ANP 1105A
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3. Homeostasis: ANS & Endocrine System

These slides contain material to be presented in lecture*. The information should be used in *combination* with the relevant chapters of the recommended Text book(s). Throughout this presentation, there are references to figures in the text book. In addition, specific animations/videos are also referenced and should be used by the student for study purposes.

**Slides marked with a STAR will not be covered in the lecture but are provided as additional learning material*

Most disease seen as a ***disturbance*** of homeostasis = **homeostatic imbalance**

Aging associated with progressive decrease in our ability to maintain homeostasis

➢ **greater risk for illness**

What is Physiological ***homeostasis***

"ability of the body to maintain relatively stable internal conditions even though there is continuous change in the outside world" …..*Walter Cannon*

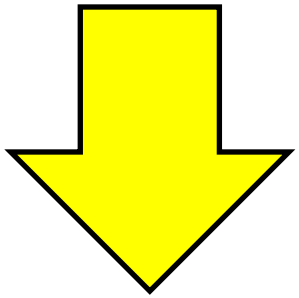
Does not mean the cellular environment is unchanging - rather **it is in a dynamic** state of equilibrium involving many systems:

(i) adequate blood levels of vital nutrients

(ii) heart activity/blood pressure monitored & adjusted as needed

(iii) wastes must not accumulate

(iv) body temperature has to be maintained



Control, Control, Control

Key Homeostatic Regulatory Systems:

- **Autonomic nervous system**
  - sympathetic & parasympathetic arms
  - sensory and motor neural pathways
  - ***fast*** response

- **Endocrine system**
  - hormones released into extracellular fluid and often travel to target organs via bloodstream
  - ***slower response*** time but response can be ***long-lived***
  - different chemical classes of hormones with associated mechanisms of action

Homeostatic Control Mechanism

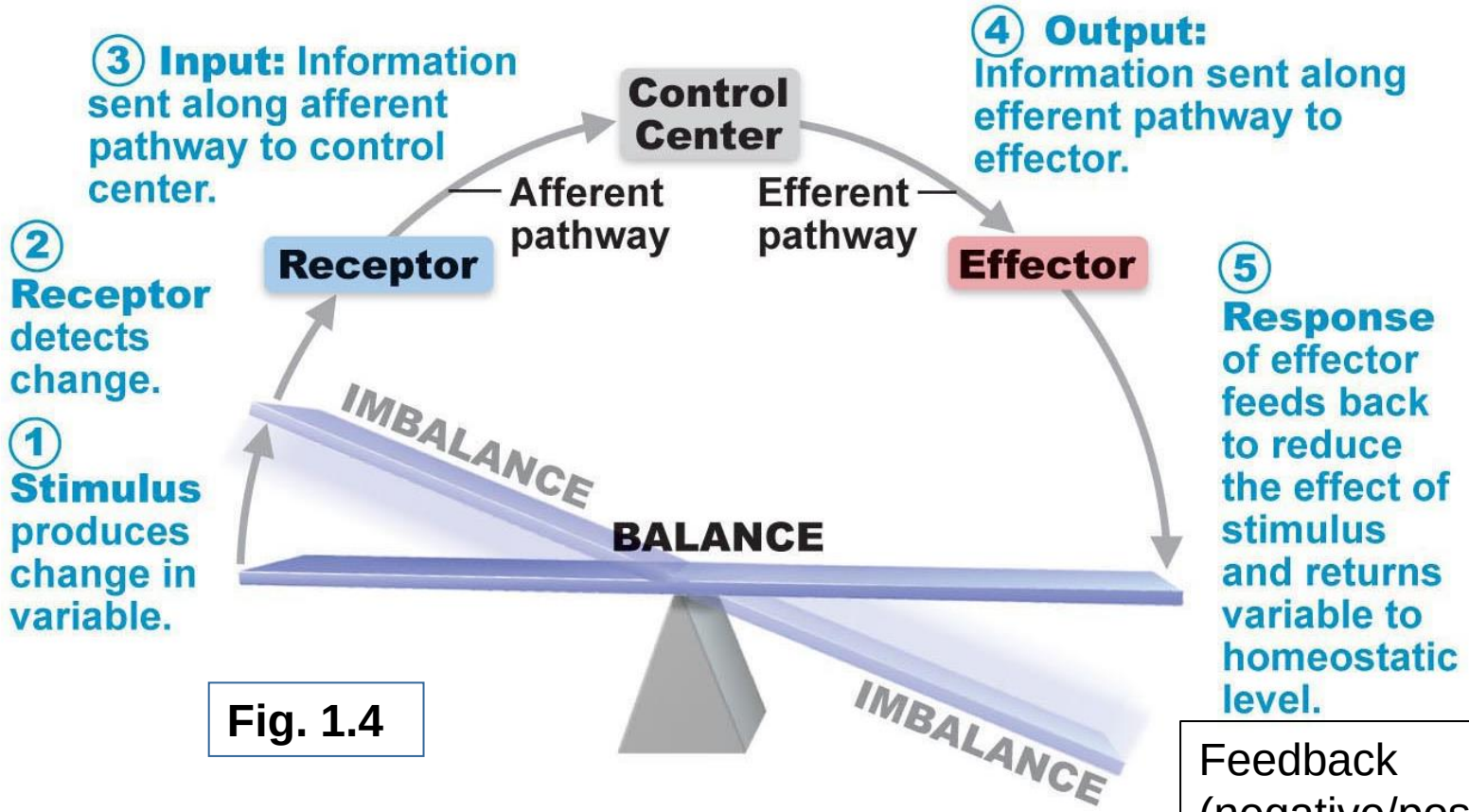


Fig. 1.4

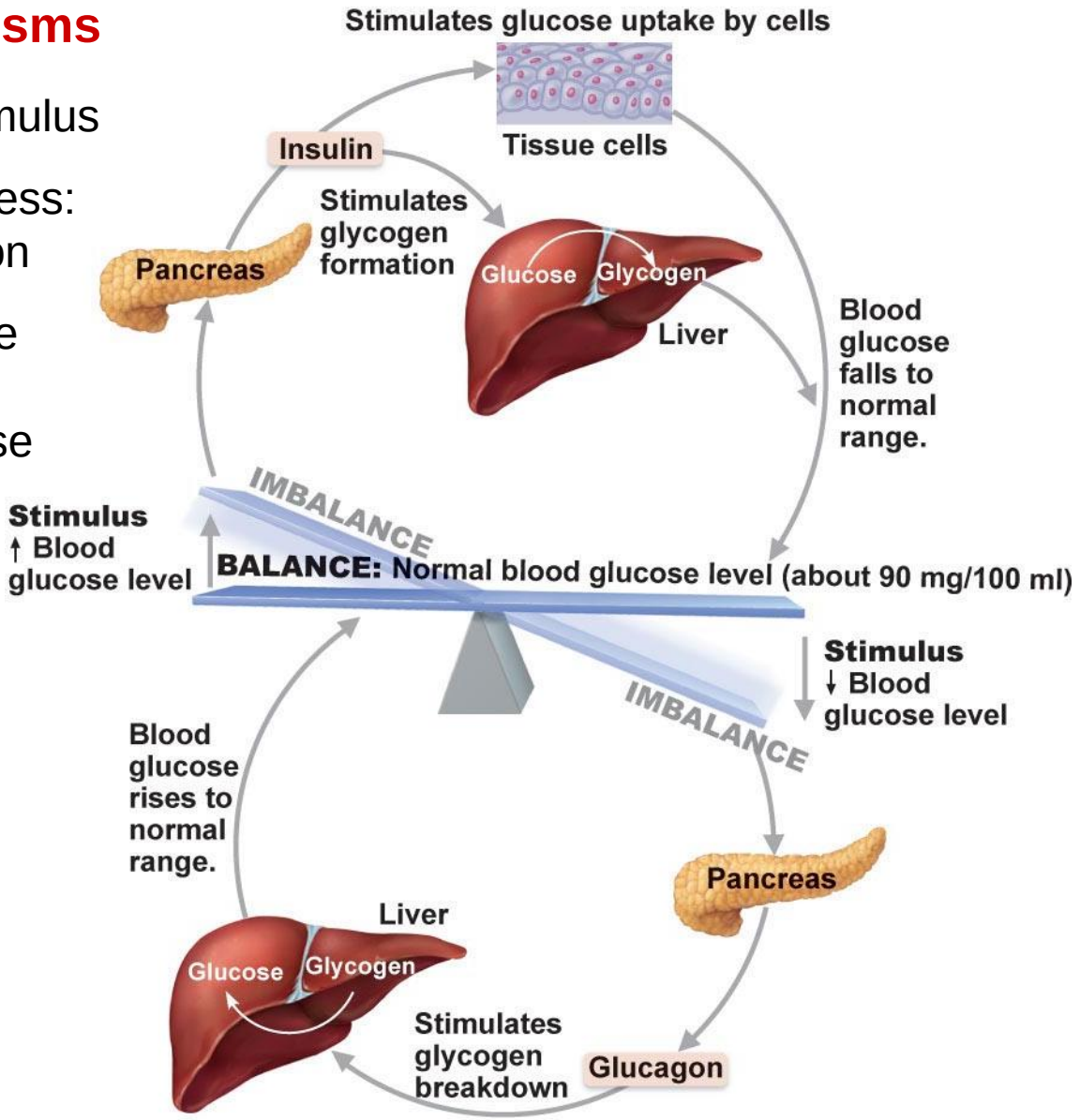
Feedback (negative/positive)

Negative Feedback Mechanisms

- output **reduces** or shuts off stimulus

(i) 1 hormone regulating a process: negative feedback ↓ secretion

(ii) process regulated in opposite directions by 2 different hormones – eg: blood glucose



Goal of negative feedback:
prevent sudden, severe changes

J. Carnegie, UofO

Fig. 16.19

Positive Feedback

- response of mechanism **enhances** original stimulus
  - ➢ output is **further stimulated**
- change occurs in **same direction** as original response
- **goal** to be attained
- eg: blood clotting - *how is this still, overall, maintaining homeostasis??*

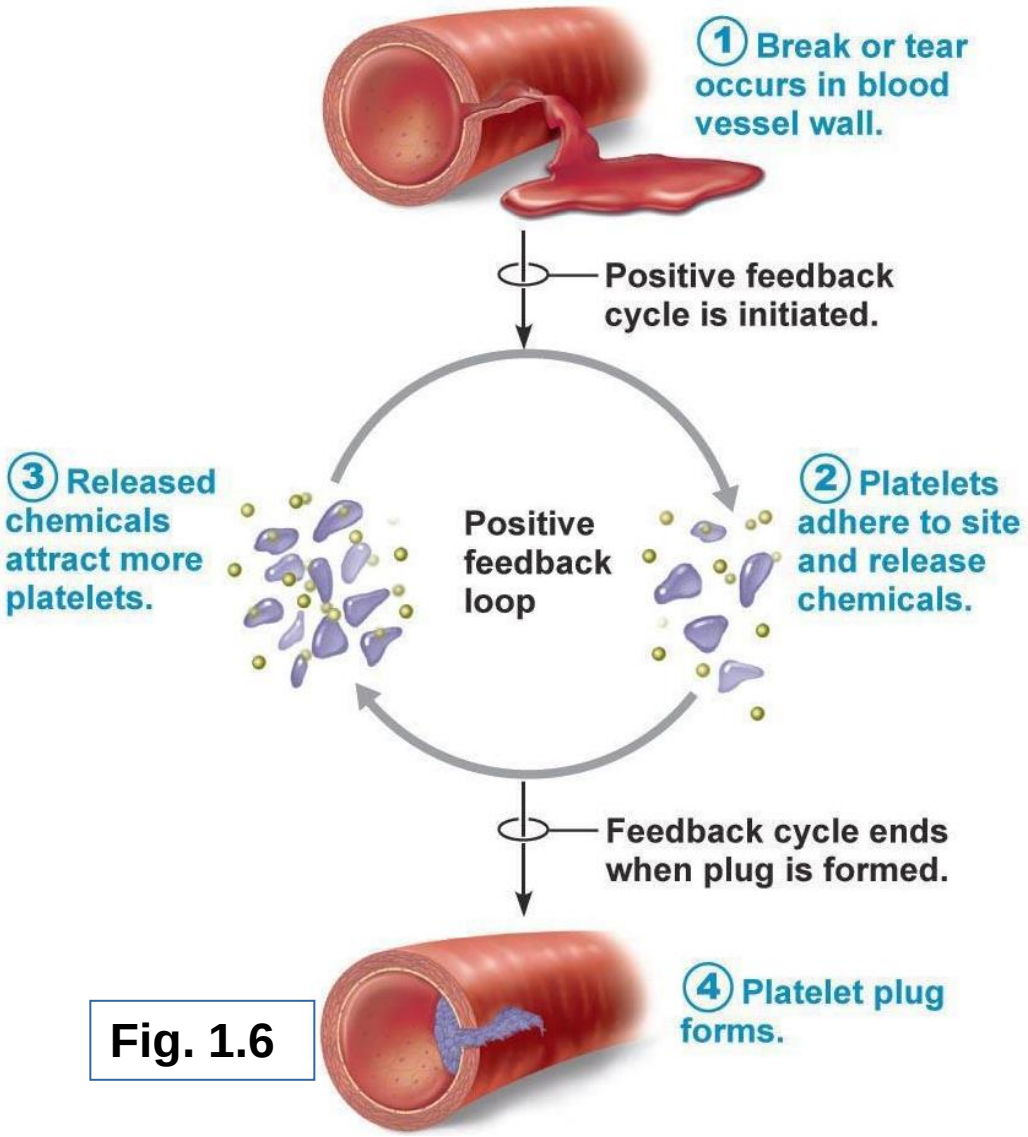


Fig. 1.6

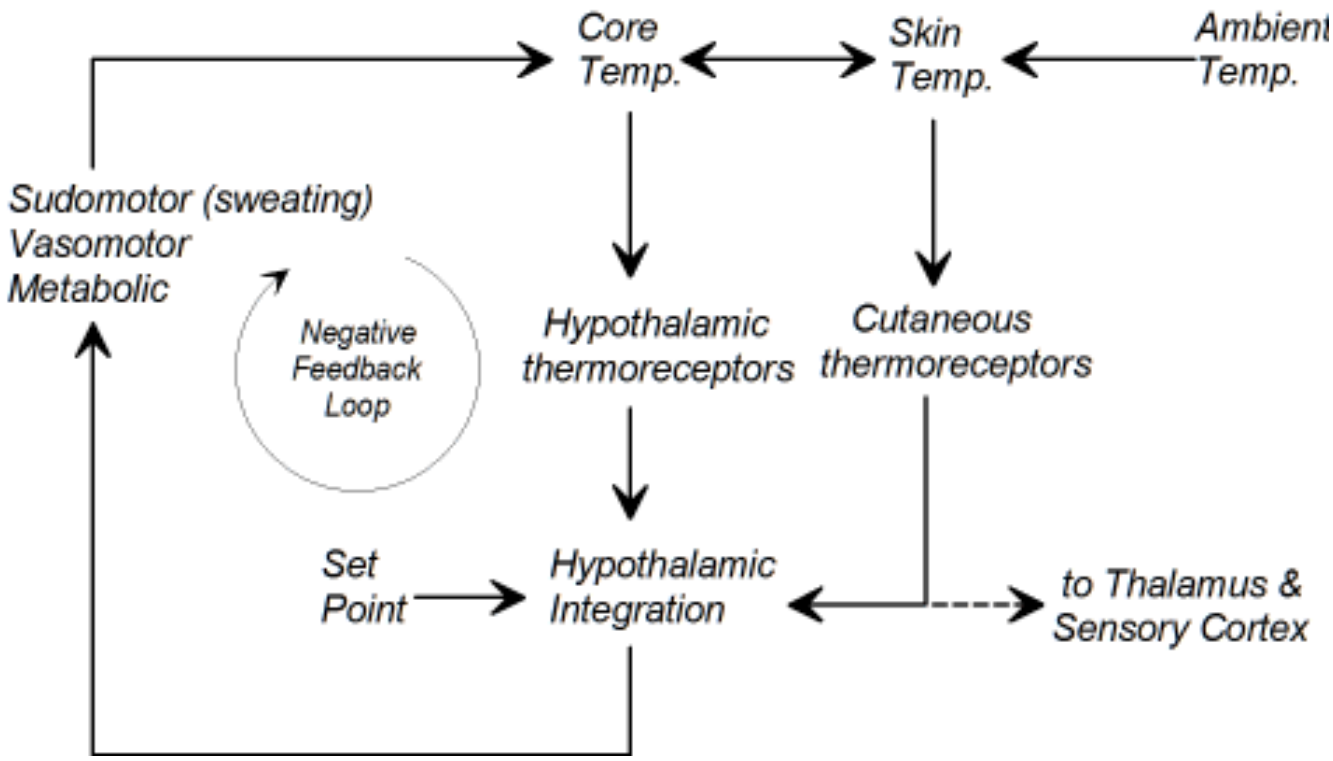
Neurons of the hypothalamus (Thermostat Center) are sensitive to changes in skin and blood T^0

The temperature-regulating centres are in the Preoptic Area (anterior hypothalamus). Receives input from peripheral T^0 receptors in the skin & mucous membranes and from Central Thermoreceptors

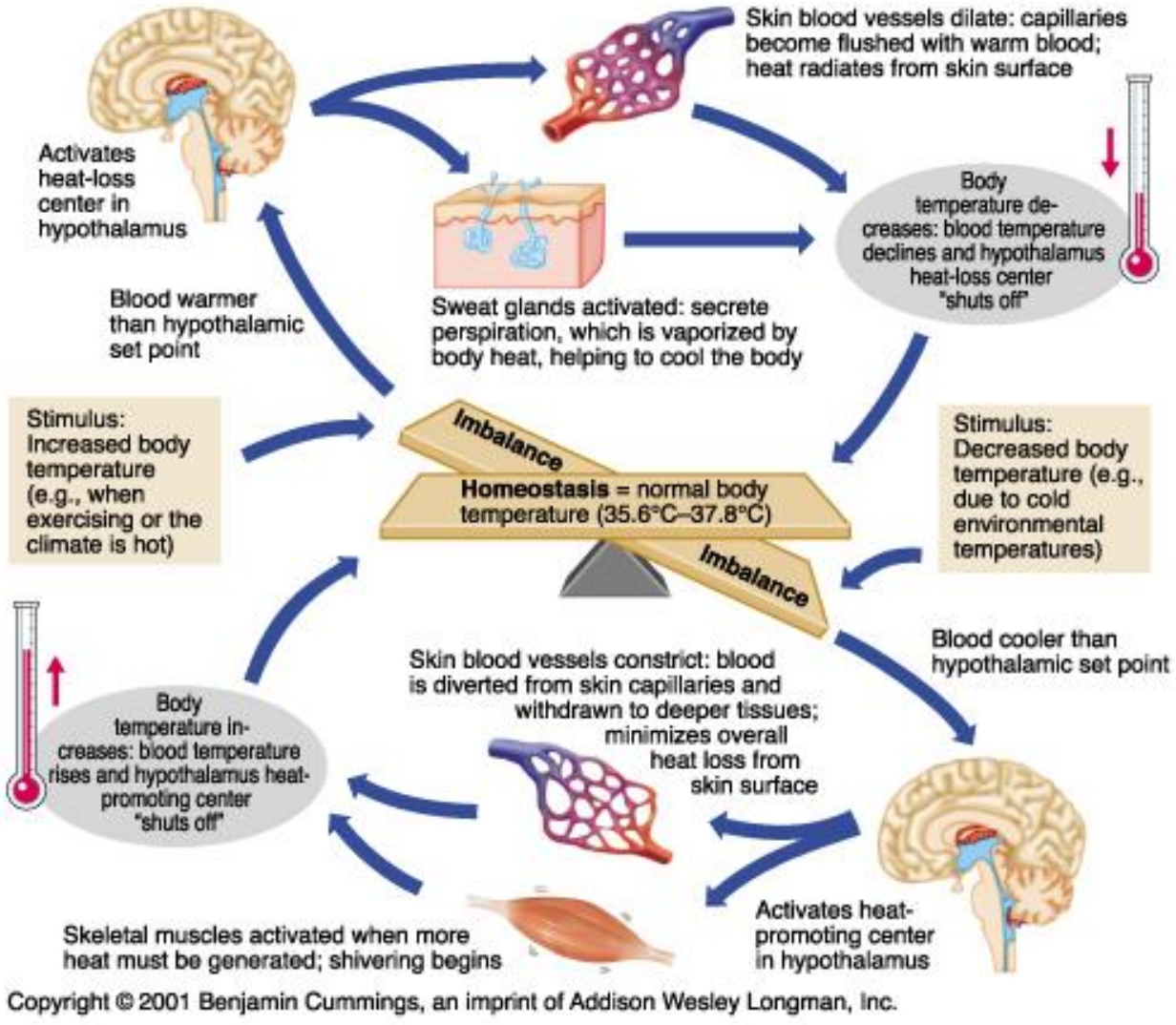
The temperature sensory signals are combined in the posterior hypothalamus to control the heat producing and conserving reactions of the body

The hypothalamic thermostat works in conjunction with other hypothalamic, autonomic and higher nervous thermoregulatory centers to keep the core temperature constant.

Some of these thermoregulatory responses are involuntary, mediated by the ANS, some are neurohormonal and others are semi-voluntary or voluntary behavioral responses



Integration center response is most sensitive to hypothalamic thermoreceptors and less sensitive to cutaneous thermoreceptor input; also cutaneous influence tends to be transcient (adapting)



http://schoolworkhelper.net/thermoregulation/

RESPONSES TO COLD:

Drop in your skin T^0 stimulates skin cold receptors (increase s their activity) and cools the blood flowing into the skin.
These signals are received by both the hypothalamic thermostat and higher cortical centers.

The thermostat is also activated by the change in blood T^0. It initiates responses that promote heat gain and inhibits centers that promote heat loss.

Involves activation of Sympathetic Centres causing

1) Constriction of skin vessels
2) Brown fat (*in infants*) oxidation increases causing thermogenesis
3) Piloerection, which traps air close to skin
4) Epinephrine secretion from adrenal medulla increases thermogenesis
5) A Shivering Center in the hypothalamus is also activated which activates the Brainstem Motor Centers

RESPONSES TO HEAT

When body T^0 rises, skin warmth receptors and blood convey these changes to the hypothalamic thermostat

The thermostat inhibits the sympathetic nerves controlling vasoconstriction and metabolic rate, thus causing cutaneous vasodilation and reducing BMR

Results in increased heat loss via skin and a decrease in core heat production

If heat is sufficiently intense, the sympathetic fibers (via cholinergic fibres), which innervate sweat glands release ACh, stimulating sweat

Sweating is the most effective involuntary heat fighting response in man
Behavioral responses to heat, such as lethargy, resting or lying down with limbs spread out, decreases heat production and increases heat loss.
What else do you do?

FEVER

To fight infection, the hypothalamus allows body temperature to climb higher than the normal value of about 38^0C.

Most common fevers are due to an increase in **temperature regulation set point**, due to agents called "pyrogens"

Pyrogenic Agents

bacterial endotoxin

bacterial debris

antigen-antibody complexes

neoplastic disease

mechanical tissue trauma

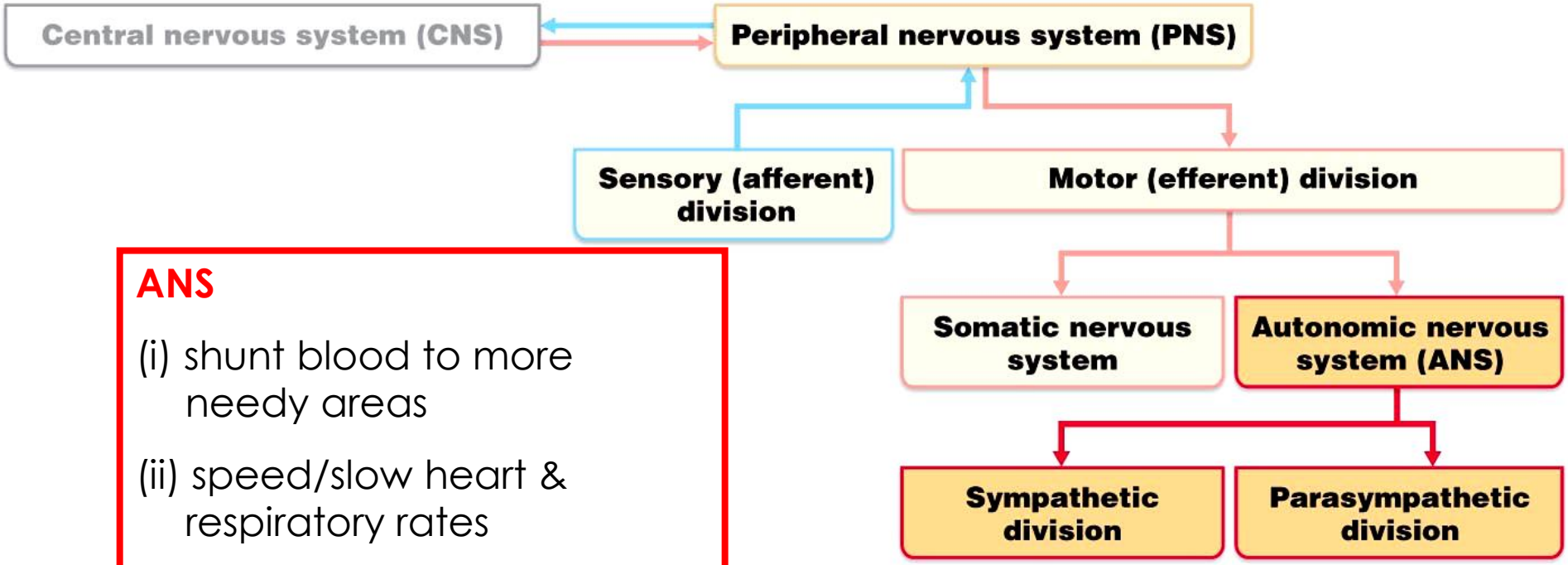
Body Temperature Changes

Body responds as if it were too cold as long as core temperature is below the new set point (vasoconstriction, shivering)

When the fever breaks, the body responds as if it were too warm (which is actually the case) to lower core temperature to the normal level (vasodilation, sweating)

Automatic neural control for homeostasis

- *auto* = self; *nom* = govern
- ANS = system of motor neurons to smooth & cardiac muscle & glands to allow responses usually *without* our awareness



ANS

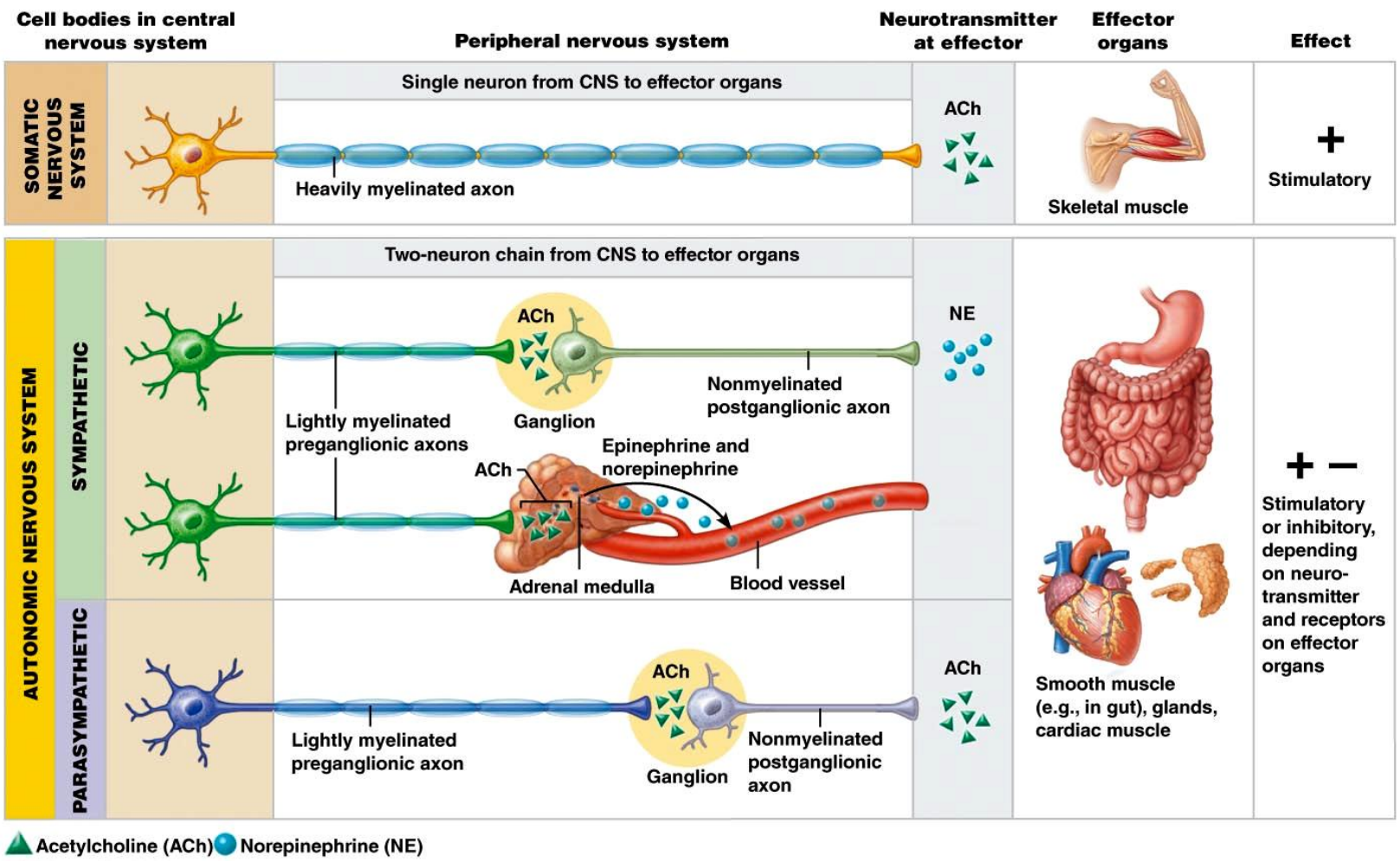
(i) shunt blood to more needy areas

(ii) speed/slow heart & respiratory rates

(iii) adjust blood pressure, body temp

(iv) increase/decrease gastric secretions

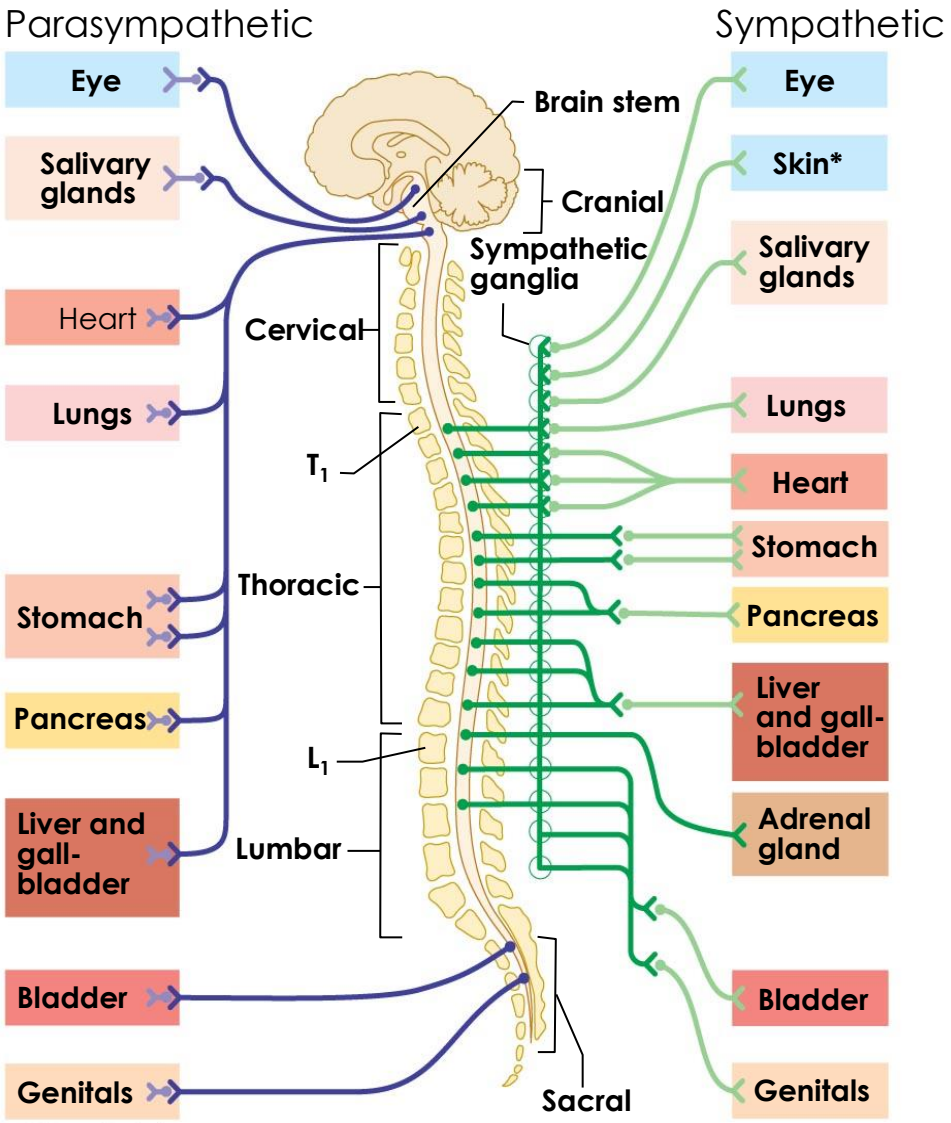
Fig. 14.1



Pathways

- ***Somatic:*** thick, myelinated axon to skeletal muscle; rapid conduction of impulses (no ganglia)
- ***ANS:*** two-neuron chain: **preganglionic neuron:** from brain or spinal cord synapses with 2nd motor neuron **(postganglionic)** in ganglion outside CNS ➢ **postganglionic axon** to effector organ
- conduction is slow; preganglionic axons are thin & lightly myelinated; postganglionic axons are thinner & unmyelinated

Figure 14.3 The subdivisions of the ANS



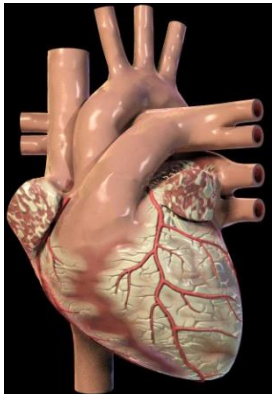
Also see
Figs 14.4 & 14.6

Parasympathetic Tone

- Parasympathetic division normally dominates heart, smooth muscle of digestive and urinary tract organs, activate most glands except for adrenal and sweat glands
  - Slows the heart
  - Dictates normal activity levels of digestive and urinary tracts
- The sympathetic division can override these effects during times of stress
- Drugs that block parasympathetic responses increase heart rate and cause fecal and urinary retention

Interactions of the Autonomic Divisions

most visceral organs receive dual innervation



Antagonistic Interactions:

- eg: activity of heart, GI system, respiratory system

	PNS	SNS
Heart	-	+
GI System	+	-
Resp. System	+ (minor -)	-

Cooperative Effects:

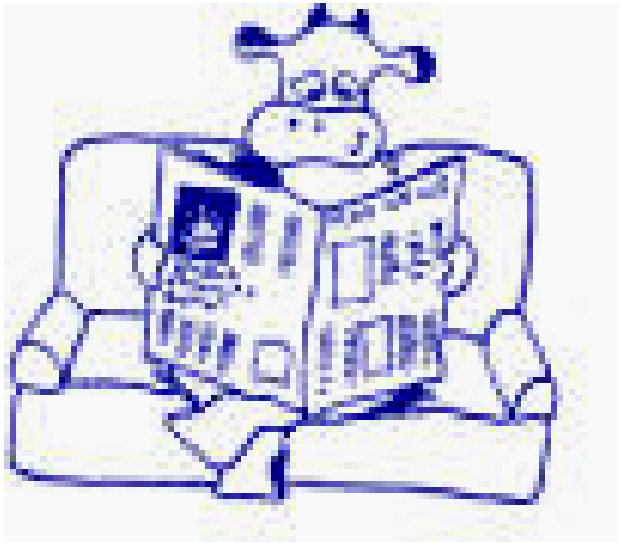
- eg: regulation of external genitalia during intercourse:
  - a) PNS: dilation of blood vessels in penis
  - b) SNS: ejaculation, reflex peristalsis of female's vagina

ANS Parasympathetic Division:

- active in non-stressful situations – *resting & digesting*
- low energy use while regulating « housekeeping » activities (digestion, elimination of feces & urine)

  what are the predominate effects of the parasympathetics when reading a newspaper after a meal??

- **"D" actions:** digestion, defecation, diuresis



ANS Sympathetic Division:

- **" fight or flight"** system; also important during exercise: increased heart rate, rapid, deep breathing, cold sweaty skin(***why?***), dilated eye pupils
- **"E" actions:** exercise, excitement, emergency, embarrassment, exams

Sympathetic Nervous Output:

Regulate adrenal medulla, sweat glands, arrector pili muscles of skin, kidneys, most blood vessels

also:

- thermoregulatory responses to heat
- renin release from kidneys - result will be increased blood pressure

metabolic effects:

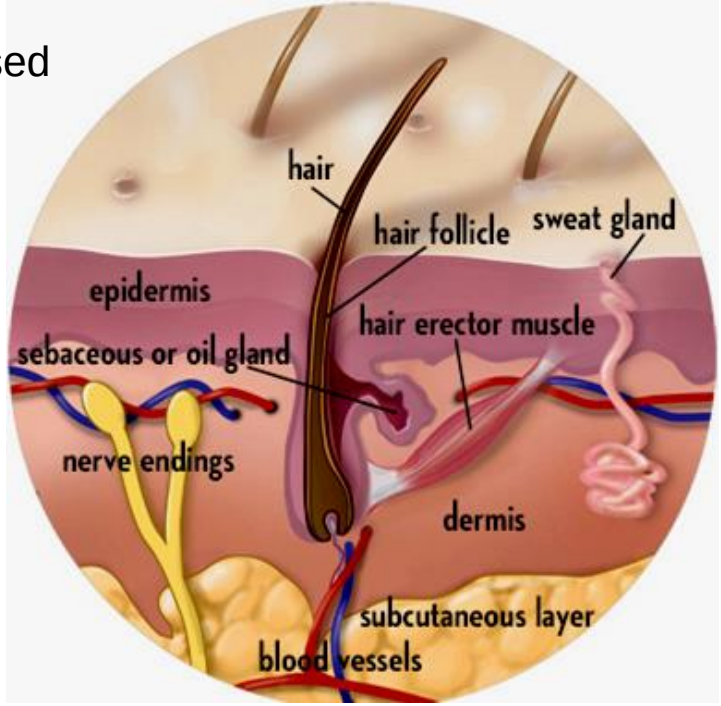
(i) increases metabolic rate of body cells

(ii) raises blood glucose levels

(iii) stimulates mobilization of fats

(iv) increases mental alertness

(v) increases speed/strength of muscle contraction



Levels Of Regulation Of Autonomic Function

1. Brain Stem & Spinal Cord Controls

- significant direct effects on ANS-regulated activities
- motor centres in ventro-lateral medulla (cardiocascular centre, blood vessels; also GI, respiratory centres)

2. Hypothalamic Controls:

- **hypothalamus = integration centre of ANS and for hormonal output**

> *anterior regions* ➢ parasympathetic

> *posterior* areas ➢ sympathetic

- hypothalamus contains centres to coordinate heart activity, blood pressure, body temp, water balance, endocrine activity; also centres that help mediate emotions & biological drives

3. Cortical Controls:

- e g: meditation & biofeedback allow some conscious control over visceral activities

> e g: during meditation, can lower heart & breathing rates, oxygen use, metabolic rate

> biofeedback to improve management of migraine headaches, stress & cardiac function

Homeostatic Imbalances of ANS

- e g: *hypertension:*

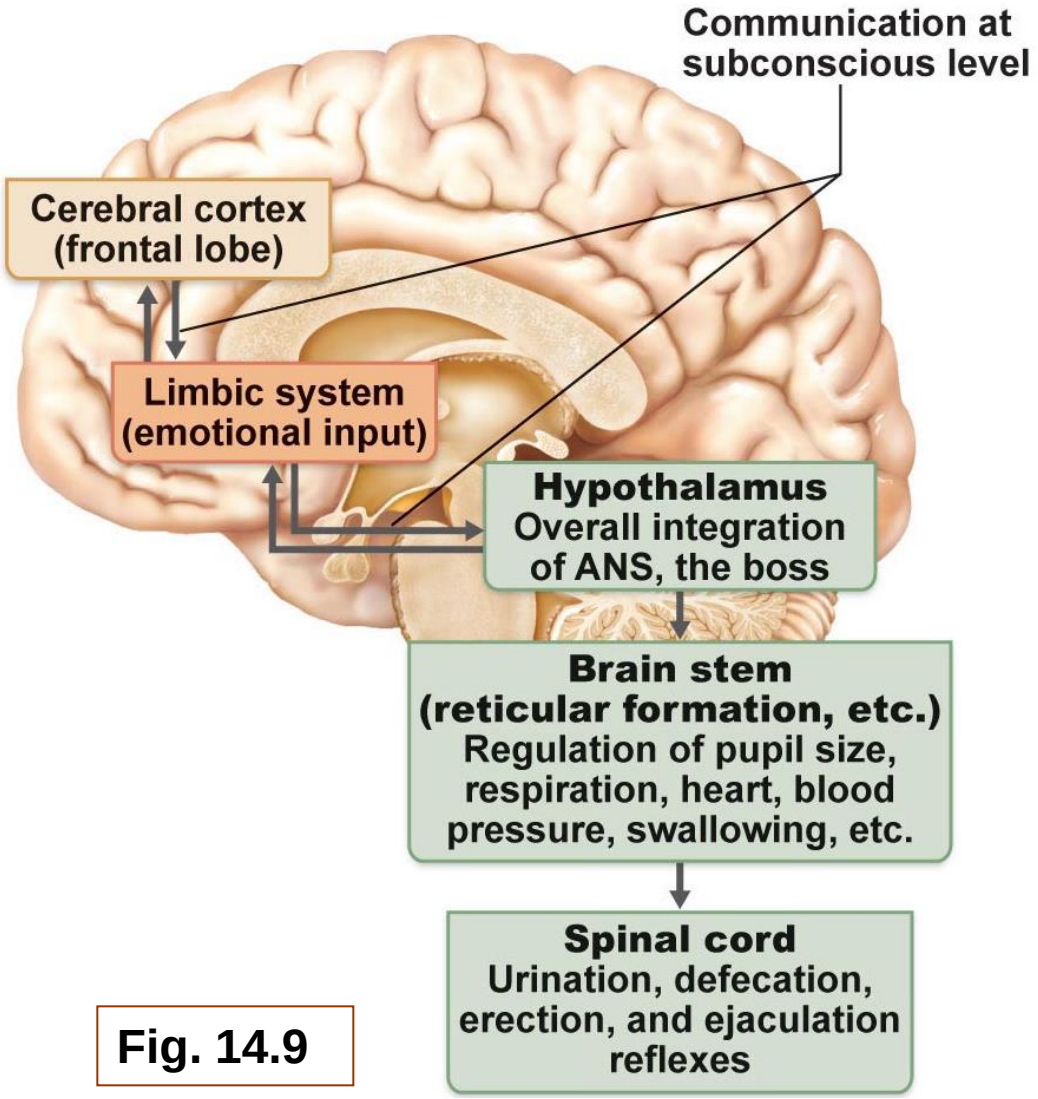


Fig. 14.9

Homeostatic Imbalances of the ANS

- Hypertension (high blood pressure)
  - Overactive sympathetic vasoconstrictor response to stress
  - Treated with adrenergic receptor - blocking drugs
- Raynaud's disease
  - Exaggerated vasoconstriction in fingers and toes
    - Pale, then cyanotic and painful
    - Treated with vasodilators

GUT-BRAIN AXIS !

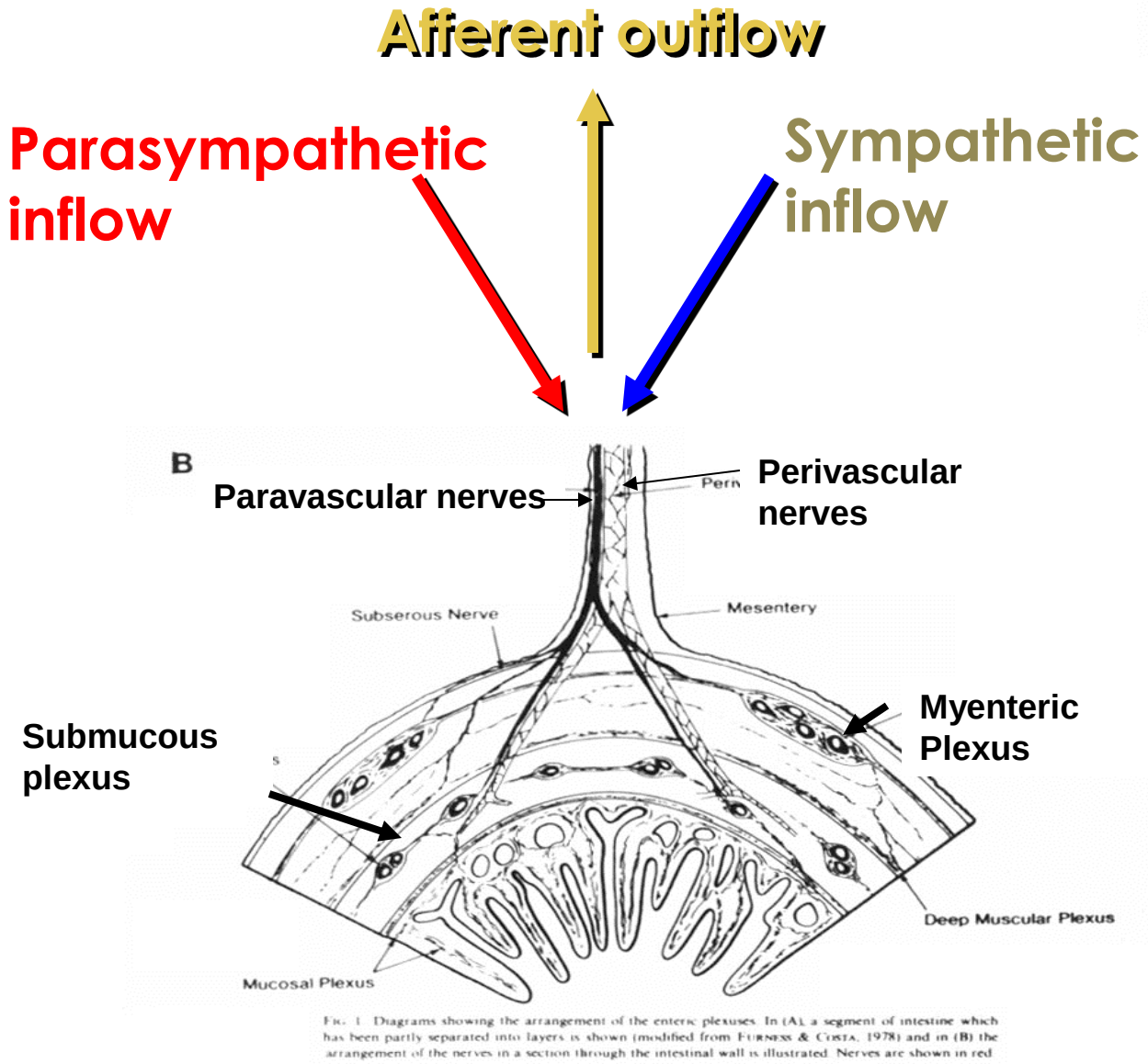
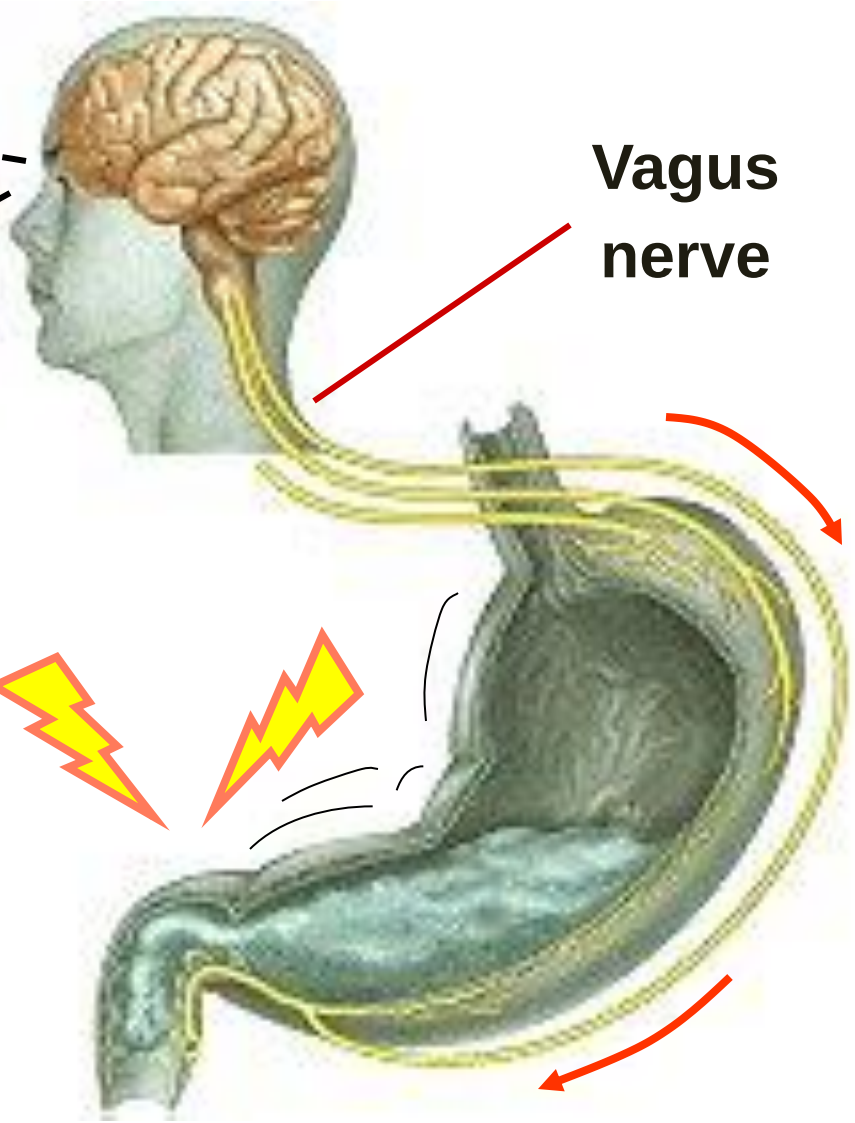


FIG. 1. Diagrams showing the arrangement of the enteric plexuses. In (A) a segment of intestine which has been partly separated into layers is shown (modified from FURNESS & COSTA, 1978) and in (B) the arrangement of the nerves in a section through the intestinal wall is illustrated. Nerves are shown in red

1. CEPHALIC PHASE



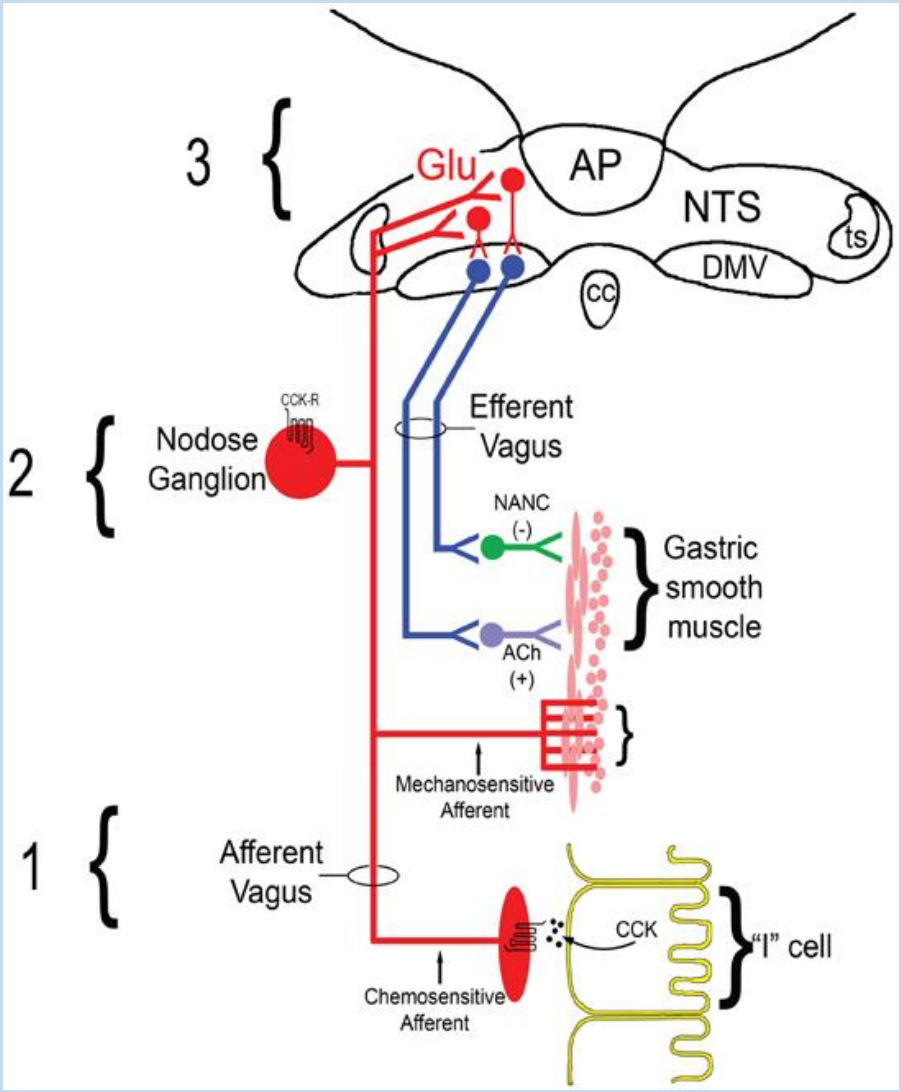
Sight, smell or thought of food

- Parasympathetic activation of gastric motility & gastric juice secretion

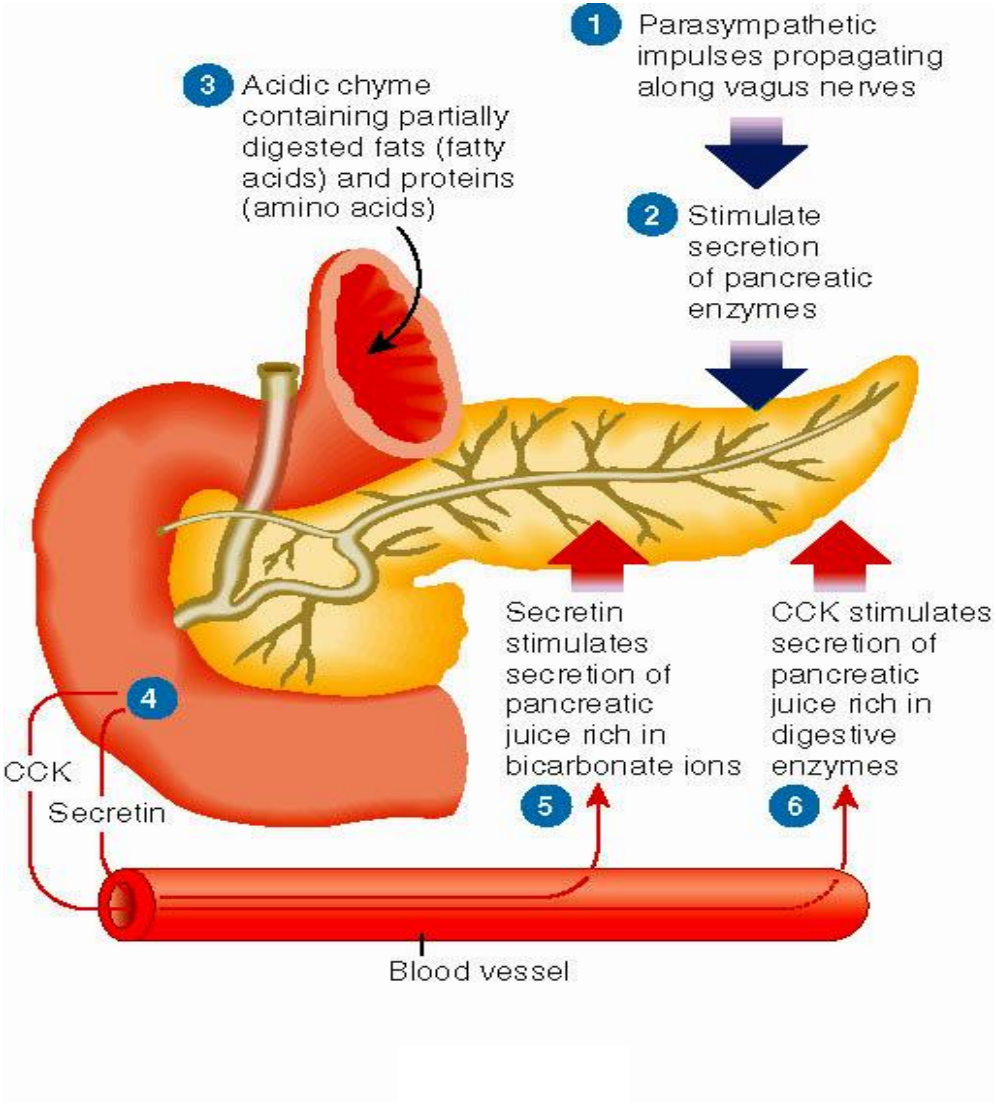
Vagovagal reflex –
Important for starting receptive relaxation of the stomach in response to swallowing of food

Food in the stomach- a "vagovagal" reflex from the stomach to the brain, and then back again to the stomach causing further *active* relaxation of the smooth muscle in the stomach wall

If vagal innervation is interrupted then intra-gastric pressure increases


3
Glu
AP
NTS
ts
DMV
cc
2
CCK-R
Nodose
Ganglion
Efferent
Vagus
NANC
(-)
Gastric
smooth
muscle
ACh
(+)
Mechanosensitive
Afferent
1
Afferent
Vagus
CCK
"I" cell
Chemosensitive
Afferent

Integration of Autonomic Neural signals with Gut Hormonal regulation of the Pancreas



ANS effects

1. post surgery, patients are often unable to urinate and bowel sounds are absent

   What division of the ANS is affected by anaesthetic?

2. Stress-induced stomach ulcers can be caused by over stimulation by parasympathetic nerves to the H^+ secreting cells of the stomach= high acid

   - can also be due due to excess sympathetic stimulation = reduced blood flow to the stomach wall

   How is this related to sympathetic function?

Developmental Aspects of the ANS

Effects of age on ANS

- Constipation
- Dry eyes
- Frequent eye infections
- Orthostatic hypotension
  - Low BP after position change
  - Pressure receptors less responsive to BP changes
  - Cardiovascular centers fail to maintain healthy BP

Effects of Drugs

- Atropine
  - Anticholinergic; blocks muscarinic ACh receptors
  - Used to prevent salivation during surgery, and to dilate pupils for examination

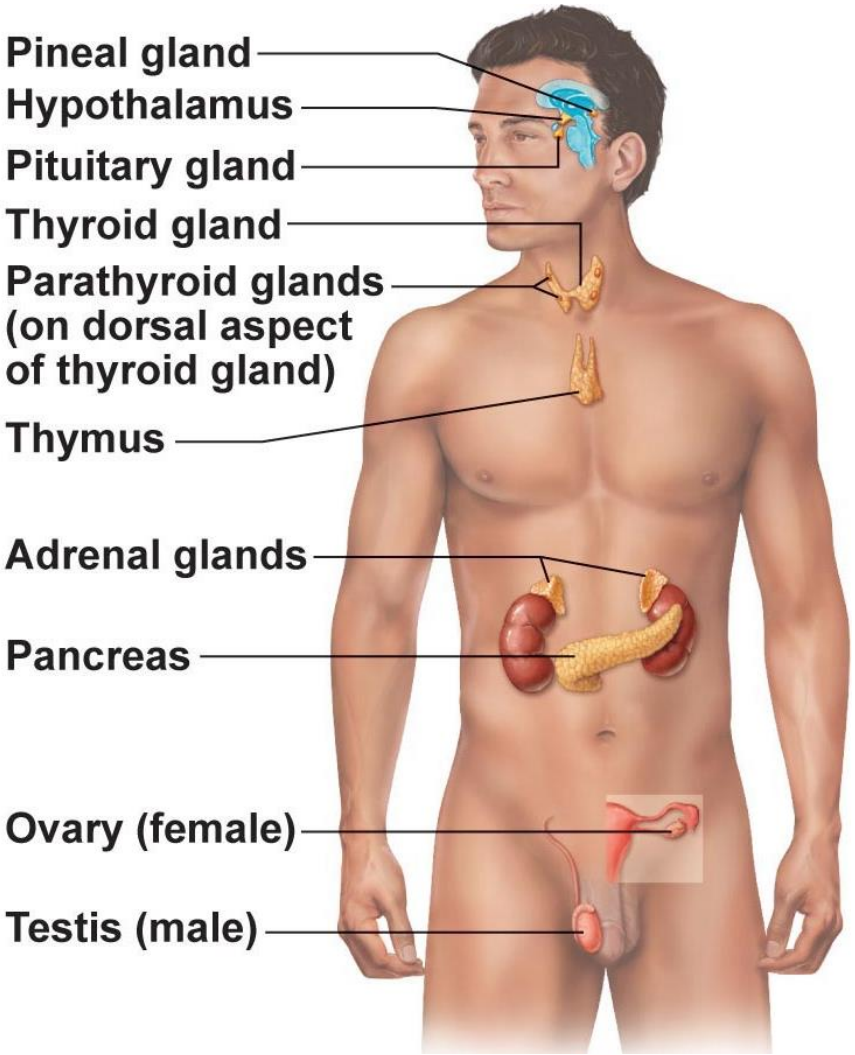
- Neostigmine
  - Inhibits **acetylcholinesterase** that breaks down ACh
  - Used to treat myasthenia gravis (*an autoimmune neuromuscular disease*)

Effects of Drugs

- Over-the-counter drugs for colds, allergies, and nasal congestion
  - Stimulate **α-adrenergic receptors**

- **Beta-blockers**
  - Drugs that attach to β_2 receptors to dilate lung bronchioles in asthmatics; other uses

THE ENDOCRINE SYSTEM



HORMONE= Chemical substance that gets to target via blood and/or the ECF: serve to regulate the metabolic function of other cells in the body

Just like all other signalling agents in the body, hormones have specific receptors; level of target cell activation depends on:

(i) **hormone concentration**

(ii) **receptor expression**

(iii) **affinity** of hormone for receptor

Fig. 16.1

Hormone Secretion

Stimulated and inhibited by:

Other hormones (stimulating- or releasing -hormones)

Plasma concentrations of ions or nutrients, as well as binding globulins

Neurons and mental activity

Environmental changes, e.g., of light or temperature

Hormone Actions in Mammals

Stimulation or inhibition of growth

Wake-sleep cycle and other circadian rhythms

Mood

Induction or suppression of apoptosis (programmed cell death)

Activation or inhibition of the *immune system*

Regulation of metabolism

Preparation for mating, fighting, fleeing, and other activity

Body transition- puberty, parenting, and menopause

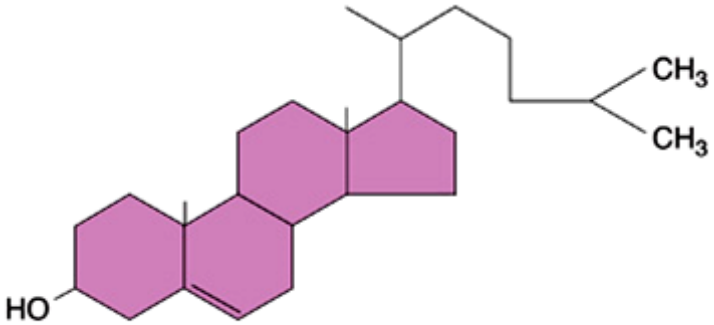
Reproductive cycle

Hunger

Sexual arousal

Hormone Action:

- hormones alter levels of cell activity:
  - » membrane permeability/potential (channels)
  - » synthesis of enzymes within cells
  - » enzyme activation/deactivation
  - » induction of secretory activity
  - » stimulation of mitosis



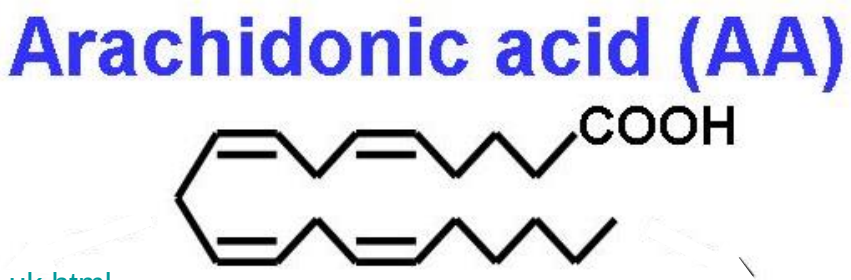
Cholesterol

3 Structural groups of hormones:

(i) amino acids, peptides, proteins

(ii) steroid hormones (derivatives of cholesterol)

(iii) eicosanoids (from arachadonic acid)



http://www.gremi.asso.fr/mediator_inflammation-uk.html

Mechanisms of Hormone Action

Water-soluble hormones (all amino acid–based hormones except thyroid hormone)

- Act on plasma membrane receptors
- Act via G protein second messengers
- **Cannot enter cell**

Lipid-soluble hormones (steroid and thyroid hormones)

- Act on intracellular receptors that directly activate genes
- **Can enter cell**

Mechanisms of Peptide/protein hormone action

Via activation of G protein » production of 2nd messenger (eg: cAMP, calcium) which activates protein kinases to regulate key enzymes

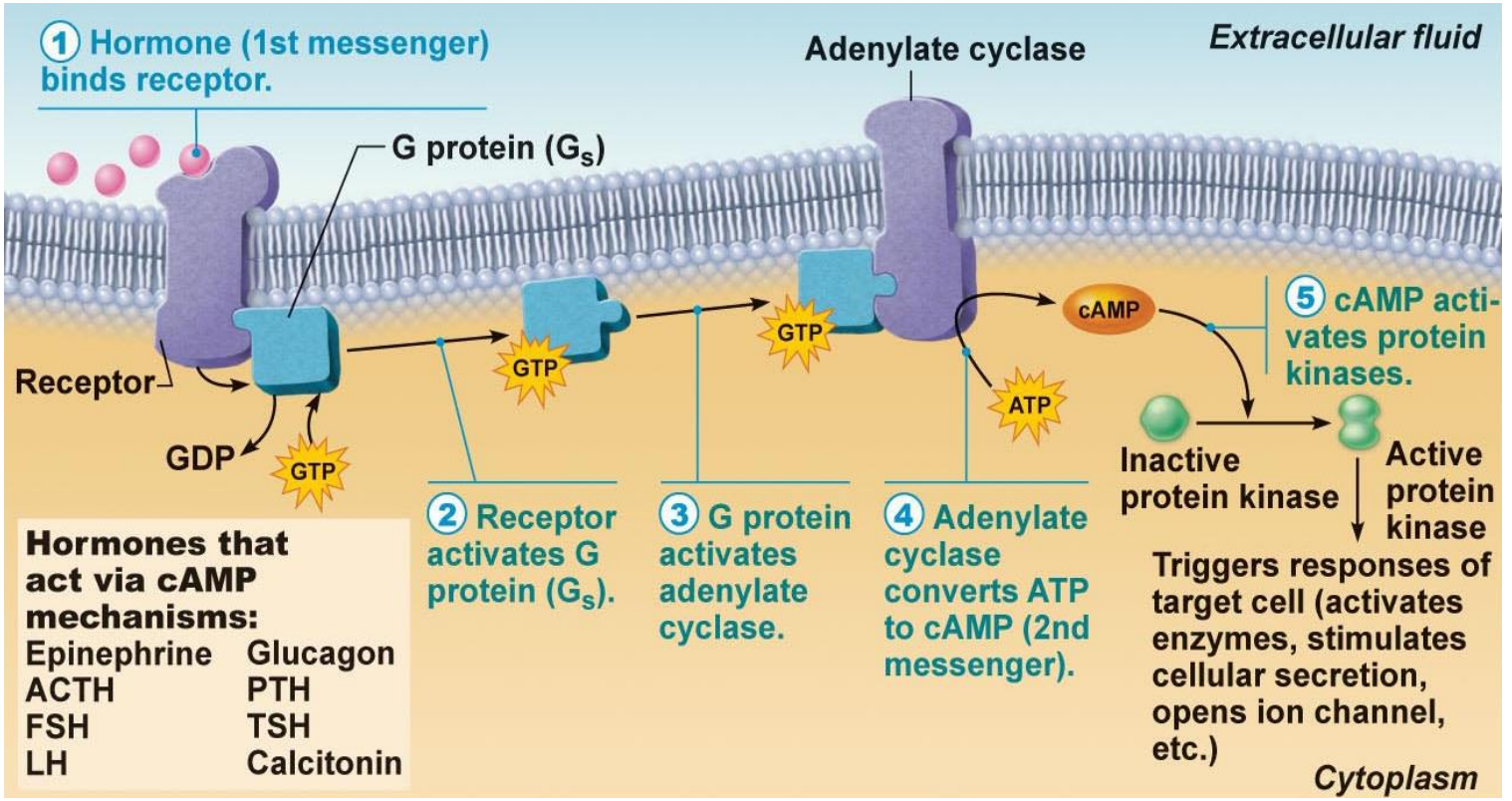


Fig. 16.2

Intracellular Receptors and Direct Gene Activation

Steroid and Thyroid hormones

1. Diffuse into target cells & bind with intracellular receptors
2. Receptor-hormone complex *enters nucleus*; binds to specific region of DNA
3. Prompts *DNA transcription* to produce mRNA
4. mRNA directs protein synthesis
5. Promote metabolic activities, or promote synthesis of structural proteins or proteins for export from cell

Steroid hormones: Mechanism of action

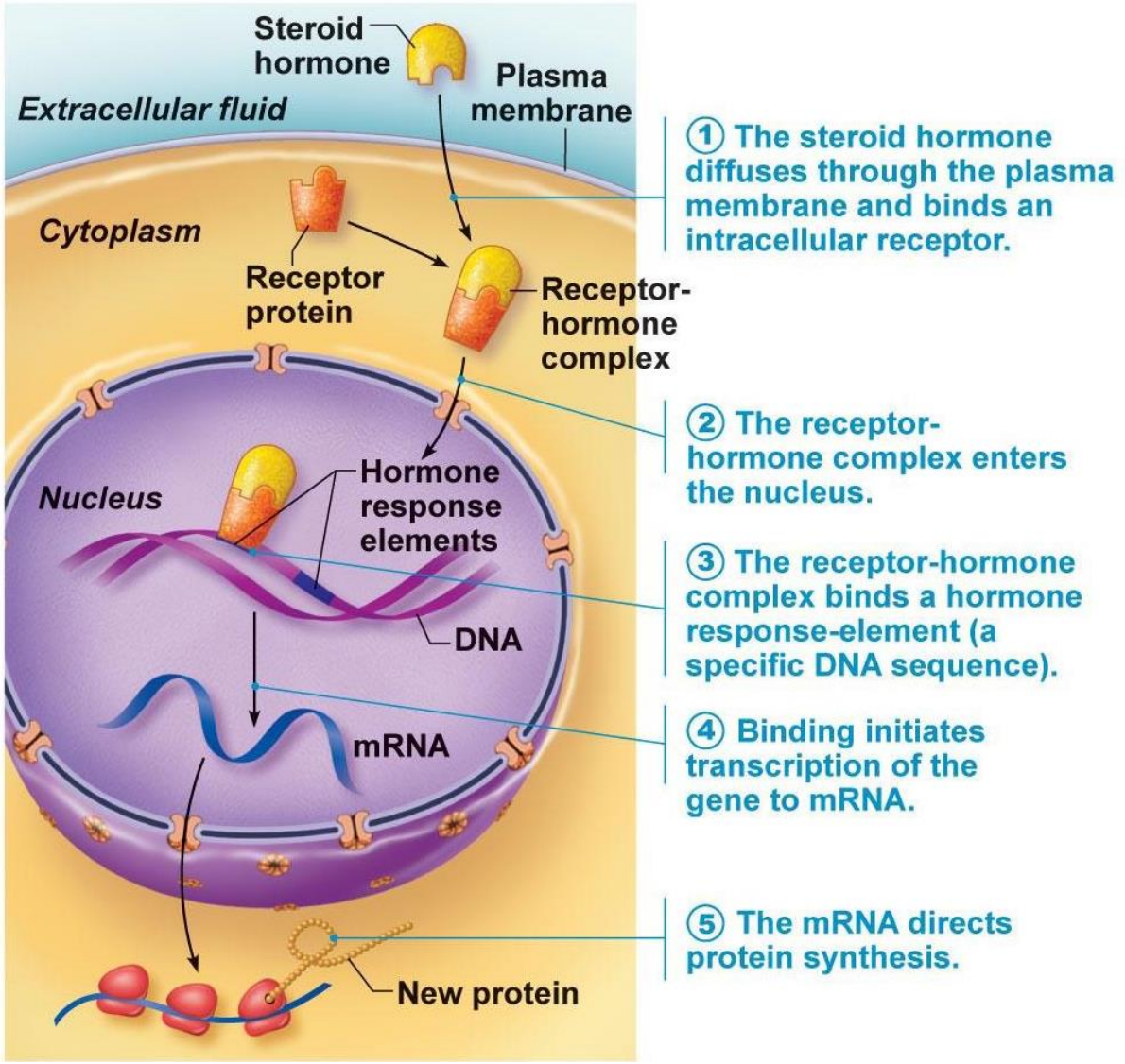


Fig. 16.3: Steroid hormones usually act in the nucleus to influence gene transcription

Other Hormone Signaling Mechanisms

- Cyclic guanosine monophosphate (cGMP) is second messenger for some hormones
  - **Atrial natriuretic peptide-initiated cGMP pathways regulate vasodilator-stimulated phosphoprotein phosphorylation and angiogenesis in blood vessels**

- Some work *without second messengers*
  - E.g., insulin receptor is tyrosine kinase enzyme that autophosphorylates upon insulin binding → docking for **relay proteins** that trigger cell responses
  - hepatic **Irs1** and **Irs2** function in a distinct manner in the regulation of glucose homeostasis
    - In type 2-diabetes and impaired glucose tolerance, the muscle, fat and liver become resistant to insulin: recent developments place dysregulation of insulin receptor substrate (IRS) expression and activation at the center of such defects

Half-life, Onset & Duration of Hormone Activity

- hormones are **potent & long acting**

- blood level depends on:
  - » rate of synthesis
  - » rate of degradation/clearance from blood

- **half-life:** in the blood; usually 1-30 min

- time to **onset** of hormone action variable: **enzyme activation** - rapid (minutes); **enzyme synthesis** - hrs to days

- some hormones secreted as ***pro-hormones:*** activated once reach target cell

- **duration** of hormone action : hrs to days

Hormones in the Blood

- Hormones circulate in blood either **free** or **bound**
  - Steroids and thyroid hormone are attached to plasma proteins
  - All others circulate without carriers

- Concentration of circulating hormone reflects
  - Rate of release
  - Speed of inactivation and removal from body

Hormones in the Blood

- Hormones removed from blood by
  - Degrading enzymes
  - Kidneys
  - Liver

Control of Hormone Release

- usually **–ve feedback** (**setpoint**); sometimes **+ve** feedback (**goal**)
- 3 types of stimuli: humoral, neural & hormonal

a) ***Humoral*** stimuli: hormone secretion in direct response to change in blood level of a nutrient, ion [eg: parathyroid hormone (**PTH**) & blood **calcium**; **insulin** & blood **glucose**]

b) ***Neural*** stimuli: not as common, eg: **sympathetics** & **epinephrine** release by adrenal medulla, **hypothalamic neurons** & **oxytocin** release

c) ***Hormonal*** stimuli: 3-tiered system involving **hypothalamus**, **pituitary** & **target endocrine gland** - concept of **hypothalamic-pituitary axis**

Nervous System Modulation

- Nervous system modifies stimulation of endocrine glands and their –ve feedback mechanisms
  - Example: under severe stress, hypothalamus and sympathetic nervous system activated
    - → body glucose levels rise

- Nervous system can override normal endocrine controls

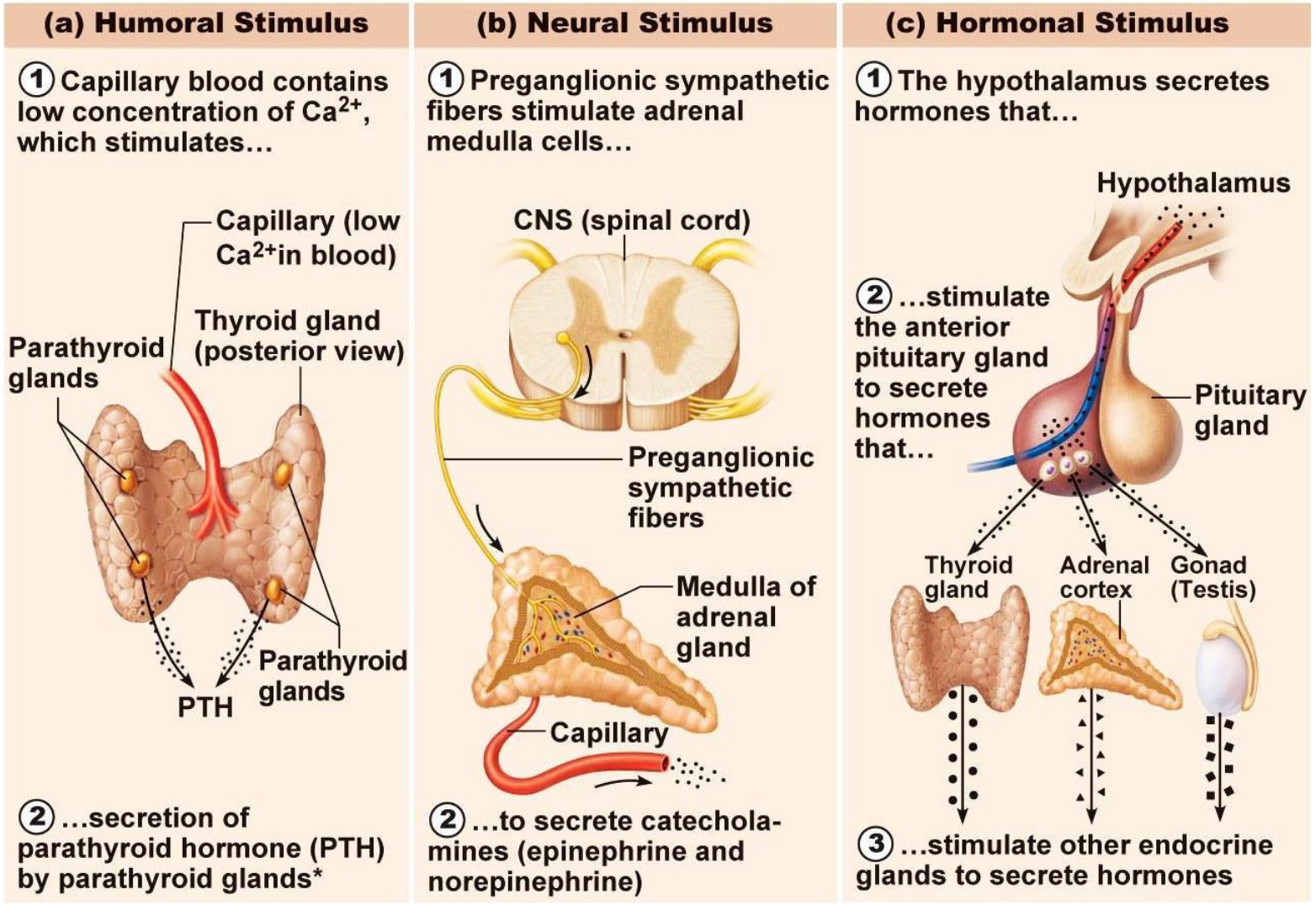
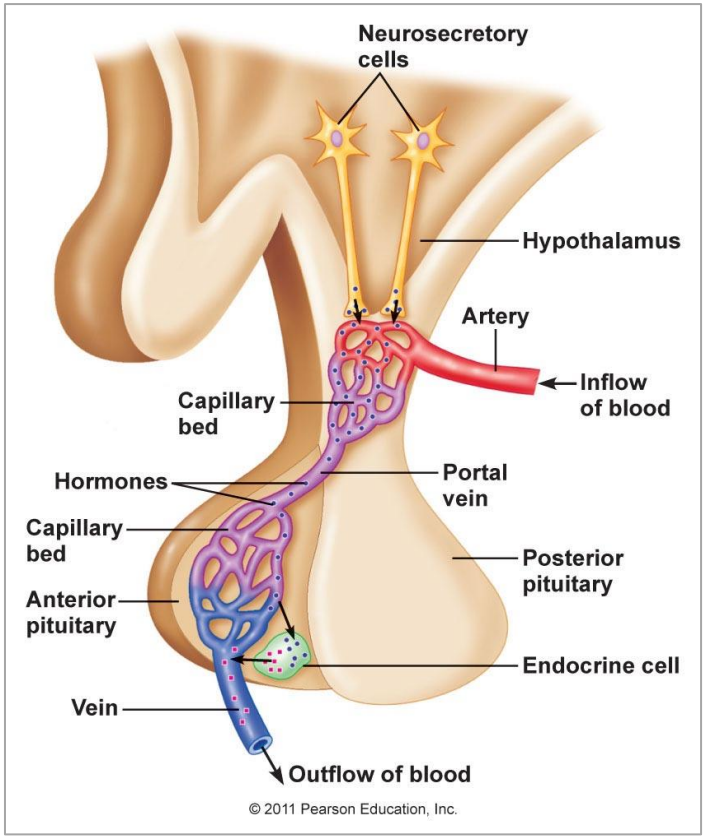


Fig. 16.4: Endocrine stimulation – 3 mechanisms

Hormonal Stimuli

Hormones stimulate other endocrine organs to release their hormones

- Hypothalamic hormones stimulate release of most anterior pituitary hormones
- Anterior pituitary hormones stimulate targets to secrete still more hormones
- Hypothalamic-pituitary-target endocrine organ feedback loop: hormones from final target organs inhibit release of anterior pituitary hormones



Hormonal Stimulus: Hypothalamus-Anterior Pituitary

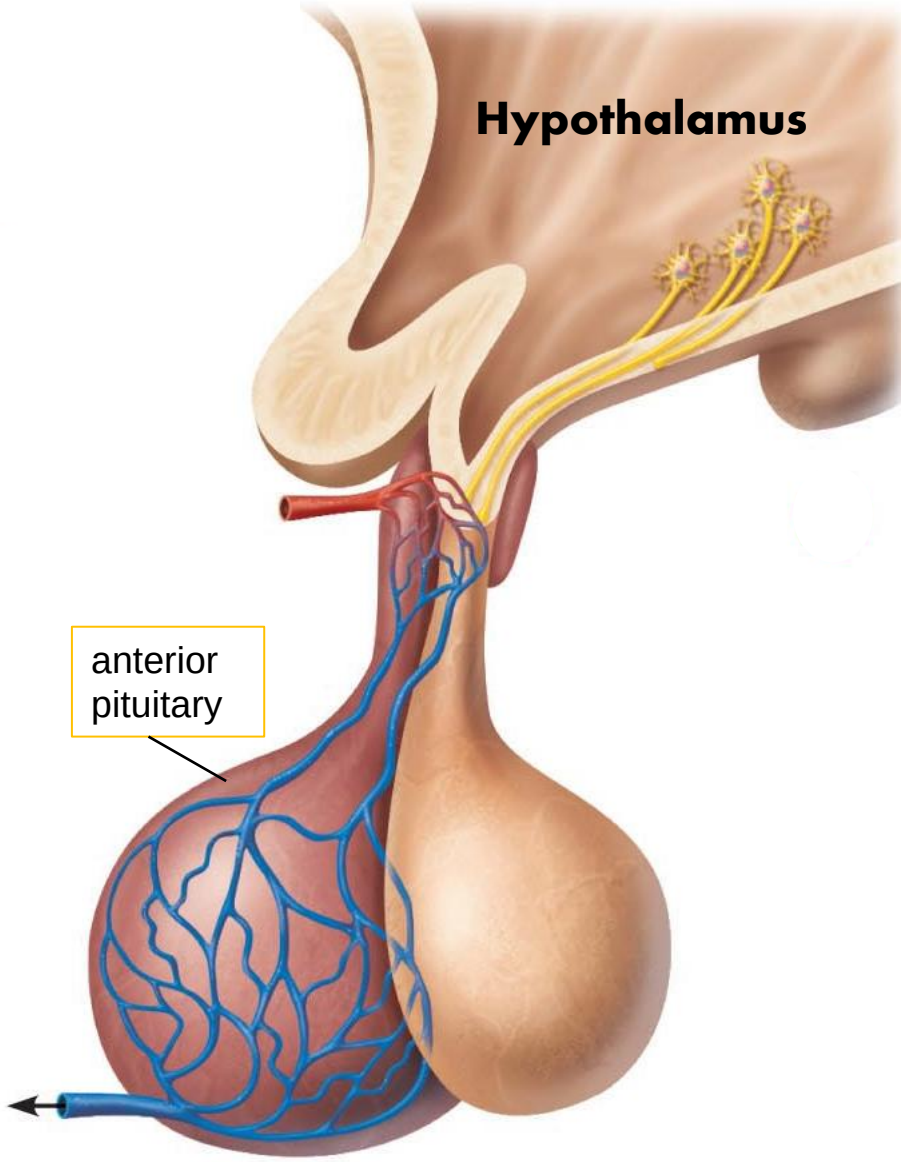
Thyroid-releasing hormone (**TRH**)
(hypothalamus)

⇩

Thyroid-stimulating hormone (**TSH**)
(anterior pituitary)

⇩

Thyroid hormones (**T_3 & T_4**)
(thyroid gland)



Hypothalamus is **neural**; produces a number of **releasing factors (hormones)** which travel to **anterior pituitary** via **hypophyseal portal system**

This system of blood vessels allows transport and exchange of hormones for a fast communication of both glands

Fig. 16.5b:

Pituitary Gland:

- size & shape of a pea
- infundibulum connects pituitary to hypothalamus

posterior lobe:

- axon terminals
- hormone storage area
- **antidiuretic hormone (SON)**

  oxytocin (PVN)

Structurally similar (both are nonapeptides); but very different functions!!

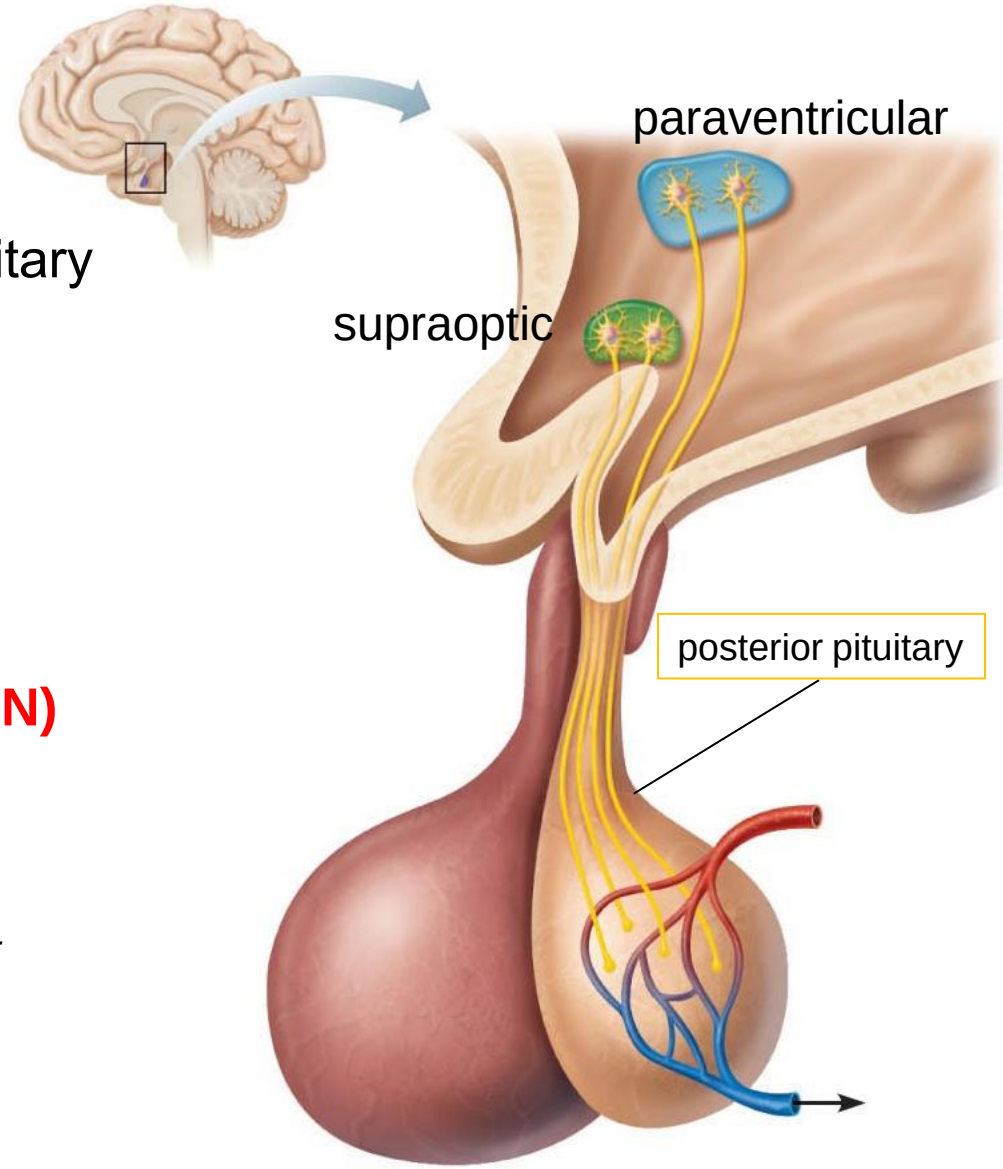


Fig. 16.5a: Hypothalamus & posterior pituitary

Hypothalamic Releasing Hormone	Anterior Pituitary Hormone	Target Gland
Thyroid releasing hormone (TRH)	Thyroid stimulating hormone (TSH)	Thyroid gland
Corticotropin releasing hormone (CRH)	Adrenocorticotropic hormone (ACTH)	Adrenal glands
GHIH (Somatostatin) GRH or GHRH	Growth Hormone	Liver
Gonadotropin releasing hormone (GnRH)	Follicle stimulating hormone (FSH) Luteinizing hormone (LH)	Ovaries Testes
PIH = dopamine PRH = TRH, oxytocin	Prolactin	Breast