ENDOCRINE DISORDERS

(CHAPTERS 37 AND 38)

QUESTION 1

What is the cause of most endocrine disorders?

Remember that the function of the endocrine system is the regulation of body systems through the production of **hormones**.

Most endocrine problems fall into one of two categories:

hypersecretion – the body produces **too much** of a particular hormone

hyposecretion – the body produces **too little** of a particular hormone

The causes of these imbalances can vary, but **most** endocrine disorders occur on the "producing" end.

However, some endocrine disorders can occur on the "receiving" end. When a hormone is produced in appropriate amounts but the target doesn't respond to it correctly, we call this **receptor resistance**.

QUESTION 2

Describe Graves' disease.

We've talked about **Graves' disease** previously in the unit on autoimmunity, but to review, it is the most common cause of **hyperthyroidism**.

Immune antibodies are formed which target and attach to the **thyroid stimulating hormone** (TSH) receptors on the thyroid gland, **mimicking** TSH and **activating** the receptors.

This causes the thyroid to **over-produce** the thyroid hormones **T_3** and **T_4.**

QUESTION 3

Would you expect thyroid-stimulating hormone (TSH) to be high or low in Graves' disease?

The thyroid gland is normally controlled by TSH production in the **pituitary gland**—but in Graves' disease, the thyroid breaks free of this control mechanism and starts **overproducing** hormones.

In response to this imbalance, the pituitary tries to throttle back the thyroid gland by **decreasing** TSH production, resulting in high T_3/T_4 but **low** TSH levels.

QUESTION 4

What is the pathophysiology of exophthalmos?

Exophthalmos is a forward "bulging-out" of the eyes that often occurs in patients with Graves' disease.

It results from autoantibodies provoking an **inflammatory response** in the tissues behind the eyes, causing swelling and fibrosis which pushes the eyes forward from behind.

QUESTION 5

What are some common causes of hypothyroidism?

Hypothyroidism, like many other endocrine disorders, can have **multiple causes**.

The root cause of low thyroid hormone levels can be in either in **the thyroid itself**, or in the **hypothalamus/pituitary gland** which regulate it.

In **primary hypothyroidism**, the problem is **in the thyroid**. The thyroid is being stimulated, but is not responding to TSH by producing T_3 and T_4 as it should.

As a result, in primary hypothyroidism, TSH levels are **elevated**, as the pituitary gland is trying harder to get the thyroid to respond, but it isn't working.

This can be **congenital**, can occur due to **surgical resection** of the thyroid, or may be due to **iodine deficiency**.

In **secondary hypothyroidism**, the problem is **in the pituitary gland** or **in the hypothalamus**. The thyroid is functioning normally, but it isn't being stimulated to produce the correct amount of T_3 and T_4.

As a result, in secondary hypothyroidism, TSH levels are **low**, as the pituitary is either failing to produce TSH, or the hypothalamus is failing to stimulate the pituitary gland with TRH.

QUESTION 6

Describe the cause of Hashimoto's thyroiditis.

Hashimoto's thyroiditis, like Graves' disease, is an autoimmune disease that affects the thyroid. However, the effect is **opposite**.

Unlike Graves' disease, which is a type II (tissue-specific) hypersensitivity, Hashimoto's is a type IV (cell-mediated) hypersensitivity in which cytotoxic T cells **attack** and gradually **destroy** the thyroid gland.

This results in primary **hypothyroidism**, and the lab values are **inverted** vs. Graves' disease. Rather than TSH being low to try to slow down the thyroid, TSH will be **high** as the pituitary gland tries to compensate for T_3 and T_4 being **low**.

QUESTION 7

Describe myxedema.

Myxedema is a type of **swelling** (edema) which can occur in severe cases of **hypothyroidism**, and occasionally in hyperthyroidism (as in Graves' disease.)

It results from an increased concentration of **proteins** and **polysaccharides** in the extracellular space, increasing IFOP and drawing water out of the cells.

This process results in the formation of **non-pitting edema**, particularly of the **face**, **hands**, and **feet**.

Swelling of the tongue and the mucus membranes of the mouth can result in difficulty speaking and slurred speech.

QUESTION 8

How is hypothyroidism treated?

If the thyroid is not producing enough thyroid hormone, the body's supply must be **supplemented**.

This is done with a drug called **levothyroxine** (Synthroid,) which is just a synthetic form of T_4.

It is usually taken orally, and requires careful monitoring of T_4 and TSH levels to achieve a therapeutic level.

Levothyroxine is one of the **most-prescribed drugs** in the U.S. and is the definitive treatment for hypothyroidism.

QUESTION 9

Describe Cushing's syndrome.

Cushing's syndrome refers to a group of symptoms associated with **hypercortisolism**—the excess of **glucocorticoids**, a type of hormone produced in the **cortex** of the **adrenal glands**.

In **primary** hypercortisolism, the problem is directly in the **adrenal cortex**. Because of this, **adrenocorticotropic hormone** (ACTH) levels will be **low**, as the pituitary gland is trying to slow down the adrenal gland, but it isn't working.

In **secondary** hypercortisolism, the problem is in the **pituitary gland**. This will result in ACTH levels being **high**, because the pituitary gland is overproducing ACTH and the adrenal cortex is simply responding to the high ACTH levels.

QUESTION 10

What are the functions of cortisol?

Cortisol is one of the body's primary **stress hormones** and the primary **glucocorticoid** produced in the adrenal cortex.

One of its main functions is the regulation of **metabolism** and the mobilization of energy stores, e.g. increasing blood glucose and enabling lipid breakdown.

It also has a suppressing effect on certain parts of the **immune system**, which reduces the body's inflammatory response.

QUESTION 11

Why are glucocorticoids prescribed to treat inflammation?

Glucocorticoid drugs, such as **prednisone**, **dexamethasone**, etc. mimic the effects of **cortisol** on the immune system, thus suppressing inflammation.

They have a **huge** array of uses, from asthma and allergies to arthritis, and many people take them as a form of long-term therapy for chronic diseases.

QUESTION 12

Describe some causes of Cushing's syndrome.

Cushing's syndrome—the symptoms of excess **glucocorticoids** in the body—can occur for a few different reasons.

One of these causes is **Cushing's disease**, a form of **secondary hypercortisolism** caused by a pituitary tumor.

The tumor tissue produces an excess of **adrenocorticotropic hormone** (ACTH,) which causes the adrenal cortex to become overactive.

It can also be caused by a secreting tumor in the adrenal cortex itself, causing **primary hypercortisolism**.

Finally, the excess glucocorticoids may be coming from outside the body; Cushing's syndrome is a possible side effect of **long-term steroid use**.

QUESTION 13

How is the body's appearance altered in Cushing's disease?

Some of the signs and symptoms can include **abdominal obesity** with stretch marks, a buildup of fat around the face known as "**moon face**," **hirsutism**, and **fatigue**.

A good mnemonic for this is that "Cushing's" sounds like "cushion"—too much cortisol makes you puffy and fuzzy like a pillow. 😂

QUESTION 14

Describe Addison's disease.

Addison's disease refers to **hypocortisolism**, or a deficit of glucocorticoid production—essentially the "opposite" of Cushing's syndrome (hypercortisolism.)

It is a **rare** condition usually caused by **autoimmune damage** to the adrenal glands (**primary adrenal insufficiency**,) resulting in decreased production of adrenal hormones.

A decrease in cortisol production can also be caused by **secondary adrenal insufficiency**, in which the adrenal glands receive insufficient stimulation from the hypothalamus and pituitary gland.

This results in a decrease of **all** of the adrenal hormones: **mineralocorticoids** (aldosterone,) **glucocorticoids** (cortisol,) and **androgens** (testosterone.)

ACTH levels may be either **high** or **low** depending on the underlying cause (primary or secondary.)

QUESTION 15

What are some causes of adrenal insufficiency?

As mentioned in the previous question, adrenal insufficiency can be caused by damage to the **pituitary gland** which is responsible for ACTH production.

Addison's disease, which is caused by autoimmune damage to the adrenal cortex itself, is actually **less common** than secondary adrenal insufficiency.

QUESTION 16

List the three main types of diabetes mellitus (DM.)

The three types of diabetes mellitus are:

- **Type 1** (insulin-dependent) diabetes
- **Type 2** (non-insulin-dependent) diabetes
- **Gestational diabetes mellitus** (GDM)

There is also a fourth type of diabetes: **diabetes insipidus**. However, this is **not** the same as diabetes mellitus and represents an entirely different disease process that has nothing to do with blood sugar.

The reason it is called diabetes is because it has **similar symptoms**. We'll talk about this more when we get to the unit on renal disorders. For now, just know that it is **not** the same as DM.

QUESTION 17

What is the underlying problem in type 1 diabetes?

Type 1 diabetes, sometimes called **insulin-dependent diabetes mellitus** (IDDM,) is caused by the destruction of the **beta cells** in the islets of the pancreas, which are responsible for secreting **insulin** into the bloodstream.

This results in **low insulin levels**, causing the cells of the body to fail to take in glucose from the blood to fuel their metabolic needs, which in turn leads to an increase in blood glucose.

Patients diagnosed with type 1 diabetes tend to develop it at a young age, with the average age at diagnosis being around 14.

QUESTION 18

How is type 1 diabetes treated?

Type 1 diabetes is unique in that the body **does not produce** (or greatly underproduces) insulin, meaning that patients **must** receive supplemental insulin via subcutaneous injection in order for normal cellular metabolism to occur.

Insulins vary by type, with some taking effect very quickly but not lasting very long, and others lasting for a much longer time, even an entire day or more. Often, multiple types are **combined** to achieve appropriate insulin levels throughout the day.

QUESTION 19

What is the underlying problem in type 2 diabetes?

Type 2 diabetes, sometimes called **non-insulin-dependent diabetes mellitus** (NIDDM,) is caused by insulin **resistance**, meaning that insulin may be produced in normal amounts, but fails to trigger the intake of glucose by the cells.

Like type 1 diabetes, this also results in an elevated blood glucose level. This excess glucose is then excreted in the urine (**glycosuria**,) and water is also lost by osmosis, leading to **polyuria**.

One of the greatest risk factors for the development of type 2 diabetes is **obesity**. Currently, about 90% of diabetes cases fall into the category of type 2 diabetes.

QUESTION 20

What are the "3 P's" of diabetes?

polyuria – high blood sugar causes glucose to be excreted by the kidneys, increasing **urine production**

polydipsia – fluid loss is balanced by increased **sensation of thirst**

polyphagia – unmet metabolic needs stimulate increased **sensation of hunger**

(In other words: DM makes you **eat a lot**, **drink a lot**, and **pee a lot**.)

QUESTION 21

What are the diagnostic criteria in type 2 diabetes?

Diabetes is, as you might expect, diagnosed based on **blood sugar measurements**.

"Random" blood glucose (taken anytime, **without fasting**) should generally be below 140 mg/dl; **> 200** indicates diabetes and anything in between (140-200) is considered "pre-diabetes."

Likewise, **fasting** blood glucose should be below 100 mg/dl; **> 125** indicates diabetes and 100-125 is pre-diabetes.

QUESTION 22

How is type 2 diabetes treated?

Ideally, type 2 DM can be caught early and corrected with **lifestyle changes** (diet, exercise) while it is still in the pre-diabetes stage.

If it persists, oral hypoglycemic agents such as **metformin** are often prescribed.

In later stages, insulin production may begin to decrease and supplemental **insulin** may be required (but often isn't.)

QUESTION 23

Describe gestational diabetes mellitus (GDM.)

Gestational diabetes is a type of diabetes that develops in non-diabetic women **during pregnancy**, particularly in the late second and early third trimesters.

It **usually** resolves after birth, but can progress to chronic diabetes in a small fraction of cases.

The underlying mechanism is similar to that of type 2 diabetes, featuring insulin resistance, and **obesity** is likewise also a risk factor.

QUESTION 24

What are the outcomes in the fetus or newborn if GDM is not treated?

One of the most common effects is that the newborn's blood glucose will **sharply drop** after birth when the baby is no longer connected to the mother's bloodstream via the umbilical cord.

Glucose in the mother's blood can pass freely through the placenta into the fetus's circulation, triggering fetal **insulin production**.

When the baby is cut off from this source of glucose, the high insulin levels will quickly deplete the available glucose, causing rapid **hypoglycemia**.

It can also cause problems such as **pancreatic hyperplasia** as the fetus has adapted to needing to produce high levels of insulin in the womb.

Abundant glucose availability can also lead to **macrosomia**, or birth of a baby who is **large for gestational age** (LGA.)

This in turn increases the likelihood of intrapartum complications and potentially the need for a Caesarean section.

QUESTION 25

Describe hypo- and hyperparathyroidism.

Hypoparathyroidism and **hyperparathyroidism** refer, respectively, to the under- or over-production of **parathyroid hormone** (PTH) in the **parathyroid glands** (adjacent to the thyroid.)

Pay attention to the **whole word** on exams: **hypoparathyroidism** and **hypothyroidism** are **completely different** conditions with different causes and symptoms!

QUESTION 26

Describe the consequences of parathyroid disorders.

The major function of **parathyroid hormone** in the body is the regulation of **calcium** absorption and storage.

Higher levels of PTH will **increase** serum calcium by stimulating **osteoclast** activity and enhancing **renal** and **intestinal** (re)absorption of calcium.

As such, **hyperparathyroidism** results in **hypercalcemia**—abdominal pain, weakness, arrhythmias, etc.—and decreased **bone density** from resorption of bone calcium.

Hypoparathyroidism results in **hypocalcemia** and the associated symptoms: numbness, spasm, hyperreflexia, seizures, or even cardiac arrest.

Primary hyperparathyroidism results from the **overgrowth** of the parathyroid glands, leading to an excessive production of parathyroid hormone.

This results in a state of **hypercalcemia**, or excessive calcium in the blood, because calcium is being reclaimed from the bones when it is not needed.

Secondary hyperparathyroidism, on the other hand, is the result of a normal physiological response to **hypocalcemia**, usually due to **kidney disease** and the excess loss of calcium in the urine.

In response to low calcium levels, the parathyroid glands initiate the normal response, which is to leech calcium from the bones to fuel the body's needs.

Over time, this can result in serious decreases in bone density, just like primary hyperparathyroidism.