



Immunology
Hypersensitivity (2)
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Hypersensitivity reactions= Policeman and the thief



Type 2
hypersensitivity



Type 3
hypersensitivity



Type II Hypersensitivity

Type II Hypersensitivity is subdivided into

Target cell depletion or
destruction without
inflammation
(cytotoxic)

Ab mediated cell dysfunction
(no cell depletion, destruction,
or inflammation) (non
cytotoxic)

Complement mediated
Inflammation (cytotoxic)

Type II Hypersensitivity

1. Target cell depletion or destruction without inflammation

Examples

1. Autoimmune Hemolytic Anemia (AIHA)
2. Autoimmune Neutropenia
3. Erythroblastosis fetalis (hemolytic disease of the newborn)
4. ABO incompatibility

Mechanism of cell destruction is mediated by

- Antibodies
- Complement
- Natural killer (NK) cells

Type II Hypersensitivity

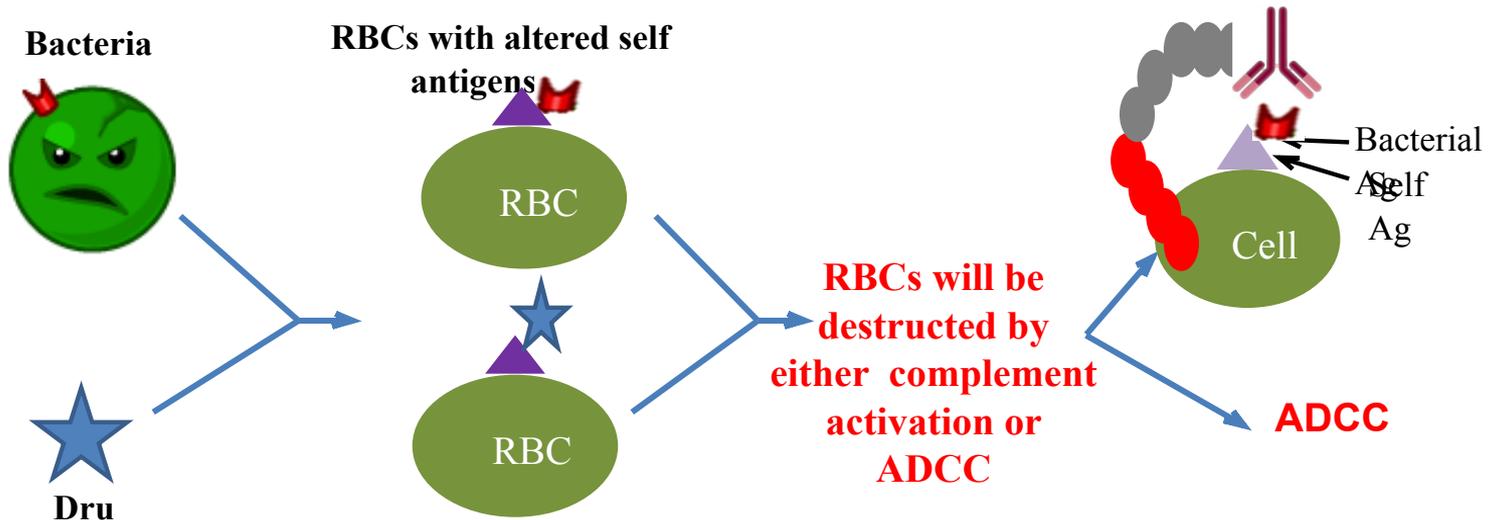
1. Target cell depletion or destruction without inflammation

Autoimmune Hemolytic Anemia (AIHA)

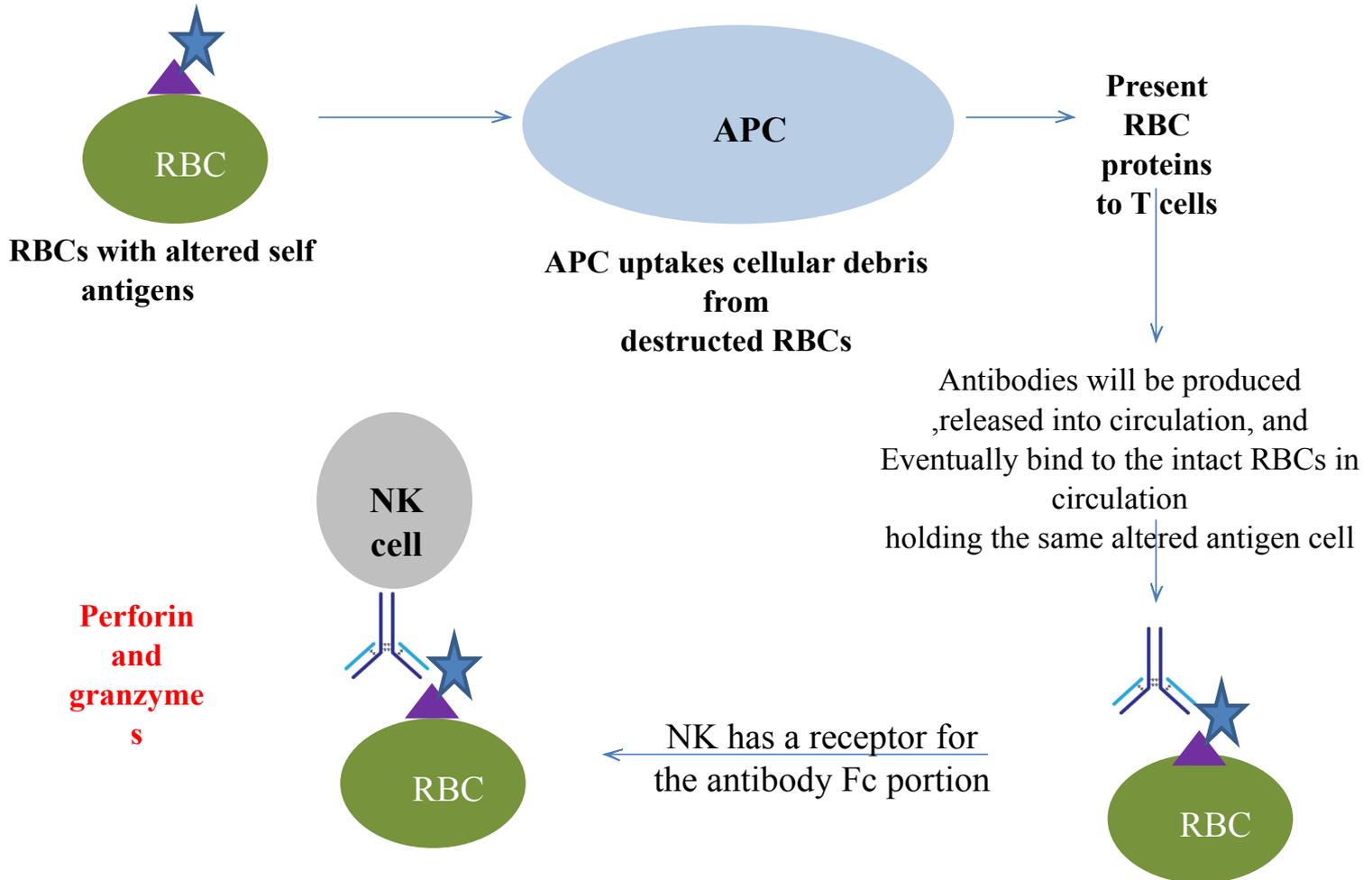
Causes of AIHA:

Idiopathic

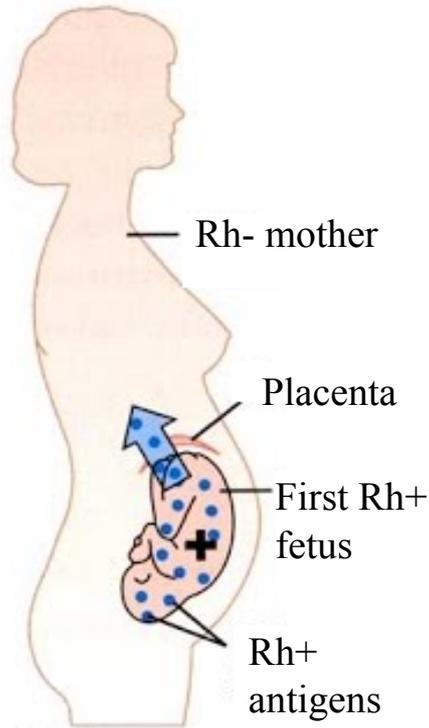
Drug or bacterial induced altered self antigens



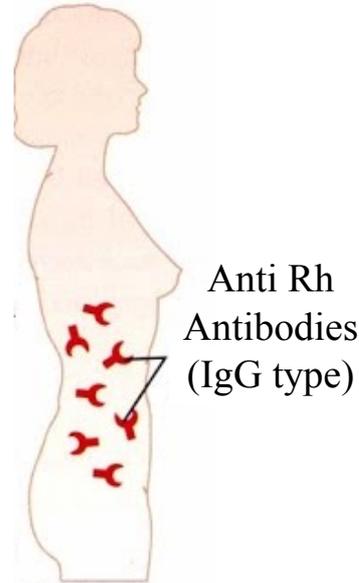
Antibody dependent cell mediated cytotoxicity (ADCC)



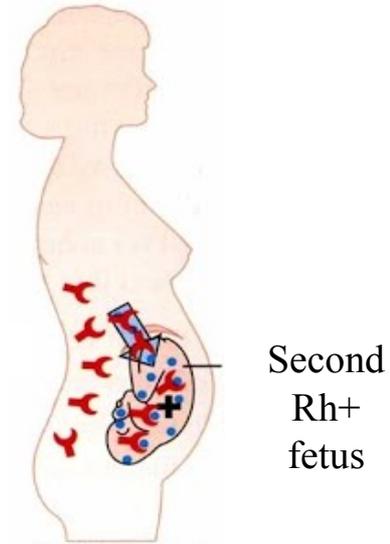
Erythroblastosis Fetalis (hemolytic disease of the newborn)



First pregnancy



Between pregnancies



Second pregnancies

Symptoms

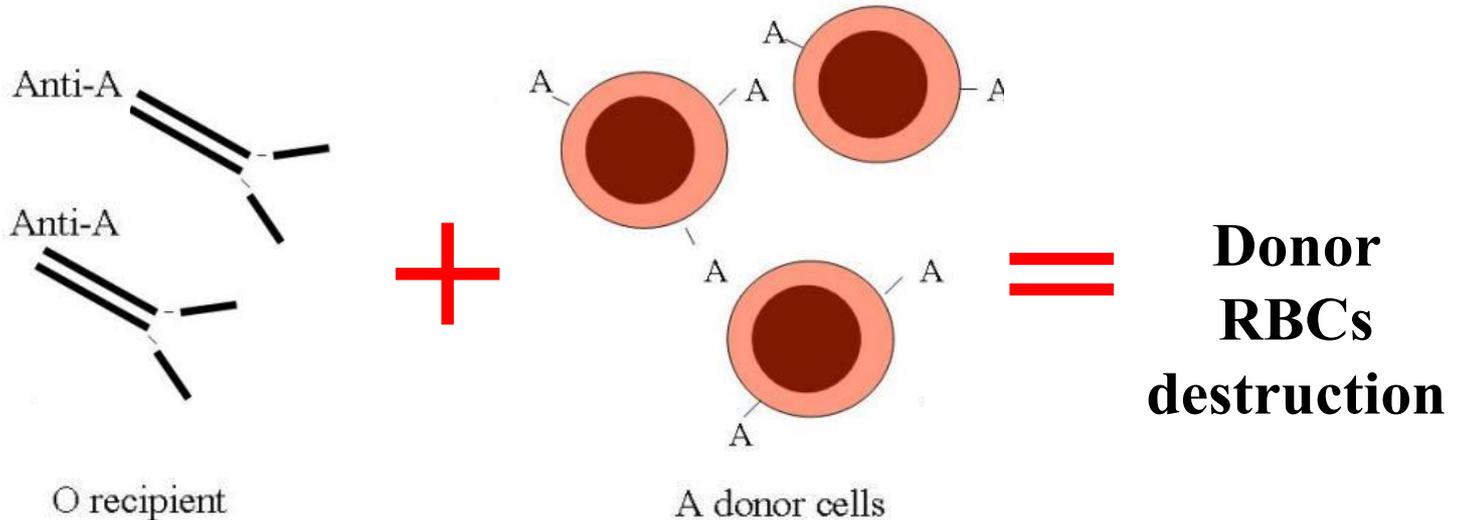
•**In the fetus:** Symptoms detected during pregnancy may include an enlarged liver, spleen, or heart, and fluid buildup in the abdomen, lungs, or scalp ([hydrops fetalis](#)).

•**In the newborn:** After birth, symptoms can include anemia, severe jaundice (due to a buildup of bilirubin), and an enlarged liver and spleen.



ABO incompatibility

- Are examples of cellular destruction that result from antibody combining with blood antigens
- **Acute hemolytic transfusion reactions** may occur **within minutes** or hours after receipt of incompatible blood



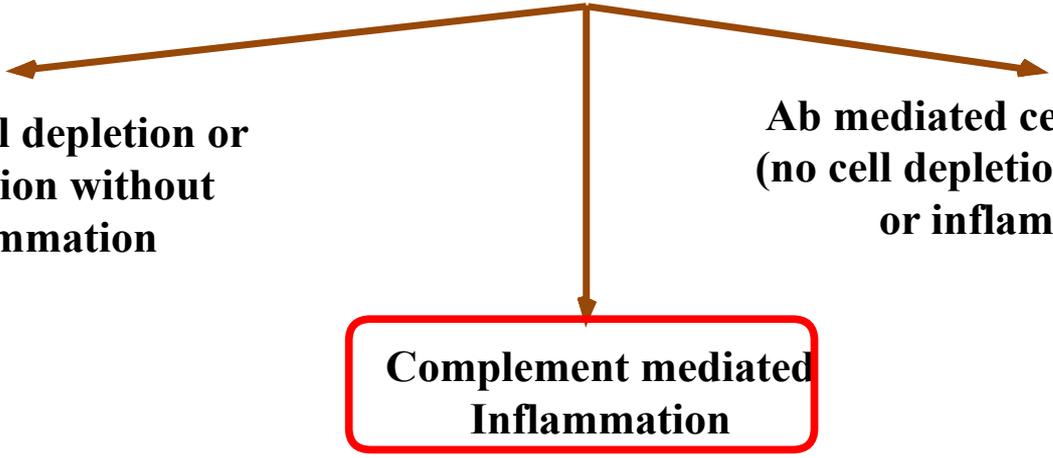
Type II Hypersensitivity

Type II Hypersensitivity is subdivided into

Target cell depletion or
destruction without
inflammation

Ab mediated cell dysfunction
(no cell depletion, destruction,
or inflammation)

Complement mediated
Inflammation



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graph TD; A[Type II Hypersensitivity is subdivided into] --> B[Target cell depletion or destruction without inflammation]; A --> C[Ab mediated cell dysfunction (no cell depletion, destruction, or inflammation)]; A --> D[Complement mediated Inflammation];
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2. Complement mediated Inflammation

2. Complement mediated Inflammation Mechanism

1. Ab directed against self antigen = complement mediated destruction.
2. Complement proteins mediate neutrophil chemotaxis to the site of Ab activation.

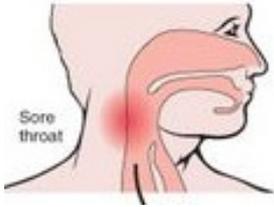
Example

s

Molecular mimicry: is a phenomenon where the immune system mistakenly attacks the body's own tissues because a foreign molecule (like from a virus or bacteria) is structurally similar to a "self" molecule. This similarity can trick the immune system into a cross-reactive response, where the immune cells and antibodies that were activated to fight the infection also target the host's cells, leading to autoimmune disease.

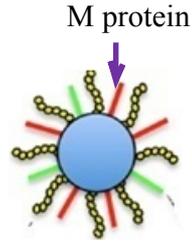
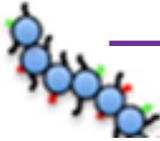


2. Acute Rheumatic Fever



Sore throat

S. pyogenes



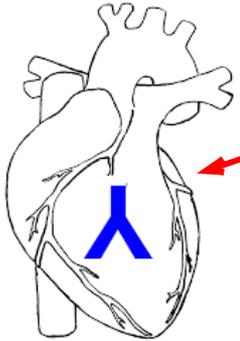
M protein



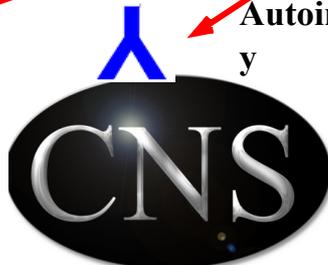
M-protein mimics the self proteins present in heart, CNS, and joints



- Anti-M antibodies start fighting against bacteria
- Anti-M antibodies also cross react with self Ag and mediate Immune destruction



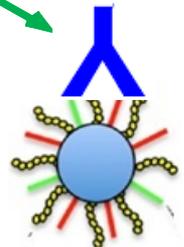
Autoimmunity



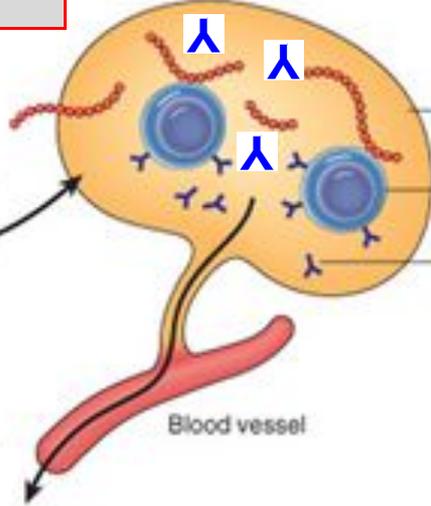
Autoimmunity



Protection



Immune response



Lymph node

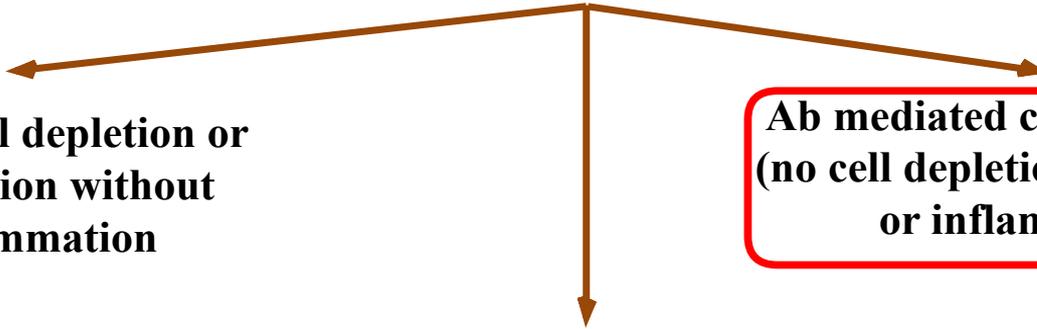
B lymphocytes

Antistrept antibodies

Blood vessel

Type II Hypersensitivity

Type II Hypersensitivity is subdivided into



Target cell depletion or destruction without inflammation

**Ab mediated cell dysfunction
(no cell depletion, destruction, or inflammation)**

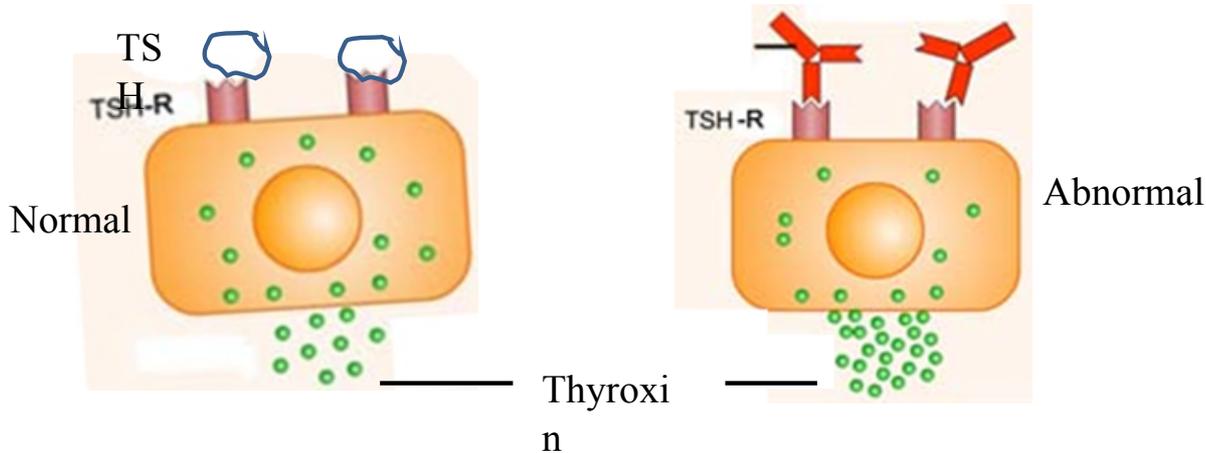
Complement mediated Inflammation

Type II Hypersensitivity

3. Ab mediated cell dysfunction (no cell depletion, destruction, or inflammation)

Examples

1. Graves' disease (Autoimmune hyperthyroidism)

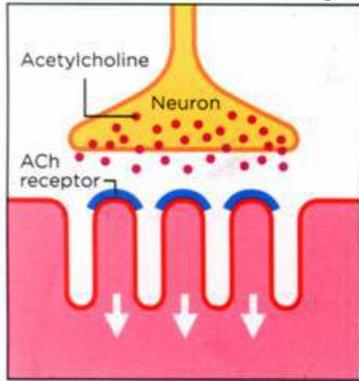


The disorder results from an antibody, called **thyroid stimulating immunoglobulin (TSI)**, that has a similar effect to thyroid stimulating hormone (TSH). These antibodies cause the thyroid gland to produce excess thyroid hormone

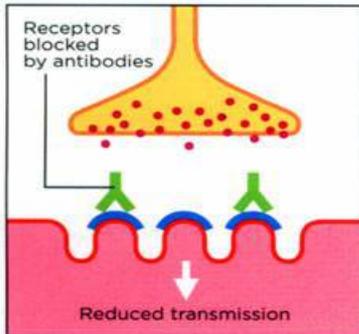
Type II Hypersensitivity

2. Myasthenia

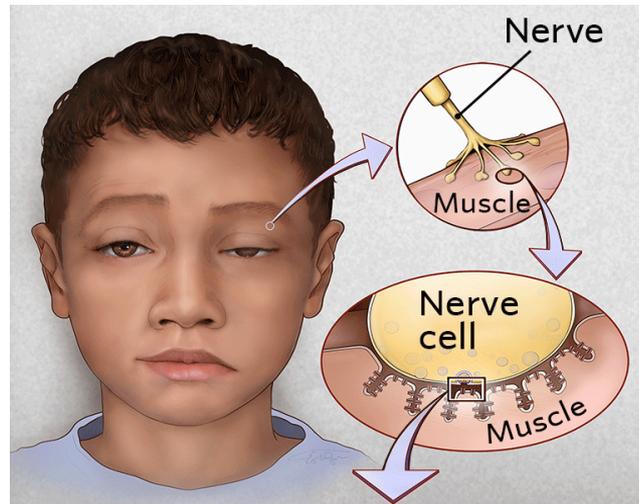
gravis
Autoantibody produced against acetylcholine (ACh) receptors which inhibits the ACh mediated muscle contraction leading to muscle weakness



Normal neuromuscular junction



Neuromuscular junction in myasthenia gravis



Type II Hypersensitivity

Table I-13-4. Type II Hypersensitivities

Disease	Target Antigen	Mechanism of Pathogenesis	Clinical Manifestations
Cytotoxic			
Autoimmune hemolytic anemia (HDNB)	RBC membrane proteins (Rh, I Ags)	Opsonization, phagocytosis, and complement-mediated destruction of RBCs	Hemolysis, anemia
Acute rheumatic fever	Streptococcal cell-wall Ag; Ab cross-reacts with myocardial Ag	Inflammation, macrophage activation	Myocarditis, arthritis
Goodpasture syndrome	Type IV collagen in basement membranes of kidney glomeruli and lung alveoli	Complement- and Fc-receptor-mediated inflammation	Nephritis, lung hemorrhage, linear Ab deposits
Autoimmune thrombocytopenic purpura	Platelet membrane proteins	Ab-mediated platelet destruction through opsonization and complement activation	Bleeding

Type II Hypersensitivity

Table I-13-4. Type II Hypersensitivities

Disease	Target Antigen	Mechanism of Pathogenesis	Clinical Manifestations
Non-cytotoxic			
Myasthenia gravis	Acetylcholine receptor	Ab inhibits acetylcholine binding, downmodulates receptors	Muscle weakness, paralysis
Graves disease	TSH receptor	Ab-mediated stimulation of TSH receptors	Hyperthyroidism followed by hypothyroidism
Type II (insulin-resistant) diabetes	Insulin receptor	Ab inhibits binding of insulin	Hyperglycemia
Pernicious anemia	Intrinsic factor of gastric parietal cells	Neutralization of intrinsic factor, decreased absorption of vitamin B ₁₂	Abnormal erythropoiesis, anemia

Hypersensitivity reactions= Policeman and the thief



Type 3
hypersensitivity



Type 3 hypersensitivity

- also known as immune-complex hypersensitivity,
- occurs when soluble antigen-antibody complexes accumulate in tissues, triggering an inflammatory response that can cause tissue damage.
- the reaction is caused by the failure of the immune system to adequately clear these circulating complexes.

Type 3 hypersensitivity

Predisposing Conditions and Exposures

- **Persistent Infections:** Chronic infections such as bacterial endocarditis, hepatitis B, or hepatitis C can cause continuous release of antigens into the bloodstream, leading to ongoing immune complex formation and disease.
- **Autoimmune Diseases:** In conditions like systemic lupus erythematosus (SLE) and rheumatoid arthritis, the immune system produces autoantibodies against the body's own soluble antigens (e.g., DNA or immunoglobulins). Because the autoantigens are constantly present, immune complex deposition continues, leading to chronic inflammation and widespread organ damage.
- **Exposure to Foreign Proteins/Drugs:** The immune system may react to foreign proteins introduced through medications, vaccines, antivenoms, certain antibiotics, or insect stings, leading to a systemic reaction called **serum sickness**.
- **Environmental/Occupational Exposures:** Repeated inhalation of environmental antigens, such as mold spores in "farmer's lung" or bird proteins can cause immune complexes to form and deposit in the lung alveoli, causing hypersensitivity pneumonitis.

Type III Hypersensitivity

Types

1- Localized reaction (Arthus reaction)

Mechanism

Exposure to an antigen

IgG production

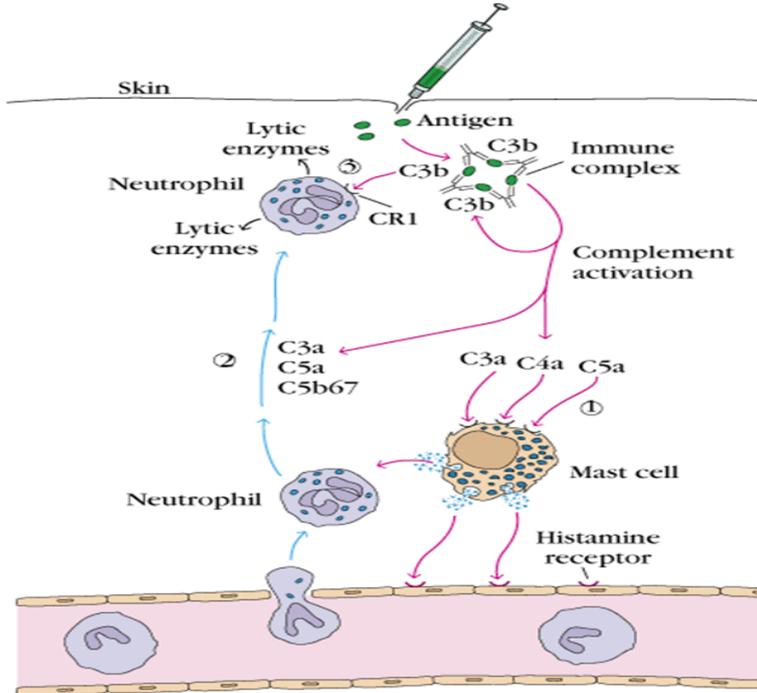
Further exposure

Enough IgG

Local reaction

4-8 hours

Arthus reaction



Types

of Arthus reaction

➔ Injected--- Vaccine, insect bite

➔ Inhaled-- Bird Breeder's Disease



Type III Hypersensitivity

Types

2- Serum sickness

- More systemic
- IgG or IgM
- Antigen
 - Drugs
 - Endogenous (SLE) or exogenous (Bacterial, viral, or fungal)
- 6-15 days (the time needed to develop Abs)

Sites in which this typically occurs include the glomerular basement membrane, vascular endothelium, joint linings, and pulmonary alveolar membranes.

Types of

Arthus

reaction



Serum Sickness



Drug Reactions



Autoimmune Diseases

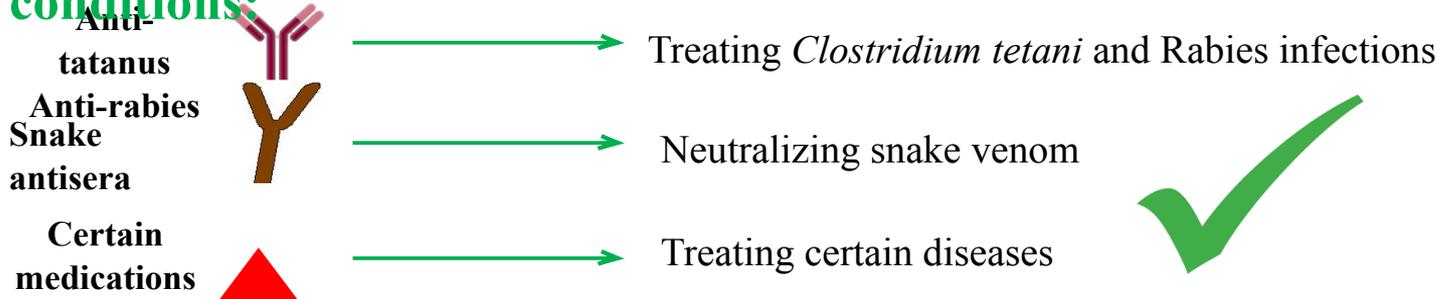
Type III Hypersensitivity

Types

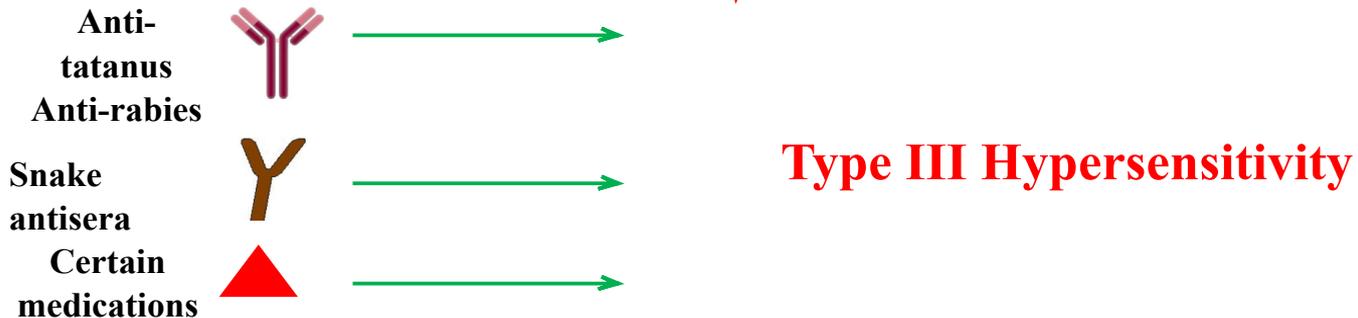
1. Generalized reaction (Serum Sickness reaction)

Antibodies and medications are useful under normal

conditions:



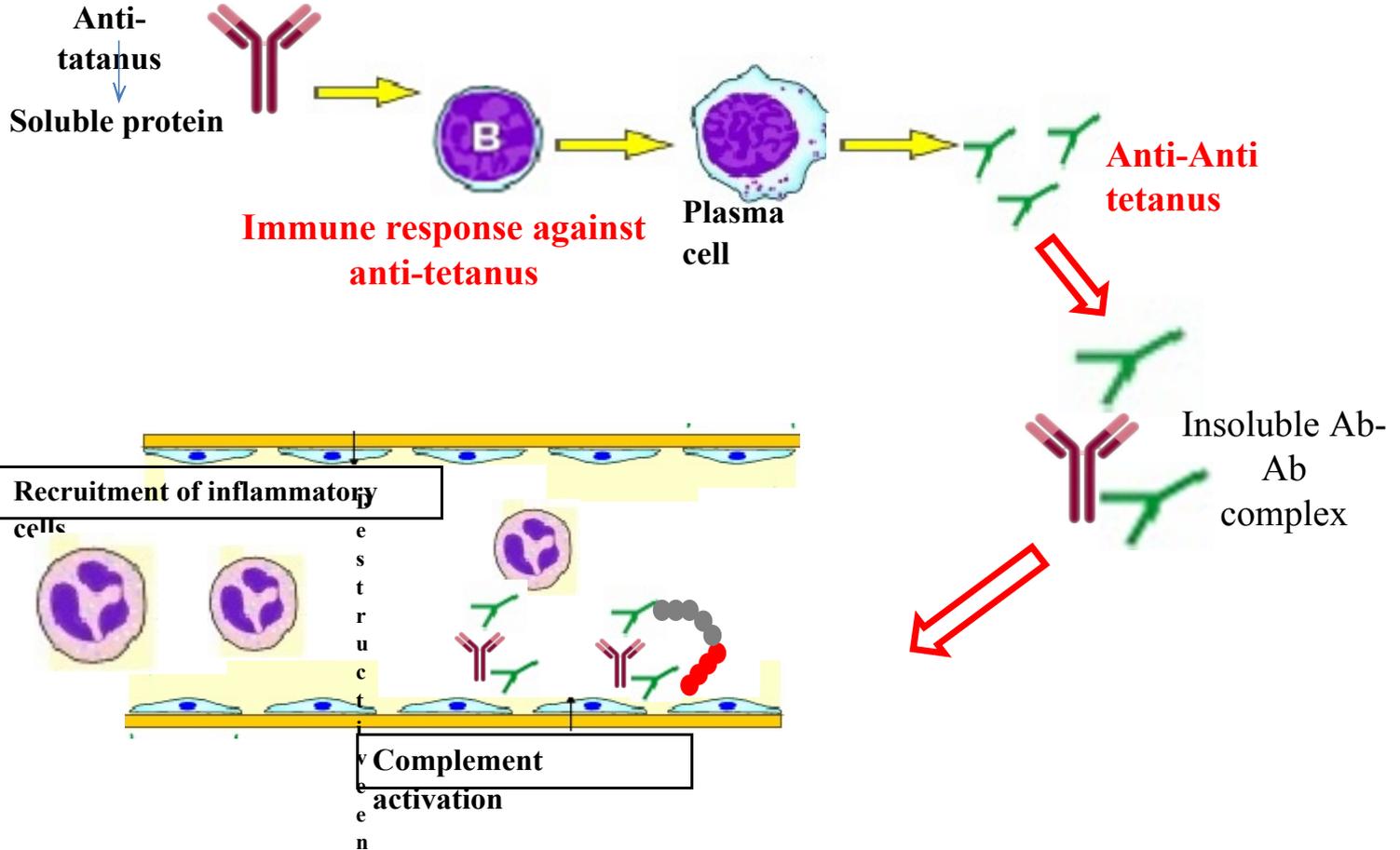
But these might have negative effect through the induction of **type III Hypersensitivity**



Types

Type III Hypersensitivity

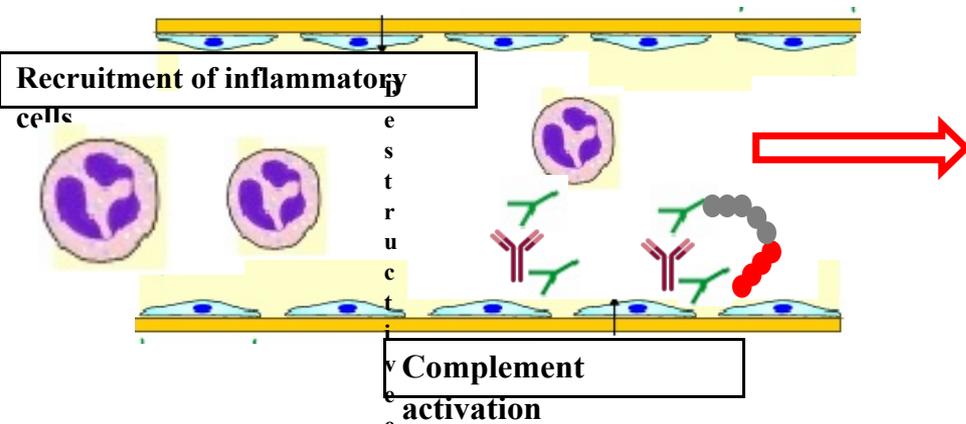
1. Generalized reaction (Serum Sickness reaction)



Type III Hypersensitivity

Types

Generalized reaction (Serum Sickness like reaction).



- Fever
- Generalized Lymphadenopathy
- Rashes
- Proteinuria and hematuria
- Polyarthritits
- Pericardial pain
- Multiple vasculitic leasions



Type III Hypersensitivities

Disease	Antigen Involved	Clinical Manifestations
Systemic lupus erythematosus ⁺	dsDNA, Sm, other nucleoproteins	Nephritis, arthritis, vasculitis, butterfly facial rash
Poststreptococcal glomerulonephritis	Streptococcal cell wall Ags (may be “planted” in glomerular basement membrane)	Nephritis, “lumpy-bumpy” deposits
Arthus reaction	Any injected protein	Local pain and edema
Serum sickness	Various proteins	Arthritis, vasculitis, nephritis
Polyarteritis nodosa	Hepatitis B virus Ag	Systemic vasculitis

- The immune complexes that cause disease may involve either self or foreign antigens bound to antibodies.
- These immune complexes are filtered out of the circulation in the small vasculature, so their sites of ultimate damage do not reflect their sites of origin.
- These diseases tend to be systemic, with little tissue or organ specificity.

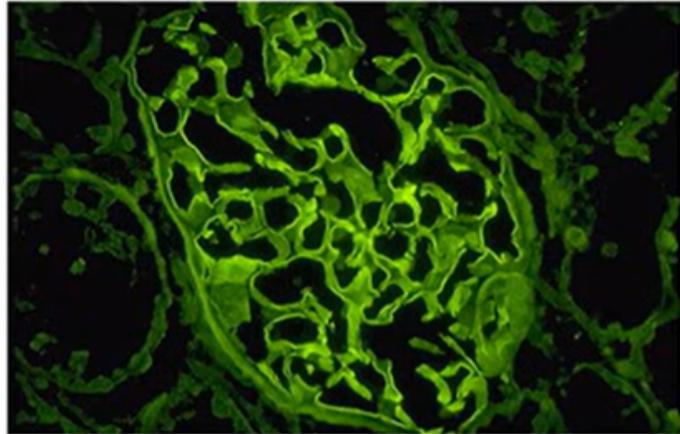
Type II vs. Type III Glomerulonephritis

TYPE 2

Goodpasture Syndrome

“linear” deposition

Good Pasture (2)

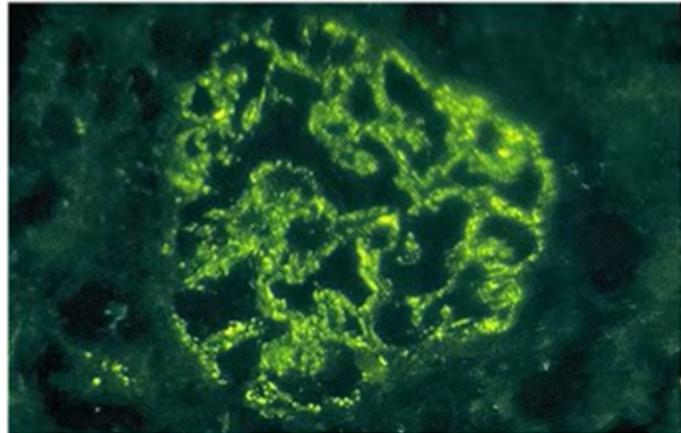


TYPE 3

Poststreptococcal Glomerulonephritis

“lumpy bumpy” deposition

PSG (3 letters)

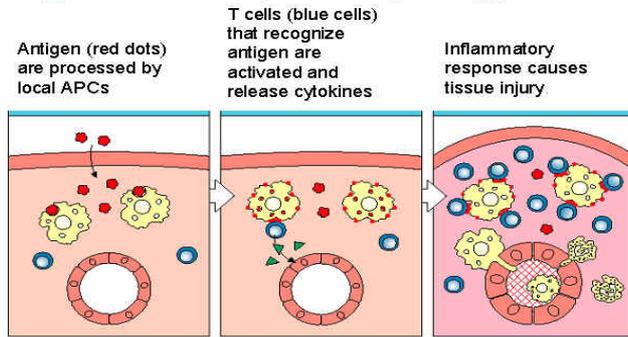


Type IV Hypersensitivity reaction

Type IV hypersensitivity

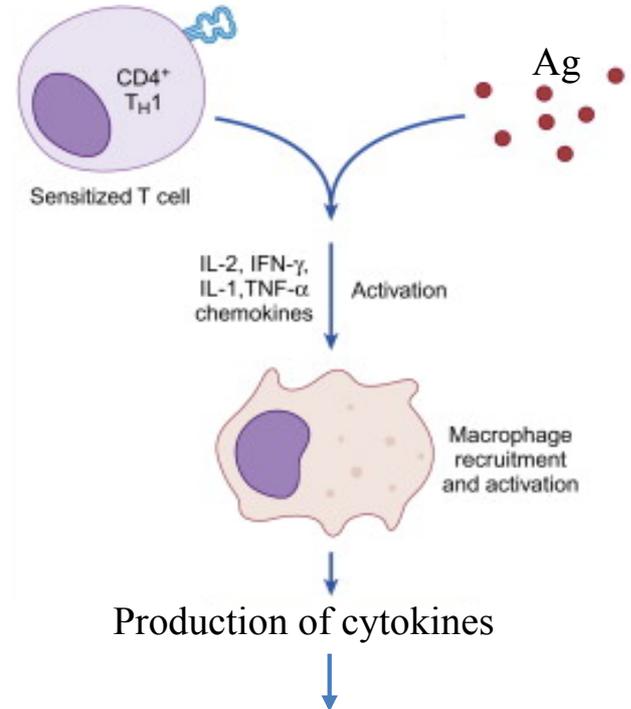
- Also known as delayed-type hypersensitivity.
- Is a cell-mediated immune response that involves T-cells
- Typically develops 48 to 72 hours after exposure to an antigen.
- Caused by T-cells, which can cause inflammation and tissue damage directly or by releasing cytokines that recruit other immune cells.
- This type of reaction is involved in defense against intracellular pathogens like bacteria and fungi, as well as conditions such as allergic contact dermatitis, transplant rejection, and some drug reactions

Type IV hypersensitivity – delayed-type or contact



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Antigen is presented by APCs to antigen-specific memory T cells that become activated and produce chemicals that cause inflammatory cells to move into the area, leading to tissue injury. Inflammation by 2-6 hours; peaks by 24-48 hours.



Activate Th1 and Tc cells

Activate phagocytosis

Inflammation

Tissue damage

Type IV hypersensitivity

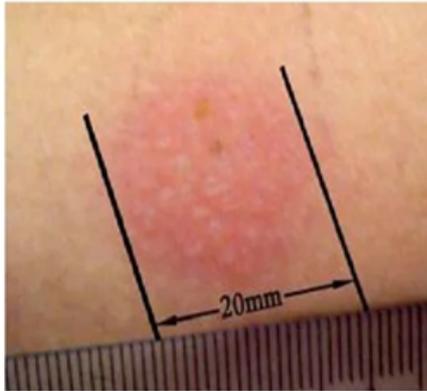
Disease	Specificity of Pathogenic T Cells	Clinical Manifestations
Tuberculin test	PPD (tuberculin & mycolic acid)	Indurated skin lesion (granuloma)
Contact dermatitis	Nickel, poison ivy/oak catechols, hapten/carrier	Vesicular skin lesions, pruritus, rash
Hashimoto thyroiditis*	Unknown Ag in thyroid	Hypothyroidism
Multiple sclerosis	Myelin Basic Protein	Progressive demyelination, blurred vision, paralysis
Rheumatoid arthritis*	Unknown Ag in joint synovium (type II collagen?)	Rheumatoid factor (IgM against Fc region of IgG), alpha-cyclic citrullinated peptide (α -CCP) antibodies, chronic arthritis, inflammation, destruction of articular cartilage and bone

Type IV hypersensitivity

Insulin-dependent diabetes mellitus (type I)*	Islet-cell antigens, insulin, glutamic acid decarboxylase, others	Chronic inflammation and destruction of β cells, polydipsia, polyuria, polyphagia, ketoacidosis
Guillain-Barré syndrome*	Peripheral nerve myelin or gangliosides	Ascending paralysis, peripheral nerve demyelination
Celiac disease	CD4+ cells—gliadin, CD8+ cells—HLA class I-like molecule expressed during stress	Gluten-sensitive enteropathy
Crohn disease	Unknown Ag, commensal bacteria?	Chronic intestinal inflammation due to Th1 and Th17 cells, obstruction

*Diseases classified as type IV pathologies in which autoantibodies are present and used as clinical markers

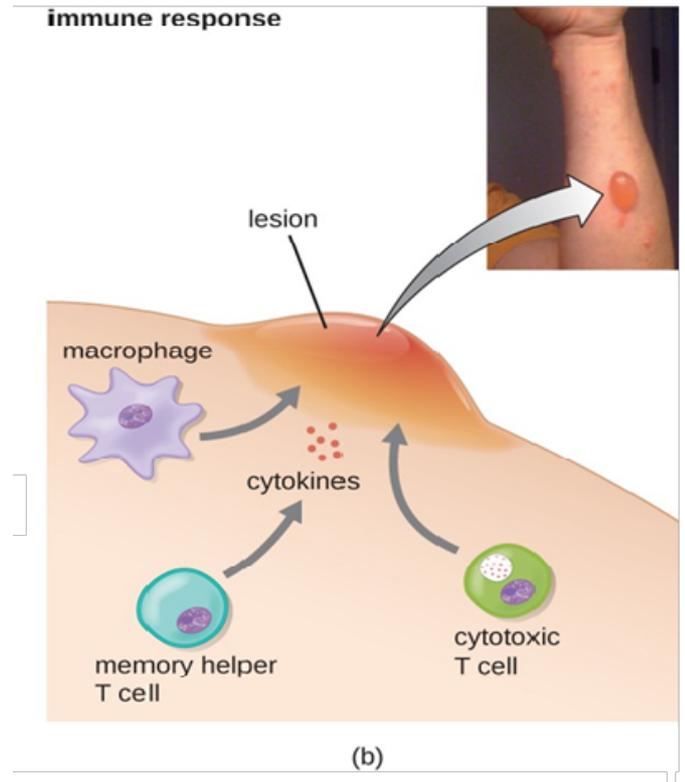
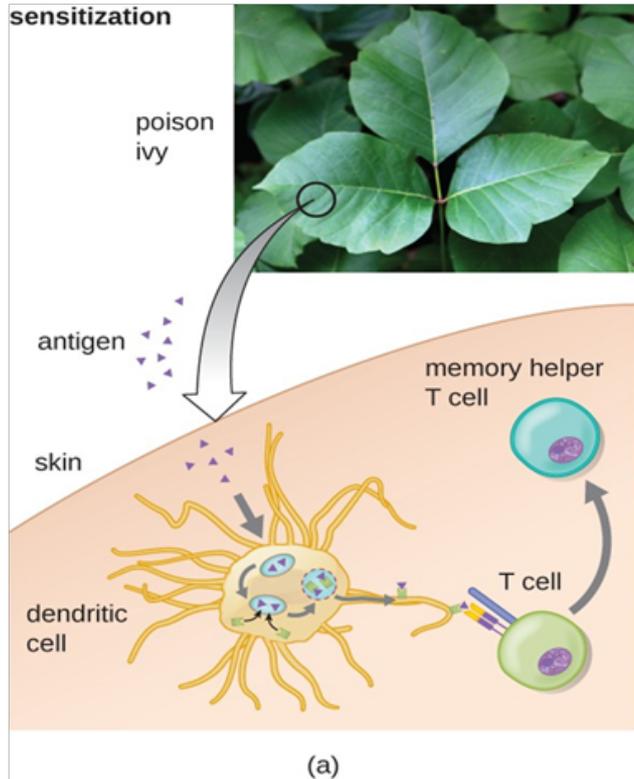
Tuberculosis Skin Test (PPD)



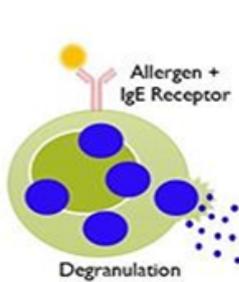
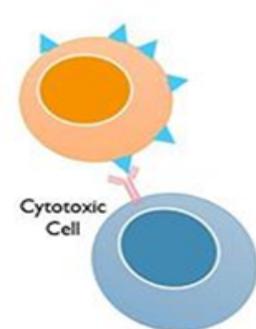
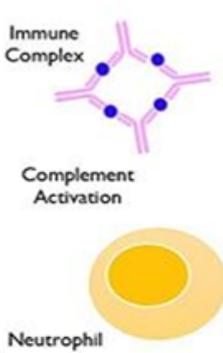
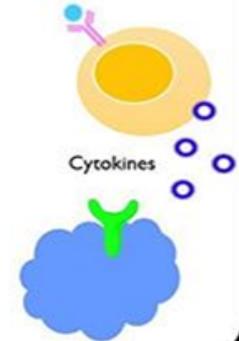
How it works

- **Antigen injection:** A small amount of PPD, a protein from the TB bacteria, is injected intradermally.
- **Immune system activation:** If the individual has a history of exposure to *M. tuberculosis*, their immune system will have memory T-cells that recognize the PPD antigen.
- **Delayed response:** These memory T-cells are activated and trigger an inflammatory response that develops over 48 to 72 hours, not immediately.
- **Cellular infiltration:** The inflammatory response involves the recruitment of macrophages and other immune cells to the injection site.
- **Visible reaction:** This cellular infiltration leads to the characteristic redness and swelling (induration) that is measured to determine if the test is positive.

Ivy Poison



Types of Hypersensitivity Reactions

	Type I	Type II	Type III	Type IV
	 <p>Allergen + IgE Receptor</p> <p>Degranulation</p>	 <p>Cytotoxic Cell</p>	 <p>Immune Complex</p> <p>Complement Activation</p> <p>Neutrophil</p>	 <p>Cytokines</p>
Mediators	IgE-Mediated	IgG or IgM Cytotoxic	Immune Complex-Mediated	T-Cell-Mediated
Onset	Within 1 Hour	Hours to Days	1-3 Weeks	Days to Weeks
Examples	Anaphylaxis	Hemolytic Anemia	Serum Sickness SLE	Rash SJS

How to remember the types of hypersensitivity?

I= Allergic Anaphylaxis

A

Atopy

B

II= antiBody

C

III= immune Complex

D

IV= Delayed

Anaphylaxis = Type I

Cytotoxic = Type II

Immune complex = Type III

Delayed = Type IV

A
c
i
d

