The Endocrine System

Interrelationship between nervous and endocrine system

- Nervous system
  - short term/ fast
- Endocrine system
  - long term/slow

Differences between systems

- Endocrine system good for gradual changes
  - Embryological changes
  - Puberty
  - Menstrual cycle
  - Water balance
- Nervous system good for split second decisions
  - Interpreting sight and sound
  - Muscles to move you out of danger
  - memory

- Hormone
  - Chemical messenger made in one place, transported by blood, to have action in another place
- Target cell
  - Cell where hormone has effect must have receptor for the hormone
  - Only cells with appropriate receptor responds to hormone

Hormone effects

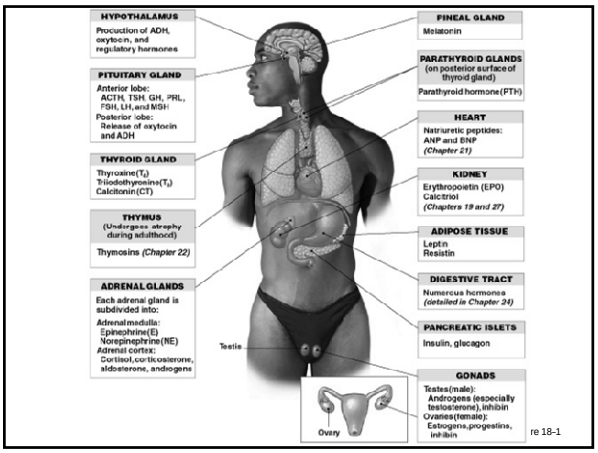
1. Stimulate synthesis of enzymes or structural proteins
2. Increase or decrease rate of synthesis
3. Turn existing enzyme or membrane channel “on” or “off”

Similarities

- Are similarly organized:
  - rely on release of chemicals
  - share many chemical messengers
  - are regulated primarily by negative feedback
  - share a common goal: to preserve homeostasis

Endocrine vs. Exocrine Cells

- Endocrine
  - Glandular secretory cells that release their secretions into extracellular fluid
  - ductless
- Exocrine
  - Secrete their products onto epithelial surfaces
  - ducted



re 18-1

Hormones

- Can be divided into 3 groups:
  1. amino acid derivatives
  2. peptide hormones
  3. lipid derivatives (steroid hormones)

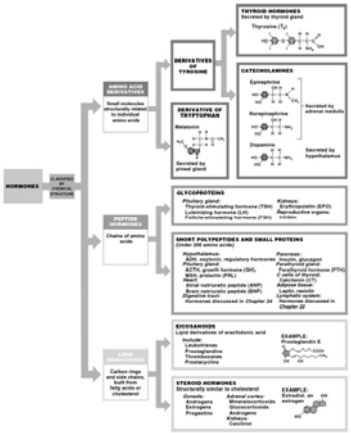
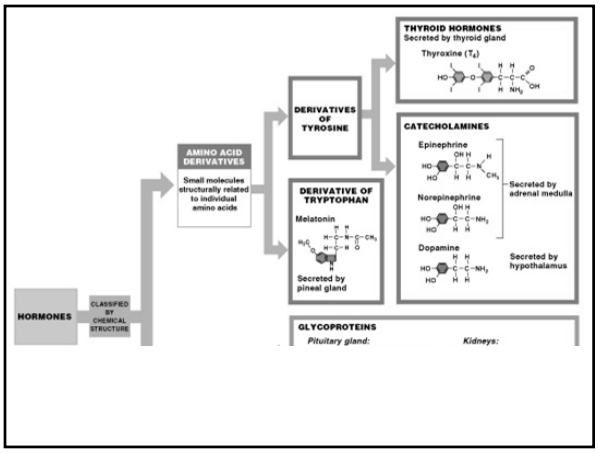
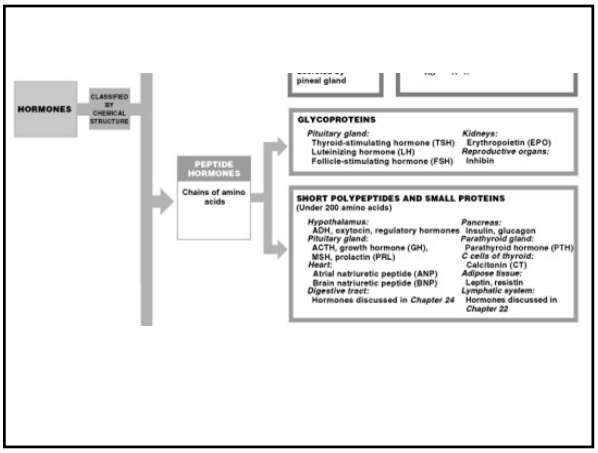
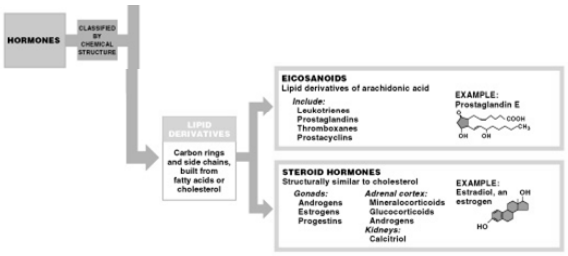


Figure 18-2







Amino Acid Derivatives

- Small molecules structurally related to amino acids
- Synthesized from the amino acids tyrosine and tryptophan

Tyrosine Derivatives

- Thyroid hormones
- Compounds:
  - epinephrine (E)
  - norepinephrine (NE)
  - dopamine, also called catecholamines

Do not memorize

Tryptophan Derivative

- Melatonin:
  - produced by pineal gland

Do not memorize

Peptide Hormones

- Chains of amino acids
- Synthesized as prohormones:
  - inactive molecules converted to active hormones before or after secretion

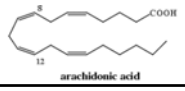
2 Classes of Lipid Derivatives

- Eicosanoids:
  - derived from arachidonic acid
- Steroid hormones:
  - derived from cholesterol

Do not memorize

Eicosanoids

- Are small molecules with five-carbon ring at one end
- Are important paracrine factors
- Coordinate cellular activities
- Affect enzymatic processes in extracellular fluids

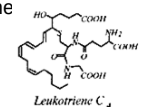


arachidonic acid

Do not memorize

Leukotrienes

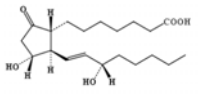
- Are eicosanoids released by activated white blood cells, or leukocytes
- Important in coordinating tissue responses to injury or disease
- SINGULAIR is a different way to treat seasonal allergies because it blocks leukotrienes instead of blocking histamine


Leukotriene C$_4$

Do not memorize

Prostaglandins

- A second group of eicosanoids produced in most tissues of body
- Are involved in coordinating local cellular activities

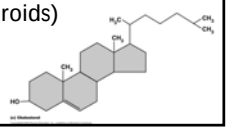


a prostaglandin

Do not memorize

Steroid Hormones

- Are lipids structurally similar to cholesterol
- Hormones differ in side chains
- Released by:
  - reproductive organs (androgens by testes, estrogens, and progestins by ovaries)
  - adrenal glands (corticosteroids)
  - kidneys (calcitriol)



Steroid Hormones

- Remain in circulation longer than peptide hormones
- Are absorbed gradually by liver
- Are converted to soluble form
- Are excreted in bile or urine

Secretion and Distribution of Hormones

- Typically released into capillary bed for fast uptake and distribution
- Circulate freely or bound to transport proteins

Free Hormones

- Remain functional for less than 1 hour:
  - diffuse out of bloodstream:
    - bind to receptors on target cells
  - are absorbed:
    - broken down by cells of liver or kidney
  - are broken down by enzymes:
    - in plasma or interstitial fluids

Thyroid and Steroid Hormones

- Remain in circulation much longer
- Enter bloodstream:
  - more than 99% become attached to special transport proteins
- Free and bound hormone state
  - As free removed, bound is released
  - Blood contains substantial reserve of bound hormones

Mechanisms of Hormone Action

- Hormone Receptor
  - Is a protein molecule to which a particular molecule binds strongly
  - Each cell has receptors to respond to several different hormones
  - Different tissues have different combinations of receptors
  - Presence or absence of specific receptor determines hormonal sensitivity

Location of Receptor

- Depends on type of hormone
- Cell membrane receptors
  - Generally water soluble hormones
- Intracellular receptors
  - Generally lipid soluble hormones

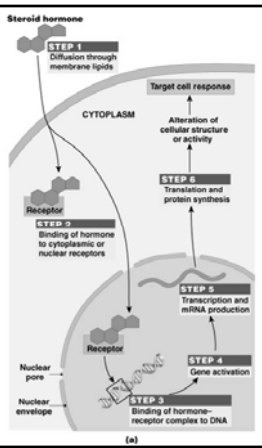


Figure 18-4a

Endocrine Reflexes

- Functional counterparts of neural reflexes
- In most cases, controlled by negative feedback mechanisms

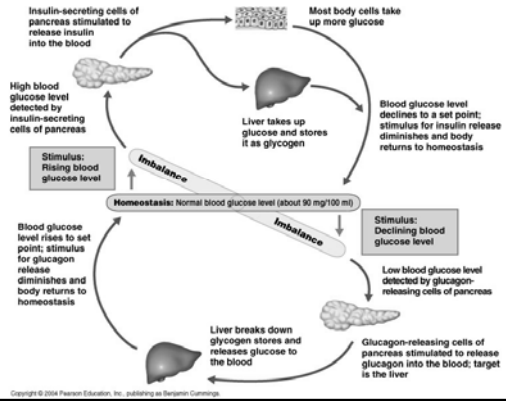
Endocrine Reflex Triggers

1. Humoral stimuli:
   - changes in composition of extracellular fluid
2. Hormonal stimuli:
   - arrival or removal of specific hormone
3. Neural stimuli:
   - arrival of neurotransmitters at neuroglandular junctions

Simple Endocrine Reflex

- Involves only 1 hormone
- Endocrine cells respond directly to changes in extracellular fluid
- Secreted hormone adjusts activities of target cell to restore homeostasis
- For example:
  - heart
  - pancreas
  - parathyroid gland
  - digestive tract

Negative feedback

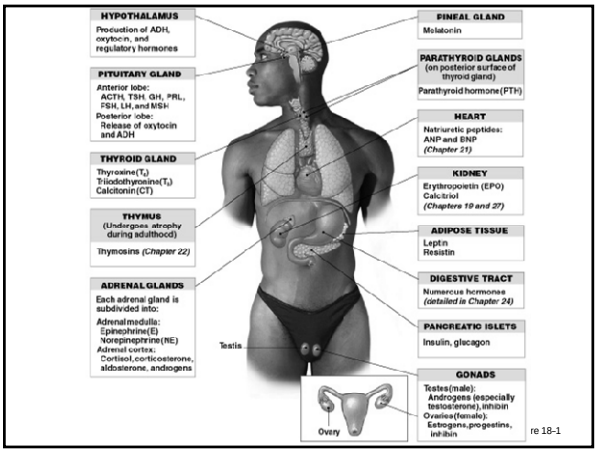


Complex Endocrine Reflex

- Involves:
  - 1 or more intermediary steps
  - 2 or more hormones

Pulses

- Hypothalamic and pituitary hormones released in sudden bursts
- Frequency varies response of target cells



Hypothalamus and Pituitary Gland

- Pituitary gland (or hypophysis) **was** thought to be “master gland”
- **Now** we know it is controlled by hypothalamus

Hypothalamus

- Integrates activities of nervous and endocrine systems in 3 ways:

1. Secretes regulatory hormones:
   - special hormones control endocrine cells in anterior pituitary gland
   - Hormones of anterior pituitary control endocrine cells in thyroid, adrenal cortex and reproductive organs

Hypothalamus

2. Acts as an endocrine organ
   - Hormones of posterior pituitary made by hypothalamus
3. Contains autonomic centers:
   - exert direct neural control over endocrine cells of adrenal medullae

Hypothalamus

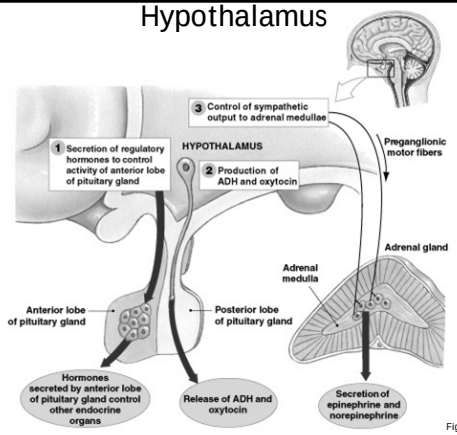


Figure 18-5

Pituitary Gland

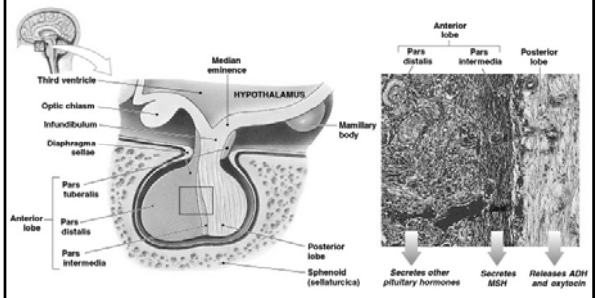
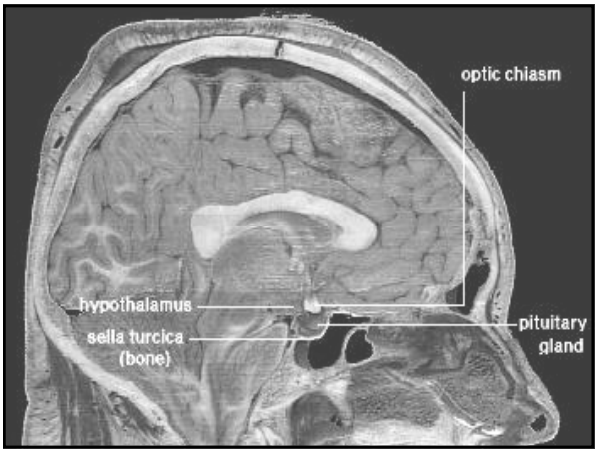


Figure 18-6



Pituitary Gland

- Also called hypophysis
- Lies within sella turcica
- Hangs inferior to hypothalamus:
  - connected by infundibulum
- Divided into anterior and posterior lobe based on function and developmental anatomy

Pituitary Gland

- Releases 9 important peptide hormones
- Hormones bind to membrane receptors

Anterior Lobe

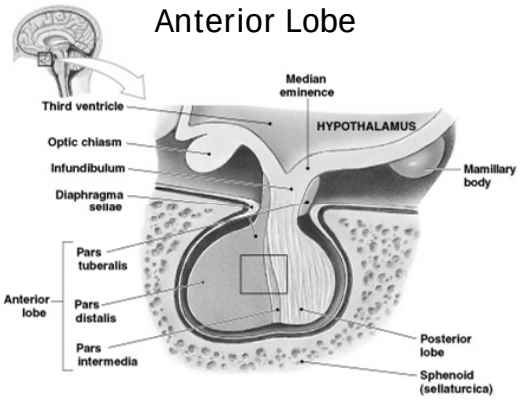


Figure 18-6

Anterior Lobe

- Also called adenohypophysis
- Hypophyseal portal system
  - Usual circulatory arrangement is heart, artery, capillary bed, vein and back to heart
  - Portal system has 2 capillary beds
  - heart, artery, capillary bed, portal veins, 2nd capillary bed , vein and back to heart

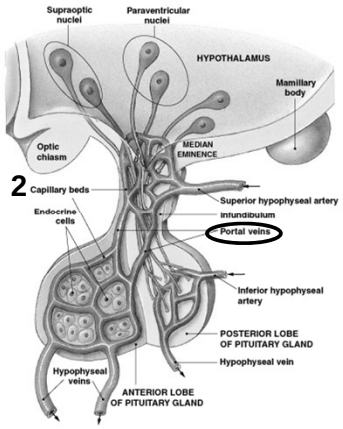


Figure 18-7

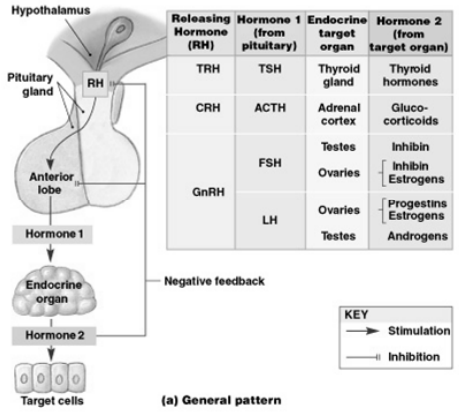
2 Classes of Hypothalamic Regulatory Hormones

1. Releasing hormones
   - Stimulates synthesis and secretion of hormone from anterior lobe
2. Inhibiting hormones
   - Inhibits synthesis and secretion of hormone from anterior lobe

- Endocrine cell in anterior pituitary may be controlled by one or the other or both
- Releasing and inhibiting hormones transported directly to anterior pituitary by hypophyseal portal system
- Rate of secretion is controlled by negative feedback

Hormones of the Anterior Lobe

- 7 hormones
  - TSH
  - ACTH
  - FSH
  - LH
  - PRL
  - GH
  - MSH
- Aka tropic or trophic hormones because they turn on or support other endocrine glands



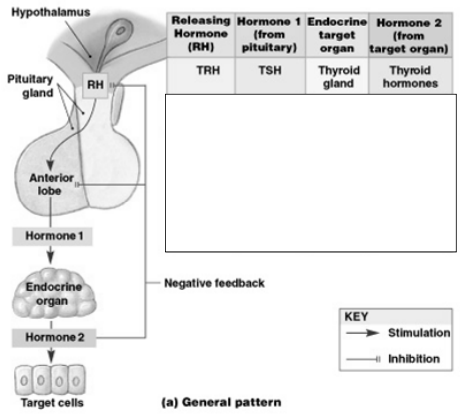
Releasing Hormone (RH)	Hormone 1 (from pituitary)	Endocrine target organ	Hormone 2 (from target organ)
TRH	TSH	Thyroid gland	Thyroid hormones
CRH	ACTH	Adrenal cortex	Gluco-corticoids
GnRH	FSH	Testes	Inhibin
		Ovaries	Inhibin, Estrogens
	LH	Ovaries	Progestins, Estrogens
		Testes	Androgens

(a) General pattern

18-8a

Thyroid-Stimulating Hormone (TSH)

- Also called thyrotropin
- Triggers release of thyroid hormones
- Released in response to Thyrotropin-releasing hormone from hypothalamus
- Negative feedback
  - As thyroid hormone rises, TSH and TRH decline



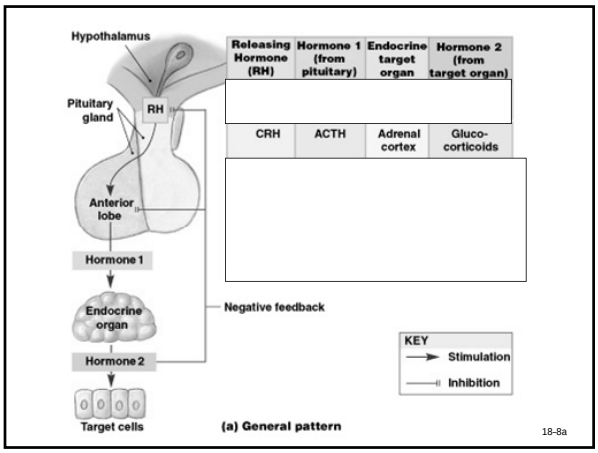
Releasing Hormone (RH)	Hormone 1 (from pituitary)	Endocrine target organ	Hormone 2 (from target organ)
TRH	TSH	Thyroid gland	Thyroid hormones

(a) General pattern

18-8a

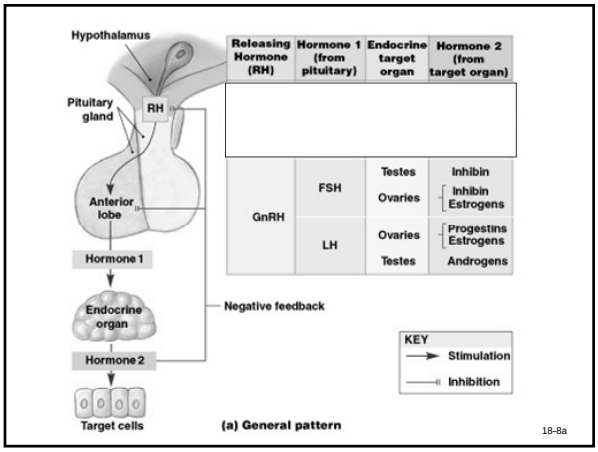
Adrenocorticotropic Hormone (ACTH)

- Also called corticotropin
- Stimulates release of steroid hormones by adrenal cortex
- Targets cells that produce glucocorticoids-affect glucose metabolism
- Released in response to corticotropin-releasing hormone from hypothalamus
- Negative feedback
  - As glucocorticoid levels rise, CRH and ACTH release declines



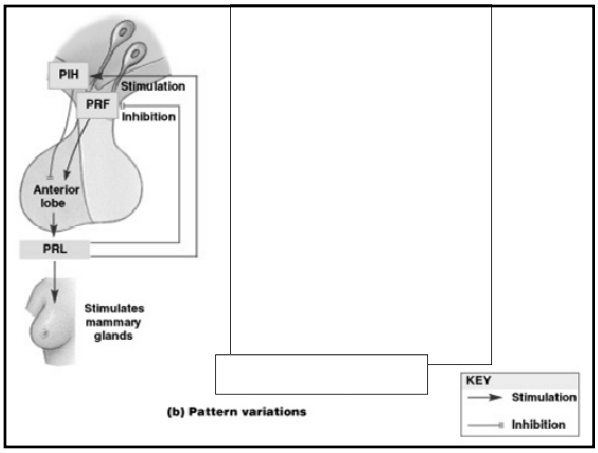
Gonadotropins

- Regulate activities of gonads (testes, ovaries)
- Follicle-stimulating hormone
  - Promotes follicle development in female
  - Maturation of sperm in males
- Luteinizing hormone
  - Trigger ovulation in females
  - Androgen production in males
- Released in response to gonadotropin-releasing hormone from hypothalamus



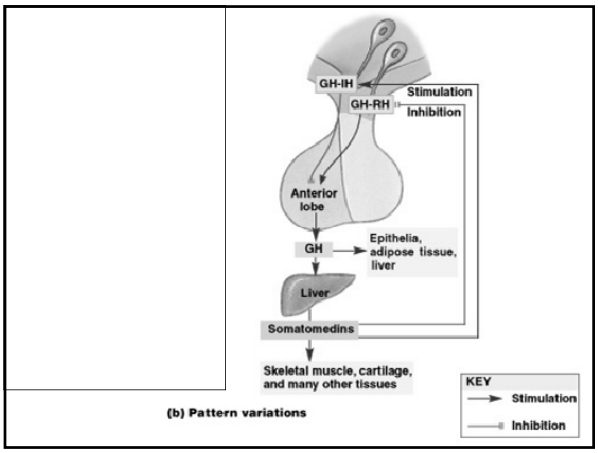
Prolactin (PRL)

- Also called mammotropin
- Stimulates development of mammary glands and milk production
- Role in males poorly understood
- Production inhibited by prolactin-inhibiting hormone (PIH)
- Prolactin-releasing factors (PRF) released by hypothalamus



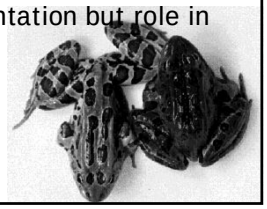
Growth Hormone (GH)

- Also called somatotropin
- Stimulates cell growth and replication
  - Primarily by increasing rate of amino acid uptake and incorporation
- Production regulated by:
  - growth hormone–releasing hormone (GH-RH)
  - growth hormone–inhibiting hormone (GH-IH)



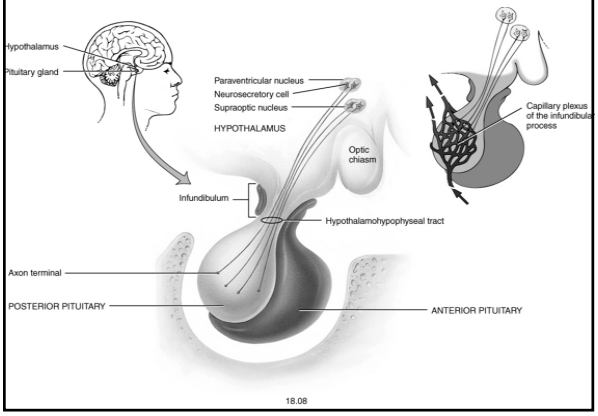
Melanocyte-Stimulating Hormone (MSH)

- Also called melanotropin
- Stimulates melanocytes to produce melanin
- Role in animal pigmentation but role in humans unknown



Posterior Lobe

- Also called neurohypophysis
- Outgrowth of brain during fetal development
- Axons of hypothalamic neurons manufacture:
  - antidiuretic hormone (ADH)
  - oxytocin (OT)
- Posterior lobe does NOT make hormones, it releases hormones made by hypothalamus

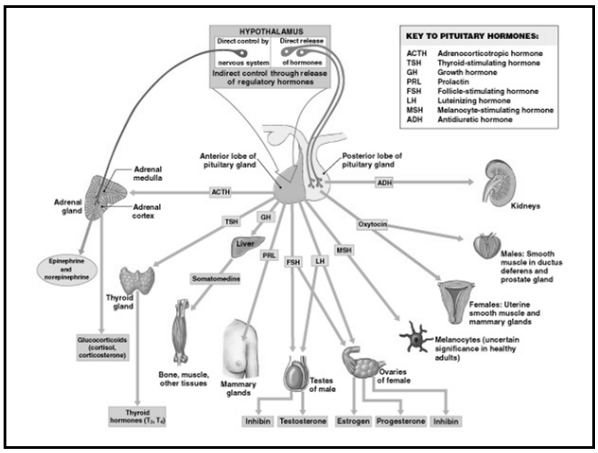


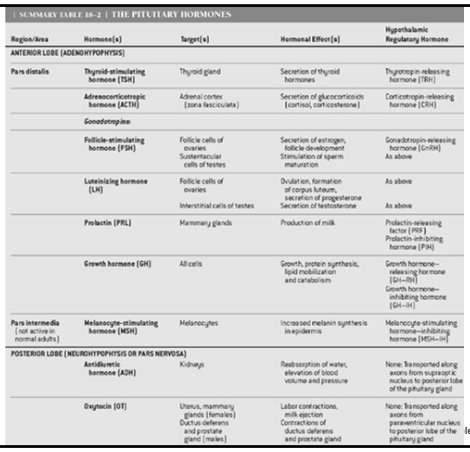
Antidiuretic Hormone

- Decreases amount of water lost at kidneys
- Elevates blood pressure
- Release inhibited by alcohol
  - Leads to increased urination
  - Hangover due to dehydration

Oxytocin

- Stimulates contractile cells in mammary glands
- Stimulates smooth muscles in uterus
- Secretion and milk ejection are part of neuroendocrine reflex
- In males, may be important in emission
  - Ejection of secretions before ejaculation





SUMMARY TABLE 18-2 | THE PITUITARY HORMONES

Region/Area	Hormone(s)	Target(s)	Hormonal Effect(s)	Hypothalamic Regulatory Hormone
ANTERIOR LOBE (ADENOHYPOPHYSIS)				
Pars distalis	Thyroid-stimulating hormone (TSH)	Thyroid gland	Secretion of thyroid hormones	Thyrotropin-releasing hormone (TRH)
	Adrenocorticotropic hormone (ACTH)	Adrenal cortex (zona fasciculata)	Secretion of glucocorticoids (cortisol, corticosterone)	Corticotropin-releasing hormone (CRH)
	Gonadotropins:			
	Follicle-stimulating hormone (FSH)	Follicle cells of ovaries Sustentacular cells of testes	Secretion of estrogen, follicle development Stimulation of sperm maturation	Gonadotropin-releasing hormone (GnRH) As above
	Luteinizing hormone (LH)	Follicle cells of ovaries Interstitial cells of testes	Ovulation, formation of corpus luteum, secretion of progesterone Secretion of testosterone	As above As above
	Prolactin (PRL)	Mammary glands	Production of milk	Prolactin-releasing factor (PRF) Prolactin-inhibiting hormone (PIH)
	Growth hormone (GH)	All cells	Growth, protein synthesis, lipid mobilization and catabolism	Growth hormone–releasing hormone (GH–RH) Growth hormone–inhibiting hormone (GH–IH)
Pars intermedia (not active in normal adults)	Melanocyte-stimulating hormone (MSH)	Melanocytes	Increased melanin synthesis in epidermis	Melanocyte-stimulating hormone–inhibiting hormone (MSH–IH)
POSTERIOR LOBE (NEUROHYPOPHYSIS OR PARS NERVOSA)				
	Antidiuretic hormone (ADH)	Kidneys	Reabsorption of water, elevation of blood volume and pressure	None; Transported along axons from supraoptic nucleus to posterior lobe of the pituitary gland
	Oxytocin (OT)	Uterus, mammary glands (females) Ductus deferens and prostate gland (males)	Labor contractions, milk ejection Contractions of ductus deferens and prostate gland	None; Transported along axons from paraventricular nucleus to posterior lobe of the pituitary gland

le 18-2

Thyroid Gland

- Lies anterior to thyroid cartilage of larynx
- Consists of 2 lobes connected by narrow isthmus

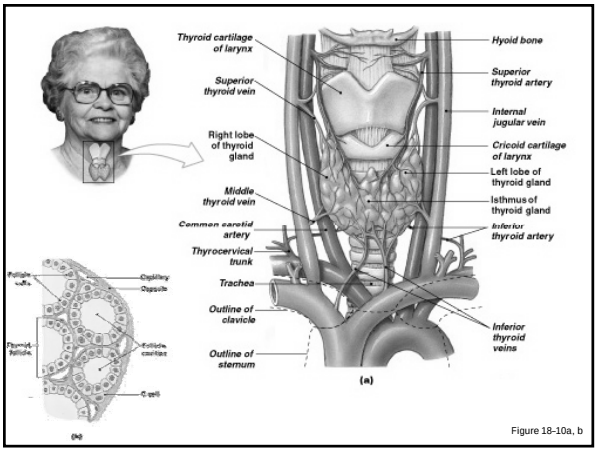
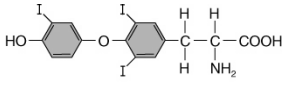


Figure 18-10a, b

Thyroid Hormones

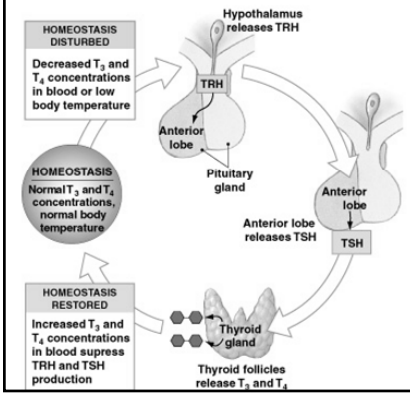
- Thyroxine (T_4)
  - Also called tetraiodothyronine
  - Contains 4 iodide ions
- Triiodothyronine (T_3)
- Contains 3 iodide ions



Triiodothyronine (T_3)

18.T02b

Rate of Thyroid Hormone Release



- Major factor:
  - TSH concentration in circulating blood

Figure 18-11b

Thyroid Hormones

- Affect most cells in body
- Calorigenic effect
  - Cell consumes more energy resulting in increased heat generation
- Is responsible for strong, immediate, and short-lived increase in rate of cellular metabolism

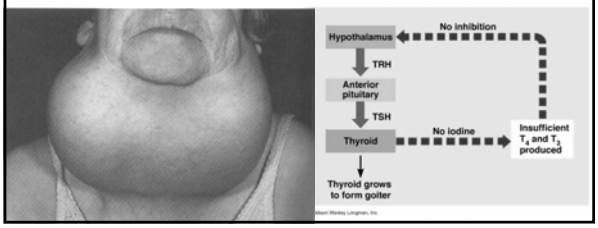
TABLE 18–3 Effects of Thyroid Hormones on Peripheral Tissues

1. Elevated rates of oxygen consumption and energy consumption; in children, may cause a rise in body temperature
2. Increased heart rate and force of contraction; generally results in a rise in blood pressure
3. Increased sensitivity to sympathetic stimulation
4. Maintenance of normal sensitivity of respiratory centers to changes in oxygen and carbon dioxide concentrations
5. Stimulation of red blood cell formation and thus enhanced oxygen delivery
6. Stimulation of activity in other endocrine tissues
7. Accelerated turnover of minerals in bone

Table 18-3

Goiters

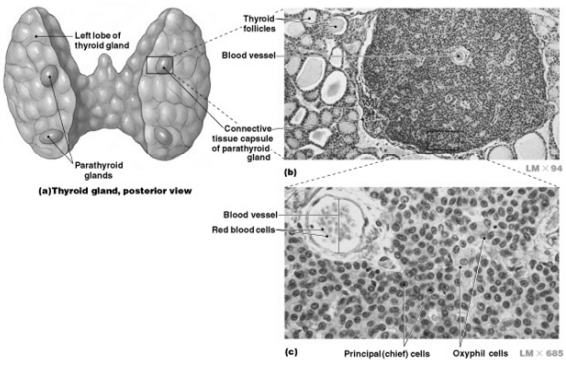
- Due to insufficient iodine in the diet
- No Iodine = no T3 or T4
- Body makes thyroid bigger to try to make more hormone



C (Clear) Cells

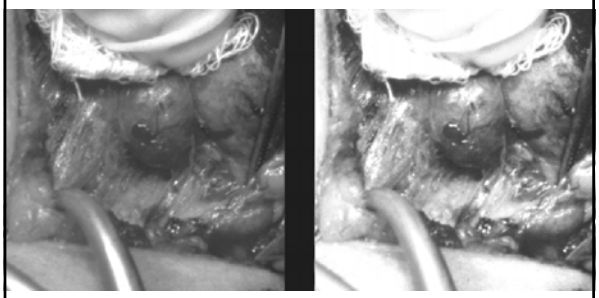
- Produce calcitonin (CT)
- helps lower concentrations of Ca^{2+} in body fluids
- Direct endocrine regulation
  - C cells respond directly to Ca^{2+} in blood

Parathyroid Glands



Parathyroid Glands

- Embedded in thyroid gland
- Didn't know gland existed until thyroidectomies for goiter



Parathyroid tissue – subsequent level of dissection; with enhanced image to highlight local contrast

Parathyroid Hormone (PTH)

- Produced by chief cells
- In response to low concentrations of Ca^{2+}

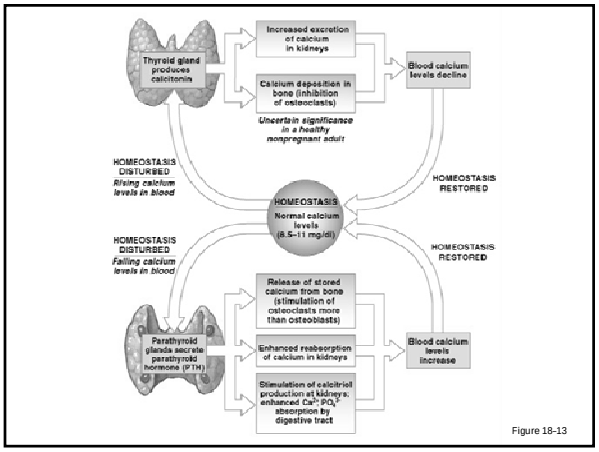


Figure 18-13

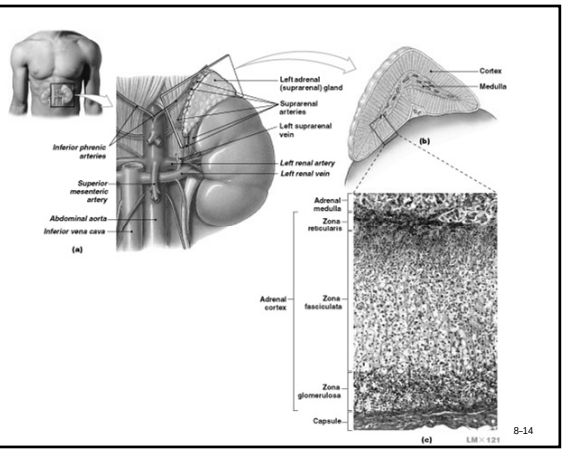
TABLE 18–4 Hormones of the Thyroid Gland and Parathyroid Glands

Gland/Cells	Hormone(s)	Targets	Hormonal Effects	Regulatory Control
THYROID GLAND				
Follicular epithelium	Thyroxine (T_4), triiodothyronine (T_3)	Most cells	Increases energy utilization, oxygen consumption, growth, and development	Stimulated by TSH from anterior lobe of the pituitary gland *(see table 18–3)*
C cells	Calcitonin (CT)	Bone, kidneys	Decreases Ca^{2+} concentrations in body fluids	Stimulated by elevated blood Ca^{2+} levels; actions opposed by PTH
PARATHYROID GLANDS				
Chief cells	Parathyroid hormone (PTH)	Bone, kidneys	Increases Ca^{2+} concentrations in body fluids	Stimulated by low blood Ca^{2+} levels; PTH effects enhanced by calcitriol and opposed by calcitonin

Table 18-4

Adrenal Glands

- Lie along superior border of each kidney
- Subdivided into outer adrenal cortex and an inner adrenal medulla



8–14

Adrenal Cortex

- Stores lipids, especially cholesterol and fatty acids
  - Gives it a yellow color
- Manufactures more than 2 dozen steroid hormones:
  - adrenocortical steroids (corticosteroids)

TABLE 18–5 The Adrenal Hormones

Region/Zone	Hormone(s)	Primary Targets	Hormonal Effects	Regulatory Control
CORTEX				
Zona glomerulosa	Mineralocorticoids (primarily aldosterone)	Kidneys	Increase renal reabsorption of Na^+ and water (especially in the presence of ADH) and accelerate urinary loss of K^+	Stimulated by antiotensin II, elevated plasma K^+, or a fall in plasma Na^+; inhibited by [ANP and BNP]
Zona fasciculata	Glucocorticoids (cortisol [hydrocortisone], corticosterone)	Most cells	Release amino acids from skeletal muscles and lipids from adipose tissues; promote liver formation of glucose and glycogen; promote peripheral utilization of lipids; anti-inflammatory effects	Stimulated by ACTH from anterior lobe of pituitary gland
Zona reticularis	Androgens		Not important in adult men.	Stimulated by ACTH
MEDULLA	Epinephrine, norepinephrine	Most cells	Increases cardiac activity, blood pressure, glycogen breakdown, blood glucose levels; releases lipids by adipose tissue	Stimulated during sympathetic activation by sympathetic preganglionic fibers

Table 18-5

Adrenal Gland Hormones

- Adrenal cortex
  - adrenocortical steroids (corticosteroids)
    - Mineralcorticoids- electrolytes in body fluid
    - Glucocorticoids- increase glucose synthesis and glycogen formation
      - corticotropin-releasing hormone (CRH) in hypothalamus
      - ACTH in anterior lobe
      - Anti-inflammatory “steroid creams”
    - Androgens- important in adult women

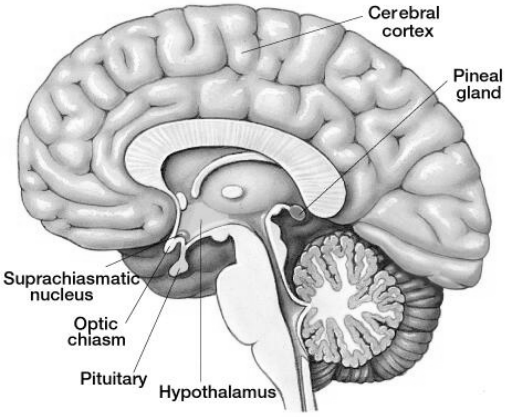
- Adrenal Medulla
  - Secretory activities controlled by sympathetic division of ANS
  - Produces epinephrine (adrenaline) and norepinephrine
    - Fight or flight reactions- mobilize glucose in muscles and liver, break down fat, increase rate and force of heart

Pineal Gland

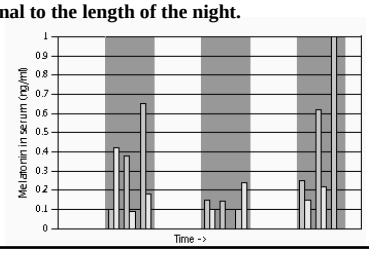
- produces hormone melatonin
- Nerves from visual pathways enter pineal and melatonin production highest at night and lowest during the day

Functions of Melatonin

- Inhibiting reproductive functions
  - In other animals, longer nights=more melatonin= winter=not the time to reproduce
- Protecting against damage by free radicals
- Setting circadian rhythms
  - May be the cause of SAD



•Examples of the circadian rhythm in melatonin secretion in humans is depicted in the figure to the right (adapted from Vaughn, et al, J Clin Endo Metab 42:752, 1976).
•The dark gray bars represent night, and serum melatonin levels are shown for two individuals (yellow versus light blue). Note that blood levels of melatonin are essentially undetectable during daytime, but rise sharply during the dark. Very similar patterns are seen in other species.
•**The duration of melatonin secretion each day is directly proportional to the length of the night.**



Seasonal Affective Disorder

- SAD
- Type of depression linked to low light in winter
- May be due to overproduction of melatonin
- Can be treated by exposure to full spectrum bright light mimicking sunlight

Pancreas

- Lies between:
  - inferior border of stomach
  - and proximal portion of small intestine
- Contains exocrine and endocrine cells
  - Exocrine- 99% of gland makes pancreatic fluid for digestive tract
  - Endocrine- pancreatic islets or islets of Langerhans

Pancreas

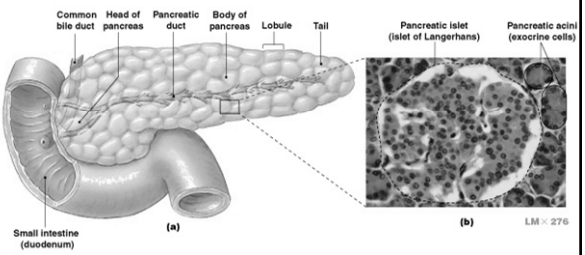


Figure 18-15

2 Major Types of Cells in Pancreatic Islets

1. Alpha cells:
   - produce glucagon
   - Increases blood sugar levels
2. Beta cells:
   - secrete insulin
   - Lowers blood glucose levels

TABLE 18–6 Hormones Produced by the Pancreatic Islets

Structure/Cells	Hormone	Primary Targets	Hormonal Effects	Regulatory Control
PANCREATIC ISLETS				
Alpha cells	Glucagon	Liver, adipose tissues	Mobilizes lipid reserves; promotes glucose synthesis and glycogen breakdown in liver; elevates blood glucose concentrations	Stimulated by low blood glucose concentrations; inhibited by GH–IH from delta cells
Beta cells	Insulin	Most cells	Facilitates uptake of glucose by target cells; stimulates formation and storage of lipids and glycogen	Stimulated by high blood glucose concentrations, parasympathetic stimulation, and high levels of some amino acids; inhibited by GH–IH from delta cells and by sympathetic activation

Table 18-6

Blood Glucose Levels

- When levels rise:
  - beta cells secrete insulin, stimulates transport of glucose across cell membranes
- When levels decline:
  - alpha cells secrete glucagons, stimulates glucose release by liver

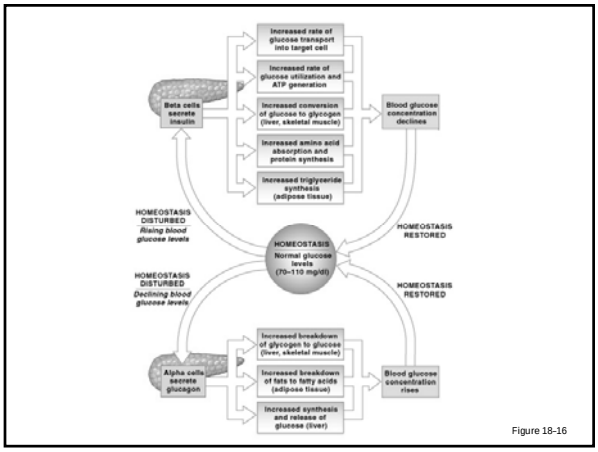
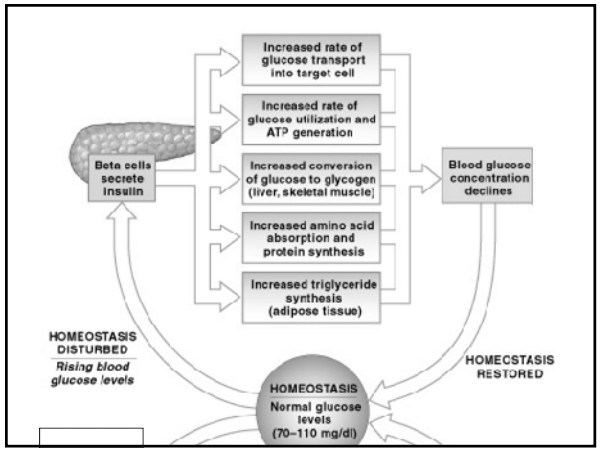
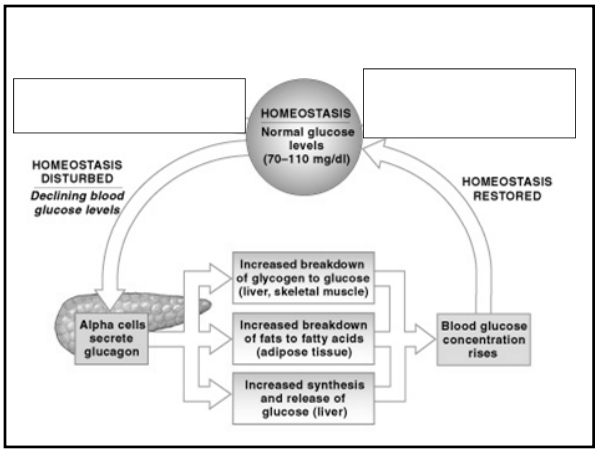


Figure 18-16





Diabetes Mellitus

- 2 major types
  - Type 1- problem is in the amount of hormone
    - Insulin dependent
    - Not enough insulin is being made
    - Very low insulin levels in blood
    - Can be treated by injection
  - Type 2 - problem is the receptor
    - Insulin independent
    - Something wrong with receptors on cells
    - Very high insulin levels in blood
    - Cannot be treated by insulin injection
    - diet

Testes

- Produce androgens in interstitial cells:
  - testosterone:
    - is most important male hormone

Ovaries

- Produce estrogens:
  - principle estrogen is estradiol
- After ovulation, follicle cells:
  - reorganize into corpus luteum
  - release estrogens and progestins, especially progesterone