VIVEKANANDA COLLEGE
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NAAC ACCREDITED 'A' GRADE

Topic: **Gell and Coombs' classification and brief description of various types of hypersensitivities**
Course Title: **CORE COURSE 10: Immunology**
Paper: **ZOOA-CC4-10-TH**
Unit: **Unit 8: Hypersensitivity**
Semester: 4
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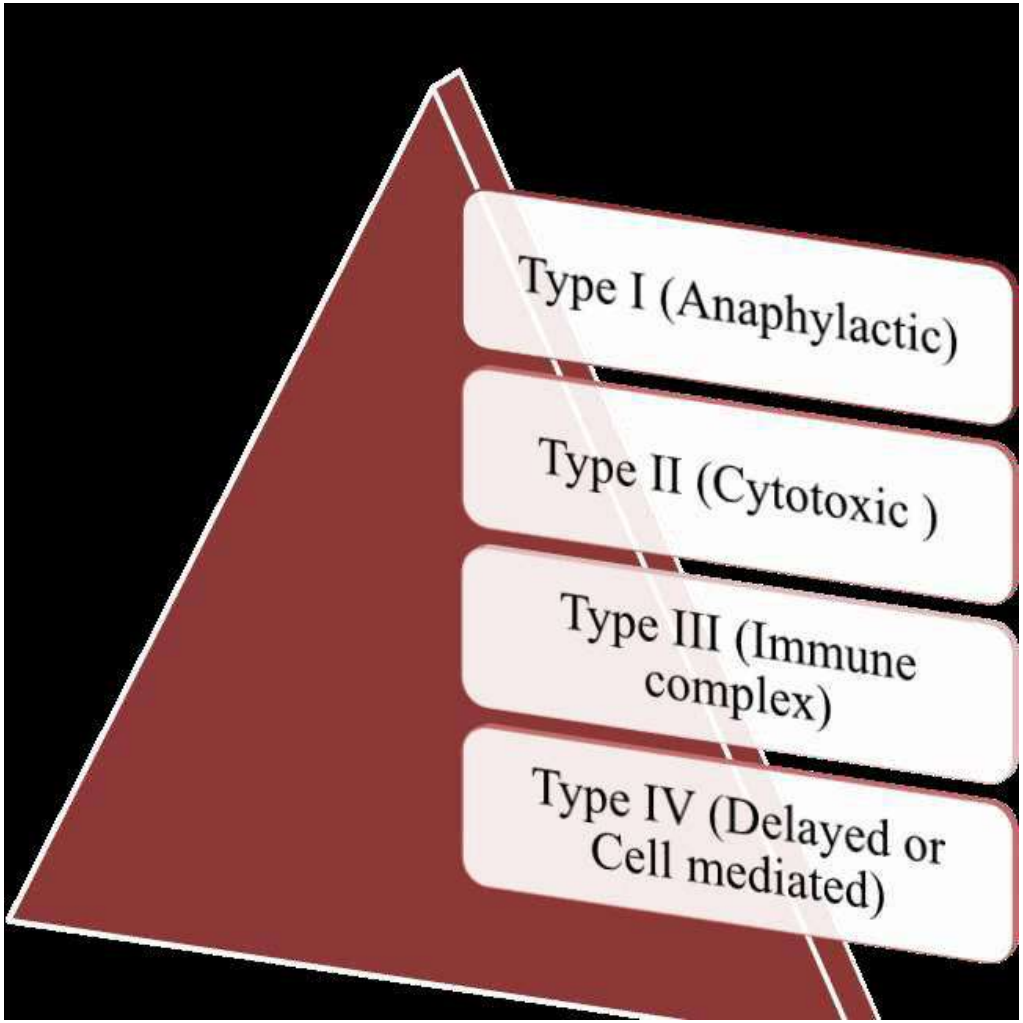
Name of the Department: Department of Zoology

Hypersensitivity

Gell and Coombs' classification and brief description of various types of hypersensitivities.

Dr.Gunjan Dhar
4th SEM UG Hons



What makes us sick?

"enemies" in the environment in the form of **microbes** and **chemicals** are constantly attacking our bodies, disrupting homeostasis

sometimes immune system homeostasis is disrupted on its own

it may over-react to antigens such as with allergies

it may under-react as with human immunodeficiency virus infection (HIV)

it may react to self proteins as with autoimmune disease

Hypersensitivities

Immune responses to innocent antigens or self antigens that lead to symptoms or tissue damage
• Term “hypersensitivity” originally used to denote acquired immune response, as was “allergy”
• “Hypersensitivity” and Allergy” most commonly refer to responses to innocent antigens
• But autoimmune diseases are sometimes subset of hypersensitivity
• Atopy is term used to describe condition of general likelihood of responding with allergic reaction

Hypersensitivity reactions are harmful antigen-specific immune responses , occur when an individual who has been primed by an innocuous antigen subsequently encounters the same antigen , produce tissue injury and dysfuntion.
• It is defined as a state of exagerrated immune response to an antigen.

Classification of Hypersensitivity
•Immediate and Delayed.
Immediate type
Also called as Immediate Hypersensitivity
Popularly called as B cell Mediated Hypersensitivity

Hypersensitivity reactions can be described by the Gell and Coombs classification. This was first put forwards as a classification in 1963 by immunologists Phillip Gell and Robin Coombs and still remains the most widely used classification for hypersensitivity. It classifies reactions depending on their timescale and aetiology producing four separate groups. Although the classes are apparently independent of each other, hypersensitivity reactions often involve more than one of the reactions

- P. G. H. Gell and R. R. A. Coombs classified hypersensitive reactions into four types.

Type I reactions

- involve immunoglobulin E (IgE)–mediated release of histamine and other mediators from mast cells and basophils.

Type II reactions

- involve immunoglobulin G or immunoglobulin M antibodies bound to cell surface antigens, with subsequent complement fixation.

Type III reactions

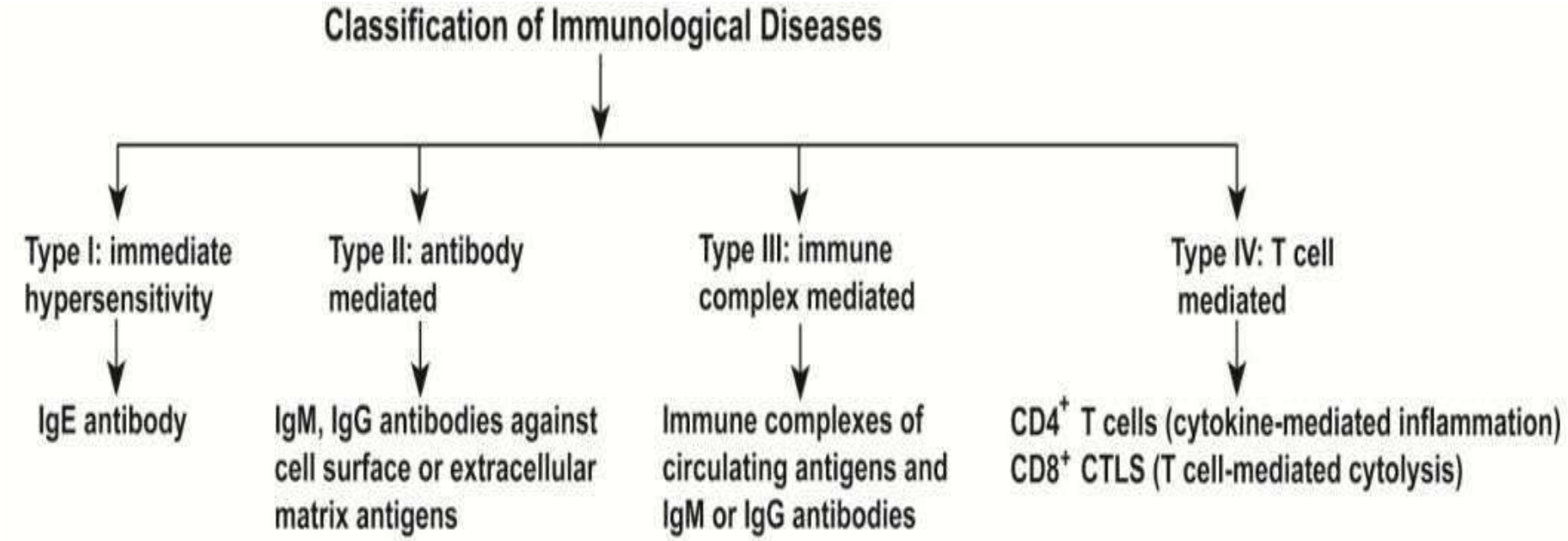
- involve antigen-antibody immune complexes that deposit in postcapillary venules, with subsequent complement fixation.

Type IV reactions

- mediated by T cells rather than by antibodies.

Hypersensitivity reactions

- Aberrant or excessive immune response to foreign antigens
- Primary mediator is the adaptive immune system T & B lymphocytes
- Damage is mediated by the same attack mechanisms that mediate normal immune responses to pathogen



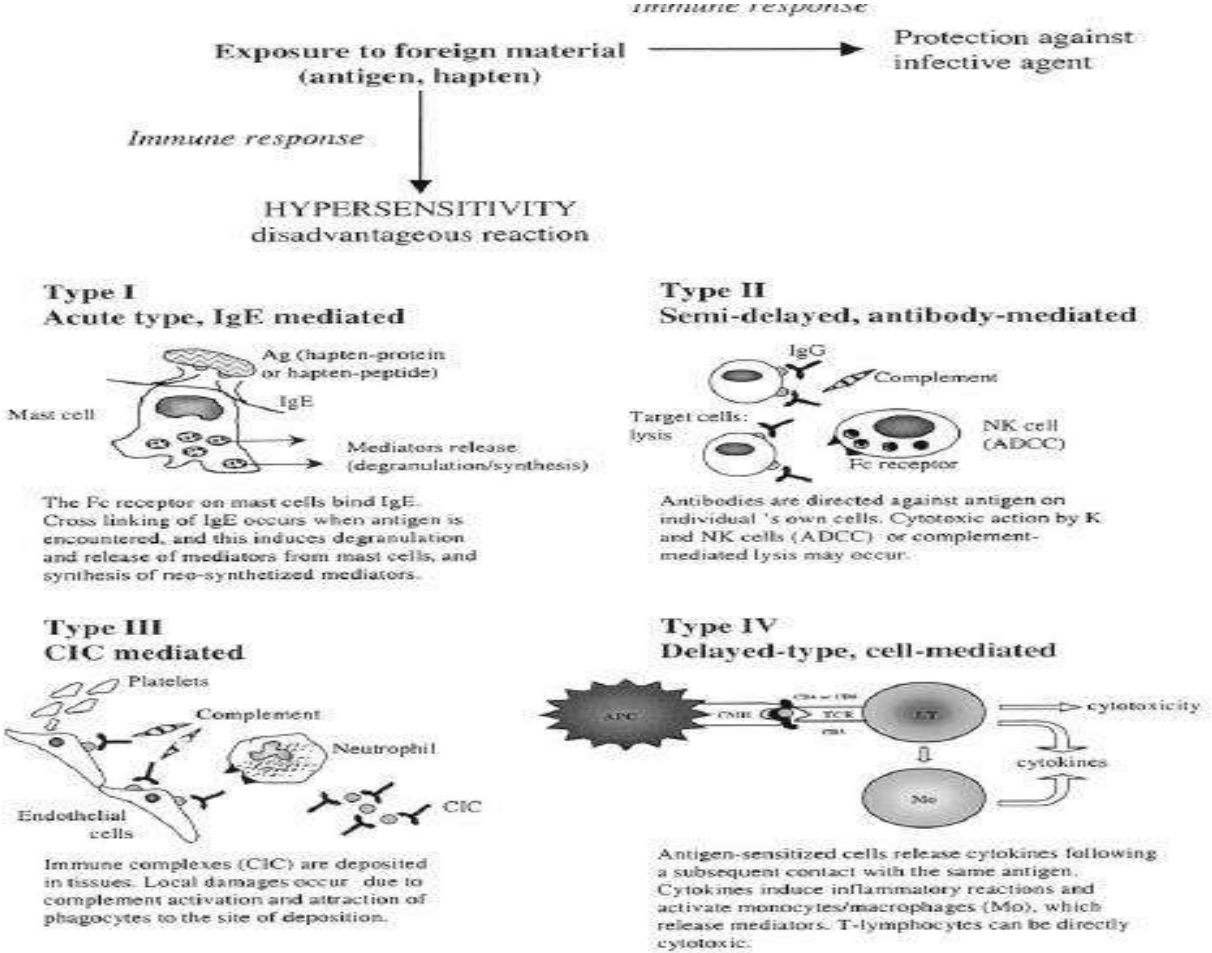
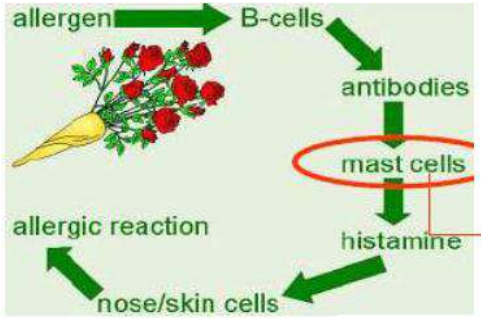


Fig. 1. Hypersensitivity reactions to foreign material (low molecular weight chemicals–drugs) according to Gell and Coombs classification.

Type I: Immediate hypersensitivity

Rapidly developing immunogenic reaction occurring within minutes after the combination of an antigen when antibody bound to mast cells or basophils in individuals.

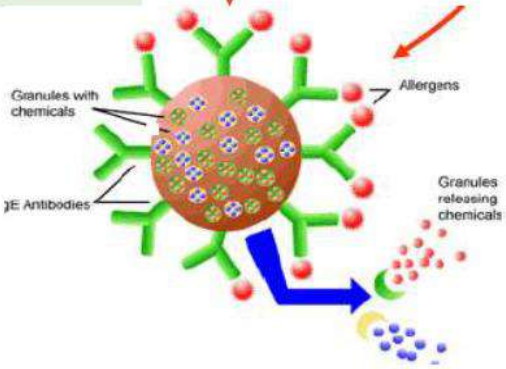
• may occur as a systemic or as a local reaction



Allergic reactions

• Reactions can be elicited by various aeroallergens(pollen, animal dander), drugs(penicillin, sulfonamides) or insect stings(bee venom, wasp venom)

• Other possible causes are latex ,foreign serum food allergy.



Allergens

• Allergens have intrinsic enzymatic activity- allergen extracts f
well as from fungi and bacteria have high protease activity.

• Protease cause the disruption of epithelial cell junctions, allo
Access the underlying cells and molecules of the innate and a

• Cleave and activate complement components at the mucosal surface.

• Allergens contain potential pathogen associated molecular patterns(PAMPS).

• Interact with receptors of the innate immune system and initiating a cascade of responses leading to an allergic response.

Type I Hypersensitivity reaction

Characteristics	IMMEDIATE OR ANAPHYLACTIC HYPERSENSITIVITY		
Antibody	IgE		
Antigen	Exogenous		
Response time	•15-30 minutes from allergen exposure •Sometimes delayed onset of 10-12 hours •Many patients also have a late phase response 5 - 8 hrs after the initial exposure which peaks at 12 hrs and subsides by 36hrs – thus NB to monitor symptoms and continue treatment		
Pathogenesis	1. **Sensitisation phase:** *1st exposure* to antigen stimulates production of IgE antibodies, which bind to mast cells and circulating basophils.	2. **Activation phase:** *Re-exposure* to antigen causes IgE molecules to become cross-linked, which triggers mast cells and basophil degranulation into surrounding fluids – triggers effector phase	3. **Effector phase:** • Histamine (H1-H4) - small blood vessel dilatation, increases permeability, and bronchiolar smooth muscle constriction; increased mucous production • Heparin prevents blood coagulation; • Enzymes break down proteins; • Signalling agents attract eosinophils and neutrophils; • Platelet activating factor (PAF) stimulates platelets to adhere to blood vessel walls and to release serotonin, which constricts arteries. • Prostaglandins and leukotrines from stimulated mast cells have potent local effects incl. capillary blood vessels leakage, smooth muscle contraction, increased granulocytes activity, and platelet adhesion.

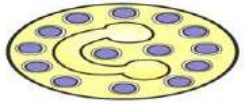
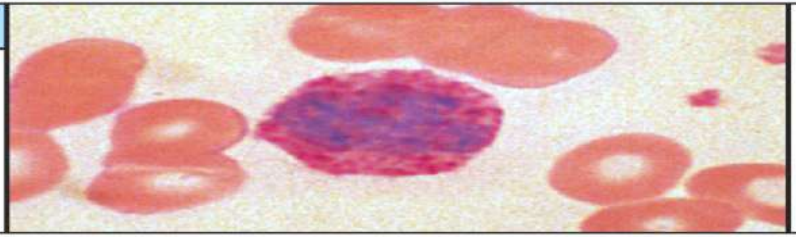
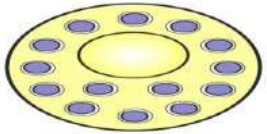
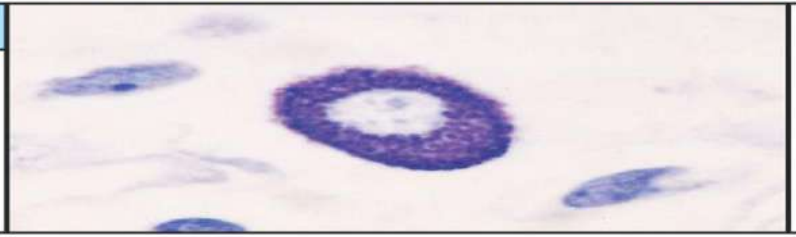
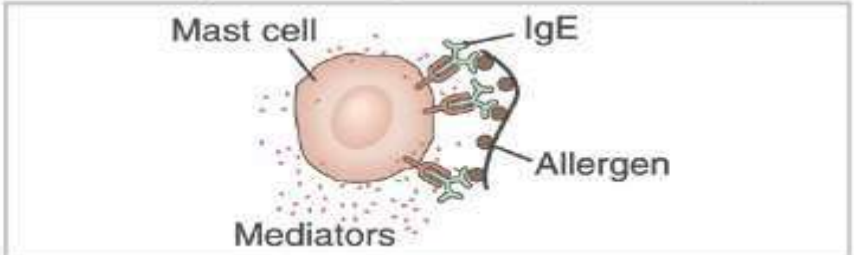
Cell		Activated function
Basophil 		Unknown
Mast cell 		Release of granules containing histamine and other active agents

Figure 1-4 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Type of hypersensitivity	Pathologic immune mechanisms	Mechanisms of tissue injury and disease
Immediate hypersensitivity (Type I)	T_H2 cells, IgE antibody, mast cells, eosinophils 	Mast cell–derived mediators (vasoactive amines, lipid mediators, cytokines) Cytokine-mediated inflammation (eosinophils, neutrophils)

Type I hypersensitivity response

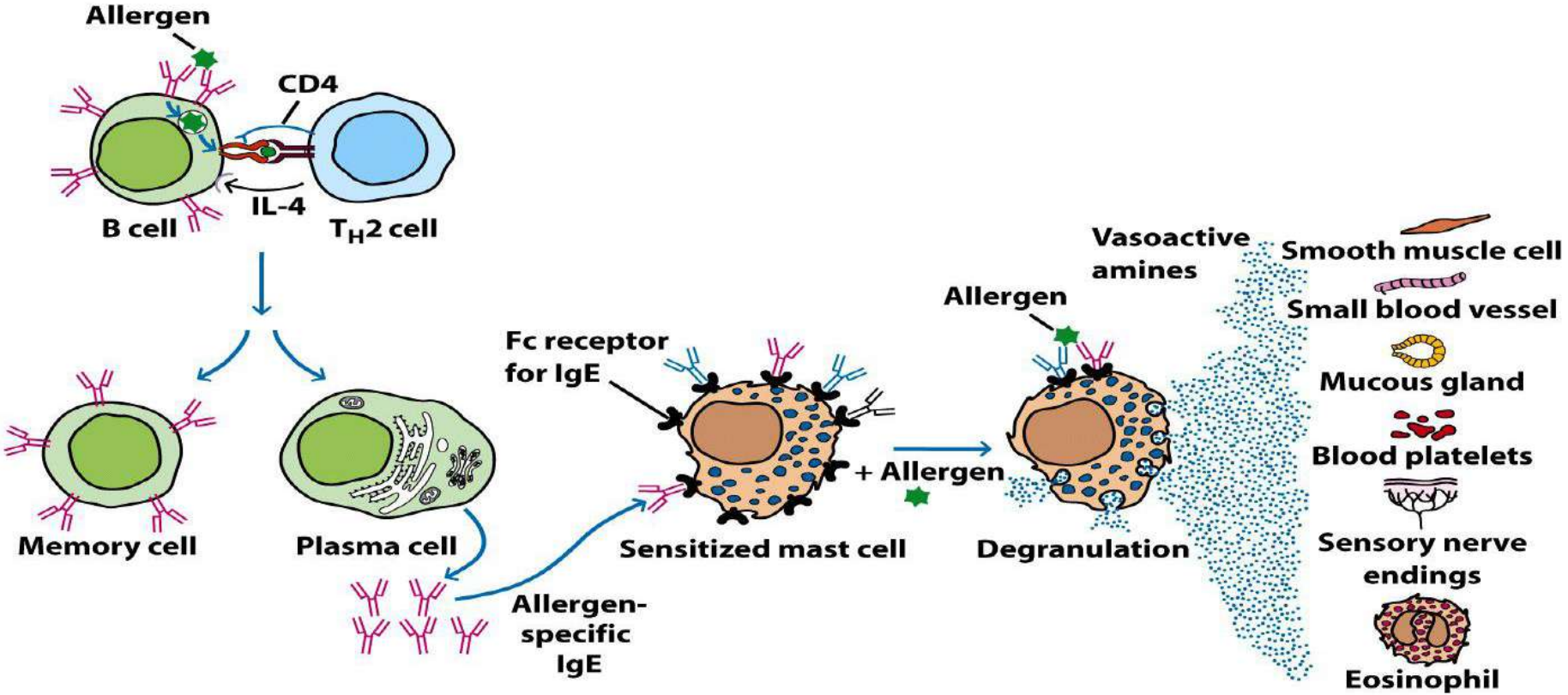


Figure 15-2
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Initiation of degranulation

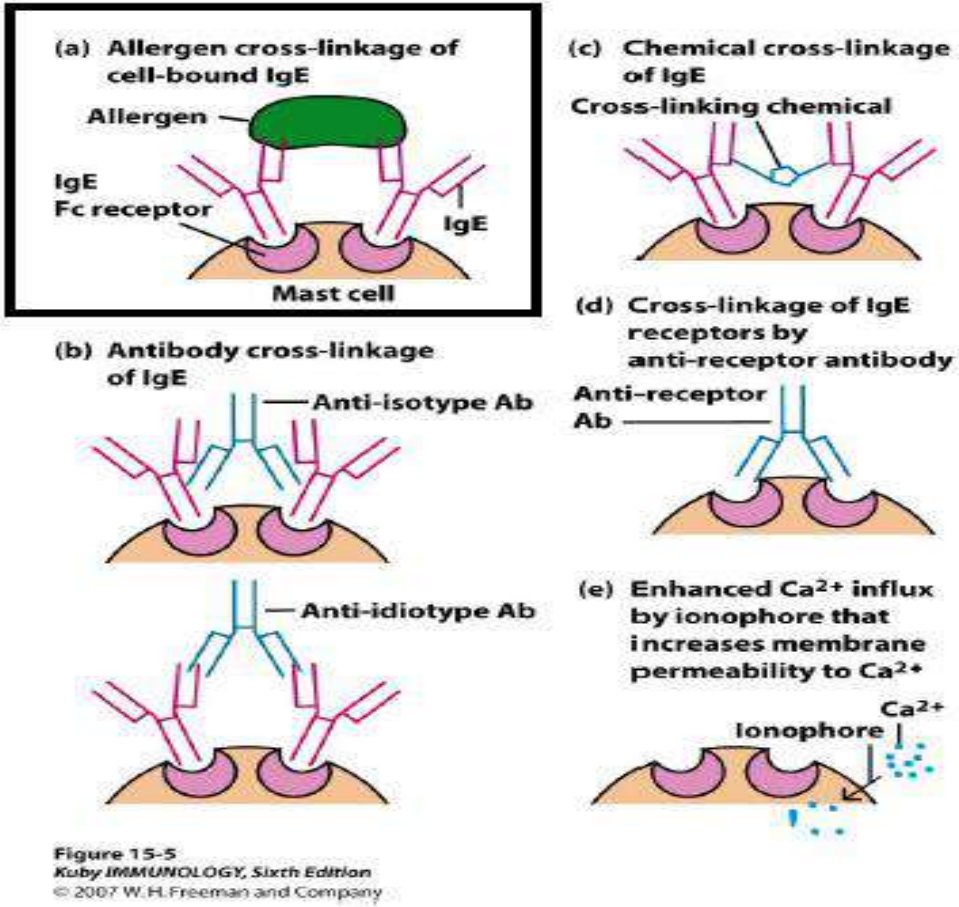

Figure 15-5
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Mediators of Type I Hypersensitivity

- Primary Mediators – produced before degranulation and are stored in the granules.
- Secondary Mediators - synthesized after target-cell activation or released by the breakdown of membrane phospholipids during the degranulation process.

Usefulness of “Type I” IgE responses:
eliminating parasites, like helminths
Propulsive smooth muscle contraction,
mucus prevent infiltration of epithelium by parasites

TABLE 15-3 Principal mediators involved in type I hypersensitivity

Mediator	Effects
	PRIMARY
Histamine, heparin	Increased vascular permeability; smooth muscle contraction
Serotonin (rodents)	Increased vascular permeability; smooth muscle contraction
Eosinophil chemotactic factor (ECF-A)	Eosinophil chemotaxis
Neutrophil chemotactic factor (NCF-A)	Neutrophil chemotaxis
Proteases (tryptase, chymase)	Bronchial mucus secretion; degradation of blood vessel basement membrane; generation of complement split products
	SECONDARY
Platelet-activating factor	Platelet aggregation and degranulation; contraction of pulmonary smooth muscles
Leukotrienes (slow reactive substance of anaphylaxis, SRS-A)	Increased vascular permeability; contraction of pulmonary smooth muscles
Prostaglandins	Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation
Bradykinin	Increased vascular permeability; smooth muscle contraction
Cytokines	
IL-1 and TNF-α	Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells
IL-4 and IL-13	Increased IgE production
IL-3, IL-5, IL-6, IL-10, TGF-β, and GM-CSF	Various effects (see Table 12-1)

Table 15-3
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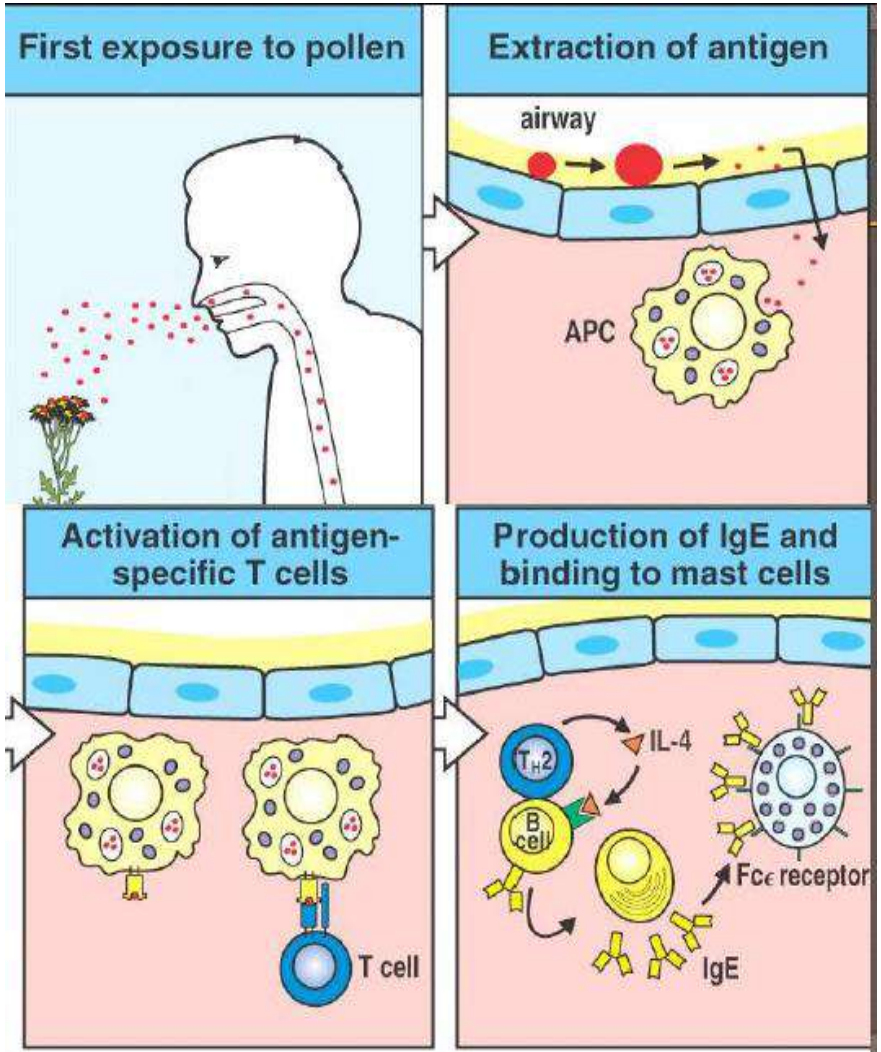
Sensitization phase:

- CD4 TH2 T cells cytokine profile leads to isotype switching to IgE

Effector phase:

- IgE triggers Mast cell degranulation



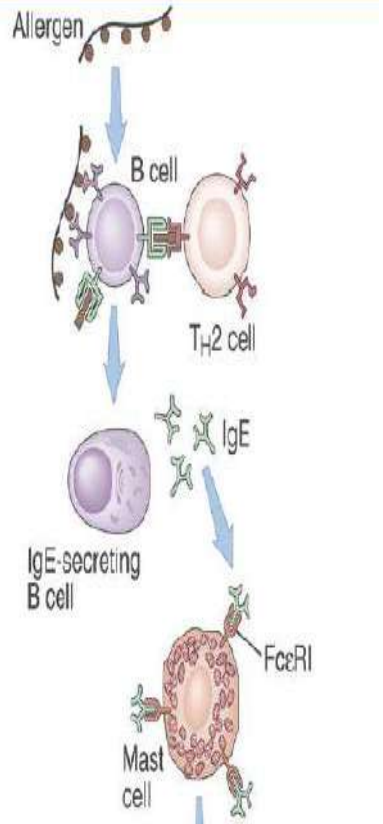
Sequence of events in Type I, "immediate hypersensitivity"

First exposure to allergen

Antigen activation of T_H2 cells and stimulation of IgE class switching in B cells

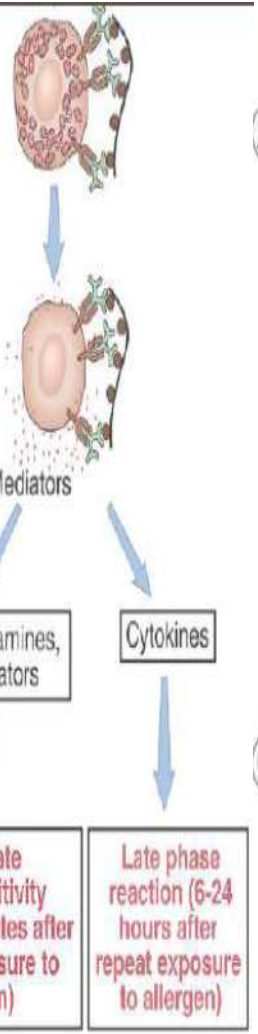
Production of IgE

Binding of IgE to FcεRI on mast cells



Repeat exposure to allergen

Activation of mast cell: release of mediators



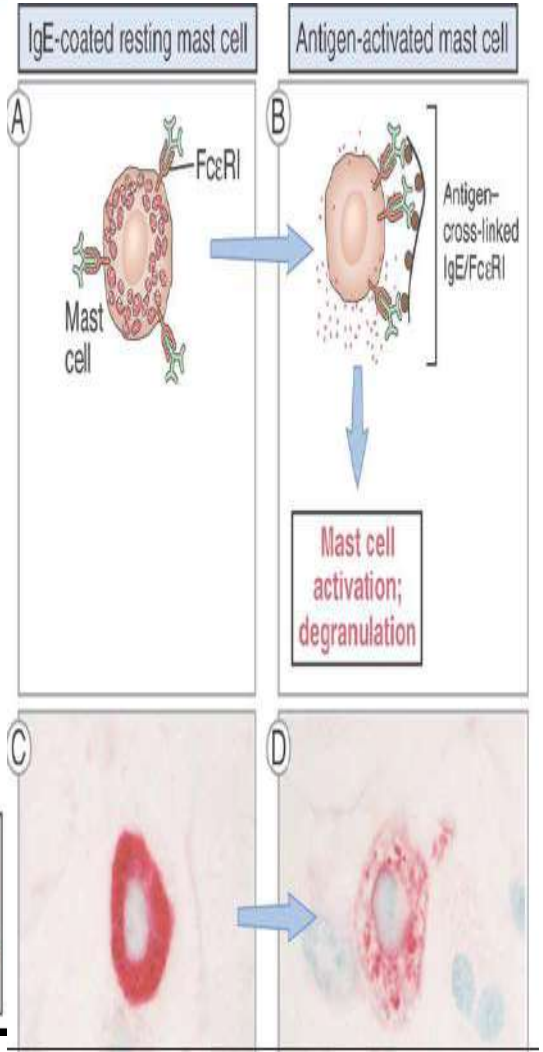


TABLE 15-1 Common allergens associated with type I hypersensitivity

Proteins
- Foreign serum
- Vaccines

Plant pollens
- Rye grass
- Ragweed
- Timothy grass
- Birch trees

Drugs
- Penicillin
- Sulfonamides
- Local anesthetics
- Salicylates

Foods
- Nuts
- Seafood
- Eggs
- Peas, beans
- Milk

Insect products
- Bee venom
- Wasp venom
- Ant venom
- Cockroach calyx
- Dust mites

Mold spores

Animal hair and dander

Latex

Table 15-1
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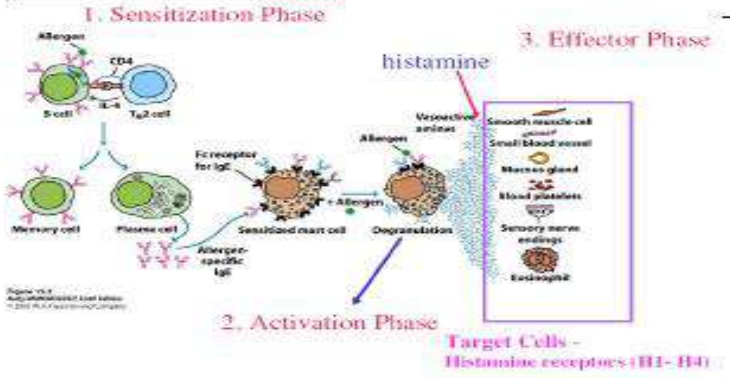
Type I Hypersensitivity reaction

Histology	•Mast cell & Basophils •The reaction is amplified and/or modified by platelets, neutrophils and eosinophils. •Biopsy of the reaction site demonstrates mainly mast cells and eosinophils)	
Examples	**1. Systemic Anaphylaxis (Anaphylactic shock)** Shock-like and **often fatal state** initiated by an allergen introduced into the blood, or absorbed by the gut or skin •**Smooth muscle contraction** (gut, bladder, bronchiole) & **systemic vasodilation** = **hypotension** **Treatment:** IM Adrenaline 0.5mg 1:1000/ Epinephrine (EpiPen)	**2. Localised Hypersensitivity reactions (Atopy)** •Localised hypersensitivity reaction to a specific target tissue or organ •Allergic rhinitis (hay fever) •Asthma •Atopic dermatitis **Treatment:** Symptomatic
	Triggers in humans: •venom from bee, wasps and ants; pollen; drugs such as penicillin; seafood; nuts ; latex	



Systemic Anaphylaxis

- It is a shock like and occurs within minutes of exposure to an allergen.
- Initiated by an allergen introduced directly into the bloodstream or absorbed from the gut or skin.
- Symptoms include labored respiration, drop in blood pressure leading to anaphylactic shock ,contraction of smooth muscles leading to defecation, urination, and bronchiolar constriction.
- Leads to anaphyxiation, which lead to death within 2 to 4 minutes of exposure to the allergen.
- venom from bee, wasp, hornet, and ant stings; drugs such as penicillin, insulin, and antitoxins; and foods such as seafood and nuts cause anaphylaxis.
- Epinephrine is used for treating anaphylaxis.

Localized Hypersensitivity Reactions (Atopy)

- The pathology is limited to a specific target tissue or organ, and often occurs at the epithelial surfaces first exposed to allergens.
- Atopic allergies include a wide range of IgE-mediated disorders, such as allergic rhinitis (hay fever), asthma, atopic dermatitis (eczema), and food allergies.
- Hay fever is the most common and results from the inhalation of common airborne allergens (pollens, dust, viral antigens).
- Allergen react with IgE molecules bound to sensitized mast cells in the conjunctivae and nasal mucosa.
- Cross-linking of IgE receptors induces the release of histamine and heparin from mast cells, which then cause vasodilation, increased capillary permeability, and production of exudates in the eyes .
- Tearing, runny nose, sneezing, and coughing are the main symptoms.

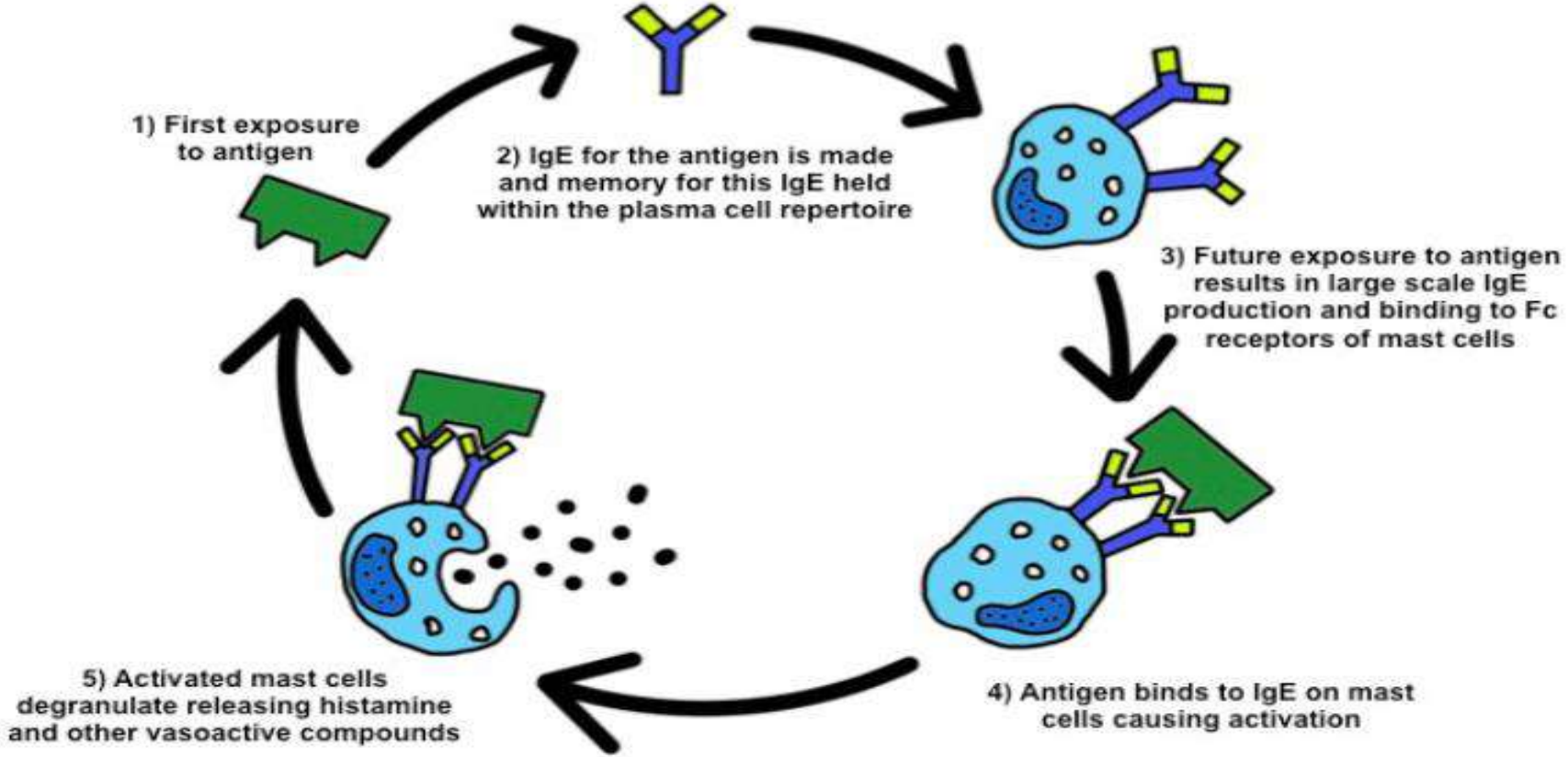


Figure 1: Diagrammatic representation of type I hypersensitivity reactions

Antibody-Mediated Cytotoxic (Type II) Hypersensitivity

• Body makes special autoantibodies directed against self-cells (antigens present on the surface of cells or tissue components)

Antigen:

• 1. may be intrinsic to the cell membrane

• 2. may take the form of an exogenous antigen adsorbed on the cell surface.

• hypersensitivity results from the binding of antibodies to normal or altered cell-surface antigens

Antibody bound to a cell-surface antigen and induce death of the antibody-bound cell by

• Activate the complement system, creating pores in the membrane of a foreign cell.

• Antibodies can mediate cell destruction by antibody dependent cell-mediated cytotoxicity (ADCC).

• Antibody bound to a foreign cell can serve as an opsonin.

Type II examples

1.Transfusion reactions

• cells from an incompatible donor react to the host's antibody

2. Erythroblastosis fetalis

• there is an antigenic difference between the mother & the fetus,and antibodies (IgG) cross the placenta & cause destruction of fetal red cells.

3. Autoimmune hemolytic anemia, agranulocytosis,thrombocytopenia

• individuals produce antibodies to their own blood cells and are then destroyed.

4. Drug reactions • antibodies are produced that react to the drug

Type II hypersensitivity

• Mediated by abs directed towards antigens present on cell surfaces or the extracellular matrix (type IIA) or abs with agonistic/antagonistic properties (type IIB).
• Mechanisms of damage:
– Opsonization and complement- and Fc receptor mediated phagocytosis
– Complement- and Fc receptor-mediated inflammation
– Antibody-mediated cellular dysfunction

Non-autoimmune type II reactions

• Transfusion reactions (ABO incompatibility
• Hemolytic disease of the newborn (erythroblastosis fetalis)

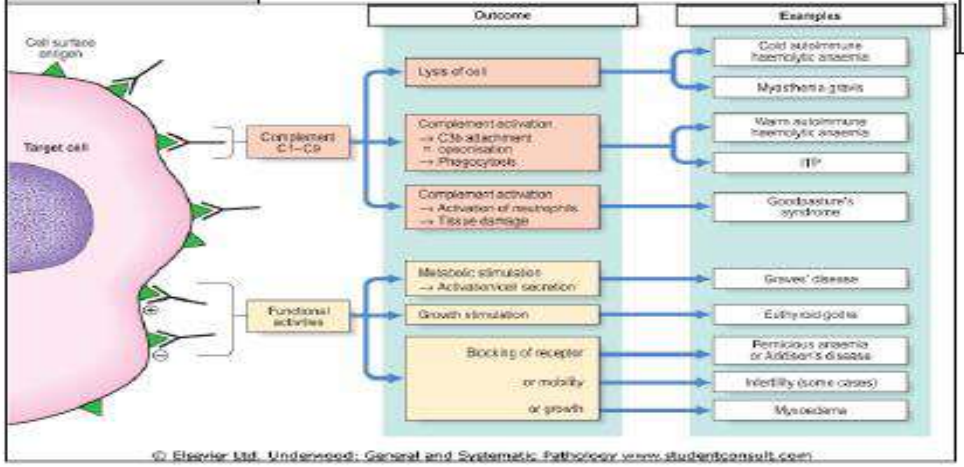
Type II Hypersensitivity reaction

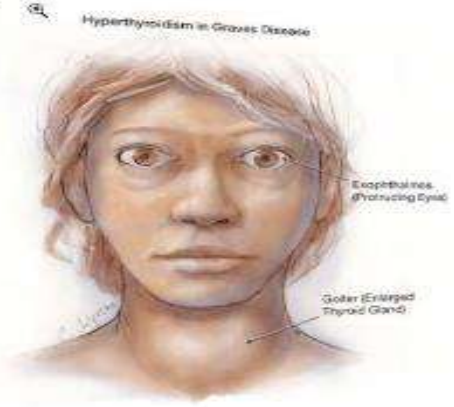
Characteristics	ANTIBODY MEDIATED CYTOTOXIC REACTION
Antibody	**IgG, IgM**
Antigen	Cell surface antigen
Response time	Minutes – hours
Pathogenesis	Antibody binds to an antigen on the surface of a target cell and can cause damage through a number of mechanisms: 1. **When IgM or IgG mediator molecules** are involved, they activate the **complete complement system**, which leads to the formation of a membrane attack complex that destroys the cell – **antibody-dependent cell mediated cytotoxicity (ADCC)**. 2. OR **IgG molecules**, which coat the target cell and attract **macrophages** and **neutrophils** to destroy it. **Not all type II reactions cause cell death, but altered** cell function (PROMOTE or INHIBIT) may occur • E.g. Antigen to which the antibody binds is a cell-surface receptor which normally interacts with a chemical messenger, such as a HORMONE. If the antibody binds to the receptor, it prevents the hormone from binding and carrying out its normal cellular function as seen in AUTOIMMUNE DISEASES OF THE THRYOID GLAND **Type I reactions:** antigens interact with **cell-bound IgE immunoglobulins** **VS** **Type II reactions:** involve the interaction of **circulating immunoglobulins** with **cell-bound antigens**.

Type II Hypersensitivity reaction

Histology	Antibody Complement (C1 - C9)
Examples	• Grave's Disease • Myasthenia Gravis • Goodpasture's Nephritis • Autoimmune Haemolytic anaemia • Erythroblastosis fetalis • Treatment: anti-inflammatory and immunosuppressive agents

- Type II reactions only rarely result from the introduction of innocuous antigens.
- **More often develop as a result of antibodies produced against body cells that have been infected by microbes** (and thus present microbial antigenic determinants) OR
- **Antibodies have been produced that attack the body's own cells.**
- This latter process underlies a number of autoimmune diseases incl. examples listed





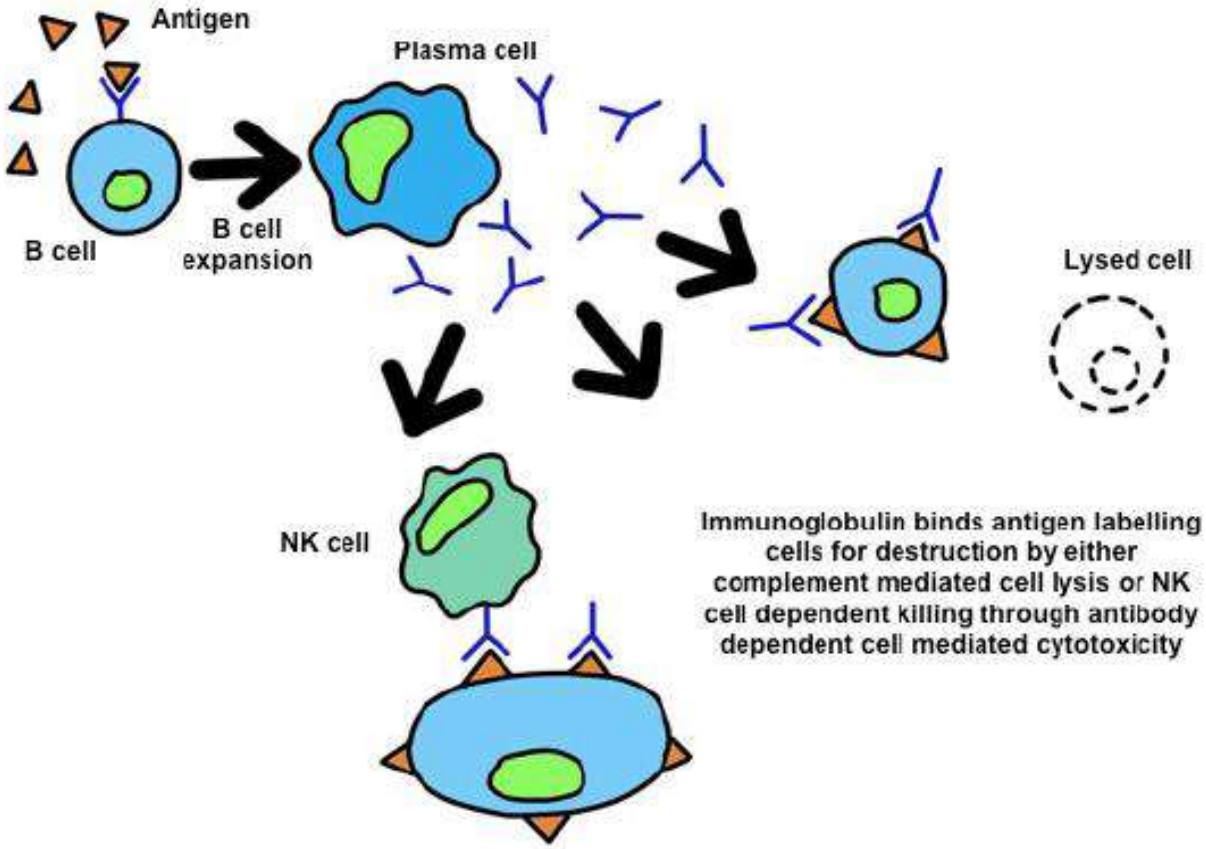


Figure 2: Type II Hypersensitivity reactions. The Presence of antigen stimulates specific B-cells. The B-cell undergoes clonal expansion and produces large amounts of immunoglobulin against the antigen. By binding antigen, the immunoglobulin labels the cell for destruction by NK cells or complement.

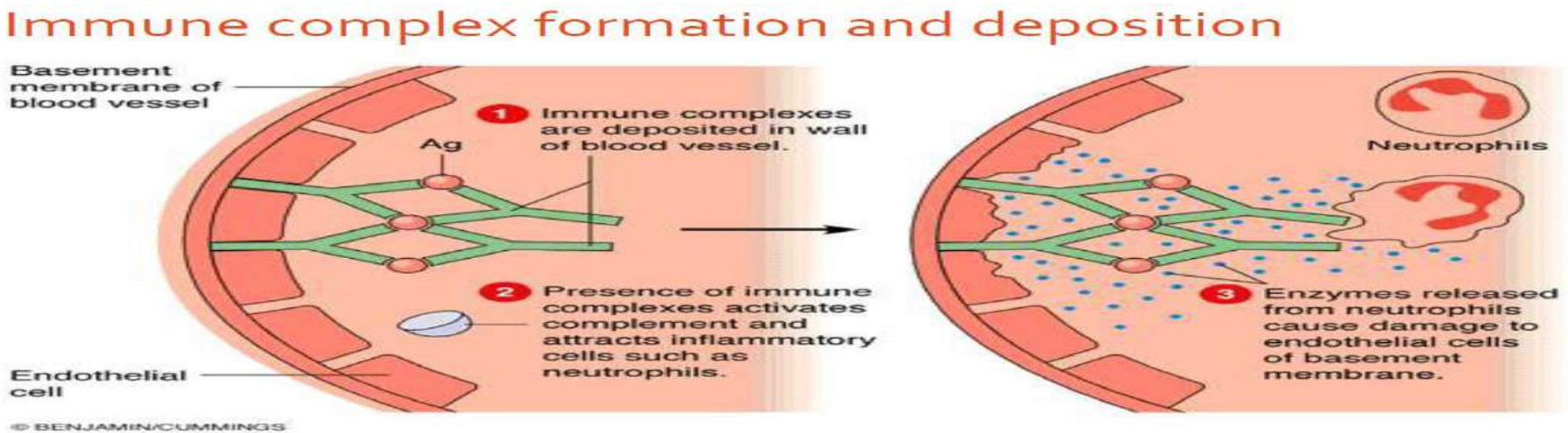
Immune Complex–Mediated (Type III) Hypersensitivity

Immune Complex Disease

- Involve reaction against soluble antigens circulating in the serum.
- Involve IgM ,IgG antibodies.
- Every time an antibody binds to antigen, an immune complex is formed .
- Under normal conditions complexes are bound by complement to RBCs and then eliminated by phagocytes.
- In Type III hypersensitivity, immune complexes are not cleared out and they become deposited in tissues.

In Type III hypersensitivity, the antibody involved is primarily IgG

- The immune complexes activates complement (C3a, C4a and C5a), leading to degranulation of mast cells.
- The products of mast cell degranulation cause blood vessels to become more permeable.
- This allows immune complexes to be deposited in the walls of blood vessels.
- The neutrophils release lysosomal enzymes into the area, causing further damage to the vessel wall



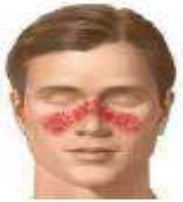
LOCATION

• The immune complexes are formed in the circulation & are deposited in many organ .
• kidney (glomerulonephritis), joints (arthritis), small blood vessels of the skin if the complexes are formed and deposited locally (local Arthus reaction)

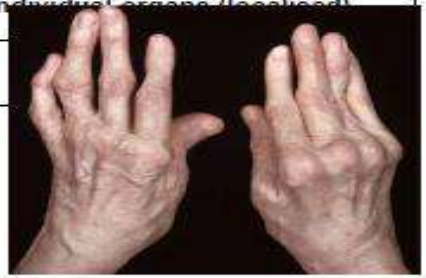
Arthus reaction

• If an animal or human is injected intradermally with an antigen to which large amounts of circulating antibodies exist(intravenous injections).
• Antigen will diffuse into the walls of local blood vessels and large immune complexes will precipitate close to the injection site.
• This initiates an inflammatory reaction that peaks approximately 4 to 10 hours post injection and is known as an Arthus reaction.
• Inflammation at the site of an Arthus reaction is characterized by swelling and localized bleeding, followed by fibrin deposition

Type III Hypersensitivity reaction



Characteristics	IMMUNCE COMPLEX REACTIONS
Antibody	IgG, IgM (same antibodies as Type II, **but the mechanism by which tissue damage is brought about is different**)
Antigen	Soluble
Response time	3 – 8 hours
Pathogenesis	1. The antigen to which the antibody binds is not attached to a cell. 2. Once the antigen-antibody complexes form, they are **deposited** in various tissues of the body, especially the **blood vessel walls, glomerular basement membrane of kidneys, lungs, skin, and synovial membranes of joints** 3. Tissue damage caused by activation of CLASSICAL COMPLEMENT PATHWAY and inflammation. 4. Inflammatory response, which leads to the **recruitment of neutrophils** to the site and **granular release** of tissue-damaging substances, such as **lytic enzymes** that **destroy tissues locally**, and **interleukin-1**, which, among its other effects, **induces fever**. 5. Magnitude of reaction is determined by the **amount** and **size** of immune complexes, and the **affinity** of antibody. 6. The **reaction may be general** (e.g.serum sickness) or **may involve individual organs (localised)**
Histology	Complement Neutrophils
Examples	**Immune complexes underly many autoimmune diseases** • **Systemic Lupus Erythematosus (SLE)** • Glomerulonephritis • **Rheumatoid Arthritis** • Addison's disease

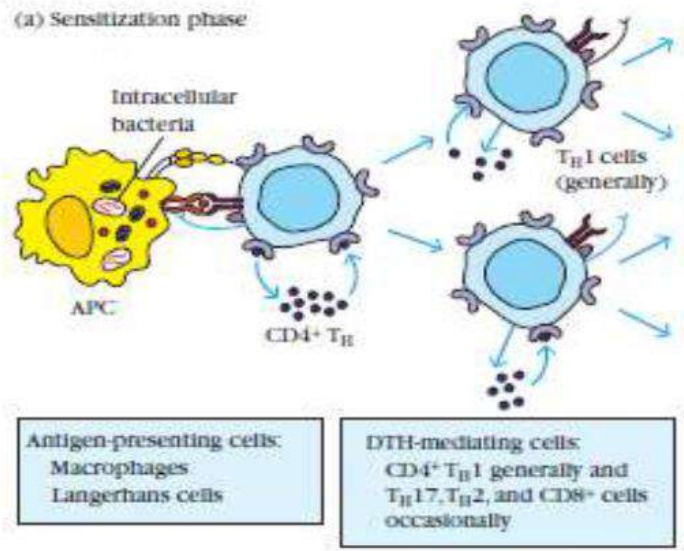


Type IV: Delayed Hypersensitivity

• The only type that is not antibody-mediated.
• contact hypersensitivity (poison ivy, poison oak and reactions to metals in jewelry);
• tuberculin-type hypersensitivity (the tuberculosis skin test);
• granulomatous hypersensitivity (leprosy, tuberculosis, schistosomiasis and Crohn's disease).
• It is called delayed because its onset may vary;
• Occurs hours to days
• The length of the delay varies from 72 hours in contact hypersensitivity and 21-28 days in granulomatous hypersensitivity.

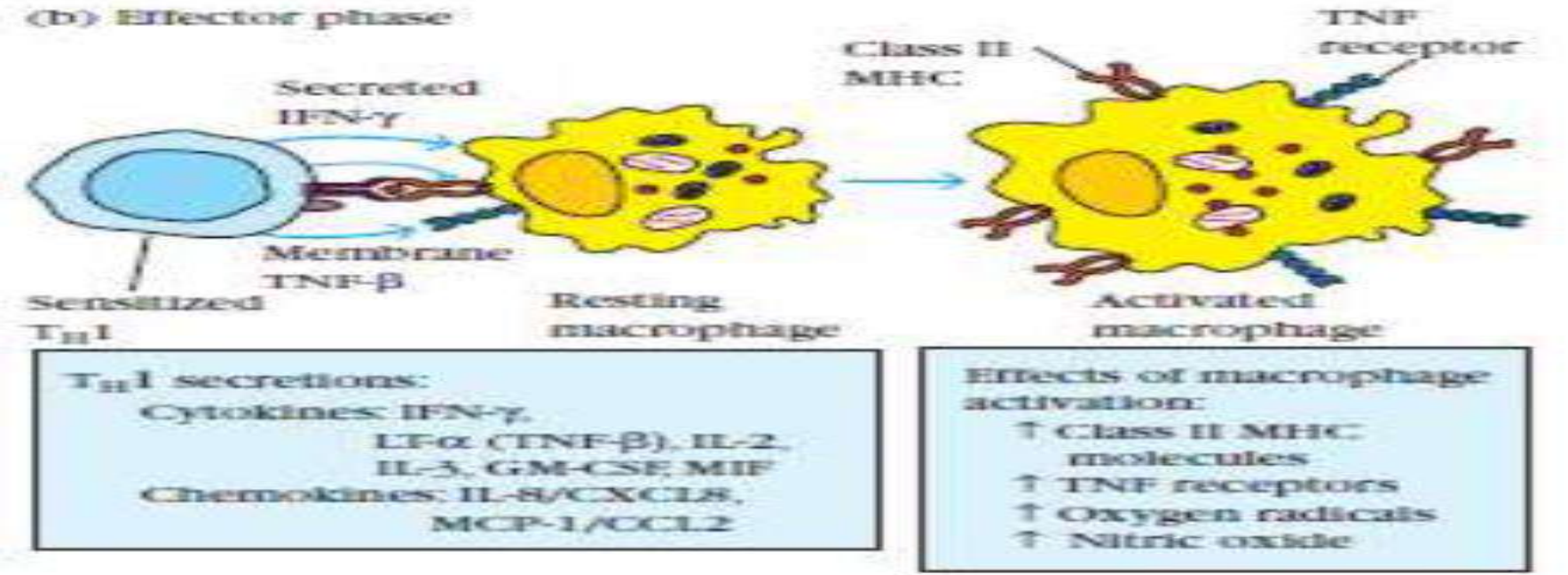
Th1 cells and macrophages

• In sensitization phase
• The dendritic cells pick up antigen and present the antigen to T cells.
• The T cells proliferate and differentiate into TH1 cells.
• These Th1 cells can activate macrophages and trigger inflammatory response.



In the effector phase ,exposure of sensitized TH1 cells to antigen.

- TH1 cells secrete a variety of cytokines and chemokines.
- IFN-g, TNF-a, and TNF-b - cause tissue destruction, inflammation.
- IL-2 - activates T cells and CTLs.
- Chemokines - for macrophage recruitment.
- IL-3, GM-CSF -increased monocyte/macrophage
- Inflamed area becomes red and fluid filled can form lesion.
- Tissue damage there is activation of clotting cascades and tissue repair.



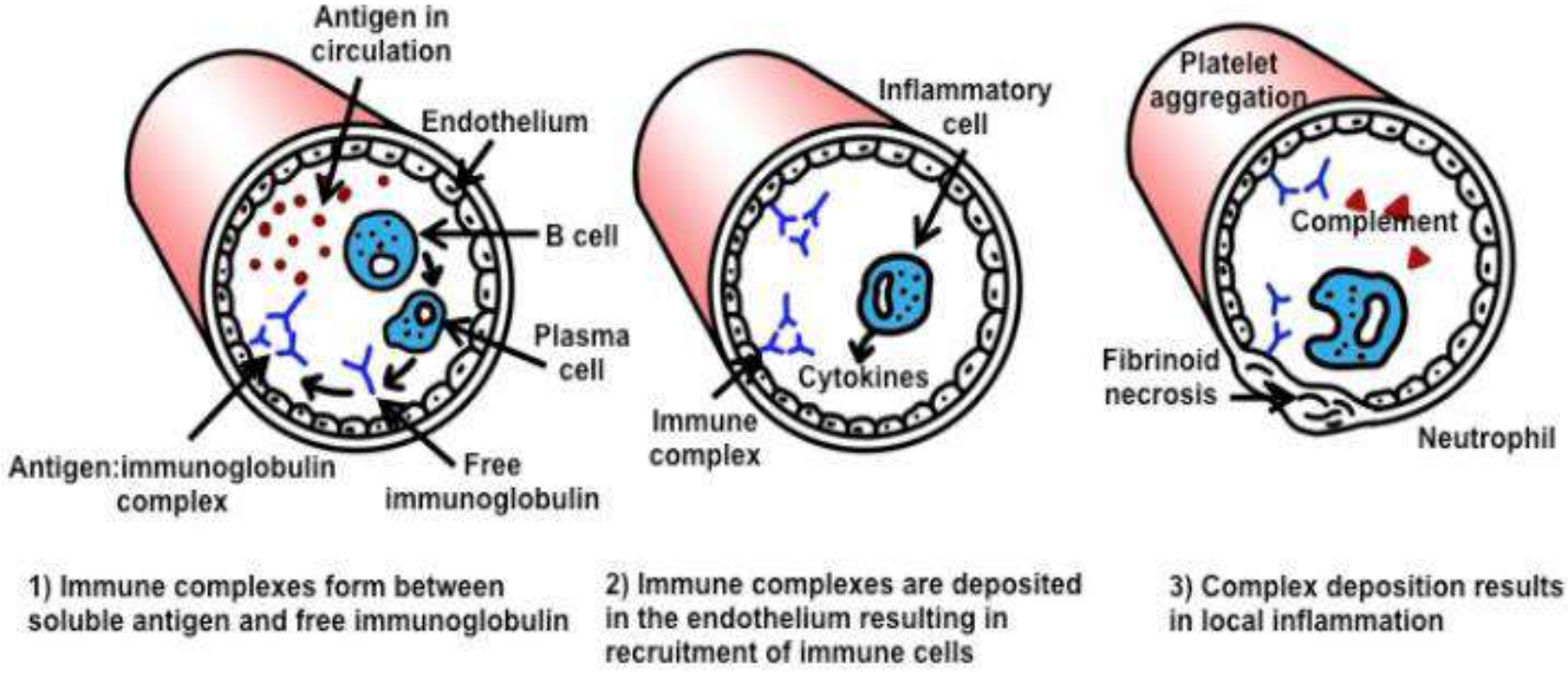


Figure 3: Pathogenesis of type III hypersensitivity.

Type IV Hypersensitivity reaction

Characteristics	DELAYED TYPE HYPERSENSITIVITY REACTION / CELL MEDIATED	
Antibody	NONE Interaction of **T cells with antigens**. Reactions of this kind depend on the presence in the circulation of a sufficient number of T helper (especially TH1) cells to be able to recognize the antigen. The specific T cells must migrate to the site where the antigen is present to induce localized inflammation.	
Antigen	Tissues and organs	
Response time	48 -72 hours	
Pathogenesis	**1. Sensitization phase (1-2 weeks):** • Macrophages and dendritic cells secrete IL-12, which induces the development of Th1 cells in regional lymph nodes. • A DTH response develops over 48-72 hours when antigen presented by a tissue macrophage in the context of IL-12 and IL-18 secretion activates sensitized **Th1 cells** in the tissue. • **Major lymphokines**: *Chemokines* (IL-8, MCP-1) and *cytokines* (IL-2, IFN, MIF and TNFß) released by the activated Th1 cells attract and activate additional macrophages.	**2. Effector Phase (starts at 24hrs, peaks at 48-72 hrs):** • Activated macrophages are the principal effector cell in a DTH response. • Activated macrophages show increased expression of class II MHC molecules, TNF receptors, oxygen radicals, and nitric oxide. • These changes enhance the antigen presenting and microbicidal activities of macrophages. • Lytic enzymes that leak from activated macrophages cause local tissue destruction. CTL induced by Th1 cells may also participate in tissue destruction.

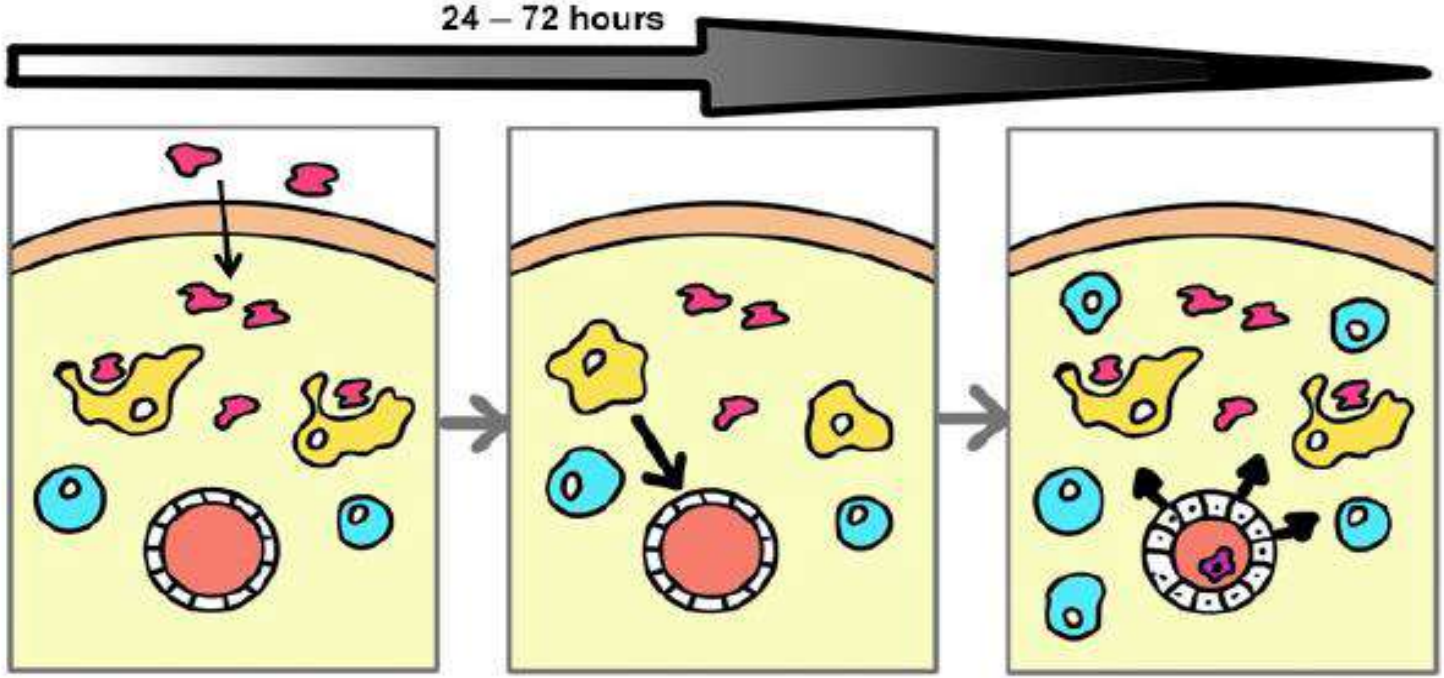
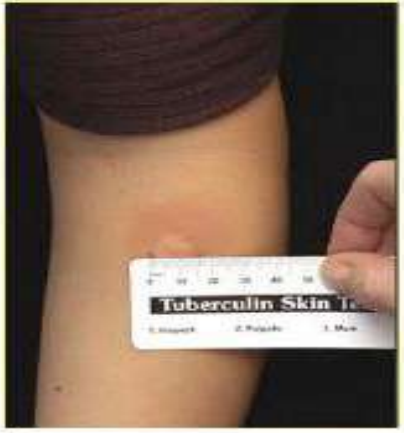
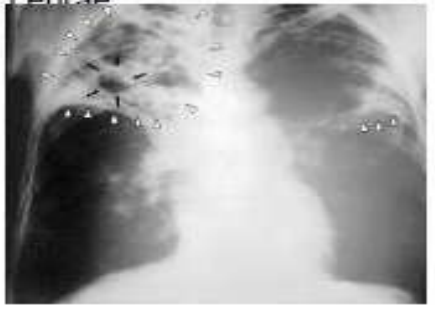
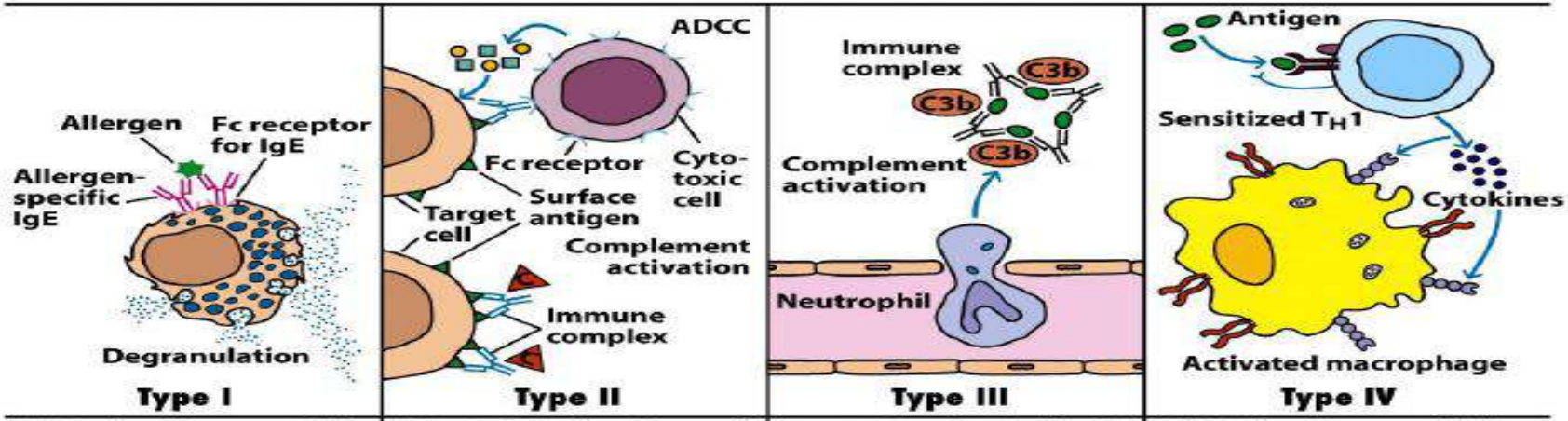


Figure 4: Pathology of cutanous type IV hypersensitivity.[4]

Type IV Hypersensitivity reaction

Histology	**Monocytes and Lymphocytes**		
Examples	**Delayed contact dermatitis** • Epidermal reaction giving eczematous appearance • **Triggers:** nickel, chromate, rubber • **First exposure:** no reaction but memory cells made in 7-14 days • **Repeat exposure:** erythematous reaction at point of contact after 48-72 hours 	**Tuberculin test** (basis of heaf test) • Given injection of antigen (mycobacterium- TB) • If previously exposed local reaction with swelling occurs at injection site. 	**Granuloma** • Develops over 21-28 days • **Pathology:** 1.micro-organisms or other particles become trapped in macrophages & cannot be destroyed 2.Epithelioid granuloma forms (or disseminated disease eg miliary TB) • **Examples:** M. TB & M. Leprae 

Hypersensitivity reactions



Type I	Type II	Type III	Type IV
IgE-Mediated Hypersensitivity	IgG- or IgM-Mediated Cytotoxic Hypersensitivity	Immune Complex–Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces cross-linking of IgE bound to mast cells and basophils with release of vasoactive mediators.	Ab directed against cell surface antigens meditates cell destruction via complement activation or ADCC.	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils.	Sensitized T_H1 cells shown above release cytokines that activate macrophages or T_C cells that mediate direct cellular damage. T_H2 cells and CTLs mediate similar responses.
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema.	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia.	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus.	Typical manifestations include contact dermatitis, tubercular lesions, and graft rejection.

Figure 15-1
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Table 1 Classification of hypersensitivity reactions

Classification	Immunoreactants	Clinical Presentation
Type I	Mast cell mediated, IgE dependent (anaphylactic, and IgE independent)	Anaphylaxis, urticaria, angioedema, asthma, and allergic rhinitis
Type IIa	Antibody-mediated cytotoxic reactions (IgG and IgM antibodies complement often involved)	Immune cytopenias
Type IIb	Antibody-mediated cell-stimulating reactions	Graves disease and chronic idiopathic urticaria
Type III	Immune complex–mediated reactions complement involved	Serum sickness and vasculitis
Type IVa	Th1 cell-mediated reactions macrophage activation	Type 1 diabetes and contact dermatitis (with IVc)
Type IVb	Th2 cell–mediated reactions eosinophilic inflammation	Persistent asthma and allergic rhinitis
Type IVc	Cytotoxic T cell-mediated (perforin/granzyme B involved)	Stevens-Johnson syndrome and TEN
Type IVd	T-cell-mediated neutrophilic inflammation	AGEP and Behcet disease

Source: Adapted from Ref. 2.
AGEP = acute generalized exanthematous pustulosis; TEN = toxic epidermal keratinocytes.

Autoimmune disease

- **Inappropriate activation** of immune response – classified by different types of hypersensitivity reactions
- Development of **auto-antibodies** and specific cells against self-protein/DNA/RNA
- **Spectrum: Organ specific** to **systemic disease**
- Individuals may have more than one autoimmune disease
- **Treatment:** variety of strategies depending on disease
  - Anti-inflammatory (corticosteroid)
  - **Immunosuppressive** drug therapy (cyclophosphamide, azathioprine, cyclosporine)
  - Immunomodulation e.g. cytokine therapy (Interferon α/β)
  - Plasmapheresis
  - IVIg
  - Autologous stem cell transplantation etc.
- In **organ specific autoimmune disorders** symptoms, it may be possible to treat some symptoms by metabolic control e.g.
  - **thyrotoxicosis** by *antithyroid drugs*
  - pernicious anaemia by *injection of vitamin B12*
  - myasthenia gravis by *cholinesterase inhibitors*
  - Insulin-dependent diabetes by *insulin administration*

Autoimmune disease

Organ-specific autoimmune disease	Systemic autoimmune disease
Type I diabetes mellitus (pancreas)	**Rheumatoid arthritis**
Goodpasture's syndrome (renal and lung basement membrane)	Scleroderma
Multiple Sclerosis (CNS)	**Systemic Lupus Erythematosus** Primary Sjogren's syndrome Polymyositis
Grave's disease (thyroid) Hashimoto's thyroiditis (thyroid) Autoimmune Pernicious anaemia (red cells) Autoimmune **Addison's disease** (Adrenal cells) Vitiligo (skin) **Myasthenia Gravis** (muscle)	