IMMUNE DISORDERS

(CHAPTER 14)

QUESTION 1

Define hypersensitivity, allergy, autoimmunity, and alloimmunity.

hypersensitivity – an umbrella term for an inappropriate or exaggerated immune response to a substance, foreign or otherwise

In general, this covers three distinct types of immune "overreaction"...

allergy – an hypersensitive immune response to a foreign but non-harmful substance (allergen)

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

List the four types of hypersensitivity. Give an example of each.

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

This is **different** from the autoimmune/alloimmune distinction! Here, we're looking at **why** the immune system is misbehaving.

Don't worry—these categories will be overwhelming at first, but we'll go into more detail on each.

Type I (**IgE-mediated**) – allergies, asthma, anaphylaxis

Type II (**tissue-specific**) – Graves' disease, transfusion reactions

Type III (**immune complex-mediated**) – lupus, rheumatoid arthritis

Type IV (**cell-mediated**) – type 1 DM, contact dermatitis

QUESTION 3

Describe type I hypersensitivity reactions.

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 4

What does it mean for an individual to be "atopic?"

Atopy (or being "atopic") refers to an individual's hypersensitivity to non-harmful environmental factors —in other words, having **allergies**.

Atopy can present itself in any number of ways depending on the particular allergen(s) someone is sensitive to:

atopic deramtitis (**eczema**,) allergic rhinitis (such as **seasonal allergies**,) extrinsic **asthma**, etc.

QUESTION 5

Describe anaphylaxis.

Anaphylaxis is a severe and potentially **life-threatening** form of type I hypersensitivity reaction, caused by an extreme immune response to an allergen.

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

QUESTION 6

Describe Graves' disease.

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 7

Describe a type III hypersensitivity reaction.

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 8

Describe a type IV hypersensitivity reaction.

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 9

Describe some examples of autoimmunity.

Autoimmunity refers to any type of hypersensitivity reaction in which the immune system is targeting or attacking the body's **own tissues**.

These are typically going to fall into categories II through IV (remember that type I represents allergies in which there is an external irritant.)

There are **many** examples of autoimmunity, some of which we've talked about already:

Type II – Graves' disease, autoimmune hepatitis

Type III – lupus, rheumatoid arthritis, scleroderma

Type IV – type 1 DM, IBD, Hashimoto's thyroiditis

and **MANY** more!

QUESTION 10

What are the four stages of rheumatoid arthritis?

Like other type III reactions, RA tends to flare up and then remit over time. However, cumulative damage can cause the symptoms to worsen as the disease progresses.

This is not a guaranteed path for everyone who suffers from RA, but generally the symptoms will gradually worsen over the course of years.

Stage 1 (**early RA**) is still mild and hasn't yet caused any permanent damage. The synovial lining of the joint becomes inflamed, causing swelling.

Stage 2 (**moderate RA**) occurs when the damage begins to affect the cartilage. Range of motion may decrease, but there is little to no deformity at this point.

Stage 3 (**severe RA**) begins to involve the bone, as the cartilage is worn down and the joint begins to malfunction. This is when the classic joint deformities of RA tend to appear.

Stage 4 (**end-stage RA**) is characterized by complete destruction of the joint, often with the bones fusing together into a permanently deformed shape.

QUESTION 11

What are transfusion reactions?

Transfusion reactions occur when the body's immune system rejects the **foreign blood cells** introduced during a blood transplant.

Acute hemolytic reactions occur when there is incompatibility in the **ABO blood types** of the donor and the recipient.

Blood type is based on the presence or absence of two different antigens on the surface of **red blood cells**, known as **A** and **B**.

Individuals are classified as **A**, **B**, **AB**, or **O** based on whether their body produces RBCs with one, both, or neither antigen present.

When a person is exposed to antigens which they do not **naturally have** on their own RBCs, this can lead to the immune system **attacking** the donated blood cells.

For this reason, the donor must not have **any** antigens the recipient does not already have: e.g. A can donate to AB, but B cannot donate to A or O.

Because type AB blood already has **both** antigens, the body of a person who naturally produces type AB blood will not recognize either antigen as foreign.

This means that they can receive from any other ABO type, making type AB the **universal recipients**.

Because type O blood has **neither** antigen, there is nothing present on type O RBCs for anyone else's immune system to react to.

This means that anyone can safely receive type O blood, making type O the **universal donor**.

QUESTION 12

How is transplant rejection classified based on time?

Graft rejection falls into three categories based on the speed with which it occurs:

Hyperacute rejection occurs fast, usually in about a day, but is uncommon as it means the host **already** has antibodies against the grafted tissue.

Acute rejection is fairly rapid and usually occurs within the first three months. The intensity varies, but it almost **always** occurs to some degree.

Chronic rejection is slower and results in slow damage to the transplanted organ over many years.

QUESTION 13

Contrast primary immunodeficiency with secondary 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.

QUESTION 14

Contrast graft-versus-host disease and host-vs-graft disease.

Graft-versus-host disease (GvHD) and **host-versus-graft disease** (HvGD) are two examples of **alloimmunity**.

The process in each is similar, but as the names suggest, they occur in **different directions**.

In **graft-versus-host disease**, some WBCs from the organ or tissue **donor** make their way into the recipient, often in bone marrow or stem-cell transplants.

These cells recognize their new environment as foreign, causing them to attack the **recipient's body**.

In **host-vs-graft disease**, it is the **recipient's** immune system that recognizes the implanted organ or tissue as foreign and attacks the new tissues.

This results in the new tissue being damaged or destroyed, in a process known as **transplant rejection**.