Al Mustaqbal Universty
Collage of pharmacy

Hypothalamic Regulation of Hormonal Function

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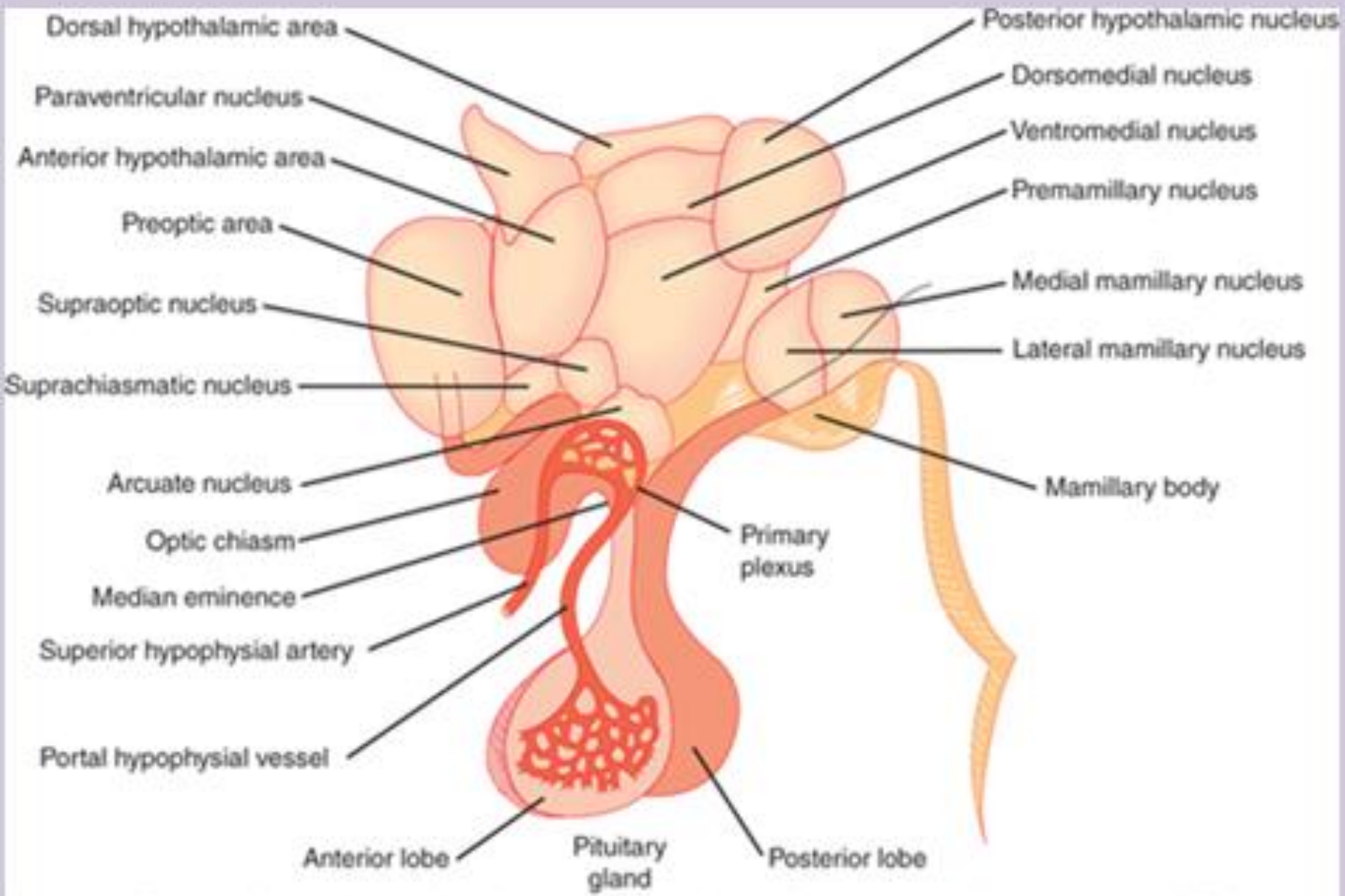
Introduction

Many of the complex autonomic mechanisms that maintain the chemical constancy and temperature of the internal environment are **integrated** in the hypothalamus. The hypothalamus also functions with the limbic system as a unit that **regulates** emotional and instinctual behavior

Relation to the Pituitary Gland

There are ***neural connections*** between the hypothalamus and the posterior lobe of the pituitary gland and ***vascular connections*** between the hypothalamus and the anterior lobe.

- Embryologically, the posterior pituitary arises as an evagination of the floor of the third ventricle. It is made up in large part of the endings of axons that arise from cell bodies in the supraoptic and paraventricular nuclei and pass to the posterior pituitary via the hypothalamohypophysial tract.



Source: Kim E. Barrett, Susan M. Barman, Scott Boitano, Heddwen L. Brooks: Ganong's Review of Medical Physiology, 25th Ed.
www.accessmedicine.com

Most of the supraoptic fibers **end** in the posterior lobe itself, whereas **some** of the paraventricular fibers **end** in the median eminence. The anterior and intermediate lobes of the pituitary arise in the embryo from the Rathke pouch, an evagination from the roof of the pharynx. **Sympathetic nerve** fiber reach the anterior lobe from its capsule, and parasympathetic fibers reach it from the petrosal nerves, but few, if any, nerve fibers pass to it from the hypothalamus.

- However, ***the portal hypophysial vessels*** form a direct vascular link between the hypothalamus and the anterior pituitary.
- **Arterial twigs** from the carotid arteries and circle of Willis form a network of fenestrated capillaries called the primary plexus on the ventral surface of the hypothalamus.
- **Capillary loops** also penetrate the median eminence. The capillaries drain into the sinusoidal portal hypophysial vessels that carry blood down the pituitary stalk to the capillaries of the anterior pituitary.

- This system begins and ends in capillaries without going through the heart and is **therefore a true portal system**.
- In birds and some mammals, including humans, there is no other anterior hypophysial arterial supply other than capsular vessels and anastomotic connections from the capillaries of the posterior pituitary.

❖ **The median eminence is generally defined as the portion of the ventral hypothalamus from which the portal vessels arise. This region is outside the blood–brain barrier**

THIRST

- Decreases in ECF volume also stimulate thirst by a pathway independent of that mediating thirst in response to increased plasma osmolality (Figure 17–4). Thus, hemorrhage causes increased drinking even if there is no change in the osmolality of the plasma.
- The effect of ECF volume depletion on thirst is mediated in part **via** the renin–angiotensin system .

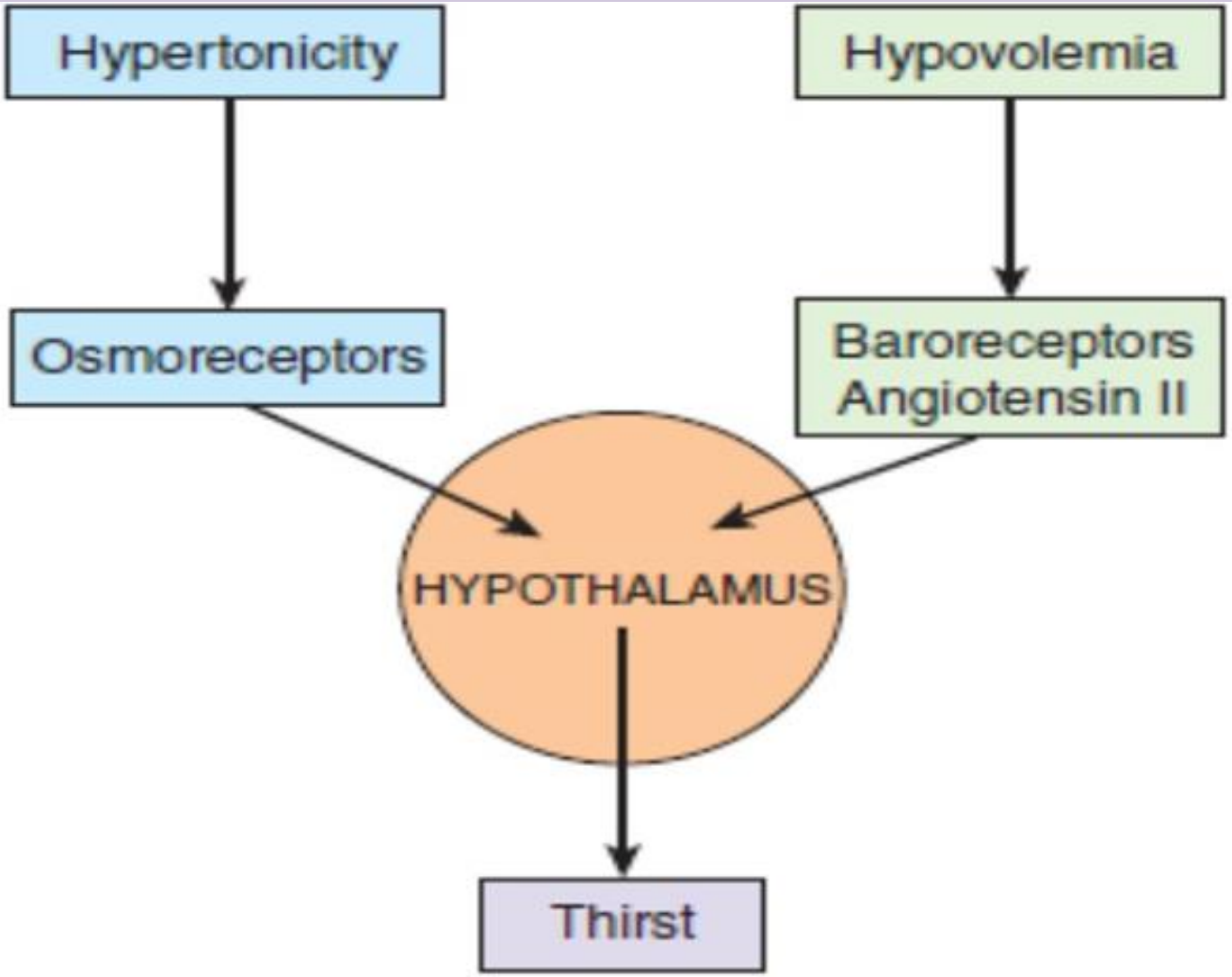


FIGURE 17–4 Diagrammatic representation of the way in which changes in plasma osmolality and changes in ECF volume affect thirst by separate pathways.

- **Renin** secretion is increased by hypovolemia and results in an increase in circulating angiotensin II. **The angiotensin II** acts on the **subfornical organ**, a specialized receptor area in the diencephalon, to stimulate the neural areas concerned with thirst.

- Some evidences suggest that it acts on the organum vasculosum of the lamina terminalis (OVLT) as well. These areas are highly permeable and are two of the circumventricular organs located outside the blood–brain barrier.

- However, drugs that block the action of angiotensin II **do not completely** block the thirst response to hypovolemia, and it appears that the baroreceptors in the heart and blood vessels are also involved.

- The intake of liquids is increased during eating (prandial drinking). The increase has been called a learned or habit response, but it has not been investigated in detail. **One factor** is an increase in plasma osmolality that occurs as food is absorbed.

- **Another may be** an action of one or more gastrointestinal hormones on the hypothalamus When the sensation of thirst is obtunded, either by direct damage to the diencephalon or by depressed or altered states of consciousness, patients stop drinking adequate amounts of fluid.

- **Dehydration** results if appropriate measures are not instituted to maintain water balance. If the protein intake is high, the products of protein metabolism cause an osmotic diuresis, and the amounts of water required to maintain hydration are large.
- Most cases of **hypernatremia** are actually due to simple dehydration in patients with psychoses or hypothalamic disease who do not or cannot increase their water intake when their thirst mechanism is stimulated.
- **Lesions of the anterior communicating artery** can also obtund thirst because branches of this artery supply the hypothalamic areas concerned with thirst.

Control of posterior pituitary secretions

vasopressin & oxytocin

- In most mammals, the hormones secreted by the **posterior pituitary** gland are arginine vasopressin (AVP) and oxytocin.
- In hippopotami and most pigs, arginine in the vasopressin molecule is **replaced by** lysine to form lysine vasopressin.
- The posterior pituitaries of some species of pigs and marsupials contain a mixture of arginine and lysine vasopressin.
- The posterior lobe nano peptides with a disulfide ring at one end.

BIOSYNTHESIS, INTRANEURONAL TRANSPORT, & SECRETION

- The hormones of the posterior pituitary gland **are synthesized in the cell bodies** of the magnocellular neurons in the supraoptic and paraventricular nuclei
- and transported down the axons of these neurons to their endings in the posterior lobe, **where they are secreted** in response to electrical activity in the endings.
- Oxytocin and vasopressin are typical **neural hormones,** that is, hormones secreted into the circulation by nerve cells.

vasopressin & oxytocin in other locations

Vasopressin-secreting neurons are found in the suprachiasmatic nuclei, and vasopressin and oxytocin are also found in the endings of neurons that project from the paraventricular nuclei to the brainstem and spinal cord. These neurons appear to be involved in cardiovascular control.

In addition, vasopressin and oxytocin are synthesized in the gonads and the adrenal cortex, and oxytocin is present in the thymus. The functions of the peptides in these organs are unsettled.

Vasopressin Receptors

- There are at least three kinds of vasopressin receptors: V1A, V1B, and V2.
- All are G-protein–coupled.
- The V1A and V1B receptors act through phosphatidylinositol hydrolysis to increase intracellular Ca2+ concentrations.
- The V2 receptors act through Gs to increase cyclic adenosine monophosphate levels.

Effects of Vasopressin

- Because one of its principal physiologic effects is the retention of water by the kidney, vasopressin is often called the antidiuretic hormone (ADH). It increases the permeability of the collecting ducts of the kidney so that water enters the hypertonic interstitium of the renal pyramids. The urine becomes concentrated and its volume decreases.
- The overall effect is therefore retention of water in excess of solute; consequently, the effective osmotic pressure of the body fluids is decreased.
- **In the absence of vasopressin**, the urine is hypotonic to plasma, urine volume is increased, and there is a net water loss. **Consequently**, the osmolality of the body fluid rises.

Effects of Oxytocin

- In humans, oxytocin acts primarily on the breasts and uterus, though it appears to be involved in luteolysis as well.
- A G-protein–coupled oxytocin receptor has been identified in human myometrium, and a similar or identical receptor is found in mammary tissue and the ovary.
- It triggers increases in intracellular Ca2+ levels.

Anterior Pituitary Hormones

- The anterior pituitary secretes **six** hormones: adrenocorticotropic hormone (corticotropin, **ACTH**), thyroid-stimulating hormone (**thyrotropin, TSH**), growth hormone (**GH**), follicle-stimulating hormone (**FSH**), luteinizing hormone (**LH**), and prolactin (**PRL**).

- An additional polypeptide, β-lipotropin (β-LPH), is secreted with ACTH, but its physiologic role is unknown

Nature of Hypothalamic Control

- Anterior pituitary secretion is **controlled by** chemical agents carried in the portal hypophysial vessels from the hypothalamus to the pituitary. These substances used to be **called** *releasing and inhibiting factors*,
- but now they are commonly called hypophysiotropic hormones.
- The latter term seems appropriate **since** they are secreted into the bloodstream and act at a distance from their site of origin. Small amounts escape into the general circulation, but they are at their highest concentration in portal hypophysial blood.

Hypophysiotropic Hormones

There are **six** established hypothalamic releasing and inhibiting hormones (Figure 17–10):

- Corticotropin-releasing hormone (**CRH**);
- Thyrotropin-releasing hormone (**TRH**);
- Growth hormone–releasing hormone (**GRH**);
- Growth hormone–inhibiting hormone (**GIH**, now generally called somatostatin);
- Luteinizing hormone–releasing hormone (**LHRH**, now generally known as gonadotropin-releasing hormone [GnRH]);
- Prolactin-inhibiting hormone (**PIH**).

In addition, hypothalamic extracts contain prolactin-releasing activity, and a prolactin-releasing hormone (PRH) has been postulated to exist.

Receptors for most of the hypophysiotropic hormones are **coupled to G-proteins**.

There are two human CRH receptors: **hCRH-RI** and **hCRH-RII**.

The physiologic role of hCRH-RII is unsettled, though it is found in many parts of the brain. In addition, a CRH-binding protein in the peripheral circulation inactivates CRH.

It is also found in the cytoplasm of corticotropes in the anterior pituitary, and in this location it might play a role in receptor internalization. However, the exact physiologic role of this protein is unknown. Other hypophysiotropic hormones do not have known binding proteins.

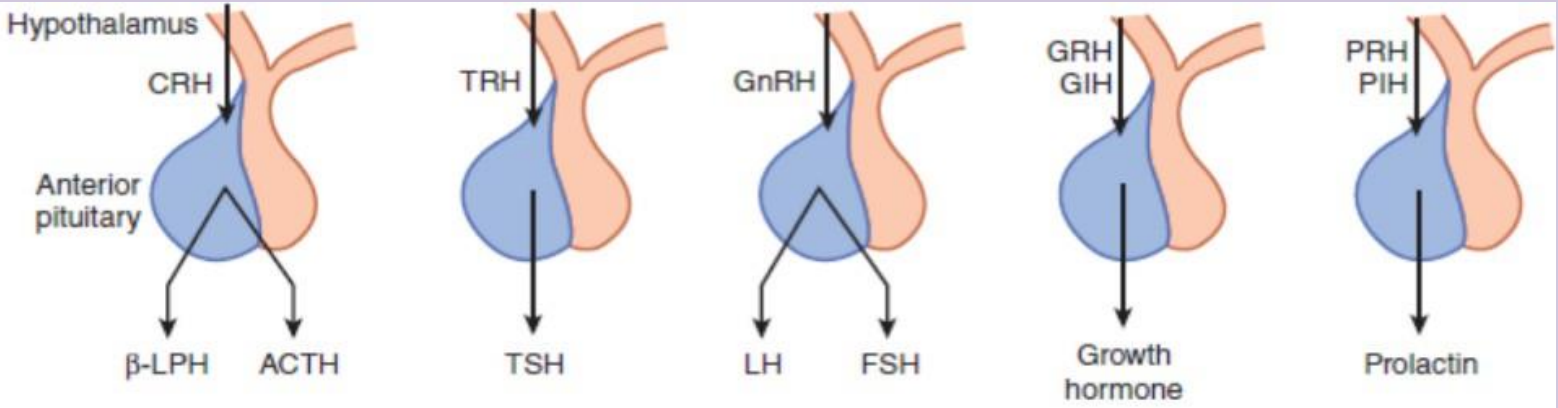


FIGURE 17–10 **Effects of hypophysiotropic hormones on the secretion of anterior pituitary hormones.**

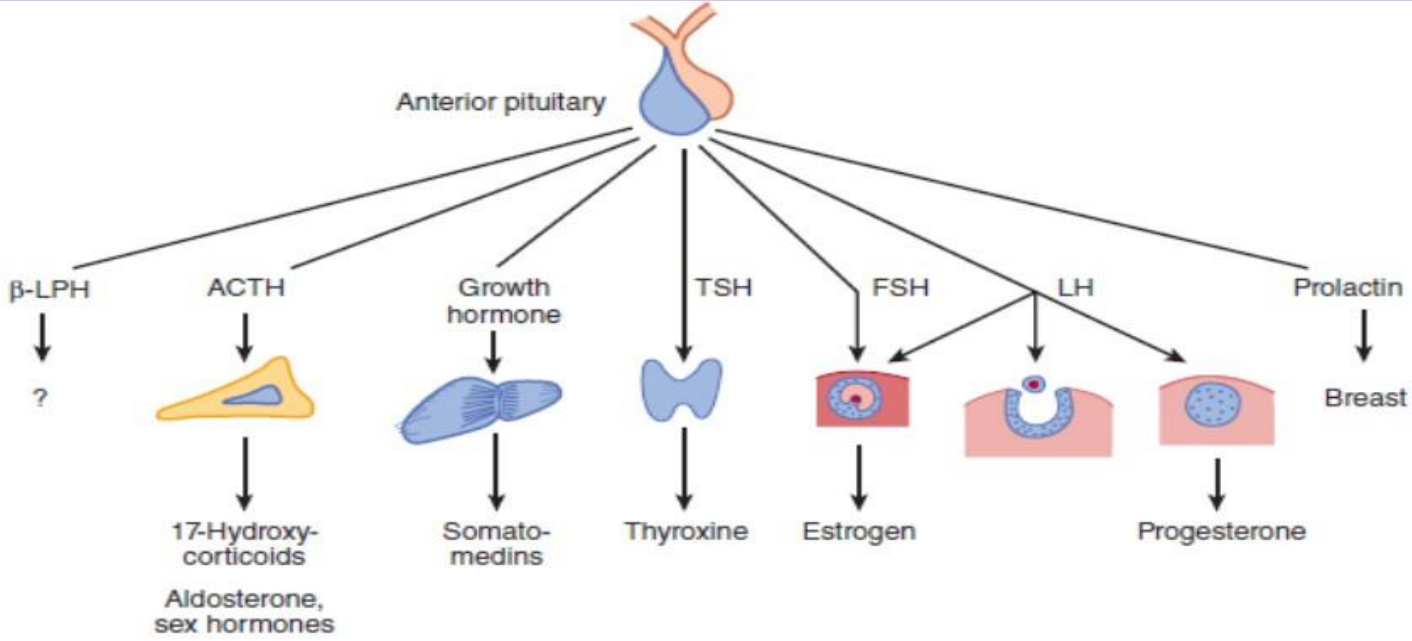


FIGURE 17–9 **Anterior pituitary hormones.** In women, FSH and LH act in sequence on the ovary to produce growth of the ovarian follicle, ovulation, and formation and maintenance of the corpus luteum. Prolactin stimulates lactation. In men, FSH and LH control the functions of the testes. ACTH, adrenocorticotropic hormone; β-LPH, β-lipotropin; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.