INTRODUCTION AND AIM OF THE WORK

Graft rejection continues to be a major problem in kidney transplantation despite steady improvements in induction therapy, post transplant patient management and immune monitoring . The average rate of kidney graft survival at the transplantation division of the University Of Tennessee was about 94%,however, many of these patients still experienced rejection episodes .

The presence in potential kidney recipient serum of preformed antibodies to donor cells can lead to early graft rejection . Many factors such as complement-dependent cytotoxicity, target cell , immunoglobulin class and titer affect the clinical relevance of these antibodies to long term graft survival. Pretransplant crossmatching has for years been done by serological methods based on complement-dependent cytotoxicity . A positive result between recipient serum and donor T cells is considered a contraindication to transplantation. However , some grafts continue to be lost to early rejection which may be caused by levels of preformed anti-donor antibodies undetectable by conventional means or which are directed to target cell populations other than T lymphocytes.

The development of flow cytometry crossmatching has allowed for greatly enhanced test sensitivity and specificity. By selecting various target cell populations with fluorescent tagged monoclonal antibodies and then using a developing antibody conjugated to a different fluorochrome, it is possible to accurately assess the nature and strength of recipient anti-donor antibodies by histogram analysis.

Our immune monitoring program has include retrospective flow cytometric crossmatching using T and B lymphocytes as well as monocytes as

donor cell targets. One of the goals of our flow cytometry crossmatch program is to establish the negative and clinically relevant positive median fluorescent channel shift ranges in the context of our pre- and post transplant immunosuppressive regimen. In addition,recent evidence indicates that initially negative crossmatches to T-cells became positive in recipients followed longitudinally posttransplantation. Those recipients with initially negative /repeat positive crossmatches developed acute rejection episodes and had poorer graft outcome than those recipients with continued negative anti-donor crossmatches . This interesting relationship with post transplant repeat crossmatching has not been documented in endothelial cell crossmatching and is probably the most important of the specific aims of this project.

The objective of this study is to determine the significance of anti-endothelial sensitization as a determinant of post transplant outcome and to develop monitoring techniques based on anti-endothelial antibody detection which will allow for early predicton of renal graft rejection episodes. Also to relate these findings to the postrevascularization biopsies of cadaveric kidney in order to improve the clinical graft outcome.