Learning Objectives:
- Identify the three major classes of hormones
- Distinguish tropic and non-tropic hormones
- Identify the hormones produced by the hypothalamus, anterior and posterior pituitary
- Describe negative feedback controls of the hypothalamic-pituitary axis
- Diagnose whether an endocrine disorder is a primary or secondary pathology

QUIZ/TEST REVIEW NOTES
SECTION 1 ENDOCRINOLOGY
[ENDOCRINOLOGY/HORMONES]
CHAPTERS 7 AND 22

CHAPTER 7

HORMONE: Chemical secreted by a cell or group of cells into the blood for transport to a distant target where it acts in very low concentrations to affect growth, development, homeostasis, or metabolism
- Hormones of the endocrine system are secreted into the blood, act slowly, and their effects may take minutes to hours to develop
- Hormones bind with appropriate receptors (which are selectively present in the cells of target organ) and induce a desired effect on growth, metabolism or other function in the organ

Endocrine Glands of the Body:
1. Pineal Gland (Melatonin)
2. Anterior Pituitary (Tropic; Growth Hormone [GH], Tropins)
3. Posterior Pituitary (Non-tropic; ADH, Oxytocin)
4. Thyroid (Thyroine, T3)
5. Parathyroid (Parathormone)
6. Adrenal Cortex (Corticosteroids)
7. Adrenal Medulla (Catecholamines)
8. Pancreatic Islets (Insulin, Glucagon)
9. Tests (Male steroids, Inhibin)
10. Ovaries (female steroids, Inhibin)

Organs with Partial Endocrine Function:
1. Kidney (Renin, erythropoietin, calcitriol)
2. Liver (Somatomedin)
3. Thymus (Thymosin)
4. Hypothalamus (Hypothalamic hormones)
5. Heart (Natriueretic peptide)
6. Stomach (gastrin)
7. Duodenum (Secretin, CCK, GIP)

(NOTE) Endocrine Gland: Clusters of endocrine cells with distinct hormonal secretory functions

Page 14 and 15 for details for peptide, steroid, and amine hormone information
I. HORMONES EXERT THEIR EFFECT AT VERY LOW CONCENTRATIONS
   a. Has the ability to act at concentrations in the nanomolar ($10^{-9}$) to picomolar ($10^{-12}$) range
   b. Most (peptide hormones) are stored in high concentrations in a parent endocrine cell then released when stimulated

II. HORMONE ACTION MUST BE TERMINATED
   a. If insulin activity would be prolonged after a meal, blood glucose levels could fall so low that the nervous system could become unable to function properly – potentially a lethal situation
      i. The body avoids this by
         1. Limiting insulin secretion
         2. Removing or inactivating insulin circulating in the blood
         3. Terminating insulin activity in the cells
      ii. Hormones in the bloodstream are usually degraded into inactive metabolites by enzymes found primarily in the liver and kidneys
         1. The metabolites are then excreted in either the bile or the urine
         2. Rate of hormone breakdown is indicated by a hormone's half-life (amount of time required to reduce the concentration of hormone by one-half)

III. CLASSIFICATION OF HORMONES
   a. Peptide (protein) Hormones
      i. Linked amino acids
      ii. The initial peptide that comes off the ribosome is a large inactive protein known as a Preprohormone which Contains:
         a. One or more copies of a peptide hormone
         b. Signal Sequence that directs the protein in the lumen of the rough endoplasmic reticulum
         c. Other peptide sequences that may or may not have biological activity
            (Inactive Preprohormone moves through E.R. and Golgi complex, and then the signal sequence is removed turning the inactive molecule into a Prohormone)
      iii. Lipophobic; usually unable to enter the cell so instead bind to surface membrane receptors (initiating cellular response by means of Signal Transduction System, CAMP Second Messenger Systems, or by Tyrosine Kinase Activity)
      iv. Can be made in advance and stored in secretory vesicles until the cell receives a signal for secretion
      v. Examples of Peptide Hormones:
         Insulin, Glucagon, Somatostatin, Pancreatic Polypeptide
b. Steroid Hormones

i. Derived from cholesterol

ii. Made in only a few organs
   1. Adrenal Cortex (Three types of steroids)
   2. Adrenal Gland
   3. Gonads (estrogens, Progesterone, Androgens)
   4. Pregnant Women’s Placenta

iii. Lipophilic; diffuse easily across membranes, both out of their parent cell and into their target cells

iv. Cannot be stored in secretory vesicles; they are synthesized as needed/on demand from precursors

v. Not very soluble in plasma/body fluids so most steroid hormones in blood are bound to protein carrier molecules
   1. Corticosteroid-binding globulin
   2. Albumin
      a. Steroid hormone binding to a carrier protein protects hormone against enzymatic degradation, extending the half-life
      b. Binding can also block their entry into target cells

vi. Receptors found in cytoplasm or nucleus; Steroid ligation actives genes for transcription and translation which induces new protein synthesis
c. Amine Hormones

i. Derivatives of one of the two amino acids: tryptophan or tyrosine

1. Tryptophan: Melatonin (pineal gland)
2. Tyrosine: Catecholamine's (One tyrosine molecule), Thyroid hormones (Two tyrosine plus iodine atom)
   a. Catecholamine Hormones: (E, NE, Dopamine) Neurohormones that bind to cell membrane receptors the way peptide hormones do
   b. Thyroid Hormones: Behave more like steroids, with intracellular receptors that active genes
IV. CONTROL OF HORMONE RELEASE

a. Hormones can be classified by their reflex pathways

i. All reflex pathways have similar components:
   1. Stimulus
   2. Input Signal
   3. Integration of Signal (Integration Center)
   4. Output Signal → (in endocrine/neuroendocrine reflexes = Hormone/Neurohormone)
   5. Response

ii. Simple Reflex Pathway
   1. The response of pathway serves as negative feedback signal that turns off the reflex

   High Plasma Glucose → Insulin → Low Plasma Glucose

   Low Plasma Calcium → PTH → High Plasma Calcium

iii. Hormones are not restricted to follow only one reflex pathway
   1. Example: Insulin
      a. Can be triggered by input signals from nervous system
      b. Can be triggered by a hormone secreted from digestive tract as meal is eaten

b. The endocrine cell is the sensor in the simplest endocrine reflexes
   i. Simplest reflex control pathways in the endocrine system are those in which an endocrine cell directly senses a stimulus and responds by secreting its hormone
   ii. In this type of pathway the endocrine cell acts as both sensor (receptor) and integration center
      1. Example: Parathyroid hormone (PTH)
      2. Example: Insulin
c. Many endocrine Reflexes Involve the Nervous System
   i. Nervous system and endocrine system overlap in both structure and function
   ii. Specialized groups of neurons secrete Neurohormones, and two endocrine structures are incorporated into the anatomy of the brain
      1. Pineal Gland
      2. Pituitary Gland

V. HYPOTHALAMIC-PITUITARY PATHWAY

a. Neurohormones Are Secreted into the Blood by Neurons
   i. Neurohormones: Chemical signals released into the blood by a neuron
   ii. Nervous System produces three major groups of Neurohormones
      1. Catecholamine’s (Made by modified neurons in Adrenal Medulla)
      2. Hypothalamic Anterior Pituitary Hormones (Tropic; Control other hormone secretion)
      3. Hypothalamic Posterior Pituitary Hormones (Non-tropic; Secrete hormones)

b. Pituitary Gland Is Actually Two Fused Glands
   i. Anterior Pituitary (Releases SIX Hormones)
      1. True endocrine gland or epithelia origin derived from embryonic tissue of the mouth
      2. Releases Six Hormones
         a. Prolactin
         b. Thyrotropin
         c. Adrenocorticotropin
         d. Growth hormone
         e. Follicle-stimulating hormone
         f. Luteinizing hormone
      3. TROPHIC Hormones (anterior pituitary)
         a. A hormone that controls the secretion of another hormone
         b. Stimulate and maintain their endocrine target tissue (organ target may atrophy if no trophic stimulation)
         c. The hypothalamic Neurohormones that control the release of Anterior Pituitary Hormones are also trophic hormones
      4. Control Growth, Metabolism and Reproduction
         a. Anterior pituitary controls so many vital functions that pituitary is often called the master gland
         b. Prolactin (PRL) and Growth Hormone (GH or Somatotropin) are the only two anterior pituitary hormones whose secretion is controlled by both releasing hormones and inhibiting hormones
c. Follicle stimulating hormone (FSH) and Luteinizing hormone (LH) are known as collectively as *gonadotropins* because both have effects on the ovaries or testes.
d. Thyroid-stimulating hormone (TSH or Thyrotropin) control hormone synthesis and secretion in thyroid gland.
e. Adrenocorticotropic hormone (ACTH or Corticotropin) act on certain cells of adrenal cortex to control synthesis and release of steroid hormone Cortisol.
ii. **Posterior Pituitary (Releases TWO Hormones)**

1. Extension of the neural tissue of the brain; secreting Neurohormones made in the hypothalamus
2. Storage and release sight for two Neurohormones (Peptides)
   a. **Oxytocin**
      i. Ejection of milk during breast-feeding
      ii. Contractions of uterus during labor and delivery
      iii. Could play role in social, sexual, and maternal behaviors
   b. **Vasopressin** (Antidiuretic Hormone)
      i. Regulates water balance in the body
3. Non-tropic hormones

c. Feedback Loops Are Different in the Hypothalamic-Pituitary Pathway
   i. Pathways in which anterior pituitary hormones act as trophic hormones are among most complex endocrine reflexes because they involve three integrating centers
      1. Hypothalamus
      2. Anterior Pituitary
      3. Endocrine target of pituitary hormone
         • Instead of response acting as a negative feedback signal the hormones themselves are the signal
         • Each hormone in pathway feeds back to suppress hormone secretion by integrating centers earlier in the reflex pathway
         • When secretion of one hormone increases or decreases in a complex pathway the secretion of other hormones also change
         • Typically in a two or three hormone sequence, the last hormone secreted will feed back to suppress the hormones that controlled its secretion [MAJOR EXCEPTION: Ovarian Hormones]

Example: Cortisol secreted from adrenal cortex feeds back to suppress secretion of the trophic hormones Corticotropin-releasing hormone and Adrenocorticotropic hormone
- Hypothalamus

- Tropic Releasing Hormone (H1)

- Anterior Pituitary

- Stimulating Hormone (H2)

- Peripheral Gland

- Non-tropic Hormone (H3)

- Target Response/Organ

- Long Loop Negative Feedback: Product (widget) or “downstream” hormone feedbacks to regulated/suppress earlier stage hormone that permitted its release
  
  [H3 inhibits H2 and H1]

- Short Loop Negative Feedback: Pituitary hormones feedback to decrease hormone secretion by hypothalamus
  
  [H2 inhibits H1]

- H1 = Releasing Hormone = TRH
- H2 = Stimulating Hormone = TSH
- H3 = Nontropic Hormone = Thyroxine

**KEY**

- Stimulus
- Integrating center
- Efferent pathway
- Effector
- Systemic response
d. **Portal System Directs Trophic Hormone Delivery**
   i. Hypothalamic trophic hormones that regulate secretion of anterior pituitary hormones are transported directly to the pituitary through special set of blood vessels known as the *hypothalamic-hypophyseal portal system*.
   1. **Portal System**: Specialized region of circulation consisting of two sets of capillaries directly connected by a set of blood vessels.
   2. **Three portal systems in the body**
      a. Kidneys
      b. Digestive System
      c. Brain
   3. Through a portal system a smaller amount of hormones can be released to elicit a given level of response.

   ![Diagram of the hypothalamic-hypophyseal portal system](image)

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VI. **HORMONE INTERACTIONS**

a. **Synergism**
   i. In synergism the effect of interacting hormones is more than additive
   ii. Example:

   Glucagon from pancreas is primarily responsible for elevating blood glucose levels, but Cortisol and epinephrine can also raise blood glucose levels. If these two/three hormones interact at their targets at the same time, the combination helps yield to a greater result; this type of interaction is called *synergism*.

   ![Graph of hormone interactions](image)
b. Permissive Hormones
   i. A hormone that cannot fully exert its effects unless a second hormone is present
   ii. Example
      1. Maturation of reproductive system is controlled by gonadotropin releasing hormones, but if thyroid hormone is not present in sufficient amounts the maturation of the reproductive system is delayed
         o Because thyroid hormone by itself cannot stimulate maturation of the reproductive system, thyroid hormone is considered to have a permissive effect on sexual maturation

c. Antagonistic Hormones
   i. Two hormones work against each other; one diminishes the effectiveness of the other
   ii. Hormones that have opposing physiological actions
      1. Example:
         a. Glucagon (↑ blood glucose) is antagonistic to Insulin (↓ blood glucose)
         b. PTH is antagonistic to Calcitonin

VII. ENDOCRINE PATHOLOGIES
a. Hypersecretion of Gland
   i. Normal effects of the hormone are exaggerated
   ii. Can be caused by
      1. Benign Tumors
      2. Immunological
      3. Substances Abuse
   iii. Can be used as treatment for
      1. Pharmacological Antagonists
      2. Radiation therapy
      3. Removal of a gland
   iv. Can also be caused from a substance coming from outside the body (exogenous) that is part of a medical treatment or an exogenous hormone agonist
      1. In this case, the condition is called iatrogenic; physician caused
      2. Example: Exogenous Cortisol
         • Exogenous Cortisol injected into the body acts as a negative feedback signal, just as Cortisol produced within the body would, shutting off the producing of CRH and ACTH
         • Without the trophic “nourishing” influence of ACTH the body’s own Cortisol production shuts down
         • It pituitary remains suppressed and the adrenal cortex is deprived of ACTH long enough the cells of both glands (adrenal cortex and anterior pituitary) will begin to shrink and lose their ability to manufacture ACTH and Cortisol; with the loss of cell mass known as Atrophy

NOTE: Exogenous Steroid hormones can be used to treat poison ivy, severe allergies, or abused for muscle gain. When treatment is complete the dosage must be tapered off gradually to allow the pituitary and adrenal gland to work back up to normal hormone production
b. Hyposecretion of Gland
   i. Hyposecretion diminishes or eliminates a hormone's effects
   ii. May occur anywhere along
      1. Endocrine control pathway
      2. Hypothalamus
      3. Pituitary
      4. Other endocrine glands
   iii. Most common cause is atrophy of the gland due to some disease process
   iv. Negative feedback pathways are affected in Hyposecretion, but in the opposite direction from Hyperecretion
      - Absence of negative feedback causes trophic hormone levels to rise as the trophic hormones attempt to make the defective gland increase its hormone output
      - **Example**: Adrenal cortex atrophies because of tuberculosis, diminishing Cortisol levels. Hypothalamus and anterior pituitary sense low Cortisol levels so they increase CRH and ACTH secretion

c. Reflex Disorders; Primary and Secondary
   i. Primary
      1. Nontropic gland disorder
      2. Ex: Tumor in the adrenal cortex begins to produce excessive amounts of Cortisol (Primary Hypersecretion)
   ii. Pituitary
      1. Tropic gland disorder
      2. Ex: Pituitary damage due to dead trauma decreases ACTH secretion resulting in Cortisol deficiency (Secondary Hyposecretion)

d. Down-regulation
   i. If hormone secretion is abnormally high for a prolonged period target cells may down-regulate (decrease the number of) their receptors for that hypersecreted hormone in an effort to diminish its responsiveness
   ii. Example: Hyperinsulinemia
      - Sustained high levels of insulin in blood cause target cells to remove insulin receptors from cell membrane
      - Patients suffering from hyperinsulinemia may show signs of diabetes (TYPE 2)

<table>
<thead>
<tr>
<th>(a) Secondary hypersecretion due to hypothalamic problem</th>
<th>(b) Secondary hypersecretion due to pituitary problem</th>
<th>(c) Primary hypersecretion due to problem with adrenal cortex</th>
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<tbody>
<tr>
<td>HYPOTHALAMUS</td>
<td>Hypothalamus</td>
<td>Hypothalamus</td>
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<tr>
<td>Anterior pituitary</td>
<td>CRH</td>
<td>CRH</td>
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<tr>
<td>Adrenal cortex</td>
<td>↑ ACTH</td>
<td>↑ ACTH</td>
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<tr>
<td>Adrenal cortex</td>
<td>Cortisol</td>
<td>Cortisol</td>
</tr>
<tr>
<td>Symptoms of excess</td>
<td>Negative feedback fails</td>
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</table>

**NOTE:**
PLACE OF DISORDER AND DOWN IF HYPERSECTION: ↑
ABOVE PLACE OF DISORDER IF HYPERSECTION: ↓
PLACE OF DISORDER AND DOWN IF HYPOSECRETION: ↓
ABOVE PLACE OF DISORDER IF HYPOSECRETION: ↑
### Peptide Hormones

<table>
<thead>
<tr>
<th>Peptide Hormones</th>
<th>Location</th>
<th>Function</th>
<th>Gland/Cell</th>
<th>Target</th>
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<tbody>
<tr>
<td>Trophic hormones</td>
<td>Hypothalamus</td>
<td>Release or inhibit hormones</td>
<td>Clusters of neurons</td>
<td>Anterior pituitary</td>
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<td>Oxytocin (OT)</td>
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<td>Milk ejection labor and delivery; behavior</td>
<td>Extensions of hypothalamic neurons</td>
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<td>Vasopressin (ADH)</td>
<td>Posterior pituitary</td>
<td>Water reabsorption</td>
<td>Extensions of hypothalamic neurons</td>
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<tr>
<td>Prolactin (PRL)</td>
<td>Anterior pituitary</td>
<td>Milk production</td>
<td>Glands</td>
<td>Breast</td>
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<tr>
<td>Growth hormone (GH, somatotropin)</td>
<td>Anterior pituitary</td>
<td>Growth and metabolism</td>
<td>Glands</td>
<td>Many tissue</td>
</tr>
<tr>
<td>Corticotropin (ACTH)</td>
<td>Anterior pituitary</td>
<td>Cortisol release</td>
<td>Glands</td>
<td>Adrenal cortex</td>
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<tr>
<td>Thyrotropin (TSH)</td>
<td>Anterior pituitary</td>
<td>Thyroid hormone synthesis and release</td>
<td>Glands</td>
<td>Thyroid gland</td>
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<td>Follicle stimulating hormone (FSH)</td>
<td>Anterior pituitary</td>
<td>Egg or sperm production; sex hormone production</td>
<td>Glands</td>
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<td>Luteinizing hormone (LH)</td>
<td>Anterior pituitary</td>
<td>Sex hormone production; egg or sperm production</td>
<td>Glands</td>
<td>Gonads</td>
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<td>Prathyroid hormone (PTH)</td>
<td>Parathyroid</td>
<td>Regulates plasma calcium and phosphate levels</td>
<td>Glands</td>
<td>Bone, kidney</td>
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<td>Thymosin; thymopoietin</td>
<td>Thymus</td>
<td>Lymphocyte development</td>
<td>Glands</td>
<td>Lymphocytes</td>
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<td>Atrial natriuretic peptide (ANP)</td>
<td>Heart</td>
<td>Increases sodium excretion</td>
<td>Cells</td>
<td>Kidneys</td>
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<tr>
<td>Angiotensinogen;</td>
<td>Liver</td>
<td>Aldosterone secretion; increases blood pressure</td>
<td>Cells</td>
<td>Adrenal cortex, blood vessels, brain</td>
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<tr>
<td>Insulin-like growth factors (IGF)</td>
<td>Liver</td>
<td>Growth</td>
<td>Cells</td>
<td>Many tissues</td>
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<tr>
<td>Gastrin; cholecystokinin (CCK), secretin, and others</td>
<td>Stomach and small intestine</td>
<td>Assist digestion and absorption of nutrients</td>
<td>Cells</td>
<td>GI tract and pancreas</td>
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<tr>
<td>Insulin, glucagon, Somatostatin (SS), pancreatic polypeptide</td>
<td>Pancreas</td>
<td>Metabolism of glucose and other nutrients</td>
<td>Glands</td>
<td>Many tissues</td>
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<td>Erythropoietin (EPO)</td>
<td>Kidney</td>
<td>Red blood cell production</td>
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<td>Inhibin</td>
<td>Tests (male)</td>
<td>Inhibit FSH secretion</td>
<td>Glands</td>
<td>Anterior pituitary</td>
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<tr>
<td>Ovarian inhibin;</td>
<td>Ovaries (female)</td>
<td>Inhibits FSH secretion</td>
<td>Glands</td>
<td>Anterior pituitary</td>
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<tr>
<td>Relaxin (pregnancy)</td>
<td>Ovaries (female)</td>
<td>Relaxes muscle</td>
<td>Glands</td>
<td>Uterine muscle</td>
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<td>Leptin and others</td>
<td>Adipose tissue</td>
<td>Food intake, metabolism reproduction</td>
<td>Cells</td>
<td>Hypothalamus, other tissues</td>
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<tr>
<td>Chorionic somatomammotropin (CS);</td>
<td>Placenta (pregnant females only)</td>
<td>Metabolism</td>
<td>Glands</td>
<td>Many tissues</td>
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<tr>
<td>Chorionic gonadotropin (CG)</td>
<td>Placenta (pregnant females only)</td>
<td>Hormone secretion</td>
<td>Glands</td>
<td>Corpus luteum of ovary</td>
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### Steroid Hormones

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<th>Target</th>
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<td>Aldosterone</td>
<td>Adrenal Cortex</td>
<td>Na⁺ and K⁺ homeostasis</td>
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<td>Cortisol</td>
<td>Adrenal Cortex</td>
<td>Stress response</td>
<td>Gland</td>
<td>Many tissues</td>
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<tr>
<td>Androgens</td>
<td>Adrenal Cortex</td>
<td>Sex drive in females</td>
<td>Gland</td>
<td>Many tissues</td>
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<tr>
<td>Vitamin D₃</td>
<td>Skin</td>
<td>Precursor of 1,25 Dihydroxy-vitamin D₃</td>
<td>Cell</td>
<td>Intermediate form of hormone</td>
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<td>Androgen</td>
<td>Testes (male)</td>
<td>Sperm production, secondary sex characteristics</td>
<td>Gland</td>
<td>Many tissues</td>
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<tr>
<td>Estrogens and progesterone</td>
<td>Ovaries (female)</td>
<td>Egg production, secondary sex characteristics</td>
<td>Gland</td>
<td>Many tissues</td>
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<td>Estrogens and progesterone (P)</td>
<td>Pregnant Only</td>
<td>Fetal and maternal development</td>
<td>Gland</td>
<td>Many tissues</td>
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<td>AMINE HORMONES</td>
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<td>LOCATION</td>
<td>FUNCTION</td>
<td>GLAND/CELL</td>
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<td>Melatonin</td>
<td>Pineal gland</td>
<td>Gland</td>
<td>Unclear in humans</td>
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<td>Epinephrine &amp;</td>
<td>Adrenal Medulla</td>
<td>Gland</td>
<td>Many tissues</td>
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<tr>
<td>Norepinephrine</td>
<td>Fight-or-flight response</td>
<td>Many tissues</td>
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<td>[IODINATED AMINES]</td>
<td>Triiodothyronine and thryoxine (T₃ and T₄)</td>
<td>Metabolism, growth, and development</td>
<td>Many tissues</td>
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