

The slide features a light green background with a vertical gradient. On the left side, there are several thin, dark, curved lines that sweep upwards and to the right, resembling stylized grass or abstract brushstrokes. The main title is centered in the upper half of the slide.

Immune Response



Introduction

- The specific reactivity induced in a host by an antigenic stimulus is known as *immune response*
- Protection against invading MCO
- It may lead to consequence which may be either beneficial, indifferent or injurious
- The immune response can be of 2 types
 - Humoral mediated immunity (HMI)
 - Cell mediated immunity (CMI)
- Usually developed together, but either may be predominant, exclusive or sometime act together or sometime in opposite

Humoral Mediated Immunity (HMI)

- Antibody mediated
- Antibody – produced from **plasma cell** present in blood and other body fluid (**Humoral – body fluid**)
- Provides defence against most **bacterial** pathogen and **virus** (respiratory and intestinal)
- Also participates in pathogenesis of type 1, 2, 3 **hypersensitivity** reaction and **auto-immune disorder**

Cell Mediated Immunity

(CMI)

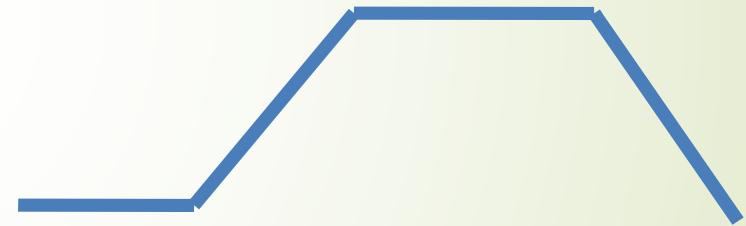
- **Specific immune** response that doesn't involve antibody
- Protects against **fungi, virus** and facultative intracellular **bacterial** pathogen
- Rejection of **homografts** and **graft-versus host reaction**
- Provides immunological surveillance and immunity against **cancer**
- Mediates pathogenesis of delayed **type 4 hypersensitivity** reaction and certain autoimmune disorder



Humoral Mediated Immunity (HMI)

Production of Antibodies

- It involves 4 step
- **Lag phase**
 - entry of pathogen, its distribution and fate in tissue
 - Contact with immunocompetent cells
- **Log Phase**
 - Steady rise in the titre of antibody
- **Plateau phase**
 - Equilibrium between antibody synthesis and catabolism
- **Decline phase**
 - catabolism exceeds production and thus titre falls



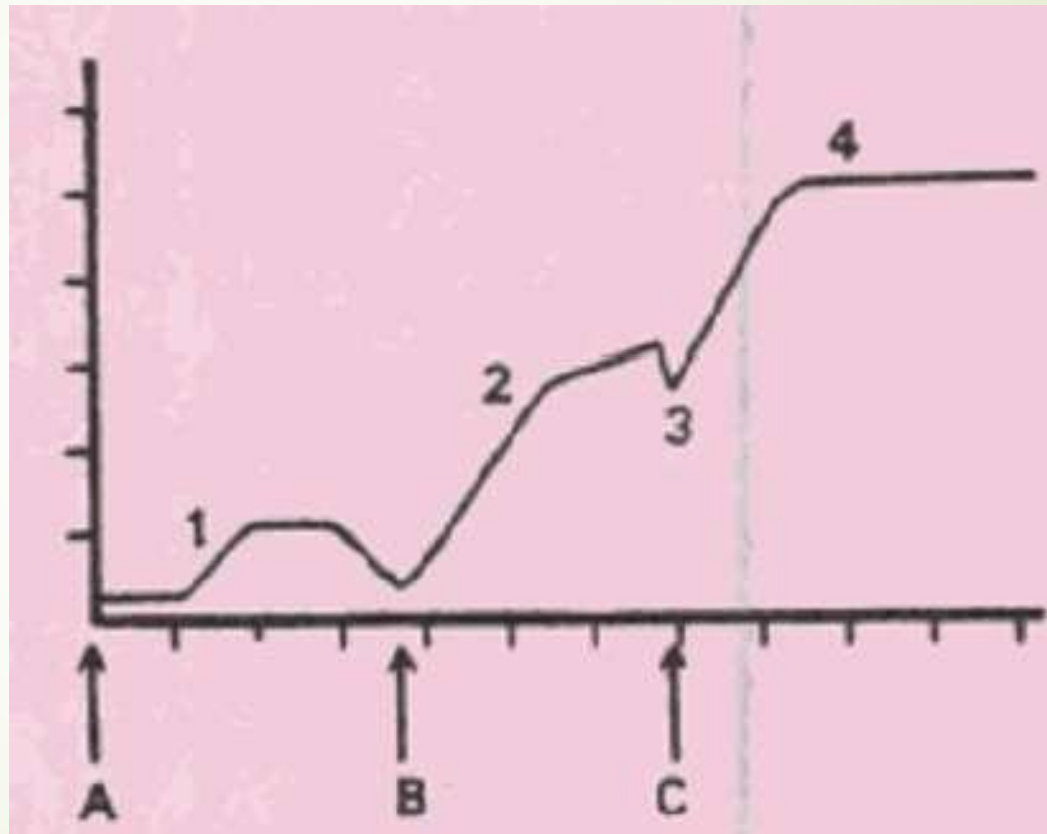
Primary and Secondary Response

- Antibody response to initial antigenic stimulus is called **primary response**
 - differs both quantitatively and qualitatively
 - Slow, sluggish and short lived
 - Long lag phase and low titre of antibody
 - Predominantly IgM
- Subsequent to primary response is call **secondary response**
 - Prompt, powerful and prolonged
 - Short or negligible lag phase
 - much higher level of antibodies for longer period
 - Predominantly IgG

Primary and Secondary Response

Negative Phase (3)

- When an antigen is injected in individual already carrying specific antibody, there is temporary fall in antibody level
- **Combination of antigen with the antibody**



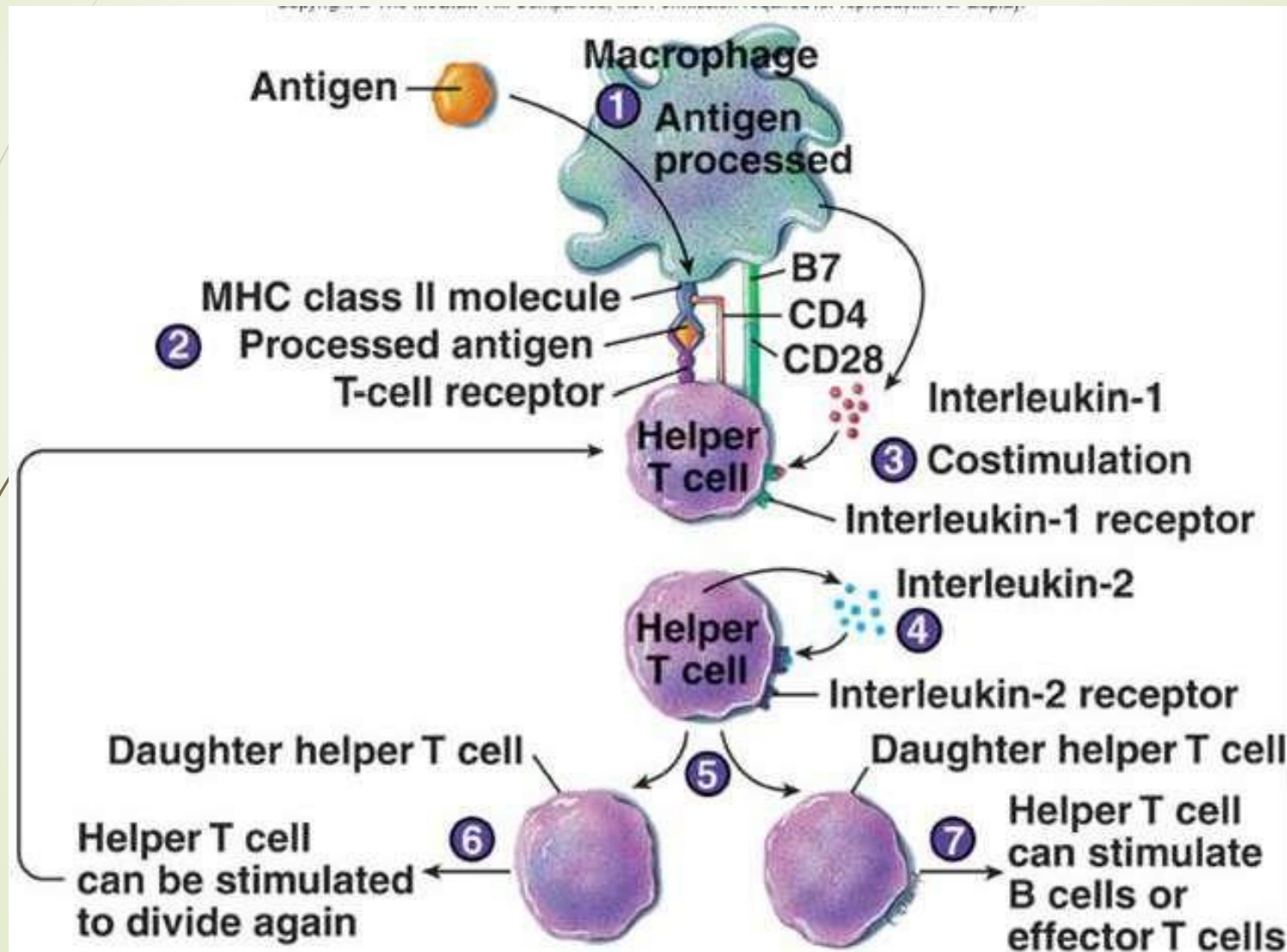
Primary and Secondary Response

- Duration of lag phase and persistence of antigen vary with nature of antigen
 - Diphtheria toxoid: 2-3 weeks
 - Pneumococcal polysaccharide – few hrs
- **Non living vaccine** – given in multiple dose
 - **Priming dose:** first injection of antigen
 - **Booster dose:** subsequent injection of antigen
- **Live vaccine:** sufficient for multiplication of organism in the body which provides continuous antigenic stimulus

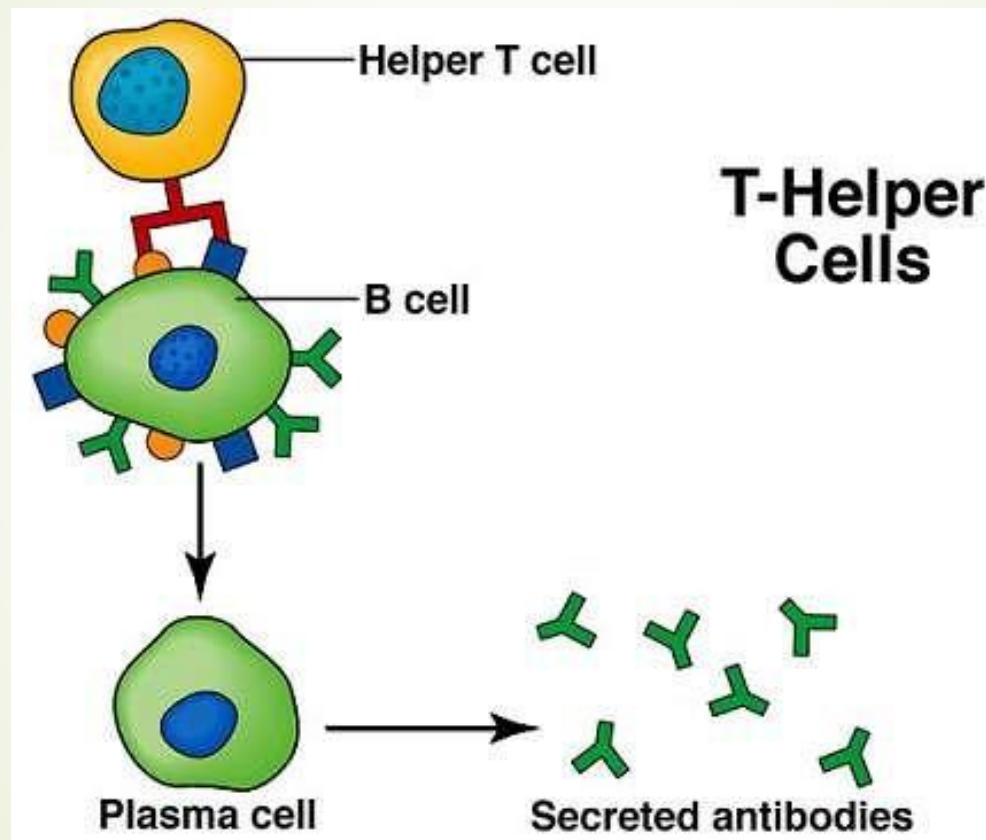
Production of Antibodies


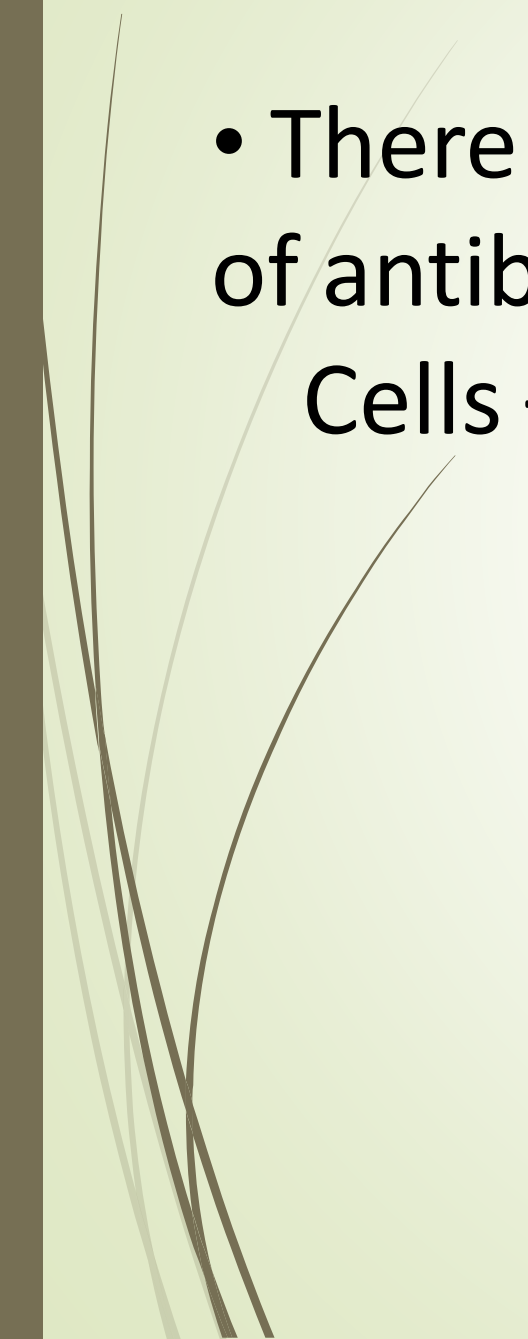
1. Antigen enters
2. **Antigen presenting cells (APC)** – activated
 - Macrophage
 - Dendritic cells
3. APC binds with **Major histocompatibility complex (MHC) II**
4. **Immature T-cell** binds with earlier formed complex with the help of **T-cell receptor** (TCR)
5. Whole complex produces signal for activation of **CD4 cells**
6. Activation of **CD4 cells** – Maturation of **T helper cell** (TH-cells)
7. Forms **IL-2, IL-4, IL-5 & IL-6: B-cell** maturation and subsequently release of **plasma cells**
 - **Plasma cells** – forms **antibodies**
 - Some of the **plasma cells** – **memory cells**

Production of Antibodies



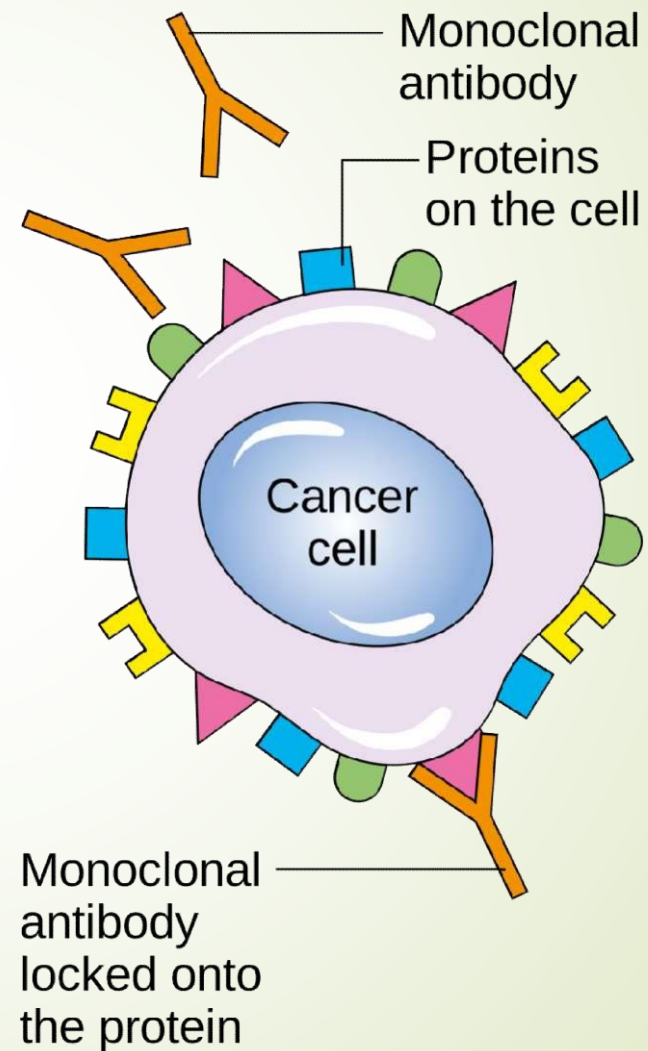
Production of Antibodies



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- There is continued production of antibody by cloning of Plasma Cells – **Polyclonal Antibodies**
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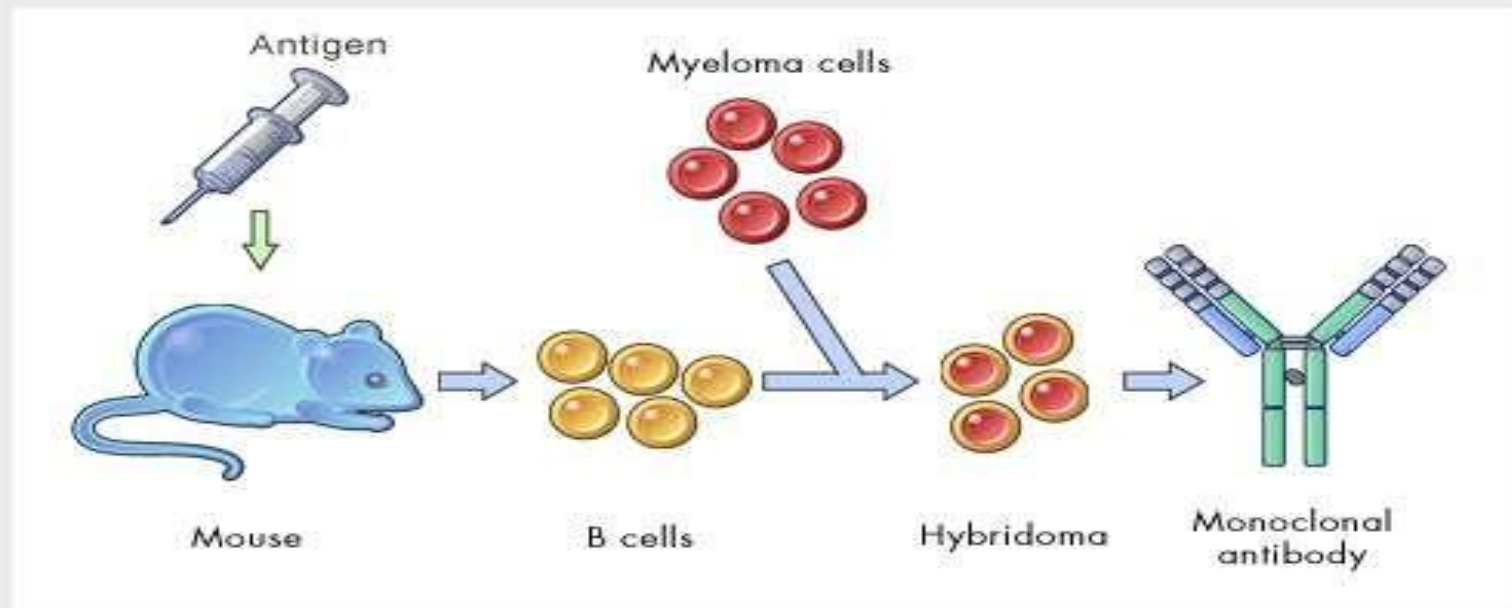
Monoclonal Antibodies

- Kohler and Milstein (Nobel Prize 1984)
- A single antibody forming cell or clone produces Antibodies against single antigen
- Antibodies are usually polyclonal,



Monoclonal Antibodies

- Prepared by fusing immortal **myeloma cells** with the spleen cells **B cells** (derived from a mouse that has been immunized with the intended antigen) to produce monoclonal antibody-producing cells, **hybridomas**.
- Hybridomas have the characteristics of both cells i.e. produce **antibodies** and reproduce infinitely.





Monoclonal Antibodies

- Diagnostic tests
 - detect small amounts of drugs, toxins or hormones
 - e.g. monoclonal antibodies to **human chorionic gonadotropin (HCG)** - pregnancy test kits
 - **AIDS** by the **ELISA test**
- Treat viral diseases
- Detection and immunotherapy of cancer
- Classify strains of a single pathogen, e.g. *Neisseria gonorrhoeae*



Factors Affecting the Antibody Production

- 1. Genetic Factor**
- 2. Age**
- 3. Nutritional status**
- 4. Route of Administration**
- 5. Size and Number of dose**
- 6. Multiple Antigens**
- 7. Adjuvants**
- 8. Immunosuppressive agents**
- 9. Effect of Antibody**



Factors Affecting the Antibody Production

- **Genetic Factor**
 - Difference in immune response to same antigen by different individual
- **Age**
 - Embryo is immunologically immature – derives immunity from maternal antibodies
 - Neonate
 - > 3-6 months Maternal antibodies
 - Ig G 5-7 years
 - Ig A 10-15 years
 - **B-cell** response to **T-cell** dependent antigen (protein and complex)
 - T-cell independent (Polysaccharide) – 2 yrs



Factors Affecting the Antibody Production

- **Nutritional status:** decreased antibody synthesis
 - Malnutrition – PEM effects both CMI and HMI
 - **Amino acid deficiency** – tryptophan, phenylalanine, methionine, glycine, isoleucine
 - **Vitamin deficiency** – Vit A & B (riboflavine, pyridoxine, biotin, pantoic acid, folic acid)
- **Route of Administration**
 - Parenteral administration of antigen – better immune response
 - Route of administration also influence the type of antibody produced
 - IgA – oral and nasal
 - IgE – Nasal
 - IgG- Parenterally



Factors Affecting the Antibody Production

- **Size and Number of dose**
 - Dose dependent – effective only above **minimum critical dose**
 - Further increase – enhances the intensity of antibody response
 - Beyond a certain level – inhibit and induce tolerance
 - **Immunological Paralysis Felton**
 - Increased antibody response – secondary stimulus but after certain stages no further increase occurs
 - **Anamnestic reaction** – antigenic reaction to a heterologous antibody that the host has produced earlier

Factors Affecting the Antibody

Production

- **Adjuvants**
 - Substances which **enhances** the **immunogenicity** of an antigen
 - Increase the concentration and persistence of **circulating antibodies**
- **Types of adjuvants**
 - **Inorganic compounds:** alum, aluminum hydroxide, aluminum phosphate, calcium phosphate hydroxide
 - **Mineral oil:** paraffin oil, Monophosphoryl lipid A
 - **Bacterial products:** killed bacteria Bordetella pertussis, Mycobacterium bovis, toxoids
- **It enhances the immune response** to the antigen in different ways:
 - extend the presence of antigen in the blood
 - help absorb the antigen presenting cells antigen
 - activate macrophages and lymphocytes
 - support the production of cytokines



Factors Affecting the Antibody Production

- **Immunosuppressive agents**
 - Inhibit the immune response
 - Essential to prevent graft rejection in transplantation
 - **X rays**: no antibody is produced till 24 hrs after exposure
 - **Corticosteroids**: depletion of lymphocyte from blood and lymphoid organ
 - **Anti-metabolites**: interfere the synthesis of DNA, RNA or both. Ex: methotrexate, 6-mercaptopurine, azathioprine, uracil and cytosine
 - **Cytotoxic Chemicals**: cyclosporine – cyclic polypeptide, most commonly used
 - **Antilymphocytic serum (ALS)**: antiserum against lymphocytes
 - **Radiomimetic drugs**: cyclophosphamide, nitrogen mustard

Factors Affecting the Antibody Production

- **Multiple Antigens:** when 2 or more antigen are given simultaneously the effect may vary
 - **No effect:** antibody will be produced separately as if they were given alone
 - **Typhoid and cholera vaccine**
 - **Enhanced:** triple vaccine **DPT**
 - **Diminished:** when only diphtheria and tetanus vaccine given together – the one in excess shows antibody production
 - person already immunised with diphtheria, will not show immune response to **triple vaccine** other than diphtheria
- **Effect of Antibody**
 - Immune response gets suppressed by **passive administration** of **homologous antibody**
 - Feedback mechanism
 - Rh(-ve) mother having Rh(+ve) fetus – early sensitization by administration of anti-Rh globulin (antibody)



Super antigens

- Certain protein Molecules that activate large number of T cells, irrespective of Antigenic specificity.
- Ex: Staphylococcal Enterotoxin
- Usually only few T-cells (0.001%) are stimulated – up to 20 % of circulating T-cells
- This exaggerated T-cell activation – outpouring of T-cell cytokines : **multisystem dysfunction**
- **Staphylococcal Shock syndrome**




Mitogens

- A **mitogen** is a chemical substance that encourages a cell to commence **cell division**.
- **B-cell mitogens:** lectin glycoproteins and lipopolysaccharide (LPS)
- **T-cell mitogens:** phytohaemagglutinin (PHA)



Cell-mediated Immunity



Cell-mediated Immunity

- Specific immune response that do not involve antibody
- It participates in following immunological functions
 - Delayed hypersensitivity
 - Immunity in infections caused by Obligate and facultative intracellular parasites
 - **Bacteria:** Tuberculosis, Leprosy, Listeriosis, Brucellosis.
 - **Fungi** – Histoplasmosis, Coccidiomycosis, Blastomycosis
 - **Parasites** – Leishmaniasis, Trypanosomiasis
 - **Virus-** measles and mumps
 - Transplantation immunity
 - Immunological surveillance & Immunity against **malignancy**
 - Pathogenesis of **Autoimmune diseases:** thyroiditis, encephalomyelitis



Induction of Cell Mediated Immunity

- Depends on Nature of Antigenic stimulus
- Best developed after following infection with **intracellular parasites**
- **Live vaccines** highly stimulating
- Killed vaccine not very effective, but effective if contains adjuvant.

Induction of Cell Mediated

1. Immunity

Antigen enters

- 2. Antigen presenting cells (APC)** – activated
 - Macrophage
 - Dendritic cells
3. APC binds with **Major histocompatibility complex (MHC) I**
- 4. Immature T-cell** binds with earlier formed complex with the help of **T-cell receptor (TCR)**
5. Whole complex initiate the formation of **CD4 (helper) & CD8 cells (cytotoxic)**
 - Former **helps** releases of **lymphokines** which activates macrophage – eats away intercellular parasites
 - **CD8 cells** - recognize antigen on surface of virus, infected cells, tumor cells, allograft cells with MHC I and secretes **lymphokines** and destroy target cells

Cytokines

- **Signalling** proteins and glycoproteins that are used extensively in **cellular communication**.
- It regulates **immunological, inflammatory and reparative** host response
- It acts like **hormone** and **neurotransmitter**
- Differ from former in being produced not by specialized glands but by widely distributed cells such as **lymphocytes, macrophage, platelets and fibroblast**
- Its grouped in 5 class
 - **Interleukin (IL)** : IL (1-13)
 - **Colony stimulating factors (CSF)**
 - **Tumor Necrosis factor (TNF)**
 - **Interferon (INF)**
 - **Others:** Transforming growth factor (TGF) & Leukemia inhibitory factor (LIF)



Interleukin (IL)

- **IL-1**
 - Secreted by macrophages, monocytes and few other multinucleated giant cell (MGC)
 - Stimulated by antigen, toxins, injury and inflammatory processes
 - Inhibited by cyclosporin A, corticosteroid and prostaglandins
 - Stimulates T-cell for production of IL-2 and other lymphokines
 - B-cell proliferation and antibody synthesis
 - Neutrophil chemotaxis and phagocytosis
 - Endogenous pyrogens
- **IL-2**
 - Powerful modulator of immune response
 - Major activator of T and B cells
 - Stimulates cytotoxic T cells and NK cells
 - Treatment of certain kind of cancers



Interleukin (IL)

- **IL-3**
 - Growth factor for bone marrow stemm cells
 - Stimulates multilineage hematopoiesis
 - Also known as multicolony stimulating factor **multi-CSF**
- **IL-4**
 - Activates resting B-cells and differentiate it
 - Growth factor for T-cells and mast cells
 - Enhances cytotoxic T cells
 - Role in atopic hypersensitivity – augments Ig E synthesis
- **IL-5**
 - Proliferation of activated B cells
 - Induces maturation of eosinophils
- **IL-6**
 - Produced by stimulated T and B cells, macrophages and fibroblasts
 - Induces immunoglobulin synthesis – activated B-cells



Colony stimulating factors (CSF)

- Stimulates growth and differentiation of **pluripotent stem cells** in bone marrow
- Induces **cascades** of other **cytokines**
- Adjusting the rate of **production of blood cells** according to requirements
 - Massive **granulocyte response** seen in **pyogenic infection**
- Treating **hematopoietic dysfunction** in infections and malignancies



Tumor Necrosis factor (TNF)

- Two types TNF α and TNF β
- Principally formed by activated macrophages and monocytes
- Induces hemorrhagic necrosis
- **Cachetin:** Serum factor – wasting syndrome (cachexia)
- Manifestation of endotoxic shock
- Immunomodulatory influence on other cytokines
- **TNF β :** produced principally by T-helper cells, effects similar to **TNF α**



Interferon (IFN)

- Antiviral agent, 3 classes
- **IFN α**
 - produced by leukocytes
 - Treat various viral infections: certain cases of acute and chronic hepatitis C and chronic hepatitis B
- **IFN β**
 - produced by fibroblast
 - virus-infected epithelial cells
- **IFN γ**
 - Produced in response to mitogens, antigen or exposure to IL-2
 - Macrophage activation and Augmentation of neutrophil
 - Monocyte function and Anti-tumor activity
 - **Treatment** : lepromatous leprosy, leishmaniasis, toxoplasmosis and certain tumours such as melanoma and Kaposi's sarcoma.

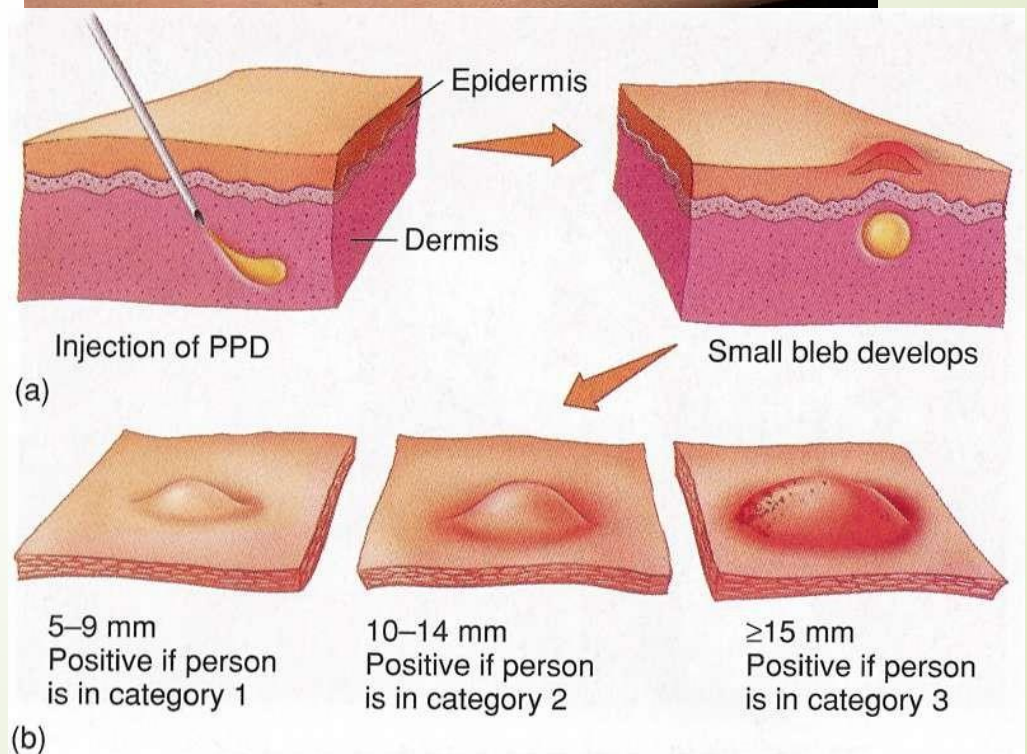


Others

- **Transforming growth factor (TGF)**
 - Transform fibroblasts
 - Growth factor for fibroblasts
 - Promotes wound healing
 - Down regulator of some immunological and hematological processes

Detection of CMI

- Earlier method was skin test – **Delayed type hypersensitivity**
 - Ex: Mantoux test (tuberculin test)
- Culture test
- Lymphocyte transformation test
- Migration inhibiting factor test.





Theories of Immune response

- Direct template theory
- Indirect template theory
- Natural selection theory
- **Clonal selection theory**
 - Nobel Prize winning
 - Most accepted theory
 - Immunological specificity to cellular level