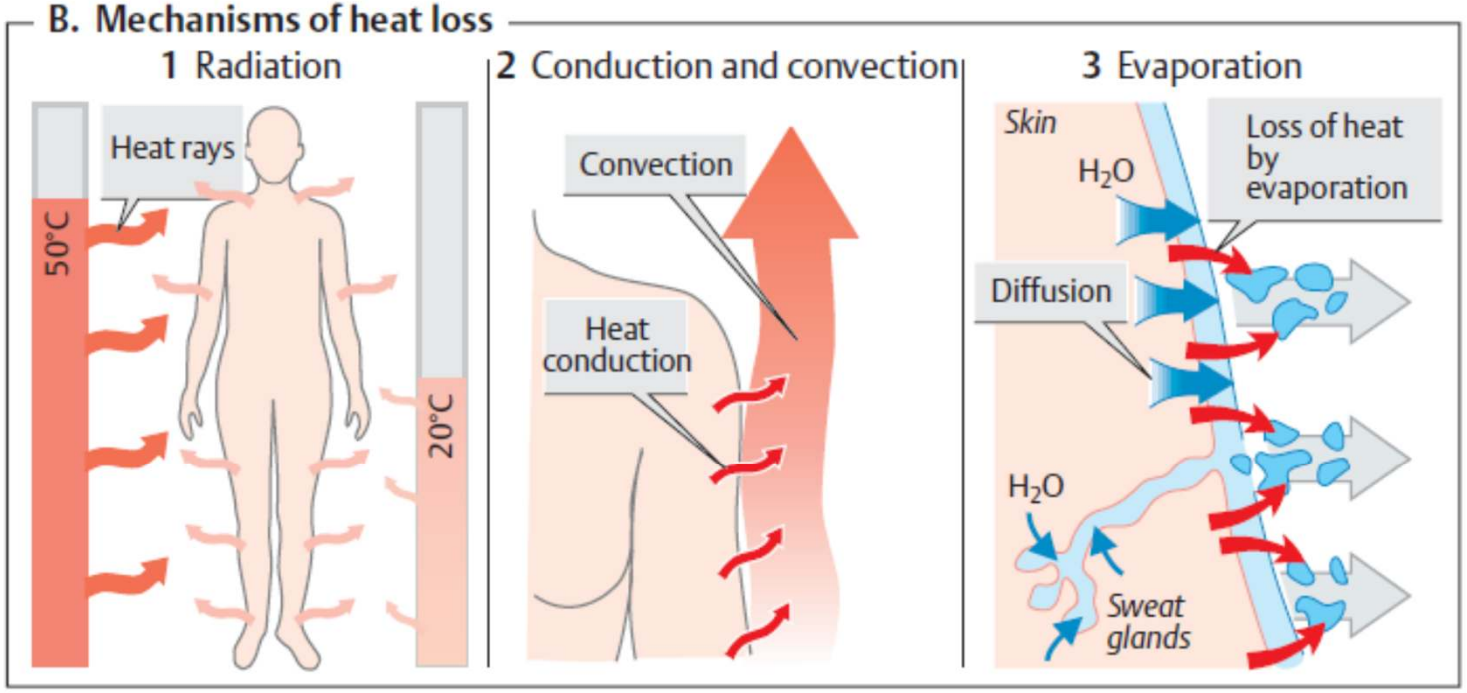
1 radiation, 2 conduction, 3 convection, 4 evaporation



core and shell



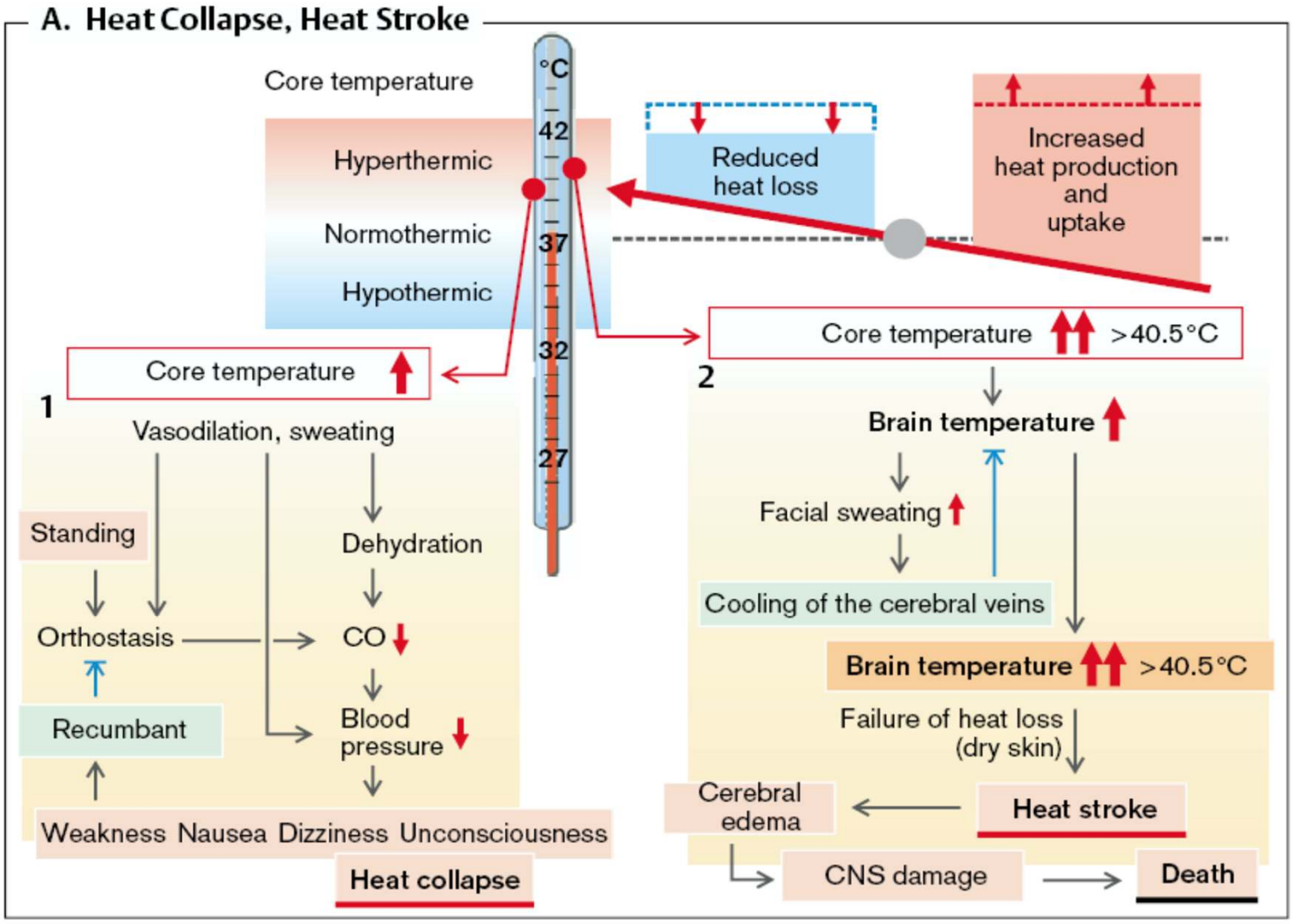
countercurrent systém



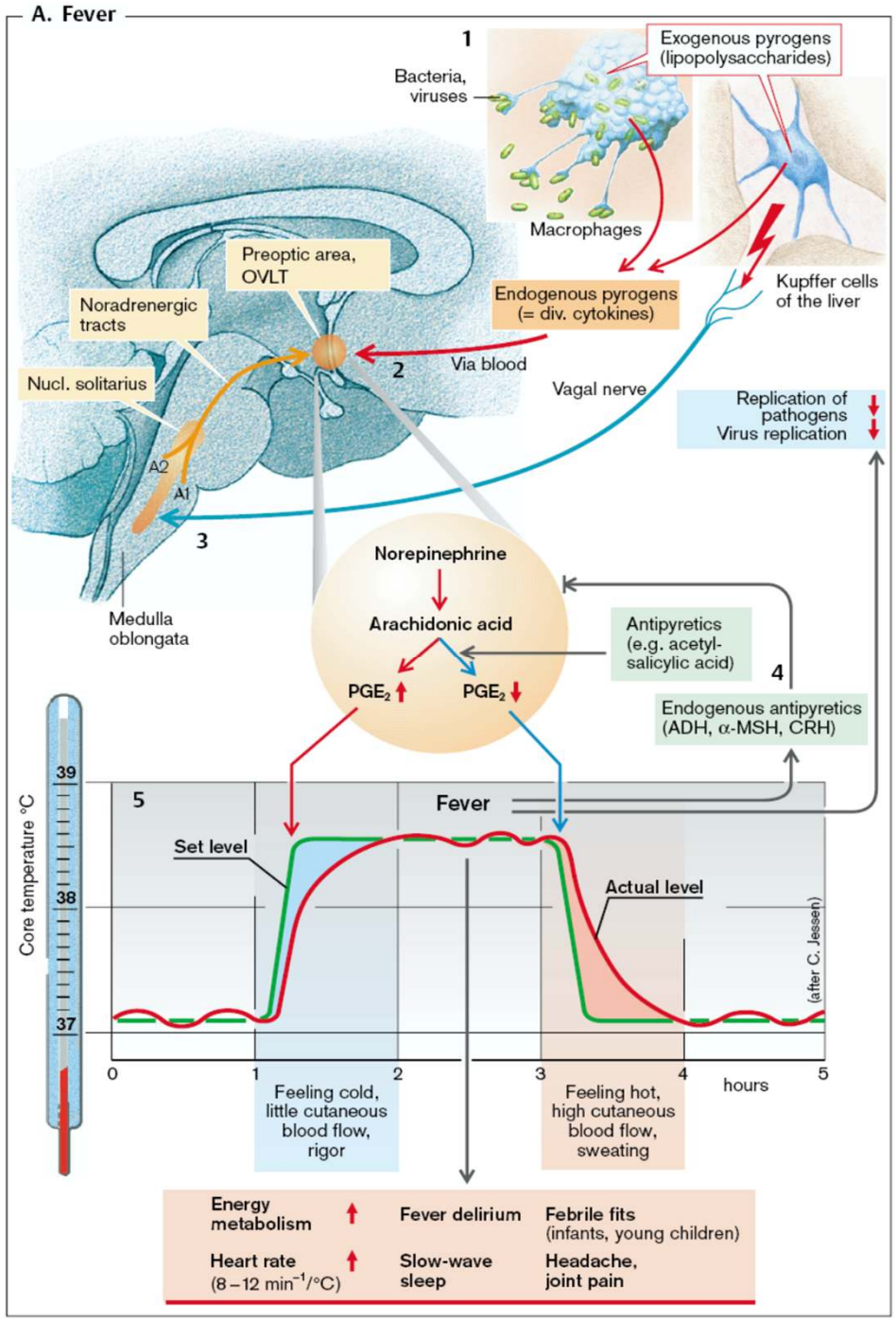
Heat transfer:

1
(radiation)
2
(conduction)
3
(convection)
4
(evaporation)

Přehřátí, úpal/ úžeh…



Vicious circles



Fever, temperature control

homo-io-termic organisms

Fever

Old defence reaction, well conserved in evolution

Correlation with better prognosis and duration of acute infection

Defense reaction → adverse environment for microbes, for their metabolism and proliferation.

Fever

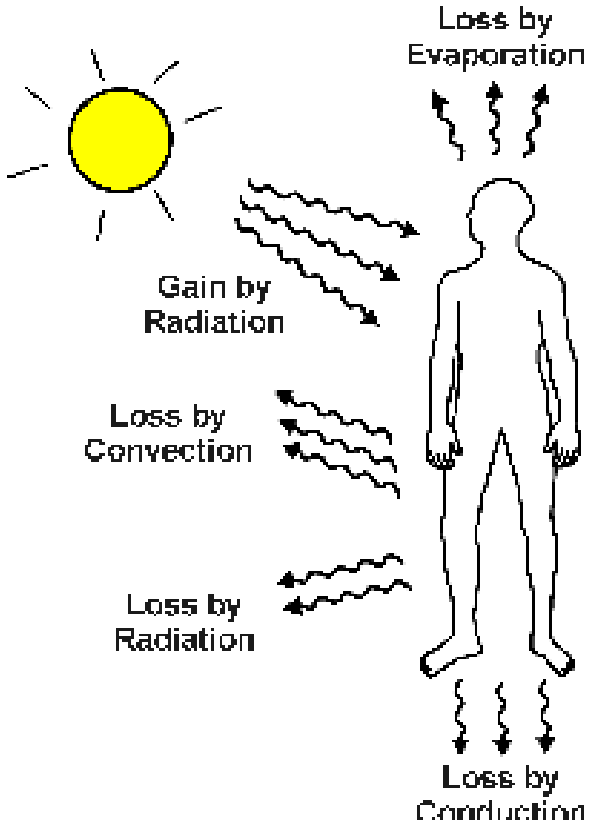
Regulation of temperature

heat production

(intensity of metabolism – catecholamines, $T_{3,4}$)

x

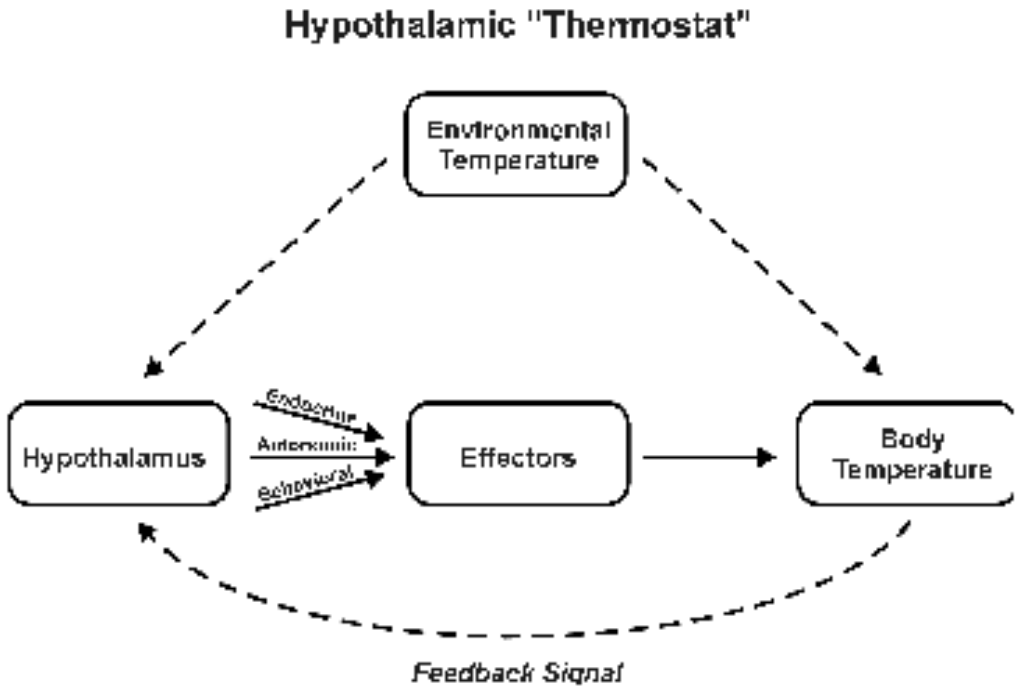
heat output



Fever

Hypothalamic thermoregulatory center

- „thermostat“



Fever

TNF, IL-1, IL-6 + microbial toxins + PG

↓

stimulation / reset of hypothalamic center

•direct effect of mediators in hypothalamus

•indirect / afferent stimulation via n. vagus from periphery to hypothalamus

↓

• peripheral vasoconstriction (cold skin, hypoperfusion)

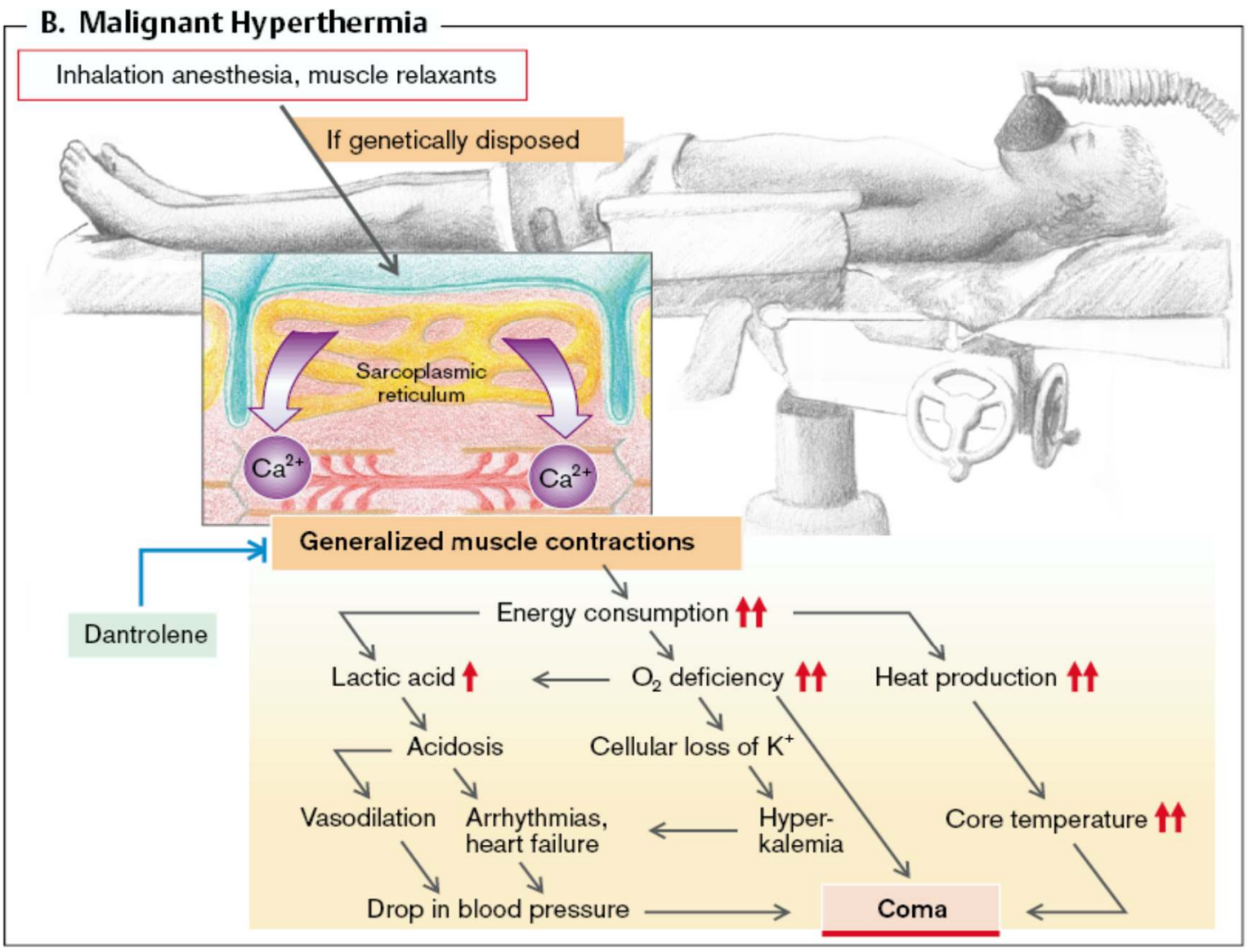
• heat production (thermogenesis)

↓

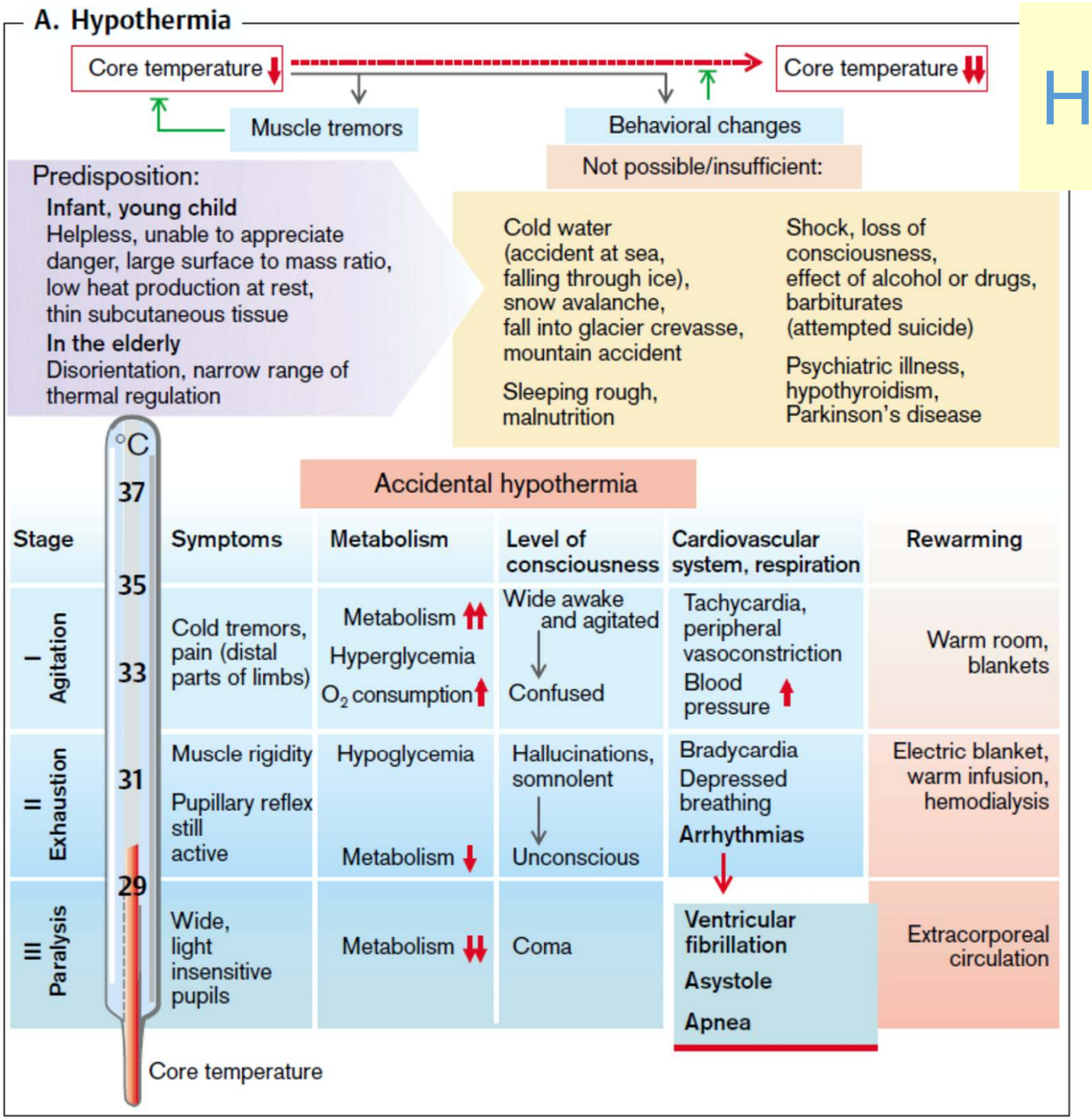
Restoration of initial status

•vasodilatation

•perspiration


B. Malignant Hyperthermia
Inhalation anesthesia, muscle relaxants
If genetically disposed
Sarcoplasmic reticulum
Ca2+
Ca2+
Generalized muscle contractions
Dantrolene
Energy consumption
Lactic acid
O2 deficiency
Heat production
Acidosis
Cellular loss of K+
Vasodilation
Arrhythmias, heart failure
Hyper-kalemia
Core temperature
Drop in blood pressure
Coma

Hypothermia



Inflammation

Inflammation

= The complex system of defense reactions of vascularized tissues against pathogenic stimulus (insult) of different character

The aim of inflammation is:

- **elimination of a cause,**
- **removal of an irreversibly damaged tissue,**
- **consecutive tissue regeneration or reparation, restoration of impaired both metabolism and function of organs, the return to dynamic balance status**

Including other defense actions: coagulation, regeneration, vs. (connective) tissue reparation, wound healing, neuro-humoral responses

Acid base balance

Fyziologické regulace se uplatňují u patologických stavů, hranice mezi fyziologickým a patologickým je neostrá

CZ

- Patologické procesy a mechanismy se podílejí v patogenezi více onemocnění
- Fyziologické mechanismy zúčastňující se tzv. patogeneze: obranné a adaptivní mechanismy, zánět, horečka, hyper-termie, hypo-termie, šok, stres, edém,

poruchy regulačních mechanismů (!, co to je?...),

poruchy metabolismu, poškození genetické informace, atd. ….

Další témata obecné patofyziologie: CZ

- aktivní transport, klidový (Nernstův) potenciál na membráně, akční potenciál, **membránové jevy** obecně
- nutrice
- růst a vývoj
- stres a jeho mechanismy

Acute phase proteins

Stimulatory effects of proinflamm. cytokines + corticoids (+ insulin) on hepatic proteosynthesis

An increase of expression of a group of important defense proteins + concurrent depression of both structural and transport protein synthesis

Acute phase proteins = plasma proteins formed in liver; its synthesis is regulated both by proinflamm. cytokines and corticoids

Due to dynamics of changes:

- positive APP (elevation of synthesis)

- negative APP (depression of synthesis).

Acute phase proteins

Importance

1. **mediators and modulators of inflamm. response - members of cytokine cascade (CRP, …)**
2. **inhibitors of leukocyte proteases – limitation of a range of proteolytic tissue destruction (a_1-antitrypsin, a_2-macroglobulin)**
3. **scavengers – binding of both circulating or tissue fragments of damaged cells, hemoglobin fragments (haptoglobin, hemopexin) or free oxygen radicals (ceruloplasmin)**
4. **some coagulation factors (e.g. fibrinogen)**
5. **reparatory proteins – a stimulation of connective tissue proliferation (a_1-acid glycoprotein) and angiogenesis (ceruloplasmin)**
6. **transport proteins - (x CpI); a moiety of other transport proteins (albumin, transferrin) represent negative APP ... their plasma concentration decline during inflammation.**

Disturbances of the growth

• genetic factors

action of the endocrine system

function of the CNS

nutrition

• genotype determines scheme of the growth, development, habit, prenatal period (development of CNS and endocrine glands)

outstanding influence of thyroid hormones, GH, insulin

T3, T4 - necessary for release of GH, for development of teeth germs, development of habit, ossification of the cartilages

• growth after birth continues two steps of accelerated growth:

till 3rd month

puberty control and stop by influence of the sex hormones

Insufficient growth 1

• influence of heredity

chondrodystrophy – disturbance of growth of long bones, skull base, vertebrae,

low production of the GH, thyroid hormones etc.

disturbance of the hypothalamus –

disturbed production GnRHs Fröhlich´s syndrome,

pubertas praecox

• neural influence, hypothalamic region

Fröhlich´s syndrome

pubertas praecox

diabetes insipidus

disturbed control of body temperature

Insufficient growth 2

• influence of the endocrine systeme

acquired diseases are manifestated at hypophysis disturbance before puberty:

separate low production of GH

low production of further hormones

(e.g. hypothyroidism, insuphiciency of the adrenal cortex, gonads etc)

• influence of the nutrition

lack of full-value proteins retarded growth, decreased synthesis of proteohormones

Excessive growth

• influence of heredity

primordial gigantism

• endocrine system

a) insufficient production of sex hormones

primary hypogonadism (late closing of growth cartilages)

b) overproduction of the GH

before closing – gigantism

after acromegaly

Causes of the ageing

- **influence of heredity**
- **defective protein synthesis** – accumulation of the defects, accumulation of the mutations
- **mutations in the immune system** – lasting accumulation of the mutations of immune-competent cells (lymphocytes, macrophages) higher frequency of the autoimmune disturbances in old age

role of the cytokines in development of diseases – IL-1, IL-6, TNF, EGF, IGF-1, fFGF, PDGF

decreased amount of heat-shock proteins (HSPs prevent protein from aggregation, from increase of the Ca2+ in ICF; they lower the amount of the free radicals, prevent from DNA breaks and accelerate DNA repair

- **pre-programmed life-span in cell populations** – interference by:

a) accumulation of free radicals

b) accumulation of the substances in ECF (Ca, lipofuscin, cholesterol)

c) cross-linkage of the macromolecules in ICS including DNA, RNA

Hypothermia in surgery

decline of *core* temperature lowering of metabolism and oxygen uptake in tissues

controlled hypothermia is used prevalently in cardiosurgery and neurosurgery

programmed cooling of blood in extracorporal circulation

temperatures 32^{o}C - 27^{o}C are commonly used

in long-term surgery – body temperature can be lowered less then 25^{o}C

after surgery – programmed relatively rapid blood rewarming

Bazální metabolismus

CZ

Bazální metabolismus = klidový metabolický obrat

hrubý odhad: asi 100 kJ na 1 kg za 1 den

- Mechanická energie: činnost srdce, plic, střevní peristaltika,…
- Transportní a osmotická práce: udržení rovnováhy na membránách
- Chemická energie: biosyntézy
- Tepelná energie: udržení tělesné teploty

The END

Thanks for your attention

Warning: neither the PDF, nor the PPT, PPTX, etc. versions of this presentation are official study materials. For internal use only. Do not distribute.

Contact: Petr.Marsalek@LF1.CUNI.CZ

First Medical Faculty, Institute of Pathological Physiology