The Posterior Pituitary and Hypothalamic Hormones

- Posterior pituitary
  - made of axons of hypothalamic neurons
  - stores antidiuretic hormone (ADH) and oxytocin synthesized & released by the hypothalamus
- ADH influences water balance
- Oxytocin stimulates smooth muscle contraction in breasts and uterus

- ADH & oxytocin differ by only 2 amino acids:
  - ADH: CYFQNCPRG
  - OXY: CYIQNCPGLG
Oxytocin

- Released at significantly higher levels during childbirth and in nursing women
- The number of oxytocin receptors peaks near the end of pregnancy
- Stretching of the uterus as birth nears sends afferent impulses to the hypothalamus which then synthesizes oxytocin & triggers its release from the neurohypophysis
- As blood levels of oxytocin rise, contractions increase
- Oxytocin is the hormonal trigger for milk ejection
- Oxytocin is often used to induce labor
Antidiuretic Hormone (ADH)

- Inhibits/prevents urine formation
- Prevents wide swings in H2O balance avoiding dehydration and H2O overload
- Osmoreceptors of the hypothalamus monitor solute concentration of the blood
- When solutes become too concentrated, osmoreceptors are excited and hypothalamic neurons synthesize ADH precursor which is ultimately released as a hormone from the neurohypophysis
Antidiuretic Hormone (ADH)

- ADH targets the kidney tubules via cAMP
- The kidney tubules respond by reabsorbing H2O from the forming urine and returning it to the blood stream
- Alcohol inhibits ADH secretion (as does excessive H2O drinking)
- ADH also targets vascular smooth muscle and causes vasoconstriction (e.g. released when high blood loss occurs)
Thyroid Gland

- The largest endocrine gland, located in the anterior neck, consists of two lateral lobes connected by a median tissue mass called the isthmus (looks like a butterfly)
- Highly vascularized (bloody surgeries)
- Composed of hollow follicles formed by follicle cells that produce the glycoprotein thyroglobulin
- Colloid (thyroglobulin + iodine) fills the lumen of the follicles and is the precursor of thyroid hormone
- Other endocrine cells, the parafollicular cells, produce the hormone calcitonin
Thyroid Gland

Figure 16.8
Thyroid Hormone (TH)

- Thyroid hormone – major metabolic hormone
- Consists of two related iodine-containing compounds
  - $T_4$ – thyroxine; has two tyrosine molecules plus four bound iodine atoms & is the major hormone secreted by thyroid follicle
  - $T_3$ – triiodothyronine; has two tyrosines with three bound iodine atoms & is formed at the target tissue by conversion of $T_4$ to $T_3$
Effects of Thyroid Hormone

- TH is concerned with:
  - Glucose oxidation
  - Increasing metabolic rate
  - Heat production

- TH plays a role in:
  - Maintaining blood pressure by increasing the number of adrenergic receptors in blood vessels
  - Regulating tissue growth
  - Developing skeletal and nervous systems
  - Maturation and reproductive capabilities
Synthesis of Thyroid Hormone

- Synthesis of TH begins w/ TSH secreted from the anterior pituitary

- Thyroglobulin is synthesized and discharged into the lumen

- Iodides (I\(^-\)) are actively taken into the cell, oxidized to iodine (I\(_2\)), and released into the lumen

- Iodine attaches to tyrosine, mediated by peroxidase enzymes, forming T\(_1\) (monoiodotyrosine, or MIT), and T\(_2\) (diiodotyrosine, or DIT)
Synthesis of Thyroid Hormone

- Iodinated tyrosines link together to form $T_3$ and $T_4$

- Colloid is then endocytosed and combined with a lysosome, where mainly $T_4$ (and relatively little $T_3$) are cleaved and diffuse into the bloodstream

- TSH stimulates RELEASE not production (when TH levels fall, synthesis begins)

  - TSH levels are low during the day and high at night…WHY?
Figure 16.9

1. Thyroglobulin is synthesized and discharged into the follicle lumen

2. Iodide ($I^-$) is trapped (actively transported in)

3a. Iodide is oxidized to iodine

3b. Iodine is attached to tyrosine in colloid, forming DIT and MIT

4. Iodinated tyrosines are linked together to form $T_3$ and $T_4$

5. Thyroglobulin colloid is endocytosed and combined with a lysosome

6. Lysosomal enzymes cleave $T_4$ and $T_3$ from thyroglobulin colloid and hormones diffuse from follicle cell into bloodstream

Thyroid follicle cell

Colloid in lumen of follicle

Capillary

Iodide ($I^-$)

Thyroglobulin colloid

Rough ER

Golgi apparatus

Lysosome

$T_3$

$T_4$

$T_3$ and $T_4$ from thyroglobulin colloid and hormones diffuse into bloodstream

To peripheral tissues
Transport and Regulation of TH

- $T_4$ and $T_3$ bind to thyroxine-binding globulins (TBGs) produced by the liver
- Both bind to target receptors, but $T_3$ has the greater binding coefficient over $T_4$
- Falling TH levels triggers release of TSH
- TSH release stops when TH levels are high
Transport and Regulation of TH

- Conditions that increase body temperature requirements, e.g. cold, pregnancy, stimulate the hypothalamus to secrete thyrotropin releasing hormone (TRH) which triggers TSH release and **overcomes** the Neg. F.B. controls

- Inhibitors of TSH release are somatostatin and glucocorticoids

- High Iodide concentrations inhibit TH release

- Lack of iodine, thyroid will swell causing an endemic goiter
Calcitonin

- A peptide hormone produced by the parafollicular (C) cells
- Lowers blood calcium levels
- Antagonist to parathyroid hormone (PTH)
Calcitonin

- Calcitonin targets the skeleton, where it:
  - Inhibits osteoclast activity (and thus bone resorption) and release of calcium from the bone matrix
  - Stimulates calcium uptake and incorporation into the bone matrix
- Low calcium levels inhibit calcitonin release
- Regulated by a humoral (calcium ion concentration in the blood) negative feedback mechanism
- Only important in children, in adults calcitonin acts as a hypocalcemic agent
Parathyroid Glands

- Tiny glands embedded in the posterior aspect of the thyroid (usually 4 of them)
- Cells are arranged in cords containing oxyphil and chief cells
- Chief (principal) cells secrete PTH (parathyroid hormone, aka parathormone)
- Oxyphil function is not understood
Parathyroid Glands

- PTH controls calcium balance in the blood
- PTH release is triggered by falling Ca++ levels
- ““ inhibited by hypercalcemia
- Increases Ca++ levels in blood by stimulating:
  - Skeleton
  - Kidneys
  - Intestine
Effects of Parathyroid Hormone

- PTH release:
  - Stimulates osteoclasts to release Ca++ from bone
  - Enhances reabsorption of Ca++ from food
  - Increases absorption of Ca++ by intestine

- Vitamin D is required for Ca++ absorption
  - Vitamin D from food or produced by skin is inactive
  - Kidneys convert Vitamin D to the active form (calcitriol)...this conversion is stimulated by PTH
Effects of Parathyroid Hormone

Figure 16.12

- Hypocalcemia (low blood calcium) stimulates parathyroid glands
- Rising $Ca^{2+}$ in blood inhibits PTH release
- PTH release from parathyroid glands
- PTH:
  - Activates osteoclasts: calcium and phosphate ions released into blood
  - Increases calcium absorption from food
  - Promotes activation of vitamin D
  - Increases calcium reabsorption

Key:
- $\downarrow$ = $Ca^{2+}$ ions
- $\uparrow$ = PTH molecules
Adrenal (Suprarenal) Glands

- Adrenal glands – paired, pyramid-shaped organs atop the kidneys

- Structurally and functionally, they are two endocrine glands
  - Inner adrenal medulla – neural tissue that acts as part of the SNS
  - Outer adrenal cortex – glandular tissue
  - Each produces its own set of hormones
    - But all help to cope with stress
Adrenal Cortex

- Over 24 steroid hormones (corticosteroids) are synthesized here from cholesterol
- The corticosteroids are NOT stored in the cells
- Different corticosteroids are produced in each of the three layers of the adrenal cortex
  - Zona glomerulosa – mineralocorticoids (chiefly aldosterone)
  - Zona fasciculata – glucocorticoids (chiefly cortisol)
  - Zona reticularis – gonadocorticoids (chiefly androgens)
Adrenal Cortex

Figure 16.13a, b

(a) Adrenal gland
- Medulla
- Cortex

(b) Capsule
- Zona glomerulosa
- Zona fasciculata
- Zona reticularis
- Adrenal medulla
Mineralocorticoids

- Regulate electrolytes in extracellular fluids (Na, K)
- Aldosterone – most abundant mineralocorticoid
  - Maintains Na\(^+\) balance by reducing excretion of sodium from the body
  - Target is the distal part of the kidney tubules where it stimulates Na reabsorption from the forming urine and its return to the bloodstream
  - Its activity involves the synthesis & activation of the Na pump
  - H2O follow Na
  - Crucial for homeostasis
Four Mechanisms of Aldosterone Release

- Four mechanisms regulate aldosterone release
- 1) Renin-angiotensin mechanism:
  - Major mechanism
  - Influences blood volume & blood pressure
  - Specialized kidney cells release renin into the blood when blood pressure declines
  - Renin cleaves angiotensinogen forming angiotensin II which stimulates aldosterone release
Four Mechanisms of Aldosterone Release

2) Plasma concentration of sodium and potassium
   - Directly influences the zona glomerulosa cells
   - Increase in K stimulates, decrease in K inhibits aldosterone release

3) ACTH causes small increases of aldosterone during stress

4) Atrial natriuretic peptide (ANP)
   - Secreted by the heart when blood pressure increases
   - Inhibits the renin-angiotensin mechanism and decreases blood pressure by releasing Na (and thus H2O) from the body
Major Mechanisms of Aldosterone Secretion

- Increased K⁺ (or decreased Na⁺) in blood
- Decreased blood volume and/or blood pressure
- Anterior pituitary
- Stress
- Hypothalamus
- CRH
- ACTH
- Kidney
- Renin initiates cascade that produces Angiotensin II
- Angiotensin II has direct stimulating effect
- Zona glomerulosa of adrenal cortex
- Enhanced secretion of aldosterone
- Targets kidney tubules
- Increased absorption of Na⁺ and water; increased K⁺ excretion
- Increased blood volume and blood pressure
- Increased blood pressure or blood volume
- Atrial natriuretic peptide (ANP)
- Inhibitory effect
Glucocorticoids (Cortisol)

- Influence energy metabolism of cells
- Keep blood glucose levels constant
- Maintain blood pressure by increasing action of vasoconstrictors
- Stress results in high output of glucocorticoids, e.g. cortisol (hydrocortisone)
- Regulated by Neg. F.B.
Glucocorticoids (Cortisol)

- Cortisol release is promoted by ACTH triggered by hypothalamus releasing hormone (CRH)
- Rising cortisol levels feedback on the hypothalamus & Ant. Pituitary preventing CRH release
- Cortisol levels peak when we awake and fall during sleep
- Stress increases release of cortisol resulting in elevated glucose, fatty acid and amino acid levels in the blood
Glucocorticoids (Cortisol)

- Prime metabolic effect is to provoke gluconeogenesis, the formation of glucose from fats and proteins

- Excessive glucocorticoids
  - Depress cartilage & bone formation
  - Inhibit inflammation
  - Depress immune system
  - Promote changes in cardiovascular, neural, and gastrointestinal function
Gonadocorticoids (Sex Hormones)

- Most gonadocorticoids secreted are androgens (male sex hormones), and the most important one is testosterone
- Converted to testosterone in the tissue cells or to estrogen and estradiol in females
- Most are made by the gonads (later in lecture)
Adrenal Medulla

- Made up of chromaffin cells (modified ganglionic sympathetic neurons) that synthesize catecholamines (epinephrine and norepinephrine)
- Stress activates the SNS releasing catecholamines which function to prolong the fight/flight responses
- Release consists of 80% E & 20% NE which exert the same effect
- E is more potent and activates bronchial dilation and blood shunting to the heart and skeletal muscles
- NE initiates vasoconstriction (blood pressure)
- Secretion of these hormones causes:
  - Blood glucose levels to rise
  - Blood vessels to constrict
  - The heart to beat faster
  - Blood to be diverted to the brain, heart, and skeletal muscle
Stress and the Adrenal Gland

**Short-term stress response**

1. Increased heart rate
2. Increased blood pressure
3. Liver converts glycogen to glucose and releases glucose to blood
4. Dilation of bronchioles
5. Changes in blood flow patterns leading to decreased digestive system activity and reduced urine output
6. Increased metabolic rate

**Long-term stress response**

1. Retention of sodium and water by kidneys
2. Increased blood volume and blood pressure

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**Further details**

- Hypothalamus
- CRH (corticotropin-releasing hormone)
- ACTH
- Adrenal cortex
- Mineralocorticoids
- Glucocorticoids
- Catecholamines (epinephrine and norepinephrine)

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Figure 16.16
Pancreas

- A triangular gland, which has both exocrine and endocrine cells, located behind the stomach
- Made up mostly of Acinar cells that produce an enzyme-rich juice used for digestion (exocrine product) in the small intestine
- Pancreatic islets (islets of Langerhans) scattered amongst the acinar cells produce hormones (endocrine products)
- The islets contain two major cell types:
  - Alpha (α) cells that produce glucagon (hyperglycemic hormone)
  - Beta (β) cells that produce insulin (hypoglycemic hormone)
    - Note: glycemia is the conc. of glucose in the blood
  - α & β secrete during times of feeding and fasting to regulate blood glucose levels
Glucagon

- A 29-amino-acid polypeptide hormone that is a potent hyperglycemic agent
- One molecule can release $1 \times 10^8$ molecules of glucose
- Its major target is the liver, where it promotes:
  - Glycogenolysis – the breakdown of glycogen to glucose
  - Gluconeogenesis – synthesis of glucose from lactic acid and noncarbohydrates
  - Release of glucose to the blood from liver cells
- Release of glucagon is stimulated by falling glucose levels in the blood
- Suppressed by rising glucose levels
- SNS can also stimulate its release
Insulin

- A 51-amino-acid protein
- Acts by enhancing membrane transport of glucose into body cells (especially muscle and fat cells)
- Inhibits the breakdown of glycogen to glucose and the conversion of a.a. & fats to glucose
Effects of Insulin Binding

- The insulin receptor is a tyrosine kinase enzyme
- After glucose enters a cell, insulin binding triggers enzymatic activity that:
  - Catalyzes the oxidation of glucose for ATP production
  - Polymerizes glucose to form glycogen
  - Converts glucose to fat (particularly in adipose tissue)
Regulation of Blood Glucose Levels

- The hyperglycemic effects of glucagon and the hypoglycemic effects of insulin
Gonads

- Produce sex hormones identical to those produced by the adrenal cortical cells
Gonads: Female

- Paired ovaries in the abdominopelvic cavity produce estrogens and progesterone
- They are responsible for:
  - Maturation of the reproductive organs
  - Appearance of secondary sexual characteristics
  - Breast development and cyclic changes in the uterine mucosa
Gonads: Male

- Testes located in an extra-abdominal sac (scrotum) produce testosterone

- Testosterone:
  - Initiates maturation of male reproductive organs
  - Causes appearance of secondary sexual characteristics
  - Is necessary for sperm production
Pineal Gland

- Small gland hanging from the roof of the third ventricle of the brain
- Secretory cells are the pinealocytes
- Secretory product is melatonin which makes us feel drowsy with peak levels occurring at night
- Receives input from the retina of the eye (indirectly)
- Melatonin is involved with:
  - Day/night cycles
  - Physiological processes that show rhythmic variations (body temperature, sleep, appetite)
Thymus

- Lobulated gland located deep to the sternum
- Major hormonal products are thymopoietins and thymosins
- These hormones are essential for the development of the T lymphocytes (T cells) of the immune system (we’ll go over this in detail in Chapt. 21)
KU Game Day!!!!