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

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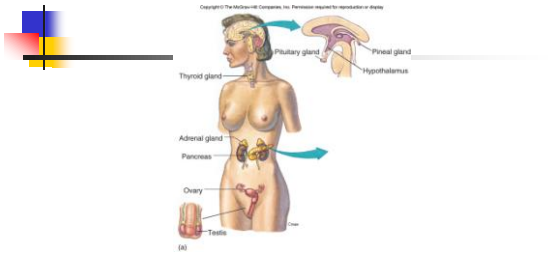
I. Endocrine Glands and Hormones



Endocrine Glands

- Ductless
- Secrete hormones into the blood
- Hormones are carried to target cells having receptors for those hormones.
- Many organs secrete hormones other than those discussed in this chapter:
  - Heart, liver, kidneys, adipose tissue

Table 11.1 A Partial Listing of the Endocrine Glands

Endocrine Gland	Major Hormones	Primary Target Organs	Primary Effects
Adipose tissue	Leptin	Hypothalamus	Suppresses appetite
Adrenal cortex	Glucocorticoids Aldosterone	Liver and muscles Kidneys	Glucocorticoids influence glucose metabolism; aldosterone promotes Na^+ retention, K^+ excretion
Adrenal medulla	Epinephrine	Heart, bronchioles, and blood vessels	Causes adrenergic stimulation
Heart	Atrial natriuretic hormone	Kidneys	Promotes excretion of Na^+ in the urine
Hypothalamus	Releasing and inhibiting hormones	Anterior pituitary	Regulates secretion of anterior pituitary hormones
Small intestine	Secretin and cholecystokinin	Stomach, liver, and pancreas	Inhibits gastric motility and stimulates bile and pancreatic juice secretion
Islets of Langerhans (pancreas)	Insulin Glucagon	Many organs Liver and adipose tissue	Insulin promotes cellular uptake of glucose and formation of glycogen and fat; glucagon stimulates hydrolysis of glycogen and fat
Kidneys	Erythropoietin	Bone marrow	Stimulates red blood cell production
Liver	Somatomedins	Cartilage	Stimulates cell division and growth
Ovaries	Estradiol-17β and progesterone	Female reproductive tract and mammary glands	Maintains structure of reproductive tract and promotes secondary sex characteristics
Parathyroid glands	Parathyroid hormone	Bone, small intestine, and kidneys	Increases Ca^{2+} concentration in blood
Pineal gland	Melatonin	Hypothalamus and anterior pituitary	Affects secretion of gonadotrophic hormones
Pituitary, anterior	Trophic hormones	Endocrine glands and other organs	Stimulates growth and development of target organs; stimulates secretion of other hormones
Pituitary, posterior	Antidiuretic hormone Oxytocin	Kidneys and blood vessels Uterus and mammary glands	Antidiuretic hormone promotes water retention and vasoconstriction; oxytocin stimulates contraction of uterus and mammary secretory units
Skin	1,25-Dihydroxyvitamin D_3	Small intestine	Stimulates absorption of Ca^{2+}
Stomach	Gastrin	Stomach	Stimulates acid secretion
Testes	Testosterone	Prostate, seminal vesicles, and other organs	Stimulates secondary sexual development
Thymus	Thymopoietin	Lymph nodes	Stimulates white blood cell production
Thyroid gland	Thyroxine (T_4) and triiodothyronine (T_3); calcitonin	Most organs	Thyroxine and triiodothyronine promote growth and development and stimulate basal rate of cell respiration (basal metabolic rate or BMR); calcitonin may participate in the regulation of blood Ca^{2+} levels

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Chemical Classification of Hormones

- **Amines hormones are derived from tyrosine or tryptophan**
  - **Include NE, Epi, thyroxine, melatonin**
- **Polypeptide and protein hormones are chains of amino acids**
  - **Include ADH, GH, insulin, oxytocin, glucagon, ACTH, PTH**
- **Glycoproteins Protein bound to Carb groups include LH, FSH, TSH**
- **Steroids lipids derived from cholesterol**
  - **Include testosterone, estrogen, progesterone, aldsoterone and cortisol**
  - **2 Glands – gonads and adrenal cortex**
  - **Steriod and thyroid hormones enter the cell**

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Prohormones and Prehormones

- Prehormones are precursors of prohormones
  - e.g. preproinsulin
- Prohormones are precursors of hormones
  - e.g. proinsulin
- Some hormones are inactive until activated by target cells
  - e.g. thyroxine (T_4) is inactive until converted to T_3 in target cells

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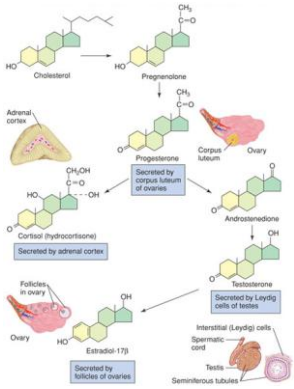

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Similarities and Differences of Neural and Endocrine Regulation

Similarities:

- **Both NS and endocrine system use chemicals to communicate**
- **Some chemicals are used as hormones and NTs**
- **Must be a way to rapidly inactivate both**
- **Targets for both NTs and hormones must have specific receptor proteins**

Differences:

- **Neural regulation is always very fast – Endocrine be**
- **Most hormones are transported in blood**
- **More diversity of effects in hormone targets vs neurons**

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Hormone Interactions

- **A tissue usually responds to >1 hormones**
- **Synergistic: work together to produce an effect**
  - **Can produce larger effect together than individually**
  - **Permissive effect: enhances responsiveness of a target organ to 2nd hormone**
  - **Antagonistic: A hormone inhibits effect of another hormone**
- **Hormone concentration is important**
  - **Weird concentrations (medically induced or other) can influence effect of hormone on target cells**

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Hormone Levels and Tissue Responses

- **Priming effect (upregulation): hormone induces more receptors in target cells**
  - **Results in greater response in target cell**
- **Desensitization (downregulation): long exposure to high levels of polypeptide hormone**
  - **Target cells can quit responding**
  - **Subsequent exposure to this hormone produces a lesser response**
  - **Due to decrease in # of receptors on targets**
  - **Most peptide hormones have pulsatile secretion which prevents downregulation (e.g., repro. Hormones)**

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Mechanisms of Hormone Action

- **Most hormones travel in blood to target site**
- **Target cell receptors show specificity, high affinity, and low capacity for a hormone**

1. High specificity for receptor proteins
2. Strong bond strength
3. High chance of fully saturating receptors (because of limited number of receptors (usually a few thousand)

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Mechanisms of Hormone Action

- **Lipophilic hormones - nonpolar (soluable in lipids)**
- **Steroid & Thyroid Hormones**
  - **diffuse thru plasma membrane**
  - **receptor is in cytoplasm**
  - **target is the nucleus - affect transcription!**

- **Hydrophilic hormones – polar (H_2O soluable)**
- **Polypeptide, glycoprotein, catecholamine**
  - **receptor on surface of target cell**
  - **act through 2nd messengers**
    - **some steroids also act on cell surface receptors**

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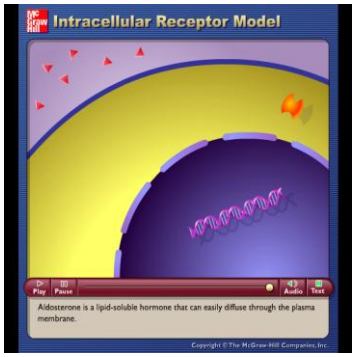
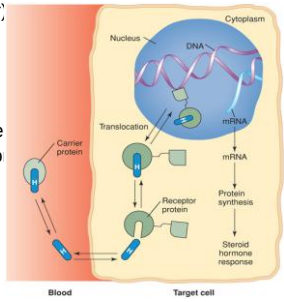


Hormones That Bind to Nuclear Hormone Receptors

- Lipophilic steroid (non-polar)
- Thyroid hormones (non-polar)
- Plasma protein carriers
  - Dissociate from carrier
  - Move through membrane
  - Attach to nuclear recepto protein
  - Transcription factors



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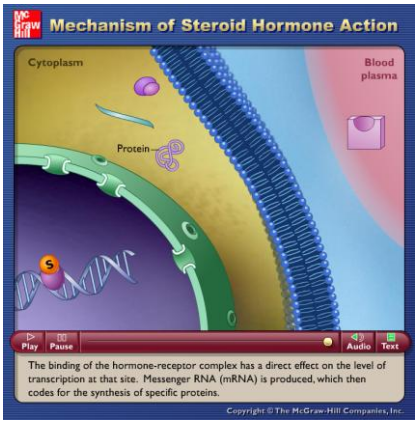
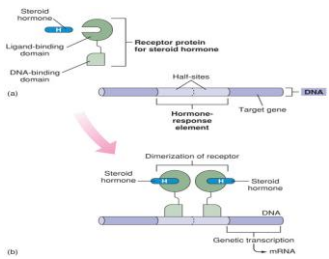


Nuclear Hormone Receptors

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

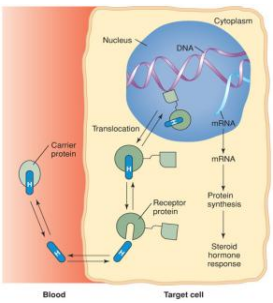
Hormone response element:
- 2 half-sites each 6 nucleotide bases long
-3 base spacer between them

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



Hormones That Bind to Nuclear Hormone Receptors

- Dimerization on hormone response elements initiation transcription
- AKA genomic action of steroids – takes >30 minutes to work.



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Coactivators and Corepressors

- Molecules are needed in addition to the steroid hormone.
- They bind to the nuclear receptor proteins at specific regions.
- This changes the effect of a given hormone in different cells.

Mechanism of Thyroid Hormone Action

- **Thyroid Hormone – another lipophilic hormone**
- **Only T3 can be used in cell to affect cell metab.**
- **Thyroid secretes:**
  - **90% T_4 (thyroxine, aka tetraiodothyronine)**
  - **10% T_3 (triiodothyronine)**
- **99.96% of T_4 in blood is bound to carrier protein (thyroid binding globulin - TBG)**
  - **Only free T_4 and T_3 can enter cells (most enters as T_4)**
  - **Protein bound T_4 serves as a reservoir**
- **T_4 converted to T_3 inside target cell**
  - **T_3 binds to binding protein & then receptor protein located in nucleus (and bound to DNA)**

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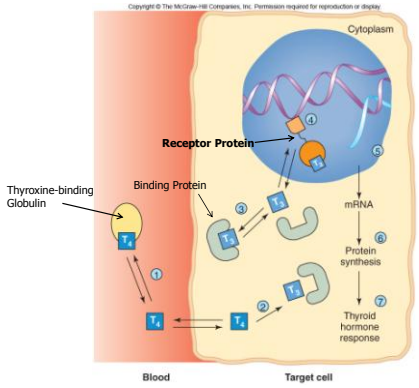
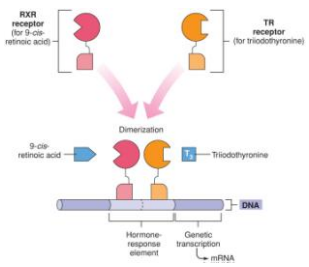


Mechanism of Thyroid Hormone Action

Hormone Response Element (1/2 sites with protein receptors)

The receptor for T_3:

- T_3 binds to TR receptor on 1 half-site
- 9-cis retinoic acit (Vit. A derivative) binds to other receptor (RXR)
  - Stimulates transcription of target gene



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Hormones That Use 2nd Messengers

- Water soluble hormones (Polar) use cell surface receptors (i.e., can't pass through membrane)
- Epi, norepi., polypeptide, and glycoprotein hormones
  - Actions are mediated by 2nd messengers
  - Hormone is extracellular signal; 2nd messenger triggers metabolic changes
- 3 different 2nd messenger systems:
  1. adenylate cyclase – cyclic AMP
  2. phospholipase C
  3. tyrosine kinase

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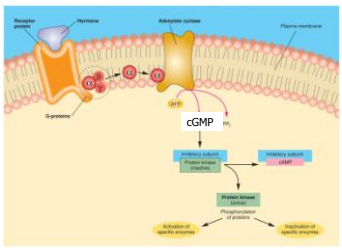
1. Adenylate Cyclase-cAMP

- **cAMP mediates effects of many polypeptide and glycoprotein hormones**
- **cAMP inactivated by phosphodiesterase**



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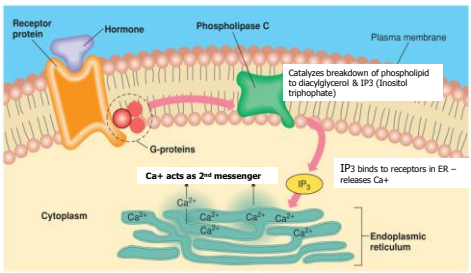
2. Phospholipase-C-Ca^{2+}

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



Ca+ acts as 2nd messenger binds to calmodulin that activates kinase enzymes

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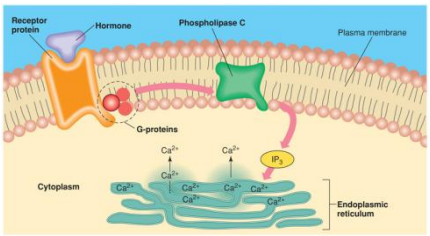
Phospholipase-C-Ca^{2+}

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



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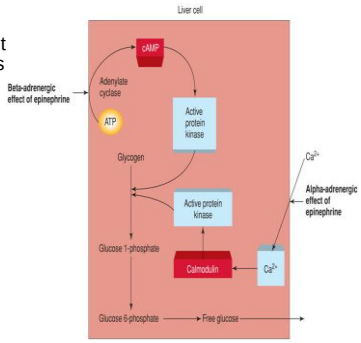
- Epi can use 2 different 2nd messeger systems
- cAMP & Ca+Calmodulin



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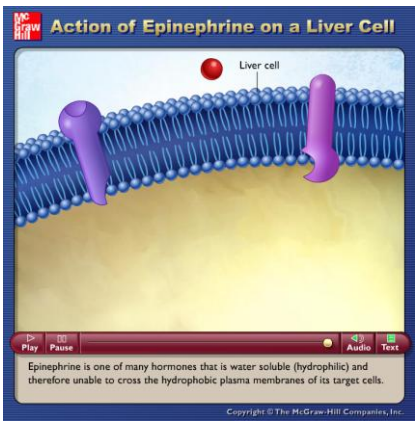

3. Tyrosine Kinase 2nd Messenger System

- insulin and many growth factors
- Surface receptor is tyrosine kinase (its an enzyme!)
  - 2 units form active dimer when 2 insulins bind
  - Phosphoralate each other
  - Now activated tyrosine kinase phosphorylates signaling molecules - induce hormone/growth factor effects