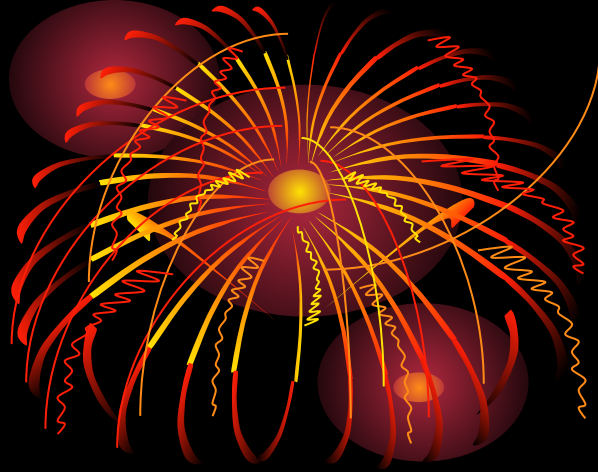
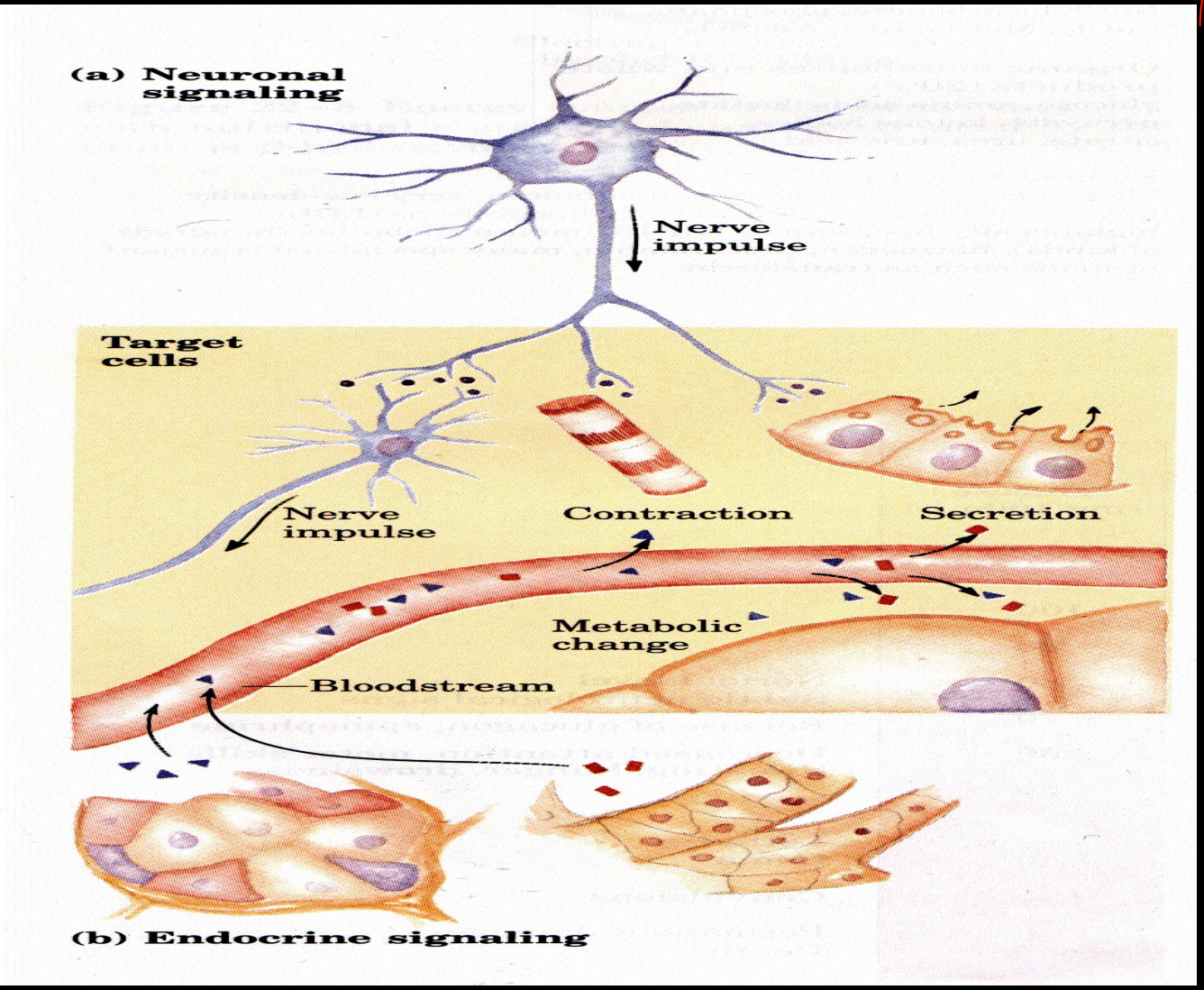


Lecture N 6

Hormones

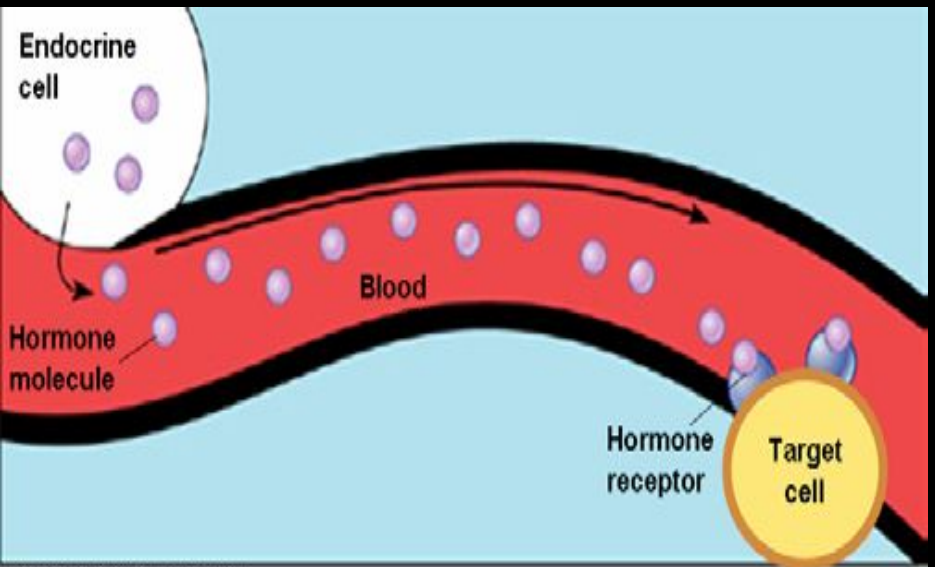
Part I

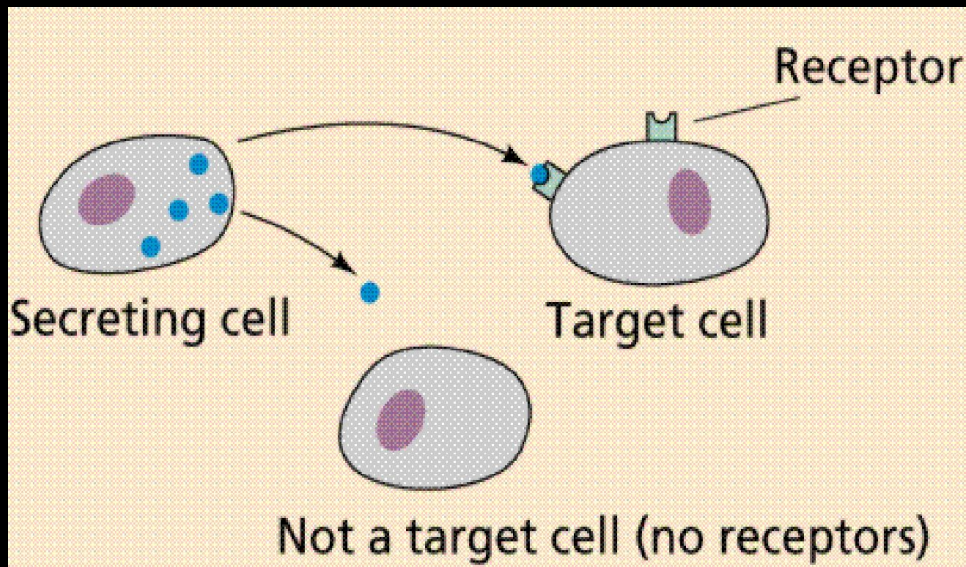
Signaling by the neuroendocrine system



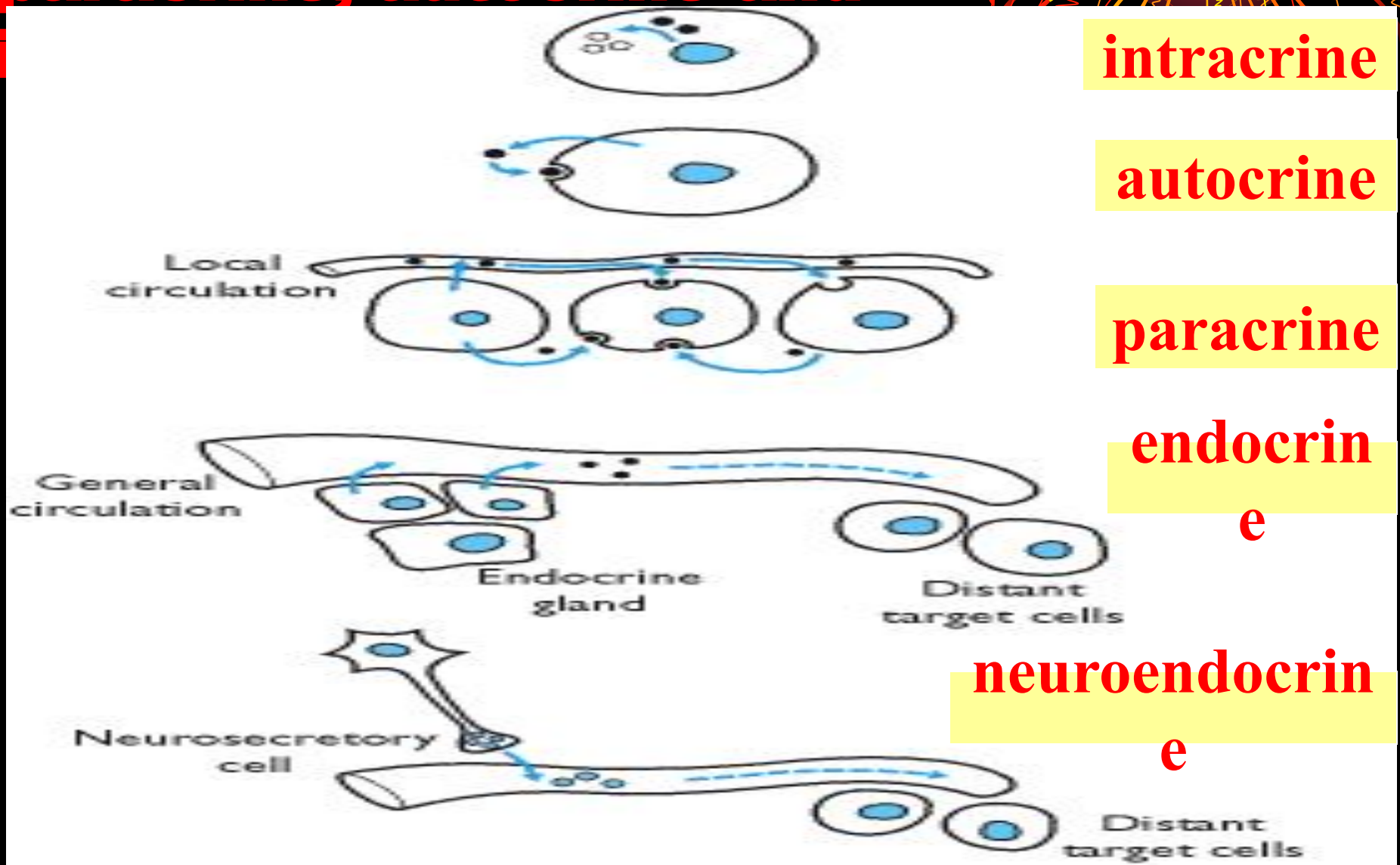
- The coordination of the body's diverse metabolic activities is achieved by hormonal and neuronal signaling

- **Hormone: A chemical substance synthesized in small amounts by an endocrine tissue and carried in the blood to another tissue, where it acts as a messenger to regulate the function of the target tissue or organ.**





Chemical signalling - endocrine, paracrine, autocrine and i



intracrine

autocrine

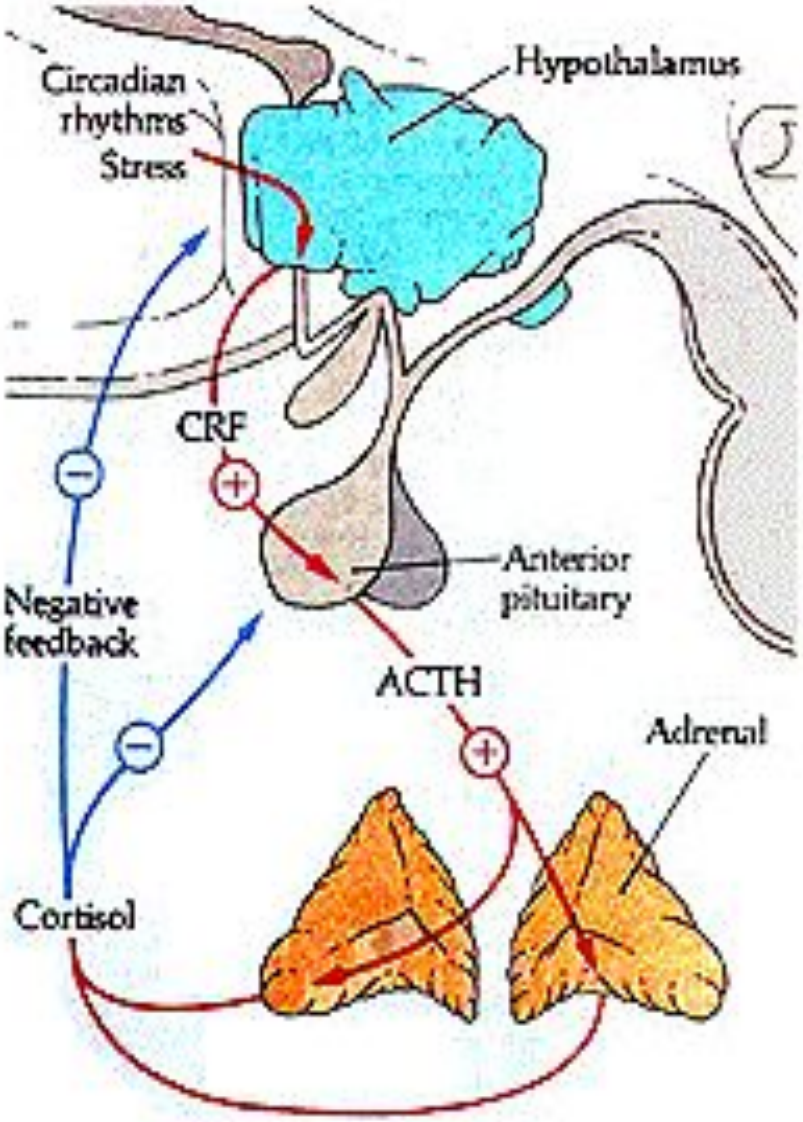
paracrine

endocrine

neuroendocrine

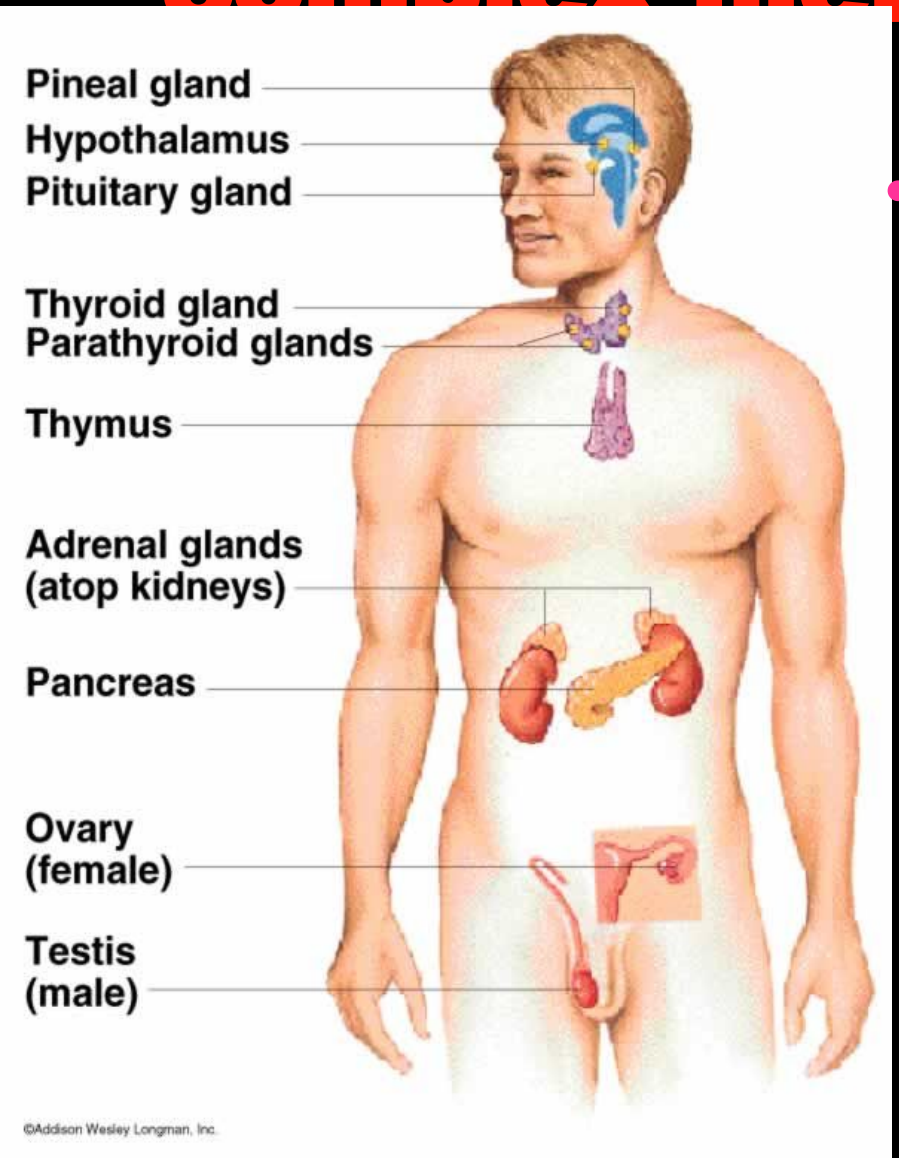
Function of hormones

- **HOMEOSTASIS**
- **Reproduction**
- **Growth and development**
- **Maintenance of internal environment**
- **Production, utilization and storage of energy**



- **At a minimum, a hormonally regulated system must include a secretary gland, a receptor for the hormone on or within the target cell, and some feedback mechanism (complex feedback loops) that regulates the secretion of the hormone in response to the function being regulated.**

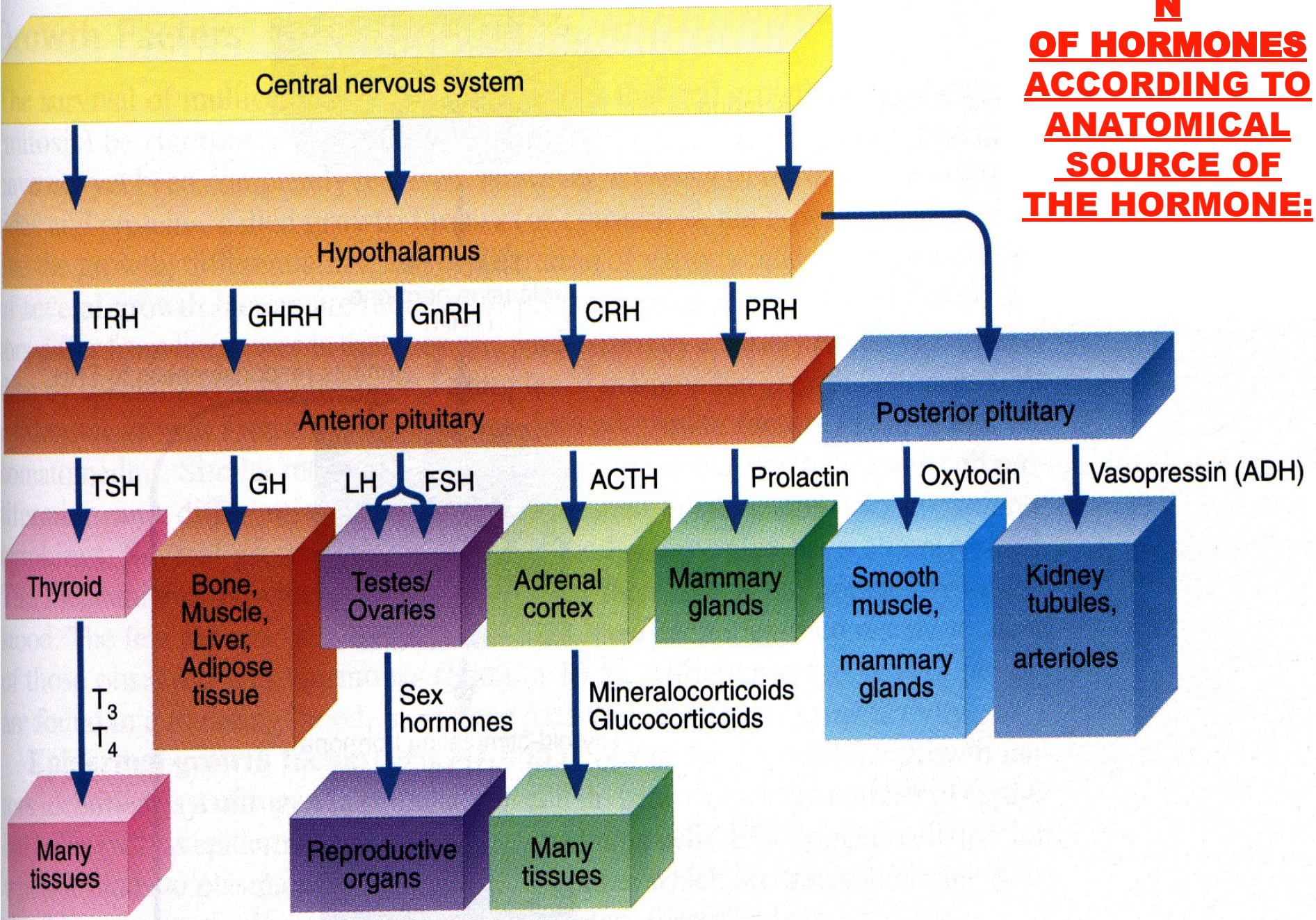
Hormones function in a complex hierarchy.



- Hormone act in hierarchy of function. The hypothala-mus functions at the top of hierarchy of many hormone-producing tissues and is the coordination center of the endocrine system. It receives neural input from diverse regions of the brain and feedback signals from hormones circulating in the blood.


CLASSIFICATION
OF HORMONES

CLASSIFICATION OF HORMONES ACCORDING TO ANATOMICAL SOURCE OF THE HORMONE:

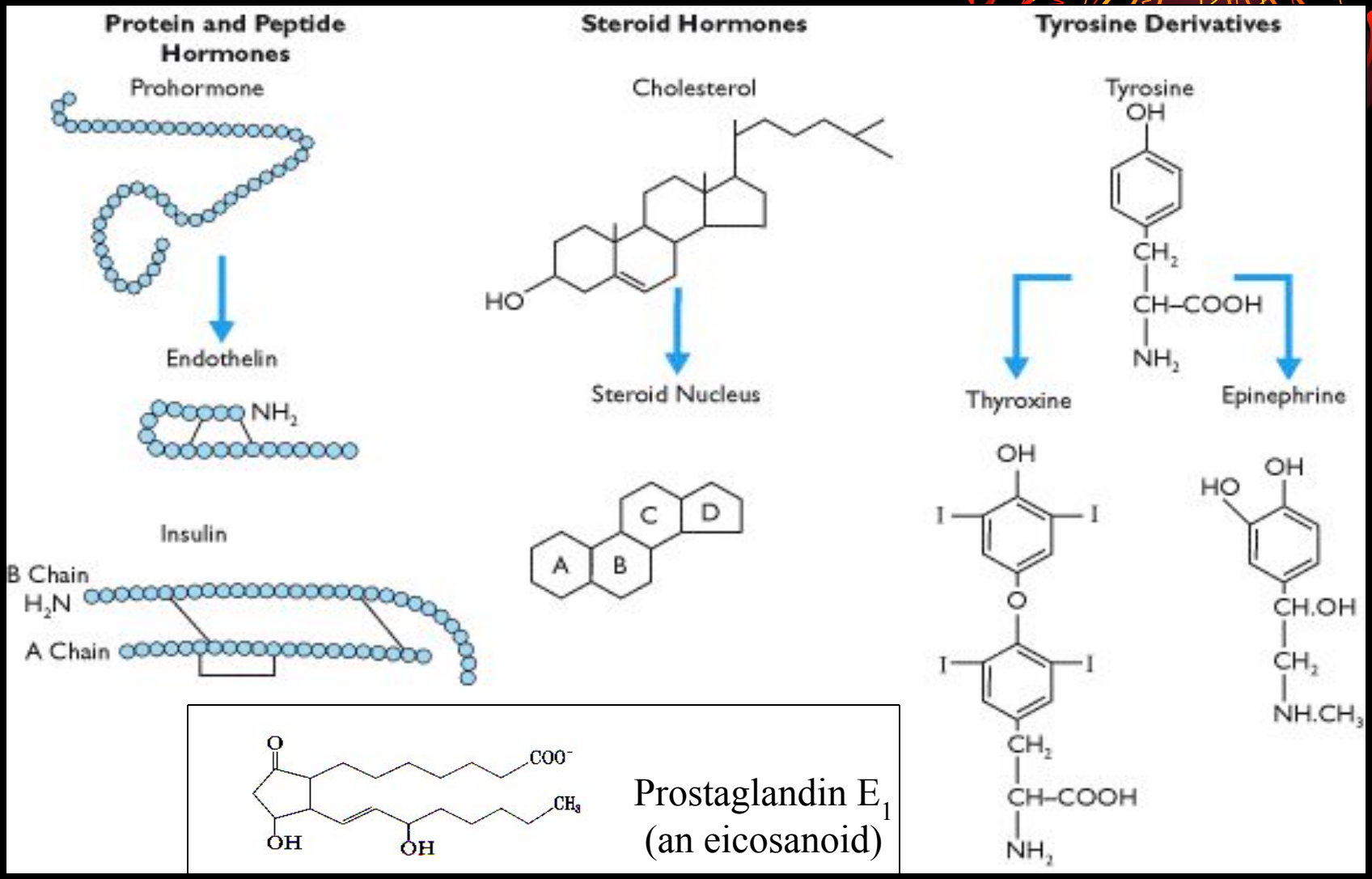


CLASSIFICATION OF HORMONES ACCORDING TO CHEMICAL COMPOSITION:

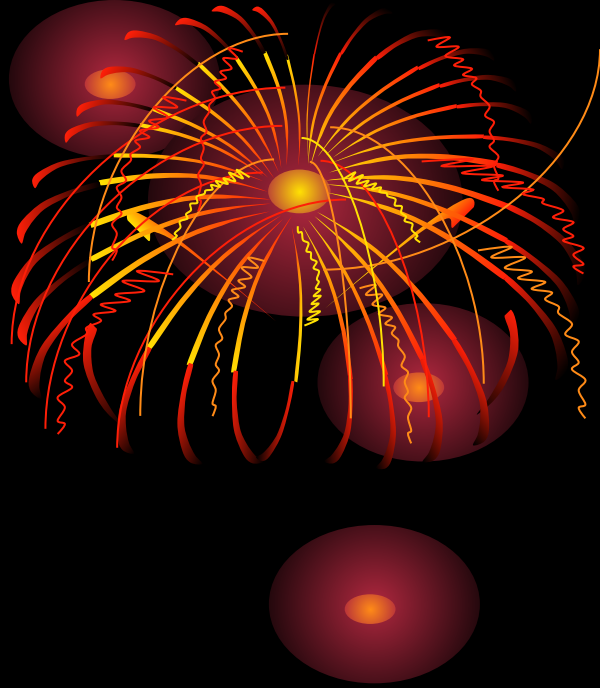
- **The peptide hormones, which may have from 3 to over 200 amino acid residues, include all of the hormones of the hypothalamus and pituitary and the pancreatic hormones insulin, glucagon, and somatostatin.**
- **The amine hormones, low molecular weight compounds derived from the amino acid tyrosine, include water-soluble epinephrine and norepinephrine of the adrenal medulla and the less water-soluble thyroid hormones.**

- The steroid hormones, which are fat-soluble, include the adrenal cortical hormones, hormone forms of vitamin D, and the androgens and estrogens (the male and female sex hormones). They move through the bloodstream bound to specific carrier proteins.
- Eicosanoids are derivatives of the 20-carbon polyunsaturated fatty acid arachidonate. All three subclasses of eicosanoids (prostaglandins, leukotrienes, and thromboxanes) are unstable and insoluble in water; these signaling molecules generally do not move far from the tissue that produced them, and they act primarily on cells very near their point of release.

CLASSIFICATION OF HORMONES ACCORDING TO CHEMICAL COMPOSITION:

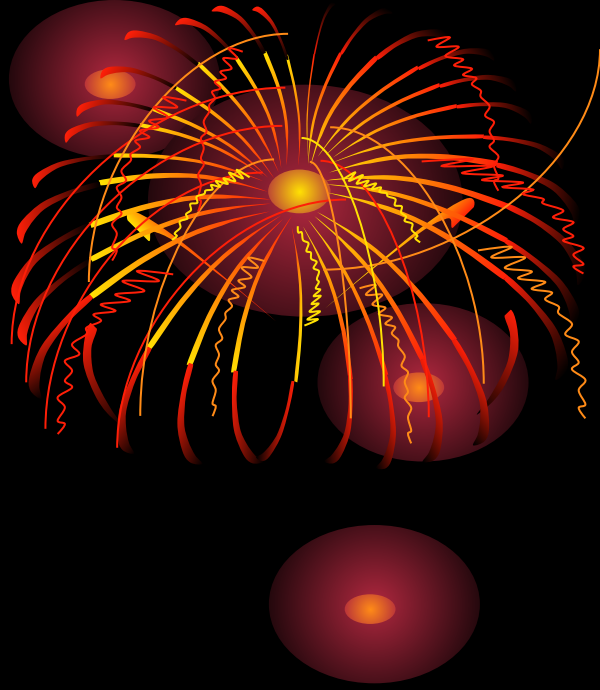


Protein/Peptide Hormones

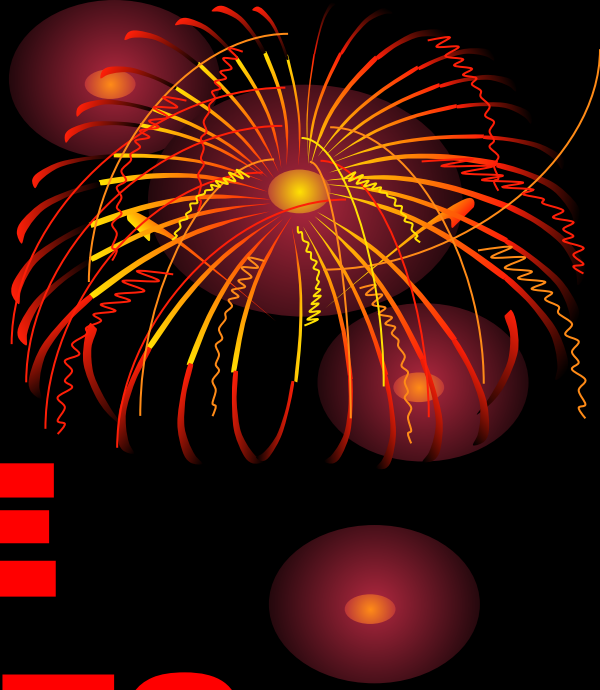


- Hydrophilic
- Large
- Can't fit through membrane
- Second messenger mechanism of action
- Most hormones
- Example: Insulin

Steroid Hormones

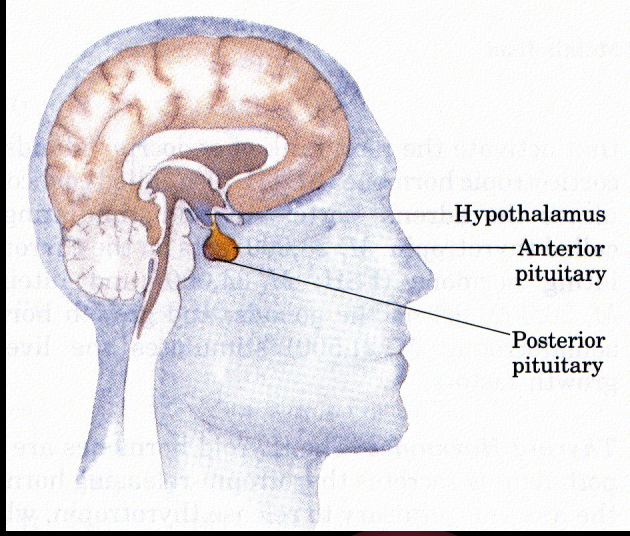


- Small
- Hydrophobic/Lipophilic
- Travel in blood w/carrier
- Cytoplasmic or nuclear receptors
- change protein synthesis
- Example: estradiol



PEPTIDE HORMONES

Why is the Hypothalamus so Important?



STIMULUS

↓

Hypothalamus

Releasing Hormone

(Release-Inhibiting Hormone)

↓

Pituitary

Stimulating Hormone

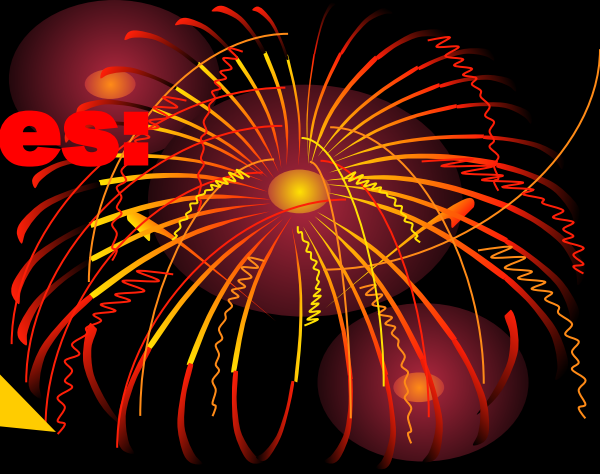
↓

Gland

Hormone

→ **Target**

Hypothalamic hormones:



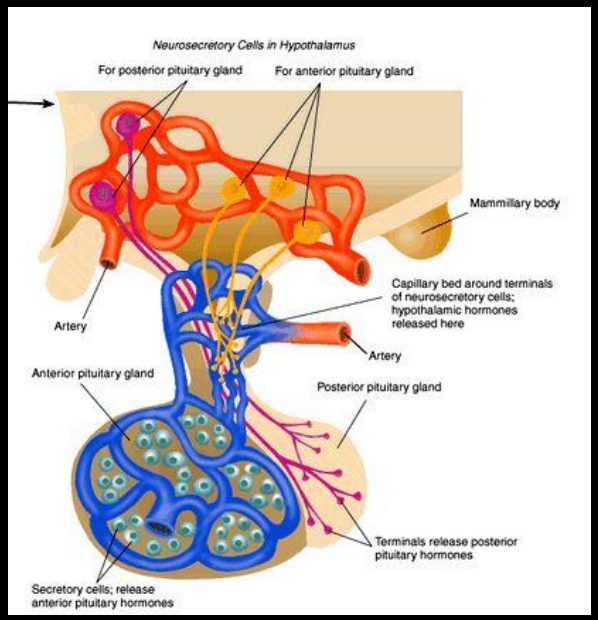
Liberins or releasing hormones:

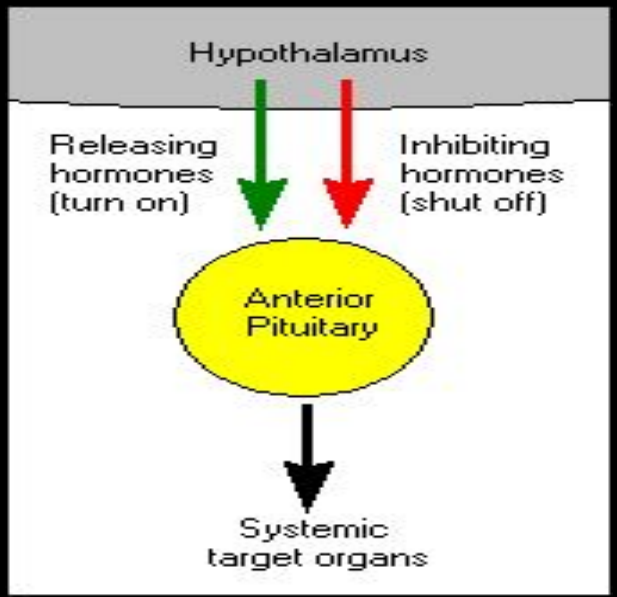
1. Corticotropin releasing factor
2. Thyrotropin releasing hormone
3. Gonadotropin releasing factor
4. Growth hormone releasings factor
5. Prolactin-reliasing factor
6. Melanotropin releasing factor

Statines or inhibiting hormones

1. Somatostatin
2. Prolactostatin

Hypothalamic hormones.

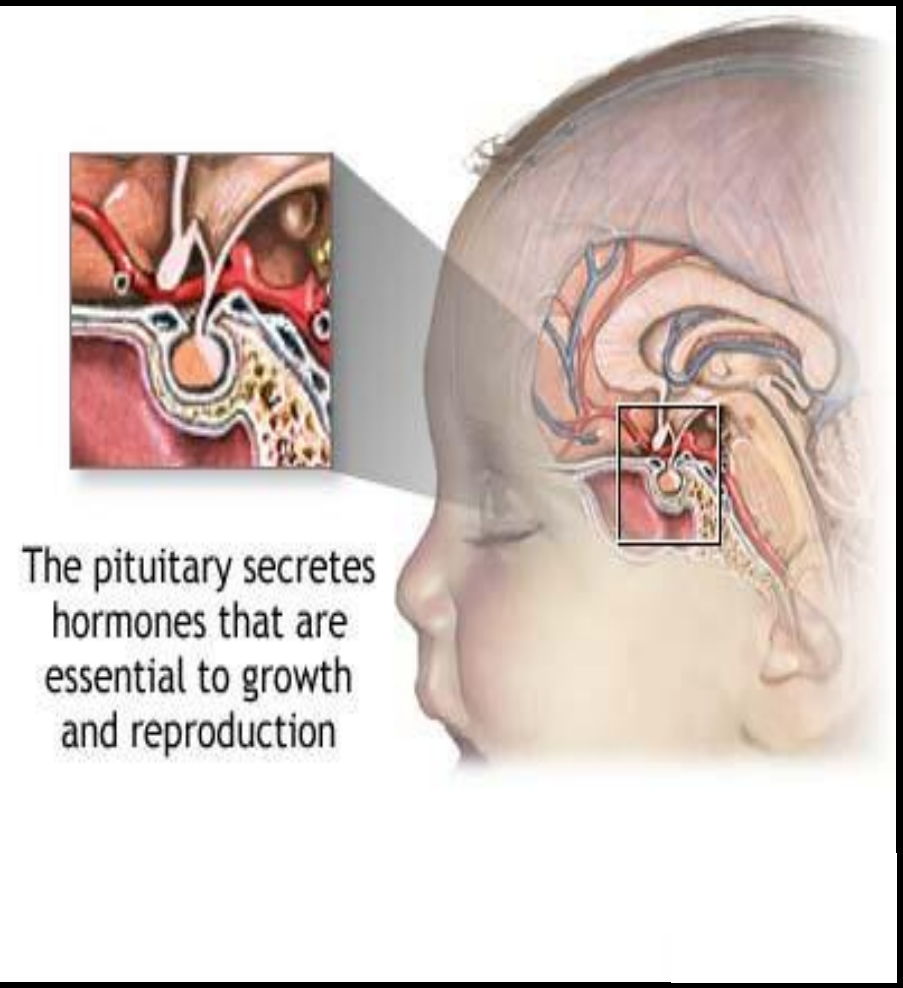




Hypothalamic releasing and inhibiting hormones are carried directly to the anterior pituitary gland via hypothalamic-hypophyseal portal veins. Specific hypothalamic hormones bind to receptors on specific anterior pituitary cells, modulating the release of the hormone they produce.

Pituitary hormones.

THE PITUITARY GLAND

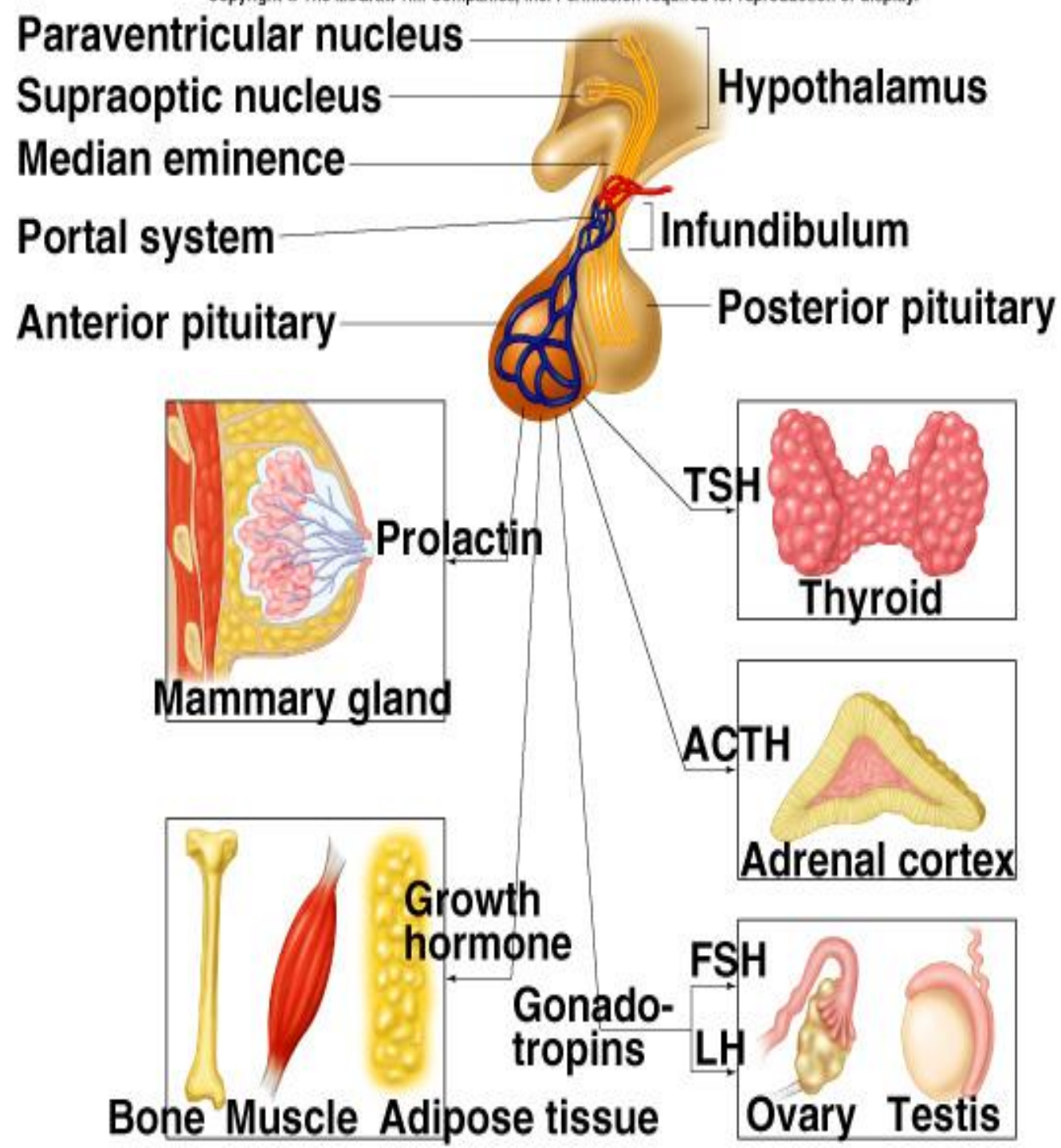


The pituitary gland is composed of distinctive parts:

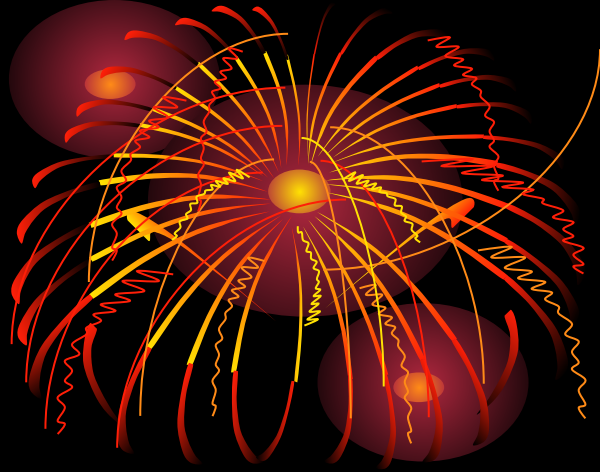
- The anterior pituitary
- The intermediate lobe
- The posterior pituitary (neurohypophysis)

- **Anterior Pituitary Hormones and Their Hormones**
  - **1. Growth Hormone**
  - **2.Thyroid Stimulating Hormone**
  - **3.Adrenocorticotropic Hormone**
  - **4.Prolactin**
  - **5.Gonadotropins: Luteinizing Hormone and Follicle Stimulating Hormone**
- **Intermediate lobe (pars intermedia)**

  1.MSH (melanocyte stimulating hormone)
- **Posterior Pituitary Hormones**
  - **1.Antidiuretic Hormone (Vasopressin)**
  - **2.Oxytocin**



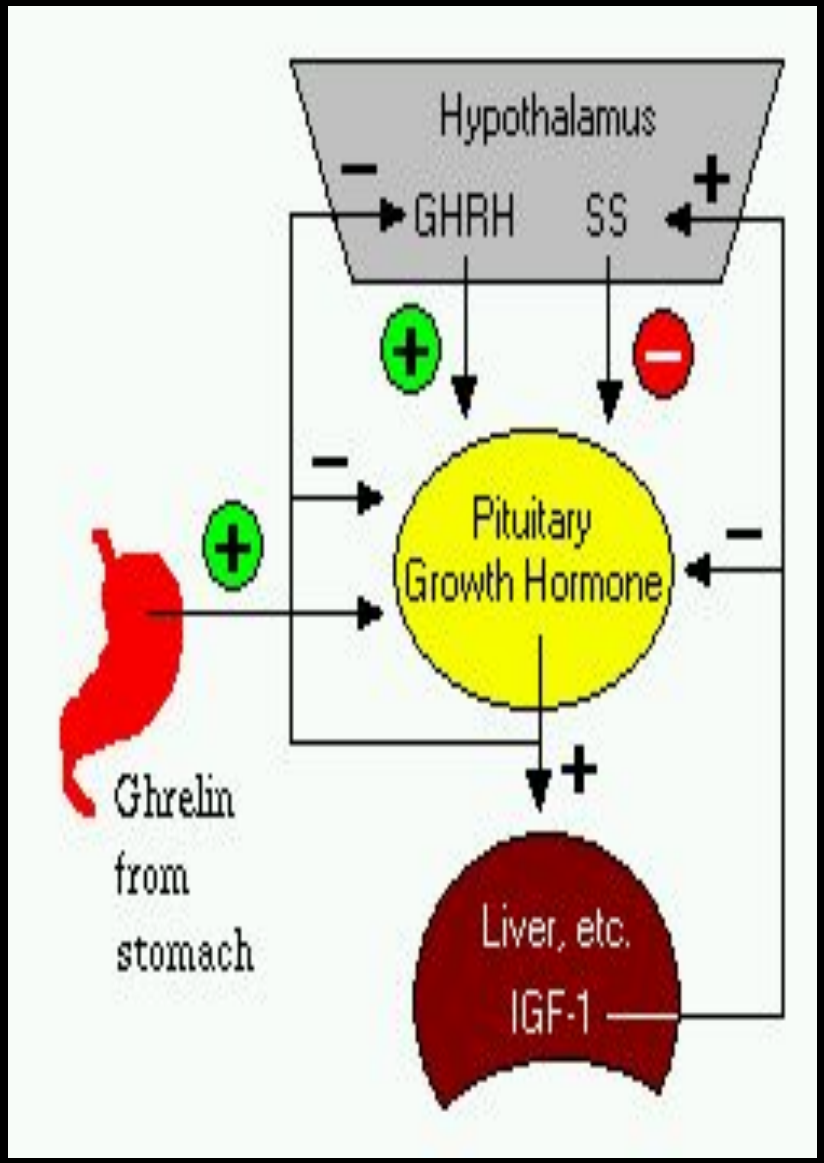
TARGET ORGAN OF PITUITARY HORMONE.



1.

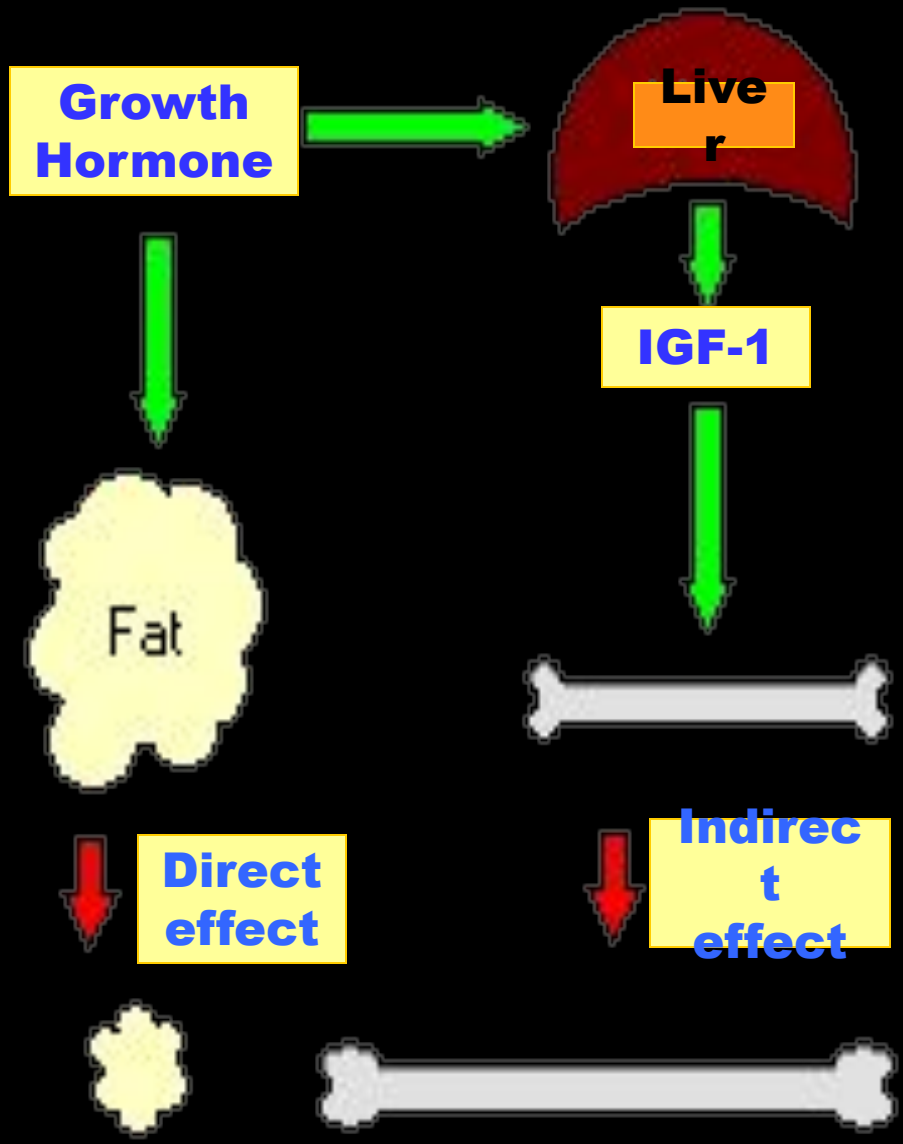
Growth Hormone (GH)

Growth Hormone (GH)



- **Human growth hormone (somatotropin) is a protein of 191 amino acids. The GH-secreting cells are stimulated to synthesize and release GH by the intermittent arrival of growth hormone releasing hormone (GHRH) from the hypothalamus.**

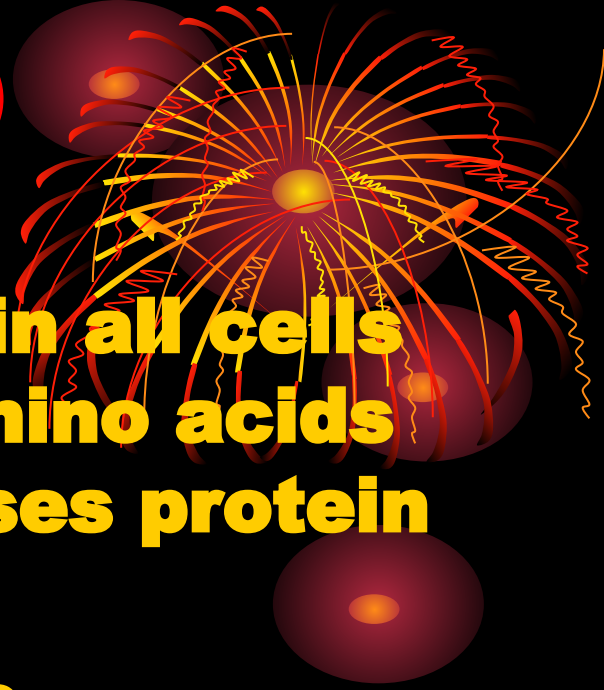
Growth Hormone (GH)



GH promotes body growth by:

- binding to receptors on the surface of liver cells
- this stimulates them to release insulin-like growth factor-1 (IGF-1; also known as somatomedin)
- IGF-1 acts directly on the ends of the long bones promoting their growth

Growth Hormone (GH)



- It promotes protein building in all cells (increase the transport of amino acids into muscle cells and increases protein synthesis)
- reduces use of carbohydrate (antagonist of insulin)
- increases use of fatty acids for energy (release of free fatty acids and glycerol from adipose tissue can increase ketogeneses if diabetes)
- GH influences on nitrogen, and mineral metabolism.

A lack of GH causes dwarfism.

- A deficiency state can result not only from a deficiency in production of the hormone, but in the target cell's response to the hormone.
- •Clinically, deficiency in growth hormone or receptor defects are as growth retardation or dwarfism.

An excess results in gigantism or acromegaly.

Gigantism, excess height and weight. Gigantism with normal body proportions and normal sexual development usually comes from excess GH in early childhood. Gigantism is usually treated with radiation, but gland surgery may also be used.

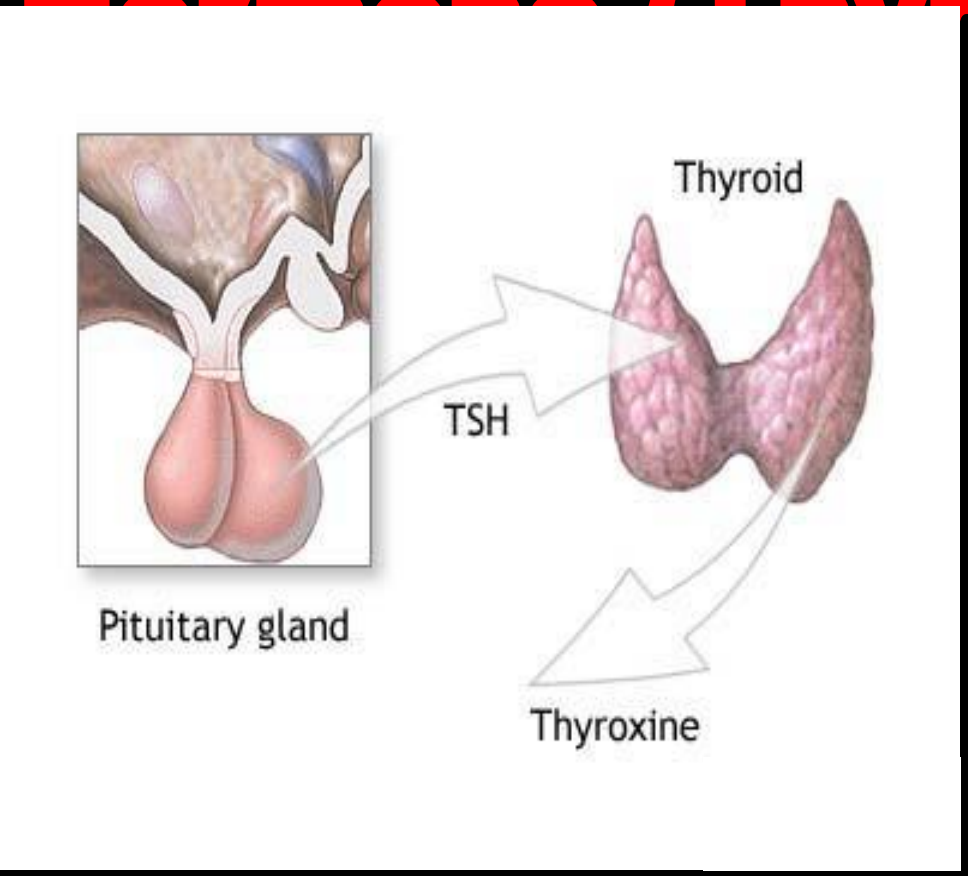
An excess results in gigantism or acromegaly.

Acromegaly , also called acromegalia. A long-term problem in which bones of the face, jaw, arms, and legs get larger. It occurs in middle-aged patients. It is caused by too much growth hormone. It is treated by x-rays to shrink the pituitary, or part of the pituitary gland is removed

2.

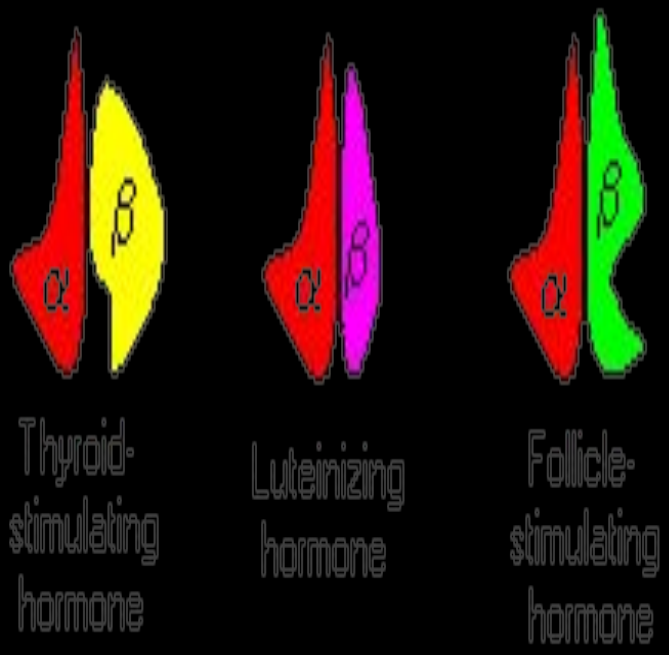
Thyroid-Stimulating Hormone (Thyrotropin)

Thyroid-Stimulating Hormone (Thyrotropin)



Thyroid-stimulating hormone, also known as thyrotropin, is secreted from cells in the anterior pituitary called *thyrotrophs*, finds its receptors on epithelial cells in the thyroid gland, and stimulates that gland to synthesize and release thyroid hormones.

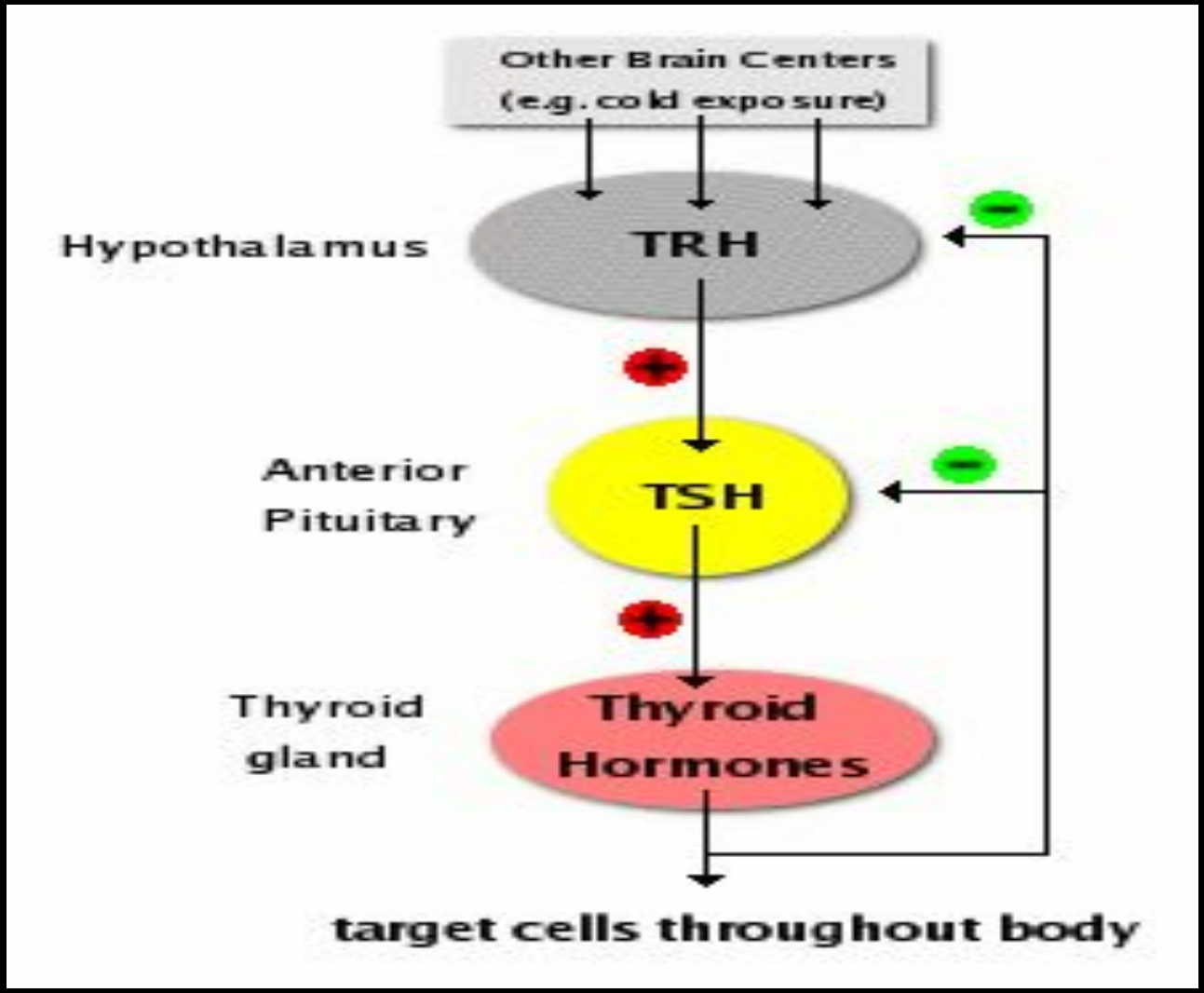
Thyroid Stimulating Hormone (TSH)



- TSH is a glycoprotein consisting of:
- a **beta** chain of 112 amino acids and
- an **alpha** chain of 89 amino acids.

The alpha chain is identical to that found in two other pituitary hormones, **FSH** and **LH** as well as in the hormone **chorionic gonadotropin**. Thus, its beta chain gives TSH its unique properties.

Regulation of secretion of thyroid-releasing hormone.



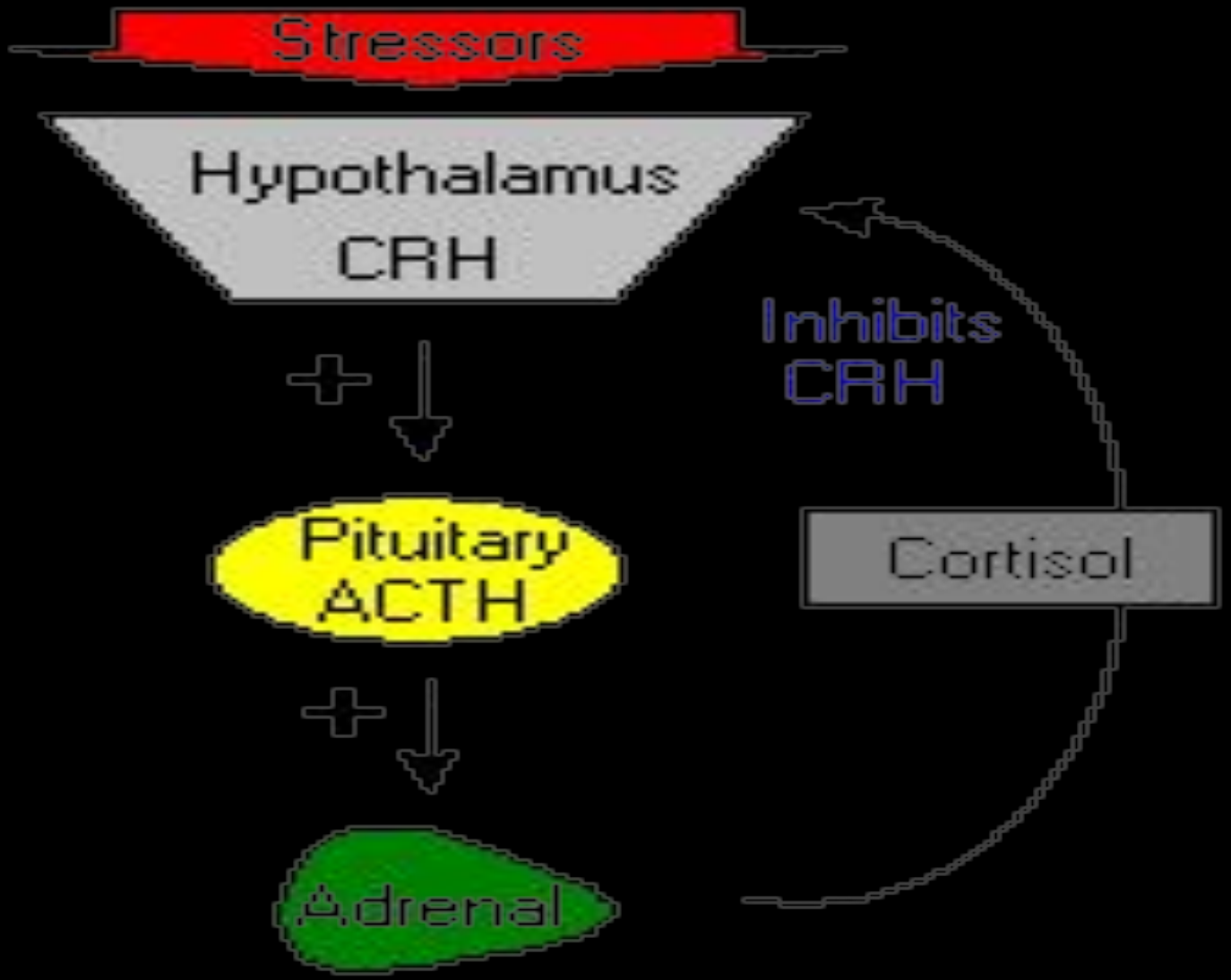
- Some people develop antibodies against their own TSH receptors. When these bind the receptors, they "fool" the cell into making more T_4 causing hyperthyroidism. The condition called thyrotoxicosis or Graves' disease.
- The deficiencies of TSH causes hypothyroidism: inadequate levels of T_4 and T_3.

3. Adrenocorticotropic Hormone (ACTH)

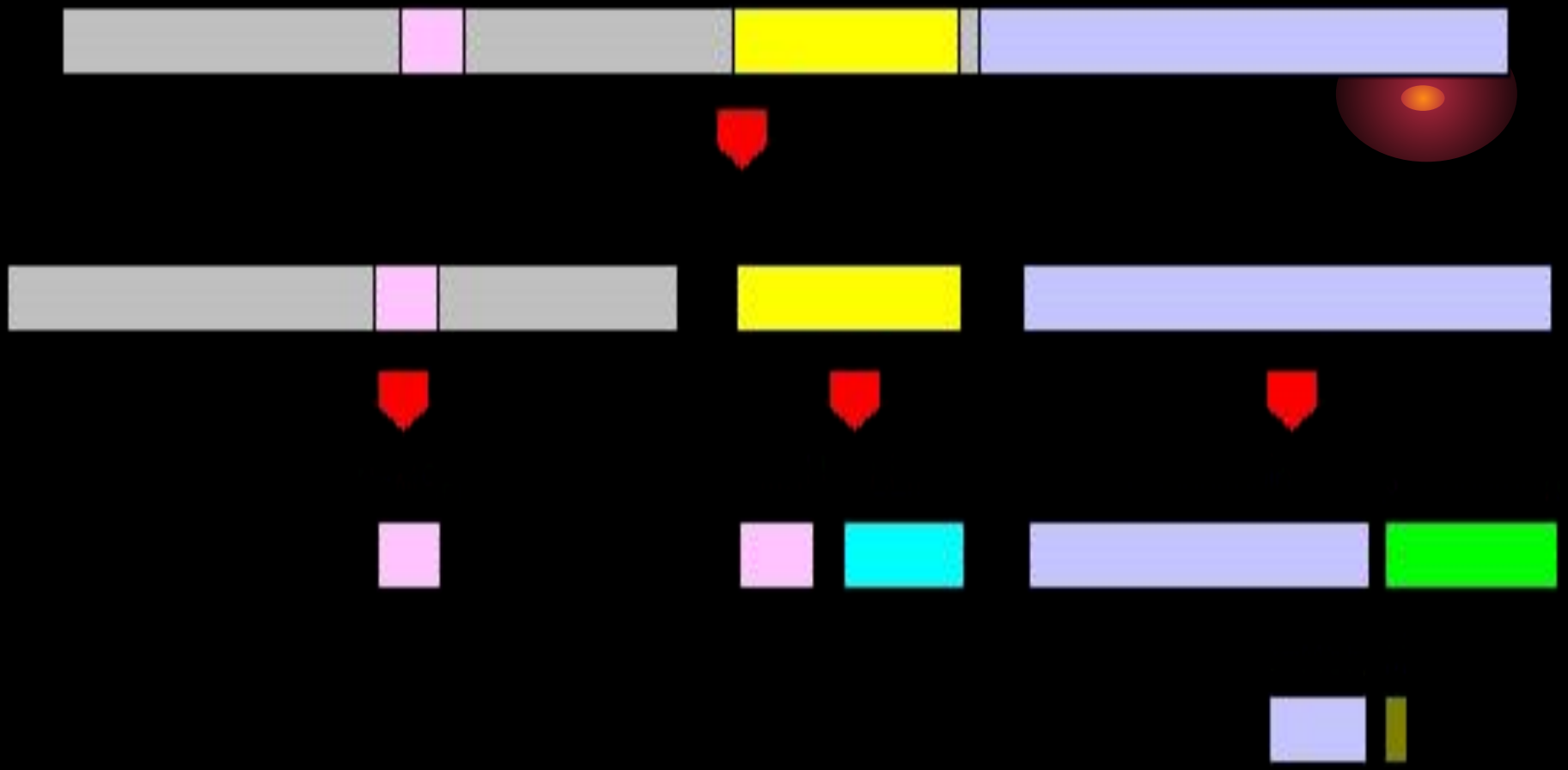
Adrenocorticotropic Hormone (ACTH)

- **Adrenocorticotropic hormone is single-chain polypeptide consisting of 39 amino acids, as its name implies, stimulates the adrenal cortex. More specifically, it stimulates secretion of glucocorticoids such as cortisol, and has little control over secretion of aldosterone, the other major steroid hormone from the adrenal cortex by enhancing the conversion of cholesterol to pregnenolone. Another name for ACTH is *corticotropin*.**

Adrenocorticotropic hormone



Adrenocorticotropic hormone



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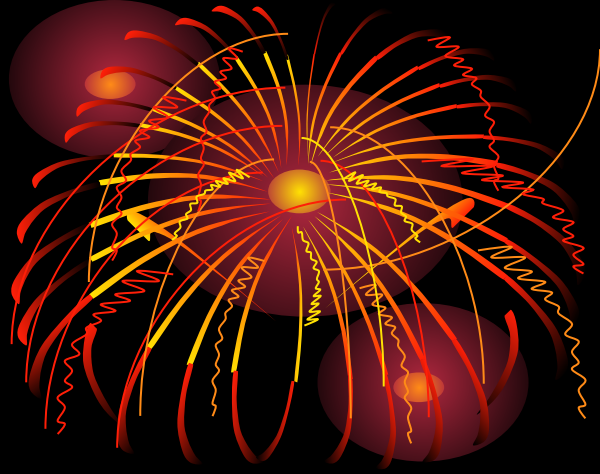


PROLACTIN

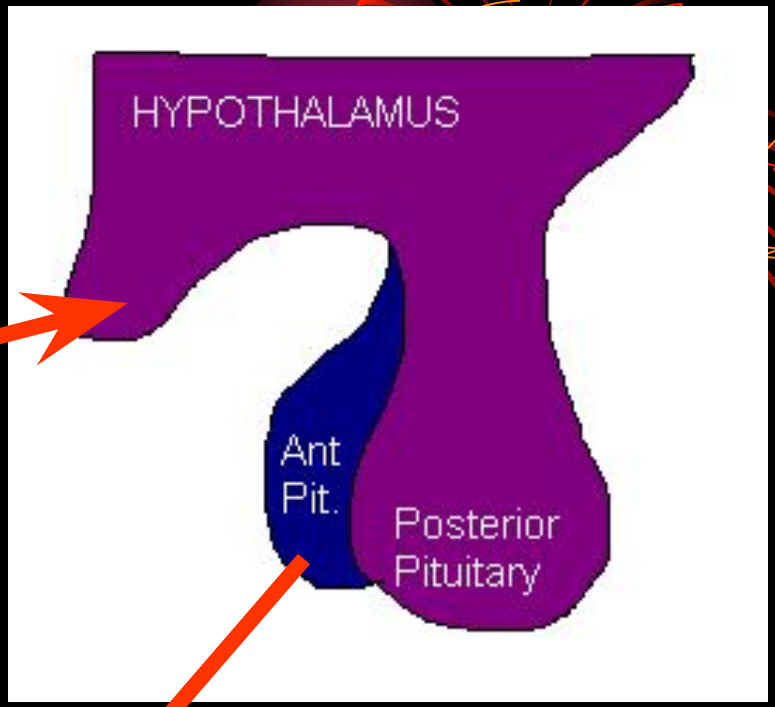
Prolactin

- **Prolactin – protein of 197 amino acids.**
- **Prolactin, acting with other hormones, starts the growth of the mammary glands. After childbirth, it helps to start and maintain the making of breast milk. This occurs in response to suckling by the infant. When suckling stops, prolactin slows and the breasts stop making milk.**

Prolactin has two major roles in milk production:

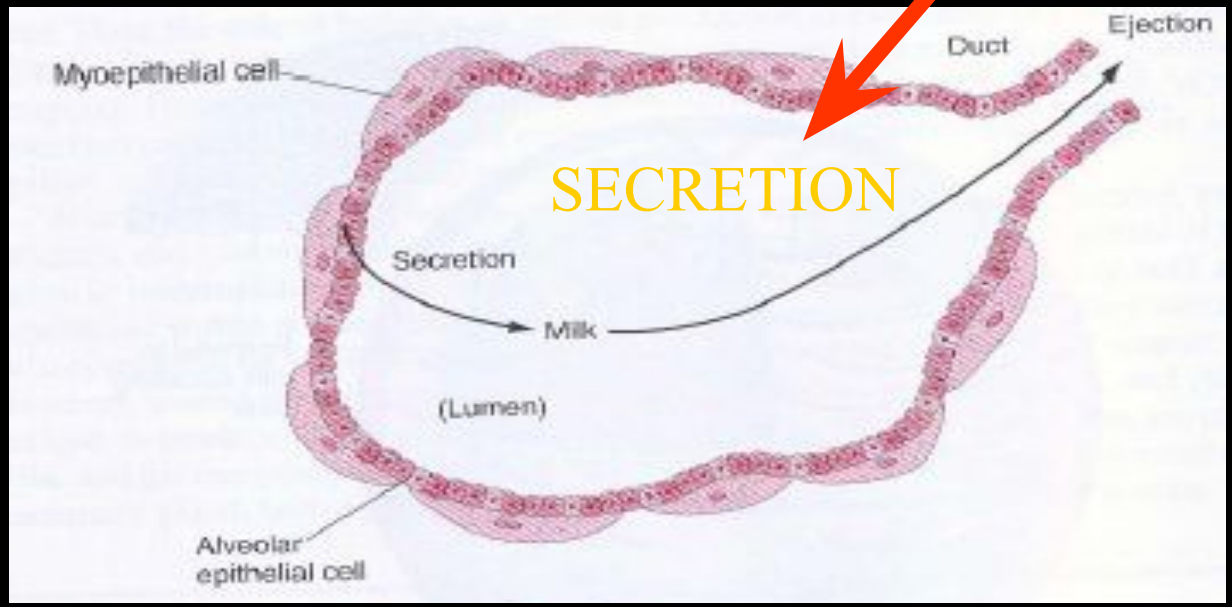
- Prolactin induces lobuloalveolar growth of the mammary gland. Alveoli are the clusters of cells in the mammary gland that actually secrete milk.

- Prolactin stimulates lactogenesis or milk production after giving birth. Prolactin, along with cortisol and insulin, act together to stimulate transcription of the genes that encode milk proteins.



PROLACTIN

SECRETION



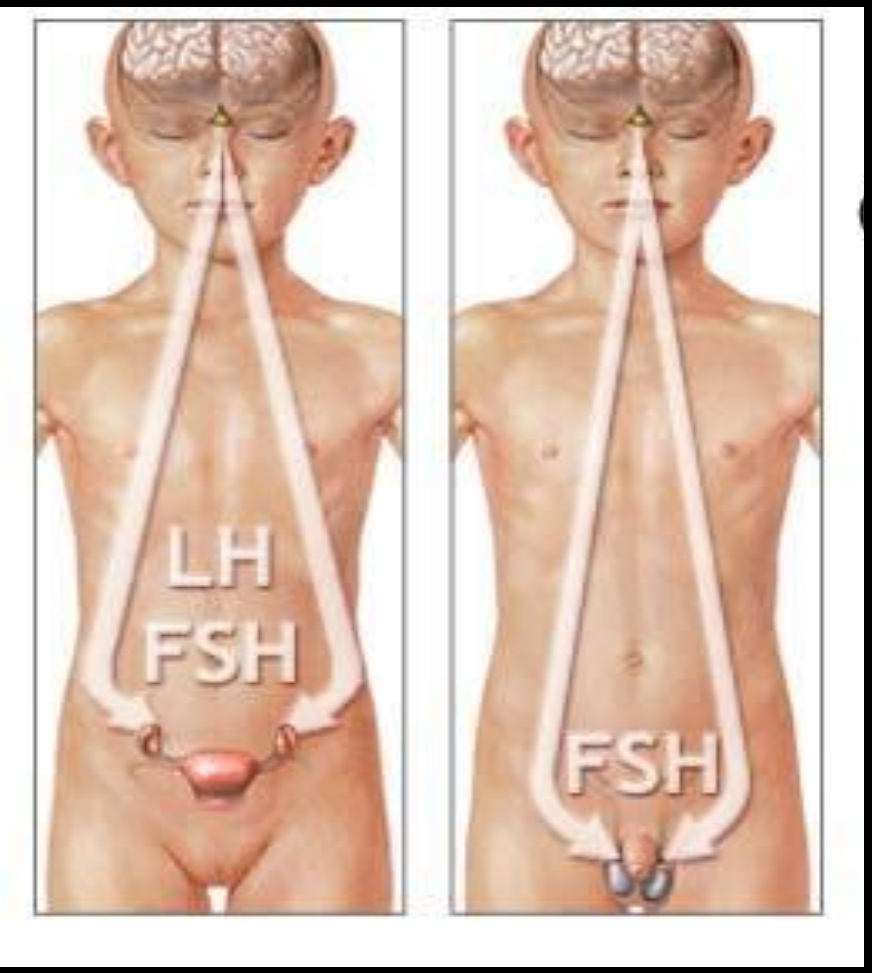
Disease States

- **Excessive secretion of prolactin - hyperprolactinemia - is a relative common disorder in humans. This condition has numerous causes, including prolactin-secreting tumors and therapy with certain drugs.**
- **Common manifestations of hyperprolactinemia in women include amenorrhea (lack of menstrural cycles) and galactorrhea (excessive or spontaneous secretion of milk). Men with hyperprolactinemia typically show hypogonadism, with decreased sex drive, decreased sperm production and impotence. Such men also often show breast enlargement (gynecomastia), but very rarely produce milk.**

5.

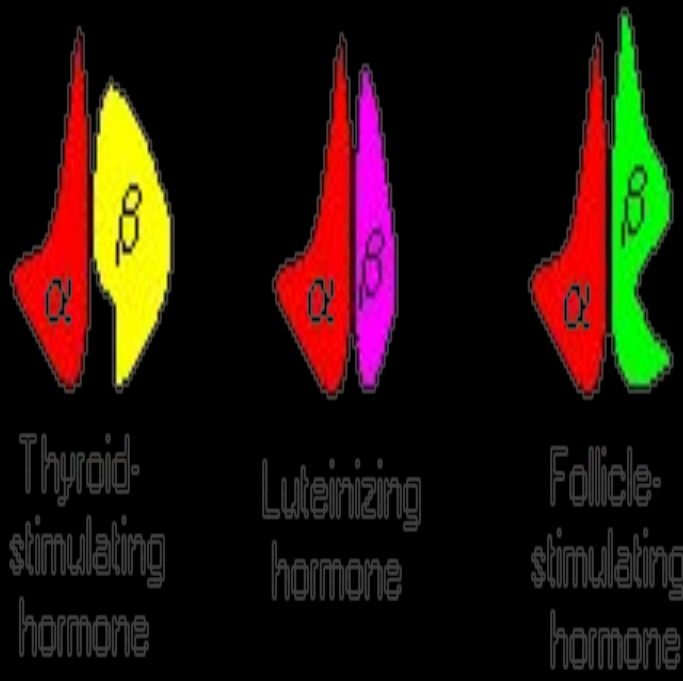
Gonadotropins: Luteinizing and Follicle Stimulating Hormones

Gonadotropins: Luteinizing and Follicle Stimulating Hormones



- **Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are called gonadotropins because stimulate the gonads - in males, the testes, and in females, the ovaries. They are not necessary for life, but are essential for reproduction.**

Gonadotropins.



- **As describef for thyroid-simulating hormone, LH and FSH are large glycoproteins composed of alpha and beta subunits. The alpha subunit is identical in all three of these anterior pituitary hormones, while the beta subunit is unique and endows each hormone with the ability to bind its own receptor.**

Physiologic Effects of Luteinizing

- **In both sexes, LH stimulates secretion of sex steroids from the gonads.**

In females, ovulation of mature follicles on the ovary is induced by a large burst of LH secretion known as the preovulatory LH surge. Residual cells within ovulated follicles proliferate to form corpora lutea, which secrete the steroid hormones progesterone and estradiol. LH is required for continued development and function of corpora lutea.

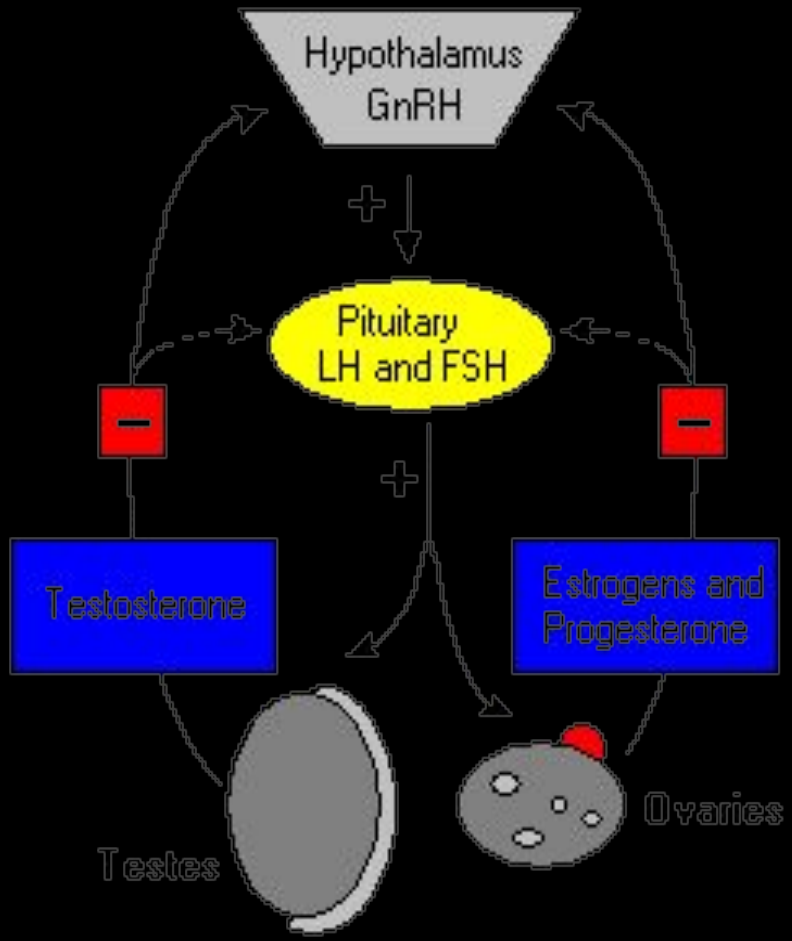
Luteinizing Hormone

- **In men In the testes, LH binds to receptors on Leydig cells, stimulating synthesis and secretion of testosterone. Theca cells in the ovary respond to LH stimulation by secretion of testosterone, which is converted into estrogen by adjacent granulosa cells.**

Follicle-Stimulating Hormone

- **As its name implies, FSH stimulates the maturation of ovarian follicles. Administration of FSH to humans and animals induces "superovulation", or development of more than the usual number of mature follicles and hence, an increased number of mature gametes.**
- **FSH is also critical for sperm production. It supports the function of Sertoli cells, which in turn support many aspects of sperm cell maturation.**

Control of Gonadotropin Secretion



- **The principle regulator of LH and FSH secretion is gonadotropin-releasing hormone or GnRH that synthesized and secreted from hypothalamic neurons and binds to receptors on gonadotrophs.**

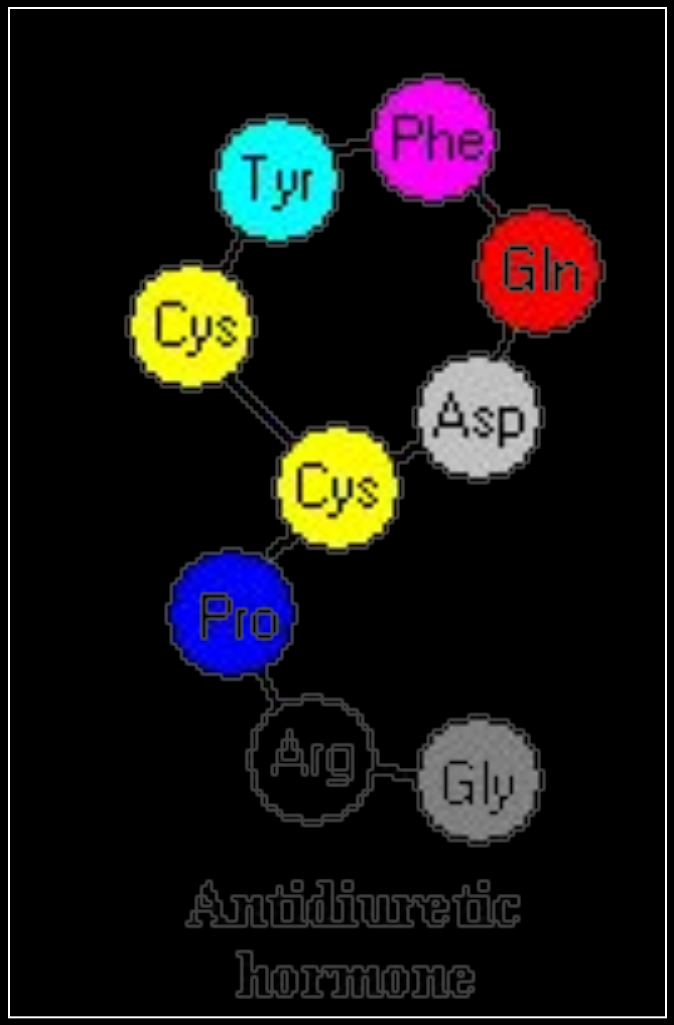
Disease States

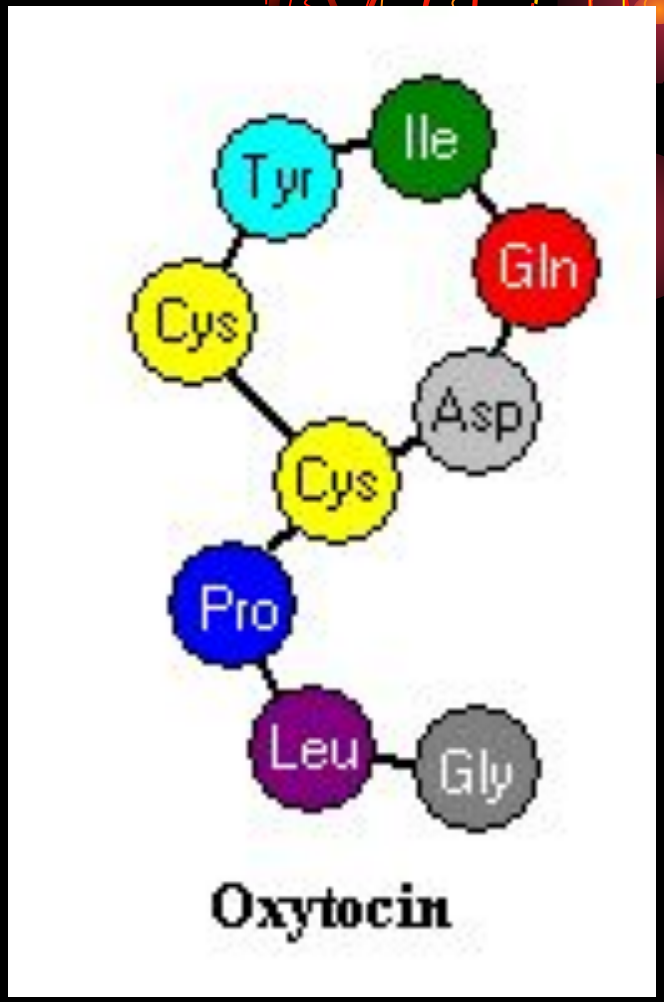
- **Diminished secretion of LH or FSH can result in failure of gonadal function (hypogonadism). This condition is typically manifest in males as failure in production of normal numbers of sperm. In females, cessation of reproductive cycles is commonly observed.**
- **Elevated blood levels of gonadotropins usually reflect lack of steroid negative feedback. Removal of the gonads from either males or females, as is commonly done to animals, leads to persistent elevation in LH and FSH. In humans, excessive secretion of FSH and/or LH most commonly the result of gonadal failure or pituitary tumors. In general, elevated levels of gonadotropins per se have no biological effect.**

Intermediate lobe: MSH (melanocyte stimulating hormone)

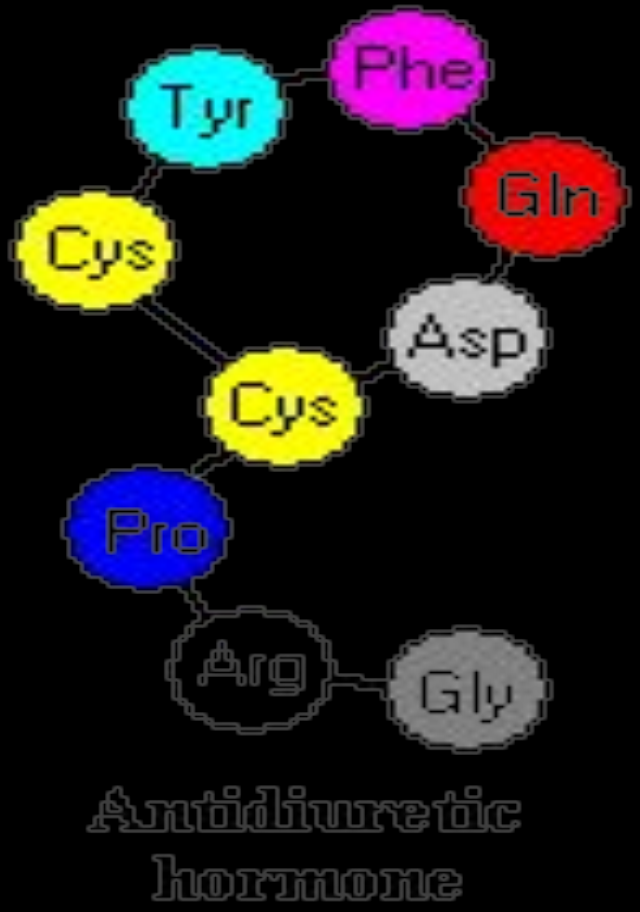
- Melanocyte-stimulating hormone (MSH): Known to control melanin pigmentation in the skin of most vertebrates.

Posterior Pituitary Hormones:



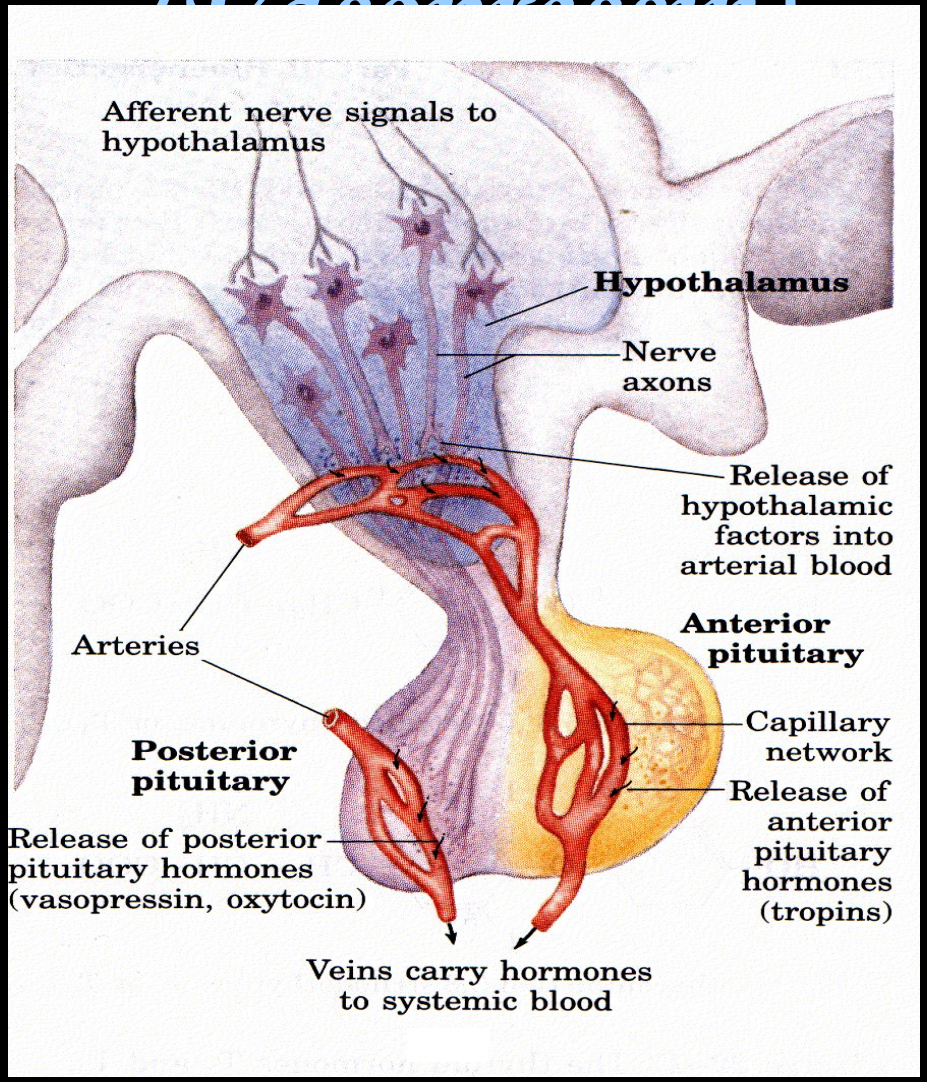


Antidiuretic Hormone (Vasopressin)



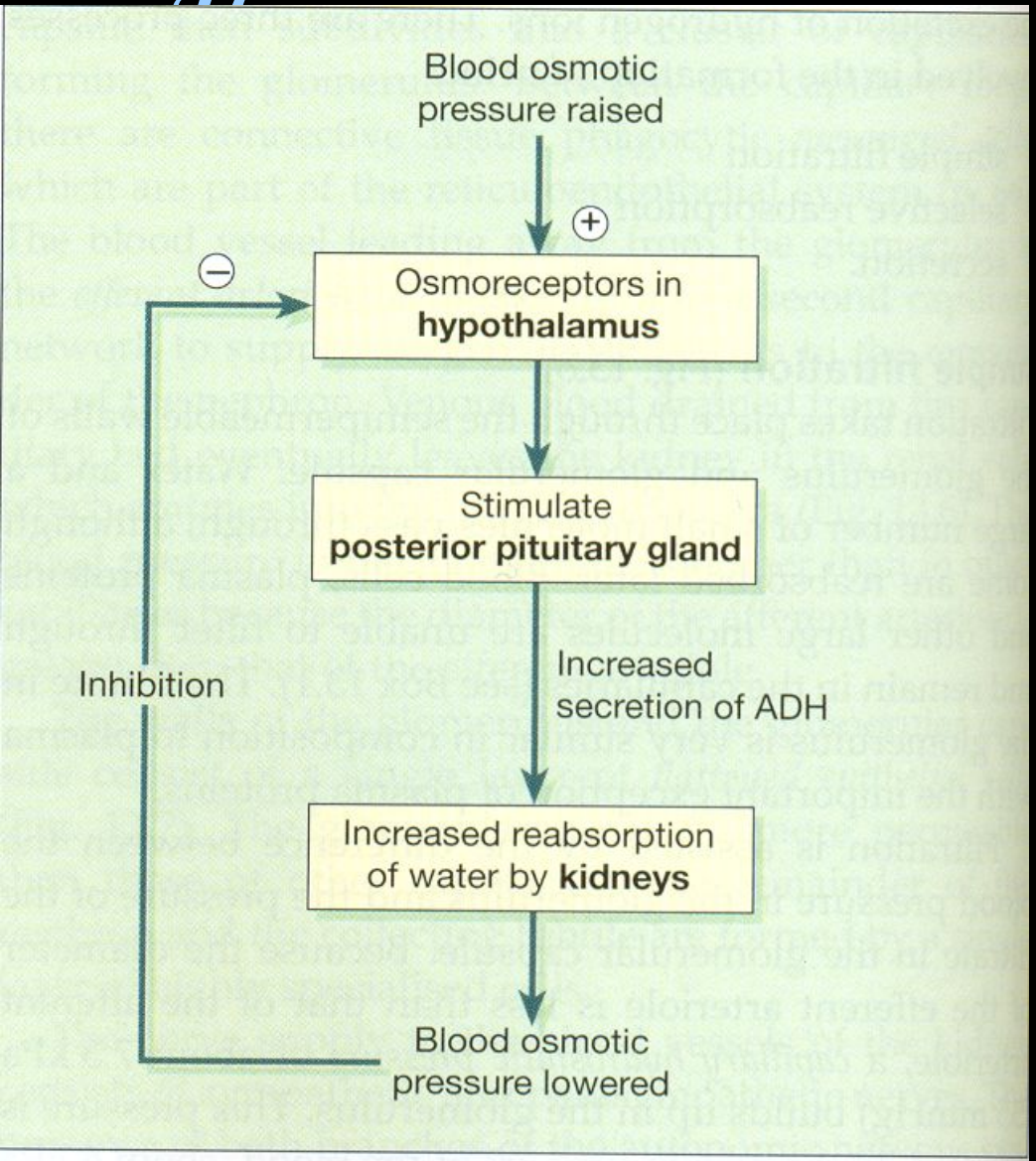
- **Antidiuretic hormone, also known as vasopressin, is a nine amino acid peptide secreted from the posterior pituitary.**

Antidiuretic Hormone (Vasopressin)



- **Within hypothalamic neurons, the hormone is packaged in secretory vesicles with a carrier protein called neurophysin, and both are released upon hormone secretion.**

Physiologic Effects of Antidiuretic

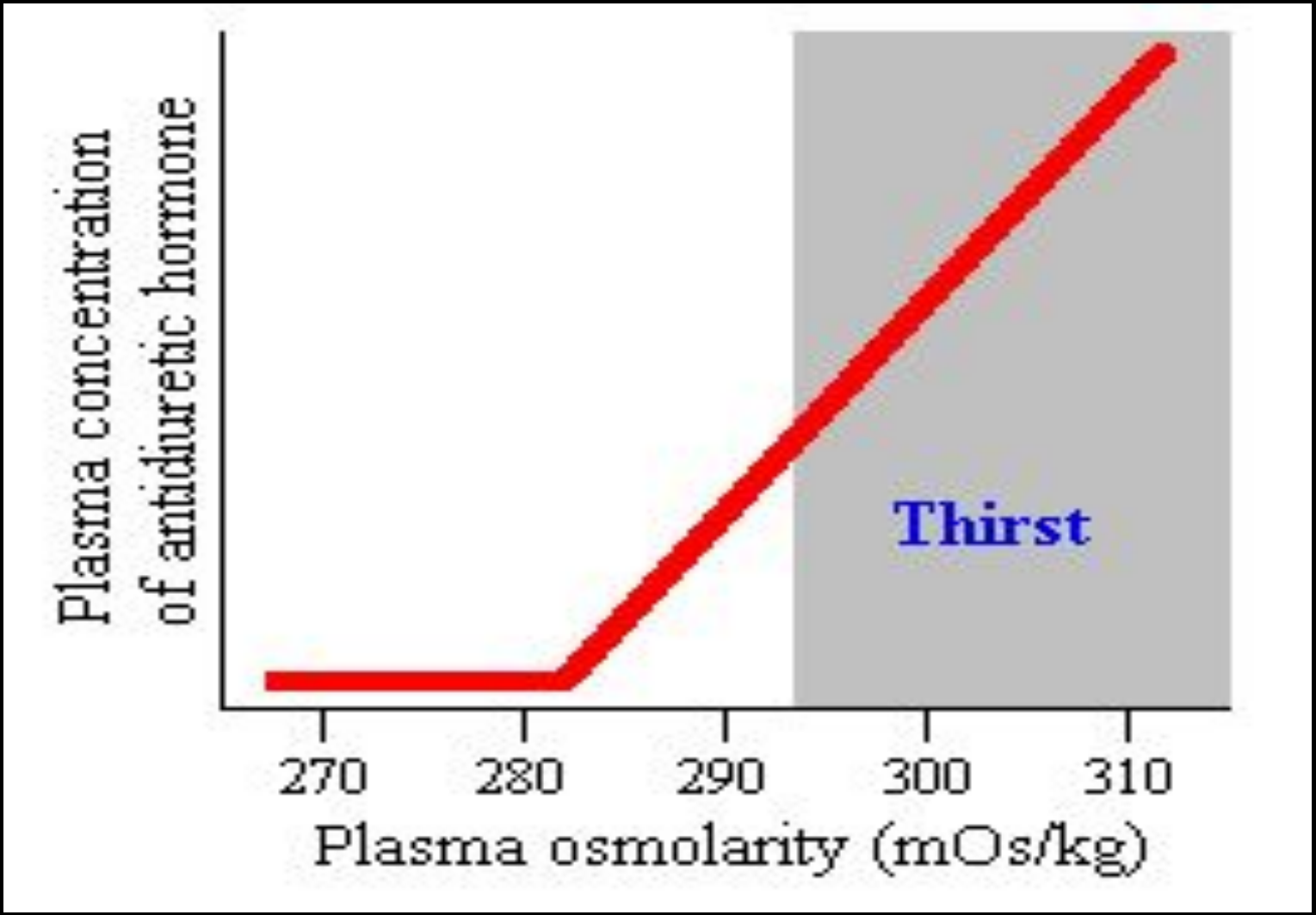


A hormone that increases blood pressure with increases reabsorption of water in kidney after signals from baro- and osmoreceptores.

Physiologic Effects of Antidiuretic Hormone

ADH is released when the blood volume falls, when a large amount of salt shows up in blood, or when pain, stress, or certain drugs are present. Nicotine, and large doses of certain drugs cause ADH to be released.

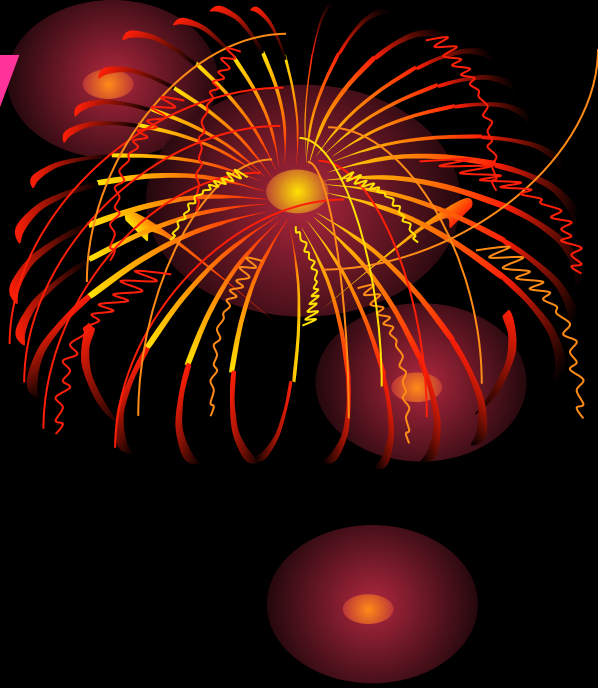
Parallel between antidiuretic hormone secretion and thirst.



Disease States

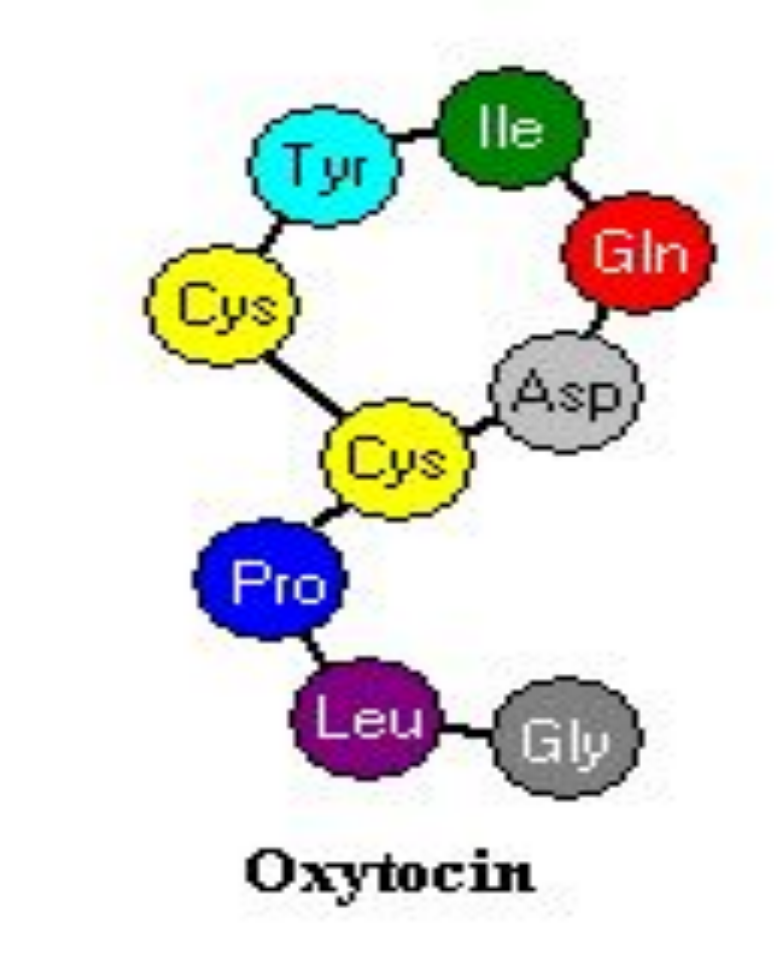
- **Diabetes insipidus is result of a lack of ADH**
- **The most common presenting signs and symptoms are**
  1. **unquenchable thirst,**
  2. **polydipsia,**
  3. **frequency of urination,**
  4. **polyuria,**
  5. **nocturia,**
  6. **dry skin,**
  7. **slight dehydration,**
  8. **constipation.**

Posterior Pituitary Hormones



Oxytocin

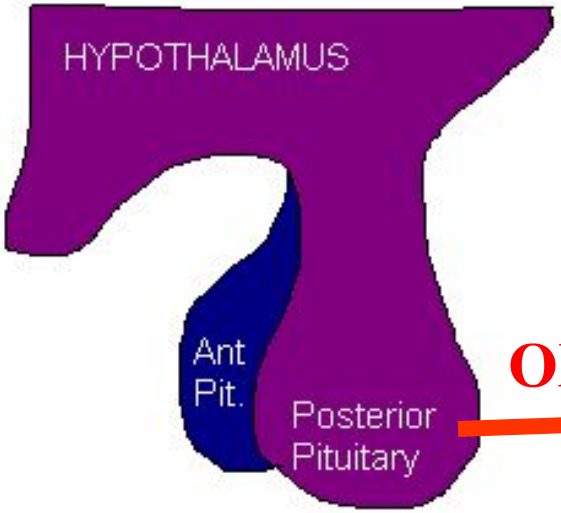
Oxytocin



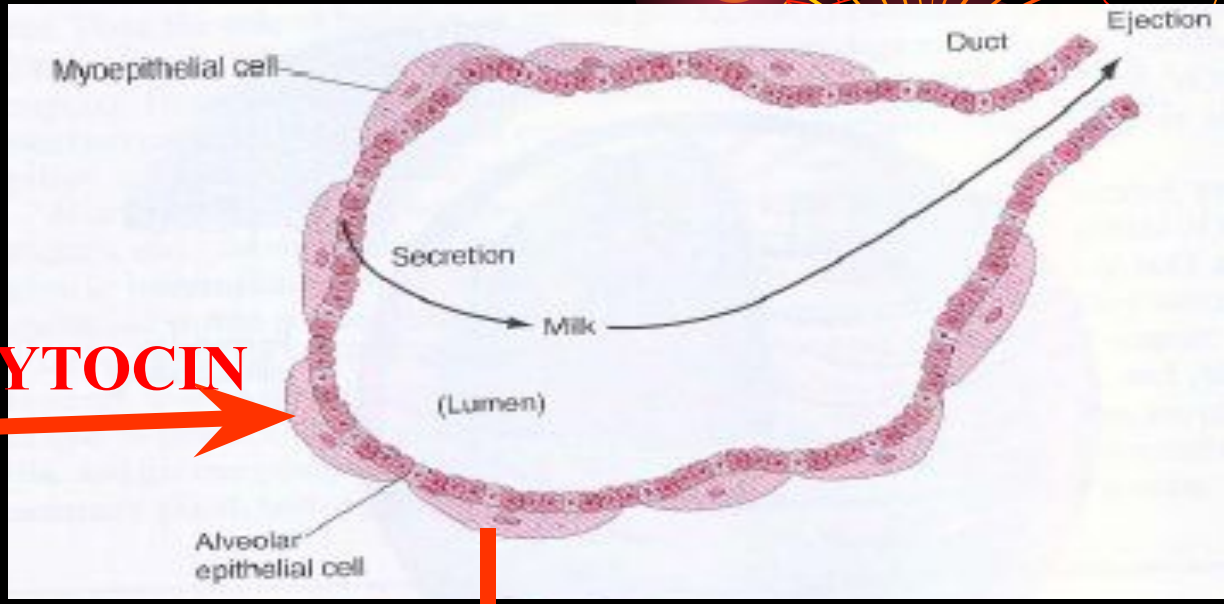
- **Oxytocin in a nine amino acid peptide that is synthesized in hypothalamic neurons and transported down axons of the posterior pituitary for secretion into blood. Oxytocin is also secreted within the brain and from a few other tissues, including the ovaries and testes. Oxytocin differs from antidiuretic hormone in two of the nine amino acids. Both hormones are packaged into granules and secreted along with carrier proteins called neurophysins**

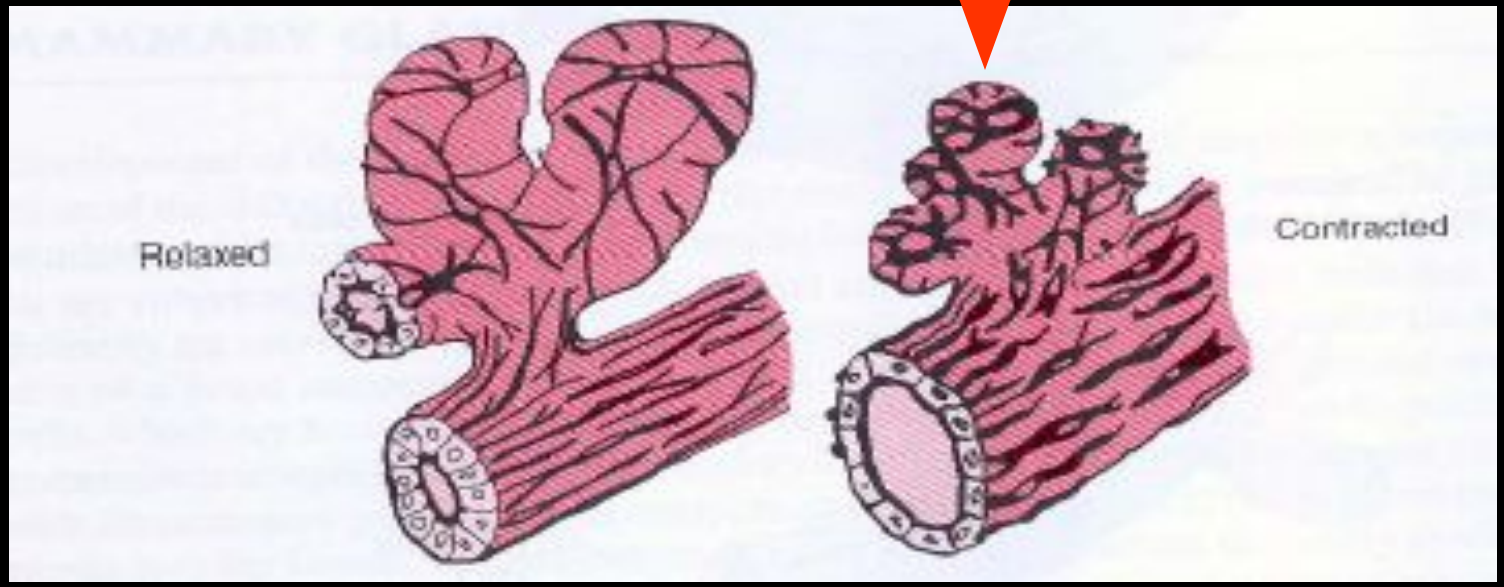
Physiologic Effects of

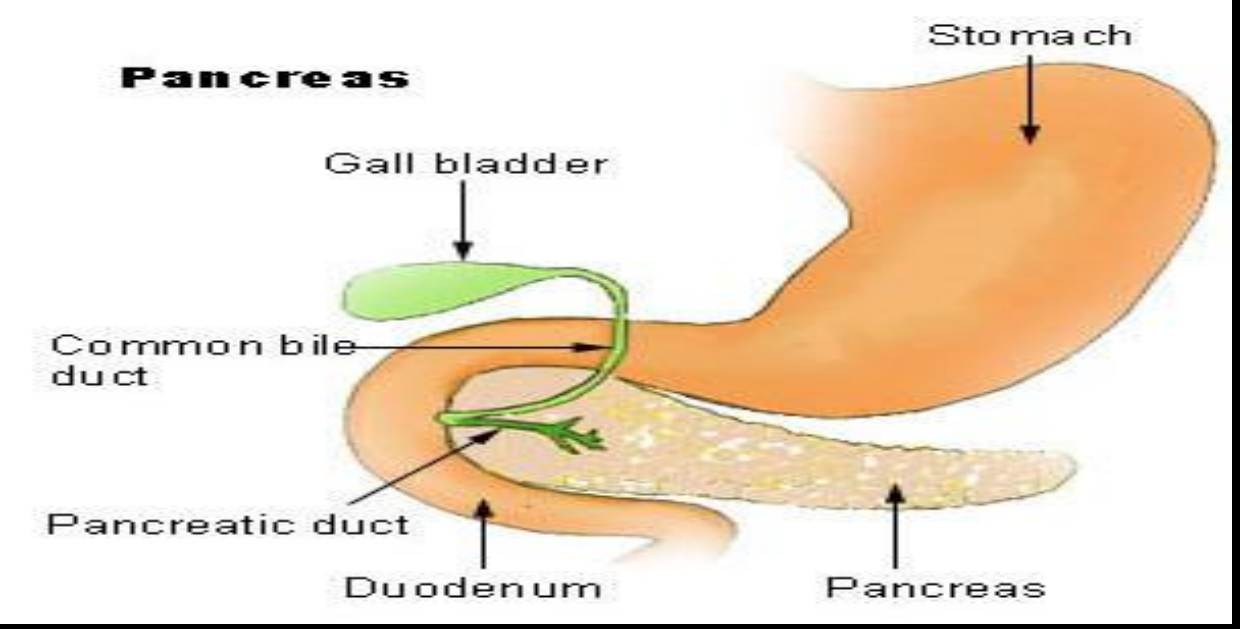
- **Oxytocin stimulates contraction of myoepithelial cells, causing milk to be ejected into the ducts and cisterns (milk letdown).**
- **Oxytocin is released during labor when the fetus stimulates the cervix and vagina, and it enhances contraction of uterine smooth muscle to facilitate parturition or birth.**

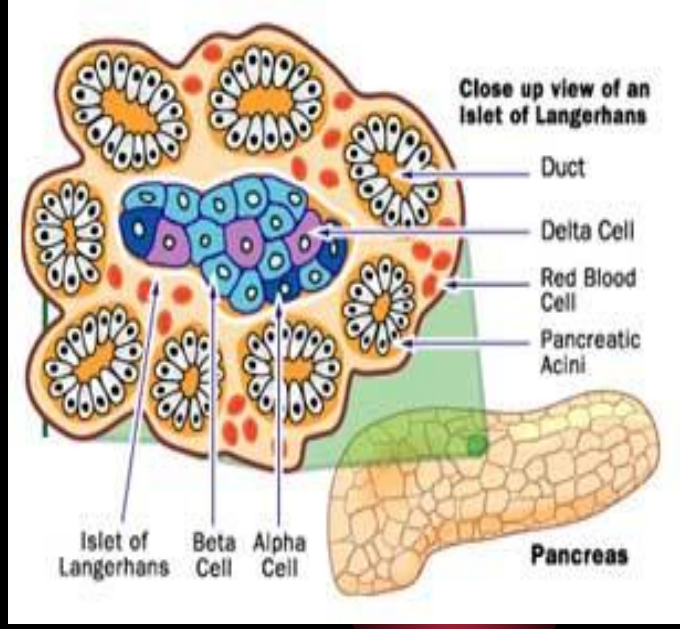

HYPOTHALAMUS
Ant Pit.
Posterior Pituitary

OXYTOCIN


Myoepithelial cell
Duct
Ejection
Secretion
Milk
(Lumen)
Alveolar epithelial cell

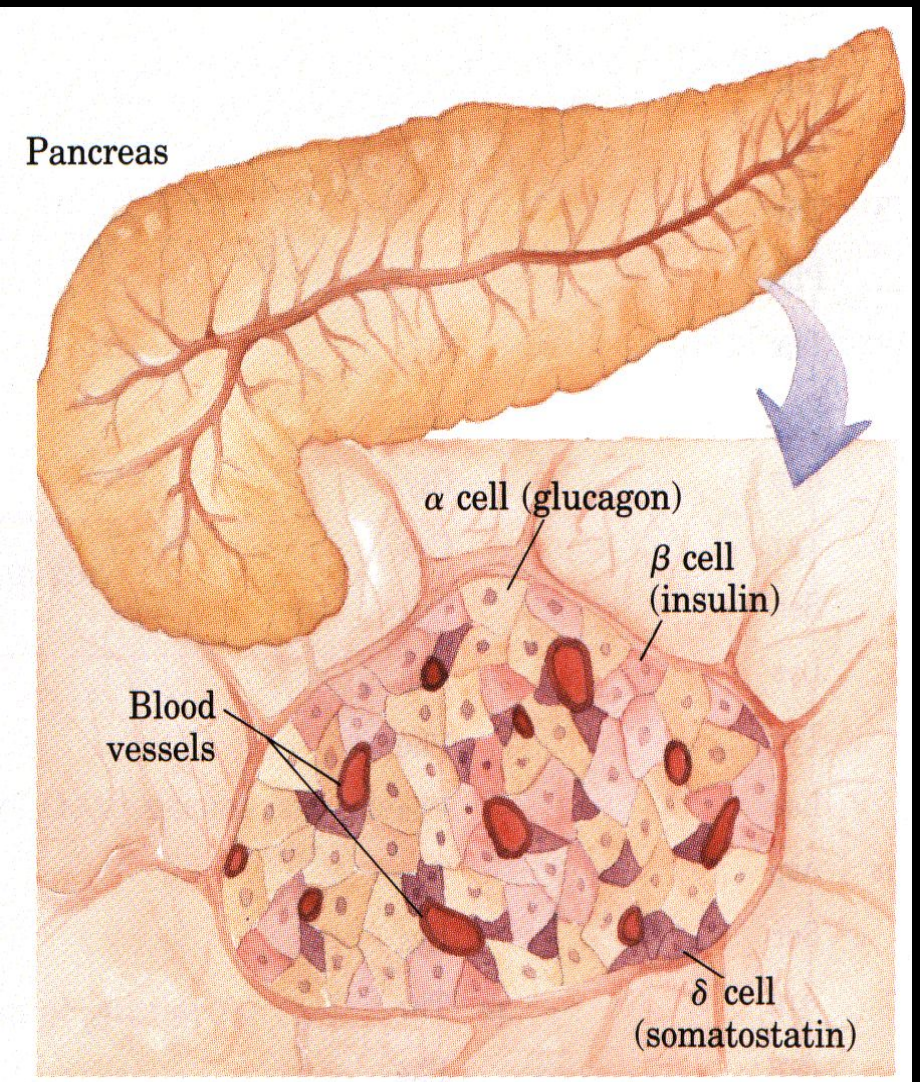

Relaxed
Contracted





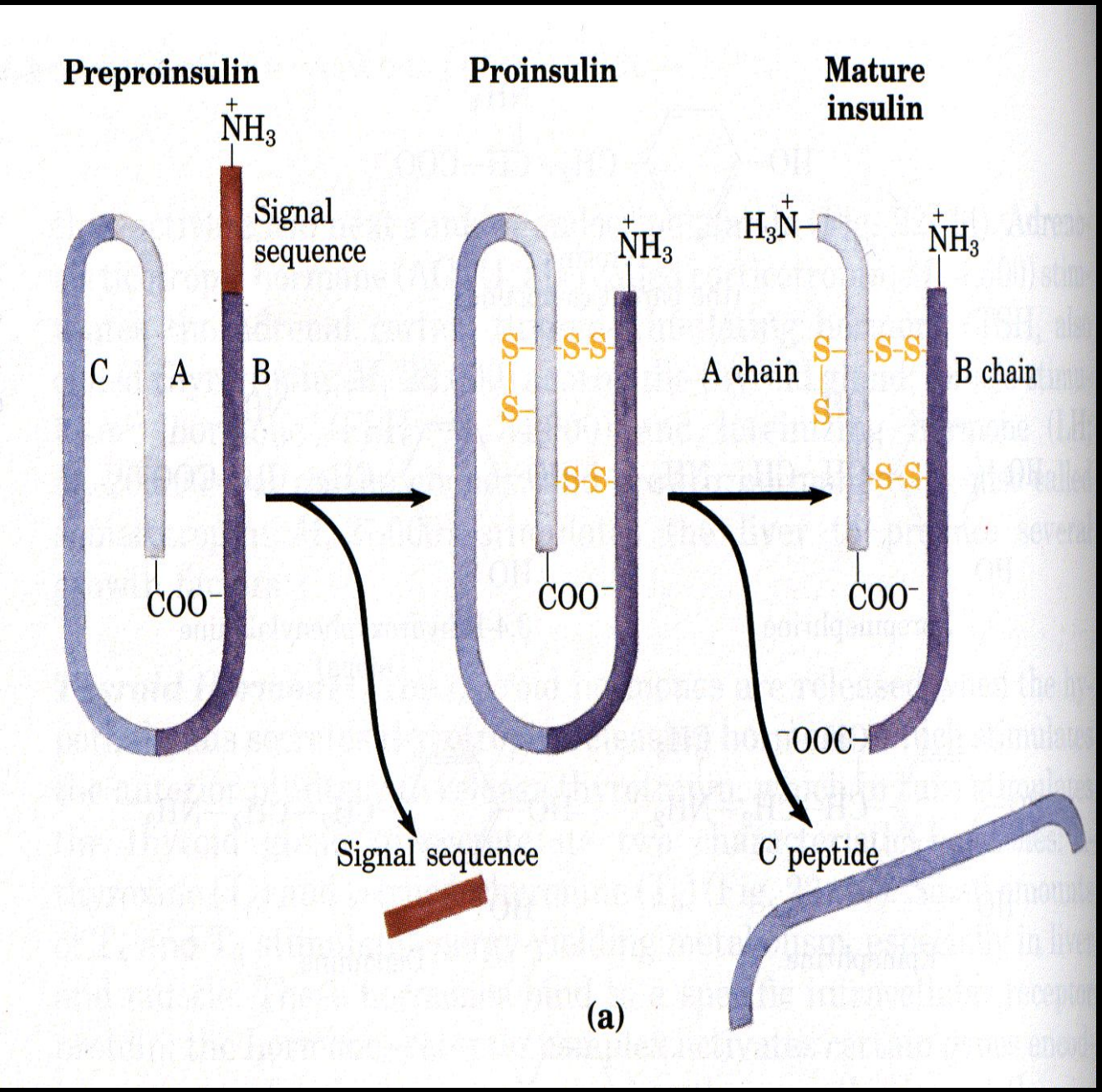
Hormones of the pancreas: insulin, glucagons, and somatostatin

The pancreas has two major biochemical functions:



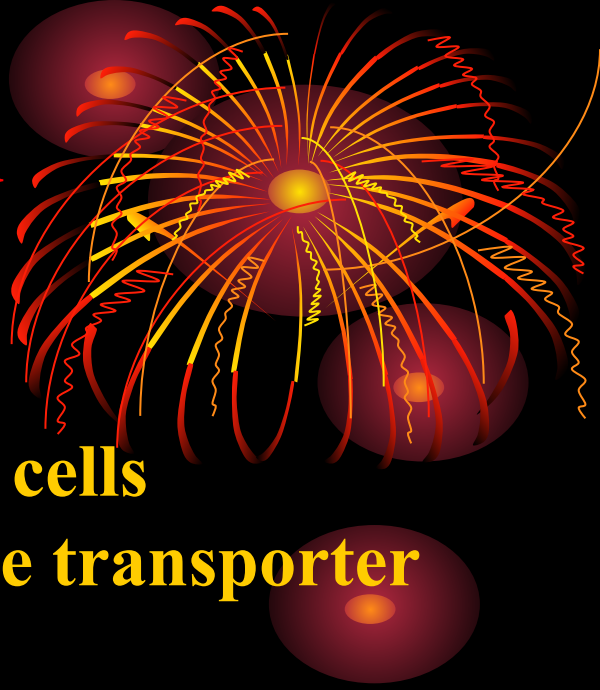
- 1. Exocrine cells produce digestive enzymes for secretion into the intestine
- 2. Endocrine cells produce and secrete peptide hormones (insulin, glucagon, and somatostatin) that regulate fuel metabo-lism throughout the body

Insulin



Insulin is a small protein with two polypeptide chains, A and B, joined by two disulfide bonds.

Insulin decreases blood level of glucose:

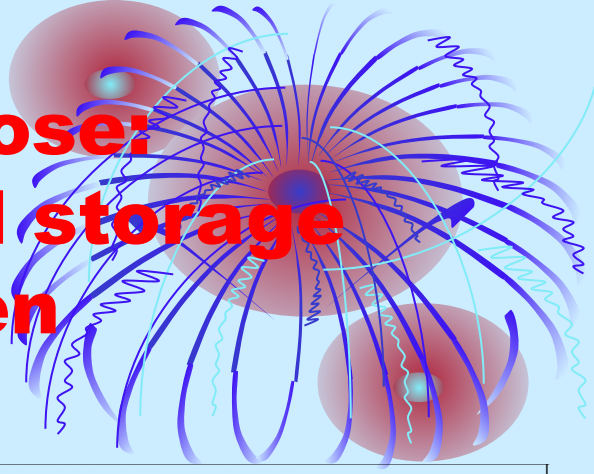


1) by increase of glucose uptake into cells triggering movement of the glucose transporter to the plasma membrane;

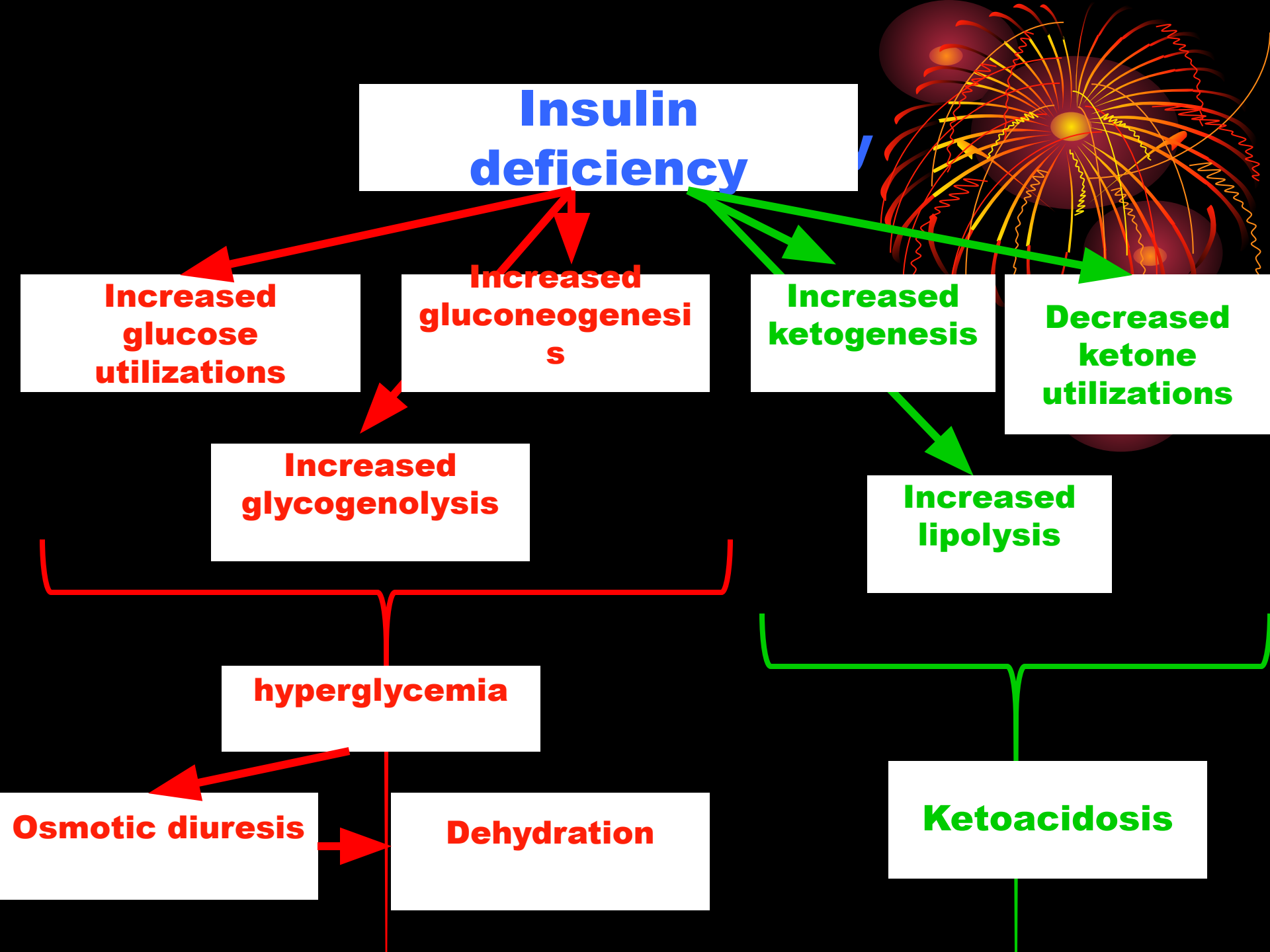
2) by stimulation of the glycolysis (increase synthesis of hexokinase, phosphofructokinase, and pyruvate kinase)

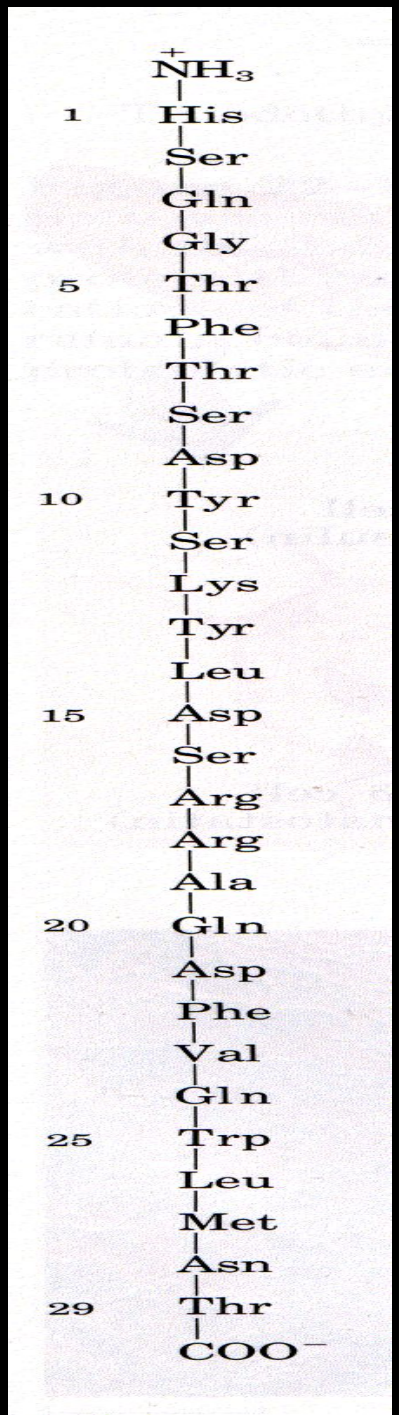
3) by stimulation of glycogen synthesis (in muscle and liver) and triacylglycerols (in adipose tissue).

Effect of insulin on blood glucose: uptake of glucose by cells and storage as triacyglycerols and glycogen



Metabolic effect	*Target enzyme*
↑ Glucose uptake (muscle, liver)	↑ Glucose transporter
↑ Glycogen synthesis (muscle, liver)	↑ Glycogen synthase
↓ Glycogen breakdown (muscle, liver)	↓ Glycogen phosphorylase
↑ Glycolysis	↑ Phosphofructokinase, hexokinase, pyruvatekinase
↑ Acetyl-CoA production (liver, muscle)	↑ Pyruvate dehydrogenase complex
↑ Fatty acid synthesis (liver)	↑ Acetyl-CoA carboxylase
↑ Triacylglycerol synthesis (adipose tissue)	↑ Lipoproteinlipase


Insulin deficiency
Increased glucose utilizations
Increased gluconeogenesis
Increased ketogenesis
Decreased ketone utilizations
Increased glycogenolysis
Increased lipolysis
hyperglycemia
Osmotic diuresis
Dehydration
Ketoacidosis



Glucagon

- is a single polypeptide chain of 29 amino acid residues, and like insulin is derived from langer precursors (preproglucagon and proglucagon) by precise proteolytic cleavages.

Glucagon

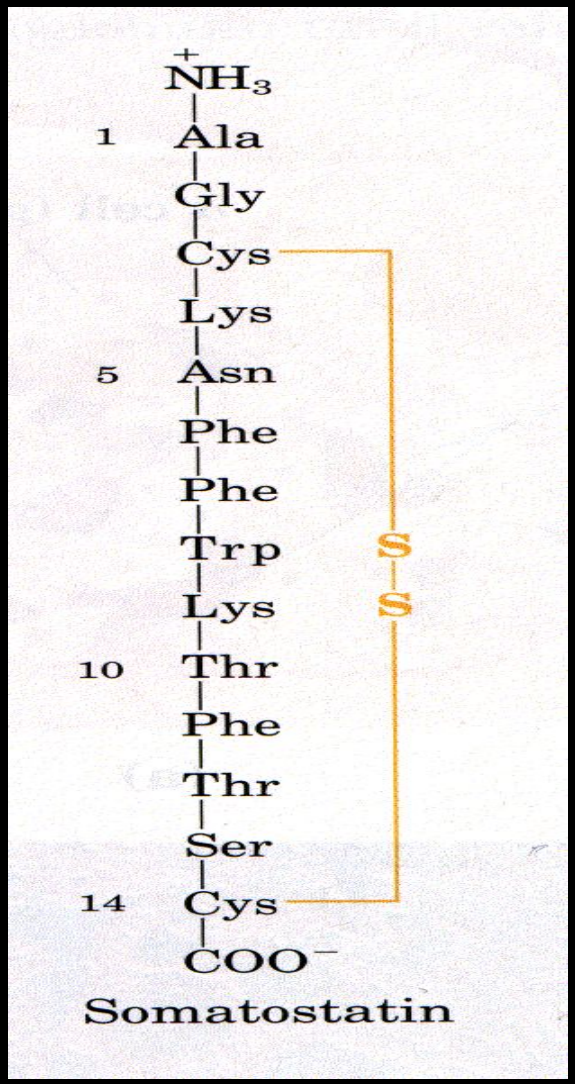
- **increases blood level of glucose:**

  1) by stimulation of the glycogen breakdown in liver;

  2) by stimulation of the gluconeogenesis.

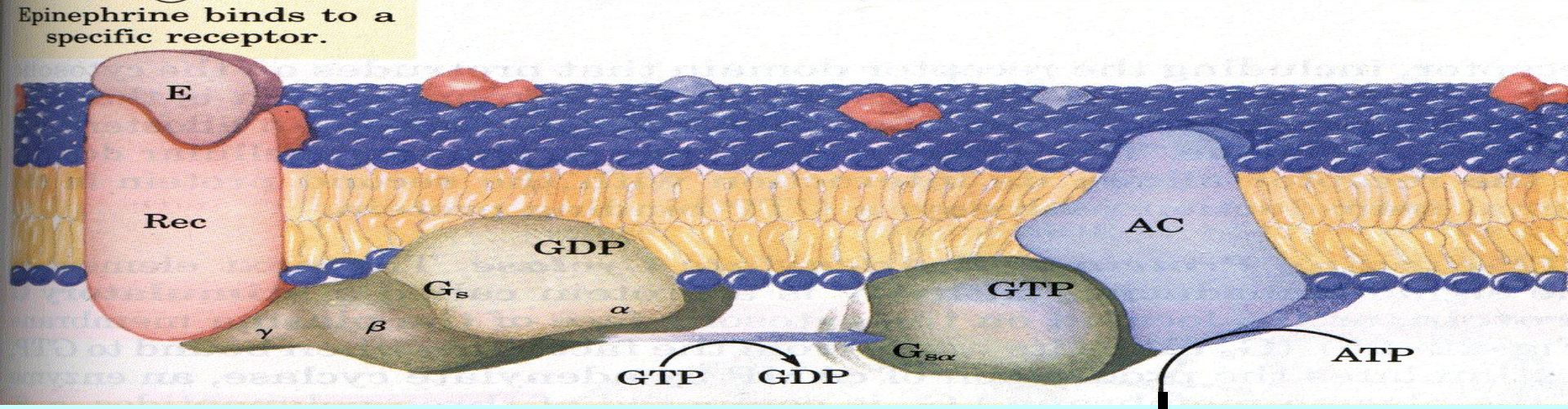
  3) by inhibition of the glycolysis (decrease activity of hexokinase, phosphofructokinase, and pyruvate kinase.

Somatostatin



Somatostatin

- **is polypeptide hormone, inhibits the secretion of insulin and glucagons by the pancreas. Somatostatin is produced and secreted not only by pancreatic δ cells, but also by the hypothalamus and certain intestinal cells.**



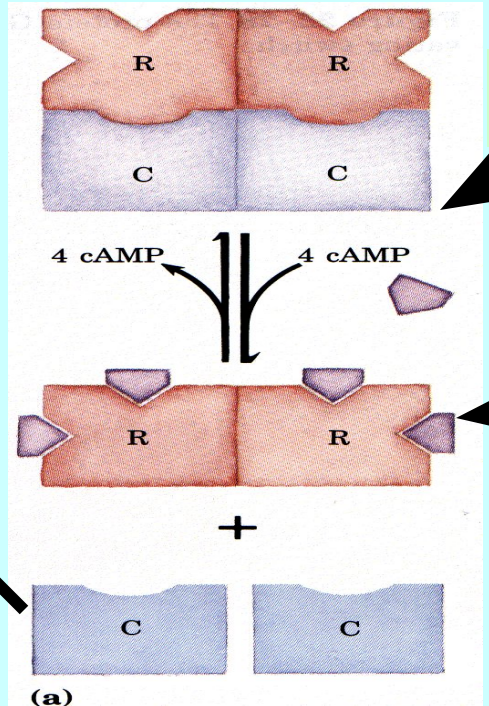
P

Active enzyme

Inactive enzyme

P

Active protein kinase in turn activates molecules of the next enzyme in the cascade



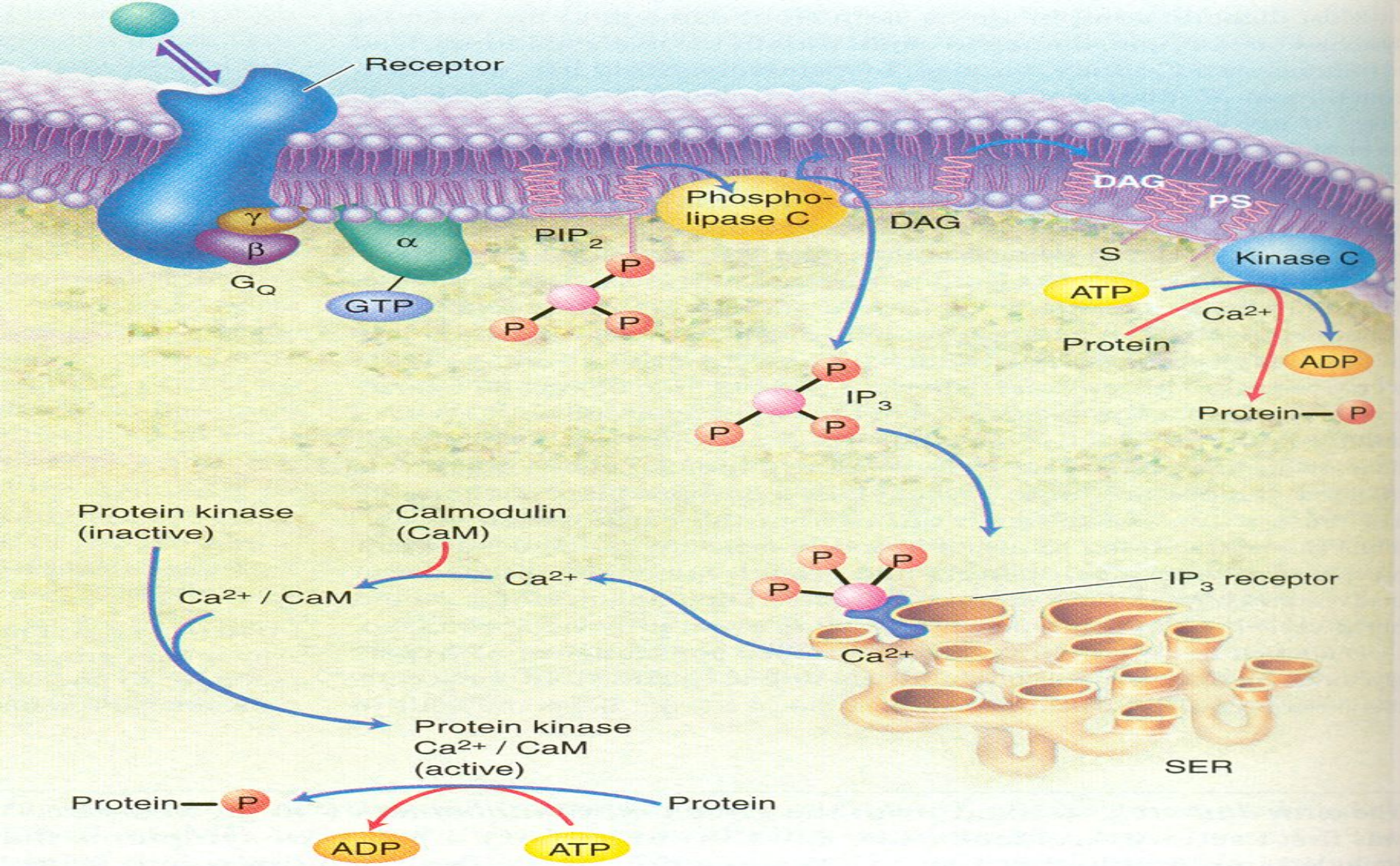
4

cAMP

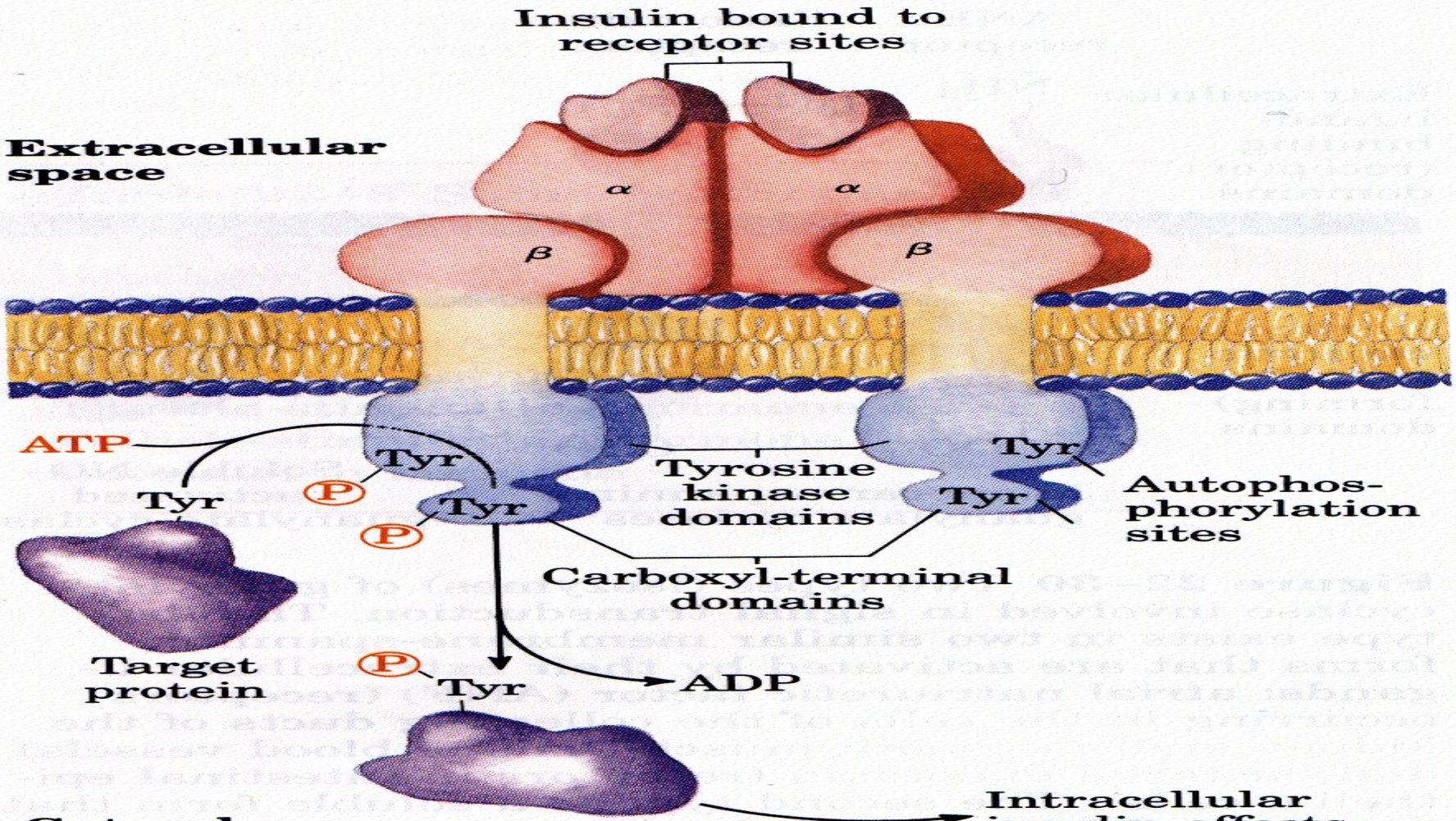
5'-AMP

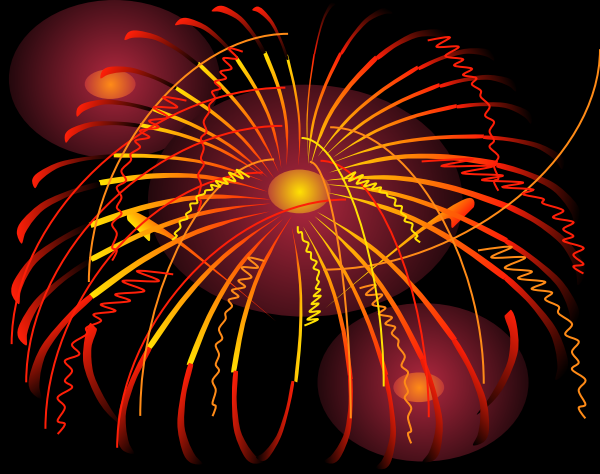
Activation of cAMP-depend protein kinase

The phosphatidylinositol pathway



The insulin receptor is a tyrosine-specific protein kinase





THE END