The Endocrine System
Overview of the Endocrine System

- System of ductless glands that secrete hormones
  - **Hormones** are “messenger molecules”
  - Circulate in the blood
  - Act on distant target cells
  - Target cells respond to the hormones for which they have receptors
  - The effects are dependent on the programmed response of the target cells
  - Hormones are just molecular triggers

- Basic categories of hormones
  - Amino acid based: modified amino acids (or amines), peptides (short chains of amino acids), and proteins (long chains of amino acids)
  - Steroids: lipid molecules derived from cholesterol
Endocrine Organs

- Purely endocrine organs
  - Pituitary gland
  - Pineal gland
  - Thyroid gland
  - Parathyroid glands
  - Adrenal: 2 glands
    - Cortex
    - Medulla

- Endocrine cells in other organs
  - Pancreas
  - Thymus
  - Gonads
  - Hypothalamus
Mechanisms of hormone release

(a) **Humoral**: in response to changing levels of ions or nutrients in the blood
(b) **Neural**: stimulation by nerves
(c) **Hormonal**: stimulation received from other hormones
Learn the 3 endocrine organs on this slide:
Hypothalamus
Pituitary (hypophysis)
Pineal
The Pituitary

Sits in hypophyseal fossa: depression in sella turcica of sphenoid bone
Pituitary secretes 9 hormones

Two divisions:

- Anterior pituitary (adenohypophysis)
  1. TSH
  2. ACTH
  3. FSH
  4. LH
  5. GH
  6. PRL
  7. MSH

  The first four are “tropic” hormones, they regulate the function of other hormones

- Posterior pituitary (neurohypophysis)
  8. ADH (antidiuretic hormone), or vasopressin
  9. Oxytocin
What the letters stand for…

- TSH: thyroid-stimulating hormone
- ACTH: adrenocorticotropic hormone
- FSH: follicle-stimulating hormone
- LH: luteinizing hormone
- GH: growth hormone
- PRL: prolactin
- MSH: melanocyte-stimulating hormone

- ADH: antidiuretic hormone
- Oxytocin
Hypothalamus controls anterior pituitary hormone release

- Releasing hormones (releasing factors)
  Secreted like neurotransmitters from neuronal axons into capillaries and veins to anterior pituitary (adenohypophysis)
  - TRH----turns on TSH
  - CRH-----turns on ACTH
  - GnRH (=LHRH)---turns on FSH and LH
  - PRF-----turns on PRL
  - GHRH----turns on GH

- Inhibiting hormones
  - PIF-----turns off PRL
  - GH inhibiting hormone ---turns off GH
What the letters mean...

- Releasing hormones (releasing factors) of hypothalamus
  Secreted like neurotransmitters from neuronal axons into capillaries and veins to anterior pituitary (adenohypophysis)
  TRH (thyroid releasing hormone) -----turns on* TSH
  CRH (corticotropin releasing hormone) -----turns on ACTH
  GnRH (gonadotropin releasing hormone) ---turns on FSH and LH
  PRF (prolactin releasing hormone) -----turns on PRL
  GHRH (growth hormone releasing hormone) -----turns on GH

- Inhibiting hormones of hypothalamus
  PIF (prolactin inhibiting factor) -----turns off PRL
  GH (growth hormone) inhibiting hormone ---turns off GH

The hypothalamus controls secretion of hormones which in their turn control the secretion of hormones by the thyroid gland, the adrenal cortex and gonads: in this way the brain controls these endocrine glands

*Note: “turns on” means causes to be released
So what do the pituitary hormones do?

The four tropic ones regulate the function of other hormones:

- **TSH** stimulates the thyroid to produce thyroid hormone
- **ACTH** stimulates the adrenal cortex to produce corticosteroids: aldosterone and cortisol
- **FSH** stimulates follicle growth and ovarian estrogen production; stimulates sperm production and androgen-binding protein
- **LH** has a role in ovulation and the growth of the corpus luteum; stimulates androgen secretion by interstitial cells in testes
The others from the anterior pituitary…

- **GH** (aka somatrotropic hormone) stimulates growth of skeletal epiphyseal plates and body to synthesize protein
  
  http://primadonablog.blogspot.com/2014/03/you-know-about-gigantism.html

- **PRL** stimulates mammary glands in breast to make milk

- **MSH** stimulates melanocytes; may increase mental alertness
When he was discovered at the age of four by P. T. Barnum, little Charles stood a mere 25 inches in height and weighed 15 pounds. His father, long embarrassed by the miniscule stature of his offspring, gladly agreed to consign his son to a month-long trial as an attraction in Barnum’s New York Museum. The agreed rate of pay was $3 as well as room and board. This was a modest financial arrangement but the elder Stratton was simply content to see his tiny toddler be of some use.
In the history of the world, little Pauline Musters is the smallest mature woman ever officially recorded. Pauline was listed in the Guinness Book of World Records as having stood only 1 foot 11.2 inches in height.
From the posterior pituitary (neurohypophysis) *structurally part of the brain*

- **ADH (antidiuretic hormone AKA vasopressin)** stimulates the kidneys to reclaim more water from the urine, raises blood pressure

- **Oxytocin** prompts contraction of smooth muscle in reproductive tracts, in females initiating labor and ejection of milk from breasts
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Now try and remember the anatomy

1. The hypothalamus secretes hormones that...
2. stimulates the anterior pituitary gland to secrete hormones that...
3. stimulates other endocrine glands to secrete hormones
The Thyroid Gland

- Anterior neck on trachea just inferior to larynx
- Two lateral lobes and an isthmus
- Produces two hormones
  - Thyroid hormone: tyrosine based with 3 or 4 iodine molecules
    - T4 (thyroxine) and T3
  - Calcitonin involved with calcium and phosphorus metabolism
• Thyroid is composed of spherical follicles
  • Follicle cells: produce thyroglobulin, the precursor of thyroid hormone (thyroxin)
  • Colloid lumen is of thyroglobulin
  • Parafollicular “C” cells: produce calcitonin
An example of a feedback loop

**generic**

- A certain item in the blood decreases
- A certain area of the brain senses this decrease
- A certain hormone is released
- This hormone stimulates the release of another hormone
- This other hormone stimulates the release of the hormone which was sensed to be decreased in the first place, causing it to be increased to desired level

**particular example: thyroid hormone**

- Thyroxine (thyroid hormone)
- Hypothalamus
- TRF from the hypothalamus
- TSH from anterior pituitary
- Thyroxine from the thyroid (TSH has caused cleavage of thyroglobulin into thyroxine)
Some Effects of Thyroid Hormone (Thyroxine)

- Increases the basal metabolic rate
  - The rate at which the body uses oxygen to transform nutrients (carbohydrates, fats and proteins) into energy
- Affects many target cells throughout the body; some effects are
  - Protein synthesis
  - Bone growth
  - Neuronal maturation
  - Cell differentiation
THYROID DYSFUNCTION

HYPO THYROIDISM
- Dry hair
- Puffy face
- Slow heartbeat
- Weight gain
- Constipation
- Brittle nails
- Arthritis
- Cold intolerance
- Depression
- Dry skin
- Fatigue
- Memory loss
- Heavy menstrual periods
- Muscle aches

HYPER THYROIDISM
- Hair loss
- Bulging eyes
- Sweating
- Rapid heartbeat
- Weight loss
- Regular gas
- Soft nails
- Sleeping difficulties
- Heat intolerance
- Infertility
- Irritability
- Muscle weakness
- Nervousness
- Scant menstrual periods
Muscle wasting

Fine hair

Exophthalmos

Goiter

Sweating

Tachycardia, high output failure

Weight loss

Oligomenorrhea

Tremor
Signs and Symptoms of HYPOTHYROIDISM

- Tiredness
- Forgetfulness/Slower Thinking
- Moodiness/Irritability
- Depression
- Inability to Concentrate
- Thinning Hair/Hair Loss
- Loss of Body Hair
- Dry, Patchy Skin
- Weight Gain
- Cold Intolerance
- Elevated Cholesterol
- Family History of Thyroid Disease or Diabetes
- Puffy Eyes
- Swelling (Goiter)
- Hoarseness/Deepening of Voice
- Persistent Dry or Sore Throat
- Difficulty Swallowing
- Slower Heartbeat
- Menstrual Irregularities/Heavy Period
- Infertility
- Constipation
- Muscle Weakness/Cramps
The Effects of Calcitonin

- Secreted from thyroid parafollicular (C) cells when blood calcium levels are high
- Calcitonin lowers Ca++ by slowing the calcium-releasing activity of osteoclasts in bone and increasing calcium secretion by the kidney
- Acts mostly during childhood
The Parathyroid Glands

- Most people have four
- On posterior surface of thyroid gland
  (sometimes embedded)
Parathyroids (two types of cells)

- Rare chief cells
- Abundant oxyphil cells (unknown function)
- Chief cells produce PTH
  - Parathyroid hormone, or parathormone
  - A small protein hormone
Function of PTH (parathyroid hormone or “parathormone”)

- *Increases blood Ca++ (calcium) concentration when it gets too low*

- Mechanism of raising blood calcium
  1. Stimulates osteoclasts to release more Ca++ from bone
  2. Decreases secretion of Ca++ by kidney
  3. Activates Vitamin D, which stimulates the uptake of Ca++ from the intestine

- Unwitting removal during thyroidectomy can be lethal

- *Has opposite effect on calcium as calcitonin (which lowers Ca++ levels)*
Adrenal (suprarenal) glands (“suprarenal” means on top of the kidney)

- Each is really two endocrine glands
  - Adrenal cortex (outer)
  - Adrenal medulla (inner)
- Unrelated chemicals but all help with extreme situations
Adrenal Gland

- Adrenal cortex
  - Secretes lipid-based steroid hormones, called “corticosteroids” – “cortico” as in “cortex”
    - MINERALOCORTICOIDs
      - Aldosterone is the main one
    - GLUCOCORTICOIDs
      - Cortisol (hydrocortisone) is the main one

- Adrenal medulla
  - Secretes epinephrine and norepinephrine
Aldosterone, the main mineralocorticoid

- Secreted by adrenal cortex in response to a decline in either blood volume or blood pressure (e.g. severe hemorrhage)
  - Is terminal hormone in renin-angiotensin mechanism
- Prompts distal and collecting tubules in kidney to reabsorb more sodium
  - Water passively follows
  - Blood volume thus increases
Cortisol, the most important glucocorticoid

(Glucocorticoid receptors are found in the cells of most vertebrate tissues)

- It is essential for life
- Helps the body deal with stressful situations within minutes
  - Physical: trauma, surgery, exercise
  - Psychological: anxiety, depression, crowding
  - Physiological: fasting, hypoglycemia, fever, infection
- Regulates or supports a variety of important cardiovascular, metabolic, immunologic, and homeostatic functions including water balance

People with adrenal insufficiency: these stresses can cause hypotension, shock and death: must give glucocorticoids, eg for surgery or if have infection, etc.
Cortisol, continued

- Keeps blood glucose levels high enough to support brain’s activity
  - Forces other body cells to switch to fats and amino acids as energy sources
- Catabolic: break down protein
- Redirects circulating lymphocytes to lymphoid and peripheral tissues where pathogens usually are
- In large quantities, depresses immune and inflammatory response
  - Used therapeutically (prednisone)
  - Responsible for some of its side effects
Cushing syndrome occurs when your body is exposed to high levels of the hormone cortisol for a long time. The most common cause of Cushing syndrome, sometimes called hypercortisolism, is the use of oral corticosteroid medication. The condition can also occur when your body makes too much cortisol. Too much cortisol can produce some of the hallmark signs of Cushing syndrome.
CUSHING'S SYNDROME

- Personality Changes
- Hyperglycemia
- Moon Face
- CNS Irritability
- ↑ Susceptibility to Infection
- Males: Gynecomastia
- Fat Deposits on Face and Back of Shoulders
- NA & Fluid Retention (Edema)
- Thin Extremities
- GI Distress - ↑ Acid
- Females: Amenorrhea, Hirsutism
- Thin Skin
- Purple Striae
- Bruises & Petechiae
- Osteoporosis
Cushings

Other signs and symptoms include:

- Fatigue
- Muscle weakness
- Depression, anxiety and irritability
- Loss of emotional control
- Cognitive difficulties
- New or worsened high blood pressure
- Glucose intolerance that may lead to diabetes
- Headache
- Bone loss, leading to fractures over time
Hormonal stimulation of glucocorticoids

HPA axis (hypothalamic/pituitary/adrenal axis)

- With stress, hypothalamus sends CRH to anterior pituitary (adenohypophysis)
- Pituitary secretes ACTH
- ACTH goes to adrenal cortex where stimulates glucocorticoid secretion
  - Sympathetic nervous system can also stimulate it
- Adrenal cortex also secretes DHEA (dehydroepiandrosterone)
  - Converted in peripheral tissues to testosterone and estrogen (also steroid hormones)
  - Unclear function in relation to stress
In general:

- Steroid-secreting cells have abundant smooth ER
  - As opposed to rough ER in protein-secreting cells
- Steroids directly diffuse across plasma membrane
  - Not exocytosis
- Abundant lipid droplets
  - Raw material from which steroids made
Adrenal medulla

- Part of autonomic nervous system
- Spherical chromaffin cells are modified postganglionic sympathetic neurons
  - Secrete epinephrine and norepinephrine
  - Amine hormones
  - Fight, flight, fright
- Vesicles store the hormones
The Pineal Gland

- At the end of a short stalk on the roof of the diencephalon
- Pinealocytes with dense calcium particles
- Can be seen on x-ray (because of Ca++)
- Melatonin helps regulate the circadian rhythm
  - The biological clock of the diurnal (night/day) rhythm
  - Complicated feedback via retina’s visual input
The Pancreas

*Exocrine and endocrine cells*

- **Acinar** cells (forming most of the pancreas)
  - *Exocrine* function
  - Secrete digestive enzymes

- **Islet** cells (of Langerhans)
  - *Endocrine* function
Pancreatic islet endocrine cells

**Alpha cells**: secrete *glucagon*
- Raises blood sugar mostly in periphery

**Beta cells**: secrete *insulin*
- Lowers blood sugar central part (are more abundant)

Also rare **Delta cells**: secrete *somatostatin*
- Inhibits glucagon
DIABETES
KNOW THE SYMPTOMS

Always hungry.
Sudden weight loss.
Wounds that won't heal.
Sexual problems.
Frequent urination.

Vaginal infections.
Blurry vision.
Always thirsty.
Numb or tingling.

CONCEIVE® EASY
Muscle unable to use glucose due to low insulin

Glycogen and protein breakdown, causing keto-acidosis

Increased glucose due to low insulin

Pancreas

Decreased insulin in the blood vessels

**TYPE 1 DIABETES**

**Type 2 Diabetes**

Obesity, inheritance & other factors leading to insulin resistance

Increased glucose in the blood stream

Muscle unable to use glucose due to insulin resistance

Sufficient insulin secreted in the blood stream

Pancreas
Insulin secreted into bloodstream

Blood capillary

Insulin-producing cells
Type 1 diabetes most often starts in childhood, before the age of 20. People with type 1 diabetes usually have a number of the following symptoms:
Frequent urination
Excessive thirst
Unexplained weight loss
Extreme hunger
Sudden vision changes
Tingling or numbness in hands or feet
Feeling very tired much of the time
Very dry skin
Sores that are slow to heal
More infections than usual
Nausea, vomiting, and stomach pains
Low blood sugar symptoms include:

- Headache
- Sweating
- Shaking
- Feeling tired
- Weakness
- Hunger
Here are some of the symptoms that can signal type 2 diabetes:
Slow healing wounds and blisters that seem to take too long to recover.
Excessive lethargy and fatigue can indicate hypoglycemia and is an indication of type 2 diabetes if these symptoms are not associated with sudden lifestyle changes.
Unexplained increased hunger and or thirst can also be an indicator of onset of type 2 diabetes.
Sudden appearance of dark patches or changes in texture of small patches of skin can be an indicator especially appearing around the neck and armpits.
Rapid unexplained weight loss even when eating the same number of calories without changes in activity level.
Persistent blurred vision or headaches can be an indicator of type 2 diabetes and often accompanies irritability or confusion.
You should make a note of any sudden change in any of the above examples, especially if you are obese (BMI above 30).
Type 2 diabetes in children and teens is on the rise thanks to childhood obesity, poor nutrition and lack of exercise. We need to educate ourselves now about diabetes and children and what we can do to help reverse the trend. - See more at: http://www.losing-weight-and-the-glycemic-index.com/type-2-diabetes-in-children.html#sthash.0tih9WCI.dpuf
The Gonads (testes and ovaries)

main source of the steroid sex hormones

- **Testes**
  - Interstitial cells secrete androgens
  - Primary androgen is testosterone
    - Maintains secondary sex characteristics
    - Helps promote sperm formation

- **Ovaries**
  - Androgens secreted by thecal folliculi
    - Directly converted to estrogens by follicular granulosa cells
  - Granulosa cells also produce progesterone
  - Corpus luteum also secretes estrogen and progesterone
Hormones can be inadequate during or after each stage of development—embryonic and adolescent. During each stage, inadequate hormone stimulation will prevent normal development. After each stage, a decrease in hormone stimulation will result in failed function and perhaps some shrinkage. The organs affected principally by sex hormones are the male and female genitals, both internal and external, and the female breasts. Body hair, fat deposition, bone and muscle growth, and some brain functions are also influenced.

Read more: [http://www.healthofchildren.com/G-H/Hypogonadism.html#ixzz3ER2YwO1c](http://www.healthofchildren.com/G-H/Hypogonadism.html#ixzz3ER2YwO1c)
Endocrine cells in various organs

- The heart: atrial natriuretic peptide (ANP)
  - Stimulates kidney to secrete more salt
  - Thereby decreases excess blood volume, high BP and high blood sodium concentration
- GI tract & derivatives: Diffuse neuroendocrine system (DNES)
Atrial natriuretic peptide hormone of cardiac origin, which is released in response to atrial distension and serves to maintain sodium homeostasis and inhibit activation of the renin-angiotensin-aldosterone system. Congestive heart failure is a clinical syndrome characterized by increased cardiac volume and pressure overload with an inability to excrete a sodium load. Circulating atrial natriuretic peptide is greatly increased in congestive heart failure as a result of increased synthesis and release of this hormone. Atrial natriuretic peptide has emerged as an important diagnostic and prognostic serum marker in congestive heart failure. In early heart failure, it may play a key role in preserving the compensated state of asymptomatic left ventricular dysfunction. Despite increased circulating atrial natriuretic peptide in heart failure, the kidney retains sodium. The mechanism for the attenuated renal response is multifactorial and includes renal hypo perfusion, activation of the renin-angiotensin-aldosterone and sympathetic nervous system.
Endocrine cells in various organs continued

- The heart: atrial natriuretic peptide (ANP)
  - Stimulates kidney to secrete more salt
  - Thereby decreases excess blood volume, high BP and high blood sodium concentration

- GI tract & derivatives: Diffuse neuroendocrine system (DNES)

- The placenta secretes steroid and protein hormones
  - Estrogens, progesterone
  - CRH
  - HCG

- The kidneys
  - Juxtaglomerular cells secrete renin
    - Renin indirectly signals adrenal cortex to secrete aldosterone
  - Erythropoietin: signals bone marrow to increase RBC production

- The skin
  - Modified cholesterol with uv exposure becomes Vitamin D precursor
  - Vitamin D necessary for calcium metabolism: signals intestine to absorb CA++
Pathology

- **Pituitary**
  - Gigantism – too much GH in childhood
  - Acromegaly – too much GH in adulthood
  - Pituitary dwarfs – too little GH in childhood
  - Diabetes insipidus - too much ADH

- **Pancreas**
  - Diabetes mellitus – one type of insulin (not enough)

- **Thyroid**
  - Hyperthyroidism, commonest is Grave’s disease (autoimmune)
  - Hypothyroidism
    - In childhood leads to cretinism
    - Endemic goiter from insufficient iodine in diet
    - Adult hypothyroidism (myxedema): autoimmune
Exophthalmos of Grave’s disease

Enlarged thyroid (goiter) from iodine deficiency
Pathology, continued

- Adrenal gland
  - Cushing’s syndrome (see next pic, more about cushings)
    - Usually caused by an ACTH-secreting pituitary tumor
    - Rarely by tumor of adrenal cortex
    - Iatrogenic
  - Addison’s disease
    - Hyposecretion (under secretion) of adrenal cortex
    - Usually involves cortisol and aldosterone: low blood glucose and sodium, severe dehydration, fatigue, loss of appetite, abdominal pain
      (Jane Austin)
Addison's disease
Chronic Hypoadrenalism

- Low [CORTISOL]
- Hypoglycaemia
- Hypercalcaemia & anaemia
- High [ACTH] / [MSH]
- Pigmentation

HYPOALDOSTERONISM
- Low serum - [Na⁺]
- High serum - [K⁺]
- Dehydration (low ECV incl. TBV)
- Postural hypotension
- Weight loss
- High plasma - [renin]

- Low [SEX HORMONE]
- Loss of body & pubes hair
- Loss of libido/amenorrhoea
- Muscle wasting & thin limbs

Adrenal Gland
Video on Cushing's and Addisons

http://www.youtube.com/watch?v=sVLpROt1IoA
Before and after onset of Cushing’s disease