Key Medical Terms Associated with the Endocrine System

Gynecomastia: Excessive development of mammary glands in a male, sometimes caused by a tumor of the adrenal gland.

Hirsutism (HER-soo-tizm): Presence of excessive bodily and facial hair in a male pattern, especially in women; may be caused by excess androgen production due to tumors or drugs.

Virilizing adenoma: Tumor of the adrenal gland that liberates excessive androgens, causing virilism. Occasionally, adrenal tumor cells liberate estrogens to the extent that a male patient develops gynecomastia. Such a tumor is called a feminizing adenoma. Virilism is the presence of mature masculine characteristics in females or prepubescent males. In a female, virile characteristics include growth of a beard, development of a much deeper voice, occasionally the development of baldness, development of a masculine distribution of the hair on the body and on the pubis, growth of the clitoris such that it may resemble a penis, atrophy of the breasts, infrequent or absent menstruation, and increase muscularity that produces a male-like physique. In prepubescent males the syndrome causes the same characteristics as in females, plus rapid development of the male sexual organs and emergence of sexual desires.

Parathyroid Gland Disorders

The parathyroid glands are 4 small glands that are embedded in the posterior wall of the thyroid gland. Chief Cells secrete parathyroid hormone (PTH), which increases blood calcium levels by 3 mechanisms: 1) Stimulates osteoclast activity to break down bone and release Ca2+ into the blood, 2) Increasing the rate of Ca2+ absorption from the intestine, and 3) Increases rate of Ca2+ reabsorption by the kidneys. Along with calcitonin, provides a dual mechanism for regulating blood calcium levels.

Hypoparathyroidism: Too little parathyroid hormone leads to a deficiency of blood Ca2+, which causes neurons and muscle fibers to depolarize and produce action potentials spontaneously. This leads to twitches, spasms, and tetany (maintained muscle contraction). The leading cause of hypoparathyroidism is accidental damage to the parathyroid glands due to trauma or blood supply interruption during thyroidectomy surgery.

Hyperparathyroidism: An elevated level of parathyroid hormone, most often is due to a tumor of one of the parathyroid glands. An elevated level of PTH causes excessive resorption of bone matrix raising the blood levels of calcium and phosphate ions and causing bones to become soft and easily fractured. High blood calcium level promotes formation of kidney stones.

Thyroid Gland Disorders – See Lecture notes for their classification and disorders of hypersecretion and hyposecretion.

Diabetes Mellitus

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. There are four forms of this disorder, Type I Type II and Type III and Gestational Diabetes. All types except type III will have an elevation of glucose in the blood (hyperglycemia) and an increase of glucose loss in the urine (glucosuria). Symptoms of diabetes mellitus (except type III) consist of the three “polys”: Polyuria, excessive urine production due to high glucose content in kidney filtrate, which results in decreased ability to reabsorb water hence large volumes of water are lost in the urine; Polydipsia, excessive thirst due to large volumes
of water lost in the urine resulting in dehydration; **Polyphagia**, excessive appetite. Even through the person is hyperglycemic, glucose cannot enter the cells. The **hypothalamus** controls appetite and if glucose cannot enter the cells of the hypothalamus then the person feels extremely hungry.

**Diabetes mellitus** is the fourth leading cause of death by disease in the United States, primarily because of its damage to the cardiovascular system. The chronic hyperglycemia of diabetes is associated with long-term dysfunction, damage, and failure of various organs, especially the eyes, kidneys, nerves, coronary heart disease, and blood vessels and stroke.

**Fasting blood glucose (FBG) levels** has a normal range of 70 to 100 milligrams per deciliter (mg/dL). Note: 100 mL = 1 dL. In a normal individual after eating, blood glucose levels generally do not get above 140 mg/dL. Thus, **Non-fasting normal blood glucose level ranges between 70 to 140 mg/100 ml** and is dependent on when the person last ate. In diabetic mellitus patients, we see both low blood glucose levels that we call **hypoglycemia**, or elevated blood sugars, **hyperglycemia**.

If the blood glucose drops below about 60 mg/100 ml, people will generally have symptoms of some shakiness, feeling of hunger, maybe a little racing of the heart. If blood sugar drops below 50 and can get down as low as 40 or 30 or even 20, then there is a **progressive loss of mental function and eventually unconsciousness and seizures**. On the other side, if blood glucose gets up above 180 to 200, then it **exceeds the capacity of the kidneys to reabsorb the glucose** and we begin to spill glucose into the urine. And if it gets way up high, up in the 400s or even 500s, it can be associated with some alteration in mental function. **So either too low or exceedingly high can cause changes in mental function.**

**Glucose Tolerance Test:** As demonstrated by the "**glucose tolerance curve**", when a normal, fasting person ingests 1 gram of glucose per kilogram of body weight, the blood glucose level rises to **120 to 140 mg/100 ml** and falls back to **below normal in about 2 hours**. In a person with diabetes, the fasting blood glucose concentration is almost always above 100 mg/100 ml and after ingestion of the glucose mixture **the glucose level falls back to the starting value only after 4 to 6 hours**. The slow fall of this curve demonstrates that either (1) insulin secretion does not occur or (2) there is decreased sensitivity to insulin. Type I and Type II diabetes can be distinguished from each other by measurements of plasma insulin levels, with plasma insulin being low or undetectable in type I and can often have increased insulin levels in Type II diabetes.

**The hemoglobin A1C test** - also called HbA1C, glycated hemoglobin test, or glycohemoglobin -- is an important blood test used to determine how well your diabetes is being controlled. **Hemoglobin A1C provides an average of your blood sugar control over a six to 12 week period** and is used in conjunction with home blood sugar monitoring to make adjustments in your diabetes medicines.

**Hemoglobin** is a substance within red blood cells that carries oxygen throughout your body. **Glycated Hemoglobin** is normal at low amounts, however when diabetes is not controlled (meaning that your blood sugar is too high), abnormal high amounts of blood glucose combines with your **hemoglobin**. **Therefore, the average amount of sugar in your blood can be determined by**
measuring a hemoglobin A1C level. If your glucose levels have been high over recent weeks, your hemoglobin A1c test will be higher.

**Hemoglobin A1C Test Results:** For people without diabetes, the normal range for the hemoglobin A1C test is between 4% and 5.6%. Hemoglobin A1c levels between 5.7% and 6.4% indicate increased risk of diabetes, and levels of 6.5% or higher indicate diabetes. People with diabetes should have this test every three months to determine whether their blood sugars have reached the target level of control. Those who have their diabetes under good control may be able to wait longer between the blood tests, but experts recommend checking at least 2 times a year.

**Type 1 Diabetes or Insulin-Dependent Diabetes Mellitus (IDDM).** Results from a deficiency of insulin usually due the person’s own immune system (autoimmune disorder) destroying the pancreatic beta cells. As a result the pancreas produces little or no insulin. Type 1 diabetes usually develops in people younger than age 20 (juvenile onset), and it persists throughout life. By the time symptoms of type 1 diabetes arise, 80-90% of the islets beta cells have been destroyed.

Untreated type 1 diabetes has symptoms that are similar to that of a starving person. Because insulin is not present to aid the entry of glucose into body cells fats and proteins are broken down to provide an energy source for metabolism, results in the wasting away of body tissues. **Hydrolysis of triglycerides** within adipose tissue releases glycerol and free fatty acids into the blood which are both used as an energy source many organs; they can also be converted by the liver into derivatives called ketone bodies which circulate through the blood and used as an energy source. Ketone bodies include acetoacetic acid, β-hydroxybutyric acid, and acetone (solvent in nail polish remover). An elevated level of ketone bodies in the blood results in a condition called ketosis. If there are sufficient amounts of ketone bodies in the blood to lower the blood pH, the condition is called ketoacidosis. Severe ketoacidosis can lead to coma and death. Cataracts can develop due to excessive glucose attaching to lens proteins causing cloudiness. A person in this condition may also have a sweet-smelling breath due to the presence of acetone, which is volatile and leaves the blood in the exhaled air.

**Treatment** involves self-monitoring of blood glucose levels, a diet of regular meals and periodic insulin injections to maintain normal blood glucose levels.

**Insulin shock:** Shock due to an insulin overdose. Hyperinsulinism most often results when a diabetic injects too much insulin. The main symptom is hypoglycemia, decreased blood glucose level, which occurs because the excess insulin stimulates too much uptake of glucose by body cells. The resulting hypoglycemia stimulates the secretion of epinephrine and glucagon and results in anxiety, sweating, tremor, increased heart rate, hunger, and weakness. As blood glucose falls, brain cells are deprived of a steady supply of glucose and can lead to mental disorientation, convulsions, unconsciousness, and shock. It should be noted that the neurons in the brain do not use insulin to upregulate the protein transporters to move glucose into the cells. The glucose transporters are always present, but requires blood
glucose to be at high enough levels for facilitated diffusion to continue. This is why a drop in blood glucose levels can directly decrease the movement of glucose into brain neuron cells.

**Type 2 Diabetes or Non-insulin-dependent diabetes mellitus (NIDDM)** is much more common than type 1, representing more than **90% of all cases**. Referred to as **adult onset diabetes because it is frequently occurs in obese people over the age of 35**. The cause of type 2 diabetes is a lack of responsiveness or sensitivity to insulin, which may be at normal or elevated levels. The symptoms are usually mild and sporadic and the condition may go unnoticed for years in a patient before diagnosis. Type II may progress to destruction of the insulin-producing cells, but is still considered Type 2, even though insulin administration may be required.

**Treatment:** Usually controlled and corrected by exercise, proper diet, and weight loss.

**Metformin (Glucophage)** is an oral anti-diabetic drug and is the drug of choice for the treatment of type 2 diabetes, in particular, in overweight and obese people. **Metformin improves hyperglycemia primarily through its suppression of hepatic glucose production (gluconeogenesis).** The "average" person with type 2 diabetes has three times the normal rate of gluconeogenesis; metformin treatment reduces this by over one third. In addition to suppressing hepatic glucose production, metformin increases insulin sensitivity, enhances peripheral glucose uptake and aids in GLUT4 deployment to the plasma membrane.

**Type III Diabetes** – largely confined to the brain

- A type of insulin resistant diabetes characterized by a decrease in insulin sensitivity and insulin production of CNS neurons. A toxic protein known as soluble oligomers or **ADDL (amyloid β-derived diffusible ligand)** found in the brains of individuals with Alzheimer’s Disease (AD) removes insulin receptors from nerve cells, rendering those neurons **insulin resistant**.
- ADDLs bind very specifically at synapses, initiating **deterioration of synapse function** and causing changes in synapse composition and shape. Represents a major pathogenic mechanism of AD neurodegeneration.
- **In the brain** (particularly the cerebral cortex and hippocampus), insulin binds to receptors at a synapse and turns on mechanisms necessary for **nerve cells to survive and memories to form**.
  - Unlike insulin receptors from the periphery, the neuronal insulin receptors of the CNS are less involved with glucose metabolism and more involved with diverse brain functions, including synaptic activities required for learning and memory.
**Gestational diabetes** Can occur during pregnancy (especially during third trimester) – women exhibit high blood glucose levels. Occurs in about 5-10% of pregnancies. **Cause:** Thought to be due to high levels of pregnancy hormones which cause insulin receptors to be less sensitive to insulin and elevate blood sugar levels. Similar to the situation in type II diabetes. Gestational diabetes generally has few symptoms and it is most commonly diagnosed by screening during pregnancy. **Risks:** Untreated – have increased risk of an enlarged baby (macrosomia) at birth which may lead to delivery complications, low blood sugar, and jaundice. Gestational diabetes usually resolves itself after pregnancy. Women with unmanaged gestational diabetes are at increased risk of developing type 2 diabetes mellitus. **Treatment** for gestational diabetes during pregnancy includes: Eating a balanced diet, getting regular exercise, checking blood sugar levels, monitoring fetal growth and well-being, and if necessary taking insulin shots or using pills called glyburide and metformin.

**Diabetes Insipidus:** Antidiuretic hormone (ADH) is produced by the hypothalamus and released from the **posterior pituitary gland** in response to **decreased blood volume** (pressure) or **increased blood osmolarity** (solute concentration). ADH stimulates the kidneys to retain water so that less water is excreted in the urine and more is retained in the blood thereby raising blood pressure. **Diabetes insipidus** is a disorder due to defects in antidiuretic hormone (ADH) receptors or an inability to secrete ADH. **Neurogenic diabetes insipidus** results from hyposcretion of ADH, usually caused by a brain tumor, head trauma, or brain surgery that damages the posterior pituitary or the hypothalamus. In **nephrogenic diabetes insipidus,** the kidneys do not respond to ADH. The ADH receptors may be nonfunctional, or the kidneys may be damaged. A common symptom of both forms is excretion of large volumes of urine, with resulting dehydration and thirst. Bedwetting is common in afflicted children. Because so much water is lost in the urine, a person may die of dehydration if deprived of water for only a day or so.

**Treatment** of neurogenic diabetes insipidus involves hormone replacement. Either subcutaneous injection or nasal spray application of ADH is effective. **Treatment of nephrogenic diabetes insipidus** is more complex and depends on the nature of the kidney dysfunction.