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ENDOCRINE SYSTEM

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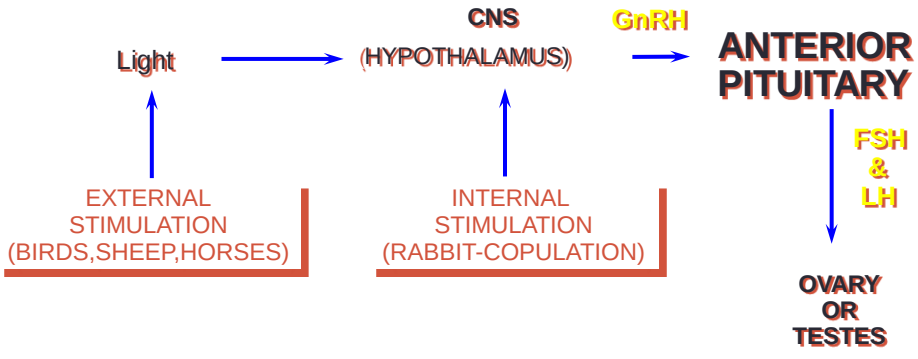
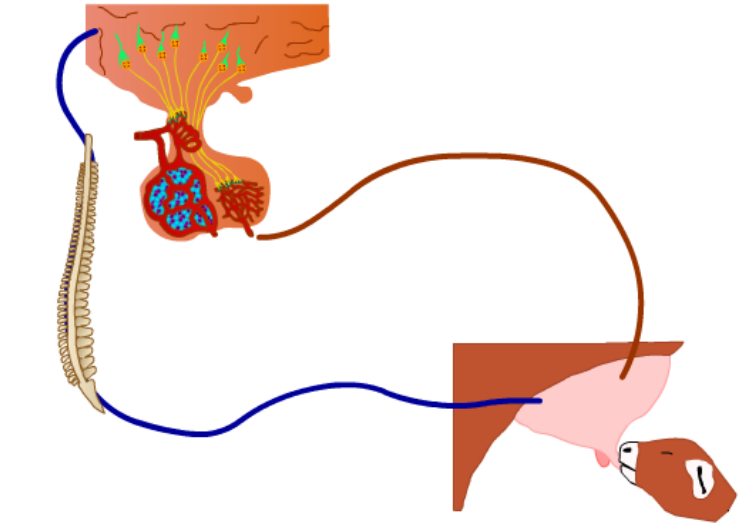
Functions of the Endocrine System - Integration of Body Functions

- nervous and endocrine system are similar
- nervous system
  - integration over seconds
- endocrine system
  - integration over minutes and hours

Neuro-humoral-interaction



Neuro-endocrine Response



Endocrine Gland

- A ductless gland
- Secretes substances into blood or lymph that affect cells elsewhere in the body
- The secretion does not involve loss of tissue

Exocrine Gland

- A gland with ducts that are used for secretion

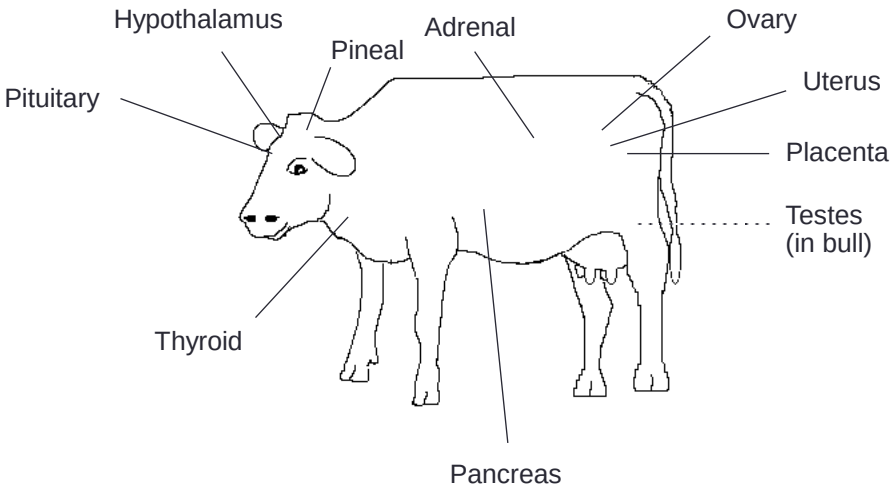
Hormone

- Substance produced by endocrine gland
- Acts on cells, tissues or organs at a place other than where produced
- Acts as a catalyst in that it is effective at small amounts and is not used up.

Endocrinology

- Study of how hormones and how, working through their receptors, they regulate body functions.

Endocrine Glands



Classification and Properties of Hormone

A. Site of Production
B. Type of action
   1. Primary hormone of reproduction
   2. Metabolic hormone
C. Chemical Structure
   1. General structure
      - *Proteins and polypeptides*
      - *Steroids*
      - *Fatty acids*
      - *Modified amino acid*
   2. Size

Classification and Properties of Hormone

C. Chemical Structure
   1. Proteins and polypeptides (hypothalamic and pituitary hormones)
   2. Steroids (gonadal and adrenal)
   3. Fatty acids (prostaglandins)
   4. Modified amino acid (melatonin)

Chemical Structure of Hormones

polypeptide	modified amino acid	protein	sex steroid	fatty acid
GnRh	melatonin	LH	Estradiol	$PGF_{2\alpha}$
TRH		FSH	Progesterone	
CRH		Prolactin	Testosterone	
GHRH		ACTH		
Somatistatin		TSH		
Oxytocin		GH or STH		
		Relaxin		
		Inhibin		

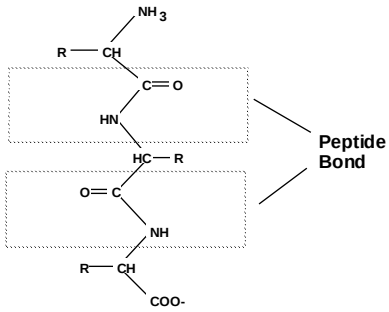
Chemical Structure of Hormones

Molecular size of hormones that regulate reproduction

Hormone	Molecular Weight
FSH	30,000 to 37,000
LH	26,000 to 32,000
Prolactin	23,000 to 25,000
HCG	37,700
eCG	28,000
Relaxin	6,500
ACTH	4,500
Inhibin	>10,000
Oxytocin	1,007
GnRH	1,200
Estradiol	300
Testosterone	300
Progesterone	300
$PGF_{2\alpha}$	300

Chemical Structure of Hormones Cont.

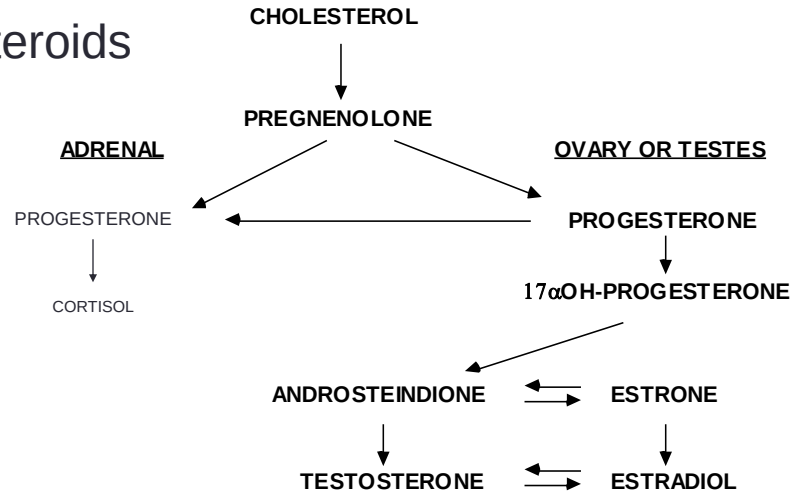
Polypeptide and protein hormones
are made of peptide bonds



These hormones can not be given orally!

Chemical Structure of Hormones Cont.

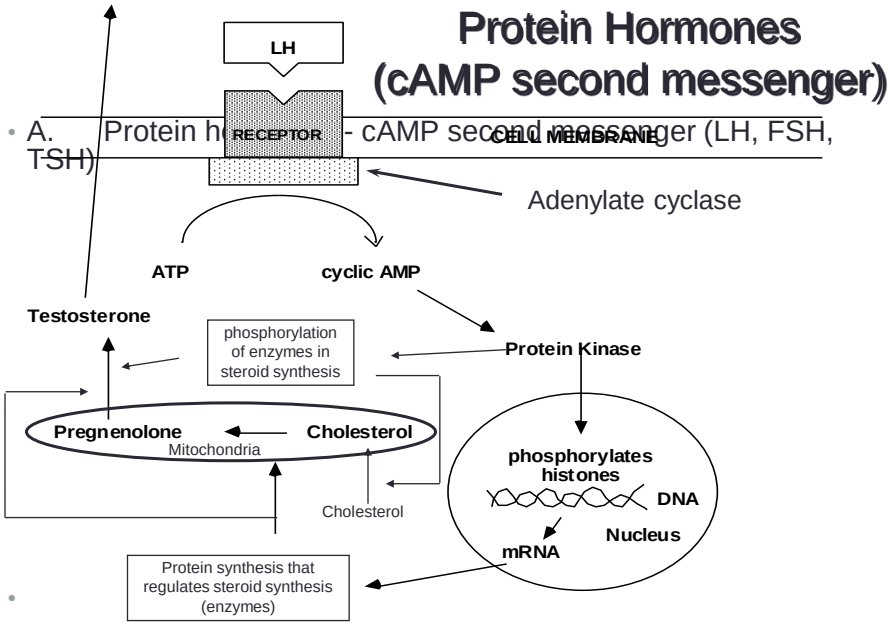
Steroids



These hormones can be given orally!

Mechanism of Hormone Action

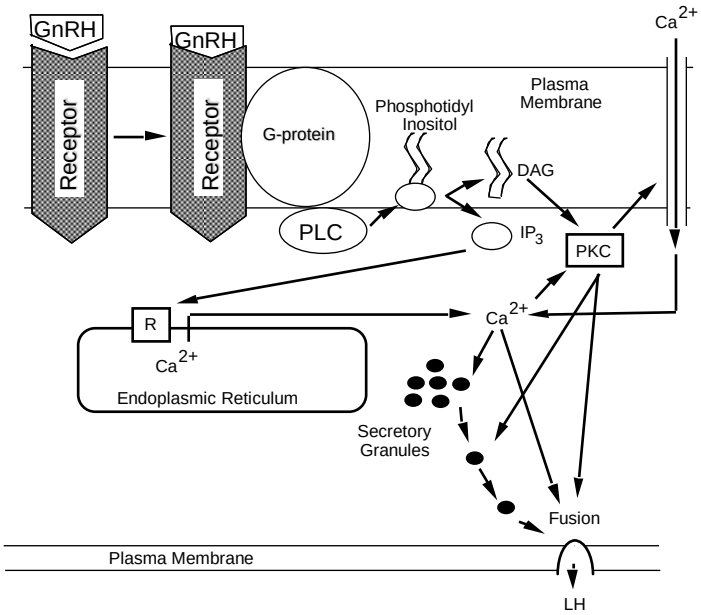
- A. Protein hormones - cAMP second messenger (LH, FSH, TSH)



cAMP Second Messenger Hormones

- Anterior Pituitary Hormones
  - LH, FSH, Prolactin
  - STH, ACTH, TSH
- Placental Hormones
  - HCG, eCG

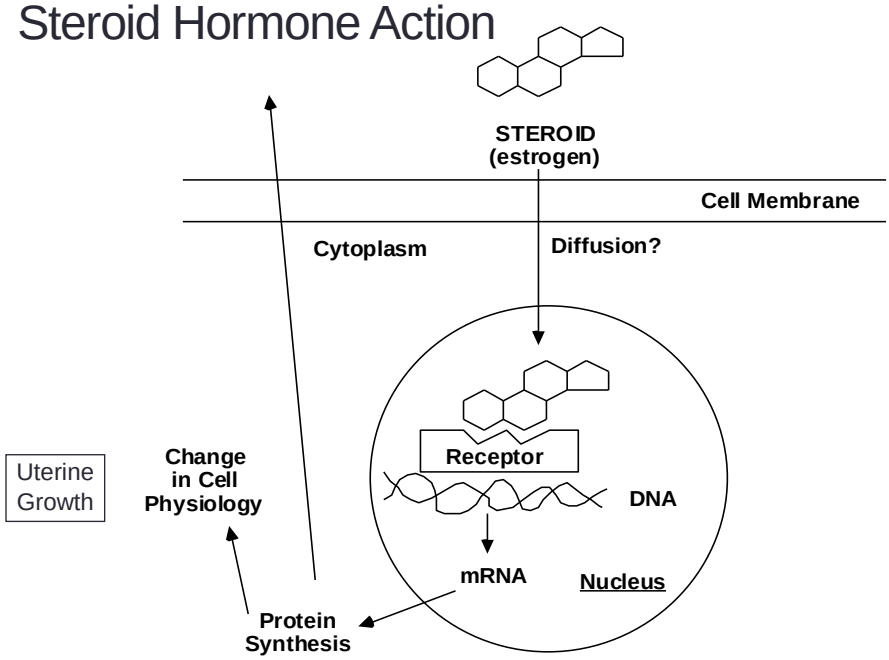
Protein Hormones (Ca^{2+} Second Messenger)



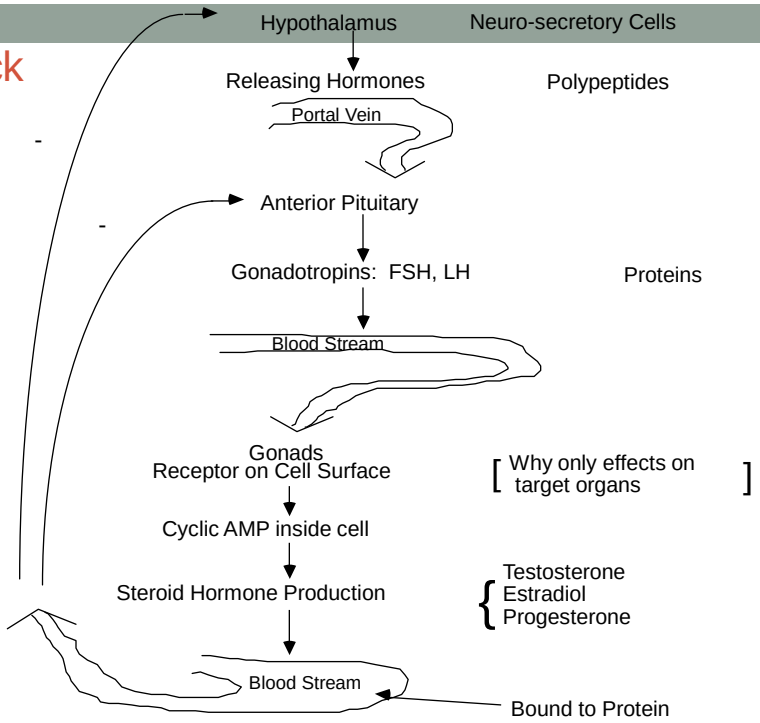
Calcium Second Messenger Hormones

- GnRH
  - triggers release of LH in anterior pituitary
- Oxytocin
  - triggers contractions of smooth muscle
- $PGF_{2\alpha}$
  - triggers apoptosis of cell
  - inhibition of progesterone synthesis

Steroid Hormone Action



Feedback Loops



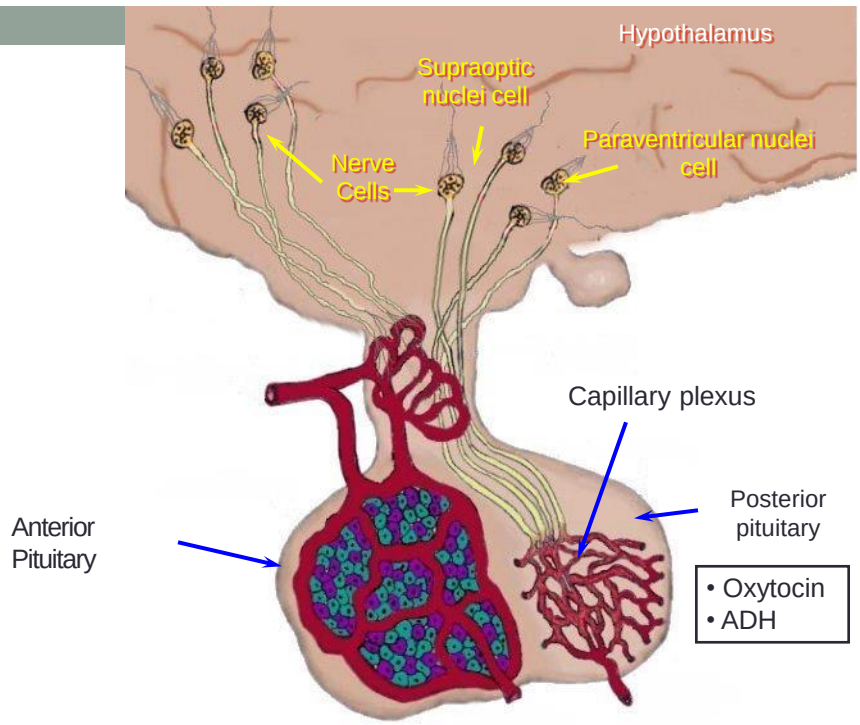
Releasing Hormones of the Hypothalamus

A. Structure

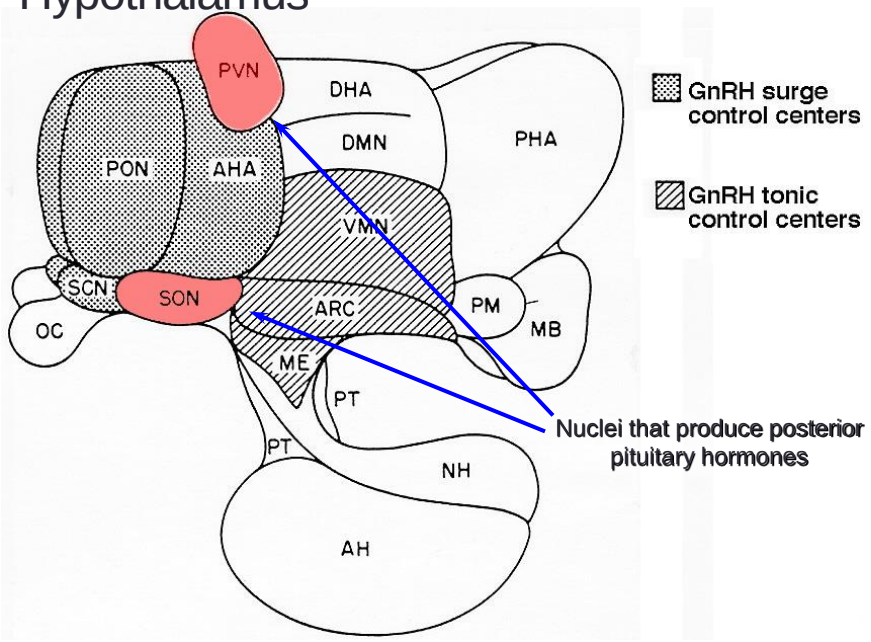
- short chain polypeptides (3 - 44 amino acids)

B. General Function

- to cause the release of trophic hormones from the anterior pituitary gland



Hypothalamus



Releasing Hormones of the Hypothalamus

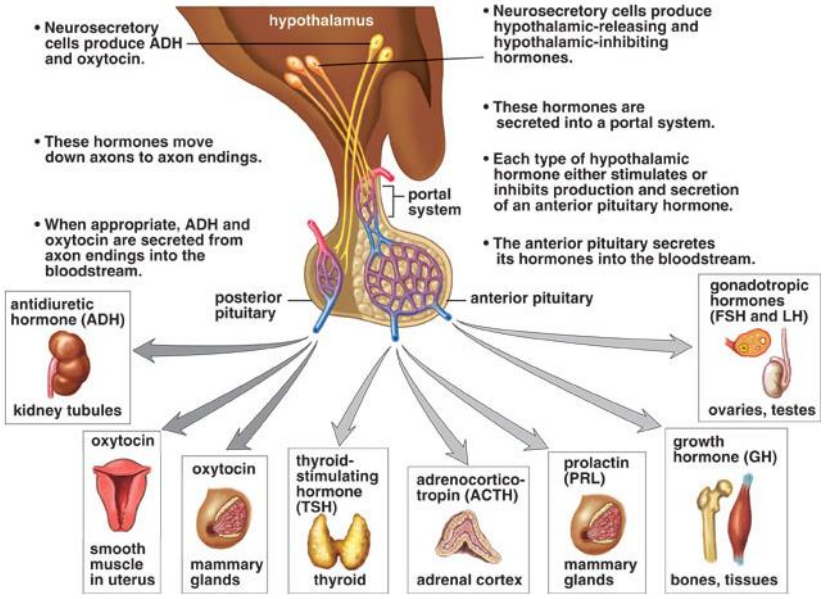
C. Hormones

- Gonadotropin releasing hormone (GnRH)
  - »LH, FSH release
- Thyrotrophin releasing hormone (TRH)
  - »TSH and prolactin release
- Corticotrophin releasing hormone (CRH)
  - »ACTH release
- Growth hormone releasing hormone (GH-RH)
- Somatostatin (growth hormone inhibiting hormone)

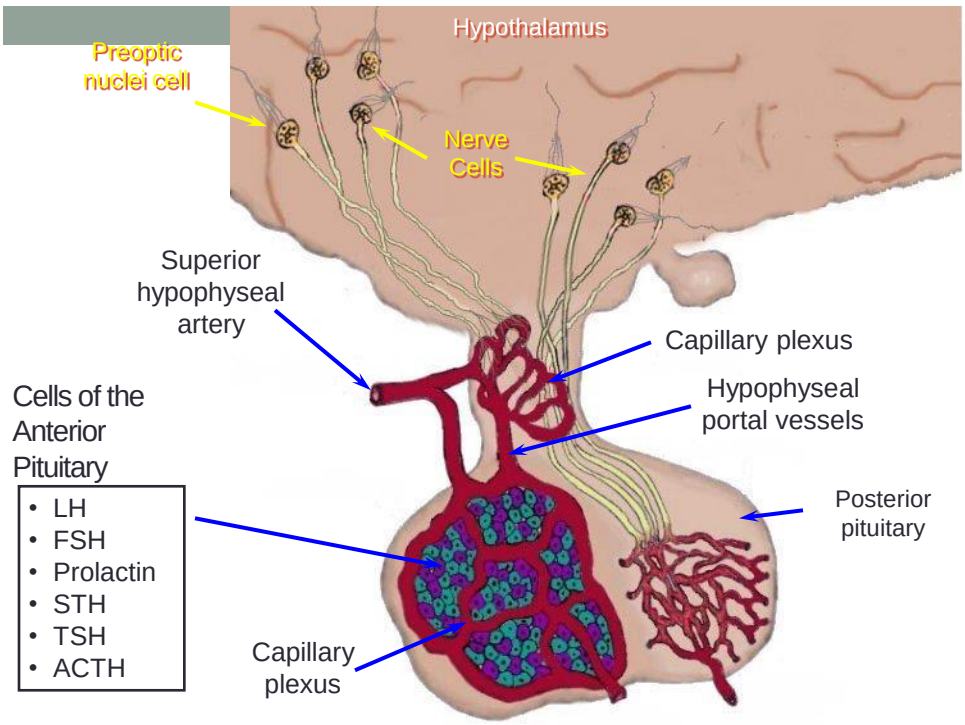
Function of Hypothalamus

- appetite
- thirst
- body temperature
- vasomotor activity
- emotion
- use of body nutrient reserves
- activity of intestine
- sleep
- sexual behaviour
- release of trophic hormones

Hypothalamus and the pituitary



- The anterior pituitary produces several hormones, some of which control other endocrine glands.
- Growth hormone is produced by the anterior pituitary; giants are due to overproduction of growth hormone during childhood, and pituitary dwarfs are due to underproduction of growth hormone.
- The thyroid produces two hormones that speed metabolism and another hormone that lowers the blood calcium level.



Anterior Pituitary (Adenohypophysis) Hormones

A. Structure
   1. glycoproteins or proteins
B. Hormones
   1. gonadotropins
      - Follicle stimulating hormone (FSH)
      - Luteinizing hormone (LH)
      - Prolactin (PRL)

Anterior Pituitary Hormones

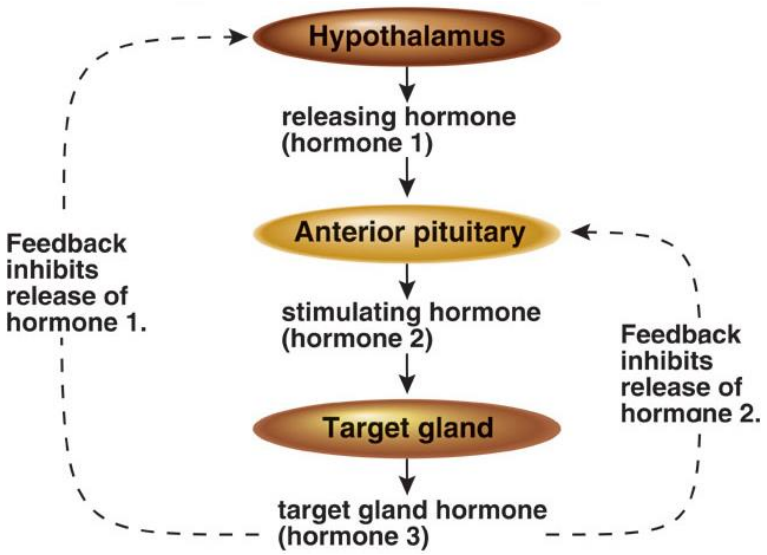
2. Other trophic hormones
   - Adrenal Corticotropic Hormone (ACTH)
   - thyroid stimulating hormone (TSH)
   - growth hormone or somatotropin (GH or STH)

Anterior Pituitary

- The hypothalamus controls the anterior pituitary by producing *hypothalamic-releasing hormones* and *hypothalamic-inhibiting hormones*.
- The *anterior pituitary* produces six hormones.
- Three of these six hormones have an effect on other endocrine glands:

1) *Thyroid-stimulating hormone* (*TSH*) stimulates the thyroid to produce thyroid hormones;

- 2) *adrenocorticotropic hormone* (*ACTH*) stimulates the adrenal cortex to produce cortisol;
- 3) the *gonadotropic hormones* (FSH and LH) stimulate the gonads to produce sex cells and hormones.
- In these three instances, the blood level of the last hormone exerts negative feedback control over the secretion of the first two hormones.



- The next three anterior pituitary hormones do not effect other endocrine glands.
- After childbirth, *prolactin* (*PRL*) causes mammary glands to produce milk.
- *Growth hormone* (*GH*) promotes skeletal and muscular growth.
- *Melanocyte-stimulating hormone* (*MSH*) causes skin color changes in fishes, amphibians, and reptiles.

Effects of Growth Hormone

- The quantity of GH is greatest during childhood and adolescence; GH promotes bone and muscle growth.
- *Pituitary dwarfism* results from too little GH during childhood.
- *Giants* result from too much growth hormone during childhood.
- If growth hormone is overproduced in an adult, it causes *acromegaly*.

Posterior Pituitary

- The *posterior pituitary* stores and releases the *antidiuretic hormone* (*ADH*) and *oxytocin* produced by the hypothalamus.
- ADH is secreted during dehydration and causes more water to be reabsorbed by the kidneys; the secretion of ADH is regulated by *negative* feedback.
- Oxytocin causes uterine contractions and milk release, and is controlled by *positive* feedback.

Posterior Pituitary Hormones

A. Structure
- polypeptides (9 amino acids)

B. Hormone
- Oxytocin - causes contraction of smooth muscle such as in mammary gland, uterus, oviduct

C. Other facts of importance
- produced in the hypothalamus but released in posterior pituitary
- also produced in the corpus luteum of some species

Placental Hormones

A. Pregnant mare serum gonadotropin (PMSG) or equine chorionic gonadotropin (eCG)
1. Contains mainly FSH-like activity but also some LH-like activity.
2. Has a longer half-life than FSH.
3. Found in the blood and not the urine.
4. Function
   - stimulates follicular development during pregnancy in the mare
   - the LH-like activity stimulates some developing follicles to ovulate and form accessory CLs

Placental Hormones (cont.)

5. Other commercial hormones from the equine placenta
   - Oestrogens (several)
     - ➢ Found in mare urine
     - ➢ Premarin is commercial name
     - ➢ Treatment of postmenopausal women
       - ✓ oestrogen replacement therapy

Placental Hormones (cont.)

B. Human Chorionic Gonadotropin (hCG)
   1. Has LH-like activity.
   2. Found in blood and urine.
   3. Function
      - prevents CL regression

C. Placental Lactogen (PL)
   1. Has both GH- and prolactin-like activity. The primary effect is to prepare the mother's mammary gland for lactation.

Gonadal Polypeptide Hormones

A. Relaxin

1. Made of 2 polypeptides that are connected with disulfide bonds. It is similar in size and structure to insulin.
2. Secreted by CL during pregnancy.
3. In some species it may be secreted by the uterus and/or placenta.
4. Generally requires tissue first be exposed to estrogens for its effects.
5. Functions
   - cervical dilation
   - inhibits uterine contractions

Gonadal Polypeptide Hormones

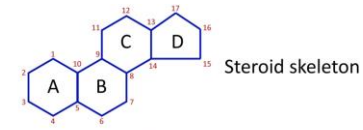
B. Inhibin

1. Secreted by sertoli cells in the male and granulosa cells in the female.
2. Function
   - inhibits FSH secretion without altering LH secretion

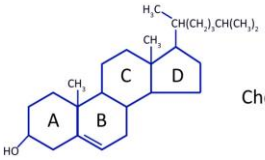
Gonadal Steroids

A. General

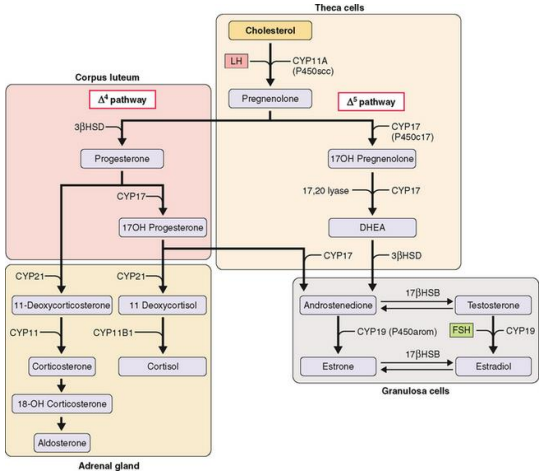
1. Origin - ovary, testis, adrenal
2. Basic structure



Steroid skeleton



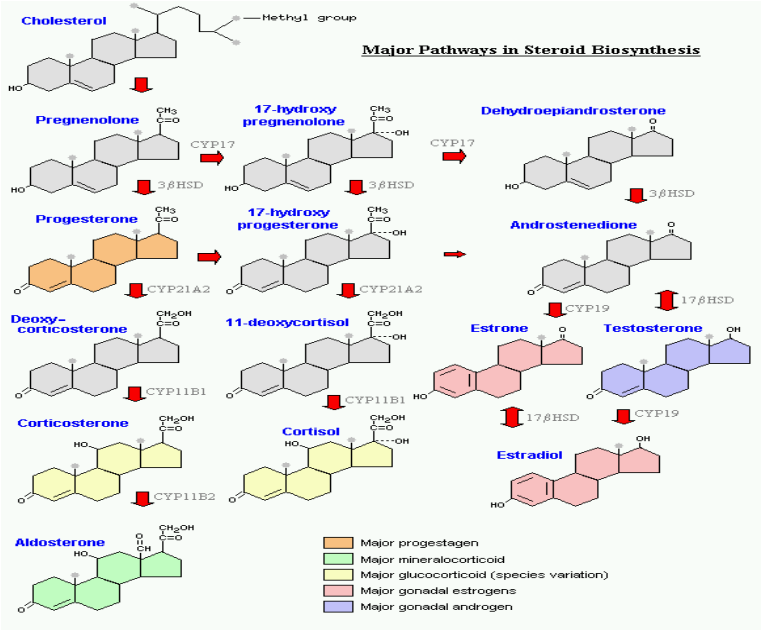
Cholesterol



Gonadal Steroids

3. Type of activity can be predicted by structure
   - cholesterol - 27 carbons
   - progestin - 21 carbons
   - androgen - 19 carbons
   - estrogen - 18 carbons

Steroid Synthesis



Gonadal Steroids Cont.

B. Androgens

1. An example is testosterone.
2. Produced by Leydig cells in the testis, theca interna in the follicle and by the adrenal gland.
3. Transported in the blood by binding to the protein, steroid binding globulin.
4. Active form is often dihydrotestosterone.

Gonadal Steroids cont.

5. Function in the male
   - stimulates spermatogenesis
   - maintain the function of the epididymis
   - promotes the growth, development, and activity of accessory sex glands and secondary sex organs
   - development of male secondary sex characteristics
   - anabolic activity
   - inhibits GnRH and LH release

Gonadal Steroids Cont.

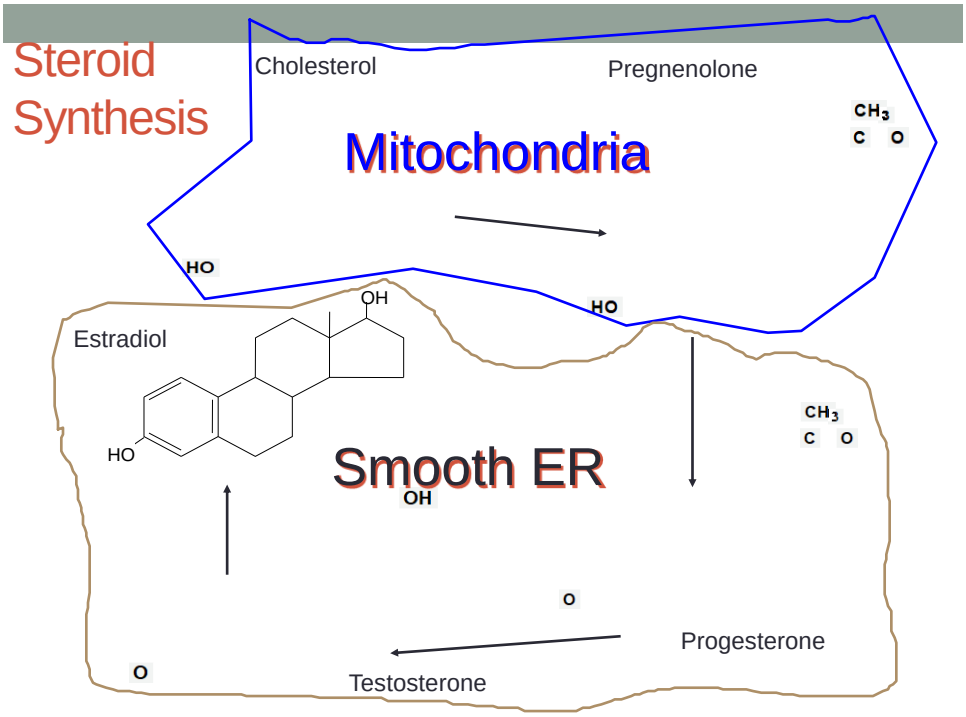
C. Estrogens
   1. An example is estradiol.
   2. Produced by granulosa cells of the follicle, sertoli cells in the testis, the placenta, and the adrenal gland.
   3. Transported in blood by steroid binding globulin

Gonadal Steroids Cont.

4. Functions
   - effects on the CNS
   - increases the mass of the uterus
   - increases the contractility of the uterus
   - development of female secondary sex characteristics
   - growth of the mammary gland ducts
   - stimulates or inhibits GnRH and LH release
   - nonreproductive
     a. calcium uptake and bone ossification
     b. anabolic and growth effects

Gonadal Steroids Cont.

D. Progestins
   1. An example is progesterone
   2. Produced in the CL, the placenta and the adrenal gland.
   3. Transported in the blood bound to steroid binding globulin.
   4. Functions
      - prepares the uterus for implantation and pregnancy
      - acts with estrogen to induce the behavior patterns of estrus
      - develops alveoli of mammary gland
      - inhibits the rise of LH that causes ovulation by inhibiting GnRH and LH release



Hormones from Other Tissues

- Leptin

- Adipose tissue (fat) produces *leptin* that acts on the hypothalamus where it signals satiety—that the individual feels "full" and has had enough to eat.
- It is possible that obese people have ineffective leptin due to a genetic mutation or that their cells lack adequate leptin receptors.

Growth Factors

- A number of different types of organs and cells produce *peptide growth factors*, which stimulate cell division and growth:
- *granulocyte and macrophage colony-stimulating factor* to fight infection,
- *platelet-derived growth factor* for wound healing,
- *epidermal growth factor* and *nerve growth factor*, both for wound healing, and
- *tumor angiogenesis factor* that causes blood vessels to grow near tumor cells.

Prostaglandins

- *Prostaglandins* are produced within cells from arachidonate, a fatty acid.
- Prostaglandins act close to where they are produced.
- They cause uterine muscle contraction and are involved in the pain of menstrual cramps; aspirin is effective against the pain by countering prostaglandins.

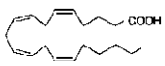
Other Hormones

A. Prostaglandins
   1. An example is $PGF_{2\alpha}$

Lipid Hormones - Prostaglandins

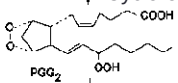
Prostaglandins
1. Produced by all tissues of body
2. Can have a local effect on tissues (same tissue which produced it)
3. Rapidly degraded in lungs

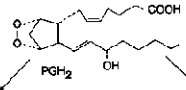
Fatty Acids
Phospholipids
↓ - Rate limiting (Phospholipase A_2)



Arachidonic Acid - Precursor to Prostaglandins

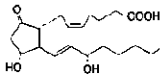
↓ Cyclo-oxygenase ⟶ Aspirin inhibits



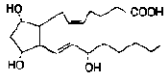


Causes vasodilatation of blood vessels

Causes vasoconstriction of Blood vessels



PGE_2



$PGF_{2\alpha}$

Maintain CL ovulation, embryo implantation

Involved with ovulation, parturition sperm transport

Effects luteal cell of CL
Lutalyse causes CL regression

Other Hormones

B. Melatonin
   1. Secreted from the pineal gland.
   2. Is a modified amino acid
   3. Functions to integrate effects of light on reproductive processes.

Other Hormones

C. Human Menopausal Gonadotropin (hMG)
   1. Secreted from the anterior pituitary gland during and after menopause.
   2. Has FSH-like activity and is actually a modified FSH molecule with a longer half-life. Results from lack of estradiol feedback.
   3. Can be collected in the urine and sold to stimulate follicular development in women.

Thyroid Gland

- The thyroid gland requires iodine to produce *thyroxine* (T_4) which contains four iodine atoms, and *triiodothyronine* (T_3) which contains three iodine atoms.
- Thyroid hormones increase the metabolic rate, and stimulate all body cells to metabolize and use energy at a faster rate.

- Effects of Thyroid Hormones
  - If *iodine* is lacking in the diet, a *simple goiter* develops.
  - Use of iodized salt helps prevent simple goiters.
  - *Hypothyroidism* in childhood produces *cretinism*; in adulthood it causes *myxedema*.
  - If the thyroid is overactive (Grave's disease) an *exophthalmic goiter* develops.

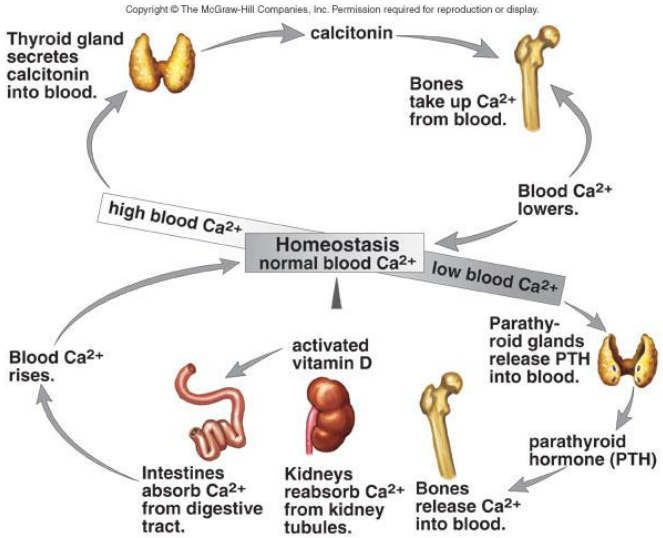
- Calcitonin

- The thyroid gland also produces *calcitonin*, which helps lower the blood calcium level when it is too high.
- The primary effect of calcitonin is to bring about the deposit of calcium in the bones; it does this by temporarily reducing the activity and number of osteoclasts.
- When the blood level of calcium is returned to normal, the release of calcitonin is inhibited.

Parathyroid Glands

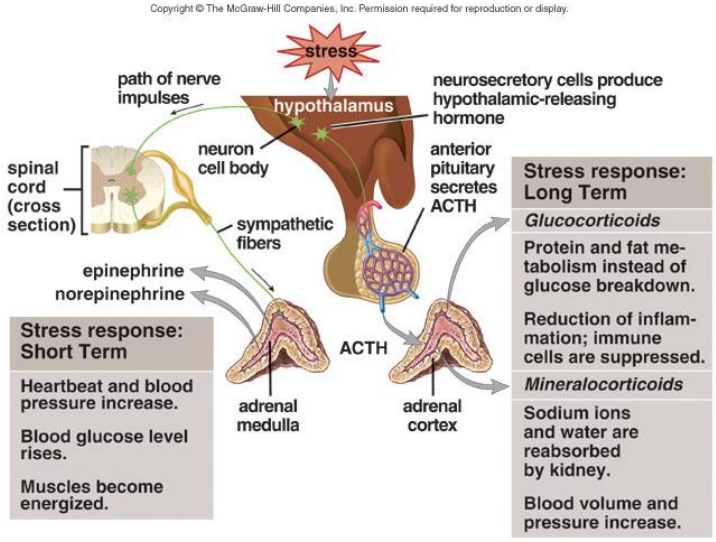
- Parathyroid glands secrete *parathyroid hormone* (*PTH*), which raises the blood calcium when it is insufficient, and decreases the blood phosphate level.
- PTH acts by stimulating the activity of osteoclasts, thus releasing calcium from bone, and stimulates the reabsorption of calcium by the kidneys and intestine.
- Insufficient parathyroid hormone will cause serious loss of blood calcium and cause *tetany*.

Regulation of blood calcium level



- The adrenal medulla secretes *epinephrine* and *norepinephrine*, which bring about responses we associate with emergency situations.
- On a long-term basis, the adrenal cortex produces *glucocorticoids* similar to cortisone and *mineralocorticoids* to regulate salt and water balance.
- The adrenal cortex also secretes both male and female sex hormones in both sexes.

Adrenal glands



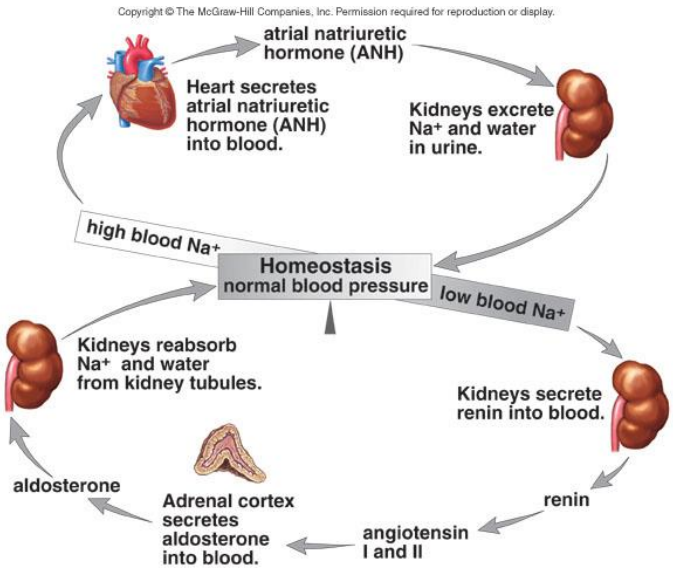
Glucocorticoids

- *Cortisol* promotes breakdown of muscle proteins to amino acids; the liver then breaks the amino acids into glucose.
- Cortisol also promotes metabolism of fatty acids rather than carbohydrates, which spares glucose.
- Both actions raise the blood glucose level.
- High levels of blood glucocorticoids can suppress immune system function.

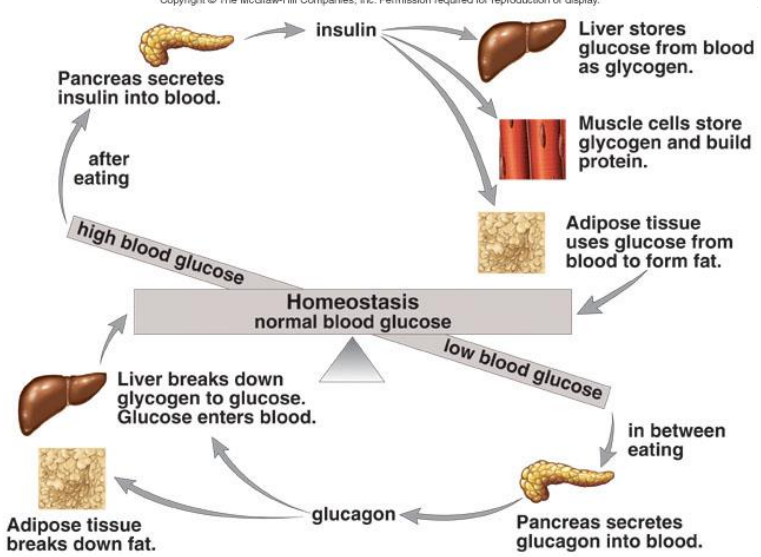
Mineralocorticoids

- *Aldosterone* causes the kidneys to reabsorb sodium ions (Na^+) and excrete potassium ions (K^+).
- When blood sodium levels and blood pressure are low, the kidneys secrete renin; the effect of the renin-angiotensin-aldosterone system is to raise blood pressure.
- The hormone *atrial natriuretic hormone* produced by the heart inhibits the secretion of aldosterone, thus reducing blood pressure.

Regulation of blood pressure and



Regulation of blood glucose level

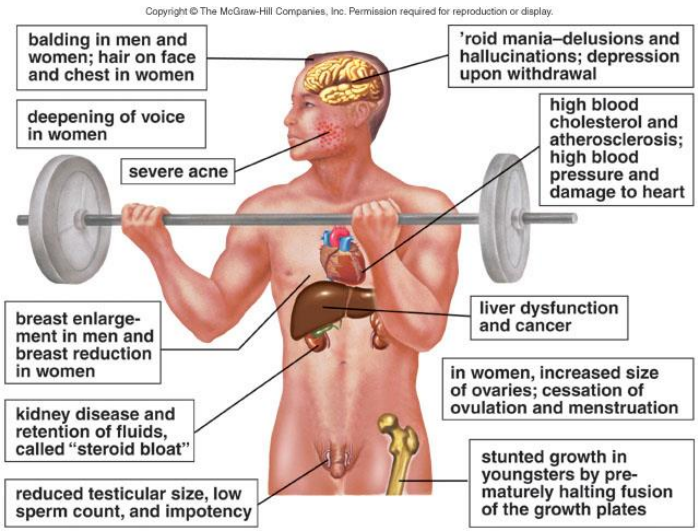


Diabetes Mellitus

- The most common illness due to hormonal imbalance is *diabetes mellitus*.
- Diabetes is due to the failure of the pancreas to produce insulin or the inability of the body cells to take it up.
- *Hyperglycemia* symptoms develop, and glucose appears in the urine.
- Diabetes is diagnosed using a glucose tolerance test.

- *Type I diabetes mellitus* occurs when the pancreas does not produce insulin and the patient requires insulin injections.
- Most people with diabetes have *Type II diabetes mellitus* where the pancreas produces insulin but the body cells do not respond.
- Both types lead to long-term serious complications.

The effects of anabolic steroid use



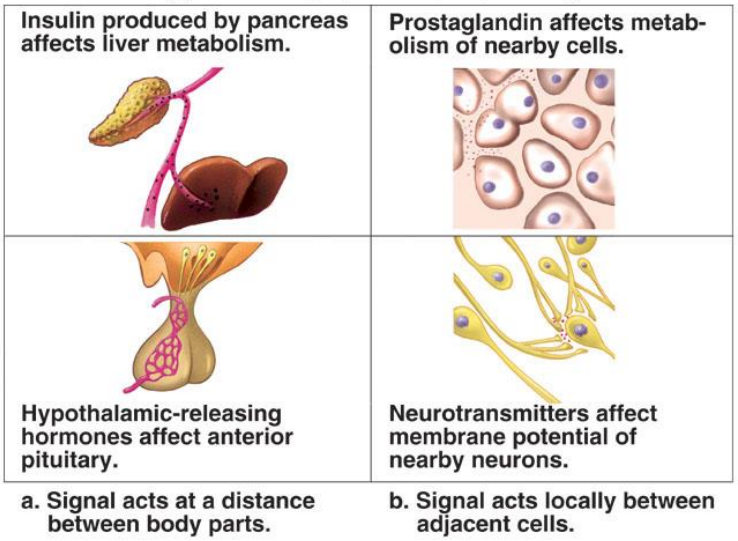
Thymus Gland

- The thymus under the sternum produces *thymosins* that stimulate T lymphocyte production and maturation.
- The thymus decreases in size with age and becomes fatty.
- There is hope that thymosins can be injected into AIDS or cancer patients where they would enhance T lymphocyte function.

Pineal Gland

- The pineal gland in the brain produces *melatonin* which is involved in circadian rhythms and the timing of development of the reproductive organs.
- Children whose pineal gland has been destroyed due to a brain tumor experience early puberty.

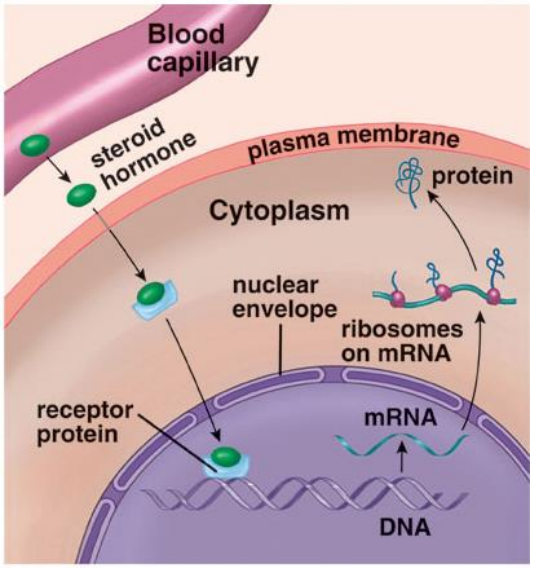
Chemical signals



The Action of Hormones

- *Steroid hormones* enter the nucleus and combine with a receptor protein, and the hormone-receptor complex attaches to DNA and activates certain genes.
- Transcription and translation lead to protein synthesis.
- *Peptide hormones* are usually received by a hormone receptor protein located in the plasma membrane.

Action of a steroid hormone



- Most often the reception of a peptide hormone leads to activation of an enzyme that changes ATP to *cyclic AMP* (cAMP).
- cAMP, as a *second messenger*, then activates an enzyme cascade.
- Calcium is also a common second messenger.
- Hormones work in small quantities because their effect is amplified by enzymes.

Action of a peptide hormone