Structure and Function of the Hypothalamus

I. Overview of Anatomical Relationship

A. Anatomy of the hypothalamus
   1. Part of the diencephalon
   2. Characteristics
      a. Lies inferior to the thalamus
      b. Contributes to the wall of the 3rd ventricle
   3. Components
      a. Hypothalamic nuclei
      b. Optic chiasm
      c. Tuber cinereum
         i. Floor of the 3rd ventricle
         ii. Median eminence is the vascular lower part of the tuber cinereum
      d. Infundibulum
         i. Stalk of tissue connecting hypothalamus to the pituitary
      e. Mammillary bodies
B. General characteristics of connections with pituitary gland

1. Pituitary is anatomically connected to the superiorly lying hypothalamus
   a. Infundibulum—stalk-like connection
      i. Physical connection between brain and endocrine system

2. Hypothalamus is part of the brain

3. Pituitary includes two major lobes
   a. Posterior
      i. Posterior lobe + infundibulum = neurohypophysis
   b. Anterior
      i. Anterior lobe (adenohypophysis) is comprised of glandular tissue

C. Functional connections between posterior pituitary and hypothalamus

1. Posterior is an outgrowth of the brain and maintains its neural connections
   a. Neurons in the supraoptic (SON) and paraventricular nuclei (PVN) of the hypothalamus give rise to the hypothalamic-hypophyseal tract (supraoptico-paraventriculohypophysial tract)
      i. Axons of these neurons terminate in the posterior pituitary
      ii. Neurohormones synthesized by these neurons are released upon stimulation (electrical)
      iii. Secretions are released into interstitial tissue and picked up by capillary plexus in the posterior pituitary

2. Oxytocin is predominantly synthesized by SON

3. Antidiuretic hormone is predominantly synthesized by PVN
D. Functional connections between anterior pituitary and hypothalamus
1. Anterior lobe is derived from epithelial tissue
2. No direct connection between anterior pituitary and hypothalamus
   a. Connection is vascular
      i. Hypophyseal portal system
      ii. Connects median eminence to secretory cells of the anterior pituitary
3. Releasing and inhibiting hormones secreted by hypothalamus are carried by portal system to anterior pituitary
   a. These hypophysiotropic factors regulate the activity of secretory cells in anterior pituitary

E. Hypothalamic nuclei
1. Magnocellular system
   a. Supraoptic nuclei (SON)
      i. Synthesize vasopressin (ADH)
   b. Paraventricular nuclei (PVN)
      i. Synthesize oxytocin
2. Parvocellular neurosecretory system
   a. Ventromedial nucleus
      i. Axons of these neurons converge toward the pituitary stalk
      ii. Abut the primary plexus of the portal system of the median eminence
      iii. Synthesize and secrete hypophysiotropic factors

F. Hypophyseal portal system
1. Primary plexus
   a. Drains interstitial space of the median eminence
2. Hypophyseal portal vein
3. Secondary plexus
   a. Delivers hypophysiotropic factors of the hypothalamus to the adenohypophysis

II. Hypophysiotropic Hormones
A. TRH—thyrotropin releasing hormone
1. Controls TSH secretion
   a. TSH release from the anterior pituitary

B. SST—somatostatin
1. Inhibits GH secretion from anterior pituitary
   a. Acts on pituitary somatotrophs
2. SST is widely distributed with diverse systemic effects

C. GHRH—growth hormone releasing hormone
1. Stimulates GH secretion from anterior pituitary

D. GnRH—gonadotropin releasing hormone
1. Stimulates the release of FSH and LH from anterior pituitary
   a. Primary brain-based control of gonadotropins
2. Functional considerations
   a. Pulsate release
   b. Frequency determines which hormone is released
      i. Low frequency causes FSH release
ii. High frequency causes LH release

E. CRH—corticotropin releasing hormone
1. Stimulates the release of ACTH from anterior pituitary
2. CRH neurons co-express vasopressin (AVP)
3. Released in response to stress

F. PIF—prolactin release inhibiting factor (DA)
1. Inhibits the secretion of PRL from the hypothalamus
2. Structure
   a. PIF is dopamine
   b. DA agonists reduce PRL secretion

G. PRF—prolactin releasing factor
1. Putative factor not established
   a. 5-HT is a candidate

H. MIF—MSH release inhibiting factor
1. MSH release inhibited hypothalamus
2. Neurons in pars intermedia extend from hypothalamus to pituitary
   a. Release DA

III. Control of Hypothalamic/Hypophyseal Hormone Secretion

A. General Mechanisms
1. Hypothalamus is controlled by other brain circuits
   a. These brain circuits are activated by circuits processing extrinsic and intrinsic cues
   b. Extra-hypothalamic neurons innervate hypophysiotropic hormone producing cells
2. Brain-based activity requires synaptic transmission
   a. Specific NT’s released by circuits terminating in hypothalamus control hormone secretion
   b. NT’s are typically monoamines
      i. NE; DA; Epi; 5-HT; Histamine; Ach
   c. Nature of effect is mediated by NT receptors
      i. Increase or decrease release

B. Feedback control of hypothalamus
1. Schema
2. Mechanisms
   a. Long loop negative feedback
      i. Three hormone systems
      ii. Third hormone can suppress the release of the first or second hormone
      iii. Peripheral hormone inhibits both the pituitary and hypothalamus
   b. Short loop negative feedback
      i. Two hormone systems
      ii. Second hormone can suppress the release of the first hormone
      iii. Pituitary hormone inhibits hypothalamus
   c. Autoinhibition
      i. Hormone can suppress its own release

3. Corticotropin secretion
   a. CRH → ACTH → glucocorticoid release
      i. Cortisol is the predominant glucocorticoid
   b. Glucocorticoids inhibit both the hypothalamus and pituitary
i. Cortisol → ↓ CRH
ii. Cortisol → ↓ ACTH

4. GnRH secretion
   a. GnRH → FSH & LH → estrogens and androgens
   b. Steroid hormones predominantly inhibit the hypothalamus
   c. In females, estrogen also acts on the pituitary
      i. Estrogen → ↓ FSH
      ii. Estrogen → ↑ LH

5. PRL secretion
   a. PRL inhibits hypothalamic release of PIF (DA)
   b. PRL may also inhibit the pituitary

6. GH secretion
   a. GH release controlled by the combined effects of SST and GHRH
   b. GHRH → GH → somatomedins from the liver
      i. Somatomedins increase tissue growth
   c. GH also activates IGF-1
      i. Insulin-like growth factor
      ii. IGF increases muscle and skeletal growth
   d. IGF-1 → ↑ SST from the hypothalamus
      i. SST → ↓ GH from the pituitary
   e. GH → ↑ SST from the hypothalamus

7. Thyrotropin secretion
   a. TRH → TSH → T3/T4
   b. T3/T4 → ↓ TSH from the pituitary
   c. T3/T4 → ↓ TRH from the hypothalamus

Structure and Function of the Pituitary Gland

I. Background
A. Embryological Development
1. Anterior lobe (adenohypophysis) forms as an out pouching of the oral ectoderm
   a. Rathke’s pouch
2. Rathke’s pouch migrates dorsally and separates from the developing oral cavity
3. Posterior lobe (neurohypophysis) forms from neuroectoderm of the floor of the forebrain
4. Infundibulum is an out pouching of the floor of the diencephalon
   a. Neuroepithelial cells proliferate and then differentiate into pituicytes
   b. Axons grow into the infundibulum from hypothalamic nuclei

B. Pituitary hormones
1. Anterior pituitary
   a. Gonadotropins
      i. FSH
      ii. LH
   b. Thyroid stimulating hormone—TSH
   c. Adrenocorticotropic hormone—ACTH
   d. Growth hormone—GH
   e. Prolactin—PRL
   f. Melanocyte-stimulating hormone—MSH
2. Posterior pituitary
   a. Oxytocin—OT
   b. Vasopressin—AVP, ADH
   c. Melanin concentrating hormone
II. Structural Classification of Anterior Pituitary Hormones

A. Peptide Growth Hormones—GH, PRL and hPL

1. Structurally similar peptides
2. Affect body growth
   a. GH
      i. Generalized effects on body cells
   b. PRL
      i. Selective effect on mammary tissue
3. GH
   a. Produced by somatotrophic cells
   b. Stimulates most cells in the body to grow and divide
   c. Major targets are bones and muscles
   d. Anabolic hormone
      i. Promotes metabolism
   e. Growth-promoting effects are mediated indirectly
      i. IGF’s—insulin-like growth factors
      ii. Produced by liver and other tissues
   f. Effects of growth hormone
      i. Stimulates uptake of amino acids from blood and their incorporation into proteins
      ii. Stimulates sulfur uptake
      iii. Mobilizes fats from fat deposits
      iv. Decreases rate of glucose uptake and metabolism
         i. Diabetogenic effect—elevation of blood glucose
   g. Regulation by hypothalamic hormones (negative feedback)
      i. GHRH—growth hormone releasing hormone (somatocrinin)
      ii. GHIH—growth hormone inhibiting hormone (somatostatin)
   h. Indirect effects mediated by IGF’s
      i. Increases amino acid incorporation into muscle
      ii. Increases collagen incorporation into extracellular tissue
   i. Direct effects
      i. Oppose effects of insulin
      ii. Increase blood glucose levels

4. Prolactin
   a. Functions
      i. Mammary gland growth
      ii. Lactogenesis
   b. Elevated during pregnancy and postpartum lactational period
      i. Estrogen → ↑ PRL release
      ii. Estrogen → ↑ mitosis in lactotrophs
   c. In males PRL affects LH receptor function
      i. LH → ↑ testosterone production
      ii. Testosterone affects the rate of spermatogenesis
   d. Release of PRL is episodic
      i. Surges during sleep

B. Glycoproteins—LH, FSH and TSH

1. Peptide hormones with carbohydrate moieties covalently bound at one or more positions on the peptides
2. TSH
   a. Synthesized and secreted by basophilic thyrotrophs in pars distalis of the pituitary gland
   b. Control thyroid function
      i. Production and release of T₃ and T₄
3. LH
   a. Control production of steroid hormones by the gonads
   b. Control gonadal function
   c. Controls corpora lutea formation in females
   d. Control testosterone secretion by interstitial cells of Leydig in males
      i. Need FSH to induce LH receptors in Leydig cells
      ii. LH indirectly control spermatogenesis in males

4. FSH
   a. Controls follicular maturation in female ovary
      i. Production of estrogen
      ii. Maturation of the oocyte
   b. Regulates differentiation of spermatogonia in males

C. Proopiomelanocortin (POMC) Derivatives—ACTH and MSH
   1. Corticotrophin—ACTH
      a. ACTH stimulates steroid biosynthesis within the adrenal cortex
         i. Controls production and release of glucocorticoids
         ii. Cortisol and corticosterone
      b. Glucocorticoids affect carbohydrate metabolism
   2. MSH
      a. Adults do not have MSH producing cells in the pituitary

III. Posterior Pituitary Hormones—Oxytocin (OT) and Arginine Vasopressin (AVP)
   A. Development and anatomy of the posterior pituitary
      1. Posterior pituitary results from the downward growth of neural ectoderm
      2. Posterior pituitary consists of neuronal terminals, blood vessels and pituicytes
         a. Pituicytes are neuroglial cells
      3. Axons that extent into the pituitary have cell bodies in the hypothalamus
         a. Cells bodies are part of the magnocellular system
         b. Cell bodies are located in two hypothalamic nuclei
            i. SON
            ii. PVN
   B. Functional relationship between posterior pituitary and hypothalamus
      1. Neurohypophysial hormones are synthesized in neuronal cell bodies
      2. Hormones are transported to axon terminals by axoplasmic transport
      3. Hormones are stored in neurosecretory vesicles
      4. Hormones are released from secretory granules by neurosecretion
         a. Depolarization of axon terminal following action potential propagation
   C. Control of posterior pituitary hormonal secretion
      1. Secretion requires activation of sensory receptors
         a. OT released in response to suckling and myometrial contraction
         b. AVP released in response to distension of vascular tissue
      2. Activation of receptors generate CNS signaling that activates neurons in SON and AVP
         a. Afferent signal from receptors activate neural pathways targeting neurosecretory cell bodies
         b. Neural pathways may be excitatory
            i. Cholinergic (ACh)
         c. Neural pathways may be inhibitory
            i. Noradrenergic (NE)
            ii. Decrease release of OT and AVP
3. Depolarization of SON and AVP in response to neurotransmission generate action potentials
   a. Action potentials are propagated along axons extending into posterior pituitary
   b. Current associated with action potential depolarize presynaptic membranes of axon terminals
   c. Depolarization opens voltage-gated Ca\(^{2+}\) channels
   d. Ca\(^{2+}\) influx acts as a molecular trigger to initiate secretory granule exocytosis

D. Physiological roles of oxytocin
1. Two major functions
   a. Let-down reflex
   b. Uterine myometrial contraction during parturition (labor)
2. OT is a female specific, transitional hormone
   a. Levels only rise appreciably during full term pregnancy

F. Milk release—Let-Down Reflex
1. Stimuli for release
   a. Suckling of areola and nipple
      i. Activates nerve endings
      ii. Primary
2. Neural pathway
   a. ST to mesencephalon targets to diencephalon (hypothalamus)
3. Through classical conditioning OT release can be associated with other stimuli
   a. Sounds and smells associated with the infant
4. Location of OT receptors
   a. Alveoli of mammary glands are surrounded by myoepithelial cells
      i. OT receptors are located on myoepithelial cells
      ii. OT receptors when bound cause contractions of myoepithelial cells
   b. Alveolar secretory cells produce milk and are hormonally controlled by PRL
5. Expression of milk
   a. Contraction of myoepithelial cells compress underlying alveolae
   b. Compression pressurizes fluid within the alveolae and pushes it through the lactiferous duct
      i. Milk exits as a pressurized stream through a single pore
6. OT is only required for expression of milk
   a. Milk can be produced without OT

G. Uterine myometrial contraction during parturition
1. OT is not required for the initiation of labor and pituitary OT may not be essential for its maintenance
   a. There is limited number of OT receptors in the myometrium prior to the term
   b. OT concentration increases only during the final stages
2. OT receptor number and sensitivity increase during terminal stages of labor
   a. Number and sensitivity parallels estradiol and progesterone levels
      i. Progesterone inhibits OT myometrial receptor formation
      ii. OT receptor formation and sensitivity increase with estradiol levels
      iii. During late term pregnancy, ↓ progesterone and ↑ estrogen
3. Pituitary OT causes myometrial contraction but primary source to initiate labor may be from direct uterine production
   a. OT in the uterus may primarily be a paracrine
   b. Rise of uterine OT concentration and OT receptor sensitivity may trigger labor
H. Physiological roles of AVP
1. Two major functions
   a. Regulation of blood pressure
      i. Control of smooth muscle contraction
   b. Regulation of osmolarity
      i. Movement of solute and water across the DCT of the medullary nephron
      ii. Increase absorption of water and Na+

I. AVP role in osmoregulation
1. Changes in blood osmolarity affect AVP release
   a. ↓ osmolarity → ↓ AVP → excretion of hypotonic urine
   b. ↑ osmolarity → ↑ AVP → excretion of hypertonic urine
2. Receptors in the anterior hypothalamus detect changes in osmolarity
   a. Osmoreceptors
      i. Unique cell population
      ii. Not SON neurosecretory cells
   b. Do not respond to changes in blood pressure
      i. Separate, unique cells that act as baroreceptors
3. SON neurosecretory cells respond to sensory inputs from either osmoreceptors or baroreceptors
   a. No unique subset of SON specific to OR or BR

J. AVP role in blood pressure
1. ↑ blood pressure → ↓ SON → ↓ AVP → increase urine output ↓ BP
2. AVP release is also affected by renin – angiotensin – aldosterone mechanism
   a. Angiotensin II → ↑ AVP → excretion of hypertonic urine → ↑ BP
   b. Aldosterone → ↑ [Na+] → activation of OR → ↑ AVP → excretion of hypertonic urine → ↑ BP

Endocrine System

I. Background:
A. There are two types of glands:
1. Endocrine
   a. Ductless
   b. Secrete hormones into surrounding tissue fluid
   c. Vascular or lymphatic drainage receive hormones
   d. Examples of endocrine glands:
      i. Pituitary
      ii. Thyroid
      iii. Parathyroid
      iv. Adrenal
      v. Pineal
      vi. Thymus
   e. Some organs also have discrete areas of endocrine tissue as well as exocrine tissue
      i. Pancreas
      ii. Gonads
      iii. Hypothalamus
2. Exocrine
   a. Have ducts
   b. Nonhormonal products are directed to membrane surfaces
II. Hormones—chemical substances secreted by cells into extracellular fluids, that regulate metabolic function of other cells in the body

A. Chemistry
1. Classification
   a. Amino acid-based hormones
      i. Most hormones
   b. Steroid hormones
      i. Gonadal and adrenocortical hormones

B. Mechanism of action—increase or decrease rates of normal cellular activity
1. Hormonal effects
   a. Alter plasma membrane permeability
   b. Alter protein or regulatory molecule synthesis
   c. Activate or inactivate enzyme
   d. Induction of secretory activity
   e. Stimulate mitosis
2. Mechanisms that transduce hormonal signal into an intracellular change
   a. G-protein linked receptor activation of intracellular second messengers
      i. Amino acid-based hormones
   b. Direct gene activation
      i. Steroid hormones

C. Target cell specificity
1. Mediated by specific protein receptors
   a. Receptors are localized to cells that are influenced by a given hormone
   b. Hormones act as molecular triggers
2. Factors affecting target cell activation
   a. Hormonal levels
   b. Number of receptors on target cell
   c. Receptor affinity
      i. Can be up or down regulated based on microenvironmental conditions

D. Hormonal activity—half-life, onset and duration
1. Half-life—measure of hormonal persistence in blood stream
   a. Depends on rate of synthesis and release
   b. Speed of removal or degradation
2. Onset of effect is dependent on hormone type
   a. Steroid
      i. Hours to days
3. Duration is generally short (e.g., 20 minutes) although depends on hormone type

E. Control of hormone release
1. Typically negative feedback
   a. Hormone secretion is triggered in response to a stimulus
   b. As hormone level increases, target organ is affected
   c. Further hormone release is inhibited
2. Types of stimuli
   a. Humoral
      i. Endocrine glands release hormones in direct response to changing levels of ions or nutrients
      ii. E.g., PTH release in response to changes in calcium levels
   b. Neural
      i. Nerve fibers stimulate hormonal release
      ii. E.g., sympathetic activated release of catecholamines from adrenal medulla
   c. Hormonal
      i. Glands release hormones in response to other hormones
      ii. E.g., hypothalamic releasing and inhibiting factors

III. Endocrine Organs Closely Associated with Nervous System Function

A. Pituitary (See Above)

B. Adrenal glands
   1. Two endocrine glands
      a. Adrenal medulla
         i. Acts as part of the sympathetic NS
      b. Adrenal cortex
   2. Involved in response to stressful conditions
   3. Adrenal cortex
      a. Corticosteroids
         i. Steroids
         ii. More than two dozen
         iii. Synthesized from cholesterol
      b. Mineralocorticoids (type of corticosteroid)
         i. Regulate electrolyte concentrations in extracellular fluid
         ii. Aldosterone is most abundant
         iii. Aldosterone reduces excretion of sodium from the body
         iv. Stimulates reabsorption of sodium in the distal tubule of kidney
      c. Mechanisms controlling aldosterone secretion (4)
         i. Renin-angiotensin mechanism: JGA releases renin in response to blood pressure decrease, initiates cascade forming angiotensin II formation, angiotensin II stimulates aldosterone release from adrenal cortex
         ii. Direct stimulation by plasma sodium and potassium ions
         iii. ACTH: at very high levels of ACTH, aldosterone secretion is increased
         iv. ANP—atrial natriuretic peptide: when blood pressure is high, heart release ANP to inhibit renin and aldosterone secretion
      d. Glucocorticoids (type of corticosteroid)
         i. Influence metabolism and mediate response to stress
         ii. Cortisol, cortisone, corticosterone
         iii. Only cortisol is secreted in significant amounts
         iv. Non-stress: CRH, ACTH, cortisol release, negative feedback
         v. Stress: Sympathetic NS overrides inhibitory effects of elevated cortisol levels and triggers CRH release
         vi. Gluconeogenesis: primary effect of cortisol; conversion of fats into glucose
4. Adrenal medulla
   a. Chromaffin cells
      i. Modified postganglionic sympathetic neurons
      ii. Secrete epinephrine and norepinephrine
   b. Initial response to stress is mediated by sympathetic NS
   c. Activation of adrenal medulla and associated release of EPI and NE prolong sympathetic response
      i. Elevated BP and heart rate
      ii. Mobilization of glucose
      iii. Shunt blood from GI

IV. Endocrine Organs Associated with Hunger
A. Pancreas
1. Contains both exocrine (GI enzymes) and endocrine cells
2. Pancreatic islets (islets of Langerhans)
   a. Two populations
      i. Alpha cells—produce glucagons
      ii. Beta cells—produce insulin
3. Effects
   a. Insulin: hypoglycemic hormone
   b. Glucagon: hyperglycemic hormone
4. Glucagon effects
   a. Breakdown of glycogen to glucose (glycogenesis)
   b. Synthesis of glucose from lactic acid, fatty acids and amino acids
   c. Release of glucose from liver
5. Regulation of glycogen
   a. Humoral response to decreased circulating glucose
6. Insulin effects
   a. Lower blood glucose
      i. Enhances membrane transport of glucose into body cells
   b. Alter protein and fat metabolism
   c. Inhibits breakdown of glycogen
   d. Triggers enzymatic activity
      i. Oxidation of glucose for ATP production
      ii. Synthesis and storage of glycogen
      iii. Conversion of glucose to fat and its storage
7. Regulation of insulin
   a. Humoral response to increased circulating glucose

V. Endocrine Organs Associated with Reproduction
A. Gonads
1. Same sex hormones as those produced by adrenal cortex
2. Ovaries produce estrogens and progesterone
   a. Sexual maturation and menstrual cycle
3. Testes produce testosterone
   a. Sexual maturation
   b. Sex drive
4. Release of gonadal hormones is regulated by gonadotropins
B. Hormones involved in menstrual cycle

1. GnRH—gonadotropin releasing hormone
   a. Produced by hypothalamus
      i. Hypothalamus is part of the brain
   b. Travels via portal vein to anterior pituitary to control release of LH and FSH

2. FSH—follicle stimulating hormone
   a. Produced by anterior pituitary
   b. Controls gonadic function

3. LH—luteining hormone
   a. Produced by anterior pituitary
   b. Controls gonadic function

4. Estrogen
   a. Produced by gonads
      i. Follicle in females
      ii. Sertoli cells in males

5. Progesterone
   a. Produced by corpus luteum
   b. Prepares uterus for implantation and pregnancy

6. Testosterone
   a. Primarily a male hormone
      i. Also produced by adrenal gland
   b. Corpus luteum produces small quantities

7. HCG—human chorionic gonadotropin
   a. Secreted by extramembryonic membranes during pregnancy

C. Menstrual Cycle Based on Ovarian Events

1. Follicular phase
   a. Hypothalamus secretes GnRH
      i. Controls activity of anterior pituitary
   b. Anterior pituitary secretes FSH & LH
      i. Controls activity of ovary
   c. FSH stimulates ovarian follicles to begin to develop
   d. As follicle develops it begins to secrete estrogen
   e. Estrogen causes further follicular development
   f. Estrogen causes the endometrium to thicken
   g. Estrogen acts to signal hypothalamus to stop releasing GnRH
      i. Negative feedback—reduced production
      ii. Causes reduced FSH release
   h. Elevated estrogen levels causes LH release from anterior pituitary
      i. Positive feedback—increases production
      ii. Estrogen levels peak 1-1.5 days prior to ovulation
      iii. Elevated estrogen causes a surge in LH release from anterior pituitary
      iv. Ovulation is a response to LH surge
   i. Although there are many follicles in the ovary, one becomes dominant
   j. Ovulation
      i. Egg is released from follicle
      ii. Follicle differentiates into corpus luteum
   k. Follicle differentiates into corpus luteum
      i. Corpus luteum produces progesterone
   l. Progesterone causes reduced LH levels
      i. Negative feedback—reduced production
m. Progesterone causes reduced GnRH levels
   i. Negative feedback—reduced production
n. Egg moved by cilia and motility of fallopian tube
   i. Egg is viable for approximately 36 hours
   ii. Sperm is viable for approximately 3 to 5 days
   iii. Window for pregnancy can be as large as 7 days
   iv. 5 days prior to ovulation
   v. 1-1.5 days after ovulation

2. Luteal phase
   a. Last 14 days of the menstrual cycle
      i. Corresponds to the life of the corpus luteum
   b. Corpus luteum—“Yellow body”
      i. Derived from the follicle
   c. Corpus luteum produces
      i. Progesterone
      ii. Estrogen (estradiol)
      iii. Testosterone
   d. Progesterone suppresses new follicle growth
      i. Prevents ovulation of other follicles
   e. Progesterone causes the maturation of glandular and blood supply to endometrium of uterus
   f. If no pregnancy:
      i. Corpus luteum degenerates into corpus albicans (“White body”)
      ii. Estrogen and progesterone levels fall
      iii. Causes endometrial lining to degenerate—menstruation
   g. If pregnant:
      i. Developing embryo produces HCG
      ii. Maintains corpus luteum
      iii. Progesterone maintains uterus