IMMUNE SYSTEM IN DISEASE: HYPER SENSITIVITY REACTIONS AND AUTOIMMUNITY

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The Immune System

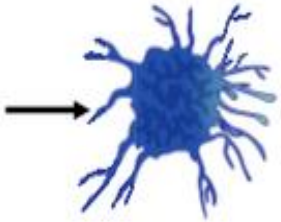
Innate Immune System

Physical barriers:
Skin; organ mucosal layers

Chemical barriers:
Stomach acid; lysozymes in eye

Innate response: Inflammatory response cells

Immune system linkage:
Dendritic cells

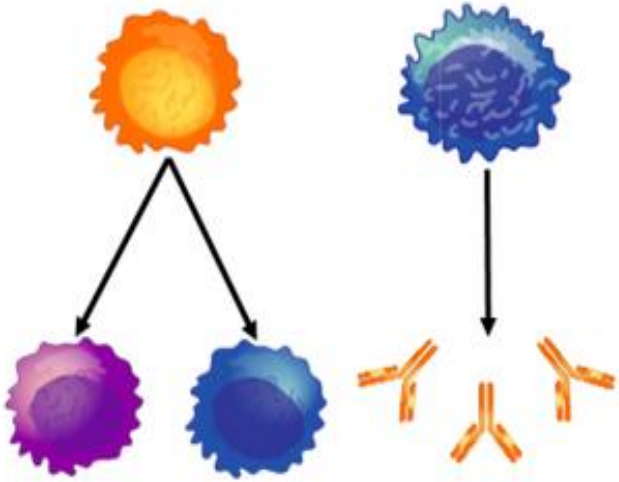


Adaptive Immune System

Adaptive response:
Cell-mediated response; humoral response

Cell mediated response:
T-lymphocytes

Humoral Response:
B-lymphocytes



Products:
CD4+ and CD8+ T-cells

Products:
Antibodies

HYPERSENSITIVITY REACTIONS

- Exaggerated immune responses against environmental antigens that are usually harmless (allergy or type 1 hypersensitivity).
- Immune system inadequately controlled and inappropriately targeted to host tissues (type , 2, 3 and 4 hypersensitivity).

Table 5 - Comparison of Different Types of hypersensitivity				
characteristics	type-I (anaphylactic)	type-II (cytotoxic)	type-III (immune complex)	type-IV (delayed type)
antibody	IgE	IgG, IgM	IgG, IgM	None
antigen	exogenous	cell surface	soluble	tissues & organs
response time	minutes30-15 hrs 2-	minutes-hours	hours 12-3	hours 72-48
appearance	weal & flare	lysis and necrosis	erythema and edema, necrosis	erythema and induration
histology	Mast cells ,basophils and eosinophils	antibody and complement	complement and neutrophils	macrophages and T cells
transferred with	antibody	antibody	antibody	T-cells

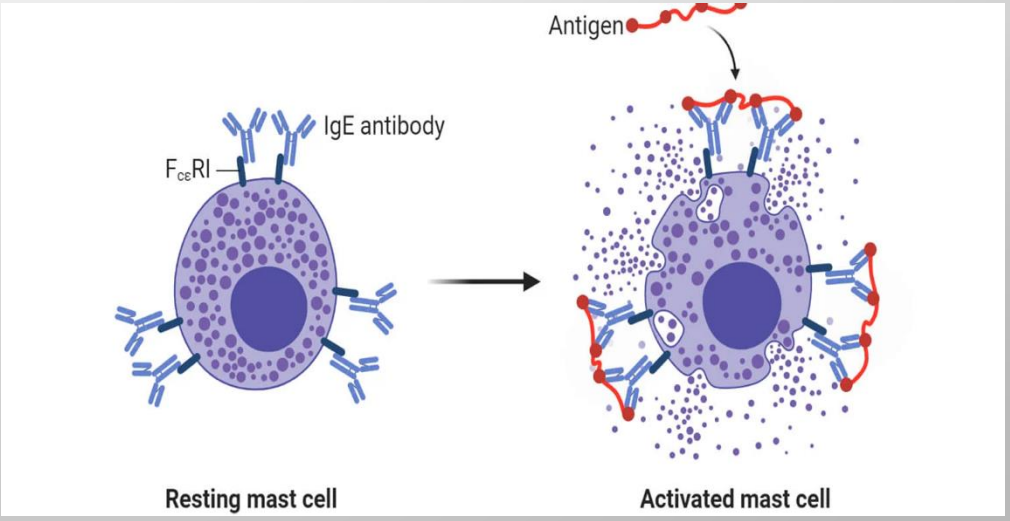
TYPE 1 HYPERSENSITIVITY REACTION
ALLERGY OR ATOPY

- The allergic reaction first requires sensitization to the specific allergen, in genetically susceptible individuals.

- The allergen is either:
- Inhaled: Pollens, house dust mite (most common allergen), cat or dog hair flakes.
- contact skin.
- Ingested: egg, milk, peanuts and fish
- Injected: penicillin and cephalosporin

- Main antibody involved: IgE.

- Main cells involved: Mast cells, basophils and eosinophils.



- **Two phases:**
- 1. Immediate reaction: start within minutes and subside within hours.
- Clinically: contraction of smooth muscles of the airway and GI tract, increased Vaso permeability and vasodilation, enhanced mucus production, and pruritus (itching)

- 2. late phase reaction: start 2-24 hours later.
- Clinically: tissue destruction (mucosal damage)

- **Examples**:
- Urticaria (eczema) causing wheals on skin.
- Allergic Rhinitis
- Allergic Conjunctivitis
- Anaphylaxis

- **Dental relevance**
- 1. Drug induced allergic reaction:
- Local anesthesia (lidocaine, preservatives) .. Causes urticaria, and edema
- Antibiotics (penicillin)
- Analgesics or NSAIDs …. May trigger bronchospasm or angioedema.
- 2. Latex allergy:
- Gloves, rubber dams ….. Cause urticaria, itching, conjunctivitis and rhinorrhea.
- 3. Anaphylaxis: life threatening after local anesthesia, antibiotics, latex exposure.
- 4. Asthma.

TYPE 2 HYPERSENSITIVITY REACTION ANTIBODY MEDIATED

- Antibodies against antigens present on the cell surface (self or foreign; like RBCs).
- Leading to cell destruction or dysfunction.

- Main antibody involved: IgG, IgM

- Examples:
- 1. Mismatched Blood Transfusion.
- 2. Autoimmune hemolytic anemia.
- 3. Goodpasture syndrome.
- 4. Grave's disease.
- 5. Pemphigus vulgaris and bullous pemphigoid

- **DENTAL RELEVANCE**
- Pemphigus vulgaris and bullous pemphigoid, often present with oral lesions first.
- Drug-induced hemolytic anemia or thrombocytopenia may appear after certain antibiotics or anesthetics

TYPE 3 HYPERSENSITIVITY REACTION
IMMUNE COMPLEX MEDIATED

- It involves soluble antigens that are not bound to cell surfaces (as opposed to those in type II hypersensitivity). When these antigens bind antibodies in the circulation, immune complexes of different sizes form
- When these Immune complex deposits in tissues, it will trigger inflammation and tissue damage.

- Main antibodies involved: IgG, IgM

- Main cells involved: Neutrophils

➢ **Examples**:

1. Autoimmune diseases:

- Post-streptococcal glomerulonephritis (after throat infection)
- Rheumatoid arthritis (deposition in synovium)
- Systemic lupus erythematosus

2. Serum sickness:

- Injection of large quantity of Ag (injection of high quantity of penicillin or antitoxins for long period)

3. Arthus reaction:

- At the site of injection of booster vaccine.

➢ **Dental relevance**:

- SLE can cause oral ulcers, mucosal petechiae, or secondary infections due to immunosuppression.

TYPE 4 HYPERSENSITIVITY REACTION OR DELAYED HYPERSENSITIVITY T-CELL MEDIATED

- Not antibody mediated.
- On re-exposure to the same antigen, the memory T-cells activate macrophages and cytotoxic T-cells.
- Leads to localized tissue destruction and granulomatous inflammation.
- **Examples:**

1. Tuberculin skin test (Mantoux).
2. Contact dermatitis: from Nickel, latex, dental resins.
3. Granulomatous inflammation: in chronic ulcers and enlarged lymph nodes in head and neck.
4. Graft rejection.

- **Dental relevance**
- Contact mucositis from acrylics or composite resins
- Latex-glove allergy causes itching, redness hours after use

AUTOIMMUNITY

- An immune response against self-antigen (self-tolerance failure) leading to tissue injury or functional disturbance.
- The body's immune system cannot distinguish self from non-self.

- Normal self tolerance (under normal conditions):
- 1. central tolerance: This process occurs in the thymus (for T cells) and bone marrow (for B cells) and involves eliminating or disabling immune cells that could attack self-antigens during their development.
- 2. Peripheral tolerance: This occurs after immune cells have matured and are circulating in the body.
- Main contributor to tolerance is CD4 T cells.

- **Mechanisms of Autoimmunity**
- 1. Loss of Self-Tolerance
- Genetic defect in deletion of self-reactive T or B cells.
- 2. Molecular Mimicry
- Microbial antigens resemble self-antigens → antibodies or T cells cross-react.
- Example: Rheumatic fever after Streptococcal infection.
- 3. Release of Sequestered Antigens
- Normally hidden antigens (e.g., lens, testes, CNS) exposed after injury → immune response
- 4. Defective T-reg Function
- Decreased suppression of autoreactive lymphocytes.
- 5. Polyclonal Lymphocyte Activation
- Certain infections (EBV, CMV) activate many B cells nonspecifically → some autoantibodies form.

- **Types of autoimmune diseases**

Type	Example	Mechanism	Key features
Organ specific	Hashimoto thyroiditis, Type 1 diabetes, Myasthenia gravis	Target limited to one organ	Local tissue destruction or dysfunction
Systemic (multiorgan)	SLE, Rheumatoid arthritis, Systemic sclerosis.	Immune complexes or autoantibodies affect many organs	Widespread inflammation, vasculitis

- Once autoimmune disease start it become chronic and progressive due to epitope spreading as a result of tissue damage.
- The symptoms is on and off, when it is on it is called flare up.

- **Lab diagnosis**
- Elevated levels of immunoglobulins
- Inflammatory markers: High CRP, ESR
- Auto-antibodies: anti-nuclear, anti-smooth muscle, anti-mitochondrial, rheumatoid factor
- Complement levels may decreased
- Biopsy: Antibody on the surface of the tissue or cells, immune complex by immunofluorescence, or lymphocyte infiltration

- **Management**
- Immunosuppression: corticosteroid
- Targeted biologics: anti-TNF
- Symptomatic: saliva substitutes in Sjogren's, pain control, topical steroid for oral lesions.
- Treat infections early due to reduced immunity.

- **Oral lesions in autoimmune diseases**
- 1. pemphigus vulgaris: intraepithelial blisters, often first seen on oral mucosa.
- 2. Sjogren's syndrome: autoimmune destruction of salivary glands ⟶ xerostomia, caries, difficulty swallowing.
- 3. SLE: oral ulcers, erythema, secondary infections.

- **Clinical cautions:**
- Many patients use immunosuppressants or corticosteroids so increase risk of infections, and delayed healing
- Dry mouth increases risk of caries, candidiasis, and mucosal ulceration.
- Use non-irritating dental materials.


THANK YOU!