Homeostasis

Homeostatic control of variables involves three components: receptor, control centre, and effector

Receptor (sensor)

- Monitors environment
- Responds to **stimuli** (things that cause changes in controlled variables) sends info **(***afferent pathway***)** to

Control center

- Determines set point for variable
- Receives input from receptor & determines appropriate response

Effector

- Receives output from control center
- provides means for response (*output along efferent pathway*)
- Response either reduces stimulus ***(negative feedback)*** or enhances stimulus ***(positive feedback)***

Homeostatic Control

Negative feedback

- Most-used feedback mechanism in body
- Response ***reduces or shuts off original stimulus***
  - Variable changes in opposite direction of initial change / Goal: prevent sudden, severe changes

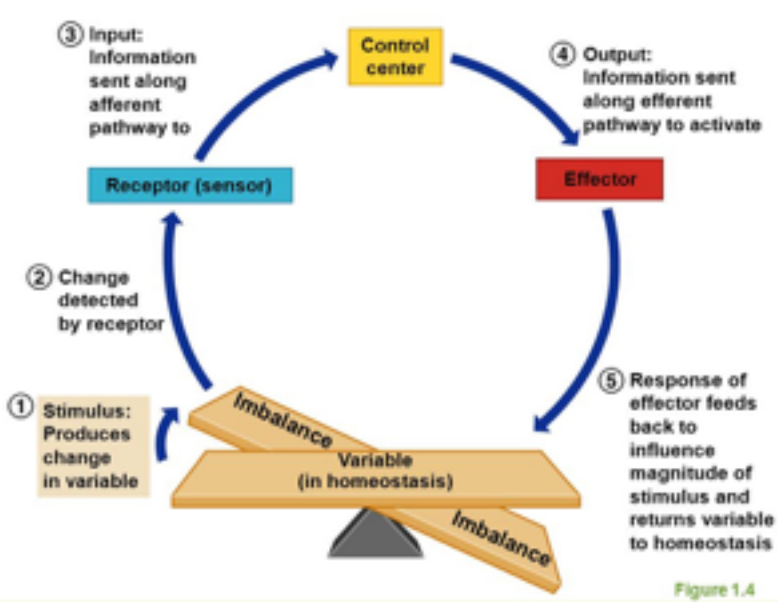


Figure 1.4

Ex: Regulation of body Temperature

Positive feedback

- Response enhances or exaggerates the original stimulus
- May exhibit a cascade or amplifying effect as feedback causes variable to continue in same direction as initial change
- Usually controls infrequent events that do not require continuous adjustment, for example

Examples:

- Enhancement of labor contractions by oxytocin
- Platelet plug formation and blood clotting

Homeostatic Imbalance

Disturbance of homeostasis

- most disease seen as a *disturbance* of homeostasis = homeostatic imbalance
- Contributes to changes associated with aging
    - Control systems become less efficient Ø greater risk for illness

– If negative feedback mechanisms become overwhelmed, destructive positive feedback mechanisms may take over

Autonomic Nervous System (ANS)

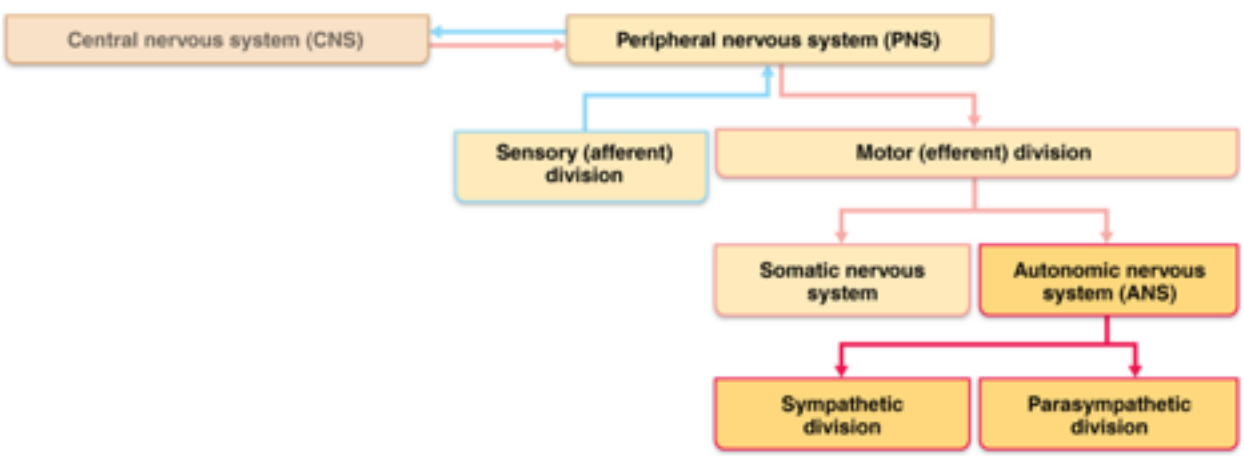
- *auto* = self; *nom* = govern

ANS = system of motor neurons

- *Innervate smooth muscles, cardiac muscle, and glands*
- allow responses usually without our awareness (subconscious control
- also called **involuntary nervous system** or **general visceral motor system**

Make adjustments to ensure optimal support for body activities

- shunt blood to more needy areas
- speed/slow heart & respiratory rates
- adjust blood pressure, body temp
- increase/decrease gastric secretions



ANS Vs. Somatic Nervous system

- Both have motor fibers but differ in:
  – Effectors / efferent pathways and ganglia / target organ responses to Neurotransmitters

	ANS	SNS
Effector	cardiac muscle, smooth muscle & glands	skeletal muscles
Efferent pathway & ganglia	**Two neuron chain** *Preganglionic neuron* • cell body in CNS • thin, lightly myelinated pre-ganglionic axon extending to ganglion *Postganglionic (ganglionic) neuron* • outside CNS: cell body synapses with pre-ganglionic axon in **autonomic ganglion** • nonmyelinated postganglionic axon that extends to effector organ	• **a single**, thick myelinated group A axon extends in spinal or cranial nerves *directly to skeletal muscle* • cell body is in CNS
Target organ responses & neurotransmitters	• Preganglionic fibers release ACh • Postganglionic fibers release NE or ACh at effectors • *Effect is either stimulatory or inhibitory, depending on type of receptors*	• All somatic motor neurons release acetylcholine (ACh) • *Effect is always stimulatory*
Conduction	• conduction is slow	• rapid conduction of impulses

Divisions of Autonomic Nervous System

Key **Anatomical** Differences Between ANS Divisions

Sites or origin of nerves

- PNS fibers: craniosacral originate in brain and sacral spinal cord
- SNS fibers: thoracolumbar originate in thoracic and lumbar regions of spinal cord

Relative lengths of pre- and post-ganglionic fibers

- PNS: long preganglionic & short postganglionic fibers
- SNS: short preganglionic and long postganglionic

Locations of ganglia

- PNS ganglia: in or near the their visceral effector organ
- SNS ganglia lie close to spinal cord

Divisions of Autonomic Nervous System

Dual innervation: all visceral organs are served by both divisions, but these divisions cause opposite effects

Parasympathetic division	**Sympathetic division**
promotes maintenance functions, conserves energy • **resting & digesting** *system* active in non-stressful situations • keeps body's energy use low while regulating « housekeeping » activities (digestion, elimination of feces & urine) • **"D" system:** digestion defecation, diuresis	mobilizes body during activity • **" fight or flight"** system; important during exercise: increased heart rate, rapid, deep breathing, cold sweaty skin(***why?***), dilated eye pupils • **"E" system:** exercise, excitement, emergency, embarrassment

Dynamic antagonism between two divisions maintains homeostasis

Parasympathetic & Sympathetic Interactions

- Most visceral organs have *dual innervation*
- One division usually predominates, but in a few cases, divisions have a cooperative effect
- Both ANS divisions are partially active, resulting in a basal **sympathetic and parasympathetic tone**
-

Antagonistic
  - **SNS** and vascular (vasomaotor) tone: continual state of partial constriction of blood vessels
    - blood shunting possible via vasoconstriction/vasodilation

- **PNS** & tone: heart, smooth muscle of GI & urinary tracts- can be overridden by SNS
    - Drugs that block parasympathetic responses increase heart rate and cause fecal and urinary retention

Cooperative Interactions

eg: regulation of external genitalia during intercourse

- PNS: dilation of blood vessels in penis
- SNS: ejaculation, reflex peristalsis of female's vagina

Unique Roles of Sympathetic NS

SNS regulation only: adrenal medulla, sweat glands, arrector pili muscles of skin, kidneys, most blood vessels

Other unique functions of sympathetic division include:

Thermoregulatory responses to heat

- When body temperatures rise, sympathetic nerves:
    - Dilate skin blood vessels, allowing heat to escape
    - Activate sweat glands
- When body temperatures drop, blood vessels constrict

Renin release from kidneys

- Sympathetic system causes release of renin from kidneys that in turn activates a system that increases blood pressure

Metabolic effects

- increases metabolic rate of body cells
- raises blood glucose levels
- stimulates mobilization of fats
- increases mental alertness
- increases speed/strength of muscle contraction

Control of ANS Function

- ANS is under control of CNS centers in:
  - Brain stem and spinal cord, hypothalamus, and cerebral cortex
  - Hypothalamus is generally main integrative center of ANS activity

Brain stem and spinal chord controls

- significant direct effects on ANS-regulated activities
- motor centres in the medulla (eg: cardiovascular centre → heart rate, blood vessels; also GI, respiratory centres)
- Spinal cord controls defecation and micturition but are subject to conscious override

Hypothalamic Controls

- hypothalamus = integration centre of ANS
  - 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

Cortical Controls

Connections of hypothalamus to limbic lobe allow cortical influence on ANS
Voluntary cortical control of some visceral activities is possible

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:

Endocrine system overview

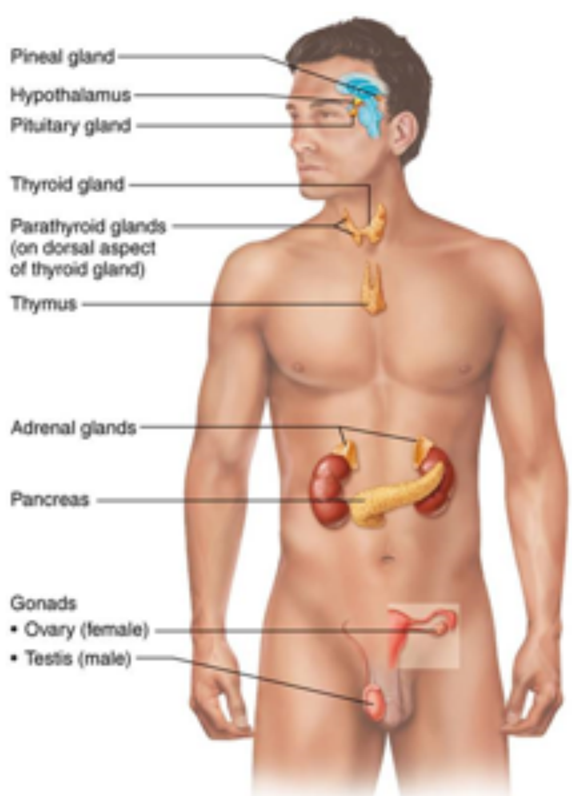
- acts with NS to coordinate and integrate activity of body cells
- Influences metabolic activities via **hormones** transported in blood
- Responses slower but longer lasting than NS responses
- Endocrine system controls and integrates:
  - Reproduction
  - Growth and development
  - Maintenance of electrolyte, water, & nutrient balance of blood
  - Regulation of cellular metabolism and energy balance
  - Mobilization of body defences

Exocrine glands

- Produce non-hormonal substances (examples: sweat, saliva)
- Have ducts to carry secretion to membrane surface

Endocrine glands

- Produce hormones
- Lack ducts; secretes hormone into surrounding tissue fluid



What is a hormone?

- Chemical substance released into the ECF that regulates the metabolic function of other cells in the body

Remember:

- hormones must bind to specific receptors to influence target cell function
- hormones are specific; level of target cell activation depends on:
    1. hormone concentration
    2. target cell receptor content
    3. affinity of hormone for receptor

Classification of Hormones

Chemical structure determine solubility in water which determines

- how it's transported
- how long it lasts before being degraded
- what receptors it can act upon

	POLAR (water-soluble)	Non-Polar (lipid soluble)
How are they made, stored and released?	• Ligands are made in advance, stored in vesicles and released by exocytosis	• Ligands cannot be made in advance, so they are made as needed and released by diffusion
How are they transported in the body?	• Dissolve in plasma with a short half life	• Carried by transport molecule with a long half life
How do they interact with their target cells?	• Cannot enter target cells; bind to surface receptors and cause signal transduction in target cells • Usually have a low lag time; hormone cause *modification of existing* proteins in target cells	• Enter cells and bind to receptors in the cytoplasm and nucleus • Usually have a high lag time, hormone cause the *induction of new proteins* in target cells

3 structural groups of hormones

1. amino acids, peptides, proteins
2. steroid hormones (derivatives of cholesterol)
3. eicosanoids (from arachadonic acid)

Hormone action on target cells may be to:

- alter membrane permeability/potential (channels)
- stimulate synthesis of enzymes within cells
- activate/deactivate enzyme
- induce secretory activity
- stimulation of mitosis

Mechanisms of Hormone Action

Peptide/protein hormones:

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

- Act on plasma membrane receptors
- Usually act via G protein/second messengers
- Cannot enter cell

Steps:

1. Hormone (first messenger) binds to receptor
2. Receptor activates a G protein
3. G protein activates or inhibits effector enzyme (adenylate cyclase)
4. Adenylate cyclase then converts ATP to cAMP (second messenger)
5. cAMP activates protein kinases that phosphorylate (add a phosphate) other proteins
6. Phosphorylated proteins are then either activated or inactivated
7. cAMP is rapidly degraded by enzyme phosphodiesterase, stopping cascade
8. Cascades have huge amplification effect

Mechanisms of Hormone Action

Steroid hormones

Lipid-soluble steroid hormones & thyroid hormone can diffuse into target cells and bind with intracellular receptors

Receptor-hormone complex enters nucleus and binds to specific region of DNA

Helps initiate DNA transcription to produce mRNA which is translated into specific protein

- Proteins synthesized have various functions
  eg: metabolic activities, structural purposes, or exported from cell

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

Hormone Release

Blood levels of hormones

– Controlled by negative feedback systems / levels vary only within a narrow range
– Hormone release is triggered by:
    - Endocrine gland stimuli
    - Nervous system modulation

Endocrine Glands are stimulated to synthesize and release horns in response to one of three stimuli;

1. Humoral stimuli: change in blood level of a nutrient, ion directly stimulates secretion of hormones [eg: parathyroid hormone (PTH) & blood calcium; insulin & blood glucose]

2. Neural stimuli: nerve fibers stimulate hormone release

- not as common, eg: sympathetic ns & epinephrine release by adrenal medulla, hypothalamic neurons & oxytocin release

3. Hormonal stimuli: hormones stimulate other organs to release their hormones
    - 3-tiered system involving hypothalamus, pituitary & target endocrine gland - concept of hypothalamic-pituitary axis

Hypothalamus/Pituitary Relationship

Hypothalamus is connected to pituitary gland (hypophysis) via stalk called infundibulum

- Pituitary secretes at least eight major hormones

It has two major lobes:

Posterior pituitary: composed of neural tissue that secretes neurohormones

- Posterior lobe+ infundibulum = neurohypophysis
  - axon terminals / hormone storage area
  - antidiuretic hormone (SON) /oxytocin (PVN)

Anterior pituitary: (adenohypophysis) consists of glandular tissue

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

Hypothalamus and Pituitary Relationship

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

Hormone Release

Nervous System Modulation

- Nervous system can make adjustments to hormone levels when needed
  - Can modify stimulation or inhibition of endocrine glands
- Nervous system can override normal endocrine controls
  - Example: under severe stress, hypothalamus and sympathetic nervous system override insulin to allow blood glucose levels to increase
    - Prepare body for "fight or flight"

Target Cell Specificity

- Target cells must have specific receptors to which hormone binds
  - Example: ACTH receptors are found only on certain cells of adrenal cortex, but thyroxin receptors are found on nearly all cells of body
- Amount of hormone that can influence number of receptors for that hormone
  - **Up-regulation**: target cells form more receptors in response to low hormone levels
  - **Down-regulation**: target cells lose receptors in response to high hormone levels
    - Desensitizes the target cells to prevent them from overreacting to persistently high levels of hormone

Half-life, Onset & Duration of Hormone Activity

Hormones

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

Blood level of hormone depends on:

» rate of synthesis
» rate of degradation/clearance from blood

Half-life:

- time required for level of hormone in blood level to decrease by half

- persistence of a hormone in the blood; usually < 1 min to 30 min

Onset

- time to hormone action variable:
  - **enzyme activation -** rapid (minutes); **enzyme synthesis -** hours to days
  - some hormones secreted as ***prohormones***; activated once reach target cell

Duration of response

- Ranges from seconds to hours to day
- Effects may disappear rapidly as blood levels drop, but some may persist for hours at low blood levels

Integration of Hormones at Target cells

Multiple hormones may act on same target at same time

- **Permissiveness**: one hormone cannot exert its effects without another hormone being present
  - Example: reproductive hormones need thyroid hormone to have effect
- **Synergism**: more than one hormone produces same effects on target cell, causing amplification
  - Example: glucagon and epinephrine both cause liver to release glucose
- **Antagonism**: one or more hormones oppose(s) action of another hormone
  - Example: insulin and glucagon