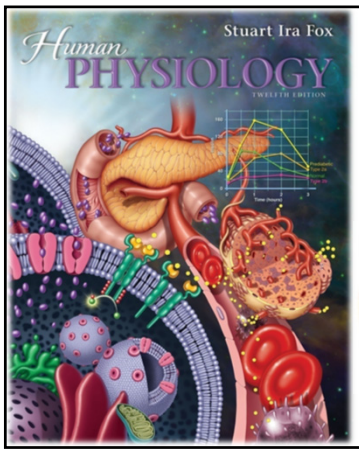
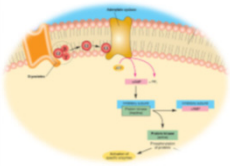


CHAPTER 11

Endocrine System



1

Chapter 11 Outline

- Endocrine Glands and Hormones
- Mechanisms of Hormone Action
- Pituitary Gland
- Adrenal Glands
- Thyroid and Parathyroid Hormones
- Pancreas and Other Endocrine Glands
- Autocrine and Paracrine Regulation

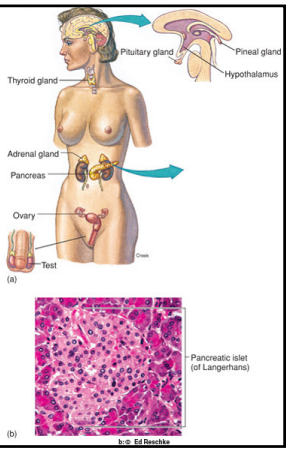
2

Endocrine Glands and Hormones

3

Endocrine Glands

- Are ductless and secrete hormones into bloodstream
- Hormones travel to target cells that contain receptor proteins for it
- Neurohormones are secreted into blood by specialized neurons
- Hormones affect metabolism of targets



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Chemical Classification of Hormones

5

Chemical Classification of Hormones

- **Amine** hormones are derived from **tyrosine** or **tryptophan**
  - Include NE, Epi, thyroxine, melatonin
- **Peptide hormones**
  - Polypeptide and protein hormones are chains of amino acids
    - Include ADH, GH, insulin, oxytocin, glucagon, ACTH, PTH
  - Glycoproteins include LH, FSH, TSH
- **Steroids** are lipids derived from cholesterol
  - Include testosterone, estrogen, progesterone, alsoterone and cortisol

6

Hormonal Actions and Interactions

7

Common Aspects of Neural and Endocrine Regulation

- Both NS and endocrine system use chemicals to communicate
- **Difference** between NTs and hormones **is transport in blood** and more diversity of effects in hormone targets
- **Some** chemicals are **used as hormones and NTs**
- **Targets** for both NTs and hormones **must have specific receptor** proteins
- Must be a way to rapidly inactivate both

8

Hormone Interactions

- Synergistic hormones:
  - They work together to produce an effect (**complementary**)
  - Produce a larger effect together than individual hormone (**additive**)
- Permissive effect if a hormone enhances responsiveness of a target organ to 2nd hormone
- Antagonistic: 1 hormone inhibits effect of another hormone.

9

Hormone Levels and Tissue Responses

- Normal tissue responses are produced only when hormones are in physiological range
- High (pharmacological) doses can cause a number of side effects
  - Probably by binding to receptors of different but closely related other hormones

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Hormone Levels and Tissue Responses

- Priming effect (upregulation) occurs when a hormone induces more of its own receptors in target cells
  - Results in greater response in target cell
- Desensitization (downregulation) occurs after long exposure to high levels of hormone
  - Subsequent exposure to this hormone produces a lesser response
- Most peptide hormones have pulsatile secretion which prevents downregulation

11

Mechanisms of Hormone Action

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Mechanisms of Hormone Action

- Target cell receptors show specificity, high affinity, and low capacity for a hormone
- **Lipophilic hormones** have receptors in target's cytoplasm and/or nucleus because can diffuse thru plasma membrane
  - Their target is the nucleus where they affect transcription
    - Called genomic action and takes at least 30 mins
- **Hydrophilic hormones** have receptors on surface of target cell
  - These act through 2nd messengers; effects are quick
  - Some steroids also act on cell surface receptors
    - Called nongenomic action

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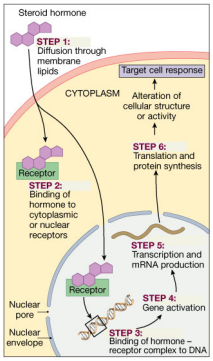
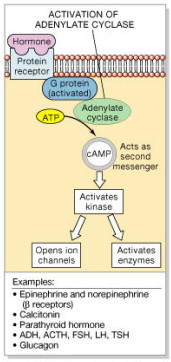
Hormone Effects on Gene Activity





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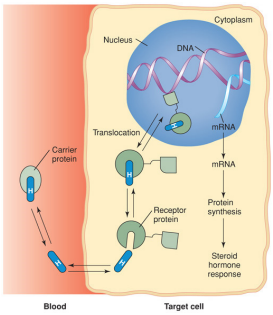
Hormones That Bind to Nuclear Receptor Proteins

- Lipid hormones travel in blood attached to carrier proteins
  - They dissociate from carriers to pass thru plasma membrane of target
    - Receptors are called nuclear hormone receptors



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Nuclear Hormone Receptors

- Serve as transcription factors when bound to hormone ligands
  - Activate transcription
- Constitute a "superfamily" composed of steroid family and thyroid hormone family (which includes vitamin D and retinoic acid)

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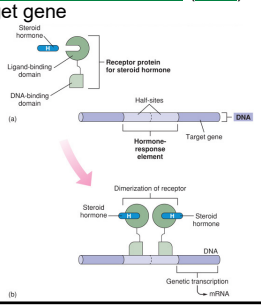
Nuclear Hormone Receptors

- Have ligand (hormone)-binding and DNA-binding domains
  - Binds hormone and translocates to nucleus
  - Binds to hormone-response element (HRE) on DNA located adjacent to target gene



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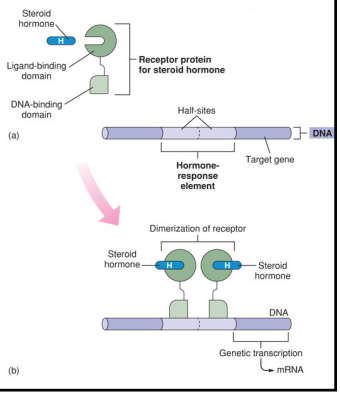
Mechanisms of Steroid Hormones

- HRE consists of 2 half-sites
- 2 ligand-bound receptors have to bind to each HRE (dimerization)
  - This stimulates transcription of target gene



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Mechanism of Thyroid Hormone Action

- Thyroid secretes 90% T_4 (thyroxine) and 10% T_3
  - 99.96% of T_4 in blood is bound to carrier protein (thyroid binding globulin - TBG)
  - Only free thyroxine and T_3 can enter cells
  - Protein bound thyroxine serves as a reservoir
  - T_4 converted to T_3 inside target cell
    - T_3 binds to receptor protein located in nucleus

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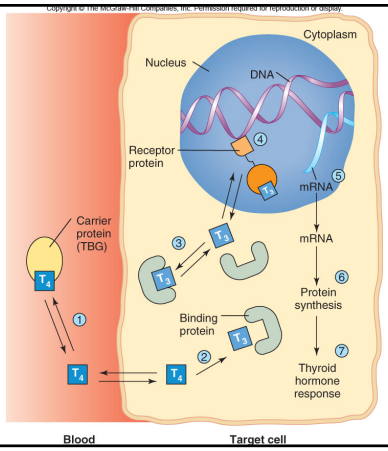

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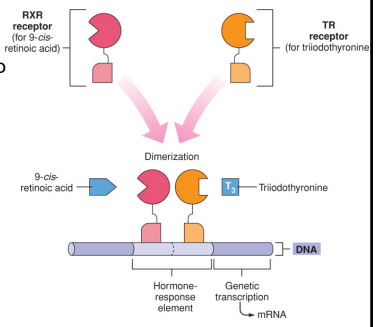
Mechanism of Thyroid Hormone Action

The receptor for T_3:

- T_3 and receptor bind to 1 half-site
- Other half-site binds retinoic acid
  - Two partners form heterodimer that activates HRE
    - Stimulates transcription of target gene



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Hormones That Use 2nd Messengers

- Water soluble hormones use cell surface receptors because cannot pass through plasma membrane
  - Actions are mediated by 2nd messengers
  - Hormone is extracellular signal; 2nd messenger carries signal from receptor to inside of cell

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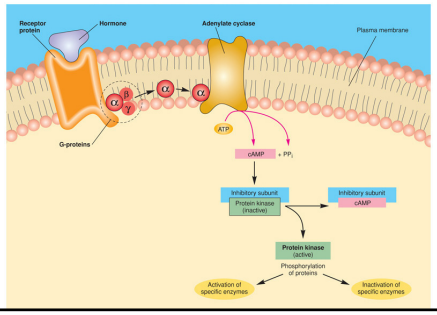
Adenylate Cyclase-cAMP

- cAMP mediates effects of many polypeptide and glycoprotein hormones
- Hormone binds to receptor causing dissociation of a G-protein subunit



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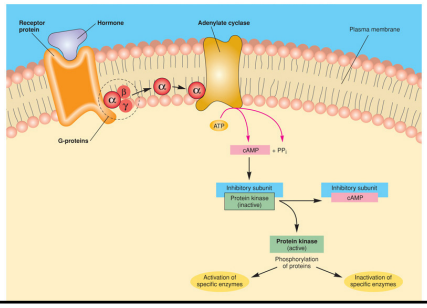
Adenylate Cyclase-cAMP

- G-protein subunit binds to and activates adenylate cyclase
  - Which converts ATP into cAMP
    - cAMP attaches to inhibitory subunit of protein kinase



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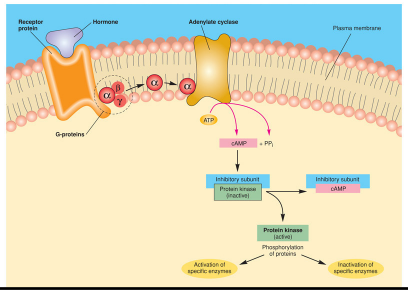
Adenylate Cyclase-cAMP

- Inhibitory subunit dissociates, activating protein kinase
- Which phosphorylates enzymes that produce hormone's effects
- cAMP inactivated by phosphodiesterase



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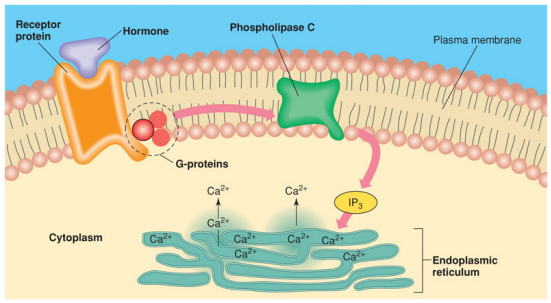
Phospholipase-C-Ca^{2+}

- Serves as 2nd messenger system for some hormones
- Hormone binds to surface receptor, activates G-protein, which activates phospholipase C



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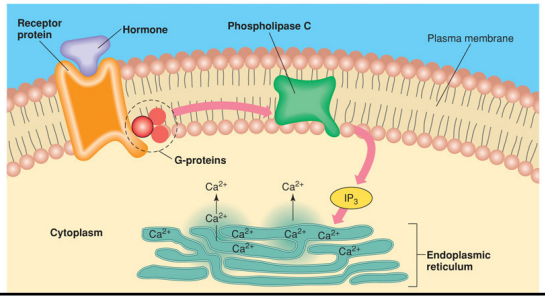
Phospholipase-C-Ca^{2+}

- Phospholipase C splits a membrane phospholipid into 2nd messengers IP_3 and DAG
  - IP_3 diffuses through cytoplasm to ER
    - Causing Ca^{2+} channels to open



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Phospholipase-C-Ca^{2+}

- Ca^{2+} diffuses into cytoplasm and binds to and activates calmodulin
- Ca^{2+}-Calmodulin activates protein kinases which phosphorylate enzymes that produce hormone's effects

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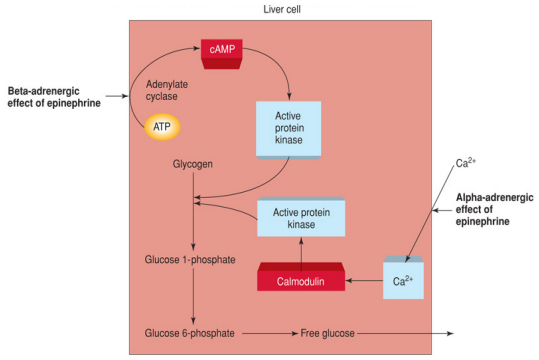
Epinephrine Can Act Via Two 2nd Messengers



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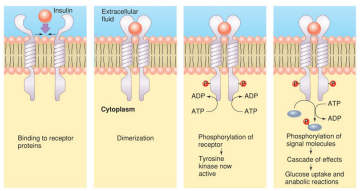
Tyrosine Kinase 2nd Messenger System

- Is used by insulin and many growth factors to cause cellular effects
- Surface receptor is tyrosine kinase
  - Consists of 2 units that form active dimer when insulin binds



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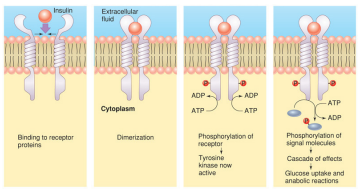
Tyrosine Kinase 2nd Messenger System

- Activated tyrosine kinase phosphorylates signaling molecules that induce hormone/growth factor effects



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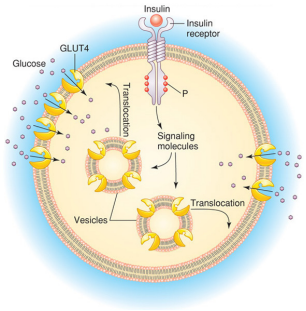
Insulin Action

- Insulin stimulates glucose uptake by means of GLUT 4 carrier proteins
  - 2nd messengers cause vesicles containing GLUT4 transporters to be inserted into plasma membrane



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Endocrine Organs

- Pituitary
- Gonads (portion of chapter 20) – Produce gametes
- Adrenal gland - Stress
- Thyroid – Metabolism and Calcium Regulation
- Parathyroid – Calcium Regulation
- Pancreas – Glucose Regulation

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Pituitary Gland

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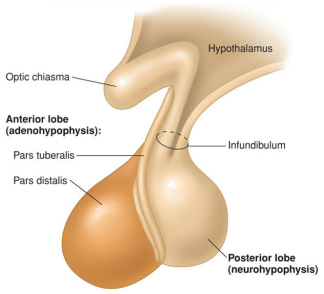
Pituitary Gland

- Is structurally and functionally divided into anterior and posterior lobes
- Hangs below hypothalamus by infundibulum
- Anterior produces own hormones
  - Controlled by hypothalamus
- Posterior stores and releases hormones made in hypothalamus



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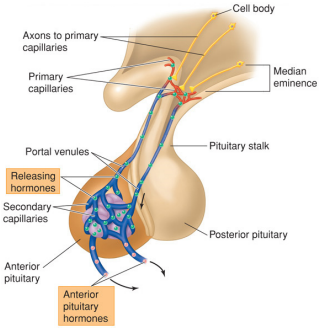
Pituitary Gland

- Pituitary gland is located beneath hypothalamus at base of forebrain



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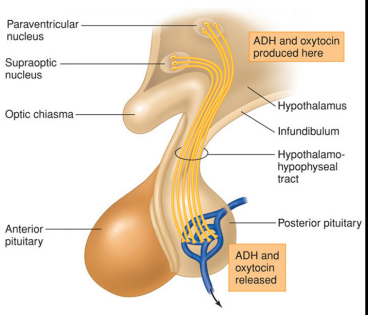
Posterior Pituitary

- Stores and releases the hormones ***vasopressin*** **(ADH)** and ***oxytocin*** that are made in the hypothalamus



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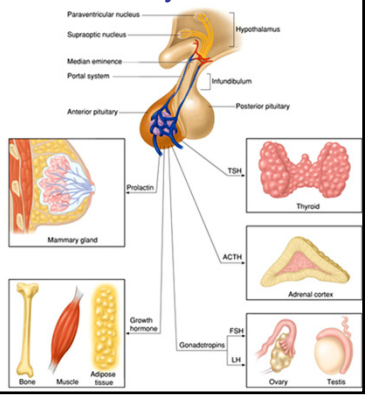
Anterior Pituitary

- **Secretes 6 trophic** hormones that maintain size of targets
  - **High blood levels** cause target to hypertrophy
  - **Low blood levels** cause atrophy



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Anterior Pituitary

- Growth hormone (GH) promotes growth, protein synthesis, and movement of amino acids into cells
- Thyroid stimulating hormone (TSH) stimulates thyroid to produce and secrete T_4 and T_3
- Adrenocorticotrophic hormone (ACTH) stimulates adrenal cortex to secrete cortisol, aldosterone
- Follicle stimulating hormone (FSH) stimulates growth of ovarian follicles and sperm production
- Luteinizing hormone (LH) causes ovulation and secretion of testosterone in testes
- Prolactin (PRL) stimulates milk production by mammary glands

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Table 11.6 | Anterior Pituitary Hormones

Hormone	Target Tissue	Principal Actions	Regulation of Secretion
ACTH (adrenocorticotropic hormone)	Adrenal cortex	Stimulates secretion of glucocorticoids	Stimulated by CRH (corticotropin-releasing hormone); inhibited by glucocorticoids
TSH (thyroid-stimulating hormone)	Thyroid gland	Stimulates secretion of thyroid hormones	Stimulated by TRH (thyrotropin-releasing hormone); inhibited by thyroid hormones
GH (growth hormone)	Most tissue	Promotes protein synthesis and growth; lipolysis and increased blood glucose	Inhibited by somatostatin; stimulated by growth hormone-releasing hormone
FSH (follicle-stimulating hormone)	Gonads	Promotes gamete production and stimulates estrogen production in females	Stimulated by GnRH (gonadotropin-releasing hormone); inhibited by sex steroids and inhibin
PRL (prolactin)	Mammary glands and other sex accessory organs	Promotes milk production in lactating females; additional actions in other organs	Inhibited by PIH (prolactin-inhibiting hormone)
LH (luteinizing hormone)	Gonads	Stimulates sex hormone secretion; ovulation and corpus luteum formation in females; stimulates testosterone secretion in males	Stimulated by GnRH; inhibited by sex steroids

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Anterior Pituitary

- Release of Anterior Pituitary hormones is controlled by
  - hypothalamic
    - releasing factors
    - inhibiting factors
  - feedback from levels of target gland hormones

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Table 11.7 | Hypothalamic Hormones Involved in the Control of the Anterior Pituitary

Hypothalamic Hormone	Structure	Effect on Anterior Pituitary
Corticotropin-releasing hormone (CRH)	41 amino acids	Stimulates secretion of adrenocorticotropic hormone (ACTH)
Gonadotropin-releasing hormone (GnRH)	10 amino acids	Stimulates secretion of follicle-stimulating hormone (FHS) and luteinizing hormone (LH)
Prolactin-inhibiting hormone (PIH)	Dopamine	Inhibits prolactin secretion
Somatostatin	14 amino acids	Inhibits secretion of growth hormone
Thyrotropin-releasing hormone (TRH)	3 amino acids	Stimulates secretion of thyroid-stimulating hormone (TSH)
Growth hormone-releasing hormone (GHRH)	44 amino acids	Stimulates growth hormone secretion

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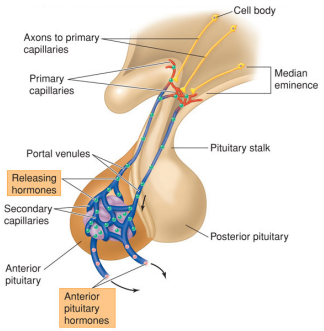
Anterior Pituitary

- Releasing and inhibiting hormones from hypothalamus are released from axon endings into capillary bed in median eminence
- Carried by hypothalamo-hypophyseal portal system directly to another capillary bed in A. Pit.
- Diffuse into A. Pit. and regulate secretion of its hormones



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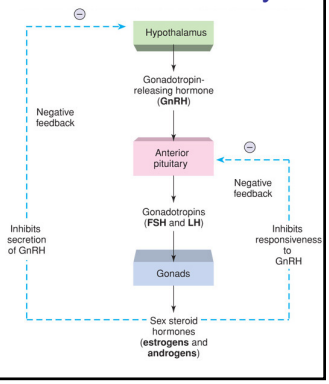
Feedback Control of Anterior Pituitary

- The hypothalamic-pituitary-gonad axis (control system)
- Involves short feedback loop in which retrograde flow of blood and hormones from A. Pit. to hypothalamus inhibits secretion of releasing hormone
- Involves negative feedback of target gland hormones
- And during menstrual cycle, estrogen stimulates "LH surge" by positive feedback



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Sex and Reproductive Hormones

- Gonads (testes and ovaries) secrete steroid hormones testosterone, estrogen, and progesterone
- Placenta secretes estrogen, progesterone, hCG, and somatomammotropin

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The Ovarian Cycle – 3 phases

- **Follicular Phase -** first ½ of ovarian cycle
  - Follicle development
- **Ovulation** – Midpoint of ovarion cycle
  - Oocyte exits from one ovary
    - Enters the peritoneal cavity
      - Is swept into the uterine tube
- **Luteal Phase** – second ½ of ovarian cycle
  - Remaining follicle becomes a corpus luteum
    - Secretes progesterone
    - Acts to prepare for implantation of an embryo

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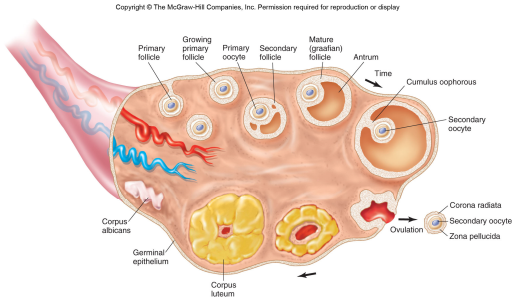
Ovarian Cycle Summary



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The Uterine Cycle

- Series of cyclic phases of the endometrium
- Phases coordinate with the ovarian cycle
- Endometrial phases directed by FSH and LH
- Phases of uterine cycle – 3 phases
  - **Menstrual phase** – days 1-5
    - Stratum functionalis is shed
  - **Proliferative phase** – days 6-14
  - **Secretory phase** – days 15-28

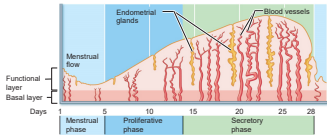

Figure 25.18c, d

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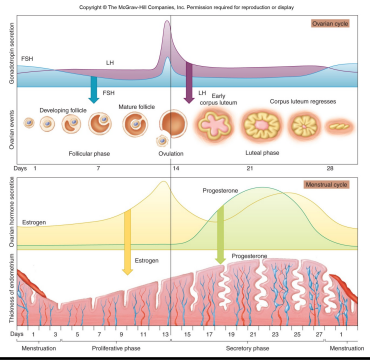
Menstrual and Ovarian Cycles



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Higher Brain Function and Anterior Pituitary Secretion

- Hypothalamus receives input from higher brain centers that can affect Anterior Pituitary secretion
- e.g. emotional states and psychological stress can affect circadian rhythms, menstrual cycle, and adrenal hormones

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Posterior Pituitary

- Stores and releases 2 hormones produced in hypothalamus:
  - Antidiuretic hormone (ADH/vasopressin)
    - Promotes H_2O conservation by kidneys
  - Oxytocin
    - Stimulates contractions of uterus during parturition
    - Stimulates contractions of mammary gland alveoli for milk-ejection reflex

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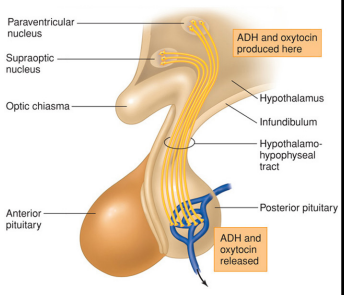
Hypothalamic Control of Posterior Pituitary

- Supraoptic nuclei of hypothalamus produce ADH
- Paraventricular nuclei produce oxytocin
- Both transported along hypothalamo-hypophyseal tract to posterior pituitary
- Release controlled in hypothalamus by neuroendocrine reflexes



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Adrenal Gland

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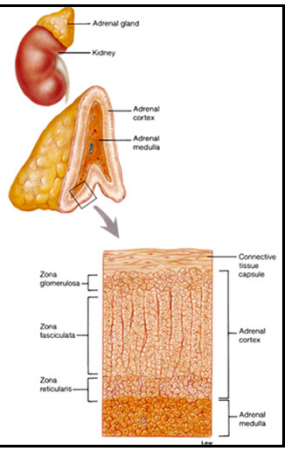
Adrenal Glands

- Sit on top of kidneys
- Each consists of outer cortex and inner medulla
- Which arise differently during development



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Adrenal Glands

- Medulla synthesizes and secretes 80% Epinephrine and 20% Norepinephrine
  - Controlled by sympathetic division of ANS
- Cortex is controlled by ACTH and secretes:
  - Cortisol which inhibits glucose utilization and stimulates gluconeogenesis
  - Aldosterone which stimulate kidneys to reabsorb Na^+ and secrete K^+
  - And some supplementary sex steroids

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Adrenal Medulla

- Hormonal effects of Epinephrine last 10X longer than Norepinephrine
- Innervated by preganglionic Sympathetic fibers
- Activated during "fight or flight" response
  - Causes:
    - Increased respiratory rate
    - Increased HR and cardiac output
    - General vasoconstriction which increases venous return
    - Glycogenolysis and lipolysis

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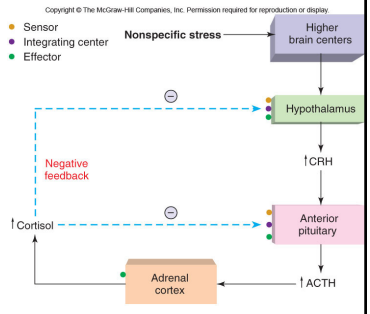
Stress and the Adrenal Gland

- Stress induces a non-specific response called general adaptation syndrome (GAS)
- Causes ACTH and cortisol release



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Stress and the Adrenal Gland

- Chronic stress can induce high levels of cortisol that cause a number of negative effects:
  - **atrophy of hippocampus** (involved in memory)
  - **reduced sensitivity** of tissues to insulin (insulin resistance)
  - **inhibition of vagus** nerve activity
  - **suppression** of growth hormone, thyroid hormone, and gonadotropins

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Thyroid Gland

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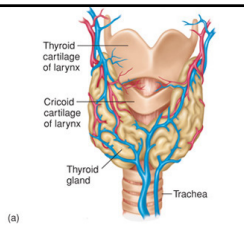
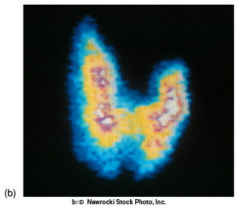
Thyroid Gland

- Is located just below the larynx
- Secretes T_4 and T_3 which set **Base Metabolic Rate** (BMR) and are needed for growth, development
- A scan of the thyroid 24 hrs. after intake of radioactive iodine (b)





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Thyroid Gland

- Consists of microscopic thyroid follicles
  - Outer layer is follicle cells that synthesize T_4
  - Interior filled with colloid, a protein-rich fluid

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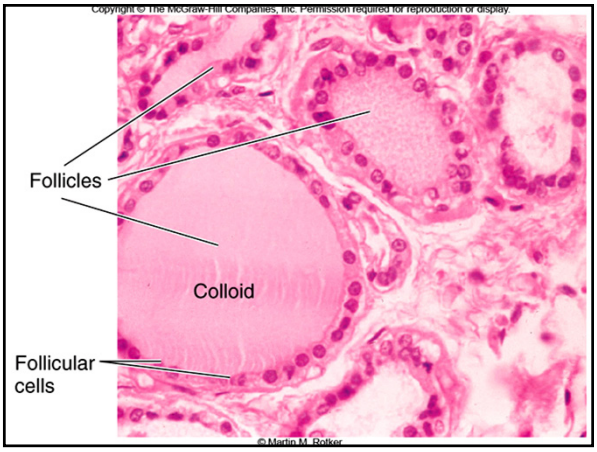

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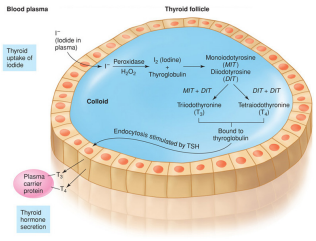
Production of Thyroid Hormones

- Iodide (I^-) in blood is actively transported into follicles and secreted into colloid
- Where it is oxidized to iodine (I_2) and attached to tyrosines of thyroglobulin
- A large storage molecule for T_4 and T_3
- TSH stimulates hydrolysis of T_4 and T_3s from thyroglobulin and then secretion



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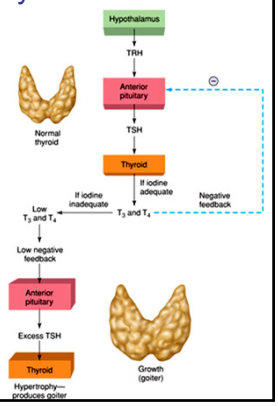
Diseases of the Thyroid - Goiter

- In absence of sufficient dietary iodide, T_4 and T_3 cannot be made and levels are low
- Low T_4 and T_3 don't provide negative feedback and TSH levels go up
- Because TSH is a trophic hormone, thyroid gland grows
- Resulting in a goiter



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Diseases of the Thyroid

- Hypothyroid - People with inadequate T_4 and T_3 levels
  - Have low BMR, weight gain, lethargy, cold intolerance
- Hyperthyroid – People with increased T_4 and T_3 levels.
  - Characterized by weight loss, heat intolerance, irritability, high BMR, exopthalmos.

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Diseases of the Thyroid

- Goiter – Enlargement of thyroid gland due to iodine deficiency
- Grave's disease
  - Autoimmune disease where antibodies act like TSH and stimulate thyroid gland to grow and oversecrete.

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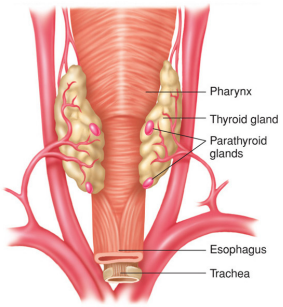
Parathyroid Glands

- Are 4 glands embedded in lateral lobes of post. side of thyroid gland
- Secrete Parathyroid hormone (PTH)
- Most important hormone for control of blood Ca^{2+} levels



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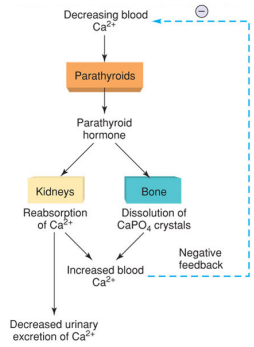
Parathyroid Hormone

- Release stimulated by decreased blood Ca^{2+}
- Acts on bones, kidney, and intestines to increase blood Ca^{2+} levels



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Islets of Langerhans

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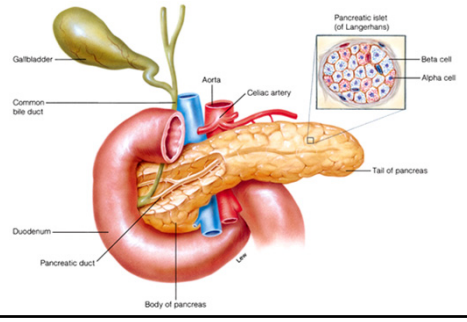
Islets of Langerhans

- Are scattered clusters of endocrine cells in pancreas
- Contain alpha and beta cells



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Islets of Langerhans

- Alpha cells secrete glucagon in response to low blood glucose
  - Stimulates glycogenolysis and lipolysis
  - Increases blood glucose

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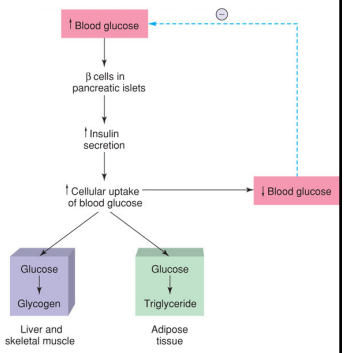
Islets of Langerhans

- Beta cells secrete insulin in response to high blood glucose
  - Promotes entry of glucose into cells
  - And conversion of glucose into glycogen and fat
  - Decreases blood glucose



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