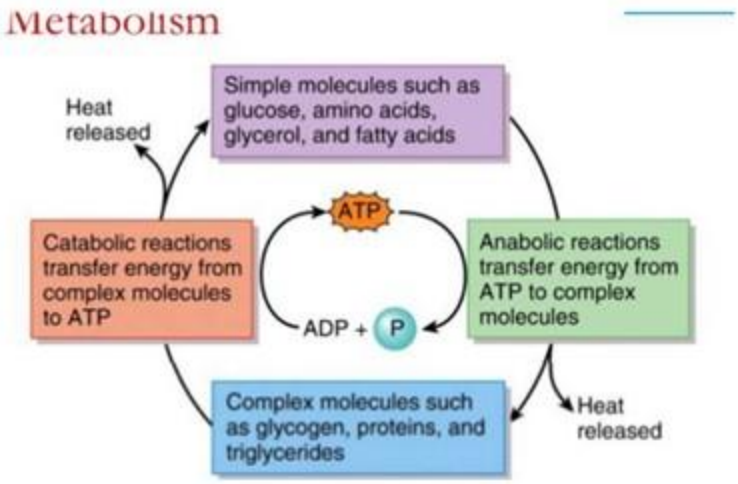
Energy balance and Metabolism

Energy intake & output are balanced, intake of different food provides energy that can be used to perform body function or stored for later use. Stability of body weight over a period of time requires that the person's energy intake be balanced with the energy consumed.

Nutrients: are chemicals the body uses for growth, maintenance, and repair. There are six major types of nutrients: carbohydrates, lipids, proteins, minerals, vitamins, and water.



Energy liberated from:

Each gram of Carbohydrates is 4.1 calories.

Each gram of Fat is 9.3 calories

Each gram of Protein is 4.3 calories.

Metabolism: the sum of the chemical reactions that take place within each cell of a living organism and that provide energy for use it to carry out activities such as movement, growth and development, and reproduction, and for synthesizing new organic material.

Metabolism: facilitated by enzymes and coenzymes NAD+ from B vitamin niacin and FAD from riboflavin (B2)

Two categories for metabolism:

Anabolism: synthesis of more complex chemicals.

Catabolism: breakdown with energy release, 40% energy use in cellular functions (ATP) and 60 energy used for heat production.

Sensation of hunger

is associated with several objective sensations such as contraction of stomach and restlessness and that's cause the person to search for food, and the person's appetite is the desire for certain type of food.

Each of these feelings (Hunger, appetite and satisfaction) influenced by environmental and cultural factors as well as specific centers in the brain (Hypothalamus):

Decreases Feeding	Increase Feeding
Serotonin, Norepinephrine Leptin Insulin Corticotropin- releasing hormone	Neuropeptide Y Melanin concentrating hormone Galanin Cortisol

A- Stimulation of the lateral nuclei of Hypothalamus (act as a feeding center) will result in hyperphagia, conversely inhibition on lateral nuclei of Hypothalamus will result in lack of desire of food, muscle weakness, weight loss and decrease in metabolism.

B- Stimulation of the ventro medial nuclei of Hypothalamus (act as a satisfaction center) will give complete feeling satisfaction even in the presence of food and the person refuses to eat (Aphagia). Conversely inhibition of this region will result in too much and continuous eating.

C- The Paraventricular and dorsomedial nuclei of Hypothalamus also involved in regulation of food intake. Example: lesions of paraventricular nuclei cause excessive eating and lesion of the dorsomedial nuclei depress eating.

Also these nuclei of Hypothalamus affect the secretion of several hormones which is important in regulation energy balance and metabolism including those from Thyroid and Adrenal gland increased feeding.

Galanin: is expressed in the brain, spinal cord, and gut.

Regulation of food intake

Hypothalamus receives neural signals from gastro intestinal tract about stomach filling and chemical signals from nutrients in blood (glucose, amino acids and fatty acids) and other signals from the gastro intestinal tract hormones and cerebral cortex (sight, smell and taste) that influence feeding behavior.

Factors regulating quantity of food intake are divided into:

A- **Short Term Regulations**: this concern with preventing overeating at the time of each meal. There are several of feedback signals as:

1. Gastro intestinal filling inhibition factor: When the gastro intestinal tract become full specially stomach and duodenum, stretching inhibition signals is transmitted to suppress feeding centers.

2. Hormonal factors Cholecystokinin a gastro intestinal hormone has an effect on suppressing feeding centers. Also presence of food in stomach and duodenum cause the pancreas to secrete glucagon and insulin which have effect on suppressing feeding centers .

3. Oral receptors meters food intake Oral factors related to feeding (salivation, chewing, tasting and swallowing) meters the food as it pass through the mouth and after certain amount it suppresses the feeding centers

B- Intermediate and Long Term Regulations: Which concerns with maintaining normal quantities of energy stored in the body.

1. Glucostatic, aminostatic and lipostatic theories: Decrease in the blood contents of glucose or amino acids or lipids (Fatty acids) will cause hunger (stimulating of feeding centers).

2. Relation between body temperature and food intake. When a person is exposed to cold, he over eats and when a person is exposed to heat he under eat. This is due to the interaction in the hypothalamus between temperature regulating system and food regulating system.

3. Feedback signals from adipose tissue regulate food intake: Most of stored energy consist of fat, so the relation between the fat and the energy storing (food intake). Hypothalamus senses the energy stored by peptide hormones called leptin. When adipose tissue increase there will be an increase in the production of leptin in the blood to reach the leptin receptors in the hypothalamus, stimulating of these receptors will cause:

a. Decrease production of appetite stimulators

b. Increase production of hormones which decreases food intake as Corticotropin-releasing hormone

c. Increase in metabolic rate.

d. Decrease in insulin secretion which decreases the energy storage.

Endocrine axis

Most organs in the body are dually regulated by the nervous system and the endocrine system. The hypothalamus's key homeostatic role requires that it be able to influence both systems. The hypothalamus functions include control of body temperature, food intake, thirst and water balance, and blood pressure, and it also controls aggression and rage. The hypothalamus exerts control through direct neural connections to autonomic centers in the brainstem, but it also controls the endocrine system. Endocrine control occurs directly through hormonal synthesis and release (oxytocin and antidiuretic hormone) and indirectly by secreting hormones that affect release of pituitary hormones.

Table 7.3: Posterior Pituitary Hormones

Pituitary Hormone Released	Pituitary Hormone Target (Effects)
Oxytocin	Uterus (contraction), mammary glands (lactation)
Antidiuretic hormone	Renal tubule (water reabsorption)

Endocrine axes:

The hypothalamus, pituitary, and a dependent endocrine gland together form a unified control system known as an endocrine axis. Most endocrine systems are organized into such axes. The advantage of this system is that it allows for both fine and gross control of hormone output. For example, the hypothalamic–pituitary–adrenal axis regulates cortisol secretion from the adrenal cortex. The hypothalamus produces corticotropin-releasing hormone (CRH), which stimulates adrenocorticotropic hormone (ACTH) release from the anterior pituitary. ACTH stimulates cortisol production by the adrenal cortex. Cortisol exerts negative feedback control on ACTH production by the anterior pituitary, and both ACTH and cortisol inhibit CRH synthesis by the hypothalamus.

Table 7.2: Anterior Pituitary Hormones

Hypothalamic Hormone	Pituitary Target Cell	Pituitary Hormone	Target Organ (Effects)
Corticotropin-releasing hormone	Corticotrope	Adrenocorticotropic hormone	Adrenal cortex (stress responses)
Thyrotropin-releasing hormone	Thyrotrope	Thyroid-stimulating hormone (TSH)	Thyroid gland (thyroxine release, metabolism)
Growth hormone–releasing hormone	Somatotrope	Growth hormone	Widespread (anabolic)
Somatostatin (release inhibitor)	Somatotrope	Growth hormone	Widespread
Somatostatin (release inhibitor)	Thyrotrope	TSH	Thyroid gland
Gonadotropin-releasing hormone	Gonadotrope	Luteinizing hormone	Gonads (androgen production)
Dopamine (release inhibitor)	Lactotrope	Prolactin	Mammary glands (milk production and letdown)
Gonadotropin-releasing hormone	Gonadotrope	Follicle-stimulating hormone	Gonads (follicle maturation, spermatogenesis)

Pituitary gland:

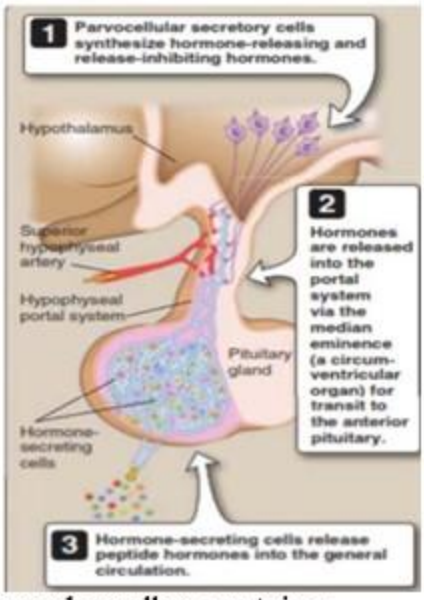
The pituitary gland (also known as the hypophysis) projects from the hypothalamus at the base of the brain and nestles in a bony cavity called the sella turcica. The hypothalamus and pituitary are connected by the pituitary (or hypophyseal) stalk, which contains bundles of neurosecretory axons. The pituitary contains two lobes. Although they lie next to each other within a common gland, they have very different embryologic origins and cellular compositions.

a. Anterior lobe:

The anterior lobe (adenohypophysis): It comprises a collection of glandular tissues that synthesize and store hormones. Hormone release is regulated by the hypothalamus using hormone releasing or release-inhibiting hormones, which travel from hypothalamus to the anterior pituitary via the hypophyseal portal system.

Hypophyseal portal system: The hypophyseal portal system directs blood from the hypothalamus to the anterior lobe of the pituitary gland. This unusual serial vascular

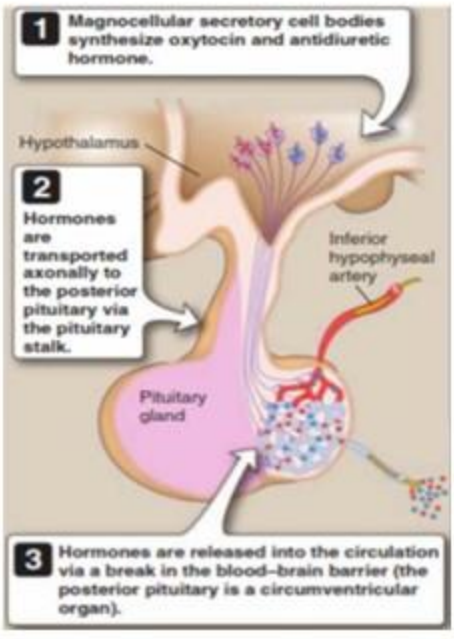
arrangement is used to carry peptide hormones synthesized by hypothalamic parvocellular (small-cell) neurosecretory cells to the anterior pituitary, where they stimulate or inhibit pituitary hormone release. Hypothalamic hormones are synthesized in neurosecretory cell bodies and then transported down their axons to terminals located in the median eminence.



Circumventricular organs (CVOs) are designed as interfaces between the brain and the periphery. They are highly vascularized, and blood flows through these regions slowly to maximize time available for exchanging materials between blood and brain. Also, CVO capillaries are fenestrated and leaky, which facilitates movement of ions and smaller proteins between blood and interstitium. It sensitive to numerous bloodborne factors(Na, Ca, angiotensin II, antidiuretic hormone, natriuretic peptides, sex hormones, and feeding and satiety signals).

The median eminence is a CVO that sits at the head of the pituitary stalk and its portal system. Given an appropriate stimulus, the hormones are released from the nerve terminals into the portal system and carried to the capillaries supplying the anterior lobe's hormone-secreting cells.

b- Posterior lobe: The posterior lobe (neurohypophysis) is neural tissue. Axons from magnocellular (large-cell) neurosecretory cells in the supraoptic and paraventricular nuclei extend down the pituitary stalk and terminate within a CVO located in the posterior lobe. Magnocellular cell bodies synthesize oxytocin (OT) and antidiuretic hormone (ADH), two related peptide hormones. The hormones are transported to the nerve terminals via the pituitary stalk and stored in secretory granules (Herring bodies) awaiting release. The posterior pituitary is highly vascular and the capillaries fenestrated. When peptides are released, they enter the general circulation directly.



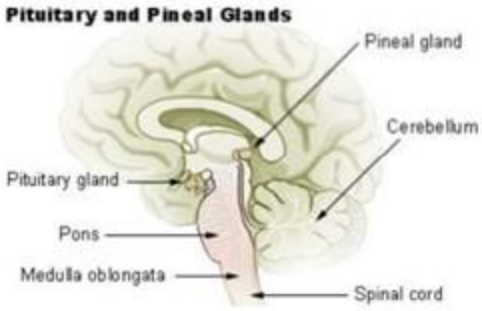
Anterior pituitary hormones: The hormones they produce can be placed in one of three structurally related groups.

A- **Adrenocorticotropic hormone:** ACTH (corticotropin) is synthesized by corticotropes, melanocyte-stimulating hormone (MSH), and β- endorphin (an endogenous opioid).

B- **Glycoprotein hormones:** Thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) are related glycoproteins. All three hormones are heterodimers that share a common subunit called α-glycoprotein subunit. TSH is synthesized in thyrotropes. FSH and LH are released by gonadotropes. Human chorionic gonadotropin (hCG) is a related placental hormone.

C- Growth hormone and prolactin: Growth hormone (GH) and prolactin are related polypeptides synthesized by somatotropes and lactotropes, respectively. A related hormone, human placental lactogen, is synthesized by the fetal placenta. GH is residue polypeptide synthesized and released in several different isoforms. Prolactin, polypeptide, is the only anterior pituitary hormone whose release is under tonic inhibition by the hypothalamus (via dopamine).

The pineal gland:



is a small pinecone shaped gland located at the midline near the posterior wall of the third ventricle. It comprises pinealocytes and glial support cells that are similar to pituicytes. It function synchronizes body functions in part through manipulation of endocrine axes .The SCN communicates with the pineal gland via neural connections to the brainstem and spinal cord. The pineal gland is a secretory CVO, which allows melatonin to be released into the circulation directly. Most bodily functions, including body temperature, blood pressure, and digestion, have daily "circadian," rhythms. The hypothalamus synchronizes these rhythms and entrains them to a circadian cycle established by suprachiasmatic nucleus (SCN). It synchronizes bodily functions in part through the endocrine system, with the pineal gland acting as a neuroendocrine intermediary.

Melatonin: is an indoleamine synthesized from tryptophan, which is regulated by the SCN via adrenergic inputs from the sympathetic nervous system. When light falls on the retina, the sympathetic pathways from the SCN to the pineal gland are activated. Melatonin synthesis and secretion fall, as a result, and do not resume until dark.

1- melatonin plays an important role in the regulation of sleep–wake cycles. Human melatonin production decreases as a person ages.

2- melatonin acts as a direct scavenger of oxygen radicals and reactive nitrogen species including $OH^{\cdot}$, O_2^{-}, and NO

3- melatonin interacts with the immune system through enhance cytokine production.

The thymus gland:

is the main organ of the lymphatic system. It is a two-lobed structure located in the upper chest above the pericardium of the heart between the lungs. The thymus functions chiefly to develop T lymphocytes. Once mature, these cells leave the thymus and are transported via blood vessels to the lymph nodes and spleen. T lymphocytes are responsible for cell-mediated immunity. T-cells contain proteins called T-cell receptors that populate the T-cell membrane and are capable of recognizing various types of antigens. The thymus produces hormone-like proteins that help T lymphocytes mature and differentiate. Some thymic hormones include thympoieitin, thymulin, thymosin, and thymic humoral factor (THF). Thympoieitin and thymulin induce differentiation in T lymphocytes and enhance T-cell function. Thymosin increases immune responses and stimulates certain pituitary gland hormones (growth hormone, luteinizing hormone, prolactin, gonadotropin-releasing hormone, and adrenocorticotropic hormone (ACTH)). Thymic humoral factor increases immune responses to viruses.