

This lecture is intended to bridge the gap between the basic sciences and clinical transplantation. By transplantation, I refer primarily to the transplantation of human organs which are designed to retain their function in the new host.

The study of any discipline begins with an understanding of the terms commonly used in the field.

TABLE 1

Grafts are termed isografts, allografts, and xenografts. These are nouns referring to the graft. An isograft is any graft between individuals that are genetically identical. In the human the only isografts are those between identical twins. Such grafts are common in the experimental laboratory which uses many inbred strains of murine species in which all members of each strain are genetically identical. The adjective relating this noun is isogeneic. An allograft is any transplant between members of the same species that are genetically different, while a xenograft is any transplant between different species. Historically allografts were referred to as homografts and xenografts as heterografts. You can see the appropriate adjective. An autograft is a transplant in which tissue is moved from one place to another in the same individual, such as skin autografts.

TABLE 2

Grafts are also often referred to as vital or static depending upon whether or not the graft is expected to retain metabolic activity or not. Static grafts are those grafts such as lyophilized bone or blood vessels which are expected to act as

struts or conduits, but are not alive. Orthotopic or heterotopic refer to whether or not the graft is anatomically placed in its normal position. For example, most liver transplants are precisely described as orthotopic vital allografts, kidney transplants are heterotopic vital allografts, while transplantation of bone would most commonly be a heterotopic static allograft.

In the natural course of events, isografts and autografts are of course not recognized as foreign by the host and are simply treated by the host as any other genetically identical material. The only abnormality of function might relate to the absence of nerve supply or the fact that the structure is not being used for its original intent, such as in a colon interposition to replace the esophagus which is a heterotopic vital autograft.

TABLE 3

Allografts under ordinary circumstances will function normally for a period of 7-10 days when a process of fairly rapid destruction occurs, which if unmodified, will be completed within 3-5 days. Function will go from normal to none over a period of days. There are some exceptions to this behavior. The natural course of xenografts, however, is hyperacute rejection. Immediately after implantation the graft will vascularize and look normal but coagulation will occur, complement will be activated and blood flow will cease within minutes to hours. These are two forms of rejection.

Rejection may be considered the process by which the host destroys the foreign material contained within the transplant.

TABLE 4

Rejection may be defined in many ways, but the most common and time-honored way of referring to rejection is by the clinical course that the graft follows. This slide shows rejection as being divided into hyperacute, acute and chronic. These are clinical syndromes which usually occur within specified time intervals. Hyperacute rejection usually begins within minutes to hours after implantation and the graft is destroyed within 24 hours. The etiology of this rejection is that of a B-cell humoral response which occurs as a consequence of either natural immunization in the case of xenografts or prior sensitization in the case of allografts. Prior sensitization may occur through immunization of the female by the paternal genetic components of the fetus. It may be acquired by infusion of leukocytes along with blood transfusions, and it be acquired by the rejection of previous transplants.

Acute rejection is the normal response which occurs when an individual is presented with a new graft to which they have had no previous exposure. In general, the earlier the onset of acute rejection the more severe the genetic disparity between donor and recipient and the more difficult the rejection will be to control. The response is a T-cell cellular response which involves specific cytotoxicity and is a part of the delayed hypersensitivity cellular immune mechanism. Under ordinary circumstances, acute allogeneic rejection occurs within 7-21 days after implantation and in the unmodified or untreated patient is completed within 3-4 days.

Table 1

| | <u>Noun</u> | <u>Adjective</u> | <u>Old Term</u> |
|---------------|-------------|------------------|-----------------|
| Terminology - | Isograft | Isogenic | |
| | Allograft | Allogenic | Homograft |
| | Xenograft | Xenogenic | Heterograft |
| | Autograft | Autogenous | |

Table 2

Grafts

- Vital
- Static
- Orthotopic
- Heterotopic

Table 3

Natural Course of Transplants

| | | |
|-------------------|----------|-----------------------------|
| Isografts | : | Acceptance |
| Allografts | : | Acute rejection |
| Xenografts | : | Hyperacute rejection |
| Autografts | : | Acceptance |

Table 4

| <u>Rejection</u> | <u>Time of Onset</u> | <u>Response</u> |
|-------------------------|-----------------------------|-------------------------|
| Hyperacute | 0-24 hours | B-cell-humoral |
| Acute | 7-21 days | T-cell-cellular |
| Chronic | >3 months | humoral/cellular |