Hypersensitivity

It refers to sensitivity beyond what is considered normal. The term **allergy** is probably more familiar & might be used in many instances as synonymous. Although it is referred to **type 1 hypersensitivity**, hypersensitivity occur in people who have been previously sensitized by exposure to an Ag which is sometimes called allergy .

Coombs & Gell have classified these damaging immunological reactions into **four major types** of hypersensitivity reactions:

a-Type I :immediate hypersensitivity reactions(Anaphylaxis).

b-Type II :cytotoxic reactions

c- type III: immune complex mediated reaction.

d-Type IV: cell mediated reaction

*stimulatory type is a 5^{th} type.

Type I(Anaphylaxis) reactions:

Often occur within **few minutes** after re exposure to the same Ag. Anaphylaxis comes from Greek word "phulaxis" which means protection, plus the prefix "ana" means against. **Anaphylaxis is occur when certain Ags combine with IgE antibodies** . Anaphylaxis can be**:**

a- systematic reactions - shock, **breathing difficulties** & are sometimes **fatal** .

b- localized reactions which include common allergic conditions such as hay **fever ,asthma** & **hives(slightly raised, often itchy & reddened areas of the skin).**

IgE antibodies are produced in response to an Ag **(allergen**) such as insect venoum or pollen bind to the surface of cells such as mast cells & basophiles. Mast cell are especially prevalent in the C.T. of the skin &respiratory tract & in surrounding blood vessel.

Basophiles circulate in the blood where they Constitute less than 1% of the leukocytes. Both are packed with granules containing a variety of chemicals called **mediators.**

The Fc region of the IgE Ab attaches to a specific receptor site on the mast cell or the basophile bearing two Ag combining sites free.

These cells can have as many as(500000) sites for IgE attachment. when an Ag such as plant pollen, binds to Ag combining sit on two adjacent IgE Abs, the mast cell or basophile is triggered to undergo "**degranulation**" .this releases the granules that pack the interior of these cells, this means the releasing of the **mediators.**

Mediators: some mediators are* **stored within the cell in an a preformed state,** i.e. histamine heparin, serotonin (5-HT),**E**asinophil **C**hemo tactic **F**actor of **A**naphylaxis **(ECF-A), N**eutrophil **C**hemo tactic Factor of Anaphylaxis**(NCF-A)** ,proteases

*. Others are **synthesized upon allergen** contain platelet activating factor (PAF),the arachidonic acid derivatives leukotrienes or prostaglandins & thrombone

Mast cells bind IgE via their Fc receptors .on encountering Ag ;the IgE becomes cross –linked ,inducing degranulation & release of mediators

_Systemic anaphylaxis (anaphylactic shock):Epinephrine (Adrenaline) counteract these effects . Penicillin is case of interest because many people are sensitive to this drug. Anyone who has had an adverse reaction to penicillin i.e. generalized **hives, swelling** of **throat ,tinnitus** or **chest constriction** should not receive the drug again.

_Localized anaphylaxis : it is usually associated with Ags that are **ingested** (food)or **inhaled (pollen).** The symptoms that developed depend primarily on the routes by which the Ag enter the body.

Asthma is an allergic reaction that affects mainly the **lower respiratory system**, such symptoms as wheezing & shortness of breath are caused by the constriction of smooth muscles in the bronchial tubes.

Therapeutic measures:

1-Avoidance:through environmental control.

2-Hyposensitization:to produce IgG blocking Ab.

3-Drug treatment :a-blocking mediators from binding to target tissue, using antihistamines for example.

A-stabilizing granules or cell memb.

B-blocking the release of mediators.

Atopy: is an immediate hypersensitivity response that occurs only in **genetically predisposed** host upon sensitization to specific allergens. This condition differs from anaphylaxis in that it cannot be induced in normal host .

The clinical manifestation of type I hypersensitivity reaction include **hay fever, eczema, asthma &rhinitis (seasonal allergy).**

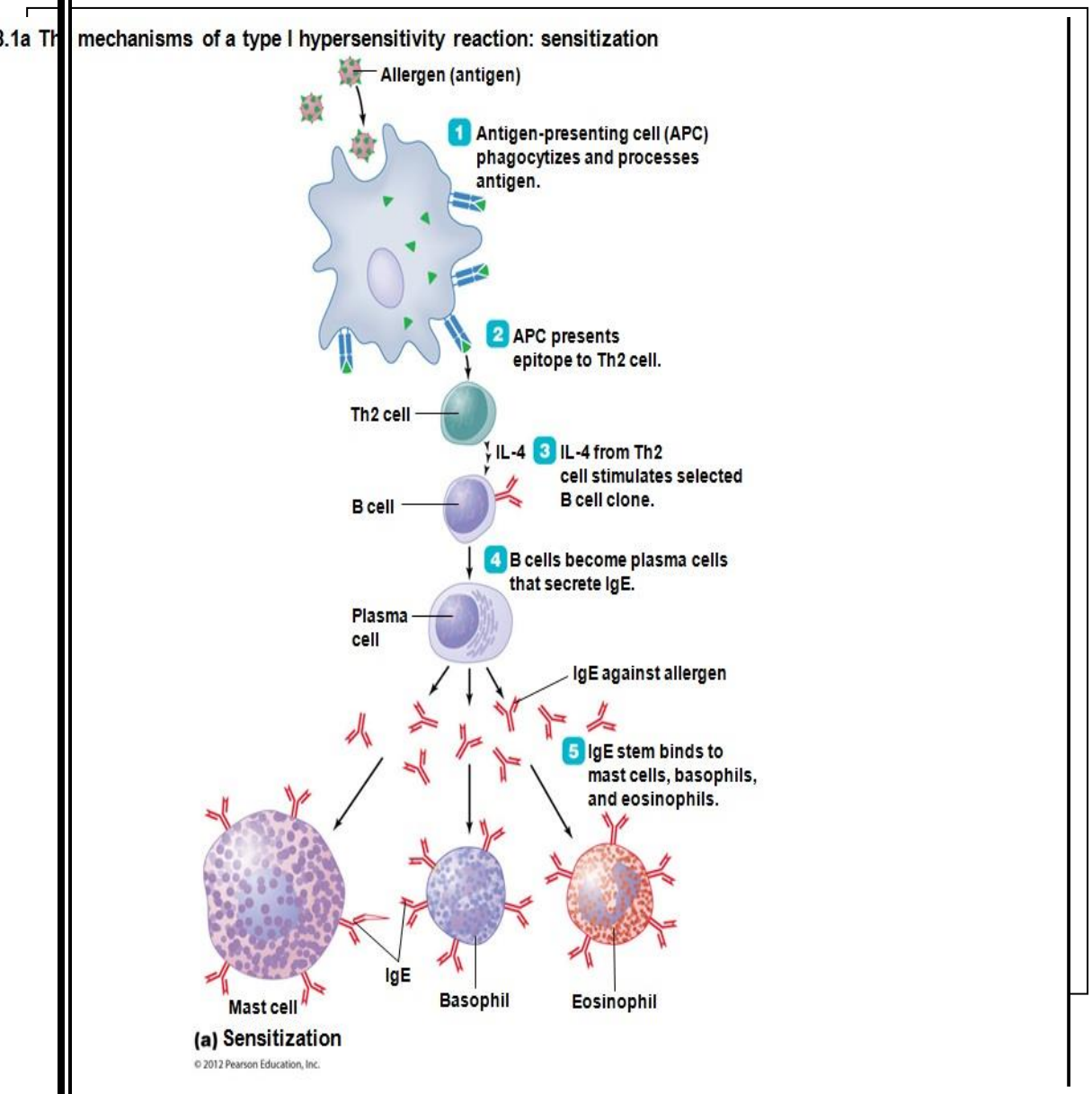
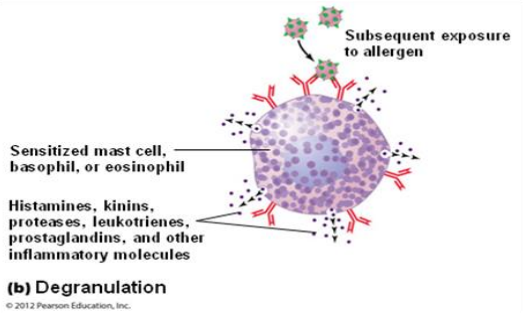


Figure 18.1b The mechanisms of a type I hypersensitivity reaction: degranulation



Type II (cytotoxic reaction):

Are initiated by Ab usually IgG or IgM react with cell bound Ag.

Cytotoxic reactions usually involve the combination o**f IgG or IgM Abs** with epitopes on cell surface or tissue or the adsorption(accumulation) of Ags or haptens to **tissue or to cell** membrane . With subsequent attachment of Abs to adsorbed Ag. This will lead to lysis via **activation of complement** or through the **action of NK** cells, killed by the ADCC antibody-dependent cellular cytotoxicity .

Clinical features: Haemolytic disease of newborn occurs when an Rh^- (mother)gives birth to an Rh^+ (infant). The mother can become sensitized to this Ag during birth ,when the Rh^+ fetal RBCs enter the maternal circulation, causing the mother to produce anti-Rh Abs of the IgG type. The mother anti-Rh Abs will cross the placenta & destroy the fetal RBCs .the fetus responds to this immune attack by producing large numbers of immature RBCs called (erythroblasts),hence the name "erythroblastosis fetalis" was used to describe the disease known now haemolytic disease of newborn(HDN).

HDN is usually prevented today by immediate passive immunization of the Rh^- mother with anti-Rh antibody. The Abs can bind with any fetal Rh^+ RBCs that have entered the mother's circulation . it might be necessary that the newborn Rh^+ blood contaminated with the maternal Abs, be replaced by transfusion of uncontaminated blood.

Figure 18.6 Events in the development of hemolytic disease of the newborn-overview

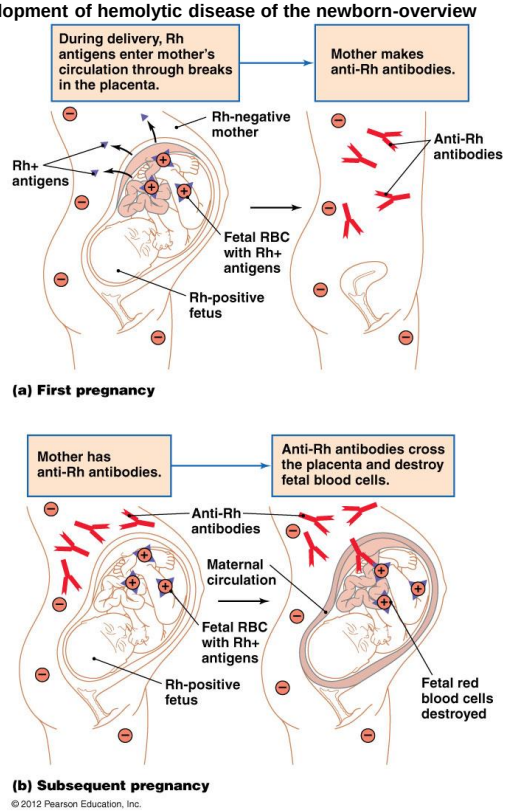
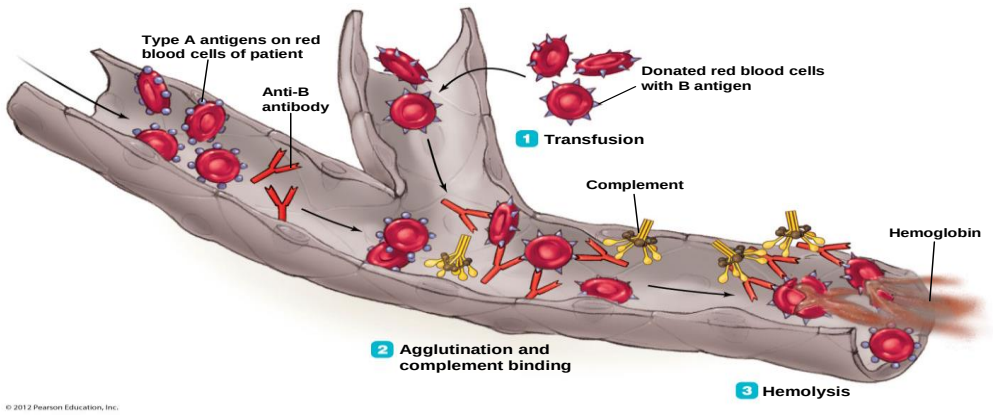


Figure 18.5 Events leading to hemolysis



Type III Immune complex mediated reactions:

Are initiated by **Ag-Ab complexes** that either are formed

- **Locally** at the site of tissue damage or are **deposited** there from the **circulation**. This complex reaction. Is present in vascular& glomerular basement membranes. The symptoms depend on the location of deposition include arthritis, vasculitis or skin lesions.

The pathogenesis involves an interplay of Ag-Ab & complement beside neutrophil, the two classic examples of these reactions are :

Arthritis reaction : is a **local** necrotic lesion resulting from a local Ag-Ab reaction & produced by injecting Ag into a previously immunized human or animal.

Ag injected intra dermally combines with specific Ab from the blood to form immune complex. the complexes activate complement & act on platelet which release vasoactive amines. Complements C3a&C5a fragments cause

1-endothelial cell retraction.2- mast cell degranulation .3-PMN chemotaxis into the tissues.

Mast cell products, including histamines, leukotrienes induce increased blood flow & capillary permeability. The inflammatory reaction is potentiated by lysosomal enzymes released from PMNs ,furthermore C3b deposited on the complexes opsonized them for phagocytosis.

Immune complexes are deposited in the tissue. complement is activated &PMNs are attracted to the site of deposition causing local damage.

Type IV cell-mediated reactions (DTH)& cell mediated cytotoxicity):

Type 4 hypersensitivity is often called delayed type hypersensitivity as the reaction takes two to three days to develop. Unlike the other types, it is not .antibody mediated but rather is a type of cell-mediated response

CD4+ helper T cells recognize antigen in a complex with Class II major histocompatibility complex. The **antigen-presenting** cells in this case are **macrophages** that secrete **IL-12**, which stimulates the proliferation of further **CD4+ Th1** cells. CD4+ T cells **secrete IL-2** and interferon gamma, further inducing the release of other Th1 cytokines, thus **mediating** the immune response. **Activated** CD8+ T cells **destroy target** cells on **contact**, whereas activated macrophages produce hydrolytic enzymes and, on presentation with certain intracellular pathogens, transform into multinucleated giant cells

.

Clinical features:

Tuberculin skin test: injection of PPD Purified protein derivative or NT intra dermally into a sensitized person, the reaction appears slowly (12 to 24 hr)& reaches maximal reactivity (24-48 hr), initially erythema then induration .

The PPD skin test is a method used to diagnose silent (latent) tuberculosis (TB) infection.

References

1-Review of Medical Microbiology and Immunology, 14e

Chapter 65: Hypersensitivity (Allergy)

2- -Essential microbiology for Dentistry 4 th edition 2012