Hypersensitivity is an exaggerated immunologic response, or overreaction, to a foreign antigen or autoimmunity (i.e., a physiological response against an endogenous "self"-antigen). This overreaction is a form of protection to alert the body to an actual or potential health problem. Hypersensitivity reactions are not due to antigens directly but from the inflammatory processes generated by antibodies, immune complexes, or cell-mediated responses.

Immediate hypersensitivity is mediated by IgE antibodies, which result in an allergy, anaphylaxis, or atopic disease. The NP should expect the client to have a type 1 hypersensitivity to recent medication use, which can include these immediate reactions as clinical manifestations: urticaria, wheezing, vomiting, and diaphoresis.

Hypertension and bradycardia are not associated with immediate hypersensitivity reactions.

Characterized by the rapid release of proinflammatory mediators like histamine, leukotrienes, and cytokines in response to allergen exposure, mast cells are the primary effector cells responsible for initiating and mediating type 1 hypersensitivity reactions.

Type 3 hypersensitivity reactions involve the formation of immune complexes that can deposit in tissues, leading to complement activation and inflammation. This process can cause tissue damage and is associated with systemic lupus erythematosus (SLE) and serum sickness.

Type 1 reactions are mediated by IgE antibodies, and type 2 are mediated by IgG or IgM antibodies. Type 4 reactions are activated by T-helper cells.

Anaphylactic Reaction

1. Antigen
2. B-cell
3. Plasma cell
4. IgE
5. Mast cell

- Histamine

Think Acid

- **A:** Allergic/Anaphylactic/Atopic (Type 1)
- **C:** Cytotoxic (Type 2)
- **I:** Immune Complex (Type 3)
- **D:** Delayed (Type 4)

A type 2 cytotoxic reaction is mediated by IgG or IgM antibodies.

1. Anti-A antibodies in type B blood mix with type A blood
2. Antibodies attach to surface antigen of type A RBC
3. Complement activated, type A RBC cell wall attacked
4. Lysis of type A RBC
5. Phagocytosis

A type 3 reaction is mediated by immune complexes.

Immune complex

1. Antibodies bind to antigens
2. Immune complexes form
3. Complexes deposit in blood vessels or tissues
4. Activation of complement
5. Inflammatory response at site of deposit
6. Release of lysosomal enzymes and chemical mediators
7. Tissue damage

A type 4 delayed reaction is mediated by cellular response.

1. Macrophage presents antigen
2. Sensitization of T lymphocyte
3. Release of lymphokines
4. Inflammation and lysis of antigen-bearing cells in the tissue
5. Tissue destruction

**Patho of Type 1 reactions**

Type 1 hypersensitivity reactions, also known as immediate hypersensitivity reactions, are characterized by the rapid release of proinflammatory mediators like histamine, leukotrienes, prostaglandins, and cytokines in response to allergen exposure. These local or systemic effects are mediated by IgE antibodies, which result in an allergic reaction, anaphylaxis, or atopic disease.

Physiological manifestations include the following:

- vasodilation
- bronchial smooth muscle contraction
- mucus production

The most common allergic reactions are type 1 reactions to environmental antigens (e.g., pollen, insects [bee venom], tree nuts, and medications). Allergic reactions can also occur to foods, latex, animal hair, and pet dander.

## Type 1: Allergic rhinitis

Allergic rhinitis, often referred to as hay fever, is a common type 1 hypersensitivity reaction and involves immunoglobulin E (IgE) mediated release of antibodies to the antigen. This results in mast cell degranulation, release of histamine, and other inflammatory mediators. Mast cells are the primary effector for initiating and mediating type 1 reactions.

**Symptoms:**

- Itchy eyes or nose
- Sneezing
- Running nose
- Watering of the eyes
- Nasal congestion

**Allergic triggers:**

- Indoor
    - Dust mites
    - Animal dander
    - Cigarette smoke
- Outdoor
    - Mold spores
    - Pollen

CASE STUDY:

Allergic rhinitis attacks are related to ongoing exposure to specific offending agents. The strongest risk factor for developing asthma is a history of atopic disease (the client has eczema, a form of atopic dermatitis). Environmental factors and allergens—such as high humidity, cold, dry weather, house dust mites, pet fur, and pollen—can place a client at risk for a new diagnosis of allergic asthma.

With prior exposure to allergens, Camille was sensitized. Chronic exposure to allergens mediated IgE antibodies to attach to sensitized cells, and with further exposure, IgE caused sensitized cells to degranulate. When degranulation occurs, inflammatory mediators like histamine, leukotrienes, and prostaglandins are released to produce several effects on the body, such as shortness of breath and wheezing. Constriction of bronchial smooth muscle also occurs, which explains her respiratory symptoms: shortness of breath, cough, and wheezing. The NP can diagnose the client with a type I hypersensitivity reaction based on localized and systemic symptoms.

The client's age and history of hypertension are not risk factors.

## Patho of Type 2 reactions

Type 2 hypersensitivity reactions are immune reactions against a specific cell or tissue. Cells express various antigens on their surfaces, while others are expressed on the membranes of only specific cells (called tissue-specific antigens). Altered tissue-specific antigens are bound by autoantibodies, resulting in tissue destruction by macrophages, neutrophils, natural killers, or complement cells.

The symptoms of many type 2 reactions are determined by the tissue or organ that expresses the antigen. For example, heparin-induced thrombocytopenia (HIT) is a tissue reaction where the immune system causes your platelets to clot when introduced to heparin, which puts a client at risk of developing life-threatening blood clots. It also results in platelet levels dropping (thrombocytopenia) and the risk of uncontrolled bleeding.

Cytotoxic hypersensitivities can occur with hemolytic transfusions. The client's blood must be typed and cross-matched to prevent possible cytotoxic hypersensitivities.

**Type 2 Cytotoxic Hypersensitivity**

1. Anti-A antibodies in type B blood mix with type A blood.
2. Antibodies attach to the surface of antigen of type A blood.
3. Complement is activated, and type A blood cell wall is attacked.
4. Lysis of type A blood occurs.
5. Phagocytosis occurs when the macrophage consumes the destroyed type A blood.

Type 2: Graves' disease

Macrophages are the primary effector cells of type 2 responses. A type 2 hypersensitivity response begins with the antibody binding to the antigen and may cause the following:

- the cell to be destroyed by the antibody
- cell destruction through phagocytosis by macrophages
- damage to the cell by neutrophils triggering phagocytosis
- natural killer cells to release toxic substances that destroy the target cell
- malfunction of the cell without destruction

For example, Graves' disease is caused by the production of IgG autoantibodies that bind to and stimulate the thyroid-stimulating hormone (TSH) receptor on thyroid follicular cells. This causes cellular malfunction without destruction, thyroid gland growth, and an overproduction of thyroid hormones (hyperthyroidism).

Graves' disease symptoms include bulging eyes, enlarged thyroid (goiter), arrythmia and tachycardia, nausea and diarrhea, tremor, change in menstrual cycles (in females), muscle weakness, headache, weight loss, anxiety and irritability, and increased perspiration.

## Type 2 hemolytic transfusion reaction

A hemolytic transfusion reaction is a severe complication that can occur after a blood transfusion. The transfused red blood cells (RBCs) are destroyed by the client's immune system.

Case Study:

M. G., a 27-year-old healthy female, required a blood transfusion 4 hours post-partum after undergoing a C-section. Twenty-four hours later, she and her newborn were released from the hospital in good health. Approximately 1 week later, she came to the primary care office complaining of fever, chills, shortness of breath (dyspnea), and a backache.

The nurse practitioner (NP) conducts an exam and the subjective and objective findings reveal the following:

**Subjective:**

- Fever
- Chills
- Shortness of breath (dyspnea)
- Backache

**Objective:**

- Fever 100.1 °F (37.8 °C)
- Blood pressure 100/64 mmHg
- Pulse 110 bmp
- Respirations 20/min
- Scleral icterus

*Lab Work:*

- Hemoglobin 6.2
- Platelet and leukocyte count are normal
- Positive direct and indirect Coombs test—revealed the presence of antibodies

Once again, let's rely on our knowledge of pathophysiology to explain why M. G. is presenting with these symptoms. The NP notes that the only new occurrence with the client was the blood transfusion that she received approximately a week ago post-