EJPMR, 2026, 13(1), 24-37 **Review Article** **Impact Factor 7.065**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

IMMUNOLOGICAL BASIS AND CLINICAL SPECTRUM OF HYPERSENSITIVITY REACTIONS: A SYSTEMATIC REVIEW

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DOI: https://doi.org/10.5281/zenodo.18092372

How to cite this Article: Dhanashree R. Patil*1, Nikhita H. Bhosale2, Sakshi M. Jakate3, Supriya B. Sabale4. (2026). Immunological Basis And Clinical Spectrum Of Hypersensitivity Reactions: A Systematic Review ". European Journal of Biomedical and Pharmaceutical Sciences, 13(1), 24–37.

Article Received on 23/11/2025 **Article Revised on 13/12/2025** **Article Published on 01/01/2026**

ABSTRACT

Hypersensitivity reactions represent exaggerated or inappropriate immune responses that result in tissue injury, chronic inflammation, or systemic complications. While the immune system primarily serves a protective role, these reactions reflect a pathological deviation where immune mechanisms themselves become harmful. Traditionally classified under the Gell and Coombs system into five types (I–V), hypersensitivity encompasses both antibody-mediated (Types I–III) and T-cell–mediated (Type IV) responses, with Type V describing stimulatory antibody activity as observed in Graves' disease. This review comprehensively explores the immunological basis, clinical manifestations, diagnostic modalities, and therapeutic interventions associated with hypersensitivity disorders. We analyse the molecular and cellular pathways underlying each type from IgE-mediated anaphylaxis to delayed-type hypersensitivity and correlate them with representative clinical entities such as autoimmune haemolytic anaemia, serum sickness, and Stevens–Johnson syndrome. Diagnostic advancements including allergen specific IgE testing, skin prick and patch assays, are critically evaluated for their precision and clinical applicability. Therapeutic strategies encompassing antihistamines, corticosteroids, epinephrine, monoclonal antibodies, and desensitization protocols are discussed with an emphasis on individualized treatment approaches. Despite significant progress, major knowledge gaps persist in predicting susceptibility and managing atypical or mixed-pattern immune responses. By delineating mechanistic distinctions among hypersensitivity types, this review underscores their diagnostic and therapeutic relevance, advocating for precision immunology and personalized care. Understanding these complex immune pathways not only enhances clinical decision-making but also paves the way for safer, targeted immunomodulatory therapies in hypersensitivity and related immune-mediated disorders.

KEYWORDS: Hypersensitivity, immune reaction, immune-complex and reaction autoimmune reaction, drug allergy, immediate response, delayed response.

INTRODUCTION

A medical condition known as hypersensitivity occurs when the immune system "over-reacts" to a foreign antigen, making the immune reaction itself more dangerous than the antigen.[1]

Most people may not experience hypersensitivity reactions, which are defined as excessive or inappropriate immune responses to a particular antigen. These reactions cause unwanted and sometimes harmful consequences on the body's tissues rather than offering protection.

Although the terms "allergy" and hypersensitivity are sometimes used interchangeably, it's crucial to keep in mind that hypersensitivity refers to the underlying immunological processes, while allergy defines the clinical symptoms.[2]

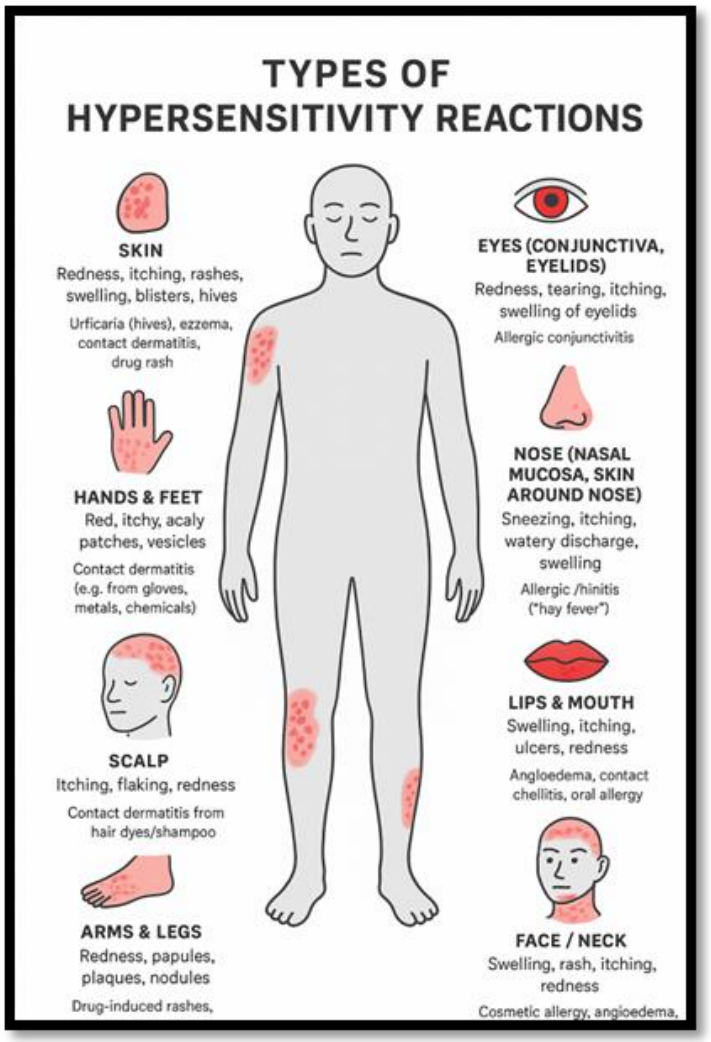
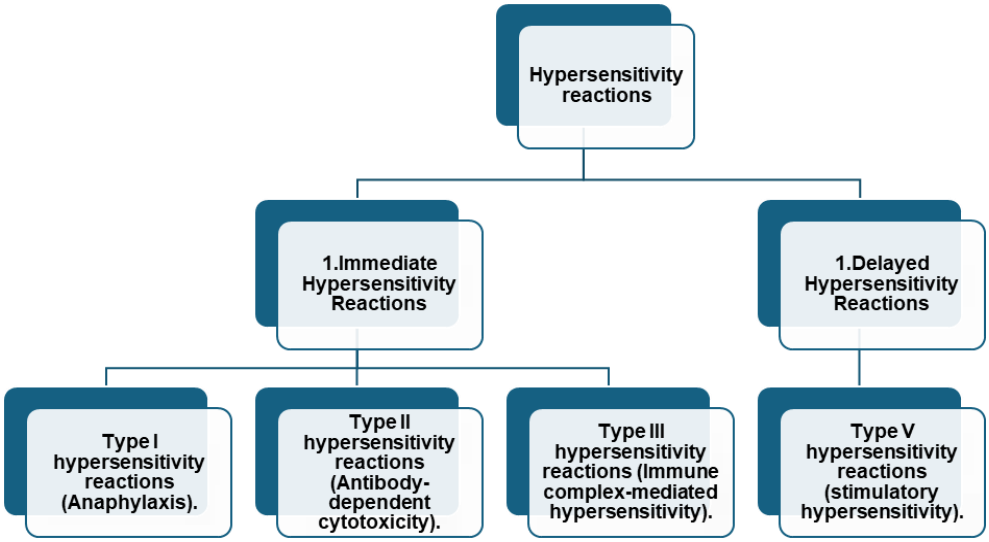


Figure no. 1: Hypersensitivity reaction.

Table no. 1: classification of hypersensitivity reaction.



Hypersensitivity reactions can be broadly manifested into two types[3-8]

1. Immediate Hypersensitivity Reactions
2. Delayed Hypersensitivity Reactions

Table no. 2: Difference between Immediate Hypersensitivity Reactions & Delayed Hypersensitivity Reactions.

Feature	Immediate Hypersensitivity Reactions	Delayed HypersensitivityReactions
Alternative Name	Also known as humeral hypersensitivity.	Commonly referred to as cell mediated hypersensitivity.
Onset of Reaction	Develops rapidly—typically within minutes to a few hours after exposure to the antigen.	Develops slowly, usually appearing 24–72 hours or even weeks after antigen exposure.
Mediating Mechanism	Mediated primarily by antibodies (IgE, IgG, IgM), complement system, mast cells, and basophils.	Mediated by T lymphocytes ($CD4^+$, $CD8^+$) and activated macrophages, rather than antibodies.
Immunologic Basis	Involves antibody-antigen interactions, leading to the release of chemical mediators and inflammatory responses.	Involves sensitized T cells that release cytokines, triggering macrophage activation and localized inflammation.
Time Course	Rapid, occurring within minutes or hours.	Delayed, developing over 1–3 days or longer.
Examples	Anaphylaxis, bronchial asthma, allergic rhinitis (hay fever), urticaria, food allergies, drug and venom allergies, autoimmune hemolytic anemia, rheumatic heart disease, serum sickness, rheumatoid arthritis, and certain types of vasculitis.	Contact dermatitis (e.g., poison ivy rash), Mantoux tuberculin skin test, graft rejection, some drug-induced hypersensitivities, and certain autoimmune conditions.

Types of hypersensitive reactions

According to the degree of harm brought about by the overreaction in the various immune system components, Phillip Gel and Robert Coombs divided hypersensitivity reactions into four categories in 1963.

These are

1) Type I hypersensitivity reactions (Anaphylaxis).
2) Type II hypersensitivity reactions (Antibody-dependent cytotoxicity).
3) Type III hypersensitivity reactions (Immune complex-mediated hypersensitivity).
4) Type IV hypersensitivity reactions (Delayed Type or Cell-mediated hypersensitivity).
5) Type V hypersensitivity reactions (stimulatory hypersensitivity).

Type IV is classified as a delayed-type hypersensitivity reaction, while the first three types of hypersensitivity reactions are classified as immediate hypersensitivity reactions.[9]

PURPOSE AND OBJECTIVES

The main purpose of studying hypersensitivity reactions is to understand, diagnose, and manage inappropriate immune responses that can cause tissue damage, chronic illness, and life-threatening conditions. This work relies on established frameworks, such as the Gell and Coombs classification, as a standard reference. purpose and objectives.

1) Decipher immune mechanisms

The main goal is to understand the cellular and molecular processes behind the four types of hypersensitivity reactions to tell the difference between a normal immune response and a harmful immune response.

2) Develop effective diagnostic tools

The objective is to create reliable ways to diagnose hypersensitivity, identify triggers like drugs or foods, and rule out other conditions. This includes testing methods like skin tests and lab assays for specific allergens.

3) Formulate targeted management strategies

The purpose is to create evidence-based treatment plans for reactions of any severity, from mild allergies to severe, life-threatening conditions like anaphylaxis or severe cutaneous adverse reactions like Stevens-Johnson syndrome. This involves researching treatments like corticosteroids, antihistamines, epinephrine, and more specific therapies.

4) Create preventative measures and patient education:

A central objective is to inform healthcare providers and patients about risk factors, prevention strategies, and the importance of trigger avoidance to reduce the frequency and severity of reactions.

5) Identify gaps for future research

By critically evaluating existing literature, studies aim to highlight unanswered questions and guide future research toward improving predictive tests, diagnostic algorithms, and therapeutic approaches to ultimately enhance patient outcomes and safety.

Type I hypersensitivity reactions (Anaphylaxis)

Anaphylactic or immediate hypersensitivity reactions, sometimes referred to as type I hypersensitivity reactions, happen 15–30 minutes and occasionally 6–8 hours after the antigen is first encountered. Antibodies against the soluble antigen are released through the action of immunoglobulin E (IgE).

Histamine and other inflammatory mediators are released as a result of mast cell degranulation.[10-11]

Type I hypersensitivity is an acute hypersensitivity brought on by an IgE antibody that causes anaphylaxis to food, medications, and insect venoms. The production of IgE antibodies to allergens causes these allergic reactions to be either local or systematic.

An antigen cross-link to a basophil or mast cell's membrane-bound IgE antibody results in the type I hypersensitivity reaction. During an anaphylactic reaction, histamine is released, which may result in internal tissue damage.[12-13]

Mechanism of Type I hypersensitivity reactions[14-17]

Table no. 3: Mechanism of Type I hypersensitivity reactions.

1] Sensitization Phase: The immune system learns to recognize a specific allergen upon initial exposure. APCs present the allergen to T-cells, which differentiate into TH2 cells. TH2 cells then instruct B-cells to produce allergen-specific IgE antibodies. These IgE antibodies then bind to the surface of mast cells and basophils, making these cells "sensitized" to the allergen.
2] Effector Phase: With subsequent exposure to the same allergen, the allergen binds to the IgE antibodies on the sensitized mast cells and basophils, causing cross-linking of the IgE receptors. This triggers the release of various chemical mediators.
3] Mediator Release: Mast cells and basophils release preformed mediators (e.g., histamine, proteases) and also synthesize new mediators (e.g., leukotrienes, prostaglandins).
4] Immediate Reactions: Histamine, a rapidly released mediator, causes effects like vasodilation, increased vascular permeability, smooth muscle contraction, itching, and increased mucus production, leading to the immediate symptoms of allergy.
5] Late-Phase Reactions: Over several hours, newly synthesized mediators lead to a more sustained inflammatory response, involving the recruitment of other inflammatory cells, contributing to chronic allergic conditions.
6] Anaphylaxis: In severe cases, systemic mediator release can cause a life-threatening reaction called anaphylaxis, characterized by widespread effects like bronchoconstriction and circulatory issues.

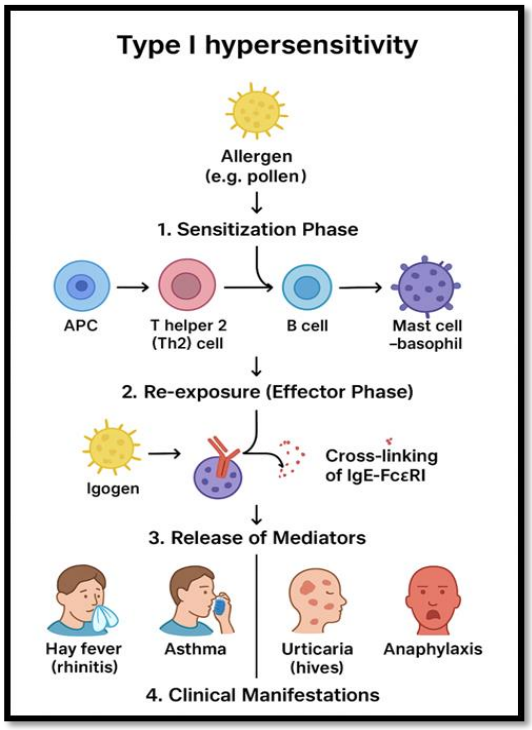


Figure no. 2: Type I hypesensitivity reactions.

Type II hypersensitivity reactions (Antibody-dependent cytotoxicity)

The term "type II hypersensitivity reaction" describes an immunological response mediated by antibodies. The destruction of cells was mediated by antibodies. Another name for this reaction is cytotoxic.

A particular antibody (IgG or IgM) attached to the cell surface antigen and killed the cell in this hypersensitive

reaction. Killing the cell is advantageous to the host if it is a bacterium.

An antibody-mediated immune response known as a type II hypersensitivity reaction occurs when antibodies (IgG or IgM) are directed against extracellular matrix or cellular antigens, leading to tissue damage, cellular death, or loss of function.[18-19]

Mechanism of Type II hypersensitivity reactions[20-22]

Table no. 4: Mechanism of Type II hypersensitivity reactions.

1] Complement Activation: Antibodies binding to target cells trigger the classical complement pathway. This leads to the formation of the membrane attack complex (MAC), which creates channels in the cell membrane, causing cell lysis and death. Complement activation also generates fragments (like C3a and C5a) that act as chemo attractants for neutrophils and other inflammatory cells. Neutrophils release cytotoxic enzymes and reactive oxygen species, leading to tissue damage. C3b acts as an opsonin, promoting phagocytosis of the targeted cells by macrophages. **2] Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC):** IgG or IgM antibodies bind to target cells, marking them for destruction. Effector cells, such as Natural Killer (NK) cells, recognize the Fc portion of the antibody via their Fc receptors. This binding triggers the release of cytotoxic granules, containing perforins and granzymes, which induce apoptosis (programmed cell death) in the target cell. **3] Antibody-Mediated Cellular Dysfunction**: In some cases, antibodies bind to cell surface receptors and alter their function without directly causing inflammation or cell lysis. Antibodies may block the receptor, preventing its normal activation. For example, in Myasthenia gravis, autoantibodies block acetylcholine receptors on muscle cells, leading to muscle weakness. Antibodies can also act as agonists, stimulating the receptor and leading to overactivity. In Graves' disease, antibodies stimulate the TSH receptor, causing hyperthyroidism.

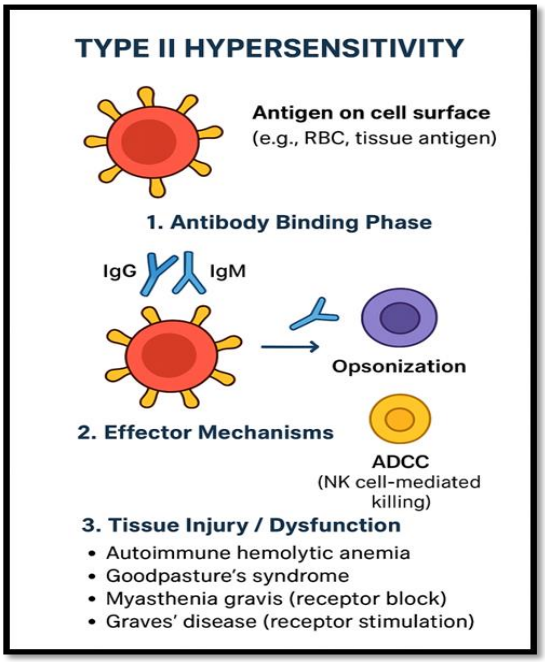


Figure no. 3: Type II hypersensitivity reactions.

Type III hypersensitivity reactions (Immune complex-mediated hypersensitivity)

An alternative name for it is immune complex hypersensitivity. Three to ten hours after being exposed to the antigen, the reaction can occur. IgG and IgM antibodies mediate type III hypersensitivities.

Comprising soluble immune complexes (aggregations of antigens, IgG, and IgM antibodies), type III hypersensitivity reaction (Immune Complex Mediate Reaction) is an abnormal immunological response.

Tissue damage during a type II immune response is caused by the production of IgG or IgM antibodies to

foreign or self antigens, which are then followed by complex formation.[23-26]

Mechanism of Type III hypersensitivity reactions[27-29]

Table no. 5: Mechanism of Type III hypersensitivity reactions.

1] Immune complex formation

Exposure to antigens (either endogenous self-antigens or exogenous foreign proteins) triggers the formation of antibodies, primarily IgG and IgM antibodies.

These antibodies bind to soluble antigens, forming immune complexes.

The size of these complexes is crucial to their pathogenicity. Smaller complexes, often formed when there is an excess of antigen, are more likely to escape the normal phagocytic clearance mechanisms of the liver and spleen.

These smaller, uncleared immune complexes circulate in the bloodstream.

2] Immune complex deposition

The circulating immune complexes deposit in various tissues throughout the body, particularly in the walls of blood vessels, glomeruli in the kidneys, and joints.

The highpressure filtration process in organs like the kidneys and joints makes them particularly susceptible to immune complex deposition.

Localized immune complex deposition in the skin at the site of antigen injection can also trigger a Type III reaction known as the Arthus reaction.

3] Inflammatory reaction and tissue damage

Once deposited in tissues, immune complexes activate the classical complement pathway.

Complement activation leads to the generation of potent inflammatory molecules, particularly C3a and C5a (anaphylatoxins).

These anaphylatoxins act as chemotaxin, recruiting inflammatory cells like neutrophils and macrophages to the site of immune complex deposition.

The recruited neutrophils attempt to engulf the deposited immune complexes. However, since these complexes are adhered to the tissues, the neutrophils are unable to fully phagocytose them.

In a process known as frustrated phagocytosis, the neutrophils release their lysosomal enzymes and reactive oxygen species into the surrounding tissues, causing inflammation and tissue injury.

This can lead to conditions such as vasculitis (inflammation of blood vessels), glomerulonephritis (inflammation of the kidney glomeruli), and arthritis (inflammation of the joints) depending on the site of immune complex deposition.

Platelet aggregation in the microvasculature can also be triggered by immune complexes, leading to the formation of blood clots and blockages, further contributing to tissue damage

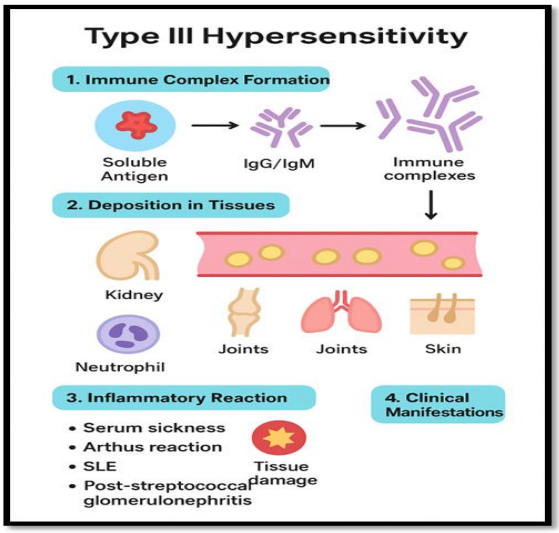


Figure no. 4: Type III hypersensitivity reactions.

Type IV hypersensitivity reactions (Delayed Type or Cell-mediated hypersensitivity)

A type IV hypersensitive reaction, sometimes referred to as cell-mediated hypersensitivity or delayed type hypersensitivity (DTH), happens when the skin comes into contact with certain allergens (contact dermatitis).

T cells that trigger an inflammatory response to antigens are the ones that cause it.

T-cell-mediated immune responses known as type IV hypersensitivity reactions usually appear 48 to 72 hours after antigen exposure, however they can appear weeks later. These reactions, in contrast to antibody-mediated reactions, include CD4+ and CD8+ T cells and result in tissue injury, inflammation, and the production of cytokines.[30]

Mechanism of Type IV hypersensitivity reactions[31-40]

Table no. 6: Mechanism of Type IV hypersensitivity reactions.

1] Initial Antigen Exposure & Sensitization Phase
Initial Antigen Exposure: The body first encounters the antigen (e.g., from poison ivy, certain pathogens).
Antigen Uptake by APCs: Antigen-presenting cells (APCs), such as dendritic cells, capture the antigen.
Antigen Processing & Presentation (MHC Class II): APCs process the antigen and present its fragments on MHC Class II molecules to CD4+ T cells.
Activation of CD4+ T cells (Th1/Th17): This interaction, along with costimulatory signals, activates specific CD4+ T cells, primarily Th1 or Th17 cells.
Differentiation into Effector & Memory T Cells: The activated T cells differentiate into effector T cells and antigen-specific memory T cells.
Sensitization Phase (Asymptomatic): This initial phase doesn't show symptoms but primes the immune system.
2] Subsequent Antigen Re-exposure & Effector Phase
Subsequent Antigen Re-exposure: The sensitized individual encounters the same antigen again.
Antigen Presentation by APCs: APCs again present the antigen.
Recognition by Sensitized Memory T Cells: The previously formed memory T cells recognize the antigen.
Activation & Proliferation of T Cells: This leads to the rapid activation and proliferation of these memory T cells. Release of Cytokines & Chemokines: Activated T cells, particularly Th1 and Th17 cells, release various cytokines (e.g., IFN-γ, TNF-α) and chemokines.
Recruitment & Activation of Macrophages: Cytokines like IFN-γ recruit and activate macrophages to the site of antigen exposure. Activated macrophages contribute significantly to inflammation.
Recruitment of Other Immune Cells (Neutrophils, Eosinophils): Chemokines recruit other immune cells, such as neutrophils and eosinophils, further amplifying the inflammatory response.
Activation of CD8+ Cytotoxic T Cells (CTLs): In some Type IV reactions (Type IVc), CD8+ T cells are activated and directly recognize and kill target cells.
Release of Inflammatory Mediators (Hydrolytic enzymes, ROS): Activated macrophages release hydrolytic enzymes, reactive oxygen species, and other inflammatory factors, which cause local swelling, redness, warmth, and potentially tissue damage.
Target Cell Killing (Perforin/Granzymes, Fas pathway): CD8+ T cells induce apoptosis in target cells using mechanisms involving perforin and granzymes or the Fas-Fas ligand pathway.
3] Tissue Damage & Visible Symptoms
Inflammation & Tissue Damage: The cumulative effects of cytokine release, macrophage activation, and immune cell recruitment lead to inflammation and tissue damage.
Tissue Damage: CD8+ T cells directly killing cells also contribute to tissue damage.
Visible Symptoms: These delayed inflammatory reactions become visible as symptoms like erythema, edema, induration, or blisters, typically 24-72 hours after re-exposure.

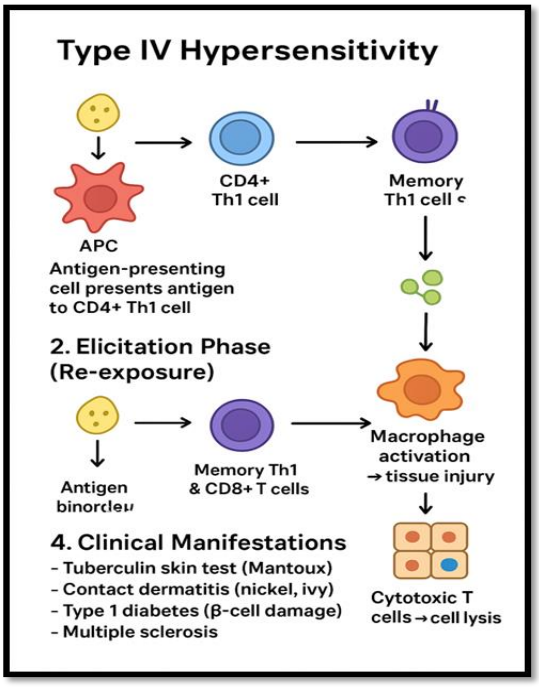


Figure no. 5: Type IV hypersensitivity reactions.

Subclassification of type IV hypersensitive reaction
Based on the predominant T cell populations, cytokines generated, and ensuing clinical symptoms, type IV hypersensitivity reactions—also referred to as Delayed-Type Hypersensitivity (DTH)—are further divided into four subgroups.[41-44]

Table No. 7: Subclassification of type IV hypersensitive reaction.

Subtype	Dominant Cells	Key Cytokines	Mechanism	Examples	References
Type IVa (Th1/Monocyte-Mediated)	Th1 cells, monocytes/macrophages	IFN-γ, TNF-α	Activated Th1 cells secrete IFN-γ and TNF-α, recruiting and activating monocytes and macrophages. This results in chronic inflammation and granuloma formation. Macrophages may form epithelioid and giant cells surrounding persistent antigens.	Sarcoidosis, tuberculosis, Crohn's disease.	[45–49]
Type IVb (Th2/Eosinophil-Mediated)	Th2 cells, eosinophils	IL-4, IL-5, IL-13	Th2 cells drive IgE production and attract eosinophils and mast cells, leading to eosinophil-dominant inflammation and tissue damage.	DRESS syndrome, allergic asthma, chronic allergic rhinitis.	[50–51]
Type IVc (Cytotoxic T Cell-Mediated)	$CD8^+$ cytotoxic T lymphocytes (CTLs)	Perforin, Granzyme B, Fas Ligand	CTLs migrate to affected tissues and induce apoptosis via perforin/granzyme B release and Fas/Fas-ligand interactions.	Stevens–Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), drug-induced hepatitis or pneumonitis, contact dermatitis.	[52–54]
Type IVd (Neutrophilic T-Cell-Mediated)	$CD4^+$ and $CD8^+$ T cells, Th17 cells	IL-8, GM-CSF	T cells release chemokines that recruit neutrophils, producing neutrophil-rich inflammation.	Acute Generalized Exanthematous Pustulosis (AGEP), pustular psoriasis.	[55–56]

Type V hypersensitivity reactions (stimulatory hypersensitivity)
It is a variant of Type-II hypersensitivity in which non-complement fixing antibodies attach to the target cell's surface receptors and cause an overabundance of cytotoxic substances to be secreted, which can activate phagocytes instead of eliminating the antigen directly.

Antibodies are produced in response to a particular hormone receptor found on a hormone-producing cell

According to Gary Kaiser (2021), "Grave's disease" is the best illustration of a type-V hypersensitivity reaction. It is brought on by antibodies attaching to certain thyroid cells at the thyroid-stimulating hormone receptor (TSH-R), which in turn causes an overabundance of thyroid hormone to be secreted.[57]

Mechanism of Type IV hypersensitivity reactions[57-59]
Table no. 8: Mechanism of Type IV hypersensitivity reactions.

1] Autoantibody Formation
The immune system produces autoantibodies that mimic natural ligands (e.g., hormones like TSH).
2] Autoantibody Binds to Receptor
These autoantibodies bind to cell surface receptors (e.g., TSH receptor on thyroid cells).
3] Receptor Activation
The autoantibody-receptor interaction activates the receptor.
Intracellular signalling is triggered (though not identical to natural ligand signaling).
4] Cell Stimulation
The cell is stimulated to produce hormones (e.g., thyroid hormone).
Leads to excessive hormone production (e.g., in Graves' disease).
5]Outcome
The stimulatory effect differs kinetically and functionally from that of natural ligands.
Results in disease symptoms due to unregulated cell activity.

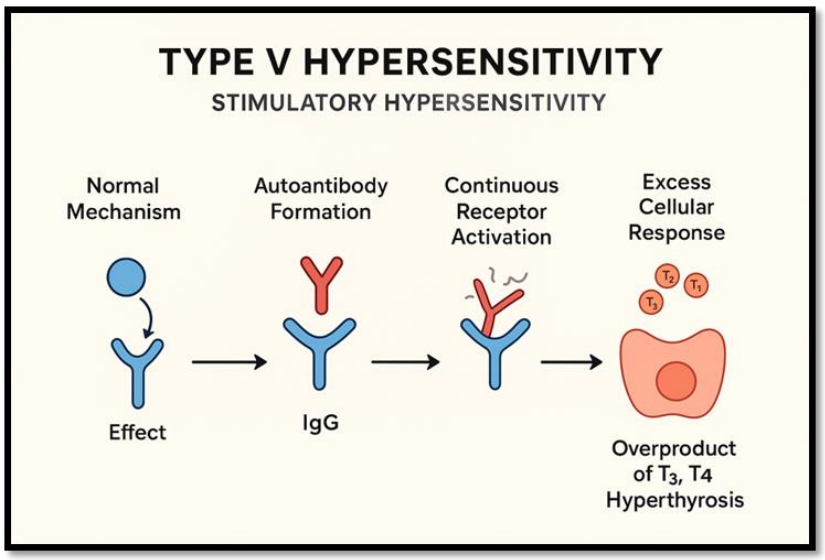


Figure no. 6: Type IV hypersensitivity reactions.

Body Parts / Organs Affected by Hypersensitivity Reactions[60-64]

Exaggerated or misguided immune responses, known as hypersensitivity reactions, have the potential to harm the body's own tissues. Almost every organ system may be impacted, depending on the underlying immunologic mechanism (Type I–V) and the type of triggering antigen (allergens, medications, infections, or self-antigens).

These reactions range from delayed T-cell-driven inflammatory responses (contact dermatitis, hypersensitivity pneumonitis, with autoimmune disorders) to acute IgE-mediated events (asthma, urticaria, and anaphylaxis). Both the tissue specificity of the antigen–antibody interaction and the kind of immune effector—antibody, complement, or T cell—affect the clinical results.

Depending on the immune response type (Type I–V) and the trigger (allergen, medication, infection, autoimmune target, etc.), hypersensitivity reactions can impact a wide range of human organs and tissues.

Given that hypersensitivity can resemble or coexist with viral and autoimmune diseases, an appropriate diagnosis, prognosis, and treatment targeting depend on an understanding of organ involvement. The main organ systems, the forms of hypersensitivity that are frequently linked to them, and typical clinical symptoms are included in the table below.

Table no. 9: Body Parts / Organs Affected by Hypersensitivity Reactions.

System / Organ	Commonly Affected Hypersensitivity Types	Examples / Manifestations
Respiratory system	Type I (IgE-mediated)	Asthma, allergic rhinitis (hay fever), airway inflammation, bronchoconstriction
Blood / Circulatory system	Type II (cytotoxic), Type III (immune-complex)	Haemolyticanaemia, transfusion reactions, serum sickness, vasculitis
Skin	Type I, II, III, IV	Urticaria (hives), eczema, contact dermatitis, drug rashes, Stevens–Johnson syndrome, toxic epidermal necrolysis
Mucous membranes (eyes, nose, throat)	Type I	Allergic conjunctivitis, rhinitis, throat swelling, angioedema
Liver	Type II, III, IV	Drug-induced hepatitis, autoimmune hepatitis
Heart	Type II	Rheumatic fever (antibodies cross-react with heart tissue), myocarditis
Nervous system	Type II, IV	Guillain–Barré syndrome, multiple sclerosis (autoimmune hypersensitivity)
Kidneys	Type III	Immune-complex glomerulonephritis, lupus nephritis
Joints	Type III	Rheumatoid arthritis (immune-complex and T-cell mediated)
Vessels (blood vessels, endothelium)	Type III, IV	Vasculitis (immune-complex or T-cell-mediated damage)
Lungs (alveoli, interstitium)	Type III, IV	Hypersensitivity pneumonitis (e.g., "farmer's lung"), drug-induced interstitial lung disease

Gastrointestinal tract	Type I, IV	Food allergies, celiac disease, inflammatory bowel diseases (autoimmune-type)

Formulation and Evaluation of a Dosage Form for the Management of Hypersensitivity Reactions[65-70]

In order to provide quick symptom alleviation, a long-lasting therapeutic effect, and patient compliance, it is essential to establish appropriate dose forms for treating hypersensitive responses. Different formulations are used, ranging from parenteral injections for life-threatening anaphylaxis to oral tablets for moderate episodes, depending on the severity, site of reaction, and pharmacokinetic requirements.

In order to make sure that every dosage form efficiently distributes the active agent to the target site, formulation science focusses on optimising drug delivery, start of action, and stability. Topical therapies lessen localised inflammation and pruritus, whereas inhalers and nebulisers offer localised airway relief in hypersensitivity related to asthma.

Analogously, ocular drops and nasal sprays minimise systemic exposure while offering tailored treatment for conjunctivitis and allergic rhinitis.

The common dose forms and their particular clinical use cases are compiled in the following table.

The following table summarizes the common dosage forms, their specific clinical use cases, and representative examples of drugs used in hypersensitivity management.

Table no. 10: Formulation and Evaluation of a Dosage Form for the Management of Hypersensitivity Reactions.

Dosage form	Use case	Example
Oral tablet / syrup	Mild to moderate allergic reactions	Cetirizine, Prednisone, Montelukast
IM/IV injection	Severe allergy, anaphylaxis	Epinephrine, Diphenhydramine, Hydrocortisone
Inhalers/nebules	Asthma, bronchospasm in allergy	Salbutamol, Budesonide
Topicalcreams/ointments	Contact dermatitis, urticaria	Hydrocortisone, Tacrolimus
Nasal sprays	Allergic rhinitis	Fluticasone, Azelastine
Eye drops	Allergic conjunctivitis	Olopatadine, ketotifen

Pharmacologic Management of Allergic and Hypersensitivity Disorders[71-83]

A complex pharmaceutical strategy is used to treat allergy and hypersensitive reactions in order to inhibit immunological hyperactivity, lower inflammation, and lessen symptoms. Drugs used to treat allergies work in a variety of ways, from suppressing histamine receptors to modifying cytokine signalling and promoting immunological tolerance.

The main therapeutic categories, their methods of action, clinical uses, administration routes, and noteworthy side effects or precautions are compiled in the table below. Knowing these classifications is crucial for maximising customised treatment plans and reducing side effects, especially in long-term allergic diseases like urticaria, asthma, atopic dermatitis, and anaphylaxis.

Table no. 11: Dosage Form and Administration in the Management of Hypersensitivity Reaction.

Category	Mechanism of Action	Examples	Common Uses	Administration	Notable Side Effects / Notes
1. Antihistamines	Block histamine receptors to prevent allergic symptoms.	First-gen: Diphenhydramine, Hydroxyzine Second-gen: Cetirizine, Loratadine, Fexofenadine	Allergic rhinitis, urticaria, conjunctivitis, angioedema	Oral, nasal spray, eye drops	First-gen can cause sedation. Second-gen are non-sedating.
2. Corticosteroids	Suppress inflammation and immune response by reducing inflammatory chemicals.	Fluticasone, Prednisone, Mometasone, Hydrocortisone	Asthma, eczema, severe allergies, nasal polyps	Oral, topical, nasal spray, inhaler, eye drops	Long-term use risks: osteoporosis, weight gain, infection, adrenal suppression.
3. Leukotriene Inhibitors	Block leukotrienes involved in inflammation and allergic reactions.	Montelukast (Singular)	Asthma, allergic rhinitis, exercise-induced bronchoconstriction	Oral	Black box warning for neuropsychiatric effects (esp. in children).
4.	Inhibit cytokine	Tacrolimus	Atopic dermatitis	Topical	Avoid long-term use

Immunomodulators	release from T-cells, dampening immune response.	(Protopic), Pimecrolimus (Elidel)		(creams/ointments)	on large areas due to potential immunosuppression and cancer risk (rare).
5. Monoclonal Antibodies	Target and block specific immune pathways (e.g., IgE, IL-4, IL-5).	Omalizumab, Mepolizumab, Dupilumab	Asthma, urticaria, nasal polyps, atopic dermatitis	Subcutaneous injection (typically by specialist)	Risk of injection site reactions, rare anaphylaxis, expensive, for moderate-severe cases.
6. Emergency Medication	Reverses life-threatening anaphylaxis by acting on alpha/beta adrenergic receptors.	Epinephrine (EpiPen, Auvi-Q)	Anaphylaxis	Auto-injector, IM/IV by professionals	Must be used immediately at symptom onset; follow with emergency care.
7. Desensitization /Immunotherapy	Gradual allergen exposure retrains immune tolerance.	Allergen-specific SCIT or SLIT protocols	Allergic rhinitis, insect sting allergy, allergic asthma	Injections (SCIT), sublingual tablets/drops (SLIT)	Requires close medical supervision; risk of allergic reaction during therapy.

CONCLUSION

Hypersensitivity reactions embody the paradox of the immune system its capacity to defend and its potential to destroy. As our understanding of immunological pathways deepens, it becomes evident that hypersensitivity is not merely an exaggerated immune response but a profound disturbance in immune regulation and tolerance. The five classical types of hypersensitivity, though well-characterized, continue to reveal new layers of complexity as emerging research uncovers overlapping mechanisms and novel mediators.

Advancements in immunodiagnostics, molecular profiling, and targeted immunotherapies are reshaping how clinicians identify and manage these disorders. Precision medicine now offers the promise of tailoring interventions to individual immune profiles, thereby minimizing adverse effects and maximizing therapeutic efficacy. Yet, significant challenges remain particularly in predicting susceptibility, recognizing atypical or mixed responses, and developing long-term, curative strategies.

A multidisciplinary approach integrating immunology, genetics, pharmacology, and clinical practice is crucial to translate scientific insights into meaningful patient outcomes. Strengthening clinician awareness, refining diagnostic accuracy, and expanding research into immune tolerance restoration are key steps toward reducing the global burden of hypersensitivity diseases.

Ultimately, the journey from understanding immune dysfunction to restoring immune balance represents the future of hypersensitivity management where prevention, precision, and personalization converge to transform patient care and improve quality of life.

Eventually, recognizing hypersensitivity not just as an overreaction, but as a dysregulation of immune tolerance, opens doors to more innovative, safe, and effective approaches to diagnosis, treatment, and prevention in the future of immunology.

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