Endocrine System

Introduction
1. Two regulatory systems involved in transmitting messages and overseeing body functions:
   a. Nervous
      1) Fast-acting via AP’s (msec)
      2) Energetically expensive
      3) Sends messages to muscles & glands
   b. Endocrine
      1) Slow-acting via hormones carried in the blood (sec-yrs)
      2) Energetically inexpensive compared to NS
      3) Affects all body tissues
      4) Action coordinated by NS

2. Endocrine functions (general)
   a. Maintains homeostasis by affecting:
      1) Concentration of body fluids
      2) Metabolism of carbohydrates, proteins, & lipids
      3) Body’s reaction to stress
      4) Growth and sexual development

3. Gland Classification
   a. Exocrine
      1) Glands that deliver secretions using ducts
      2) Examples: Salivary, sweat, pancreas
   b. Endocrine
      1) Ductless glands that release chemical messengers called hormones directly into blood
      2) Examples: Pituitary, thyroid, adrenal pancreas

4. Hormones and chemistry
   a. Defined: “I arouse”
   b. Chemical messengers secreted into the blood by one cell (gland cell) and causes a physiological response in other cells (called target cells).
   c. Chemically divided into:
      1) Biogenic amines
         a) Made from aa tyrosine w/o carboxyl group
         b) Simplest molecules
         c) Come from endocrines that have ectodermal origin
         d) Examples: Epinephrine, Thyroid H, Melatonin, Serotonin
      2) Proteins/polypeptides
         a) Polymers of aa
         b) Come from endocrine glands of endodermal origin
         c) Examples: oxytocin, ADH, Insulin, Glucagon, Adenohypophysis H’s, Parathyroid H., etc
3) Steroids
   a) Derived from cholesterol
   b) Come from endocrine glands of mesodermal origin
   c) Share 4 carbon rings
   d) Examples: estrogen, progesterone, testosterone, aldosterone, cortisol, etc

4) Eicosanoids
   a) Derived from 20 C fatty acid & 5 C ring molecule called arachidonic acid
   b) Local type hormones (as opposed to circulating hormones in first 3 groups)
   c) Examples: prostaglandins, leukotrienes, thromboxane, etc

5. Mechanisms of hormone action
   a. Regulated so that over or under secretion is avoided
   b. Carried by the blood; therefore every cell could be affected
   c. Cells that respond to a particular H are called target cells
   d. Two factors to consider:
      1) H’s do not usually affect every cell. Why?
         a) Receptor must be present
      2) Of the cells affected, the physiological response may be very different. For example:
         a) Insulin causes fat cells to stimulate glucose transport & lipid synthesis
         b) Insulin causes liver cells to stimulate aa transport & glycogen synthesis
         c) Insulin causes pancreatic cells to inhibit secretion of glucagon
      3) What causes these different responses by same H?
         a) Different # of receptors
         b) Different G proteins
         c) Different secondary messengers
         d) protein kinases
   4) Two kinds of hormonal interactions:
      a) Interaction with receptors on the plasma membrane
      b) Interaction with intracellular receptors (=direct gene activation)
   e. Interaction with receptors on the plasma membrane
      1) H carried by the blood to the target cell; the H is called the first messenger
      2) H binds to receptor on the plasma membrane
      3) Receptor uses a G protein link to activate an internal EZ called adenylate cyclase
         a) G protein is a molecule within the membrane that links 1st messenger and the EZ that activates the 2nd messenger
4) Adenyl (ate) cyclase converts ATP to 3’5’ cAMP
   a) 3’5’ cAMP is called the 2\textsuperscript{nd} messenger
   b) One of the more common 2\textsuperscript{nd} messengers
      i. Ca++ and cGMP are others
   c) One H molecule can lead to formation of many 2\textsuperscript{nd}
      messengers, a process called amplification
5) 3’5’ cAMP activates intracellular EZ’s called protein kinases
6) Protein kinases often add Pi from ATPs to other proteins (EZ’s)
   activating a metabolic pathway
   a) Many kinds of protein kinases in a cell; some excitatory,
      some inhibitory
7) Possible physiological responses by target cell:
   a) Increase synthesis of a product for export
   b) Decrease synthesis of a product to slow down
   c) Open an ion channel, often Ca++
8) Process is stopped when 3’5’ cAMP is inactivated by the EZ
   phosphodiesterase turning it into 5’ AMP
f. Interaction with intracellular receptors (=direct gene activation)
   1) H is lipid-soluble (e.g. steroids or some biogenic amines)
   2) H is carried by the blood to the target cell
   3) Since H is lipid-soluble, it can diffuse through plasma membrane
   4) H binds to a intracellular receptor forming a hormone-receptor
      complex
      a) A second pathway is that the H diffuses directly into the
         nucleus where it binds to a receptor on DNA causing
         transcription
      b) Both pathways end up the same
5) The H-R complex moves into the nucleus and interacts with specific
   receptors on DNA causing transcription of a gene
6) Gene \(\rightarrow\) Protein (EZ) \(\rightarrow\) runs or stops metabolic pathway causing
   target cell to increase or stop production
7) Possible physiological responses by target cell:
   a) Increase synthesis of a product for export
   b) Decrease synthesis of a product to slow down
   c) Open an ion channel, often Ca++
6. Prostaglandins
   a. First discovered in semen
   b. Associated with plasma membranes of most cells
   c. Derived from arachidonic acid
   d. These are paracrine or locally active H’s targeting cells mostly in vicinity
      of release
   e. Not synthesized by a gland, but by most cells
   f. Rapidly inactivated in lungs, liver, and kidney
   g. Kinds:
1) PGA – PGI
2) Also A1 and A2, B1 and B2, etc
3) Total number is:

h. PG/Eicosanoid synthesis

1) Released from plasma membranes and 2 EZ’s affect:
   a) Lipooxygenase-converts arachidonic acid to leukotrienes that mediate allergic and inflammatory reactions
   b) Cyclooxygenase
      i. prostacyclin: produced by blood vessel walls; inhibits clotting and vasoconstriction
      ii. thromboxanes: produced by platelets after injury; they override prostacyclin and stimulate vasoconstriction and clotting
      iii. prostaglandins: diverse group but examples would be PGE’s that relax smooth muscle in bladder, intestines, bronchioles, uterus, and stimulate contraction of blood vessels AND PGF’s do opposite of PGE’s

7. Feedback mechanisms
   a. Disorders occur when too much or too little of a H is released (usually)
   b. 4 kinds of control:
      1) Negative feedback
         a) Most common of 4 mechanisms
         b) Example: Parathyroid H (PTH)
            i. Released in response to low blood Ca++
            ii. PTH released from parathyroid glands
            iii, PTH brings Ca++ levels back to normal
            iv. Increased Ca++ levels inhibit PTH release
         c) The body’s response (raising Ca++) is opposite to the stimulus (low Ca++)
      2) Nervous System direct stimulation
         a) SNS innervates adrenal medulla
         b) Adrenal medulla releases E/NE
      3) NS control by regulating H’s
         a) Hypothalamus releases releasing and inhibiting H’s that control adenohypophysis
      4) Positive feedback
         a) Disruptive to homeostasis
         b) Example: oxytocin (OT)
            i. OT released from neurohypophysis in response to nerve impulses from hypothalamus caused by infant sucking on mother’s nipple
            ii. Increased sucking, more AP’s, more OT released
            iii. Also parturition (birth)
Pituitary Gland
1. Also called hypophysis cerebri
2. Sometimes called master gland because it releases several H's that turn on (tropin) other cells or glands
   a. However, hypothalamus controls pituitary by regulatory H’s
3. Small, (~1 g, 1 cm), rounded body residing in sella turcica of sphenoid bone
4. Attached to brain by stalk called infundibulum
5. Divided into:
   a. Adenohypophysis = anterior pituitary
   b. Neurohypophysis = posterior pituitary
6. Development
   a. Adenohypophysis develops as an upward outpocketing of mouth called Rathke’s pouch
   b. Neurohypophysis forms as downward extension of hypothalamus (brain)
   c. They eventually join
7. Adenohypophysis
   a. Controlled by hypothalamus by use of regulating H’s
      1) Regulating H’s delivered by hypothalamo-hypophyseal portal system
      2) 6 major H’s released: FSH, LH, TSH, ACTH, GH, PRL
   b. Growth H = Somatotropin (GH)
      1) Polypeptide of 191 aa
      2) General function: Causes body cells to grow (divide), especially muscle and bone; in adults, maintains muscle & bone mass and helps with tissue repair
      3) Hypothalamus controls by:
         a) GHRleasingH (somatocrinin)-increases release
         b) GHIhbitingH (Somatostatin)-decreases release
   4) GH specific functions:
      a) Proteins
         i. increases entry of aa into cells
         ii. causes protein synthesis
      b) Fats/lipids
         i. Makes use of adipose tissue for E
         ii. Therefore, causes catabolism of fatty acids
      c) Carbohydrates
i. Speeds conversion of glycogen to glucose in liver-releases into blood
   ii. Increases entry of glucose into cells, but cells do not use; they use fatty acids
   iii. Leads to diabetogenic effect where blood glucose elevates (like diabetes and over long term could lead to diabetes mellitus)

d) Converts other substances into growth-promoting messengers called somatomedins
   i. Peptide H made in liver that binds to receptors on plasma membranes causing cells to take in aa
   ii. Somatomedins cause cartilage & bone growth stimulating chondroblasts at epiphyseal plates

5) Hyposcretion causes pituitary dwarfism
   a) Hyposcretion during prepuberty (growing) years
   b) Most dwarfs are genetic, not pituitary
   c) Proportional body features, but short stature
   d) Often do not pass thru puberty; 1/3 sexually mature
   e) Treated by genetically engineered GH

6) Hypersecretion during prepuberty years causes pituitary gigantism
   a) Most tall people are genetic
   b) Proportional features, but very tall
   c) Often diabetic & die as young adults
   d) Treated by surgery to remove tumor and/or somatostatin (GHIH)

7) Hypersecretion during adult years causes acromegaly
   a) Normal height, but enlarged soft cartilage in hands, feet, nose, forehead, lower jaw, etc
   b) 30% diabetic
   c) Treated by surgery for tumor and/or somatostatin

C. Thyroid stimulating H (TSH)-stimulates thyroid gland to release thyroid H's

D. Adrenocorticotrophic H (ACTH)-stimulates the adrenal cortex to release mostly cortisol

E. Prolactin (PRL)
   1) F: Initiation and maintenance of milk
   2) M: Possibly makes testes more sensitive to LH

F. Melanocyte stimulating H (MSH)-stimulates melanocytes to release melanin leading to darkening of skin
   1) Production in humans is limited and only causes darkening in disorders such as Addison’s disease (see later)

G. Follicle stimulating H (FSH)
1) **F**: promotes follicle development & production of estrogen by ovaries
2) **M**: causes maturation & production of sperm

**h. Luteinizing H (LH)**
1) **F**: causes ovulation & promotes secretin of estrogen & progesterone by ovaries
2) **M**: known as Interstitial Cell Stimulating H (ICSH) causing production & release of testosterone from interstitial cells in testes

**8. Neurohypophysis**

a. Direct extension of hypothalamus
b. H's made in hypothalamus are carried to neurohypophysis by hypothalamo-hypophyseal nerve tract where they are released
   1) H's internally attached to protein carrier called neurophysin
c. Two nuclei in hypothalamus:
   1) Paraventricular-makes OT
   2) Supraoptic-makes ADH
d. Two major H's: Oxytocin (OT) and Antidiuretic H (ADH)
e. **Oxytocin**
   1) Small polypeptide-9 aa
   2) Stimulates powerful contractions of uterus during birth; relaxes cervix
   3) Prevents hemorrhaging after labor
   4) Causes milk expression from breasts
   5) Increases during sexual arousal causing ejaculation and vagina contractions (orgasm)
f. **Antidiuretic H**
   1) Peptide of 9 aa
   2) Stimulates water reabsorption by kidney tubules-reduces urine volume
   3) Diabetes insipidus-disorder of reduced ADH release
      a) Polyuria-10L + urine/day (normal = ~1 L)
      b) Polydipsia-increased thirst
c) Treated with synthetic ADH
   4) Also known as vasopressin in very high doses
      a) Stimulates contraction of smooth muscle of arterioles to increase BP
      b) Doses 100X normal??

**Hypothalamus**

1. Controls adenohypophysis by regulating H's
   a. Delivered by the hypothalamo-hypophyseal portal system
1) Portal system:
   a) Normal: Heart→arteries→capillary bed→veins→heart
   b) Portal: Heart→arteries→1st capillary bed→portal vessels (veins)→2nd capillary bed→veins→heart
2) 1st capillary bed in hypothalamus→portal vessels→2nd capillary bed in adenohypophysis→hypophyseal veins
3) Significance: Direct delivery and only low conc. of H's required

2. There are 8 H's: TRH, CRH, GHRH, LRH, FSHRH, PRLRH, GHIH, PRLIH

3. Thyroid releasing H (TRH)-causes adenohypophysis to release TSH
4. Corticotropin releasing H (CRH)-causes adenohypophysis to release ACTH
5. Growth H releasing H (GHRH)-causes adenohypophysis to release GH
6. Luteinizing releasing H (LRH)-causes adenohypophysis to release LH
7. Follicle stimulating H releasing H (FSHRH)-causes adenohypophysis to release FSH
   a. Both LRH & FSHRH are collectively called Gonadotropin Releasing H's
8. Prolactin releasing H (PRLRH)-causes adenohypophysis to release PRL
9. Growth H inhibiting H (GHIH) or somatostatin-reduces release of GH from adenohypophysis
10. Prolactin inhibiting H (PRLIH)-reduces release of PRL from adenohypophysis
    a. Also called dopamine
    b. This H decreases during late menstrual cycle allowing increase of PRL; as a result breasts become tender

**Thyroid Gland**

1. Located at a level between 5th & 7th vertebrae, anterior & inferior to larynx
2. Divided into 2 lobes connected by isthmus
3. 25-34 g, one of largest endocrine glands
4. Produces 3 H's: 2 Thyroid H's and Calcitonin
5. Thyroid gland histology and function
   a. Organized into follicles-ball-like structure with lumen in center
      1) Lumen filled with colloid
      2) Each cell is called a follicle cell
      3) Parafollicular (or C) cells found outside follicles on edges
   b. In apical edge of follicle cell is an iodide pump; a transmembrane protein that removes I- from blood & concentrates (25-40X) in cell
c. Central space (= lumen) in follicle is filled with colloid that houses the protein thyroglobulin (TGB)
   1) TGB is ~ 5000 aa protein first synthesized on rER inside follicle cell; about 140 of the 5000 aa are tyrosines
   2) Also inside follicle cell, TGB is transported to Golgi body where a carbohydrate group is attached
   3) TGB is then delivered to colloid by exocytosis

d. Inside lumen, TGB is iodinated & then folds, bringing 2 tyrosines into contact
   1) I$_2$'s came from follicle cell
   2) Some tyrosines received one iodine and are called moniodothyrosines (MIT)
   3) Some tyrosines received two iodines and are called diiodothyrosines (DIT)
   4) If MIT contacts a DIT, Triiodothyronine (or T3) is formed
   5) If two DITs meet, Tetraiodothyronine (or T4) is formed
      a) T4 is also known as thyroxine
      b) T4 makes up ~ 90% of thyroid H's

6) Note that T3 & T4 are still physically part of TGB

e. TGB taken back into follicle cell by endocytosis

f. Lyzosomes with EZ's join vesicle with TGB's and cleave T3 & T4 from large protein

g. T3 & T4 are lipid soluble and diffuse out of follicle cell into the blood where they are picked up by a transport protein called Thyroid Binding Globulin (TBG)

h. TBG delivers T3 & T4 to target cells
   1) T3 is more active form; T4 gets converted to T3 by target cell
   20 Why? Step on metabolic accelerator with T3 to gain speed (in metabolism), then maintain speed (metabolism) with T4 conversion

6. Thyroid H functions
   a. General: Increases overall metabolism by stimulating synthesis of over 100 metabolic EZ's
   b. Specific funtions:
      1) Proteins
         a) Increases protein synthesis are low/normal doses
         b) Increases protein catabolism at high/abnormal does because of gluconeogenesis
      2) Lipids
         a) Increases lipid metabolism from adipose tissue
         b) Decreases levels of cholesterol, PPL, & triglycerides in blood
      3) Carbohydrates
a) Increase all aspects of carbohydrate breakdown  
b) Glyogenolysis-conversion of glycogen to glucose  
c) Glycolysis-Breakdown of glucose to pyruvate  
d) Gluconeogenesis-formation of glucose from fats & proteins  
e) Increases absorption of glucose from GI tract

4) Increases  
a) size & # of mitochondria; also binding to receptors on mitochondria to increase E output  
b) Synthesis of many metanolic EZs especially ATP synthetase  
c) Na+ transport  
d) Basal Metabolic Rate

5) Stimulates growth because of effects on protein synthesis

7. Thyroid H production/control  
a. Overall control by negative feedback  
b. Hypothalamus controls (adenohypophysis) by TRH  
c. Adenohypophysis controls by TSH  
d. TSH stimulates release of Thyroid H’s  
e. Elevated metabolism detected by hypothalamus  
f. Hypothalamus reduces TRH→reducing TSH→reducing TH’s  
g. Too much TH = hyperthyroidism; too little TH = hypothyroidism

8. Hypothyroidism  
a. Undersecretion of TH during fetal development or after birth results in severe physical & mental retardation  
   1) Distorted facial features, swollen tongue, irregular epiphyses  
   2) Possibly autoimmune, but insufficient iodine during pregnancy can also cause  
   3) If caught early & treated with synthetic TH, normal development occurs  
b. Undersecretion of TH as an adult is also called Goiter or Myxedema  
   1) Autoimmune or dietary causes  
   2) 50 mg l/yr required  
   3) Table salt now iodinated  
   4) Endemic goiter in few areas of world: Great Lakes (historically), Andes, Africa; soil with low iodine content  
   5) Symptoms: sleep 14-16 h/day, slowed heart rate, increased wt, mentally sluggish, husky voice, enlarged thyroid  
c. In blood tests for a person with hypothyroidism, what blood concentrations (high, low, normal) would you expect to see in:  
   1) TRH (high)  
   2) TSH (high)
3) TH (low)

9. Hyperthyroidism
   a. Oversecretion of TH as an adult is also called exophthalamic goiter or Grave’s disease
   b. Causes: autoimmune/tumor
   c. Symptoms: heat intolerance, increased sweating, wt loss, muscular weakness, nervousness. Deposition of mucopolysaccharides behind eyes causing eyeball protrusion
   d. Treatment: surgical removal of tumor or inject radioactive iodine to kill cells

10. Thyroid gland: Calcitonin
    a. Polypeptide 32 aa
    b. Produced by parafollicular or C cells
    c. Released in response to high (2-3X normal levels) blood Ca++
    d. Reduces blood Ca++ by:
       1) Inhibiting osteoclasts
       2) Stimulating osteoblasts
       3) Preventing formation of new osteoclasts
    e. Of minor importance in adults because kidney is so efficient at eliminating excess Ca++
    f. Sometimes given for treatment of osteoporosis

Parathyroid Glands
1. 4 (usually) glands located on posterior surface of thyroid gland
2. Secretes parathyroid H (=Parathormone) PTH
3. Polypeptide 84 aa
4. Secreted by chief cells (=principle)
5. Second cell type, oxyphils, of unknown function
6. Released in response to low blood Ca++
   a. Returns blood Ca++ to normal by increasing:
      1) Activity of osteoclasts
      2) Formation of osteoclasts
      3) Reabsorption of Ca++ in kidney
      4) Absorption of Ca++ in GI tract
   b. PTH increases formation & secretion of calcitriol at the kidneys; calcitriol is formed from Vitamin D in the skin
      1) Calcitriol increases GI tract absorption
7. Disorders
   a. Hypoparathyroidism
      1) Causes: surgery to remove thyroid or cutting of vessels to PTH glands during surgery
2) Symptoms: Decreased Ca++ causes increased Na+ in extracellular fluid making membranes more excitable
   a) Tetanic spasms of cardiac muscle leading to cardiac arrest
3) Treatment: Hormone Replacement Therapy (HRT)

b. Hyperparathyroidism
   1) Cause: tumor
   2) Increased Ca++ causes decreased Na+ in ECF making membranes less excitable
      a) Fatigue, fever, headaches, extreme osteoclast activity, & kidney stones
3) Treatment: surgery

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**Adrenal Glands**

1. Located superior to kidneys; ~ 4-7.5 g
2. Divided into 2 distinct glands functionally and embryologically:
   a. Adrenal cortex
   b. Adrenal medulla
3. Adrenal medulla
   a. Inner region of adrenal
   b. Derived embryologically from neuroectoderm
   c. Releases 2 H's: epinephrine/norepinephrine
   d. Both H's are sympathetically controlled during fight or flight reflex
   e. Effects (a few):
      1) Increased heart rate
      2) Dilates bronchi & bronchioles
      3) Glycogenolysis
      4) Dilates pupils
   f. Stains purple on slides
4. Adrenal cortex
   a. Outer region of adrenal
   b. Derived embryologically from lateral mesoderm, the same tissue that forms the gonads
   c. Releases over 25 steroid H's divided into 3 major groups:
      1) Glucocorticoids
      2) Mineralcorticoids
      3) Sex H's
   d. Histology
      1) 3 major H groups correspond to 3 distinct zones in cortex
      2) Capsule-outer protective layer of CT
      3) Zona glomerulosa-outermost where cells are arranged into ball-like glomeruli
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a) 15% volume
b) Secrete mineralcorticoids

4) Zona fasciculate-pale cells arranged in columns (fasciculi)
a) 78% volume
b) secrete glucocorticoids

5) Zona reticularis-innermost zone of cellular cords that branch (reticulate)
a) 7% volume
b) Secrete sex H's
e. Zona glomerulosa-secrete mineralcorticoids
   1) Main H is aldosterone
   2) Absence causes death in 3 days
   3) Functions:
      a) Increases reabsorption of Na+ by kidneys
      b) Enhances K+ secretion in kidney for exit in urine
      c) Reduces loss of Na+ from sweat & salivary glands and GI tract

4) Aldosterone regulation
   a) Increased K+ in ECF
   b) Renin-angiotensin system
      i. Kidneys release H called renin
      ii. Renin activates intermediates that lead to the formation of angiotensin II
      iii. Angiotensin II stimulates release of aldosterone
   c) Na+ conc in blood
d) ACTH
e) Atrial Natriuretic Peptide (ANP)-from heart & adjust BP by controlling Na+

f. Zona fasciculate-secrete glucocorticoids
   1) Main (95%) H is cortisol
   2) Metabolic effects on:
      a) Proteins
         i. Reduces stores
         ii. Decreases protein synthesis
         iii. Increases catabolism of stored proteins
         iv. Excess cortisol causes muscular (actin/myosin) weakness and a suppressed immune system (proteins in antibodies)
      b) Lipids
         i. Mobilization of fatty acids from adipose tissue
         ii. Using fats for E instead of glucose
      c) Carbohydrates
         i. Increases gluconeogenesis
ii. Increase glycogen formation
iii. Increases blood sugar possibly leading to (adrenal) diabetes

3) Stress
a) Mental or physical stress causes increased CRH release by hypothalamus
b) Increased CRH causes increased release of ACTH by adenohypophysis
c) Increased ACTH causes increased release of cortisol by adrenal cortex

4) Effects of elevated cortisol
a) Decreases inflammation and slows healing
b) Decreases capillary permeability preventing vasodilation (important in diapedesis & healing)
c) Because of protein catabolism:
   i. Immune system is depressed and you are prone to illnesses that you usually do not get
   ii. CT regeneration is slowed (collagen is a protein)
   iii. Muscles become weak (actin/myosin are proteins)
d) Synthetic versions often used to reduce inflammation and allergies

g. Zona reticularis-sex H’s
1) Release small amts of estrogen, progesterone, & testosterone
2) In women, 50% of androgen requirement met by this zone
   a) Important in sex drive
   b) This estrogen becomes more important after menopause
3) Very minor importance in males
4) Adrenogenital syndrome and Bearded lady-tumors in this zone most noticed in women

h. Disorders:
1) Hyperadrenalism
   a) Also called Cushing’s syndrome
   b) Cause: a tumor or excessive use of glucocorticoid drugs for an autoimmune disease/allergies
c) Symptoms:
   i. Mobilization of fats from lower body to thoracic region-Buffalo torso/hump
   ii. Edema in face: Moon Face
   iii. Elevated glucose-adrenal diabetes
   iv. Muscle weakness
   v. Diminished immunity
d) Treatment: reduce steroids or dosage or surgery for tumor

2) Hypoadrenalism
   a) Also called Addison’s disease
   b) Cause: Autoimmune or insufficient ACTH from adenohypophysis
   c) Symptoms:
      i. Na+ loss in urine, water follows, BP plummets
      ii. Blood glucose fluctuates widely
      iii. Large amounts of ACTH released, but because precursor molecule is the same as the one for making MSH, the effect is increased melanin secretion by melanocytes-skin darkens
   d) Treatment: HRT

Pancreas
1. Located along greater curvature of stomach and 1st region of small intestine called duodenum
2. Two part gland:
   a. Exocrine-98% of cells are acinar (pancreatic acini) that secrete digestive EZ’s
   b. Endocrine-Islets of Langerhans (Pancreatic Islets), 1-2%
      1) Alpha cells-glucagon
      2) Beta cells-insulin
      3) Delta cells-somatostatin
      4) F cells-H that regulates composition of pancreatic juice
3. Insulin
   a. Polypeptide in 2 aa chains; 51 aa
   b. Effects on:
      1) Proteins
         a) Similar to GH
         b) Increases aa transport into cells
         c) Increases transcription & therefore protein synthesis
      2) Lipids
         a) Enhances transport of glucose into fat cells; promotes fat storage
         b) Excess glucose, not converted to glycogen, is stored as fat
      3) Carbohydrates
         a) Enhances transport of glucose into cells by facilitated diffusion
            i. Exceptions are brain, RBC’s, & kidney
b) Inhibits breakdown of glycogen
c) Inhibits gluconeogenesis
c. Released in response to high (2-3X) blood glucose; normal fasting levels = 90-110 mg/dl
d. Disorders
   1) Diabetes Type I
      a) Also called Juvenile Onset or Insulin-dependent
      b) Cause: autoimmune where beta cells destroyed
c) Symptoms:
         i. Glycosuria-increased glucose in urine
         ii. Polyuria-increased glucose in urine draws more water causing higher urine volume
         iii. Polydipsia-with loss of water in urine, thirst increases
         iv. Polyphagia-excessive hunger with loss of glucose and inability of glucose to move into cells creates starvation conditions
         v. Acidosis-shift from glucose metabolism to fat metabolism creates ketone bodies that drops pH
         vi. Cataracts
         vii. Atherosclerosis-poor circulation to extremeties
d) Treatment: insulin injections; transplants
   2) Diabetes Type II
      a) Also called Adult Onset or Noninsulin-dependent
      b) Cause: Generally a poor lifestyle where individuals are typically over 40, overweight, very sedentary, and have a poor diet
      c) Receptors are less sensitive to insulin
      d) Symptoms: similar to Type I, but usually not as extensive; can become insulin-dependent if untreated
e) Treatment: change lifestyle
         i. Exercise
         ii. Lose weight
         iii. Modified diet away from processed foods
         iv. Medications that help control glucose levels

4. Glucagon
   a. Similar effects to E; is synergistic
   b. Antagonist to insulin
c. Increases blood sugar by:
      1) Glycogenolysis
      2) Gluconeogenesis
d. Released in response to low (< 70 mg/dl) blood glucose, but also high aa levels
e. Glucagon levels are also elevated in Type I diabetics

5. Insulin shock
   a. Usually results from injecting too much insulin which so lowers blood glucose that brain is effected
   b. Pancreatic tumors also cause

Ovaries
1. Description: paired oval glands resembling unshelled almonds in size & shape
2. Location: in upper pelvic cavity; one on each side of uterus
3. Hormones:
   a. Estrogen
      1) Kinds: Beta estradiol, estrone, estriol (placenta)
      2) Functions:
         a) Primary & secondary sexual characteristics
         b) Fluid and electrolyte balance
         c) Inhibits FSH during menstrual cycle
   b. Progesterone
      1) Produced by corpus luteum in ovaries, but main source is placenta
      2) Small amounts come from adrenal cortex
      3) Functions:
         a) Prepares uterus for implantation of embryo; known as the pregnancy H
         b) Lobule development in breasts

Testes
1. Description: Paired oval glands (~5 X 2.5 cm) located in scrotum
2. Hormones:
   a. Androgens—best known is testosterone
   b. Released from the Interstitial cells of Leydig
   c. Functions:
      1) Primary & secondary sexual characteristics
      2) Sex drive
      3) Aggressive behavior

Thymus
1. Located in upper mediastinum posterior to sternum and between lungs
2. Relatively large in infants, but proportionally decreases in size with growth; enlarges again in old age
3. Group of H’s called Thymosins
4. Functions: Regulates development of immune cells called T lymphocytes; activates your immune system

**Pineal Gland (Body)**
1. Located in roof of 3\textsuperscript{rd} ventricle and part of diencephalon
2. Description: Cone-shaped mass (5-8 mm X 5 mm) that calcified at puberty
3. Innervated by SNS
4. Also receives collaterals from optic nerve
5. Pineal secretions peak between 1 & 5 yrs; decline by 75% at puberty
6. Functions & H's
   a. In nonhuman vertebrates (creatures with vertebrae in their backs), it regulates seasonal breeding
   b. May regulate the timing of puberty in humans
   c. Melatonin
      1) Blood levels low in day, high at night
      2) Affects secretion of H's by ovaries
   d. Serotonin-converted to melatonin at night
7. Disorders:
   a. Seasonal Affective Disorder (SAD)
      1) Symptoms: Depression, sleep disruption, irritability, carbohydrate craving
      2) Observed frequency in people living at high latitudes (Portland, Alaska, Maine, etc) where sunlight in winter months is less than 8 hours/24 hours
      3) Treatment: Phototherapy-exposure to 2-3 hours of bright light each day
   b. Premenstrual syndrome (PMS)
      1) Melatonin elevated in both SAD and PMS
      2) Similar symptoms
      3) Relieved by phototherapy
   c. Melatonin often taken for jet lag, but not controlled experiments to justify safety