UNIT -3

Immune response: Innate, acquired, active and passive immunity - mechanism of humoral and cell mediated immune responses - immunity to infections - immunoprophylaxis, vaccines and immunization schedule. Immunological disorders.

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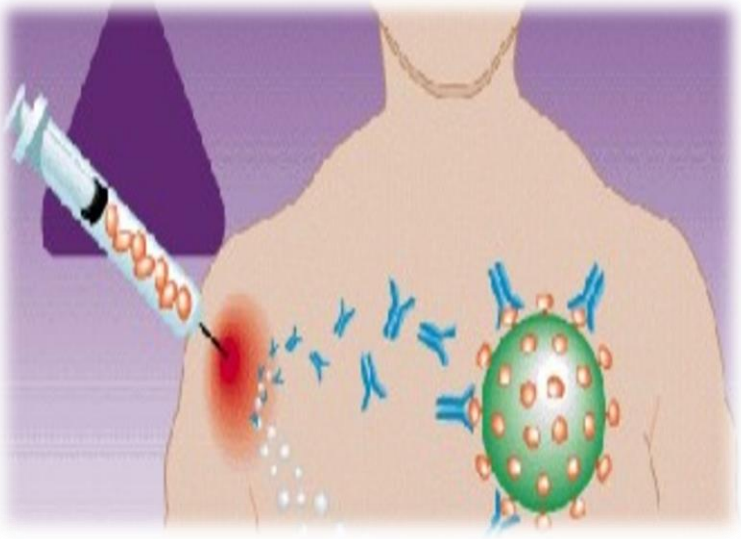


Immunoprophylaxis

Immunoprophylaxis

Protection against infectious diseases by (immunization) acquired by the individual either passively or actively:

I- Passive acquired immunity
II- Active acquired immunity

I- Passive acquired immunity

Ready made Ab transferred to individual giving rapid protection and short lasting immunity:

a-Naturally acquired passive immunity

Occurs when antibody are transferred from mother to fetus (IgG) or in colostrum (Ig A).

b- Artificially acquired passive immunity

Short-term immunization by injection of antibodies, For examples:

- injection of antitoxic serum for treatment of diphtheria or tetanus.
- injection of gamma globulin that are not produced by recipient's cells, to hypogammaglobulin children.

II- Active acquired immunity

- Individual actively produces his own Ab.
- Immunity develop slowly and long lasting due to development of immunological memory:

a-Natural active acquired immunity

The person becomes immune as a result of previous exposure to a live pathogen

b-Artificially active acquired immunity

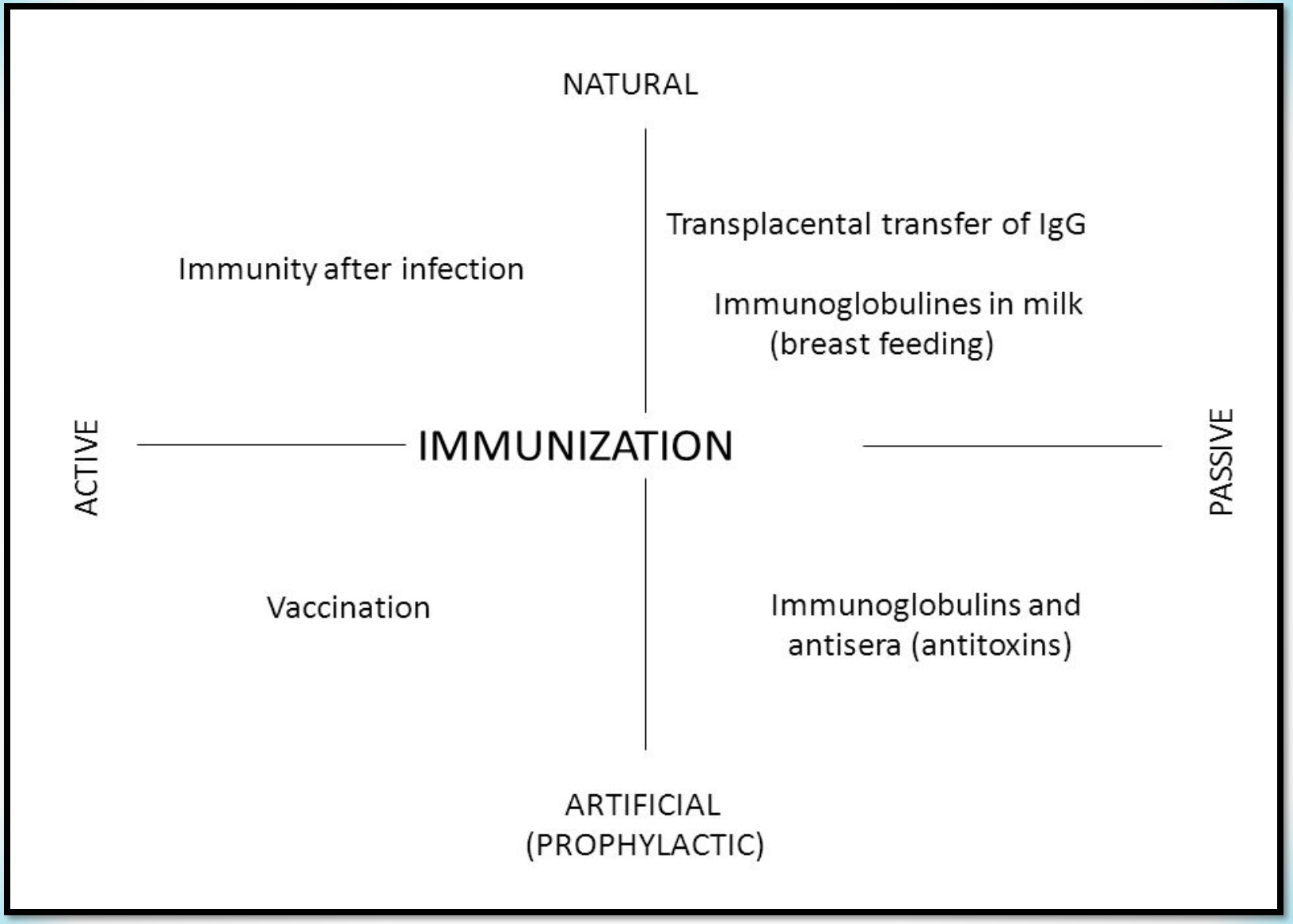
A vaccine stimulates a primary response against the antigen without causing symptoms of the disease.

IMMUNIZATION

IMMUNIZATION

- Immunization is defined as the procedure by which the body is prepared to fight against a specific disease.
- It is used to induce the immune resistance of the body to a specific disease.
- Immunization is of two types:

1. Passive immunization
2. Active immunization


NATURAL
Transplacental transfer of IgG
Immunity after infection
Immunoglobulines in milk
(breast feeding)
ACTIVE
IMMUNIZATION
PASSIVE
Vaccination
Immunoglobulins and
antisera (antitoxins)
ARTIFICIAL
(PROPHYLACTIC)

Passive immunization

- Passive immunization or immunity is produced without challenging the immune system of the body.
- It is done by administration of serum or gamma globulins from a person who is already immunized (affected by the disease) to a non-immune person.
- Passive immunization is acquired either naturally or artificially.
- Passive Natural Immunization • Passive natural immunization is acquired from the mother before and after birth.
- Before birth, immunity is transferred from mother to the fetus in the form of maternal antibodies (mainly IgG) through placenta. After birth, the antibodies (IgA) are transferred through breast milk.

Passive artificial immunization

- It is developed by injecting previously prepared antibodies using serum from humans or animals.
- This type of immunity is useful for providing immediate protection against acute infections like tetanus,measles, etc.

Active immunization

- Active immunization or immunity is acquired by activating immune system of the body.
- Body develops resistance against disease by producing antibodies following the exposure to antigens.
- Active immunity is acquired either naturally or artificially.

Active Natural Immunization

- Naturally acquired active immunity involves activation of immune system in the body to produce antibodies.
- It is achieved in both clinical and subclinical infections

Active Artificial Immunization

- Active artificial immunization is a type of immunization that is achieved by the administration of vaccines or toxoids.

Vaccine

Vaccine

- Vaccine is a substance that is introduced into the body to prevent the disease produced by certain pathogens.
- Vaccine consists of dead pathogens or live but attenuated (artificially weakened) organisms.
- The vaccine induces immunity against the pathogen, either by production of antibodies or by activation of T lymphocytes.
- Edward Jenner produced first live vaccine. He produced the vaccine for smallpox from cowpox virus.
- Nowadays, vaccines are used to prevent many diseases like measles, mumps, poliomyelitis, tuberculosis,smallpox, rubella, yellow fever, rabies, typhoid, influenza,hepatitis B, etc.

Vaccination:

The process of distributing and administrating vaccines is reffered to as Vaccination

- immunity against pathogens (viruses and bacteria) by using: live attenuated, killed, altered antigens, that stimulate the body to produce antibodies

- Vaccines work with the immune system's ability to recognize and destroy foreign proteins (antigens)

- Vaccination prevents and control such diseases as cholera , rabies , poliomyelitis, diphtheria, tetanus, measles, and typhoid fever

- Vaccines can be:

a- prophylactic (e.g. to prevent or ameliorate the effects of a future infection by any natural or wild pathogen

b- Therapeutic (e.g. vaccines against cancer are also being investigated

Live vaccines	Live Attenuated vaccines	Killed Inactivated vaccines	Toxoids	Cellular fraction vaccines	Recombinant vaccines
•Small pox variola vaccine	•BCG •Typhoid oral •Plague •Oral polio •Yellow fever •Measles •Mumps •Rubella •Intranasal Influenza •Typhus	•Typhoid •Cholera •Pertussis •Plague •Rabies •Salk polio •Intra-muscular influenza •Japanise encephalitis	•Diphtheria •Tetanus	•Meningococcal polysaccharide vaccine •Pneumococcal polysaccharide vaccine •Hepatitis B polypeptide vaccine	•Hepatitis B vaccine

Types of vaccines:

-Killed vaccines:

Virulent bacteria or viruss used to prepare these vaccines may be killed by heat (60 °C) or by chemicals (formalin, phenol or merthiolate). examples:

a-TAB vaccine against entric fever (heat)
b-Salk vaccine against poliomylitis (formaline)
c-Semples vaccine against rabies (phenol)
d-pertussis vaccine against whooping cough (merthiolate)

Killed vaccine are:

- Do not stimulate local immunity.
- Short lasting
- Do not stimulate cytotoxic T cell response in contrast to live attenuated vaccines.
- safe can be given to pregnant woman and immunocompromised host.
- It is heat stable

-**live attenuated vaccines:**

- living lost its virulence so do not produce disease but produce immunity.
- stimulate both humoral and cell mediated immunity, local and systemic.
- not given to pregnant women and immunocompromised hosts (may cause diseases)
- heat unstable
- It is prepared by:

a- repeated subculture in unsuitable condition (chemical or media) e.g BCG vaccine against T.B and 17 D vaccine against yellow fever .

b- growing at high temp . (above optimum temp) e.g Pasteur anthrax vaccine

c- selection of mutant strains of low virulence e.g Sabin vaccine against poliomylitis.

-Toxoids

- It is prepared by detoxifying bacterial toxins.
- Bacterial exotoxins treated by formalin to destroy toxicity and retain antigenicity. e.g.diphtheria and tetanus toxoid. These vaccines are used when a bacterial toxin is the main cause of illness.
- When the immune system receives a vaccine containing a harmless toxoid, it learns how to fight off the natural toxin.
- The immune system produces antibodies that block the toxin. E.g Vaccines against diphtheria and tetanus.

Gene deleted vaccines

These are genetically engineered vaccines which involve the removal or mutation of virulence gene of the pathogen

Peptide vaccine:

These are the subunit vaccine prepared by chemical synthesis of short immunogenic peptides

Microbial products

❖ vaccines are prepared from bacterial products or viral components . e. g:

a-Capsular polysaccharide vaccines are:

- Poor immunogen in children below 2 years age e. g H. influenza
- do not respond to T cell independent antigens inspite of its generation of Ig M
- produce anticapsular opsonizing antibodies. examples : *meningiococci, pneumococci* and *H. influenza*

b-cellular purified proteins of pertussis

c- purified surface Ag of hepatitis B virus

d-influenza viruses

DNA Vaccine

- when the genes for a microbe's antigens are introduced into the body, some cells will take up that DNA.
- The DNA then instructs those cells to make the antigen molecules. The cells secrete the antigens and display them on their surfaces.
- In other words, the body's own cells become vaccine-making factories, creating the anti gens necessary to stimulate the immune system.

Recombinant vaccines

- Recombinant vector vaccines are experimental vaccines similar to DNA vaccines, but they use an attenuated virus or bacterium to introduce microbial DNA to cells of the body.
- "Vector" refers to the virus or bacterium used as the carrier.

-prepared by recombinant DNA technology for improvement vaccines

e.g:

A- subunit vaccines : in which microbial polypeptides are isolated from the infective material hepatitis B and influenza viruses

B-Recombinant DNA-derived antigen vaccines: in which Ag are synthesizing by inserting the coding genes into E. coli or yeast cell as HBV vaccines

C-Recombinant DNA a virulent vector vaccines: in which the genes coding for the Ag is inserted into genome of an avirulent vector such as BCG vaccine

D-Synthetic peptide vaccines: synthesis of short peptides that corrospond to antigenic determinants on a viral or bacterial proteins

e.g cholera toxins and poliovirus to produce Ab response.

Combined immunization (Vaccination)

Immunization against diseases is recommended in combination (for young children) as :

- diphtheria , tetanus (lockjaw), and pertussis (whooping cough), given together (DTP).
- measles , mumps , and rubella , give together as MMR
- Haemophilus influenzae b (Hib) with DTP .
- Influenza b (Hib) with inactivated poliomyelitis vaccine (IPV)
- Influenza; and Neisseria meningitidis (meningococcal meningitis).

Routes of Administration

- Deep subcutaneous or intramuscular route (most vaccines)
- Oral route (oral BCG vaccine)
- Intradermal route (BCG vaccine)
- Scarification (small pox vaccine)
- Intranasal route (live attenuated influenza vaccine)

Scheme of immunization

- Primary vaccination
- One dose vaccines (BCG, measles, mumps, rubella, yellow fever)
- Multiple dose vaccines (polio, DPT, hepatitis B)
- Booster vaccination
- To maintain immunity level after it declines after some time has elapsed (DT, MMR)

Schedule

Name of vaccine	Name of disease	Dosage and administration	Immunization schedule
Hepatitis b vaccine (booster dose isn't recommended)	Hepatitis b	0.5 ml IM injection child <10 years, 10 mcg/dose child> 10 years, 20 mcg.	Second dose is given 1month after first and third after 5months(Three doses) Babies:1,2,12 month
Hepatitis A	Hepatitis A	0.5ml (1st dose) 1.0ml(2nd dose)	2yrs or above and6 to 12 months after first(two doses)
BCG vaccine	tuberculosis	0.1ml ID injection	Younger than 3-5 years
Yellow fever vaccine	Yellow fever	0.5ml SC injection	9 months or older before traveling to epidemic area (Single dose)
Measles vaccine	Measles	0.5 ml SC injection	First dose 12-15 months and second dose 4-5 years age (Two doses)
Measles Rubella vaccine	Measles and Rubella	0.5ml SC injection	(two doses)

Name of vaccine	Name of disease	Dosage and administration	Immunization schedule
Diphtheria – tetanus toxoid vaccine (DT)	Diphtheria and tetanus	0.5ml IM injection	6weeks to 7yeras old(single doses)
MMR vaccine	Mumps , Measles and Rubella	0.5ml SC injection	12 to 15 months first dose and 4-6 years second dose(Two doses)
Haemophilus influenza type b vaccine (hib)	Haemophilus influenza b	0.5ml IM injection	First three doses at intervals of every three months and final dose 12-15 months of age (Three to four doses)
Inactivated Polio Vaccines (IPV)	Polio(booster dose is required at the age of 4-6 years)	0.5ml IM/SC injection	1st dose 2 month,2nd dose 4 month,3rd dose 6-18 months of age (Three doses)

Name of vaccine	Name of disease	Dosage and administration	Immunization schedule
Typhoid vaccine	Typhoid fever	0.5ml IM injection	1 week before travel to the area sensitive. (Single dose)
Cholera vaccine (Sachets are available and dissolved in water to take orally)	cholera	3ml Oral route of administration	2 years and over Three doses(2 for adults)

Periods of maintained immunity due to vaccines

- Short period (months): cholera vaccine
- Two years: TAB vaccine (typhoid-paratyphoid A and B vaccine)
- Three to five years: DPT vaccine (diphtheria, pertussis (whooping cough), and tetanus)
- Five or more years: BCG vaccine(Bacillus Calmette–Guérin is a vaccine against tuberculosis)
- Ten years: yellow fever vaccine

Toxoids

- Toxoid is a substance which is normally toxic and has been processed to destroy its toxicity but retains its capacity to induce antibody production by immune system.
- Toxoid consists of weakened components or toxins secreted by the pathogens.
- Toxoids are used to develop immunity against diseases like diphtheria,tetanus, cholera, etc.

Immunologic Disorders

A. There are three types of immunological disorders

1. Hypersensitivity
2. Autoimmune disease
3. Immunodeficiency

B. Hypersensitivity reactions to usually harmless substances are often called allergies or allergic reactions

1. allergens – antigens that cause allergic reactions

C. Most allergic reactions fall into one of four major types:

1. Type I: Immediate IgE-mediated
2. Type II: Cytotoxic
3. Type III: Immune complex-mediated
4. Type IV: Delayed cell-mediated

Type I Hypersensitivities

- Also called IgE Mediated Hypersensitivity

Mechanism

1. First exposure to antigen induces an IgE antibody response leading to sensitization
    A) Antigen is taken up by dendritic cells (APC) and merged with MHC molecules
    B) APC presents the antigen to T-cells
    C) Activated T-cells release cytokines that stimulate B-cells to produce plasma cells which secrete large amounts of IgE
    D) IgE antibodies bind to mast cell receptors and the individual is now "sensitized
2. During the subsequent exposures, antigens activate IgE antibodies on the mast cell causing it to degranulate
    A) Histamines, leukotrienes, prostaglandins, and/or cytokines are released
    B) These chemicals are the cause of hives, hay fever, asthma and anaphylactic shock
3. Reactions generally occur within 30 minutes of exposure

Localized Anaphylaxis

1. Hives – an allergic skin condition characterized by the formation of a wheal and flare pattern

    A) Frequently the result of seafood allergies
    B) These reactions are due to the release of histamine which causes dilation of tiny blood vessels and the leaking of plasma into the area

2. Hay fever – itchy, teary eyes, sneezing, and runny nose; occurs when allergic person inhales an antigen rather than ingests it

    A) also mediated by histamine

3. Asthma – inhaled allergen causes chemical mediators from IgE to stimulate increased mucus secretions and spasms of the bronchi

    A) leukotrienes and prostaglandins are responsible

Generalized Anaphylaxis

1. Antigen enters the bloodstream and becomes widespread and the reaction affects almost the entire body (systemic)
2. Loss of fluid from the blood vessels into tissues causes swelling and possibly shock
3. Reactions may be fatal within minutes
4. Bee sting, peanut, and penicillin allergies account for most cases
5. Can usually be controlled by epinephrine injections

Immunotherapy

Desensitization or immunotherapy is often effective in decreasing the Type I hypersensitivity state

A) Repeated injections of very small amounts of antigen are given over several months
B) This regimen leads to the formation of specific IgG antibodies
C) The IgG reacts with antigen before it can bind to IgE and therefore it blocks the IgE reaction that might result in allergic reactions

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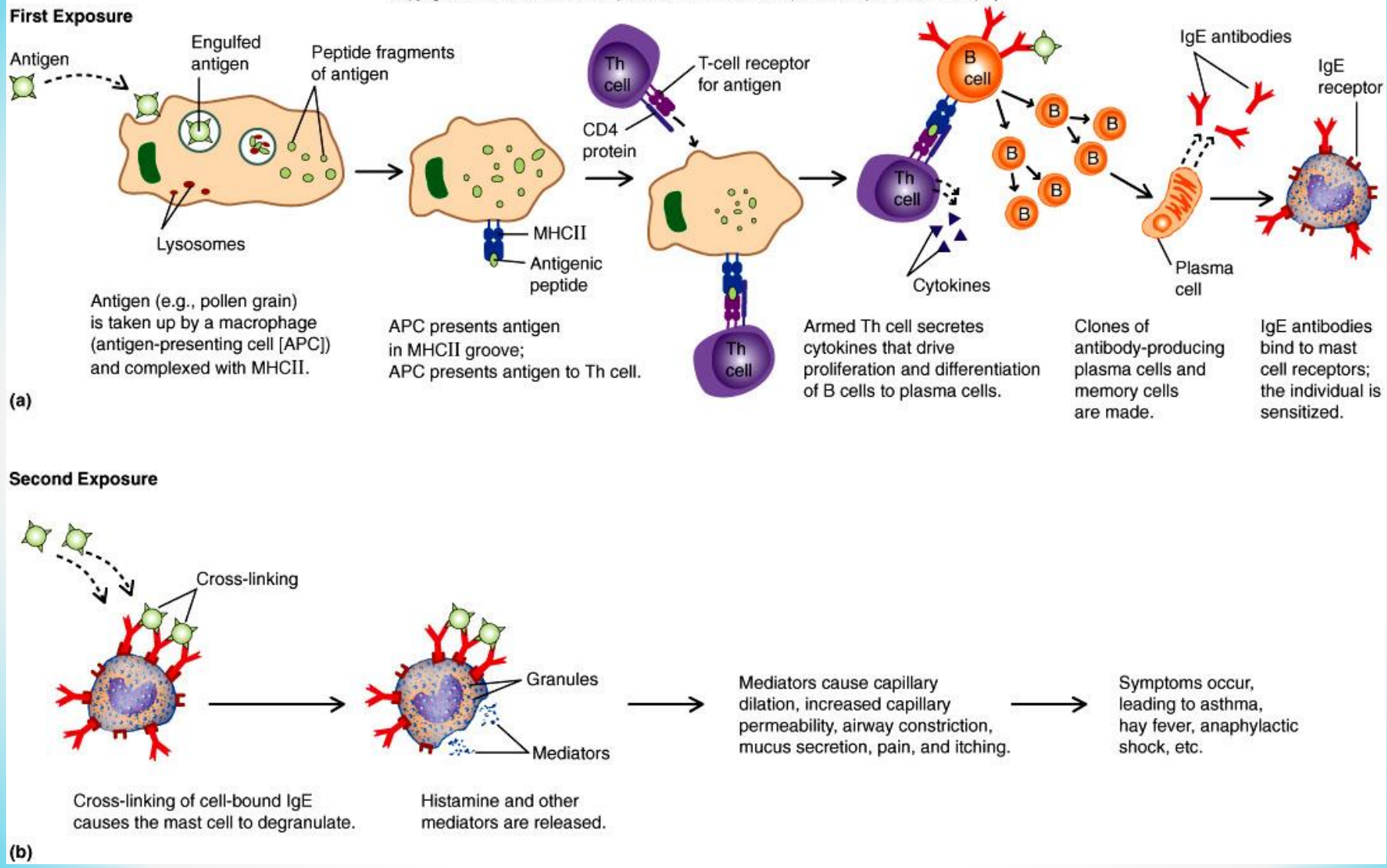

Type II Hypersensitivity

- Also called Cytotoxic Hypersensitivity because it utilizes antibodies that can destroy normal cells by complement lysis or by antibody-dependent cellular cytotoxicity (ADCC)

- Generally occur within hours after exposure

- Transfusion Reactions – the ABO blood groups are the major cause of hemolytic anemia in blood transfusion patients

1. Recall that persons with A type blood possess the A antigen and the natural antibody anti-B
2. Persons with B type blood possess the B antigen and the natural antibody anti-A
3. Persons with O type blood lack both the A and B antigens but possess both the natural antibodies anti-A and anti-B
4. Persons with AB type blood possess both the A and B antigens but posses no natural antibodies
5. In the case of ABO incompatibility, the antibodies cause reactions that include fever, low blood pressure, pain, nausea, and vomiting
6. Cross-matching the bloods and other techniques are used to ensure compatibility of donor and recipient

Hemolytic Disease of the Newborn

- Also called Erythroblastosis fetalis.
- Results when mother is Rh^- and baby is Rh^+
- Upon delivery, Rh^+ antigens are transferred to the mother's bloodstream which causes her to produce anti-Rh antibodies
- If the mother becomes pregnant again with an Rh^+ child, the antibodies cross the placenta, enter the circulation of the fetus, and cause extensive fetal erythrocyte damage
- RhoGAM may be administered to prevent this reaction

  A) contains Rh antibodies and prevents the mother's natural production of them

  B) widely used at 28 weeks and after delivery during all susceptible pregnancies

Type III Hypersensitivity

- Also called Immune Complex-Mediated Hypersensitivity
- Occurs within hours or days after exposure
- When there is a slight excess of antigen, the antigen-antibody complexes activate complements and stimulate neutrophil and basophil degranulation
    1. Results in vasodilation, increased vascular permeability, and inflammation
- Small antigen-antibody complexes are often deposited in the walls of small blood vessels in skin, joints and kidneys where they continue to cause inflammation and eventually tissue damage

E. The complexes can also precipitate causing clots to form in the small blood vessels leading to failure or death of the organ

1. Known as disseminated intravascular coagulation

F. Examples of Type III Hypersensitivity are:

1. Arthus reaction – localized tissue death

   A) ex. Chronic Obstructive Pulmonary Disease (COPD)

2. Serum sickness – seen in individuals immunized/treated with animal serum

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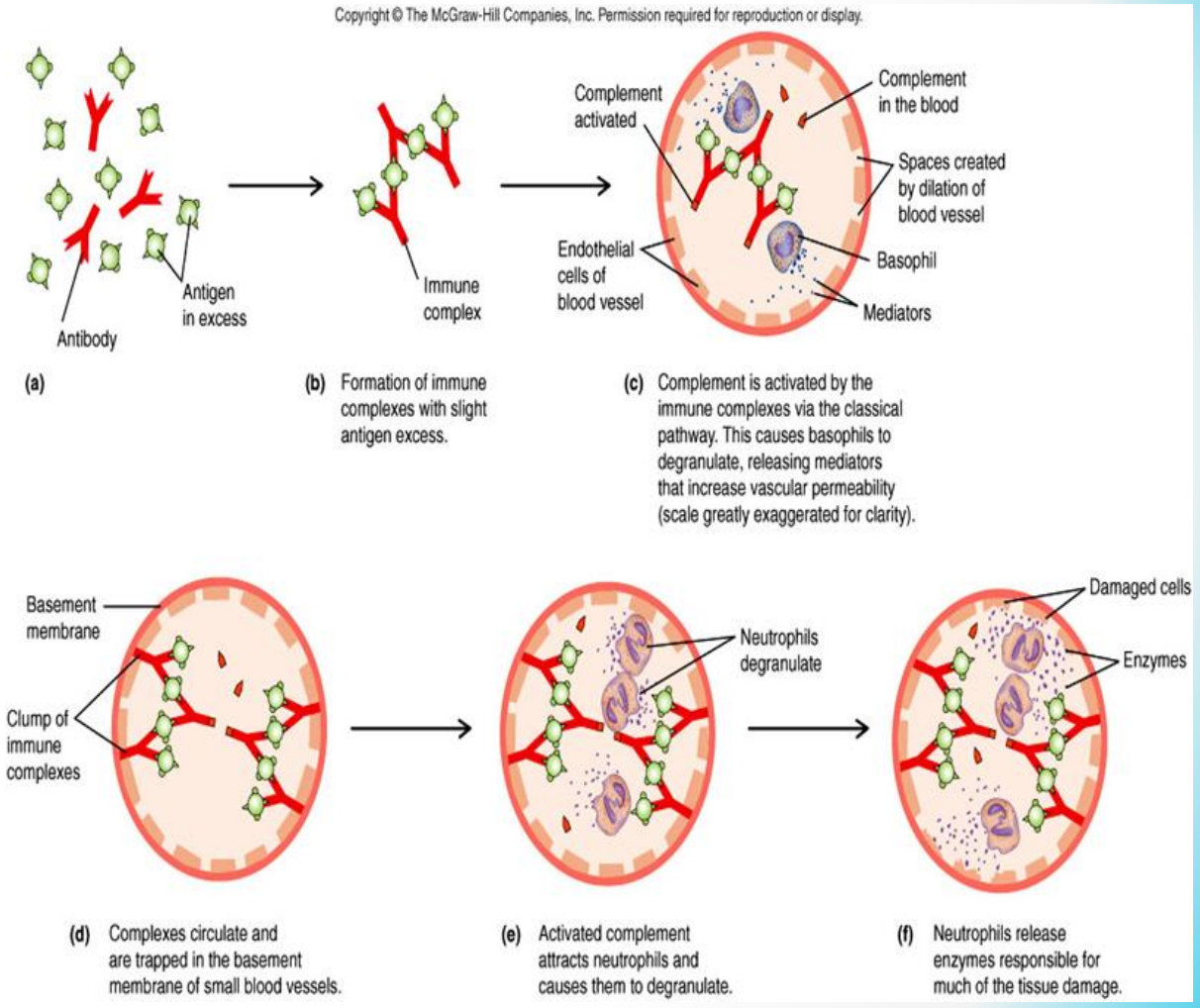

Type IV Hypersensitivity

- Also called Delayed Cell-Mediated Hypersensitivity
  1. occurs within days after exposure

- T-cells rather than antibodies are involved with this type

- Examples of delayed hypersensitivity are:

1. Tuberculin skin test – a positive test results when circulating antibodies (which are only present if the person has been exposed) bind to the protein antigens of the tuberculosis bacteria introduced under the skin

A) peaks 2-3 days after exposure

B) the redness results mainly from sensitized T-cell reactions, the release of cytokines and the influx of macrophages to the injection site

C) false positive tests can result from exposure to another species of *Mycobacterium* or use of the BCG vaccine

Contact hypersensitivity

– mediated by T-cells that release cytokines when they come into contact with the same antigen

A) the cytokines cause inflammation which attracts WBC to the site

B) these then release chemicals that result in allergic dermatitis or contact dermatitis

C) Examples: poison ivy, poison oak, nickel reactions, and latex reactions

Delayed hypersensitivity to infectious diseases

T-cells destroy macrophages and sick body cells, tissue damage results. Examples: leprosy, tuberculosis, and herpes simplex infections

Transplant Immunity

1. Autografts – grafts from the same person

2. Isografts – grafts donated by a genetically identical twin

3. Allografts – grafts between non-identical humans

4. Xenografts – transplantation of tissue from a non-human organism

- Transplantation rejection of allografts and xenografts are caused largely by Type IV cellular reaction

- Transplant success is dictated by the similarity of the MHC antigens on the surface of human cells

    1. MHC tissue typing is done in an effort to ensure that no major tissue incompatibilities exist between patient and donor

- Often immunosuppressive drugs are taken to reduce rejection

    1. These drug treatments however, make the patient susceptible to opportunistic infections

Autoimmune Diseases

- Autoimmune diseases occur when the immune system of the body responds to its own tissues as if they were foreign

- May result from normal reactions to antigens that are similar, though not identical, to the host's normal antigens

- Autoimmune reactions occur over a spectrum ranging from organ-specific to widespread response not limited to any one tissue

1. Grave's disease (thyroid) and Insulin-dependent diabetes mellitus (pancreas) are organ specific

2. Lupus and rheumatoid arthritis are considered widespread

- Treatment of Autoimmune diseases

    1. Usually treated with immunosuppressive drugs that kill dividing T-cells and thus control the response

    2. Also treated with drugs that interfere with T-cell signaling such as cyclosporin

    3. Steroids and other anti-inflammatory drugs are often used to relieve symptoms

- Some patients require replacement therapy (ex. insulin for diabetics)

- Transplantation of damaged organ is a last resort