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Immediate and cell mediated hypersensitivity

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Abstract
Body produces too much of antibody, wrong kind of antibody, large number of antigen antibody complexes and antibodies to proteins that aren't really foreign. A hypersensitivity reaction is an extreme or unnecessary immune response that the body has to an antigen. Each type of hypersensitivity reaction is an extreme immune response to an antigen. Each type of reaction differs based on the type of antigen the body identifies, what type of immune response the body generates, and how quickly the body produces the response. Sometimes hypersensitivity reactions are referred as allergies, as these are a form of hypersensitivity. But these terms can be used interchangeably, an allergic reaction typically refers to the signs and symptoms an animal may experience, while a hypersensitivity reaction describes the immunological process that occurs in the body.

Keywords: Antibody, immune response, antigen, allergy, hypersensitivity reaction, immunological process

Introduction
Type I hypersensitivity occurs as a result of exposure to an antigen. The response to the antigen occurs in two stages: the sensitization and the effect stage. In the "sensitization" stage, the host experiences an asymptomatic contact with the antigen. Subsequently, in the "effect" period, the pre-sensitized host is re-introduced to the antigen which then leads to a type I anaphylactic or atopic immune response (Connors *et al.,* 2018) [3]. Type IV hypersensitivity reactions are, to some extent, normal physiological events that help fight infections, and dysfunction in this system can predispose to multiple opportunistic infections. Adverse events can also occur due to these reactions when an undesirable interaction between the immune system and an allergen happens (Gulsen *et al.,* 2020) [5].

Type I (Immediate) hypersensitivity
Reaction is immediate and severe. Symptoms are due to histamine and vasoactive amines. Reaction is generally termed as 'Allergy' (Mertes *et al.,* 2019) [10].

Anaphylaxis
Rare, life threatening, immediate allergic reaction to something injected or ingested. It can cause shock, respiratory & cardiac failure, death. It is caused by stinging insects, antibiotics, vaccines, hormones, medications, foods. It is characterised by fast heart rate, weak pulse rate, pale gums and cold limbs with no facial swelling (Joshi and Khan, 2021) [6].

Fleabite allergy or fleabite dermatitis
Seasonal allergy that is worse during peak flea times (summer)**.** Flea and flea dirt (faeces) act as allergen. Animal bite at base of tail and scratch frequently. It is characterised by itch over whole body, generalised hair loss and red inflammed skin (Tsao *et al.,* 2022) [13].

Urticaria and Angio-oedema
It is caused by hypersensitivity to drugs, chemicals, some food and even to sunlight. It develop within 20 minutes of exposure to allergen. Not life threatening and go away by themselves. Urticaria is characterised by small areas of swelling within skin. Hair stand erect over these swellings. and itching is noticed in these areas. Angio-oedema is characterised by swelling of face, especially muzzle and around eyes. Swelling is so severe – animal cannot open its eyes. It can affect throat, which leads to difficulty in breathing (Mayorga *et al.,* 2019) [8].

Atopy/Flea allergy dermatitis
It is caused due to inhalation of pollens and cat dander. Allergic reaction occurs within few minutes of exposure (Broyles *et al.,* 2020) [1].

Mechanism of immediate hypersensitivity
The sequence of mechanisms involved in immediate hypersensitivity are: a) Production of allergens (reagens) & IgE (reagenic antibody). b) Formation of mast cells, eosinophils and basophils. Mast cells have receptor for Fc portion of IgE. Mast cells have large granules in cytoplasm. Histamines and other amines responsible for allergic reactions are present in these granules. c) Generation of activated mast cells, which cause vascular leakage, vasodilation and broncho- constriction (Trivedi *et al.,* 2021) [12].

Type IV (Delayed/Cell mediated) hypersensitivity
No role of antibody in this type of hypersensitivity
It is mediated by Th1 cells that have been sensitized by a previous encounter with an antigen. Antigens eliciting Type IV reactions are those that cannot be removed by acute inflammatory response such as virus, fungi, bacteria, parasites, chemicals and foreign tissues (Garvey *et al.,* 2019) [4].

Contact hypersensitivity
It is an epidermal reaction characterized by eczema at site of contact with an allergen. Reaction occurs 48-72 hours after exposure of allergen. It is caused by nickel, chromate and chemicals in rubber. They are generally haptens that would not themselves be antigenic. They penetrate epidermis and become conjugated to normal body proteins and become antigenic (Pichler, 2022) [11].

Tuberculin type hypersensitivity
It is characterised by a firm red swelling of skin, 48-72 hours after exposure to allergen. Lesion resolves in 5-7 days, but if antigen persists, it develop into granulomatous reaction. The infiltrate of tuberculin reaction is composed of 80-90% monocytes (Chung *et al.,* 2022) [2].

Granulomatous hypersensitivity
This is clinically the most important form of Type IV hypersensitivity. During prolonged antigenic stimulation, activated macrophages differentiate into epithelioid cells and then to multinucleate giant cells in granulomatous tissue. Maximum time for granuloma development is 21-28 days (McNeil and Stefano, 2018) [9].

Mechanism of Delayed/Cell mediated hypersensitivity
The sequence of mechanisms involved in delayed/cell mediated hypersensitivity are: a) Following initial exposure to an antigen, a specific pool of memory T cells remain. Re-exposure to the antigen causes rapid proliferation of specific T cells at antigen entry site. b) Macrophages present processed antigen in association with MHC II to T cells. c) Production of basophils and eosinophils. d) Cytokines from lymphocytes and macrophages enhance inflammatory process in the affected area (Macy, 2020) [7].

Sensitisation
Haptens adsorbed to body proteins, processed by special cells, leave epidermis and migrate to paracortical areas of regional lymph nodes. Processed hapten-protein conjugates are presented to Th1 lymphocytes, producing a population of memory T cells. It's duration is 10-14 days (Broyles *et al.,* 2020) [1].

Elicitation
Langerhans' cells present allergen to memory Th1 cells. At the site of affected skin, activated T cells produce chemokines such as Migration Inhibition Factor (MIF) and Macrophage Chemotactic Factor (MCF). Keratinocytes are activated to produce a number of pro-inflammatory cytokines. It's duration is 48-72 hours (Mertes *et al.,* 2019) [10].

Suppression of inflammatory reaction
Suppression is mediated by PgE and TGF alpha. PgE is produced from macrophages and keratinocytes, while TGF alpha from keratinocytes and T lymphocytes. Ultraviolet light inactivates Langerhans' cells and the allergen undergoes natural degradation (Garvey *et al.,* 2019) [4].

Specific tests
These tests confirm sensitivity to a particular allergen. Skin tests are most convenient way to confirm specific sensitivity. The test solutions are extracts of inhaled, ingested or injected materials (Mayorga *et al.,* 2019) [8].

Prick/Puncture test
This test is usually performed first. Drop of dilute allergenic extract placed on skin. It is then pricked or punctured through the extract.: Diluent alone is used as negative control. The positive control employed is 10 mg/ml histamine (Trivedi *et al.,* 2021) [12].

Intradermal test
Dilute sterile extract is injected to produce 1-2 mm bleb (small blister). Diluent alone is used as negative control. The positive control employed is histamine (0.1 mg/ml). Positive result is indicated with a wheal and flare formation within 15 minutes, with a wheal diameter atleast 5mm larger than control (Gulsen *et al.,* 2020) [5].

Radio-allergo sorbent test (RAST)
It is performed when direct skin testing is impossible because of generalised dermatitis. Polymer-allergen conjugate is mixed with serum to be tested. It detects the presence of allergen- specific serum IgE. Quantity of allergen-specific IgE in circulation is determined by adding I125 labelled anti-IgE antibody (Joshi and Khan, 2021) [6].

WBC Histamine release
It is an *in-vitro* test, which detects allergen-specific IgE on sensitized basophils by measuring allergen- induced histamine release from patient's WBC (Garvey *et al.,* 2019) [4].

Provocative challenge
This is performed when a positive skin test raises question about the role of the particular allergen in the production of symptoms. Allergen may be applied to eyes, nose or lungs (Chung *et al.,* 2022) [2].

Conclusion
Type I hypersensitivity involve IgE immune reactant, heterologous antigens, mast cells and basophils as cells

involved in initiation, eosinophils as inflammatory cells. The target tissues are vascular endothelium and bronchial smooth muscle. Mechanism involves the production of antigen, IgE and mast cell release. The beneficial effects are parasitic immunity. Type
IV involve T lymphocytes as immune reactant, auto/heterologous antigens, APC and Th1 cells as cells involved in initiation, macrophages and keratinocytes as inflammatory cells. The target tissues are allografts. Mechanism involves cell mediated cytotoxicity and macrophage activation. The beneficial effects are immunity to *Mycobacterium tuberculosis*, viruses and other intracellular pathogens.

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