**Donor & Recipient Screening to Reduce the Risk of Infections Post-Transplant**

Screening of donors and recipients for latent infections can allow for optimized donor utilization and post-transplant interventions to reduce the impact of the infection. Although there are OPTN policies and recommendations to screen donors and recipients for endemic infections such as strongyloidiasis and Chagas disease that occur in underdeveloped regions of the world, there is limited data on the yield and challenges of such screening practices. An ongoing retrospective epidemiologic study is describing the yield and post-transplant outcomes of our foreign born screening algorithm and comprehensive QuantiferonTB screening program. Likewise, there has been significant controversy over the optimal use of nucleic acid testing (NAT) in addition to serology to screen both live and deceased organ donors. The prevailing literature hypothesizes that there will be a significant number of organs lost because of false positive NAT results without a significant reduction in the frequency of disease transmissions through transplantation. Since the transplant programs in NY state were the first to adopt repeat testing with NAT of all live donors, Drs. Ison and Echenique conducted a survey and documented that such repeat testing was feasible and resulted in few delays and no cancellations of planned transplants. Likewise, Drs. Ison & Theodoropoulos collected national data on the yield of NAT screening of deceased donors. From this survey, we identified 10 donors with possible false positive results; this was counterbalanced by 126 donors with either false positive serologic results or cleared prior infection that were only detected by the use of NAT. In a separate study, we were able to demonstrate that NAT is generally available at most OPOs in the United States. A collaborative study between the NU CTC and our local organ procurement organization (Gift of Hope) has also identified an improved process for screening deceased organ donors for syphilis.

**Epidemiology Studies of Post-Transplant Infections**

The Northwestern Transplant Infectious Diseases group has a number of studies focused on defining the epidemiology and outcomes of a range of infectious diseases affecting transplant recipients. Perhaps the most important component of this research is our participation, spearheaded by Dr. Stosor, in the NIH-funded Solid Organ Transplantation in HIV: Multisite Study. This prospective observational study of liver and kidney HIV-seropositive recipients has demonstrated feasibility of organ transplantation for HIV-infected patients with end-stage organ disease. Based on the findings and outcomes of this study, the investigators are planning future studies aimed at reducing rejection rates in renal allograft recipients, improving outcomes in HIV-hepatitis C co-infected patients after liver transplantation, and strategies for optimizing antiretroviral and immunosuppressive therapy while minimizing complicated drug interactions between these drugs.

Dr. Stosor has also collaborated in the NIH-supported *Cryptococcus neoformans* Infection in Organ Transplant Recipients: Impact of Immunosuppressive Agent Resistance and Virulence Factors on Tissue Tropism and Outcome. The findings generated by this study are reported in numerous publications and have been instrumental in defining the epidemiology and outcomes of cryptococcosis in organ recipients and led to specific treatment recommendations for transplant patients with this infection. More recently, Drs. Stosor, Angarone and Penugonda have continued to study cryptococcosis in patients with advanced liver disease.

In collaboration with the CTC Bioinformatics Core, the group has been researching the epidemiology and outcomes of a range of infections affecting the transplant populations. One large project has been focusing on the safety and efficacy of valganciclovir prophylaxis for CMV. The group is increasingly using the tools available through the CTC Bioinformatics Core to define the epidemiology and outcomes of early nosocomial infections following SOT, the epidemiology and outcomes of BK virus nephropathy, norovirus infections in SOT recipients, and endemic fungal infections, such as histoplasmosis and blastomycosis, following SOT in addition to the efficacy of various therapies to treat BK virus nephropathy. Two separate collaborations, one with ViraCor-IBT Laboratories, Inc and another with the University of Alberta, allowed us to study the epidemiology of CMV in our SOT population and to study host responses to CMV to predict which patients are more likely to develop CMV post-transplant and which patients are more likely to have a recurrent infection after antiviral therapy is discontinued.

Lastly, the group is getting ready to launch a collaborative epidemiology study with Johns Hopkins University, the Cleveland Clinic and the University of Washington. This collaborative study is the first of its kind to prospectively collect data and laboratory samples of transplant recipients to understand the epidemiology and outcomes of infections in the era of modern immunosuppression and antiretroviral prophylaxis. The availability of additional specimens, which will be stored in the CTC Biobank, collected in patients who develop CMV and BK virus infections will facilitate future studies to identify novel markers for identify risk and outcomes of these infections.

**Clinical Trials of Novel Antimicrobial Agents**

Lastly, the group is engaged in ongoing studies to advance the development of novel antimicrobials to prevent and treat infections following transplantation in collaboration with the CTC Clinical Research Support Core. In the past, we have participated in studies of oseltamivir to prevent influenza and maribavir to prevent CMV in the SOT population. We have studies ongoing or starting in the near future to assess maribavir to treat ganciclovir-resistant CMV, nitazoxanide for the treatment of norovirus, CMX001 to prevent CMV in the HSCT population, and novel vaccines to reduce the risk of CMV post-transplant.