The Endocrine System

The Thyroid, Parathyroid and Pancreas
The thyroid and parathyroid glands are found in neck. The thyroid gland straddles the trachea on both sides while the parathyroid glands are four small glands attached to the posterior wall of the thyroid.
Anatomically, the thyroid gland consists of two lobes connected by an **isthmus**. Histologically, there are two types of cells in the thyroid gland: **thyroid follicle cells** and **parafollicular cells**. The thyroid follicle cells produce and store thyroxine (also called T4, or just “thyroid hormone”) while the parafollicular cells produce calcitonin.

Follicle cells secrete The T4 into empty, colloid-filled spaces (follicles) where the hormone is stored until TSH (secreted by the anterior pituitary) stimulates its release. The thyroid is unusual in that it stores lots of hormones for later release. Right now, you have months worth of thyroid hormones in your thyroid follicles.
Chemistry of thyroid hormone: In the follicular cells, thyroxine (T4) is made by attaching four iodine atoms to a tyrosine amino acid. The hormone is stored in this (inactive) state in the thyroid follicles and is released into the bloodstream gradually (it's rate is determined by TSH, remember?) T4 enters almost every cell in the body, where one iodine atom is removed by an enzyme, converting the T4 into triiodothyronine (T3), the active form of the hormone. Some T4 is converted to T3 in the thyroid gland, but most is converted inside the target cells.

Thyroid hormones are unique because they are amino acid-derived, but they can still enter their target cells.

Important point: Iodine is required to make T4. If there is not enough iodine available, T4 production slows down or even stops.
Hormones of the Thyroid Gland

- **Thyroid hormones** (T3, T4)
  - Effects:
    - Metabolism
    - Growth & development
    - Heart rate
  - Target tissues: Most, esp. heart & liver

The general effect of thyroid hormone release is to increase metabolism and heart rate. The increase in metabolism occurs in most cells of the body (carbohydrates are metabolized into ATP more quickly), and liver cells also break down glycogen into glucose more quickly. Thyroid hormone also plays a role in the proper growth of bones, muscle, the brain and other internal organs in infants.
Hormones of the Thyroid Gland

- **Thyroid hormones (T3, T4)**
  - Pathology
    - **Hyperthyroidism**: overproduction
      - *E.g.* Graves disease
    - **Hypothyroidism**: underproduction
      - *E.g.* iodine deficiency
      - In children: **cretinism**

Overproduction of thyroid hormones is called **hyperthyroidism**. Classic symptoms include rapid weight loss despite a huge appetite and a lot of eating, hyperactivity, nervousness, anxiety and sometimes paranoia, tremor and even stroke. The eyeballs may bulge in their sockets as well as connective tissue builds up behind the eyes or the eyelid muscles become too active.

Underproduction is called **hypothyroidism**. In young children, growth and development occurs abnormally, causing mental retardation and small size (**cretinism**). In adults, hypothyroidism causes slow metabolism, weight gain, sluggishness and depression.
Hormones of the Thyroid Gland

- **Thyroid hormones** (T₃, T₄)
  - Control
    - TRH $\rightarrow$ TSH $\rightarrow$ T₄
    - TRH release inhibited by presence of T₄ in the blood

A classic direct negative feedback loop: If circulating levels of thyroid hormones are low, the hypothalamus releases **thyroid releasing hormone** into the hypothalamic-pituitary portal where it moves to the anterior pituitary. The TRH stimulates the ant. Pit. to release **thyroid stimulating hormone** into the blood stream. Circulating TSH stimulates the thyroid gland to release thyroid hormones into the blood stream. As blood levels of thyroid hormones rise, the hypothalamus is inhibited from releasing further TRH. This causes the anterior pituitary to stop releasing TSH, which causes the thyroid gland to stop releasing thyroid hormones.
Hormones of the Thyroid Gland

- **Calcitonin**
  - Parafollicular cells.
  - Target tissues: Bone, kidneys.
  - Bone sparing:
    - Inhibits osteoclasts; stimulates osteoblasts.
    - Calcium/phosphorus $\rightarrow$ urine.
  - Control: Blood calcium levels.

**Calcitonin** is not produced or stored in the thyroid follicles. Instead, it is produced by the parafollicular cells *when needed* and released directly into the blood stream. The general effect of calcitonin is to *decrease* the amount of calcium in the blood. It does this by inhibiting osteoclasts (preventing them from breaking down the hydroxyapatite of bone) and by stimulating the movement of calcium and phosphorous into the urine by the kidneys. Control is a straightforward indirect feedback loop: an increase in blood calcium levels stimulates the release of calcitonin from the parafollicular cells. As bone resorption slows and calcium is moved into the urine, blood calcium levels drop, so the thyroid gland is no longer stimulated to release calcitonin.
The **parathyroid glands** are four (number can vary) small glands attached to the posterior wall of the thyroid. The main hormone secreted is **parathyroid hormone**, which acts antagonistically (opposite) calcitonin: it *increases* blood calcium levels. Both calcitonin and PTH work together to regulate blood calcium levels, but PTH is the more important of the two hormones.

PTH acts on the bone and kidneys. At bones, it stimulates osteoclasts to break down bone matrix, which releases stored calcium into the blood. At the kidneys, PTH has two effects. 1) excretion of calcium into the urine is inhibited, so existing blood calcium is sequestered; 2) vitamin D is released, which allows the small intestine to absorb calcium during digestion. This second effect increases the amount of new calcium introduced to the blood.

PTH control is a straightforward negative feedback loop: high circulating levels of calcitonin inhibit PTH production, so when calcium levels are low, PTH is secreted, resulting in a rise in calcium concentration. Another hormone, estrogen, acts antagonistically to PTH as well. Estrogen inhibits PTH secretion, keeping it in check. This is why postmenopausal women are at risk for osteoporosis: estrogen levels drop during menopause, so PTH levels rise and bone is broken down more quickly.
Hyperparathyroidism is an overproduction of PTH. The main effect is osteoporosis, but since it increases the concentration of calcium outside muscle and nerve cells, it also affects these cells’ excitability. The increased calcium ion concentration can also result in calcium deposits in tissues (such as kidney stones).

Hypoparathyroidism is underproduction of PTH, which results in too little calcium in the blood.
Pancreas

- Location
- Exocrine vs. endocrine functions
  - Islets of Langerhans
  - α vs. β cells

Most of the pancreas cells are **exocrine** cells: they secrete digestive juices into the small intestine. A small number of cells, though, are **endocrine** cells. These cells make up the **islets of Langerhans**. (They’re called that because they look kind of like small islands of endocrine cells among a sea of exocrine cells.) There are two types of endocrine cells in the islets of Langerhans: alpha-cells (which secrete glucagon) and beta cells (which secrete insulin).
Insulin is produced by beta cells in the islets of Langerhans. Its general effect is to lower blood glucose level by moving glucose from the blood into muscle, liver and adipose cells (as well as other cells, but not brain cells). Since glucose cannot diffuse across the cell membrane, it has to rely on transport proteins to get into cells – these transport proteins only become active when bound by insulin. In addition to helping move glucose into muscle and fat cells, insulin stimulates the anabolism of glycogen from glucose in liver cells.

A lack of functional insulin is diabetes. One form of diabetes is diabetes mellitus, in which functional insulin is not produced. Without functional insulin, glucose cannot be taken into cells, so blood glucose level is very high. The kidneys don’t stand for hypertonic blood, so they move excess glucose out of the blood and into the urine. Since this makes the urine hypertonic, large amounts of water also move from the blood into the urine, resulting in dehydration, thirst and frequent urination. Since glucose cannot get into cells to be used as a fuel, the body begins to catabolize lipids and proteins for their fatty acids and amino acids (most cells can use fatty acids and amino acids as a food source in a pinch). This results in wasting of body tissues. Diabetes mellitus is usually treated with either oral insulin or insulin injections.

The beta-cells in the pancreas are stimulated by the presence of circulating glucose, so control is humoral. As glucose levels rise (such as after a meal), insulin is produced, which results in the movement of the glucose into tissues. As the blood glucose levels fall, insulin production slows.
Glucagon is antagonistic to insulin – it increases blood glucose levels by stimulating the breakdown of glycogen (starch) in liver cells. Glycogen breaks down into glucose, which causes an increase in blood glucose levels. Control of glucagon is straightforward – glucagon production is inhibited by blood glucose. If blood glucose level drops, production is no longer inhibited, so glucagon is produced by the alpha cells. As glycogen is broken down and glucose is released, blood glucose level rises and further glucagon production is inhibited. Insulin and glucagon work together to ensure a steady supply of glucose for the body’s cells.