AUTOIMMUNITY & HYPERSENSITIVITY

(CHAPTER 14)

QUESTION 1

Compare autoimmunity with hypersensitivity. Give some examples of each.

hypersensitivity – an umbrella term for an inappropriate or exaggerated immune response to a substance, foreign or otherwise (e.g. allergies, or...)

autoimmunity – a hypersensitive immune response to the body's **own tissues** (e.g. lupus, type 1 diabetes)

alloimmunity – a hypersensitive immune response to the presence of **someone else's tissues** (e.g. organ rejection, HDN)

QUESTION 2

What characterizes a type I hypersensitivity reaction? Give an example.

Hypersensitivity reactions are categorized according to the **underlying process** that causes them.

Type 1 reactions are classified as "**IgE-mediated**" due to the role of **immunoglobulin E** in causing them.

Type I reactions include things such as **seasonal allergies**, **food allergies**, and **asthma**.

These reactions develop due to improper activation of **antibody production** in the presence of an unrecognized substance.

Helper T cells (CD4 cells) "notice" the foreign substance and trigger **B cells** (another type of lymphocyte) to begin producing IgE antibodies to the allergen.

After repeated exposures, the amount of IgE in the blood steadily increases until it is enough to produce an immune response.

When these antibodies detect the presence of the allergen again, they bind to and trigger **mast cells**, a type of granulocyte (also a form of WBC.)

The mast cells then **degranulate**, dumping **histamine** into the extracellular space and producing **leukotrienes** and **prostaglandins**, leading to an inflammatory response.

This reaction can include:

- **swelling**, **pruritus** (itching,) **runny nose**
- **urticaria** (hives)
- cardiac **dysrhythmias**
- drop in blood pressure (**hypotension**)

QUESTION 3

Identify a severe example of a type I reaction.

The most severe form of type I hypersensitivity reaction is **anaphylaxis**.

Swelling and bronchospasm contribute to **respiratory distress**, and combined with a sudden drop in BP can lead to **anaphylactic shock**.

QUESTION 4

What characterizes a type II reaction? Give an example.

Type II reactions are classified as **tissue-specific**, because they are caused by the immune system responding to a **particular type** of tissue (either autoimmune or alloimmune.)

Unlike type I reactions, type II reactions are mediated by **IgG** and **IgM**.

This type of response can lead to the **destruction** or **malfunction** of the target cell, depending on the nature of the specific disorder.

One example of a type II reaction is **Graves' disease**, a type of **hyperthyroidism**.

Antibodies form that target the **receptors** for **thyroid stimulating hormone** (TSH) on the thyroid, **triggering** them and causing the thyroid to become **overproductive**.

This category also includes:

- **transfusion reactions** and **hemolytic disease of the newborn** (but **not** transplant rejection)
- Many autoimmune disorders that result in damage to a **specific organ**:
  autoimmune hepatitis, autoimmune hemolytic anemia, myasthenia gravis

QUESTION 5

What characterizes a type III reaction? Give an example.

Type III reactions are classified as **immune complex-mediated** and typically have **systemic** effects, targeting more than one organ (although the effect may be **greatest** in one organ.)

Immune complexes are clumps of antibodies bound together with free-floating antigens in the blood.

When antibodies are created targeting the body's **own** proteins (autoantigens,) immune complexes can accumulate **faster** than the immune system can deal with them.

These complexes can get "stuck" in various tissues, leading to **inflammation** and **tissue damage** when leukocytes show up to deal with them.

Examples of type III reactions include **systemic lupus erythematosus** (SLE,) **rheumatoid arthritis**, and **serum sickness** (an adverse reaction to certain types of drugs or blood plasma donation.)

QUESTION 6

What characterizes a type IV reaction? Give an example.

Type IV reactions are classified as **cell-mediated** and are the only type of hypersensitivity reaction which **do not** directly involve antibodies.

Rather, they are caused by **overactive** CD4 "helper T" cells triggering CD8 cytotoxic "killer T" cells to induce **apoptosis** of healthy cells.

In contrast to types I-III, which tend to occur fairly quickly in response to a stimulus, type IV are also known as **delayed hypersensitivity reactions** and can take several **days** to develop after exposure.

Examples include **contact dermatitis** (e.g. poison ivy,) **type 1 diabetes mellitus**, **inflamatory bowel disease**, **Hashimoto's thyroiditis**, and **multiple sclerosis**.

Type IV hypersensitivity is also responsible for the induration and erythema seen in a positive **TB skin test**, which is why you need to return in 2-3 days after placement of the intradermal tuberculin to have the test read.

QUESTION 7

What makes an anaphylactic reaction life-threatening?

The primary reasons that anaphylaxis is so dangerous are **respiratory distress** due to inflammation of the airways and bronchospasm, and **anaphylactic shock** (sudden, severe drop in blood pressure.)

Combined, these two factors can lead to extreme systemic hypoxia and ultimately death, if the patient's oxygenation status is not improved.

QUESTION 8

What are the two types of immunodeficiencies? What is the hallmark of immunodeficiency?

primary (congenital) immunodeficiency – an **inherited** immunodeficiency that is **present at birth** and not caused by an underlying condition

This includes **DiGeorge syndrome** (decreased/absent production of T-cell lymphocytes,) as well as problems with **B-cell or complement production**.

secondary (acquired) immunodeficiency – an immunodeficiency which is **caused by** (secondary to) another condition which was not present at birth

This includes **acquired immunodeficiency syndrome** (AIDS,) **leukemia**, **stress** or **trauma**, etc.

The typical result of any type of immunodeficiency (primary or secondary) is the occurrence of **opportunistic infections**.

Impaired immune response makes it **easier** for pathogens to invade the body and multiply before the immune system can stop an infection from happening.

QUESTION 9

Give an example of an acquired immunodeficiency. Why is this a concern in elderly patients?

Some examples:

In **HIV/AIDS**, the virus attacks and kills CD4 T cells in the bloodstream.

Leukemia prevents the bone marrow from producing WBCs that function properly.

Multiple myeloma is a cancer of the B cells which results in impaired antibody production.

Acquired immunodeficiency is a concern in elderly patients because the immune system naturally **slows down** with age, leaving older patients **more susceptible to infection** and less capable of fighting off infection when it occurs.

QUESTION 10

What is scleroderma? Which sex is more likely to be affected? Is it common?

Scleroderma is an autoimmune disease primarily affecting the **skin**, although it is a **type III hypersensitivity** so it can also have systemic effects.

It results in **hardened patches of skin**, sometimes involving the underlying muscle and bone causing apparent deformity, as well as shortness of breath, kidney failure, and a wide range of other problems.

Scleroderma is **fairly rare**, affecting roughly 40/100,000 people, and like almost all forms of autoimmunity, **primarily affects women**.

QUESTION 11

What is systemic lupus erythematosus (SLE?) How does this disorder affect the body?

Systemic lupus erythematosus (SLE) is another form of **type III hypersensitivity** with diffuse systemic effects. It involves the production of antibodies to several types of autoantigens, resulting in the immune system damaging tissues **throughout the body**.

The most common symptoms include **fatigue**, **joint pain**, **photosensitivity** of the skin, and **chest pain**/**dyspnea**.

As a type III hypersensitivity, the severity of lupus symptoms tends to fluctuate with the level of immune complexes in the body, with periodic **flares** interspersed with periods of remission.

Like autoimmunity in general, SLE is also **more common in women** than in men.

QUESTION 12

What is the hallmark of SLE?

The most immediately recognizable sign of lupus is called a **malar rash** or "butterfly rash" across the upper cheeks, just below the eyes.

It appears in **about half** of SLE patients, and may persist for years or can come and go, especially with exposure to sunlight.