Endocrine Systems

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Three classes of hormones

Amines

- Derived from **tyrosine or tryptophan**

Polypeptides

- **Most hormones**

Steroid hormones

- **Cholesterol derivatives**
- **Less soluble** in water – require carriers

Chemical Classes of Hormones

Class	Chemical properties	Location of target cell receptors	Mechanism of action	Examples
Amines	**Derived from tyrosine or tryptophan**; small, **water-soluble** (**except thyroid hormones, which are lipophilic**)	**Plasma membrane (except thyroid hormones,** which act via intracellular receptors)	Stimulate **second-messenger pathways (except thyroid hormone,** which acts via changes in **gene transcription**)	Epinephrine, norepinephrine, dopamine, thyroid hormone, melatonin
Polypeptides	Water-soluble	Plasma membrane	Stimulate **second-messenger pathways**	Insulin, glucagon, leptin
Steroids	Synthesized from cholesterol; **lipid-soluble**	Cytosol or nucleus	Usually stimulate **gene transcription directly**	Aldosterone, cortisol, androgens, estrogens

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Anterior pituitary

6 hormones are secreted into **blood circulation from anterior pituitary** to act on other glands or structures

Hormones of the Vertebrate Anterior Pituitary Gland and Hypothalamus

Anterior pituitary gland hormone	Stimulatory neurohormone from hypothalamus	Inhibitory neurohormone from hypothalamus	Major functions
Adrenocorticotropic hormone (ACTH)	Corticotropin-releasing hormone (CRH)	None known	Stimulates adrenal cortex to make glucocorticoids
Follicle-stimulating hormone (FSH)	Gonadotropin-releasing hormone (GnRH)	None known	Stimulates germ cell development and sex steroid production in gonads
Luteinizing hormone (LH)	GnRH	None known	Stimulates release of eggs in females; stimulates sex steroid production from gonads
Growth hormone (GH)	Growth hormone-releasing hormone (GHRH)	Somatostatin	Promotes linear growth; regulates glucose and fatty acid balance in blood
Thyroid-stimulating hormone (TSH)	Thyrotropin-releasing hormone (TRH)	None known	Stimulates thyroid gland to make thyroid hormone
Prolactin (PRL)	TRH and other factors have been suggested as stimulators of PRL in some species, but this is not certain.	Dopamine	Stimulates milk formation in mammals; participates in mineral balance in other vertebrates

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Hormonal Control of Metabolism/Energy Balance

- Thyroid gland lies in neck of vertebrates
- Consists of follicles containing the colloid, with large amounts of **thyroglobulin**

a) Location and structure of the thyroid gland

- **Thyrotropin-releasing hormone (TRH)** stimulates **thyroid-stimulating hormone (TSH)** which stimulates the thyroid to make thyroid hormones:
  - **Thyroxine** (T_4) – 4 iodine atoms
  - **Triiodothyronine** (T_3) – 3 iodine atoms

HPT axis: Hypothalamus-Pituitary-Thyroid axis

- Thyroid hormone **stimulates metabolism/**energy expenditure:
- **Increase** number and **activity of the** Na^+/K^+-ATPase **pumps** in membranes
- **Heat production** is also increased

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Adrenal glands

Energy availability regulated by hormones of the **adrenal glands and pancreas**

Adrenal glands are **multifunctional** glands

- Inner **adrenal medulla** secretes amine hormones **norepinephrine and epinephrine**
  - Fight-or-flight reactions
  - Stimulate glycogenolysis and gluconeogenesis
- Outer **adrenal cortex** subdivided into 3 zones
  - Glomerulosa – **aldosterone** maintains **mineral and water balance**
  - Reticularis – some **androgens**
  - Fasciculata – **glucocorticoids** like **cortisol**

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Hypothalamus-Pituitary-Adrenal cortex Axis

HPA axis

Glucocorticoids (secreted by the adrenal cortex)

Liver	Stimulate gluconeogenesis, thus providing glucose to the blood
Adipose tissue	Stimulate breakdown of triglycerides into fatty acids and glycerol for fuel
Muscle and adipose tissue	Inhibit sensitivity to insulin, making more glucose available to brain cells, which do not require insulin to transport glucose across their plasma membranes
Bone	Inhibit bone growth and formation, because such processes require large amounts of nutrients that could be used to combat stress instead
Lungs	Stimulate lung maturation in the fetus
Immune	Suppress immune system function and reduce inflammation
Other	Regulate Na^+ and Cl^- balance in migratory fishes; stimulate nervous system development in most vertebrates; stimulate protein breakdown to provide amino acids to the liver for gluconeogenesis; inhibit reproduction

- **Glucocorticoids** are catabolic hormones promote ti**ssue breakdown**
- **Break down proteins and lipids** of bone, immune, muscle, and adipose tissue **to provide energy**
- **Promote gluconeogenesis in liver** during stress **to raise blood glucose**
- Expressed with **circadian rhythm during the day – low at night**

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Insulin/ Glucagon

Responsible for **maintaining normal blood concentrations of glucose**, fats, and amino acids → **homeostasis**

<u>Insulin</u> binds to **plasma membrane receptors** to **facilitate transport of glucose into cytosol**

- **Involves actions of glucose transporters (GLUTs)** in cytosolic membrane-bound vesicles
- Insulin stimulates fusion of vesicles with plasma membrane
- When insulin concentration decreases, GLUTs return to vesicles in the cytosol
- Also stimulates transport of amino acids and promotes fat deposition

<u>Glucagon</u> has **opposite effects on blood glucose levels**

- **Promotes liver glicogenolysis**
- **During starvation** it promotes **liver gluconeogenesis from non-carbohydrates sources**

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Hormonal Control of Ca++ Balance

- **Bones lose** Ca^{2+} **if not present** in the **blood**
- Among the most **tightly regulated** ions
- **1,25-dihydroxyvitamin D** (the active vitamin D derivative) **facilitates calcium transport in small intestine**
- 1,25-dihydroxyvitamin D **may considered a hormone** as it is:
  - **produced by kidney** from precursors modified in liver
  - **released in bloodstream**
  - **act distally at the intestinal level**

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Other hormones involved in Ca^{2+} homeostasis

Parathyroid hormone (PTH)

- Made by **parathyroid glands**
- Acts on **bone to stimulate** Ca^{2+} **release** and also to increase reabsorption from kidney filtrate

Calcitonin

- Functions **in calcium homeostasis in fishes** and **some mammals (in humans only in children** – not in adulthood)
- Produced by **thyroid gland**
- **Lowers blood** Ca^{2+} by promoting excretion and **deposition into bones**

Location of the parathyroid glands

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Regulation of Na^+

- Also tightly **regulated**
- **No large reservoirs** like calcium in bone
- Key is **altering rate of reabsorption** of water, Na^+ and K^+ from the urine at the **kidney level**

- **Antidiuretic hormone (ADH)** – secreted from posterior pituitary to increase reabsorption of water in kidney
- **Aldosterone** – from the adrenal glands increases sodium reabsorption in kidney
- **Atrial natriuretic peptide (ANP)** – secreted from heart to decrease sodium reabsorption in kidney

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Hormonal Control of Growth and Development

- In vertebrates, anterior pituitary produces **growth hormone (GH) under the control of hypothalamus**
- GH acts on liver to produce **insulin-like growth factor-1 (IGF-1)**
- **IGF-1 stimulates elongation of bones**, especially **during puberty**
- Eventually, **gonadal hormones will seal growth plates preventing further elongation**
- **In adults**, **GH serves metabolic functions** in regulating **glucose and fatty acid levels in blood**
- Hypothalamic hormone **somatostatin** inhibits GH release as part of a **negative feedback**

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Immune System

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Immunity

Ability of an animal to **ward off** internal **threats** such as microbes, microbial toxins, or cancerous cells

Immune system – cells and organs in an animal's body that contribute to these defenses

Innate (nonspecific) immunity – defenses present at birth that function the same way regardless of invader

Acquired (specific) immunity – develops after exposure and targets an invader specifically

- Repeated exposure elicits greater defense responses

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Cells involved in innate immunity

- All derived from adult hematopoietic stem cells

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Inflammation

- **Innate local response** to infection or injury:
  - **Destroys** or **inactivates pathogens**
  - **clears area** of dead cells
  - sets stage for **tissue repair**
- **Characterized by red-ness, swelling, heat and pain**
- Key cellular components of this process are **neutrophils, macrophages, dendritic cells,** and **mast cells**
- Induced and regulated

  by **cytokines**

1. An injury introduces bacteria beneath the skin. Mast cells secrete histamine, and endothelial cells secrete nitric oxide.
2. Capillaries dilate and become leaky. Fluid and neutrophils exit the capillaries and enter the site of the wound. Further recruitment of phagocytes is induced
3. As neutrophils and macrophages engulf and destroy bacteria, capillaries return to normal, and the infection is brought under control.

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Lymphocyte types

B cells

- **Mature in bone marrow**
- Some differentiate into **plasma cells** that synthesize and secrete **antibodies** (proteins that help destroy foreign molecules)

T cells

- **Mature in thymus gland**
- **Cytotoxic T cells** directly kill target cells using secreted chemicals
- **Helper T cells** assist in activating B cells and cytotoxic T cells

NK cells

- Similar to cytotoxic T cells
- Perform mainly **nonspecific actions** as well (innate immunity)

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Stages of acquired immune response

Antibodies

Immunoglobulin (Ig) protein family

Each composed of 4 interlinked polypeptides:

- 2 long **heavy chains**
- 2 short **light chains**

Constant region –identical amino acid sequences for given class – **binding to immune cells and complement proteins**

Variable region – varies among different B cells – specifically **recognizes antigen**

Activated B cells (humoral immunity)

Divide into **plasma cells** and **memory cells**

Clonal selection

- Antigen-stimulated lymphocyte divides and replicates itself
- Progeny of this lymphocyte all express the same receptor

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Histocompatibility complex class and T-cells response

FIGURA 6-21 Presentazione di antigeni extracellulari e citosolici a differenti sottopopolazioni di linfociti T. A. Gli antigeni citosolici sono presentati dalle cellule nucleate ai CTL CD8+, che uccidono (lisano) le cellule che esprimono gli antigeni. **B.** Gli antigeni extracellulari sono presentati dai macrofagi o dai linfociti B ai linfociti T helper CD4+, che eliminano gli antigeni attivando i macrofagi o i linfociti B.

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Central tolerance of T-cell in Thymus

- **Negative selection** of **self-reacting T-lymphocytes** occurs in the **thymus**
- The thymus is **reduced** in size **after puberty**, but a **remaining ability** to negatively and positively select is present also **in adulthood** and can be **exploited in hematopoietic stem cell transplantations**

T lymphocytes mature in the thymus

- B and T lymphocytes develop in bone marrow
- Lymphocytes mature and develop immunocompetence (ability to recognize specific antigen) in different locations
  - **B** cells mature in the **b**one marrow and provide *Ab-mediated* immunity
  - **T** cells mature in the **t**hymus and provide *cell-mediated* immunity

FIGURA 15-2 Tolleranza centrale dei linfociti T. Il riconoscimento degli antigeni self nel timo da parte dei linfociti T immaturi porta alla morte delle cellule (selezione negativa o delezione) o allo sviluppo di linfociti T regolatori che si localizzano nei tessuti periferici.

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Peripheral tolerance of T-cell

- Occurs **outside thymus (peripheral)**
- **Peripheral** tolerance is induced by **3 main mechanisms:**
- **Abnormal** (excessive or absent) **costimulation** or **repetitive stimulation** may induce:
  - **irresponsiveness (anergy)**
  - **apoptotic death (deletion) in self-reacting** T cells
- **Regulatory T-cells** may act peripherally by controlling specifically self-reactive T-cells possibly escaped from the developmental central tolerance

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