E) THYROID GLAND

1. “THYROID HORMONE” - triiodothyronine (T3) and thyroxine (T4)  
   **Target** - Body cells  
   **Main Variable(s)** – Growth, glucose metabolism, and development of the nervous system.  

**Notes:**  
Production of the hormone detail:  

1. **Occurs in the colloid and in the follicular cells.** Follicular cells make thyroglobulin, and release it into the colloid.  

2. **Iodide ion (I−) is necessary.** Do not worry about the details. In the colloid, it is attached to a molecule that will become a precursor molecule. T3-side precursor has 3 I’s attached, T4-side precursor has four I’s attached.  
   3. The precursor molecule is brought back into the follicular cells via endocytosis. **Here, they are modified into the active T3 & T4 molecules**, and released into the bloodstream.  

4. **Both T3 & T4 are active hormones.** T4 is more common, but T3 is stronger acting, which is why they usually treat hypothyroidism with T3.
Effects
1. The Thyroid Hormones have effects on the body's regulation of metabolism and energy balance (increase carbohydrate & lipid metabolism)
   - Increases blood sugar (breakdown of glycogen)
   - Hyperglycemia
   - Increases cardiac output
   - Increases heart rate
   - Increases ventilation rate
   - Increases basal metabolic rate

2. Help GH in regulation of growth and development
   - Involved in brain development
   - Increases metabolism of proteins and carbohydrates

3. Regulation of the activity of the nervous system.
   - Increases the effects of catecholamines (i.e. increases sympathetic activity)

4. These effects cause an increase in oxygen utilization and increased ATP and heat production (temperature) by tissues in general.

Pathologies:

Dietary: ENDEMIC GOITER - low iodine in diet = low thyroxine levels = low metabolism = increase in thyroid stimulating hormone = enlarged thyroid gland. Seen in areas w/ low iodine in soil. Classic case: Great Lakes Region of U.S. Michigan began iodizing salt in 1924, rest of country soon after. IQ in US went up an estimated 15 points, as thyroxine is important in CNS development.

Hypersecretion, adult - Irritability, insomnia, high BP, exophthalmos, personality changes.

One type is GRAVES' DISEASE [which is an autoimmune disorder].

The person produces antibodies that mimic the action of TSH, but the antibodies are not turned off by the negative feedback loop, which causes the thyroid gland to grow and produce thyroid hormones.

A primary sign is an enlarged thyroid, (= GOITER) which may be two to three times its normal size. The patient often has a peculiar edema behind the eyes, called EXOPHTHALMOS. This occurs because the tissues of the eye sockets and extrinsic eye muscles swell.

The metabolic rate and heart rate increase, there is loss of weight, and the autonomic nervous system induces sweating.

Treatments include surgical removal of part or all of the thyroid gland, using radioactive iodine (131I) to selectively destroy thyroid tissue, and using antithyroid drugs to block synthesis of thyroid hormones.
Hyposecretion, prepuberty [fetal life or infancy] - Congenital hypothyroidism ("CRETINISM"). Cretins exhibit dwarfism because the skeleton fails to grow and mature, and they are severely mentally retarded because the brain fails to develop fully. Cretins also display retarded sexual development and a yellowish skin color (jaundice). If diagnosed early, cretinism can be prevented by giving oral thyroid hormone.

Hyposecretion, adult – MYXEDEMA (severe). BMR below normal, weight gain, decreased metabolism, edema, & sterility. Edema occurs in the facial tissues and they swell and look puffy. A patient with myxedema has a slow heart rate, low body temperature, sensitivity to cold, dry skin and hair, muscular weakness, general lethargy, and a tendency to gain weight easily. Oral thyroid hormones reduce the symptoms.

2. CALCITONIN (CT)

**Target** - Blood calcium

**Main Variable(s)** – Seral calcium.

**Effects** - Homeostasis of blood calcium and phosphate levels. It lowers the amount of blood calcium and phosphates by inhibiting bone breakdown (inhibit osteoclast activity) and accelerating uptake of calcium and phosphates by bones.

Probably more important in regulating seral calcium in children than it is in adults, where Vit. D is more important.

**Pathologies:**

hyper: TETANY. This disorder causes neurons to depolarize without the usual stimulus. As a result, nerve impulses and muscle action potentials arise spontaneously, leading to muscle twitches, spasms, and convulsions.

Sign: Carpal spasms.
F) PARATHYROID GLANDS

1. PARATHYROID HORMONE (PTH) or Parathormone
   
   **Target** - Blood Calcium
   
   **Main Variable(s)** – Seral calcium.
   
   **Effects** - If adequate amounts of vitamin D are present, it increases the rate of calcium, phosphate, and some magnesium absorption from the digestive tract into the blood by INCREASING osteoclast activity. As far as calcium is concerned, Parathyroid Hormone and Calcitonin are antagonists.
   
   **Pathologies:**
   
   Hypersecretion - **OSTEITIS FIBROSA CYSTICA**. Severe bone decalcification [demineralization] occurs. The bone tissue that is destroyed is replaced by cavities that fill with fibrous tissue.
   
   Hyposecretion - **TETANY**.

G) ADRENAL GLANDS

**Adrenal, Part I. ADRENAL CORTEX**

The adrenal cortex produces corticosteroids from three distinct regions: the zona glomerulosa, the zona fasciculata, and the zona reticularis.

1. zF: **GLUCOCORTICOIDS** - CORTISOL [HYDROCORTISONE], CORTICOSTERONE, CORTISONE. [Cortisol is the most abundant and is responsible for about 95% of glucocorticoid activity.]
   
   **Target** - Body cells
   
   **Main Variable(s)** – Metabolism, blood glucose, and lowered immune response (in several ways).
   
   **Effects** - The Glucocorticoids regulate metabolism and resistance to stress.
   
   Recall: **Glucocorticoids are released in response to stress through the action of ACTH**.
   
   **Glucocorticoids, together with other hormones, promote metabolism.**
   
   If the body's reserves of glycogen and fat are low - **gluconeogenesis**.
   
   **Glucocorticoids provide resistance to stress.**
   
   * Vessel constricting chemicals. They thereby raise blood pressure, which is important if there is blood loss.
* An anti-inflammatory compound that inhibits the cells and secretions that participate in inflammatory responses. They reduce the number of mast cells, thus reducing release of histamines; stabilize lysosomal membranes to reduce release of enzymes; decrease blood capillary permeability; and depress phagocytosis. They also stop repair of connective tissues.

**Pathologies:**
Hypersecretion of glucocorticoids - CUSHING’S SYNDROME.
They have a rounded "moon face," and spindly arms and legs, due to catabolism of muscle proteins. The individual bruises easily and wound healing is poor. Other symptoms include: hyperglycemia, osteoporosis, weakness, hypertension, increased susceptibility to infection, decreased resistance to stress.

Low blood glucose & Na. Severe dehydration.

Hyposcretion - ADDISON’S DISEASE. Symptoms include: mental lethargy, anorexia, nausea and vomiting, weight loss, hypoglycemia [which leads to muscular weakness], hypotension.

High BP, brain edema.

2. zG: ALDOSTERONE (one of the mineralocorticoids). Also, see the Mineralocorticoids in your book

**Target:** The kidneys
Aldosterone increases the reabsorption (conservation) of sodium and the elimination of potassium, which increases blood pressure.

**Main Variable(s)** – Sera sodium and BP.

**Effects:** Mineralocorticoids, mostly aldosterone, are essential to regulation of electrolyte concentrations of extracellular fluids. As sodium is conserved at the kidney, water follows, and increases water conservation.

**Pathologies:**
Hyper- = Aldosteronism: High retention of sodium, but low levels of K+, leading to extreme hypertension, kidney failure, muscle weakness. Opposite of Addison’s disease.
3. zR: Gonadocorticoids are mostly weak androgens, which are converted to testosterone and estrogens in the tissue cells.

**Pathologies:**

One cause of Androgen Excess (or Adrenal Virilism), although not the most common: caused by a low usage of glucocorticoids, which “shunts” the precursor molecule into testosterone production.

No matter what the cause, most noticeable in women, as it causes the growth of facial hair, and possibly enlargement of the clitoris (“masculinization of genitalia”).

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**Adrenal, Part II. ADRENAL MEDULLA**

1. The Catecholamines (cat - a - col - amines) - EPINEPHRINE [ADRENALINE] (80%) and NOREPINEPHRINE [noradrenaline]

   **Target** - Body cells

   **Main Variable(s)** - many, including blood glucose.

   **Effects** - These two hormones mimic the effects brought about by the Sympathetic Division of the ANS. They are responsible for the flight-or-fight response. Like the glucocorticoids, they help the body resist stress. Unlike the adrenal cortex hormones, they are not essential for life.

   **Pathologies:**

   See “STRESS RESPONSE” box later.
Not On Exam: A Look At Stress

Cortisol counteracts insulin, contributes to hyperglycemia-causing hepatic gluconeogenesis and inhibits the peripheral utilization of glucose (insulin resistance) by decreasing the production of glucose transporters to the cell membrane.

Sympathetic Nervous Response leads to:
- Lowered function of:
  - Gastrointestinal track
  - Reproductive track
  - Cardiovascular issues

Brain Function:
- Perceptions are altered: Anxiety, Depression
- Lowers cerebral output (ability to use conscious brain for concentration and learning)

Recall, from the Nervous Chapter:
Psychosomatic Illness: Some physical diseases are believed to have a mental component derived from the stresses and strains of everyday living.
This is the case, for example, of lower back pain, Irritable Bowel Syndrome, Fibromalacia, sleep dysfunction, and Chronic Fatigue Syndrome.

* Drugs the lower “feeling” of bad: nicotine, alcohol, anidepressants, anti-anxiety medications, morphine, codeine, hydrocodone.

Lowered Immunity & Repair:

Immunity:
- Allergies
- Celiac disease
- DM1
- Systemic lupus erythematosus

Repair:
- Possible scenario: lowered normal repair process leads to increase mitosis → cancer
- and the positive feedback loop continues!!

Who needs “environmental toxins” or “chemicals” to explain the increases in many of the diseases we’ve seen increasing lately?
H) PANCREAS - Islets of Langerhans

1. GLUCAGON - produced by the alpha cells of the islets

   **Target** - Blood glucose.

   **Main Variable(s)** – Blood glucose.

   **Effects** - To increase the blood glucose levels. It does this by stimulating liver cells to convert stored glycogen into glucose - glycogenolysis, which is then released into the blood. It also stimulates the conversion of amino acids and lactic acid into glucose - gluconeogenesis.

   **Pathologies:** Inappropriate hypersecretion of glucagon is a well-documented problem in patients with type 1 and type 2 diabetes. See discussion on diabetes below. Probably a result of low blood sugar (i.e., secondary).

2. INSULIN - produced by the beta cells of the islets

   **Target** - Blood glucose

   **Main Variable(s)** – many, including blood glucose.

   **Effects** - To lower the blood glucose levels. It accelerates the transport of glucose from the blood into cells, especially skeletal muscle. It also accelerates the conversion of glucose into glycogen - glycogenesis.

   **Pathologies:**
   - Hypersecretion - results in a decrease of blood glucose - HYPOGLYCEMIA.
   - Hyposecretion - results in an increase of blood glucose - DIABETES MELLITUS.
Diabetes Mellitus (DM)

Diabetes refers to "excessive discharge of urine".

There are several types of diabetes. All are characterized by HYPERGLYCEMIA.

The more common types are "Diabetes mellitus type 1" (juvenile onset) and Diabetes mellitus type 2 (adult onset). Both type 1 & 2 are characterized by a decrease in insulin production, but for different reasons.

**Type 1** is characterized by an **absolute deficiency of insulin secretion.** "Insulin Dependent" diabetes.

Type 1 is an autoimmune disorder, with the islets being destroyed by immune cells. There is a genetic link (probably just 1 or 2 genes), although some environmental cue seems to be needed that starts the autoimmune response (may be as simple as a viral infection).

* Glucose cannot enter the cells readily.

* As insulin is also the main regulator of lipolysis, fatty acids build up in the bloodstream. If not controlled, **nitrogen buildup in the bloodstream**, and there is muscle wasting due to protein catabolism (proteolysis). Ketoacidosis results from lipolysis and synthesis of ketones by the liver (refer to the Nutrition chapter and Liver section later). **Ketosis** is the presence of ketones in their urine.

* This leads to "osmotic diuresis". Water is not reabsorbed at the kidney, as it follows these metabolites into urine during the formation of urine (see the Kidney section later). Dehydration is characteristic of DM1.

* As pH is lowered due to the ketoacidosis, there can be general systemic enzyme and organ dysfunction.

* If an identical twin has DM1, the other twin has approximately a 50% chance of having DM1 also. DM1 has been linked to several genes. There have been 3 other genes found, all dealing with regulation of immune response. Probably, this is only 1 of many.

**Type 2** is characterized by a **lack of insulin receptor activity** (which varies in severity). "Adult Onset" diabetes. More common than DM1.

* Due to breakdown in system, insulin secretion in response to meal ingestion is decreased and delayed.

* This is exacerbated by poor diet and exercise. However, usually the insulin concentrations in DM2 are high enough to prevent proteolysis, so tissue catabolism and tissue wasting doesn’t occur as with DM1.

* Over time, the Beta cells lose function and most also need insulin injections. They "require insulin injections, but do not depend on them".

* Most common = genetic form In this case, If an identical twin has DM2, the other twin has almost a 100% chance of having DM2 also.

Gestational diabetes and “alcoholic” diabetes are other forms. Also, several illnesses can lead to this (Cushing’s, acromegaly) as well as any disease of the pancreas (cystic fibrosis, pancreatitis).
I) THYMUS GLAND

- The thymus gland is relatively large at birth, growing only slowly until puberty. After puberty, it begins to decrease in size as its tissues are replaced by fat and loose connective tissue. In middle-aged and older people, the thymus gland may be so reduced in size that it is difficult to recognize.

1. Four hormones: Thymosin, Thymic Humoral Factor (THF), Thymic Factor (TF), Thymopoietin
   - **Target**: T cell Lymphocytes
   - **Main Variable(s)**: Immune system response.
   - **Effects**: Increased immune response. These four hormones promote the maturation of T cell Lymphocytes, enabling them to recognize and attack foreign proteins (antigens).
   - **Pathologies**: None discussed here.

J) PINEAL GLAND

1. MELATONIN - Produced during darkness; 70% between 11 p.m. and 7 a.m.
   - **Target**: Pituitary gland
   - **Main Variable(s)**: Many. Timing of reproduction.
   - Some role in sleep/wake cycle, but less than people think.
   - More important in the elderly.
   - **Effects**:
     1. Melatonin can suppress libido. It inhibits reproductive activity by inhibiting the release of gonadotropic hormones (FSH, LH, ICSH) by the pituitary gland.
     - it seems to play a role in prohibiting females from reaching sexual maturity before their bodies can handle it.
     - So it is believed it may play a role in the timing of puberty.
     2. The release of melatonin is based on a cycle of active and non-active periods occurring about every 24 hours. The "melatonin signal" forms part of the system that regulates the sleep–wake cycle by chemically causing drowsiness and lowering the body temperature, but it is the CNS that controls the daily cycle in most components of the paracrine and endocrine systems, not melatonin.
     - Melatonin does seem effective in helping with insomnia in older people.
   - **Pathologies**: Not much known. Deficiency in melatonin is responsible for some types of insomnia.
K) PLACENTA

1. HUMAN CHORIONIC GONDROTROPIN (hCG)
   
   **Target** - Ovary, specifically the corpus luteum

   **Main Variable(s)** – Female reproductive cycle.

   **Effects** - It stimulates the ovary to produce progesterone from the corpus luteum proper and estrogen from the theca cells of the corpus luteum. As pregnancy continues, the placenta makes increasing amounts of estrogen and progesterone, while decreasing its chorionic gonadotropin output.

   **Pathologies:** Failure to produce hCG may result in a spontaneous abortion.

L) HEART - cardiac muscle fibers of the atria

1. ATRIAL NATRIURETIC FACTOR (ANF)
   
   **Target** - Blood vessels, kidneys, among others

   **Main Variable(s)** – blood pressure.

   **Effects** - Decreases blood pressure. Atrial Natriuretic Factor is secreted when the atria are stretched, as might occur when blood volume or blood pressure increases. ANF increases sodium and water excretion in the urine [natriuresis and diuresis] and dilates blood vessels.

   **Pathologies:** None discussed here.

M) PROSTAGLANDINS

   **Target** - Prostaglandins are a family of compounds that are autocrine regulators: they act within the same organ in which they are produced. For this reason, they are commonly known as "local hormones."

   They are activated by 2 enzymes: COX-1 and COX-2.

   **Main Variable(s)** – Many (see below). Especially immune response (inflammation and blood clotting) and pain sensation (increases pain).

   **Effects** - The action of prostaglandins supplement the regulatory effects of the immune, endocrine and nervous systems.

   Prostaglandins have regulatory functions on the following: inflammation; reproductive system; gastrointestinal tract (especially upkeep of stomach lining); respiratory system; blood vessel dilation & constriction; blood clotting; kidneys, sensitize the nervous system to pain.

   Prostaglandin are involved in fear, nerve impulse, and other reactions

   **Notes** – All tissues make some prostaglandin. All nucleated cells can make them.

   Aspirin, and other NSAIDs (Non-steroidal antiinflammatory agents – ibuprofen, etc.) are COX inhibitors – lower inflammation, fever and pain by inhibiting the prostaglandins. Not very toxic. Cannot be taken near surgery, as they inhibit clotting. Repeated use can cause stomach lining problems.
Tylenol (acetaminophen) is not an NSAID. Inhibits pain only, Acetaminophen does not affect clotting or inflammation, however less problems with stomach lining. However, must not be taken with alcohol. Toxic with alcohol!

**Pathologies:**
There are too many prostaglandins to talk about “hyper” or “hypo” secretions. Affects vary widely. Often, hypersecretion associated with joint pain of some arthritis.

COX inhibition can cause problems with stomach lining.

N) The skin produces cholecalciferol, an inactive form of vitamin D3 or Calcitriol. It must be activated by sunlight.

**Target** – Blood calcium levels

**Main Variable(s)** – Increases blood seral calcium. Homeostasis of bone strength.

**Effects** – Increases calcium reabsorption at kidney and absorption in gut. Works with PTH.

**Notes:**
Although vitamin D is commonly called a vitamin, it is not actually an essential dietary vitamin in the strict sense, as it can be synthesized in adequate amounts by our body if exposed to sunlight.

Our skin makes vitamin D3 and supplies about 90 percent of our vitamin D. This molecule occurs naturally in the skin of animals and in milk. Vitamin D3 can be made by exposure of the skin to UV.

It is necessary for bone strength, so a lack of it causes bone strength problems (see below). **Its role is on maintaining seral levels necessary for healthy bones.**

Taking supplementation does not prevent osteoporosis if the person is not Vit. D deficient. Taking Vit. D and calcium supplement may prevent fractures in women after menopause, however.

**Pathologies:**
Osteomalacia (or rickets when it occurs in children) became a problem as smog worsened in cities during the Industrial Revolution, and exposure to sunlight was lessened.
O) The gastrointestinal tract contains enteroendocrine cells throughout the mucosa that secrete hormones to regulate digestive functions.

We will talk about some of these during the Digestion Chapter.

P) The kidneys produce erythropoietin, which signals the bone marrow to produce red blood cells.

Recall this from the Blood Chapter.

*There are many other hormones that we will discuss as the semester continues!*