Hypersensitivity

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- The term hypersensitivity refers to the **injurious consequences** in the sensitized host.
- For this injurious reaction **Von Pirquet** used the term allergy(i.e. altered reaction)
- Hypersensitivity reactions are divided into two types:- 1) I**mmediate** hypersensitivity(B cell or antibody mediated)

2**) Delayed** hypersensitivity

For occurrence of hypersensitivity reaction, host have had contact with **allergin**(antigen). Initial contact with allergin known as **sensitising** or **prime dose** (which sensitize B and T lymphocytes). Subsequent contact or secondary contact with the same allergen called **shocking dose**(which causes clinical reaction).

Classification of hypersensitivity

1) Immediate hypersensitivity

2) Delayed hypersensitivity

1)Immediate hypersensitivity:-

-Appears rapidly

-induced by antigen or hapten by any route

-passive transfer possible with serum

e.g. Anaphylaxis reaction, Atopy, Antibody mediated cell damage, Arthus reaction, Serum sickness.

2)Delayed hypersensitivity

-Appears slowly

-Induced by intradermally, by skin contact

-can't transfer by serum, can transfer with T cells

e.g. Infection type (Tuberculin type), Contact dermatitis.

- **Coomb's and Gell (1963)** classified hypersensitivity reaction into four types:-

I) Type I -- (Anaphylaxis)

II) Type II – (Cytotoxic)

III) Type III – (Immune complex or toxic complex disease)

IV) Type IV – (Delayed or cell mediated hypersensitivity)

Anaphylaxis:

(ana=without)(phylaxis=protection)

- Term anaphylaxis first explained by **Rechet(1902)**
- Dog sensitized with sea anemone extract second time, get died.
- Sensitization is more effective when antigen (allergen) introduced parent rally.
- Shocking dose is not effective when infected intra -venous.
- There should be time interval between sensitized dose and shocking dose of 2-3 weeks . **E.g.** Guinea pigs-are highly susceptible to hypersensitivity reaction

Mechanism of anaphylaxis reaction

- IgE molecules are bound to surface receptors on mast cells and basophiles.
- IgE attaches to the receptors on (Fc ER) mast cells, following contact with allergen (i.e. antigen) with this Ab i.e. IgE
- Increases permeability of cells to calcium ions leads degranulation which releases phamocologically active substances(Vasoamines).
- "Target tissue"i.e. tissue or organ targated or showed clinical manifestation.
- **Symptoms or clinical manifestation are** – **edema(tissue damage due to accumulation fluid in tissues),** decreased coagubility of blood, fall in blood pressure and temperature**, leucopenia(low level of WBCs),** irritation, sneezes, coughs and respiratory distress.
- Pharmacological mediators are **e.g. histamine, serotonin , heparin, acetyl-cholin and prostagladins.**

Mechanism of anaphylaxis

IgE molecules bind to the surface receptors of mast cells and basophils

↓

Shocking dose

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Antigen combines with cell bound IgE

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Cross linking between adjacent antibody molecules

↓

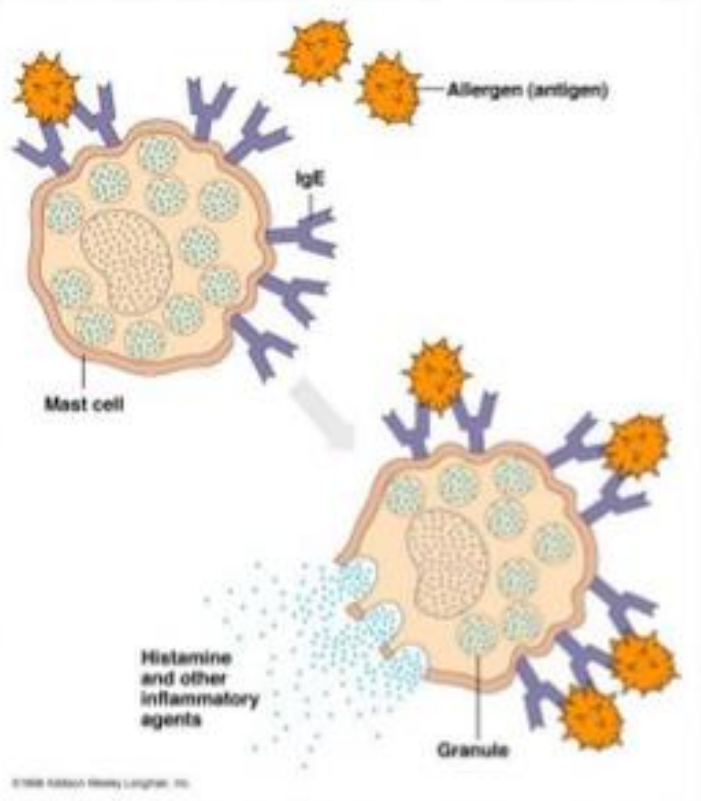
Increased permeability of cells to calcium ions

↓

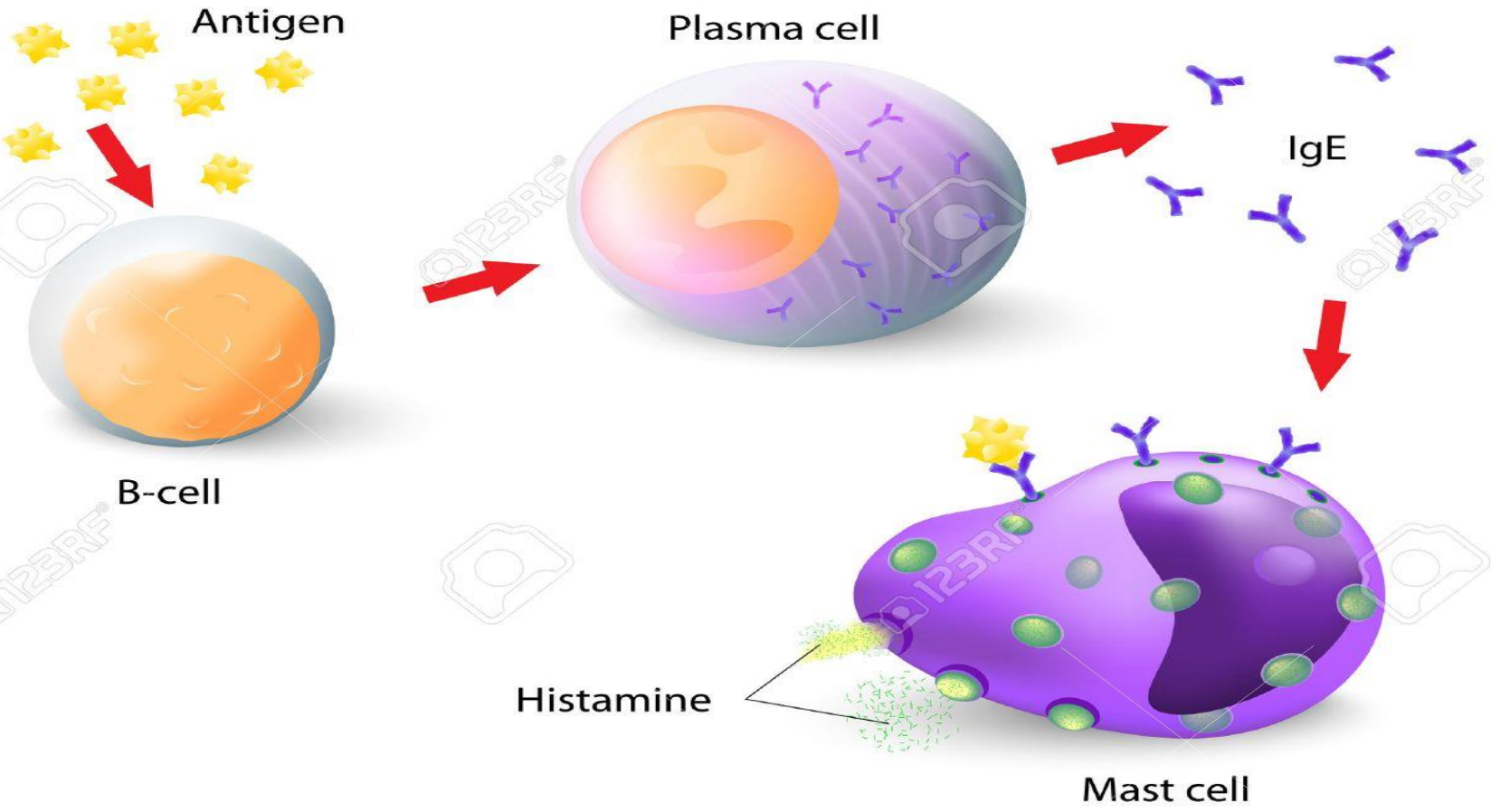
Degranulation

↓

Release of inflammatory mediators

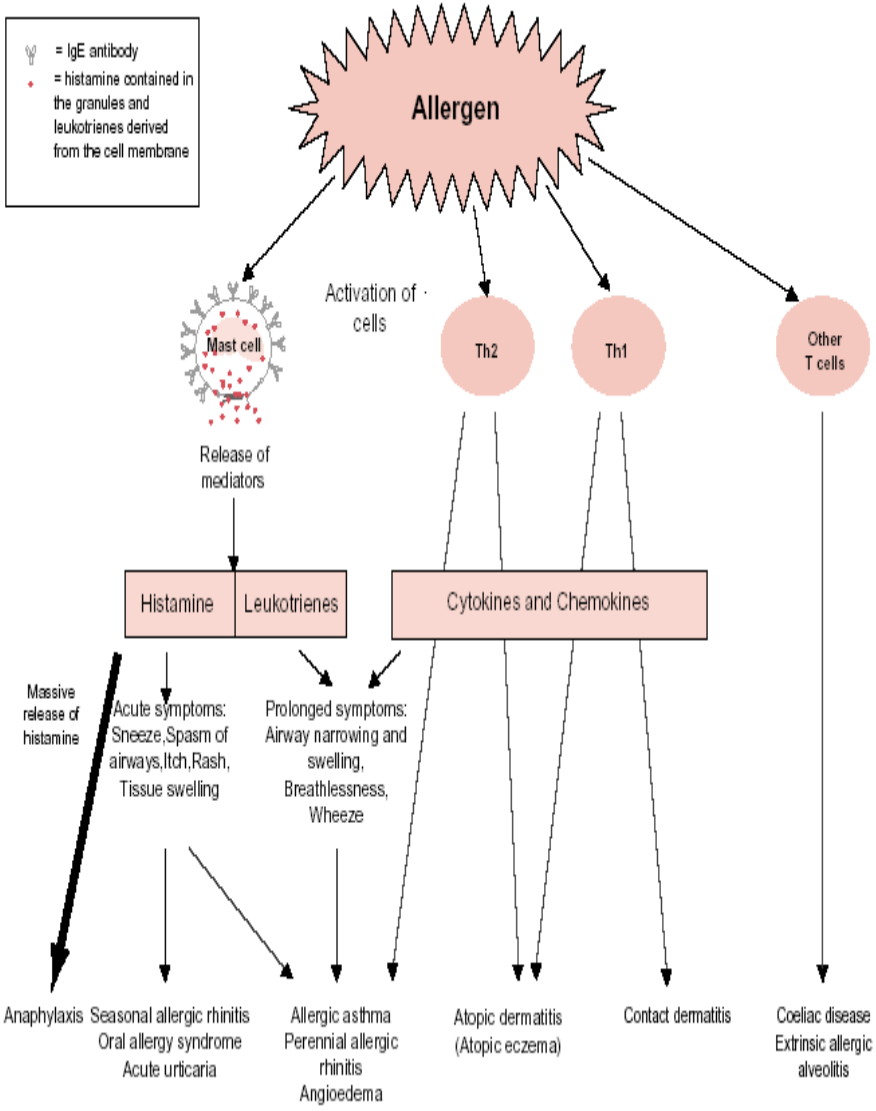


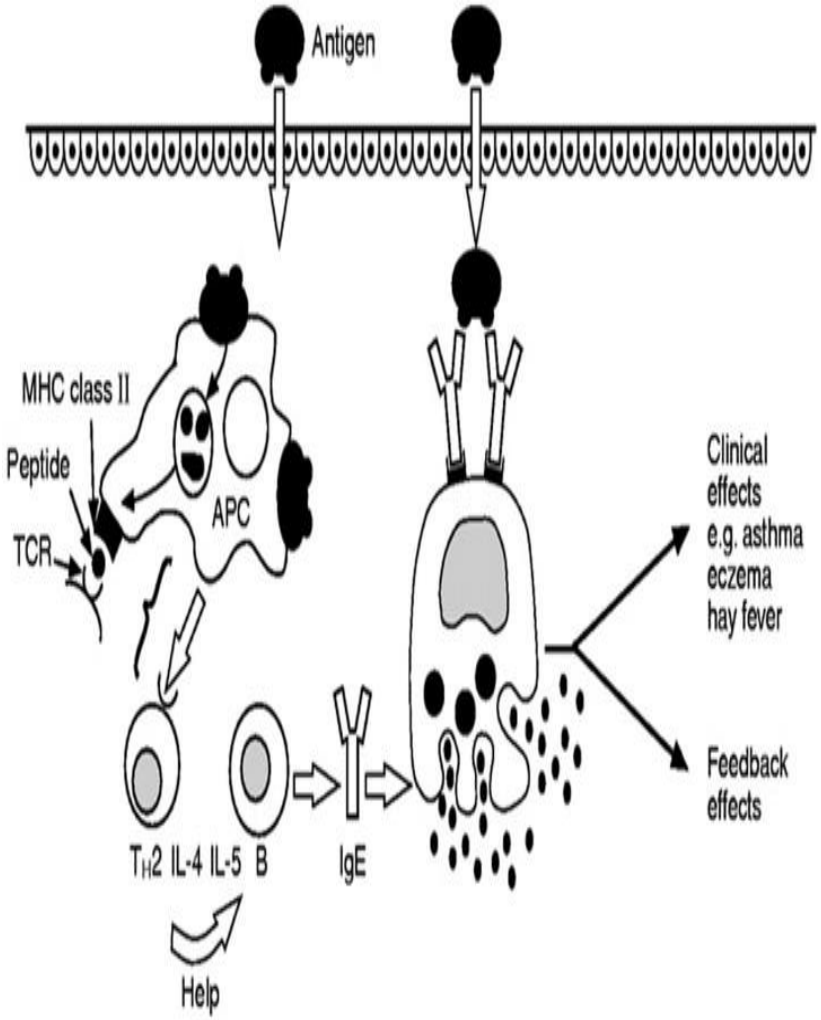
ANAPHYLACTIC REACTION



Atopy -(out of place or strangeness)

- Naturally occuring hypersensitivity to human beings (e.g. asthama. Hay fever)
- Allergens are-moulds spores, pollens, grasses, house dust, feathers , eggs etc.
- Antigen entered by inhalation ingestion or by direct contact. E.g. inhalation-asthama, ingerstion-gastric distress, contact-itching eruption.
- 10% persons have tendency to over produce IgE Ab which causes Atopic reactions.
- Over production of IgE is associated with deficiency of IgA.


= IgE antibody
= histamine contained in the granules and leukotrienes derived from the cell membrane
Allergen
Activation of cells
Mast cell
Th2
Th1
Other T cells
Release of mediators
Histamine
Leukotrienes
Cytokines and Chemokines
Massive release of histamine
Acute symptoms: Sneeze,Spasm of airways,Itch,Rash, Tissue swelling
Prolonged symptoms: Airway narrowing and swelling, Breathlessness, Wheeze
Anaphylaxis
Seasonal allergic rhinitis
Oral allergy syndrome
Acute urticaria
Allergic asthma
Perennial allergic rhinitis
Angioedema
Atopic dermatitis (Atopic eczema)
Contact dermatitis
Coeliac disease
Extrinsic allergic alveolitis

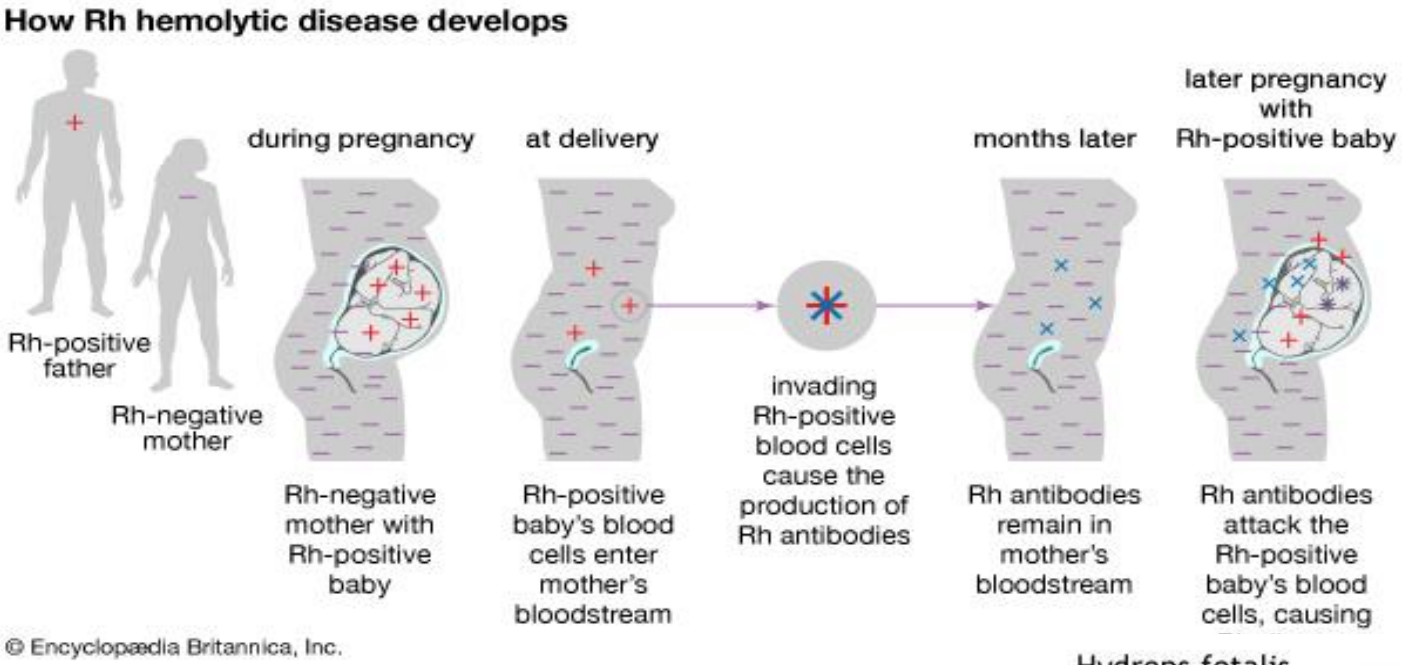

Antigen
MHC class II
Peptide
TCR
APC
Clinical effects
e.g. asthma
eczema
hay fever
Feedback effects
TH2 IL-4 IL-5 B
IgE
Help

3) Antibody mediated cell immunity

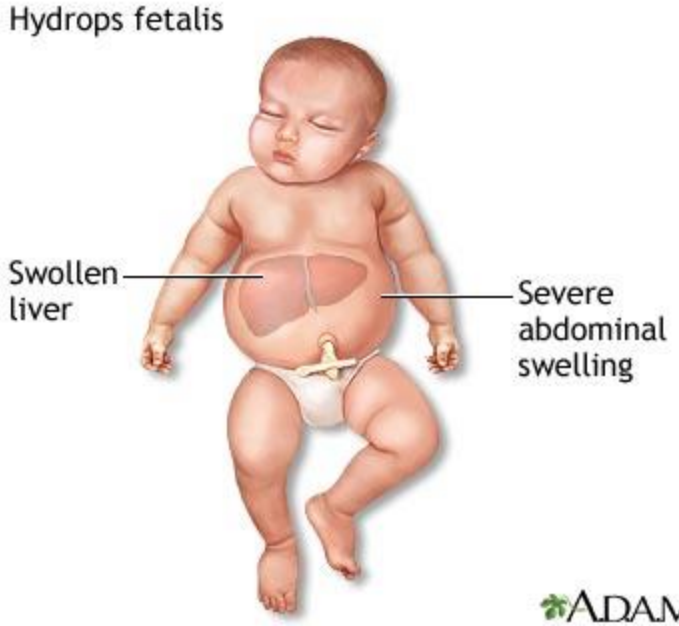
(Cytolytic or cytotoxic) Type II reaction

- Reaction involves conbination of IgG with antigenic determinants on the surface of cell leading to cytotoxic effects e.g. lyses of red cells caused by anti-erythrocyte antibodies in autoimmune anemia and hemolytic diseases of new born.
- (e.g. Erythroblasto fetalis: Rh –ve mother and Rh+ve fetus)

- Erythroblastosis fetalis- also called hemolytic disease of the new born, type of anemia in which the red blood cells of a fetus are destroyed in a maternal immune reaction resulting from a blood group incompatibillity between fetus and its mother.
- Rh incompatibility- Rh factor is a protein on red blood cells. If you are Rh –ve, and your baby is Rh +ve, your body will react to the baby's blood as a foreign substance.
- Babies who experiences erythroblastosis fetalis symptoms are swollen, pale or jaindiced after birth.
- Symptomps during pregnancy may show up by routine testing e.g. yellow amniotic fluid with traces of billirubin, an enlarge liver and spleen and heart.
- Treatment options for new borns- blood transfusion, intravenous fluids (IV), immunoglobulines (IVIg)

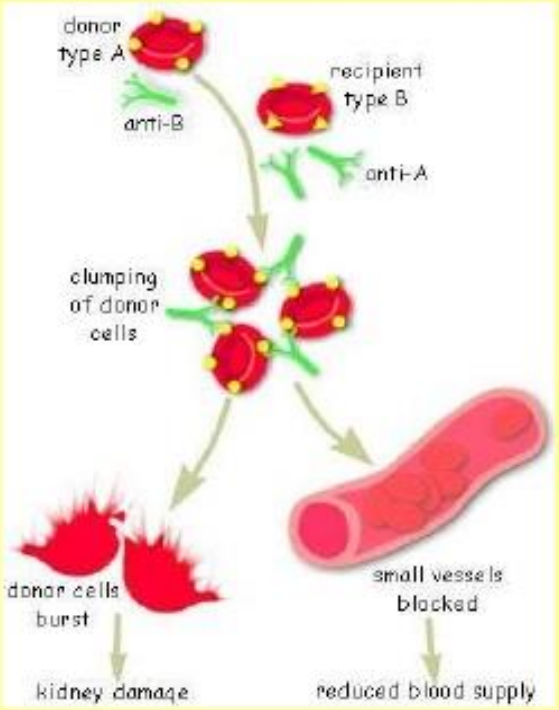


Babies who experiences erythroblastosis fetalis symptoms are- swollen, pale or jaundiced after birth



Type II- Cytotoxic Antibody Reaction

- Antigen is on the patient's own cell surfaces
- Mediated by IgG and IgM
- Complement activation
- Cell lysis and death
- Reaction takes hours to a day



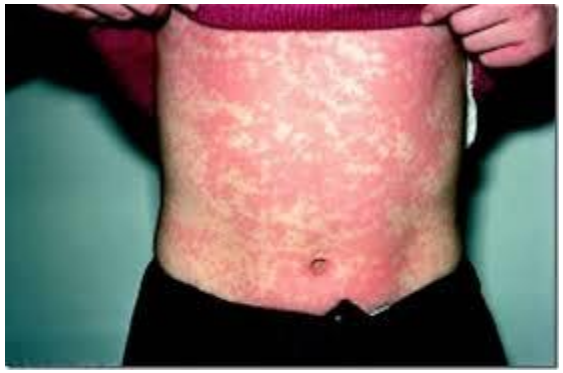
Arthus reaction: (Immune complex diseases) Type III reaction.

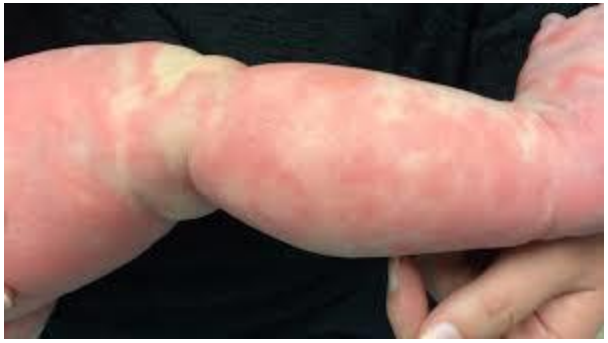
In **1903** when **Arthus** observed that rabbit were repeatedly injected subcutaneously with normal horse serum**, with initial dose**, there is **no local effect** but **later doses**, there occur **local reactions such as**- edema, indurations (hard, raised area with clearly defined margins at and around the infection site) and hemorrhagic necrosis, tissue damage.

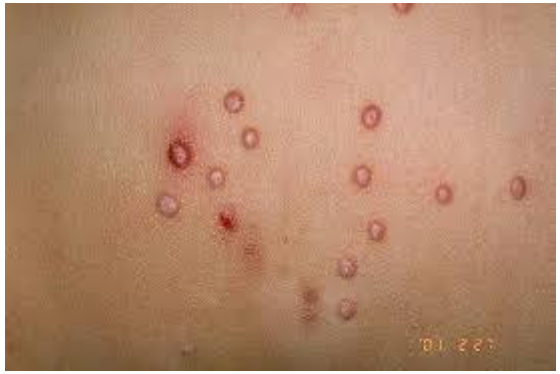
This occur due to **Ag-Ab complex** causing **complement activation** and **due to release of inflammatory molecules.**

Serum sickness:

- Plasma concentration of complement falls due to massive complement activation and fixtation by Ag-Ab complex.
- There is rise in Ab.
- E.g. following single injection of high concentration of diptheria antitoxin for 7-12 days, clinical syndromes like fever, arthritis, endocarditism(inflamation of heart valve) lymphadenopathy(Enlarment of lymph node), splenomagaly(enlargement in spleen), utricarial rashes(skin rashes by food infectios), abdominal pain, nausea and vomiting etc.
- Formation of immune complex consisting of foreign serum and Ab which get deposited on the endothelial lining of blood.





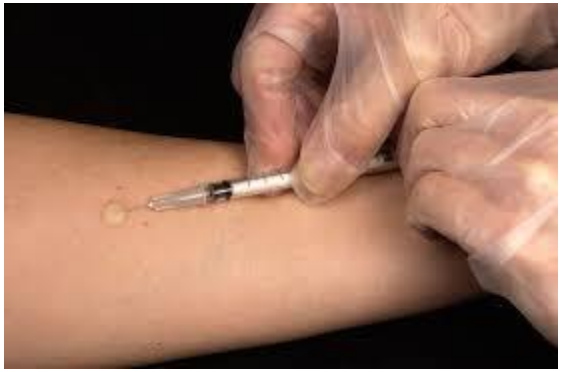


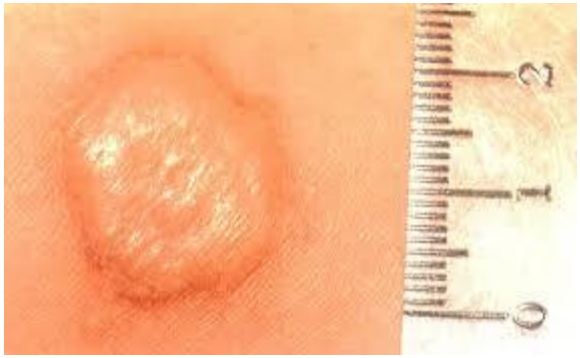
Utricarial skin rashes

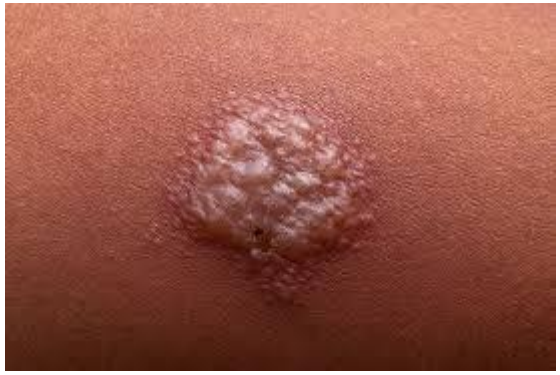
Tuberculin Test(tuberculin infection type)(Perquet Test, PPD test(Purified protein derivatives test)

- Infection by bacteria, viruses, fungi.
- This type of delayed response is tuberculin reaction.
- Person infected with mycobacterium becomes hypersensetive to tuberculo-protein(tuberculin) Degree of hypersensitivity for tuberculin.
- Inflamatory reaction develops at the site when tuberculin injected intradermaly within 48-72hrs. E.g**. Mantaux test.**

- Mantoux test is performed by injecting std. dose of 5 tuberculin units (0.1ml) into skin intradermally.
- The result should be read between 48-72 hrs. after the test, and the indurated area is measured in mm units.
- Cell mediated delayed type IV hypersensetivity reactions are mediated by skin macrophages, monocytes and T-cells
- Tcelss which are sensitized by prior TB infections, migrate to the test site and release lymphokines, which induces inflammatory process, which includes erythema, oedema, fibrine deposites and macrophages migrate at site, the reaction takes 72 hrs. to complete by formation of induration.







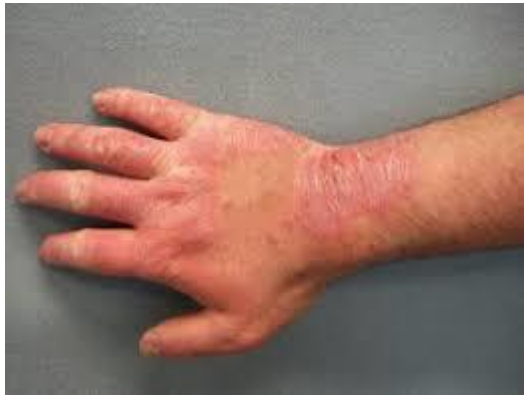
- Mantaux test: measurement of indurated area in mm.

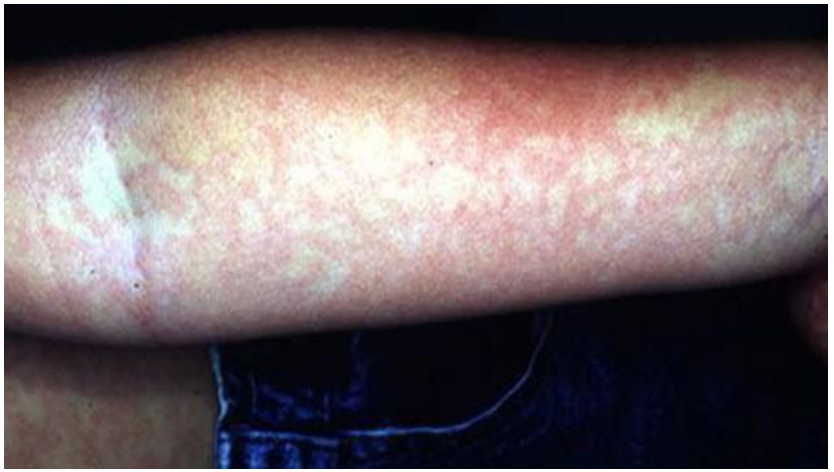
Contact dermititis:

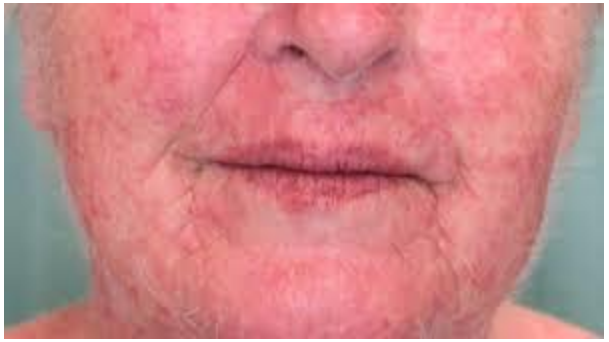
- Due to skin contact with chemicals, metals such as Nickel, Chomium, dyes like picryl chloride, drugs e.g. Penicillin.
- These all are not antigenic in nature bur when combine with skin proteins , become antigenic i.e. now it is new or ‘foreign’ to the body (very specific)
- Contact with such allergen, the lesions varying from **macules** and **papules** like **acute eczematous dermititis.** E.g. Patch test – itching,

Erythema (redding of skin usually in patches as a result of injury and irritation causing dilation of blood capillaries), bllister formation etc.

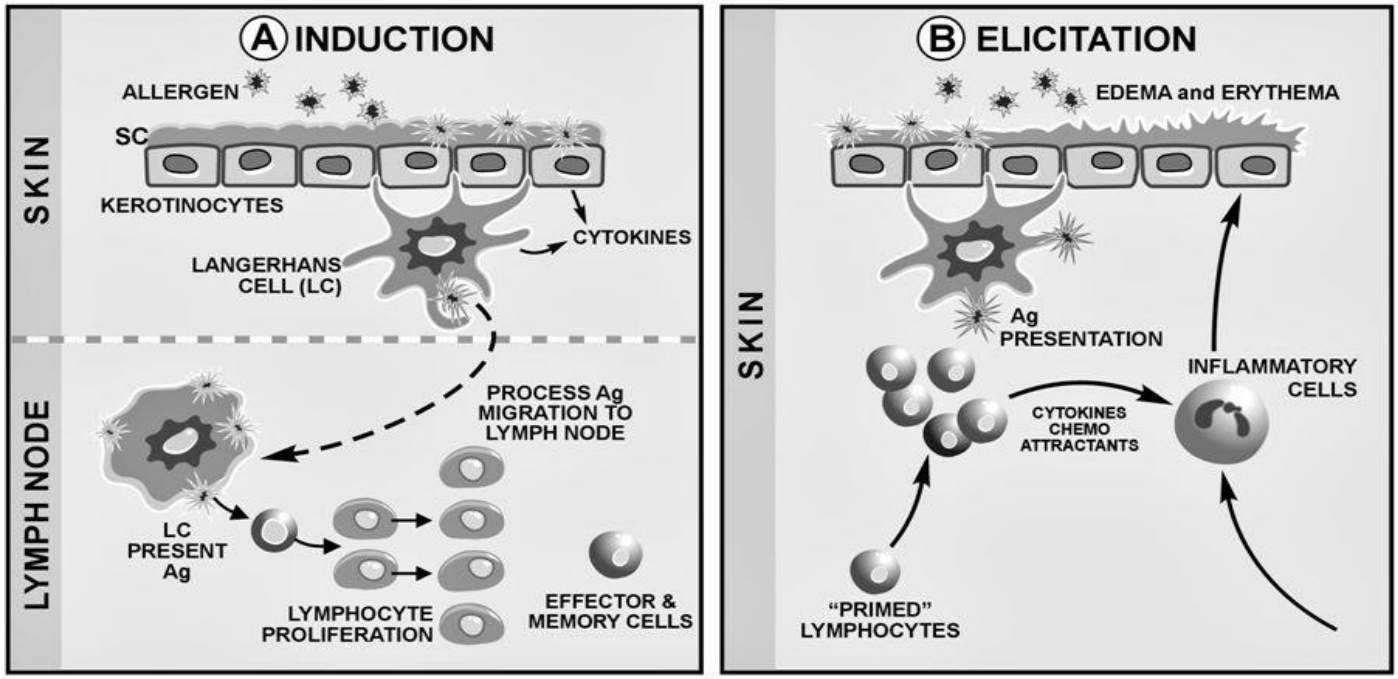
Contact dermititis: Macules and papules formation







Contact Hypersensitivity
Allergic Contact Dermatitis (ACD



Summary

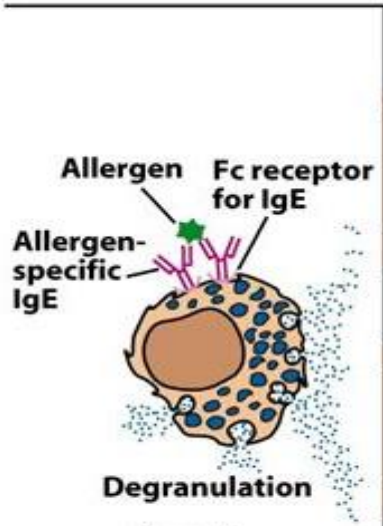
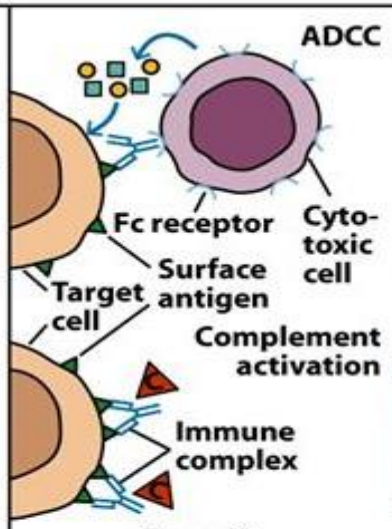
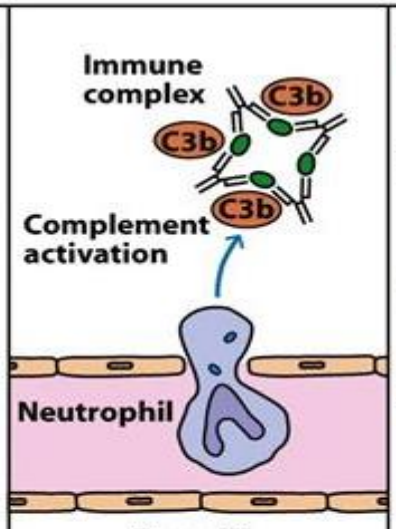
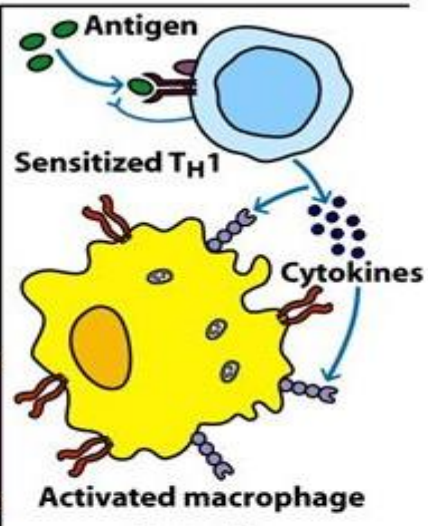
 Type I	 Type II	 Type III	 Type IV
IgE-Mediated Hypersensitivity	IgG- or IgM-Mediated Cytotoxic Hypersensitivity	Immune Complex–Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces cross-linking of IgE bound to mast cells and basophils with release of vasoactive mediators.	Ab directed 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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Thank You!