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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



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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**



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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



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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



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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



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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



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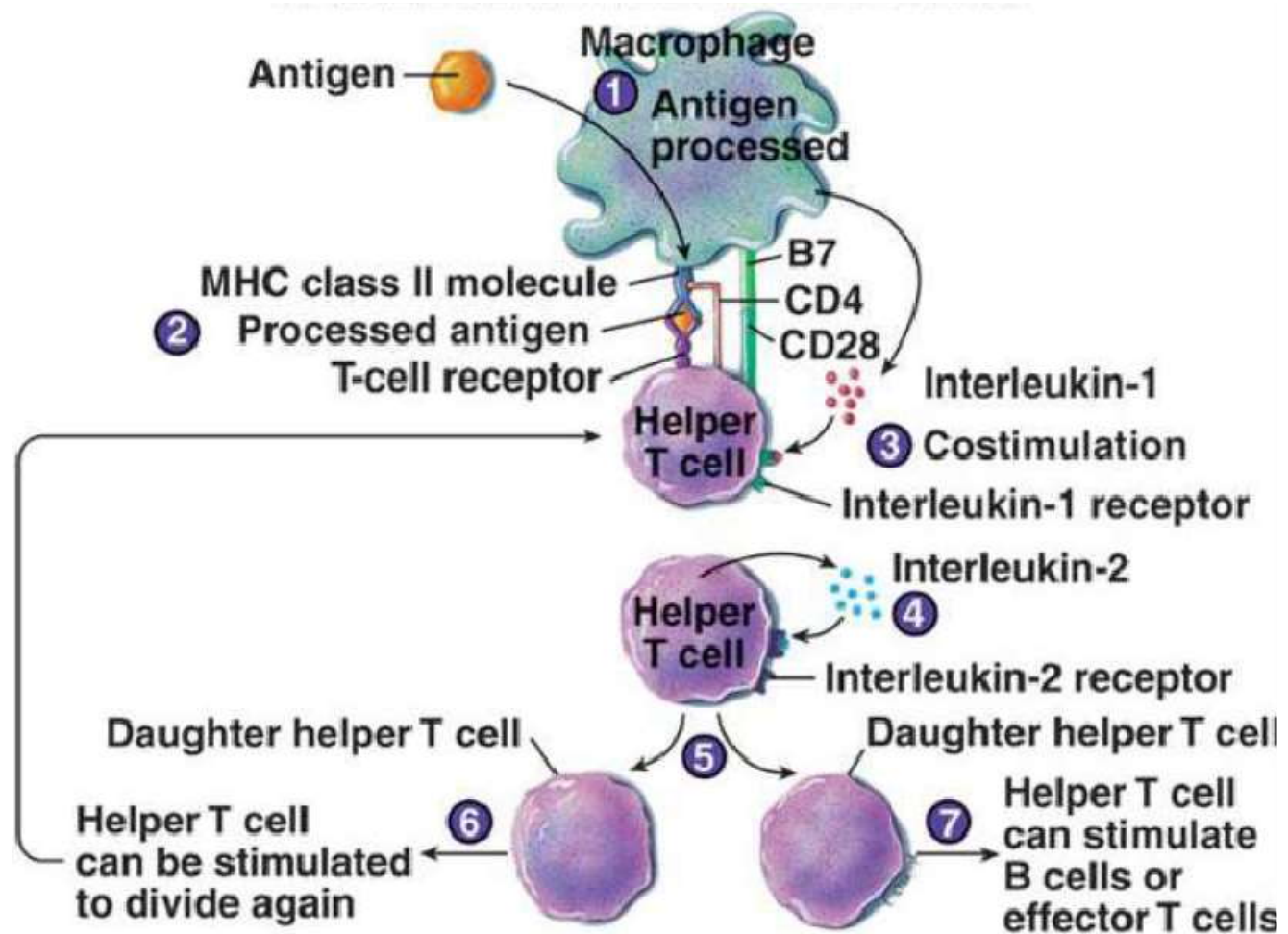
Production of Antibodies

- 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**



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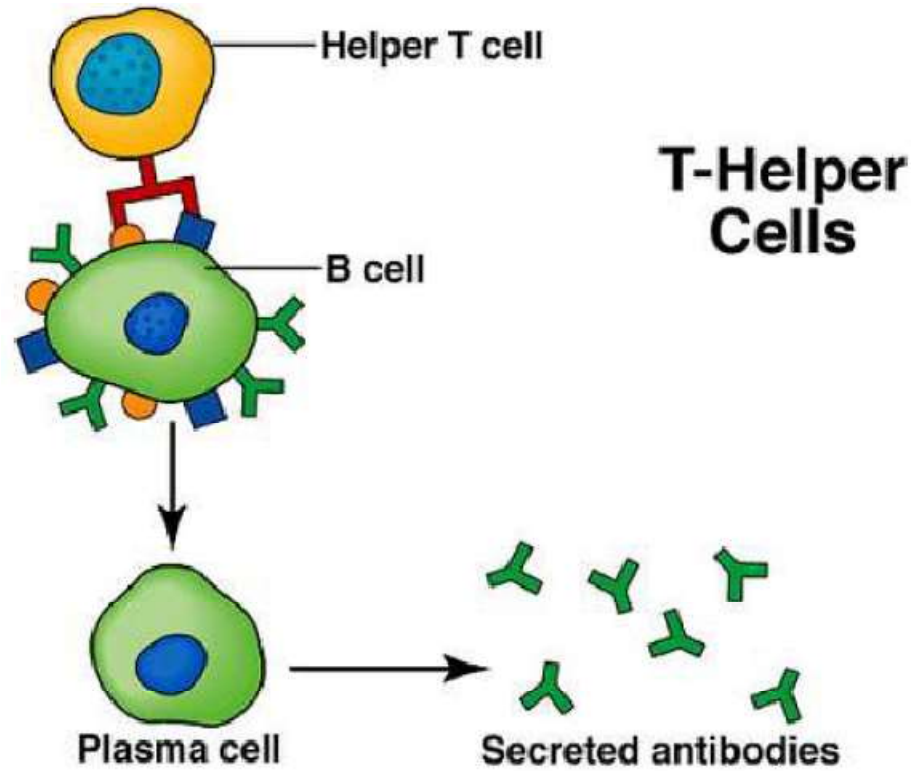
Production of Antibodies





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Production of Antibodies

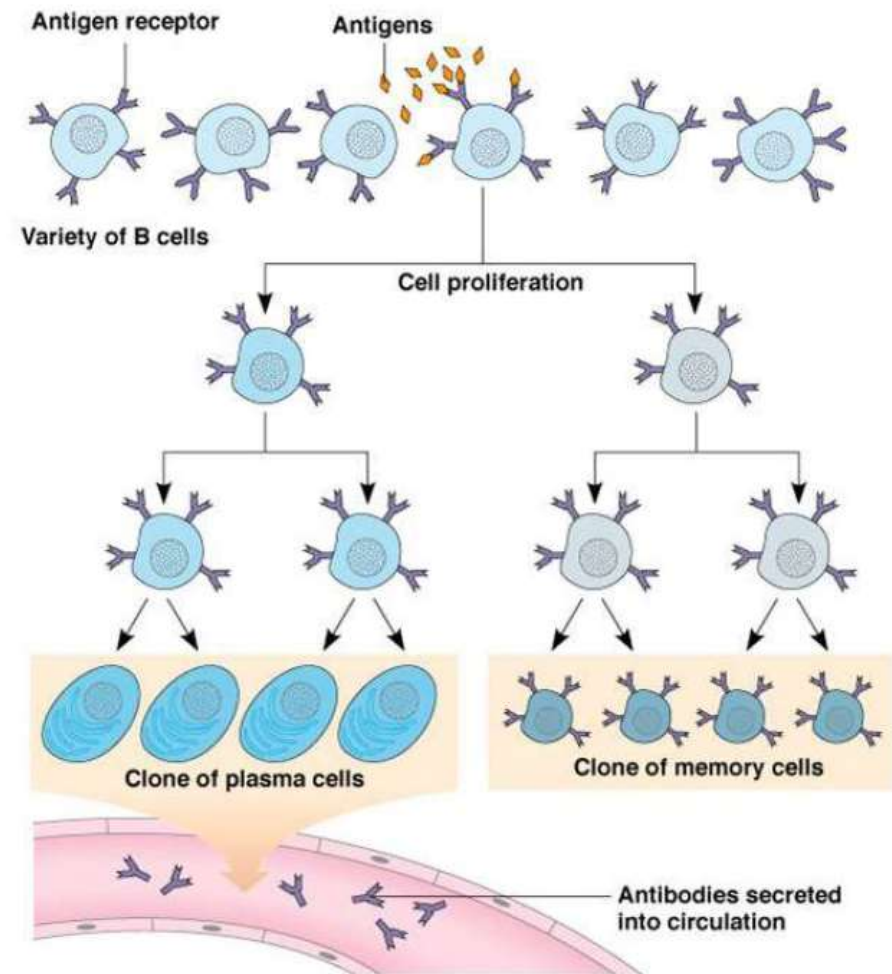




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Production of Antibodies

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



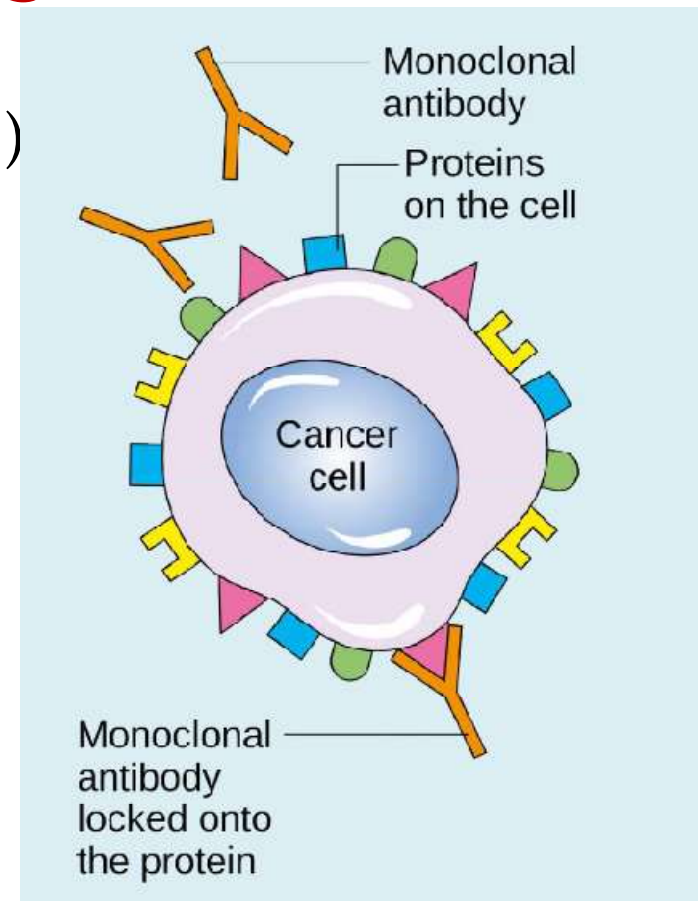


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Monoclonal Antibodies

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

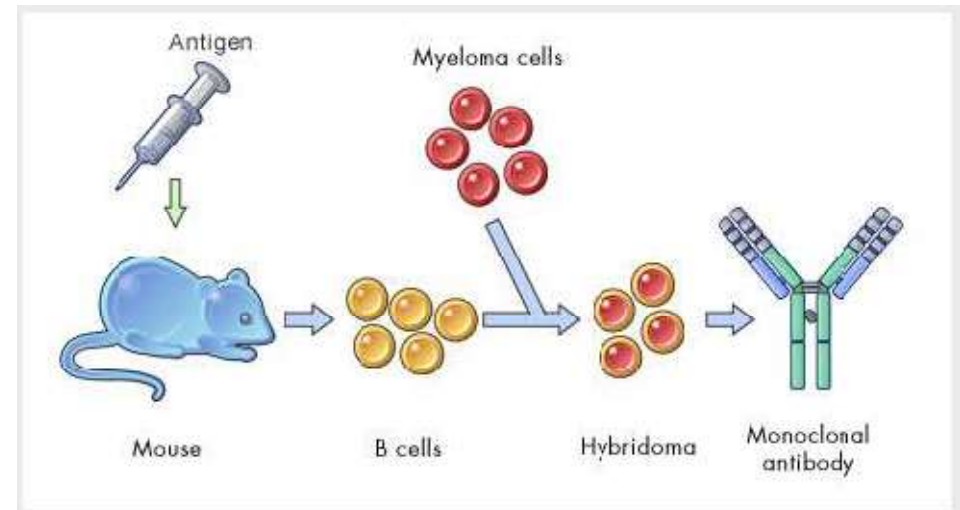




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Monoclonal Antibodies

- 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.





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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*



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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



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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.



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Induction of Cell Mediated Immunity

- 1. 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



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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)



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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



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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



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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



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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



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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.



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Others

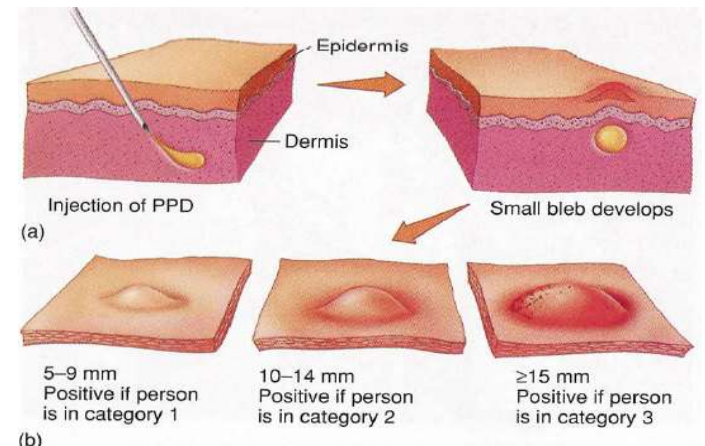
- **Transforming growth factor (TGF)**
 - – Transform fibroblasts
 - – Growth factor for fibroblasts
 - – Promotes wound healing
 - – Down regulator of some immunological and hematological processes



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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.





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THANK YOU

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