Immune Response

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Introduction

- The specific reactivity induced in a host by an antigenic stimulus is known as *immune response*

- Protection against invading Microorganism

- 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 anitibody
- 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

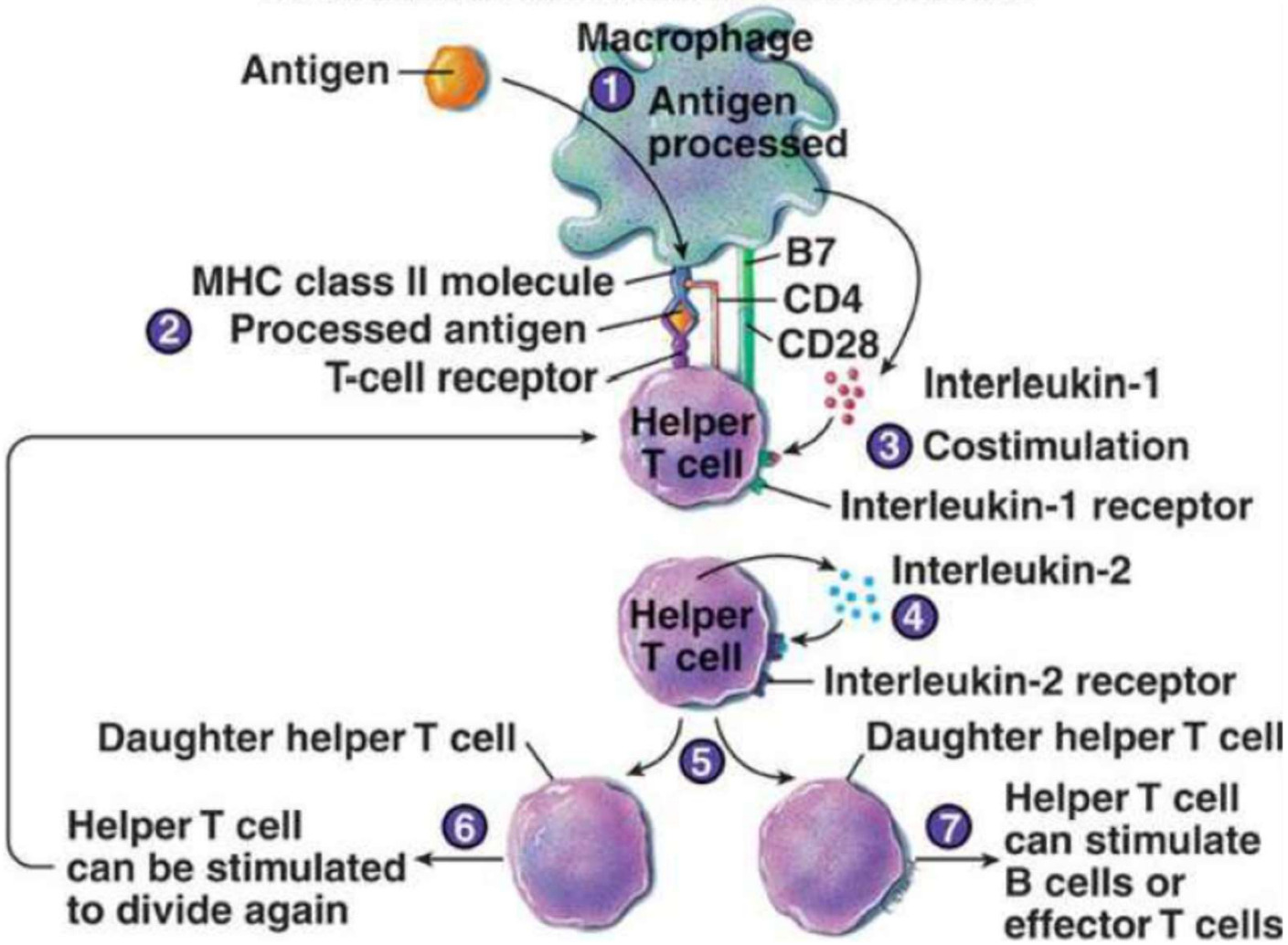
Primary and Secondary Response

- Duration of lag phase and persistence of antigen vary with nature of antigen
- – Diptheria 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

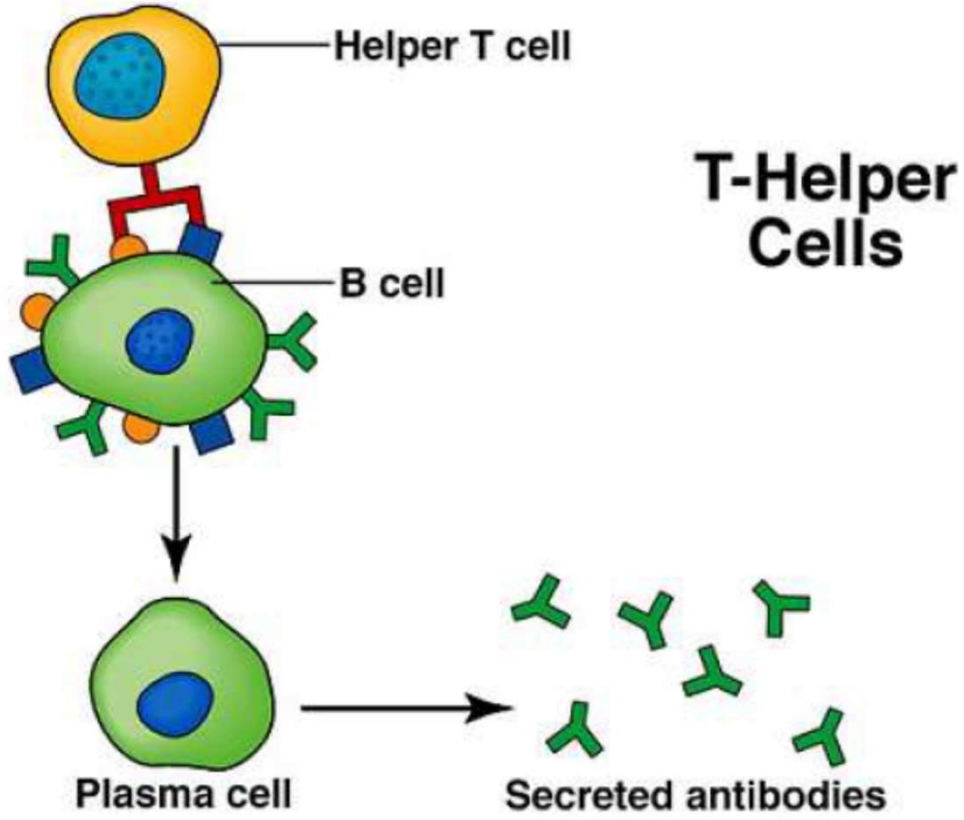
Production of Antibodies

- 1. Antigen enters
- **2. Antigen presenting cells (APC)** – acivated
- – Macrophage
- – Dendritic cells
- 3. APC binds with **Major histocompatablity 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

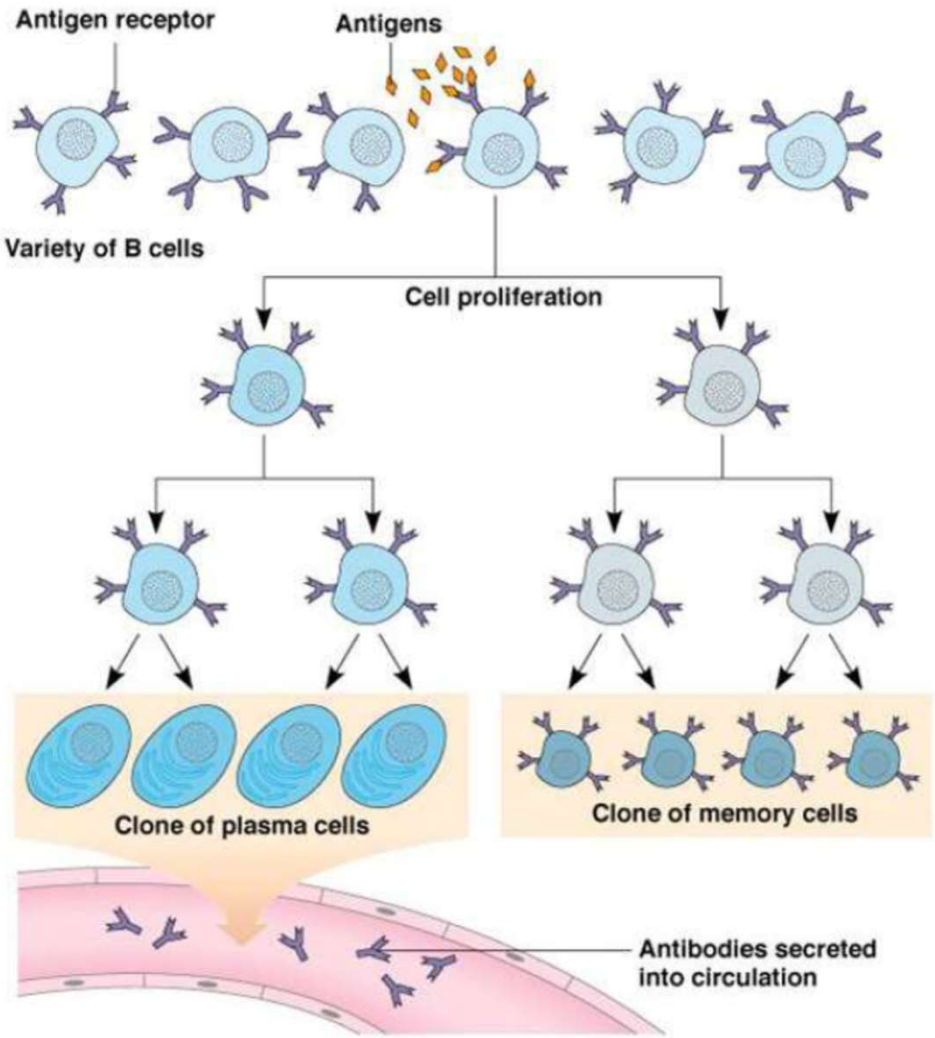


Production of Antibodies



Production of Antibodies

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

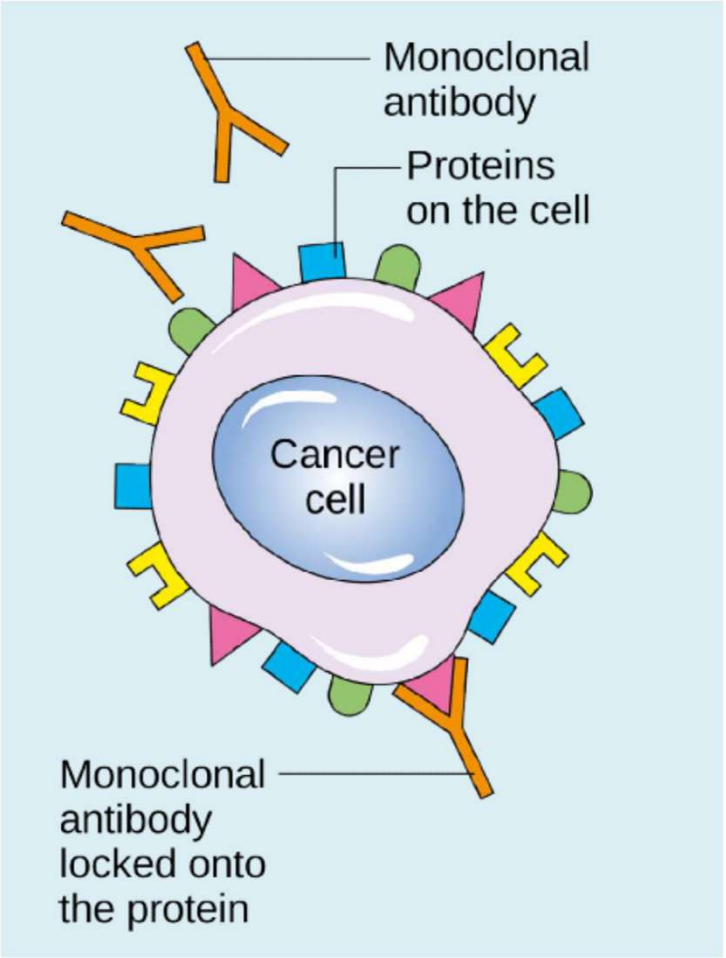


Monoclonal Antibodies

- Kohler and Milstein (Nobel Prize 1984)

- A single antibody forming cell or clone produces Antibodies against single antigen

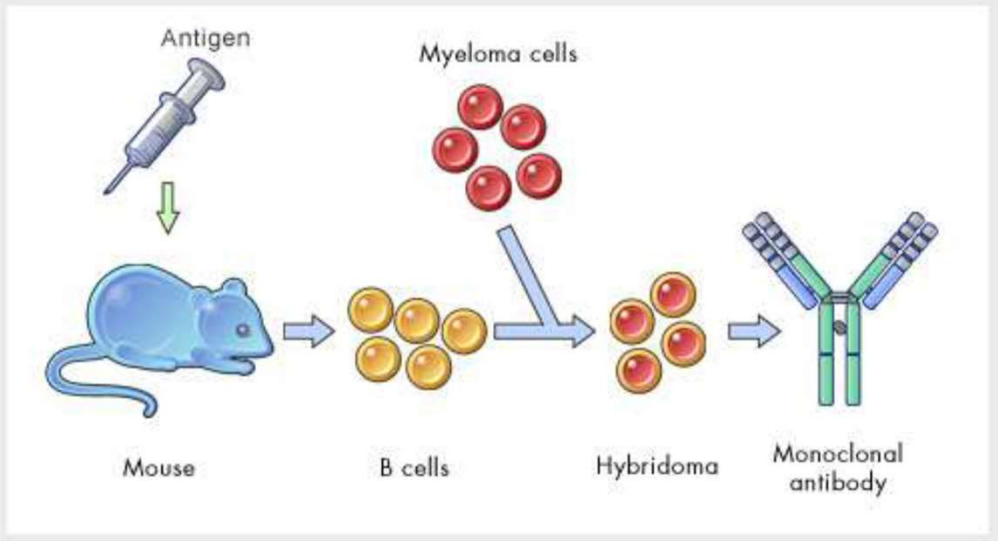
- Antibodies are usually polyclonal



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

Ex. 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*

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, Cocccidiomysosis, 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 Immunity

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- **2. Antigen presenting cells (APC)** – acivated
  - Macrophage
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- 3. APC binds with **Major histocompatablity 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 **CD_4 (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

• **Signaling** 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 stem 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

Tumour 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

IFNγ

- – 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

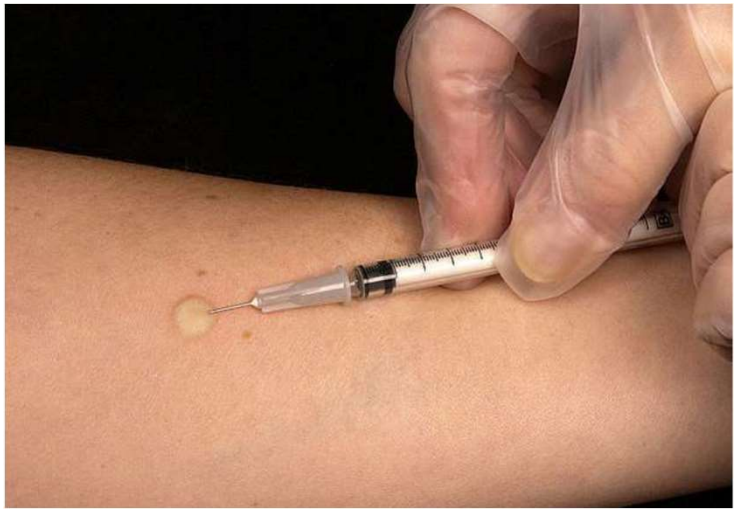
- **Transforming growth factor (TGF)**
- – Transform fibroblasts
- – Growth factor for fibroblasts
- – Promotes wound healing
- – Down regulator of some immunological and hematological processes

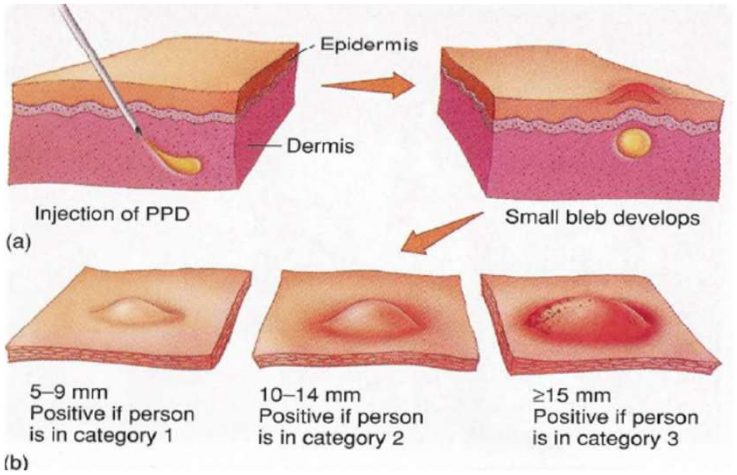
Detection of CMI

- Earlier method was skin test – **Delayed type hypersensitivity**

– Ex: Mantoux test (tuberculin test)

- Culture test
- Lymphocyte transformation test
- Migration inhibiting factor test.





THANK YOU

Happy to Answer if You have any Question....?