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# Transplant rejection

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Academic year: 2021/2022

# Transplantation

Organ or tissue transplantation is the replacement of an organ or a defective tissue by an organ taken from a donor.

- The term “ **transplantation** ” implies a restoration of **vascular continuity** (organs)
- The term “ **transplant** ” implies **the absence of this recovery** (transplant of hematopoietic stem cells)
- “**Graft**” means the grafted organ or fragment of tissue.

# Types of grafts

## 1) Orthotopic graft

The graft is brought in place of the receiver's organ to which it is substitute

## 2) HETEROTOPIC TRANSPL

The graft is placed in an anatomical site different from the natural site

## 3) Autologous or autologous transplant

Transplant from the donor organism itself and transplanted on the same organism. Ex: Skin burn treatment (**It is never rejected**)

## 4) Syngenic or isograft

Transplanted between genetically similar individuals with the same Histocompatibility

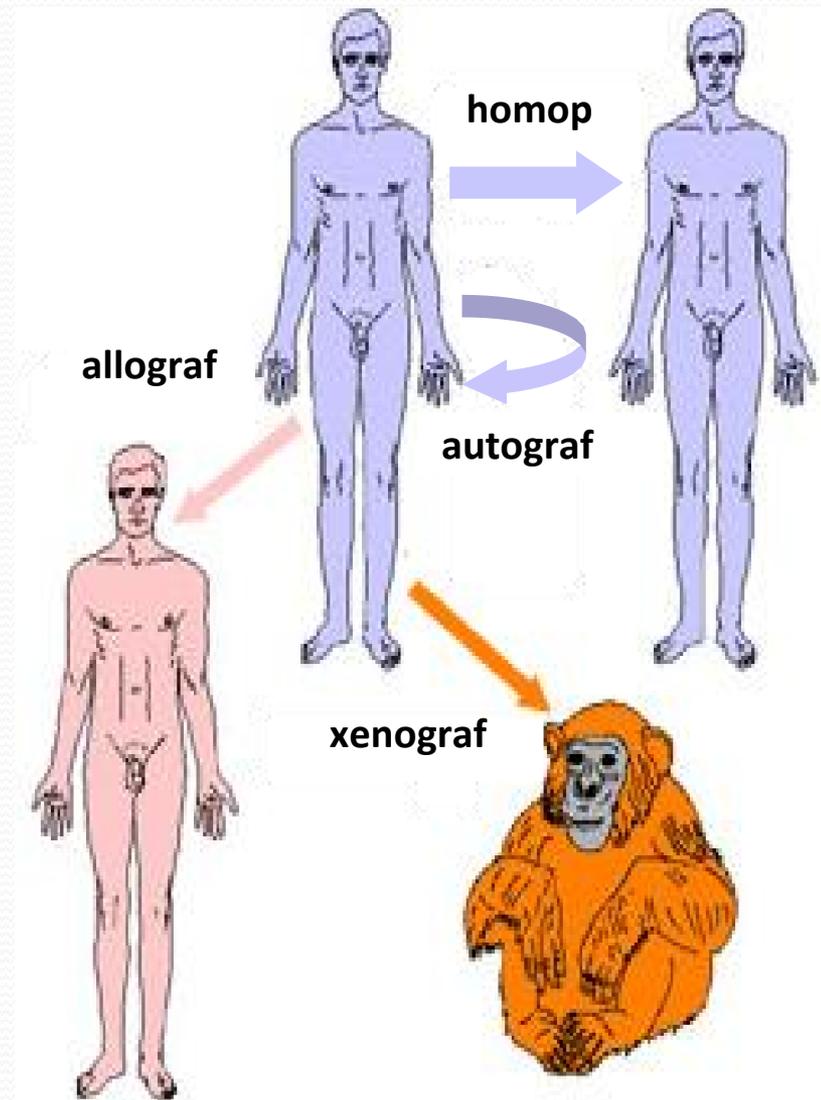
Ag (HLA): Monozygous twins

## 5) Allogeneic transplant or allograft

Transplanted between 2 individuals of the same species but genetically different.

## 6) Xenogenic or xenograft

Transplantation between individuals of different species.



## **Cellular graft rejection**

It is the destruction of the grafted tissue by the receiver's immunological reactions or by the destruction of the receiver's tissues by the graft's immunological reactions (GVHD)

### **The Different Forms of Rejection**

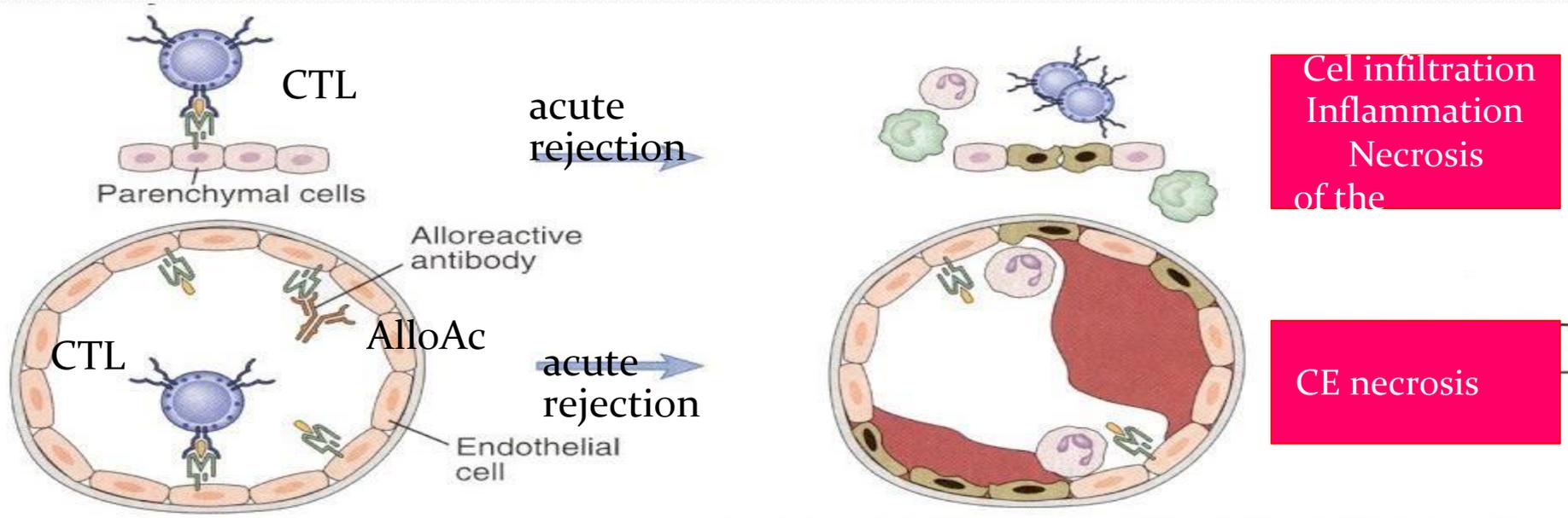
The clinical aspects vary depending on:

- the degree of tissue compatibility between Donor and Receiver
- the level of immunocompetence of the Receiver

# 1 – Acute rejection

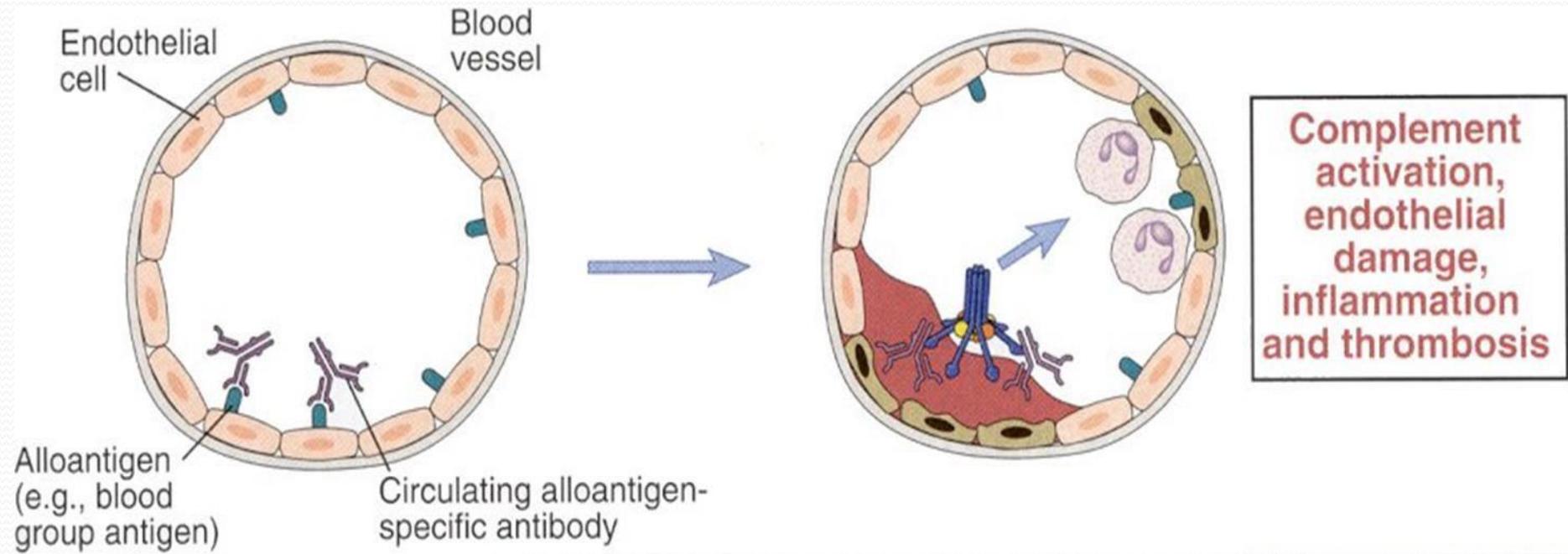
- Within 8 to 15 days of transplantation in the absence of pre-sensitization and Immunosuppression
- Delayed acute rejections, often reversible after treatment in patients treated with IS
- Essential role of LyT in acute rejection

Preferred target: CE of capillaries, venules



## 2 – Superacute rejection

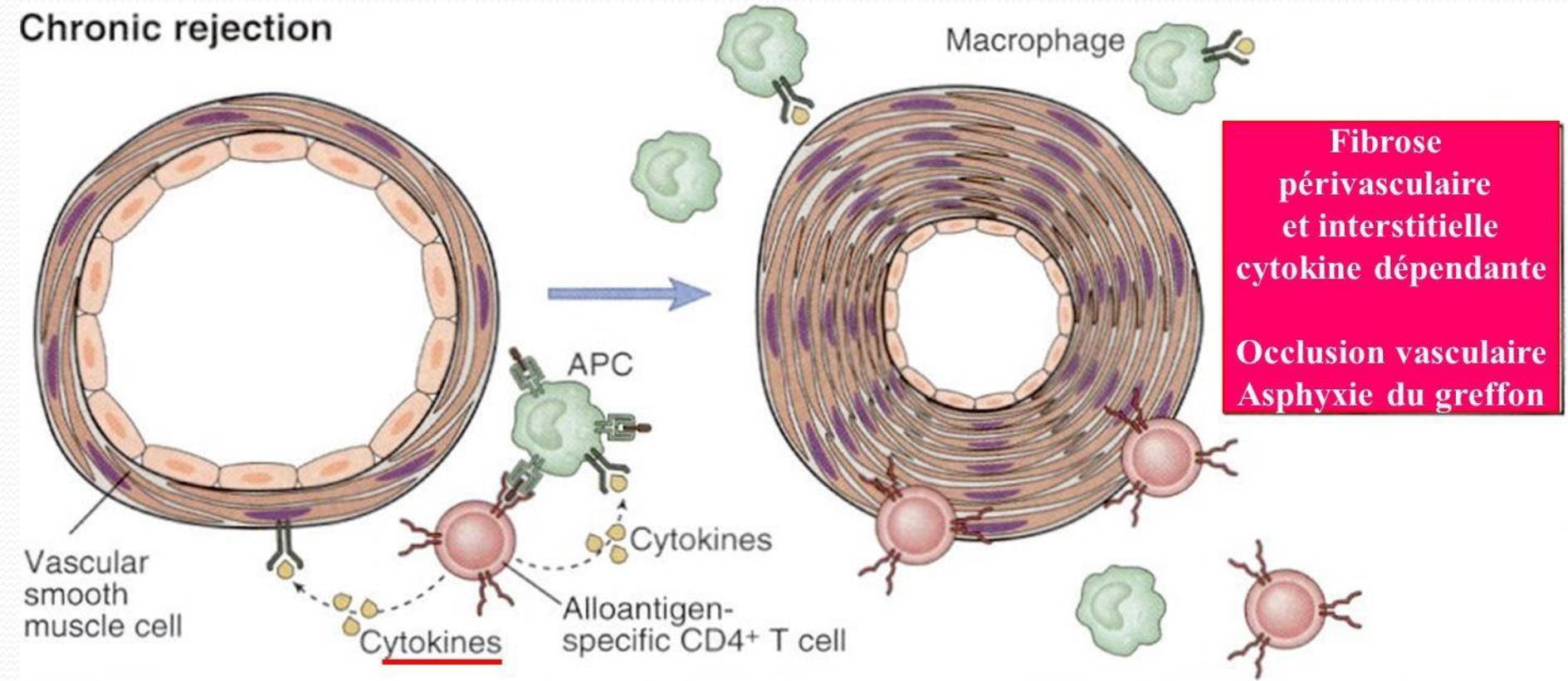
- Early and brutal, within hours of transplantation
- Occurrence in case of pre-sensitization (previous transplant, transfusion, pregnancy)
- Presence of pre-formed anti-HLA antibodies binding to the endothelium and activating the Preferred Target Complement: **CE of capillaries, venules**



### 3 - Chronic rejection

- Long-term loss of graft functional efficiency with fibrosis build-up

Preferred Target: Arterial Wall



# Graft Recognized Antigens

## 1 – Major Histocompatibility Complex antigens: major transplantation antigens

- ❖ Antigens, Class I
- ❖ Class II HLA antigens expressed on presenter cells of occupational antigens
- ❖ Very immunogenic, inducing a strong cell-mediated and humoral response

## 2 – Minor antigens

- ❖ Protein antigens with allelic polymorphisms presented as peptides by the Receiver's HLA molecules
- ❖ Not very immunogenic but cumulative effect, e.g.: Male H-Y Ag on Chr Y

### 3 – Blood group antigens

- ❖ Erythrocyte blood groups: A, B, O
- ❖ Incompatibilities —→ strong humoral response
- ❖ Expressed on the vascular endothelium

## Transplant rejection effector mechanisms

### 1) Allo-antigen presenting cells

Dendritic cells + Monocytes / macrophages + Endothelial cells Express Ag on MHC.I and MHC.II

### 2) The TCD4+ lymphocyte

- ❖ recognizes HLA.II Ag presented by graft APC cells
- ❖ undergoes activation, proliferation and differentiation of anti-HLA TCD4+ Clones.II of donor

### 3) The TCD8+ lymphocyte

- ❖ recognizes HLA.I Ag carried by APC cells and graft target cells
- ❖ its activation is dependent on anti-HLATCD4 +.II

### 4) The B lymphocyte

- ❖ B-cell recognizes HLAI + HLA.II Ag presented by graft APCs
- ❖ its proliferation and differentiation is dependent on anti-HLA.I TCD4+ in Plasmocytes producing anti-HLA.I Ac and anti-HLA.II Ac

### 5) Anti-HLA.I and Anti-HLA.II cytotoxic antibodies

- ❖ C- dependent cytotoxicity and Ac- dependent cytotoxicity (ADCC) of graft target cells
- ❖ Formation of CI and Inflammatory Phenomena

## 6) Cell mediated cytotoxicity

Direct cytotoxicity to cells of the endothelium and parenchyma of the hairplug