Endocrine

Hormones secreted from glands

Glands we will discuss
- Hypothalamus/pituitary
- Thyroid & Parathyroid
- Pancreas
- Adrenals
- Pineal
- Gonads

Hormones are secreted by glands directly into the blood.

Hypothalamus and Pituitary

The hypothalamus is the master controller of... everything.

INPUTS include
- Visceral sensory info
- Somatic sensory info
- Light (optic nerve)
- Smells
- Limbic (emotional info)
- Circumventricular organs (parts of the brain outside the blood brain barrier to detect ions, toxicants, and other variables).

OUTPUTS to:
- ANS to immediately modulate homeostasis
- Cortex to modulate behavior
- Endocrine to facilitate longer lasting changes
  - Anterior pituitary produces hormones in response to signals from hypothalamus
  - Posterior pituitary acts as warehouse of hormones synthesized by hypothalamus

Pituitary Hormones

Anterior Pituitary
- Adrenocorticotropic hormone (ACTH)
- Human Growth Hormone (hGH)
- Thyroid Stimulating Hormone (TSH)
- Follicle Stimulating and Luteinizing Hormones (FSH/LH)
- Prolactin
- Melanocyte Stimulating Hormone

Posterior Pituitary (modified ends of hypothalamic neurons)
- Antidiuretic Hormone (ADH)
- Oxytocin
Hypothalamus & Pituitary

**Leuprolide (Lupron)** is a gonadotropin releasing hormone (GnRH) agonist. The gonadotropins are FSH & LH, which are synthesized by the anterior pituitary in response to the hypothalamus secreting GnRH. FSH & LH then promote a variety of reproductive functions including stimulating the synthesis of sex steroids by the gonads. Lupron is used off label as a fertility drug.

**Somatropin (Nutropin)** is rDNA or synthetic form of hGH. Be careful to not confuse Somatropin with somatostatin which is the hormone that shuts off hGH synthesis.

**Vasopressin, ADH (Pitressin)** is a synthetic form of ADH used to treat diabetes insipidus as well as to dispel gas from the GIT for radiography. Diabetes insipidus is a condition where the body produces insufficient ADH or does not respond to ADH. Patients will produce copious volumes of dilute urine (up to 30L/day).

**Melatonin** is a synthetic version of the natural hormone available OTC to help correct circadian rhythm sleep disorders in the blind and due to jet-lag.

The Adrenal Gland

The adrenal cortex responds to ACTH by releasing Cortisol (a glucocorticoid) and Aldosterone (a mineralocorticoid). Excess secretion leads to Cushing’s, insufficient secretion leads to Addison’s.

**Fludrocortisone (Florinef)** is a synthetic aldosterone replacement.

**Dexamethasone (Deltasone) and Prednisone (Deltasone)** are synthetic cortisol (glucocorticoid) replacements.
Conditions of the Thyroid

Hyperthyroidism is typically an autoimmune condition called **Graves’ Disease**.

Hypothyroidism may also be an autoimmune condition, if so, it is called **Hashimoto’s thyroiditis**.

The thyroid gland produces two hormones. One is thyroid hormone, which is actually two chemicals we will just call T4 and T3. The other is Calcitonin. Thyroid hormone has many functions related to modulating metabolism. Calcitonin decreases blood calcium levels in concert with the parathyroid hormone (produced by the parathyroid gland and which increases blood calcium).

**Levothyroxine (Synthroid)** is a synthetic form of thyroid hormone (of T4). It is used to treat hypothyroidism as well as to provide negative feedback to the hypothalamus and shut off the release of thyroid stimulating hormone (TSH). It has a very long half life of around 1 week, so there is a latency of 4-6 weeks before therapeutic effects stabilize.

**Propylthiouracil (PTU)** is used to treat Graves’.

**Potassium-iodide solution** is used to protect the thyroid during radiation exposures.

Osteoporosis is a condition in which the density of bone is reduced. Paget’s is also a disease that alters bone density, but in general Paget’s is a problem with remodeling. In Paget’s the bones typically become dense but brittle, in Osteoporosis, the bones become thinned and fragile. Both diseases are common and treated using the same drugs.

**Alendronate (Fosamax)** is one of many bisphosphonate drugs used to treat osteoporosis and Paget’s. Alendronate is given PO SID, but other bisphosphonates may be given monthly or annually. When bisphosphonates are given as an IV, they must be given slowly (up to 24 hour infusion). When given PO, the patient must be able to sit or stand for 30 minutes after taking the product.

**Salmon Calcitonin (Miacalcin, Fortical)** is a natural product isolated from fish. It turns out the fish calcitonin is more potent than human calcitonin. Calcitonin acts by several mechanisms to reduce blood calcium.
Drugs related to reproduction

Most hormonal Birth Control is given orally, hence OBC, and most are a combination of a synthetic estrogen and progestin. There are a number of synthetic estrogens and progestins. Typically the estrogen is ethinyl estradiol.

There are many different progestins including norethindrone, norelgestromin, medroxyprogesterone, etonogestrel and drospirenone. Drospirenone is interesting because it has antimineralocorticoid (anti-aldosterone) and anti-androgen activity. The anti aldosteronism makes it resemble the potassium sparing diuretic spironolactone (Aldactone).

Patients taking drospirenone-containing OBC should be monitored for serum potassium at least once after initiation of therapy. These products require more patient teaching and compliance than other OBC including the avoidance of potassium supplements or other potassium-sparing medications.

**Loestrin** (ethinyl estradiol and norethindrone) is a daily pill as are **Ortho-Tri-Cyclen Lo** (ethinyl estradiol and norgestimate in three dosage levels) and **Yaz** (ethinyl estradiol and drospirenone).

A number of female reproductive conditions are also treated with OBC including, Turner’s syndrome, polycystic ovary syndrome, and hypothalamic amenorrhea.

Another treatment for Polycystic Ovary Syndrome is **Metformin (Glucophage)**, a top selling oral diabetes mellitus type 2 drug.

**Testosterone (Duratest)** is a C-II androgen, mainly used to replace endogenous hormone.

**Oxandrolone (Oxandrin)** is a C-III anabolic steroid with many uses.

**Sildenafil (Viagra, Revatio)** is a 5-Phosphodiesterase (5-PDE) inhibitor used to treat erectile dysfunction and pulmonary arterial hypertension.
Diabetes Mellitus

Historically, insulin was used for Diabetes Mellitus Type 1, and only rarely for DMT2. It is becoming increasingly common for patients to have DMT2 and need insulin in addition to the antihyperglycemic medications traditionally used in DMT2.

Please make sure to carefully look through the lecture notes and diabetes background notes for the discussion on insulin. Here are the insulin links for lecture:

- Humalog
- Novolog
- Humulin-r
- Humulin-n
- Humulin-l
- Lantus

The following are antihyperglycemic medications used to treat DMT2. Most are oral, a few (Liraglutide) are parenteral. All are indicated as ADJUVANTS in conjunction with alterations to diet and exercise to provide glycemic control.

**Chlorpropamide (Diabinese)** is a 1st generation sulfonylurea. **Glyburide (Micronase)** is a 2nd generation sulfonylurea. Patients must have a functional pancreas to take a sulfonylurea. These drugs increase the risk of cardiovascular death.

**Metformin (Glucophage)** is the best selling diabetes drug in the world. It is generally very well tolerated, but the patient must have good kidney function. Metformin can cause lactic acidosis.

**Pioglitazone (Actos)** targets a nuclear receptor to decrease insulin resistance but insulin must be present for it to work (so the patient must have a functional pancreas). Pioglitazone is associated with heart failure.

**Sitagliptin (Januvia)** is an interesting drug that inhibits an enzyme that breaks down naturally occurring chemicals produced by the GIT called incretins. The incretins promote insulin secretion and delay gastric emptying (which slows the absorption of carbohydrates).

**Liraglutide (Victoza)** is an incretin mimic. It is given as an SC injection. Incretin mimics are glucose-dependent meaning that they only increase insulin levels in the presence of glucose.

**Acarbose (Precose)** inhibits the enzyme alpha-glucosidase in the GIT. Alpha-glucosidase breaks down carbohydrates and by inhibiting this enzyme, you can slow the rapid rise of blood glucose following a meal. Acarbose may be used in both DMT1 and DMT2.

**Glucagon (GlucaGen)** is another pancreatic hormone. Glucagon has the opposite effects as Insulin, it causes blood glucose levels to RISE. It is given to counter HYPOGLYCEMIA. Glucagon raises blood glucose by promoting liver glycogenolysis (the breakdown of glycogen into glucose). An interesting thing about injecting exogenous glucagon: it triggers transient catecholamine release from the adrenal medulla.
Insulin is complicated... 
and not just for DMT1 anymore

Human insulin is known as “REGULAR” insulin. It is called “short-acting" which means the onset is from 30-60 minutes after injection and it lasts for 5-8 hours.

Rapid-acting insulin refers to forms that have been modified (usually by substituting an amino acid or two) so the onset is faster (10-30 minutes) and duration shorter (3-5 hours) compared to REGULAR insulin. Aspart and Lispro are the two rapid-acting insulin forms.

Intermediate-acting insulin refers to insulin that has been greatly modified, usually by combining it with zinc and/or a protein called protamine, to slow the onset and lengthen the duration. The most common type here is NPH (Neutral Protamine Hagedorn).

Long-acting forms are also greatly modified and are designed to provide BASAL insulin. Lantus (insulin glargine) is the best selling insulin in the world and it is a long-acting form.

An ultra-long acting analog called insulin Degludec will be coming on the market in 2013. It is given only 3 times/week and is intended to replace basal insulin secretion.

The top four drugs associated with medication errors:

1. INSULIN
2. Morphine
3. Fentanyl
4. Metoprolol tied with albuterol and potassium chloride

Homework and Exercises

1. Read the “START HERE” announcement in Laulima for updates and instructions.
2. Read about Endocrinology in Unit 10, Pharmacology of the Endocrine System. Adams & Urban, PHARMACOLOGY Connections to Nursing Practice. This Unit has eight chapters covering two lectures.
3. Review the Powerpoints and listen to the audio from the face-to-face lecture. You may opt to watch the appropriate videos for this lecture. Review any handouts available for this lecture in the Course Index.
4. Complete the SLO practice sets for Endocrine 1&2 in Tasks, Tests and Surveys.
5. Use “Chat,” “Discussions and Private Messages” or the lecture “Forum” to ask questions and find answers or to seek assistance.
6. Complete the online quiz in Laulima, Tasks, Tests and Surveys.

If you have any questions, email me at abeale@hawaii.edu