

**LECTURE SIX: PATHOLOGY OF RENAL TRANSPLANTATION**

**BY**

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The major barrier to transplantation of organs from one individual to another of the same species (called allografts) is immunological rejection of the transplanted tissue.

The word allograft refers to transplantation of organs within the same species while xenografts refer to transplantation between different species.

Rejection is a complex phenomenon involving both cell and antibody mediated hypersensitivity reactions directed against the histocompatibility molecules on the foreign graft.

The key to successful transplantation has been the development of therapies (drugs) that prevent or minimize rejection.

#### Mechanisms of graft (renal allograft) rejection:

Donor class I and class II major histocompatibility antigens on antigen-presenting cells in the graft (donor) are recognized by host (recipient) CD8<sup>+</sup> and cytotoxic or suppressor T cells and CD4<sup>+</sup> helper T cells respectively. CD4<sup>+</sup> cells proliferate and produce cytokines (like interferon gamma  $\gamma$ ) which induce tissue damage to renal blood vessels and tubules by a local hypersensitivity reaction.

In addition, graft antigens are taken by the antigen presenting cells in the host (recipient). These APC's activate CD4<sup>+</sup> cells which damage the graft (renal transplant) by a local delayed hypersensitivity reaction and stimulate B lymphocytes to produce antibodies.

#### Renal allograft transplant rejections are divided into:

- A] **Hyperacute rejection:** occurs within minutes to a few hours after transplantation in a presensitized host and is typically recognized by the surgeon just after the vascular anastomosis is completed. Grossly, the kidney becomes cyanotic. Microscopically, there is widespread acute arteritis and arteriolitis, vessel thrombosis and ischemic necrosis.
- B] **Acute rejection:** acute rejection may occur within days to weeks of transplantation and sometimes after months or years later. This rejection is divided into:
  - (1) **Cellular rejection:** interstitial oedema and mononuclear (lymphocytic) infiltration of the renal interstitium.
  - (2) **Humoral rejection:** associated with vasculitis.

- C] **Chronic rejection:** patients usually presents late after transplantation (months to years) with a progressive rise in serum creatinine levels. Chronic rejection is dominated by vascular changes, interstitial fibrosis and loss of renal parenchyma. Chronic rejection does not respond to standard immunosuppression treatment.