

## Transplantation

### Immunology of transplantation

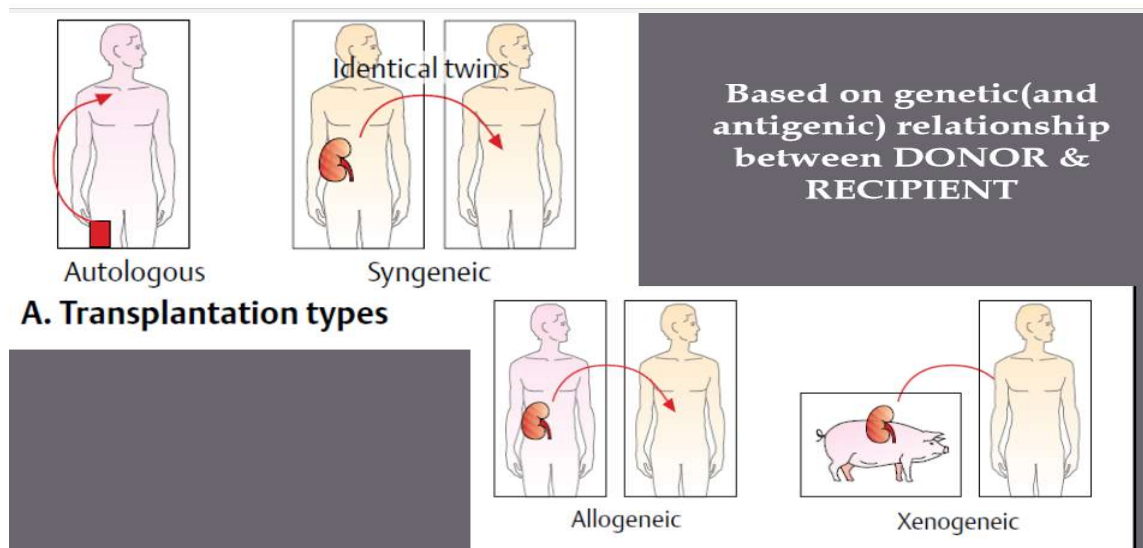
Graft or Transplant: Transfer of living cells, tissues and organs from one part of the body to another or from one individual to another.

#### The transplantation mainly based on:

1. Organ or tissue transplanted
2. Anatomical site of origin of transplant & site of its placement:
  - a. Orthotopic: normal sites
  - b. Heterotopic: abnormal sites
3. Genetic compatibility and antigenic relationship.
4. Fresh or stored transplanted tissue :

#### Types of Transplantation:-

1. Autologous .
2. Syngeneic.
3. Allogenic .
4. Xenogeneic .



## **Auto grafting ( Autologous ) -**

Transfer of self-tissue from one body site to another in the same individual, it should:

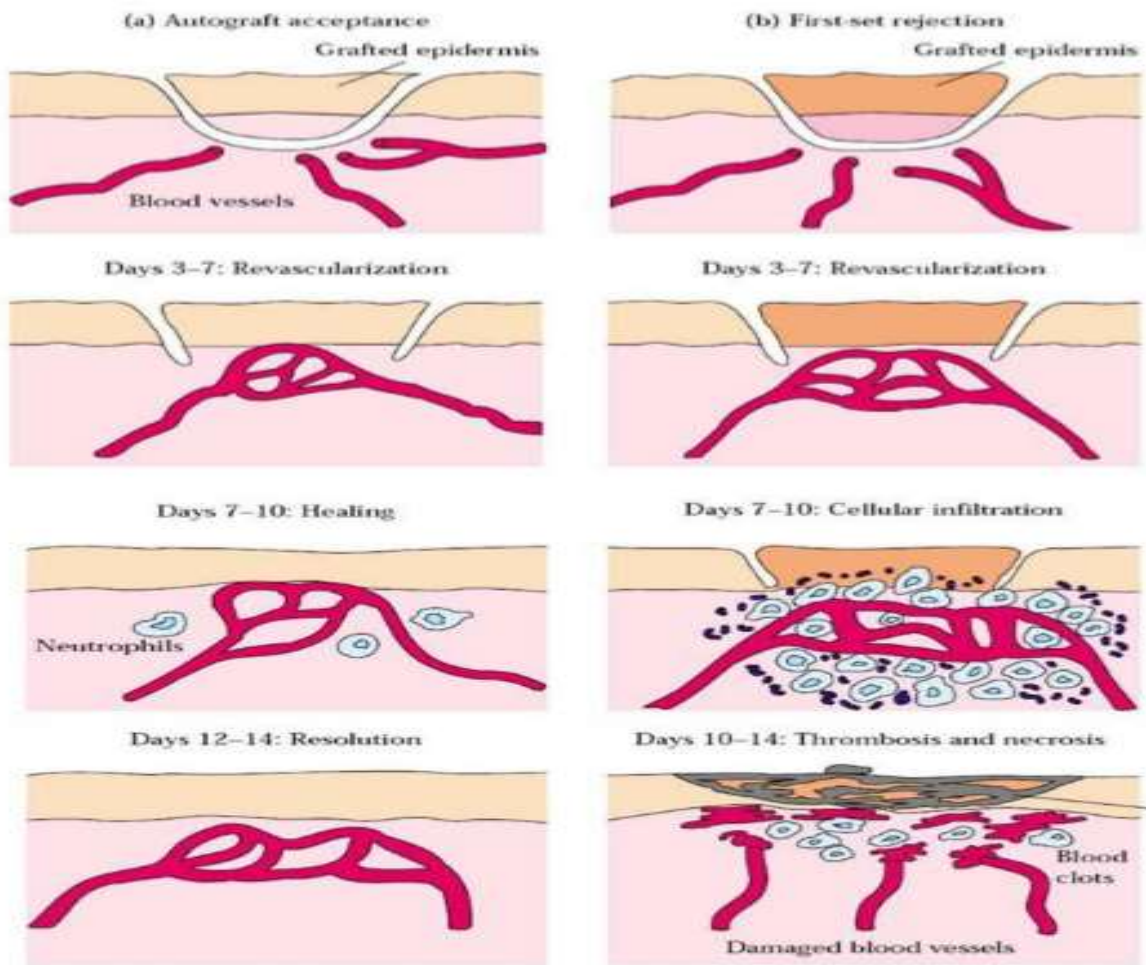
• **Genetic homology** of the tissue- immune system does not respond (Skin, hair grafts) Auto graft acceptance epidermis:-

1. After 3- 7 days have revascularization of blood vessels.
2. 7 – 10 days healing.
3. 12 -14 neutrophil resolution,

## **Allograft reaction:-**

**First Set Response** :- Skin graft from a genetically unrelated animal of same species . Initial acceptance , Thrombosed and necrosed Mainly by T lymphocytes .

- After 3- 7 days have revascularization of blood vessels .
- 7 – 10 cellular infiltration ,
- 10 -14 thromboses and necrosis ,
- > 14 day damaged blood vessels and rejection the implanted tissues.



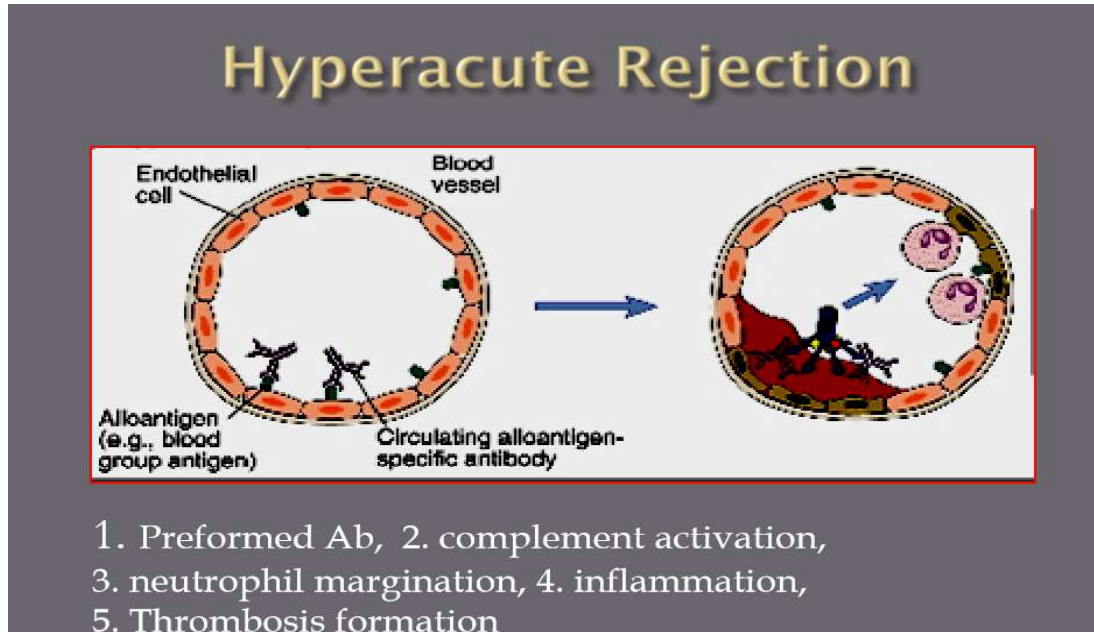
**Second Set Response :-** If an animal has rejected a graft by the first set response, another graft from the same donor is applied – rejected in an accelerated manner , Mainly by antibodies

### **Effector mechanism of allograft rejection:-**

- **Hyper acute Rejection**

- a. Pre-existing specific antibodies in high titers in the host circulation bind to donor endothelial antigens.
- b. Activates Complement Cascade.
- c. Characterized by thrombotic occlusion of graft
- d. Graft remains pale

- e. Rejected within minutes or hours, even without an attempt at vascularization



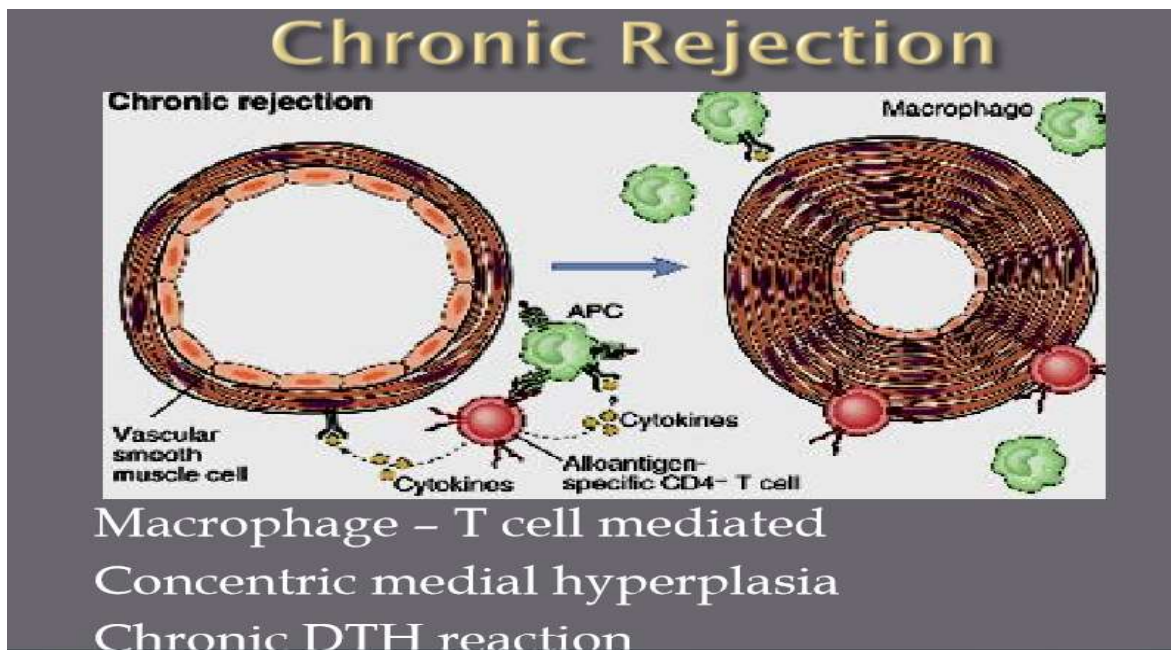
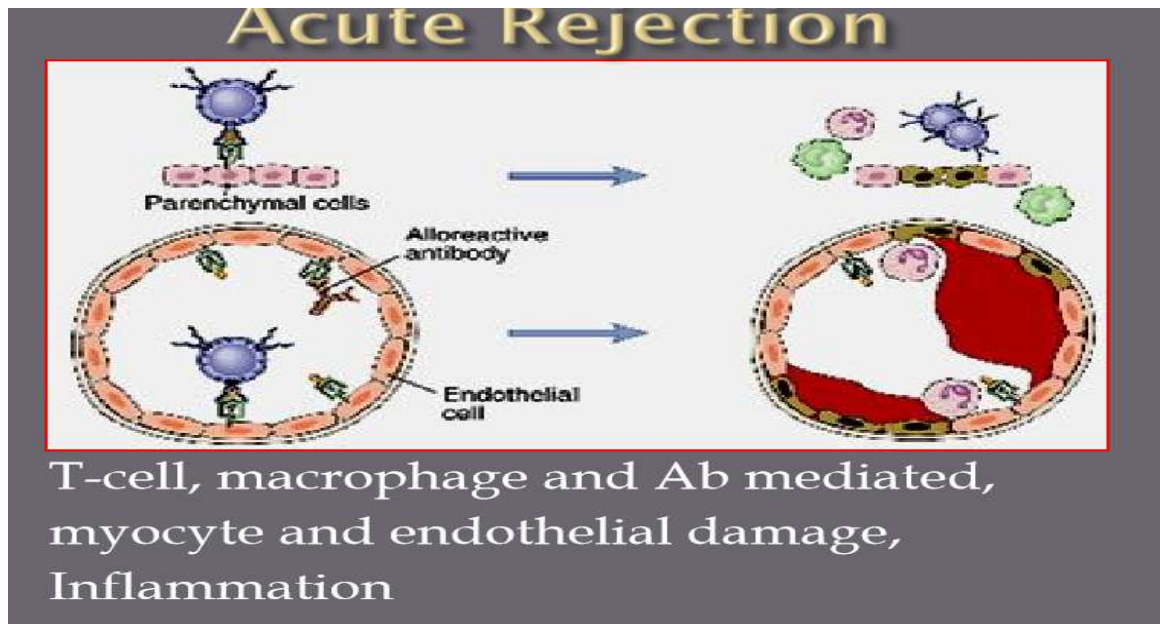
### Immunological Enhancement: -

Humoral antibodies can **act in opposition to CMI by inhibiting graft rejection.**

- **Afferent inhibition:** Combine with antigens released from graft so that they are unable to initiate an immune response
- **Central inhibition:** Antibodies may combine with lymphoid cell, by a negative feedback, render them incapable of responding to the antigens of the graft.
- **Efferent inhibition:** By coating the surface of cells in the graft so that sensitized lymphocytes are kept out of contact with them .

### Acute Rejection: -

- Vascular and parenchymal injury mediated by T cells and antibodies that usually begin after first week of transplantation if **no immunosuppressant therapy**
- Incidence is high (30%) for the first 90 days.



### Chronic Rejection :-

- Occurs in most solid organ transplants
- Heart, Kidney, Lung, Liver
- Characterized by :
  - a. Fibrosis

- b. Vascular abnormalities
- c. Loss of graft function over a prolonged period.

## **Histocompatibility antigens.**

Antigens that participate in graft rejection are called transplantation or histocompatibility antigens :

- ABO blood group
- HLA system (MHC restricted allograft Rejection )

## **Histocompatibility Testing :-**

- ABO blood grouping
- HLA compatibility:
- Tested by HLA typing and tissue matching
- HLA typing identifies the HLA antigens expressed on the surface of leucocytes

## **Methods of HLA – Typing :-**

- Microcytotoxicity test .
- Molecular methods
  - a. RFLP with southern blott
  - b. PCR using sequence specific primers.
- Tissue matching .

## **Micro Cytotoxicity: -**

Tests for complement mediated lysis of peripheral blood lymphocytes with a standard set of typing sera. Micro-cytotoxicity assay, utilizes serum with known anti-HLA antibodies that recognize particular HLA loci (HLA-A, HLA-B, HLA-C, HLA-DQ, HLA-DR /not DP) in order to match genetically similar individuals in hopes of performing a tissue transplantation.

### **Graft-versus-host (GVH) reaction: -**

Graft rejection is due to the reaction of the host to the grafted tissue, Host-versus-graft response , The contrary situation, in which the graft mounts an immune response against the antigens of the host, is known as: Graft-versus-host (GVH) reaction.

### **Essential Component Required for (GVH)**

The GVH reaction occurs when the following conditions are present:

1. The graft contains immunocompetent T cells.
2. The recipient possesses transplantation antigens that are absent in the graft.
3. The recipient must not reject the graft.

When grafted tissue has mature T cells, they will attack host tissue leading to GVHR. Major problem for bone marrow transplant.

### **Methods to overcome GVHR :**

- Treat bone marrow to deplete T cells.
- Use autologous bone marrow.
- Use umbilical cord blood.

Caused by the reaction of grafted mature Tcells in the marrow inoculum with alloantigens of the host

- **Acute GVHD** :- Characterized by epithelial cell death in the skin, GI tract, and liver .
- **Chronic GVHD** :- Characterized by atrophy and fibrosis of one or more of these same target organs as well as the lungs+