Introduction

- Since it was first recognized, the human immunodeficiency virus (HIV) has rapidly spread to all corners of the globe.
- End-stage organ dysfunction has become an increasingly common problem in this growing patient population.
- Early attempts at solid-organ transplantation in HIV+ patients were plagued with complications and yielded disappointing results.
- With the development and broad implementation of highly active anti-retroviral therapy (HAART), a dramatic decrease in the morbidity and mortality associated with HIV has been observed.
- This has spawned new interest in solid-organ transplantation in HIV+ patients and also yielded improved results.
The HIV Pandemic
The first description of patients in the United States with what is now recognized as the Acquired Immunodeficiency Syndrome (AIDS) was reported in 1981.

This report described a series of 5 homosexual men with *Pneumocystis carinii* pneumonia (PCP) and other unusual opportunistic infections.

In the following months, several more cases of PCP and Kaposi’s sarcoma were reported in California and New York.

In May 1983, a novel retrovirus was isolated from a patient with AIDS and was eventually implicated in the pathogenesis of the disease.

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The HIV Pandemic

- Since the 1980’s, HIV has spread across the world at an alarming rate.
- The United Nations Joint Program on HIV/AIDS (UNAIDS), estimates that there were 40 million people living with HIV as of 2004 with an incidence of roughly 5 million new cases per year\(^5\).
- 14,000 new HIV infections occur daily across the world.
- Almost 2,000 of these are in children under the age of 15.
- There were approximately 3.1 million deaths related to AIDS in 2004.

Should All HIV-infected Patients With ESRD Be Excluded From Renal Transplantation?

*TRANSPLANTATION, 65:1187, 1998*

**VIEWS OF U.S. TRANSPLANT CENTERS**

- Transplant Center Response Rate: 149/248 (60%)
- Is HIV testing required for prospective recipients? YES 100%
- Would a patient who refuses HIV testing be considered for transplantation? YES 12% NO 84% UNSURE 4%
- Would an HIV-infected ESRD patient be considered for deceased-donor transplantation? YES 9% NO 91% UNSURE 3%
The Impact of Highly Active Antiretroviral Therapy (HAART)
Highly Active Antiretroviral Therapy (HAART)

- The management of patients with HIV was profoundly changed with the development of HAART.
- Three classes of drugs are commonly used to treat HIV infection:
  - Nucleoside reverse-transcriptase inhibitors (NRTI)
  - Non-nucleoside reverse-transcriptase inhibitors (NNRTI)
  - Protease Inhibitors (PI)
- HAART regimens usually consist of 3 (or more) drugs from these classes.
- Although they may vary, regimens usually include a PI or an NNRTI with two NRTIs.
HAART has improved survival of patients with HIV

- Mortality of patients with HIV has decreased with the increasing use of combination antiretroviral therapy including protease inhibitors.

HAART has decreased infectious complications in patients with HIV

- The incidence of opportunistic infections also decreased with increasing use of combination anti-retroviral therapy\(^6\)

Renal Transplantation in HIV+ Recipients
HIV and End-Stage Renal Disease

- 40 million people are infected with HIV worldwide
- 5 million new cases were reported in 2003
- Survival of patients with HIV on HD is poor
- Age adjusted data suggest that ESRD patients with HIV have a 97% higher risk of death than HIV-negative patients with ESRD
- HIV-associated nephropathy has become an important cause of ESRD

Outcomes Prior to HAART

- Several cases of renal transplantation were reported in the literature prior to the development of HAART.
- In some instances, HIV infection occurred in the perioperative period.
- Others were HIV+ at the time of transplant.
In 1990, Tzakis and colleagues at the University of Pittsburgh reported a series of 25 HIV+ recipients of solid organ transplants. 8 of these patients were kidney transplant recipients. Three of the 5 kidney patients in this study were HIV+ at the time of transplant. With a mean follow-up of 3.4 ± 2.2 years, 4 out of 5 patients were alive. One patient died of generalized tuberculosis 5 months after transplantation. Two of these 5 patients survived 5 or more years after transplantation.

Outcomes Prior to HAART

- A number of cases of both living-donor and deceased-donor transplants were reported in HIV+ recipients in the following years with variable results\(^9,10\)
- Swanson and colleagues performed a large historical cohort analysis of the United States Renal Data System (USRDS) involving 63,210 recipients of deceased-donor renal transplants\(^11\)
- Despite having better HLA matching and younger donors, 3-year patient and graft survival were reduced in HIV+ versus HIV- recipients (83% vs. 88% patient and 53% vs. 73% graft survival, respectively)

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Recently, there has been renewed interest in renal transplantation in HIV+ patients, prompted by several factors:

- The increasing prevalence of HIV disease
- The increasing frequency of ESRD in patients with HIV
- The decrease in morbidity and mortality in patients with HIV that has occurred with the widespread implementation of HAART
Renal Transplantation in the HAART Era

- At University of California San Francisco, a pilot trial was conducted to evaluate the safety and efficacy of liver and kidney transplantation in HIV+ patients\(^\text{12}\).
- Mean follow-up: 480 days
- Induction therapy was not used
- Maintenance immunosuppression consisted of cyclosporine and mycophenolate mofetil
- Ten patients received renal transplants:
  - 4 living donor
  - 6 deceased donor, some with high-risk factors

Renal Transplantation in the HAART Era

- Patient and graft survival was 100%
- Rejection occurred in 50% of renal transplant recipients
- 3 of the 5 patients that experienced rejection received Thymoglobulin to treat vascular rejection
- CD4 counts dropped transiently in all 10 patients, but soon returned to normal levels
- In patients that received Thymoglobulin, CD4 counts dropped below 220 cells/mm$^3$ and were slow to recover
- No AIDS-defining infections occurred in this series
- One patient developed *S. aureus* endocarditis and another developed *Pseudomonas* pneumonia and sepsis
- There were also 2 cases of *S. Aureus* wound infection and one case of influenza B pneumonia
Kumar and colleagues have conducted one of the largest trials of renal transplantation in HIV+ patients to date. 40 patients with HIV underwent renal transplantation, including 4 received living donor transplants and 36 deceased donor transplants. 8 donors had a history of drug abuse, 3 had a history of alternative lifestyle, and 8 were expanded criteria donors. 39 of the 40 recipients were African American. Basiliximab induction therapy was employed. Maintenance immunosuppression consisted of cyclosporine, sirolimus, and steroids.

Renal Transplantation in the HAART Era

- Patient survival at 1 and 2 years: 85% and 82%, respectively
- Graft survival at 1 and 2 years: 75% and 71%
- Viral loads remained undetectable
- CD4 counts remained > 400 cells/µL
- No AIDS-defining illnesses occurred
- 25% of patients experienced acute rejection
At the University of Pittsburgh Medical Center (UPMC), we have identified several barriers that present special problems for transplantation in HIV+ recipients, including:

- Scarcity of donor organs
- Immunosuppression

To overcome these barriers, we have employed two key strategies:

- Laparoscopic live-donor nephrectomy (LLDN)
- Antibody preconditioning with minimal posttransplant immunosuppression
Minimal Posttransplant Immunosuppression

- Recipient pretreatment with lymphocyte depleting agents followed by minimal posttransplant immunosuppression permits weaning of immunosuppressive agents\textsuperscript{16-18}

- Alemtuzumab (Campath-1H)
  - Humanized anti-CD52 monoclonal antibody
  - Excellent early outcomes
  - Lower incidence of acute rejection\textsuperscript{17,18}

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8 consecutive cases between 1998 and the present\textsuperscript{19,20}
- 4 deceased-donor cases
- 4 living-related donor cases
- All recipients had CD4 counts > 200
- All recipients had undetectable viral loads

Renal Transplantation in Patients with HIV at UPMC During the HAART Era

- **Immunosuppression:**
  - **Deceased-donor recipient:**
    - Current practice utilizing a tacrolimus-based regimen without antibody induction
  - **Living-related recipient:**
    - Pretreatment with alemtuzumab 30 mg IV, premedicated with 1 g methylprednisolone, followed by 1 g methylprednisolone prior to reperfusion
    - Tacrolimus monotherapy, starting with BID dosing, to achieve levels of 10 ng/ml
<table>
<thead>
<tr>
<th>Recipient</th>
<th>Age</th>
<th>Race</th>
<th>Indication</th>
<th>Maintenance</th>
<th>Cr (lowest)</th>
<th>Cr (most recent)</th>
<th>Anti-retrovirals</th>
<th>CD4 Pre Tx</th>
<th>CD4 Post Tx</th>
<th>Viral load Copies/ml</th>
<th>Complications</th>
<th>Follow up months</th>
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<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>C</td>
<td>PKD</td>
<td>Tacrolimus mycophenolate prednisone</td>
<td>1.6</td>
<td>4.0</td>
<td>lamivudine, stavudine nevirapine</td>
<td>&gt; 500</td>
<td>482</td>
<td>&lt; 50</td>
<td>Delayed graft function, Periallograft hematoma following biopsy, ACR, plantar fasciitis, cellulitis</td>
<td>39</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>AA</td>
<td>HTN, DM</td>
<td>Tacrolimus prednisone mycophenolate</td>
<td>1.7</td>
<td>5.6</td>
<td>lamivudine, zidovudine abacavir</td>
<td>1054</td>
<td>172</td>
<td>&lt; 50</td>
<td>Delayed graft function, multiple episodes of ACR, chronic allograft nephropathy, dialysis dependent</td>
<td>51</td>
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<tr>
<td>3</td>
<td>32</td>
<td>AA</td>
<td>HTN, HIVAN</td>
<td>Tacrolimus sirolimus prednisone</td>
<td>1.3</td>
<td>9.2</td>
<td>lamivudine, zidovudine efavirenz</td>
<td>391</td>
<td>98</td>
<td>5774</td>
<td>Multiple episodes of ACR, severe chronic rejection, dialysis dependent</td>
<td>39</td>
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<tr>
<td>4</td>
<td>46</td>
<td>C</td>
<td>PKD</td>
<td>Tacrolimus</td>
<td>1.3</td>
<td>1.5</td>
<td>nevirapine, lamivudine stavudine</td>
<td>411</td>
<td>944</td>
<td>&lt; 50</td>
<td>Basal cell carcinoma, s/p excision</td>
<td>69</td>
</tr>
</tbody>
</table>

- Mean follow-up: 49 ± 14 months
- Mean age: 45 ± 11 years (range 32-58)
- Only 1 patient continues to have good graft function
- Three patients experienced decreased CD4 counts
- One patient experienced an increased viral load
- Three patients experienced at least one episode of acute rejection
## Living-Related Donor HIV+ Renal Transplant Recipients at UPMC

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Age</th>
<th>Race</th>
<th>Sex</th>
<th>Indication</th>
<th>Maintenance</th>
<th>FK506 level (mg/dL)</th>
<th>Cr</th>
<th>Anti-retrovirals</th>
<th>CD4 Pre-Tx</th>
<th>CD4 Post-Tx</th>
<th>Complications</th>
<th>Duration of follow-up (days)</th>
<th>HLA</th>
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<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>C</td>
<td>M</td>
<td>DM</td>
<td>FK506 0.05 mg PO qod</td>
<td>7.7</td>
<td>1.7</td>
<td>lamivudine, lopinavir/ritonavir, abacavir, efavirenz</td>
<td>692</td>
<td>230/44</td>
<td>Tacrolimus toxicity by bx</td>
<td>620</td>
<td>A2,3, B8,27, DR16,17</td>
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<td>2</td>
<td>40</td>
<td>AA</td>
<td>F</td>
<td>HTN</td>
<td>FK506 16 mg PO qod</td>
<td>4.0</td>
<td>0.9</td>
<td>lamivudine, zidovudine, efavirenz</td>
<td>304</td>
<td>155</td>
<td></td>
<td>557</td>
<td>A30,36, B18,35, DR1,11</td>
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<tr>
<td>3</td>
<td>58</td>
<td>C</td>
<td>M</td>
<td>Reflux nephropathy</td>
<td>FK506 4 mg PO qod</td>
<td>&lt; 1</td>
<td>1.8</td>
<td>lamivudine, zidovudine, efavirenz</td>
<td>1843</td>
<td>110</td>
<td>Tacrolimus toxicity by bx</td>
<td>447</td>
<td>A2,3, B8, DR1,17</td>
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<tr>
<td>4</td>
<td>37</td>
<td>C</td>
<td>M</td>
<td>ADPKD</td>
<td>FK506 5 mg PO qod</td>
<td>8.6</td>
<td>1.0</td>
<td>Lamivudine, Zidovudine, Efavirenz</td>
<td>713</td>
<td>164</td>
<td></td>
<td>188</td>
<td>A24,31 B8,65 DR1,17</td>
</tr>
</tbody>
</table>

- Mean follow up: 453 ± 191 days
- Mean age: 45 ± 9 years (range 37-58)
- Patient and graft survival: 100%
- Mean creatinine: 1.4 ± 0.5 mg/dl
- HIV viral loads have remained undetectable
- CD4 counts are recovering
- No opportunistic infections
- No episodes of graft rejection have been observed
- Two patients developed tacrolimus toxicity
  *This patient subsequently underwent PAK
Campath Pretreatment
38 y.o. Live Donor Kidney Graft

Immunosuppression

- Tac. qod
- Tac. qd
- Tac. bid
- Tac. Level

Graft Function

- Creatinine

Biopsy and Additional Treatment

- Steroid PO
- Biopsy
- Steroid Bolus

Steroid Dose mg

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<th>Dose mg</th>
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<th>100</th>
<th>10</th>
<th>1</th>
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<tr>
<td>Date</td>
<td>11/03</td>
<td>5/04</td>
<td>11/04</td>
<td>5/05</td>
</tr>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Campath Pretreatment
Pancreas after Live Donor Kidney

**Immunosuppression**
- Tac. Dose
- Tac. Level

**Graft Function**
- Creatinine
- Lipase

**Biopsy and Additional Treatment**
- Steroid PO
- Biopsy
- Pancreas TX
- Campath
- Steroid Bolus
Renal Transplantation in Patients with HIV at UPMC During the HAART Era

- Our data demonstrate that LLDN is an effective means of providing organs for patients with ESRD who are infected with HIV.
- An immunosuppressive regimen involving recipient preconditioning with alemtuzumab followed by low-dose tacrolimus monotherapy appears to be safe and effective for preventing graft rejection in patients with HIV.
- Long-term follow-up is required.
Renal Transplantation in the HAART Era

- Taken together, these recent trials have demonstrated promise for renal transplantation in HIV+ patients.
- A number of areas clearly require further investigation:
  - Immunosuppression
  - Anti-retroviral therapy
  - Antimicrobial prophylaxis
  - Recipient/graft immune interactions
  - Mechanisms of graft rejection
Liver Transplantation in HIV+ Recipients
HIV and End-Stage Liver Disease

- Along with ESRD, end-stage liver disease (ESLD) has also become an increasingly pressing problem in patients with HIV.
- Co-infection with hepatitis C (HCV) and HIV is frequent.
- Hepatitis B (HBV) and HIV co-infection is not uncommon.
- Progression to ESLD appears to be accelerated in patients that are co-infected with HIV.
- ESLD has become a leading cause of death in patients with HIV.

22. Ragni MV, Belle SH. Impact of human immunodeficiency virus infection on progression to end-stage liver disease in individuals with hemophilia and hepatitis C virus infection. J Infect Dis. 2001 Apr 1;183(7):1112-5.
Liver Transplantation Prior to HAART

Prior to the development of HAART, there were several cases of liver transplantation performed in HIV+ patients (see reference 24 for an excellent review).

In general, these early trials were plagued with multiple infectious complications and overall poor results, but some HIV+ recipients maintained good graft function for long periods of time.

Reference:
One of the largest early experiences was described by Tzakis and colleagues from the University of Pittsburgh\(^8\). The report described 25 solid-organ transplant recipients between 1981 and 1988 with an overall mean follow-up of 2.75 years. 15 of the patients were liver transplant recipients. Survival was 7/15 (47%). Four of the liver recipients died of AIDS-related complications. CMV and PCP were among the infectious causes of death. Other causes of death in this report included immunoblastic sarcoma, pneumonitis of unknown cause, and 1 case of hepatic artery thrombosis.

In 1991, Erice and colleagues reported a series of 5 cases of HIV+ organ recipients from the University of Minnesota and performed a review of the literature.

In the review, 12 recipients of liver transplants that were HIV negative prior to transplantation were described.

Mean follow-up for this group was 36.8 months (range: 1.6-78).

Four patients (33%) in this group died at a mean of 17.6 months posttransplant.

Two of the deaths occurred secondary to HIV-related diseases.

Progression to AIDS occurred in 3 (25%) of patients.

Liver Transplantation Prior to HAART

- Erice et al. also described 10 patients that were known to be HIV+ prior to receiving a liver transplant\(^9\).
- Mean follow-up in this cohort was 19 months (range: 0-68 months).
- Progression to AIDS occurred in 4 patients (40%) after a mean time of 19.2 months posttransplant.
- 9 patients (90%) died after a mean period of 14.2 months.
- Of these, 4 patients had developed AIDS.
- Sepsis, aspiration, drug toxicity, and hemorrhage were among the causes of death in patients who died of causes unrelated to HIV.

Liver Transplantation in the HAART Era

- The overall poor outcomes in trials of liver transplantation in the pre-HAART era led many centers to consider HIV infection a contraindication to liver transplantation.

- However, after the improvements in survival and morbidity that followed widespread use of HAART therapy, renewed interest in liver transplantation developed.
Liver Transplantation in the HAART Era

- One of the largest reports of liver transplantation in HIV+ patients in the HAART era involves a multicenter experience (Pittsburgh, Miami, San Francisco, and others) with 24 patients\(^{25}\)
- Median follow-up was 17 months
- 15 of the patients were HCV+, 7 had HBV, and 3 patients suffered from fulminant hepatic failure
- Survival after 12, 24, and 36 months was 87.1%, 72.8%, and 72.8%, respectively
- This was similar to that of age- and race-comparable HIV- recipients
- Survival was poorer in patients with post-OLTx anti-retroviral therapy (ART) intolerance, CD4 count < 200 cells/µl, viral load > 400 copies/ml, and HCV infection

Liver Transplantation in the HAART Era

- 1 patient died of an invasive fungal infection
- 5 patients died due to ESLD
  - Due to hepatotoxicity and ART intolerance: 3
  - Complicated by HCV infection: 3
  - Complicated by rejection: 2
  - Other complications: 3

- 12 patients (50%) experienced rejection
  - 10 patients had acute rejection
  - 2 patients had chronic rejection

- Median CD4 count at follow-up: 281 cells/µl
- Median HIV load at follow-up: <400 copies/ml
Liver Transplantation in the HAART Era

- In a recent pilot study by Stock and colleagues from San Francisco, a series of 4 liver transplants in HIV+ patients was reported\(^{12}\).
- Mean follow-up was 380 days.
- Immunosuppression consisted of cyclosporine, mycophenolate mofetil, and prednisone.
- 3 patients were alive at follow-up.
- One patient died from recurrent HCV at 480 days post-transplant.
- While the rejection rate was high in their kidney transplant cohort, no rejection was observed in the liver recipients.
- Viral loads remained undetectable and CD4 cell counts remained stable.

Liver Transplantation in the HAART Era

- The largest reported single center experience with liver transplantation in HIV+ patients comes from the University of Pittsburgh.\(^\text{26}\)
- Since 1997, 29 patients with HIV and ESLD have received a liver transplant.
- Mean follow-up was 18 months (range 1-69 months).
- Indications for transplant were as follows:
  - HCV: 89%
  - HBV: 7%
  - Fulminant liver failure: 4%
- Overall survival: 69%
- 1 year survival: 76%
- Of those that survived more than 30 days post-transplant, 1-year survival was 89% and overall survival was 77%.

Liver Transplantation in the HAART Era

- Recurrent HCV was the cause of death in 4 patients
- Three early deaths (within 30 days of transplant) occurred:
  - Sepsis (2)
  - Accelerated humoral rejection (1)
- In all cases, liver transplantation reversed the stigmata of liver failure in the recipients
## Reported Worldwide Experience with Liver Transplantation in HIV Patients in the HAART Era to 2004

<table>
<thead>
<tr>
<th>Center</th>
<th>Year</th>
<th>Number</th>
<th>% HCV</th>
<th>% Surviving</th>
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<tbody>
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<td>King’s College</td>
<td>1996</td>
<td>1</td>
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<td>100%</td>
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<td>Milan</td>
<td>1998</td>
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<tr>
<td>Pittsburgh</td>
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<td>100%</td>
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<td>1</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Sweden</td>
<td>2000</td>
<td>1</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Bonn</td>
<td>2000</td>
<td>1</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>King's College</td>
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<td>5</td>
<td>60%</td>
<td>40%</td>
</tr>
<tr>
<td>Birmingham</td>
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<td>100%</td>
<td>100%</td>
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<td>Japan</td>
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<td>1</td>
<td>100%</td>
<td>100%</td>
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<tr>
<td>Barcelona</td>
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<td>NA</td>
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<td>2004</td>
<td>1</td>
<td>100%</td>
<td>100%</td>
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</table>

**Total Number** 51  
68%  
80%  

US - 21 patients  
Europe - 27 patients  
Asia - 2 patients
Liver Transplantation in the HAART Era

- Together, these recent trials of liver transplantation in HIV+ patients are encouraging.
- While further studies are required, these data suggest that liver transplantation is a viable option for the management of ESLD in patients with HIV.
- To improve patient and graft survival, a number of areas will require further investigation, including:
  - Optimal immunosuppressive strategies
  - Antiretroviral management
  - Prevention and management of HCV
## Participating Centers

(visit the study website for updated lists of centers and contact information)

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<thead>
<tr>
<th>City</th>
<th>Institution</th>
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<tbody>
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<td>Atlanta</td>
<td>Emory University (K)</td>
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<tr>
<td>Baltimore</td>
<td>University of Maryland (K)</td>
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<td>Boston</td>
<td>Beth Israel Deaconess Medical Center (K, L)</td>
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<td>Charlottesville</td>
<td>University of Virginia (K, L)</td>
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<td>Chicago</td>
<td>University of Chicago (K, L, Peds K, Peds L)</td>
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<td>Rush University (K, L)</td>
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</table>
Immunosuppression in HIV+ Recipients of Solid Organ Transplants
The optimal strategy for the management of immunosuppressants in HIV+ solid-organ transplant recipients has yet to be determined. Several unique aspects must be considered, including:

- An unusually high rejection rate in this patient population
- A recipient with an already immunocompromised state
- Pharmacokinetic interactions between antiretroviral medications and immunosuppressive drugs
Immunosuppression

- Cyclosporine
  - A molecular interaction between the viral Gag protein and cyclophilin A is thought to be necessary for HIV to propagate itself
  - Cyclosporine has been shown to prevent this interaction in vitro\textsuperscript{27,28}
  - A retrospective review performed prior to the development of HAART indicated that cyclosporine may slow the progression to AIDS in transplant recipients\textsuperscript{9}
  - In a more recent study, cyclosporine was shown to have beneficial effects on CD4 counts in HIV+ patients\textsuperscript{29}
  - Other studies have failed to confirm these benefits\textsuperscript{30}
  - Significant interactions between cyclosporine and protease inhibitors occur

27. Franke EK, Luban J. Inhibition of HIV-1 replication by cyclosporine A or related compounds correlates with the ability to disrupt the Gag-cyclophilin A interaction. Virology. 1996 Aug 1;222(1):279-82.
Immunosuppression

- **Tacrolimus**
  - Protease inhibitors also inhibit metabolism of tacrolimus\(^{31}\)
  - NRTIs and NNRTIs have much less of an effect
  - Some data also suggest that tacrolimus might interfere with the HIV life cycle\(^{32}\)

Immunosuppression

- Mycophenolate Mofetil (MMF)
  - Evidence is accumulating suggesting that MMF might have inhibitory effects on HIV replication through distinct mechanisms:
    - Enhancing the activity of some anti-virals, either synergistically or in an additive fashion\(^{33}\)
    - Depleting the pool of activated CD4+ cells that are susceptible to HIV infection\(^{34}\)
  - Clinical data are conflicting and further studies are required


Sirolimus

- CCR5 is a chemokine co-receptor that is required for propagation of R5 strains of HIV
- Sirolimus is thought to inhibit HIV replication by preventing transcription of CCR5
- It may also directly inhibit transcription of HIV gene products
- Protease inhibitors may also increase sirolimus levels

<table>
<thead>
<tr>
<th>AGENT</th>
<th>TOXICITY</th>
<th>INTERACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Didanosine</td>
<td>GI, neuropathy</td>
<td>Oral ganciclovir, azoles, MMF</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>GI, neuropathy</td>
<td>Bactrim, dapsone, AZA</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Neuropathy, leukopenia, hepatotoxicity</td>
<td>Dapsone, Flagyl</td>
</tr>
<tr>
<td>Zalcitabine</td>
<td>Neuropathy, rash, pancreatitis</td>
<td>CsA, FK506, Bactrim, Flagyl</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Anemia, neutropenia, GI, myopathy</td>
<td>AZA, Bactrim, dapsone, azoles, ganciclovir</td>
</tr>
<tr>
<td>Indinavir</td>
<td>GI, nephrolithiasis</td>
<td>Azole, CsA, FK506, Prozac, Dilantin</td>
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<tr>
<td>Nelfinavir</td>
<td>GI, fatigue</td>
<td>Same</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>GI, asthenia, lipid abnormalities</td>
<td>Same, rapamycin?</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>GI, mouth sores</td>
<td>Same</td>
</tr>
<tr>
<td>Delaviridine</td>
<td>Rash, GI, hepatotoxicity</td>
<td>CsA, FK506, MMF, AZA</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Dizziness, GI, hepatotoxicity, rash</td>
<td>Same</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>GI, rash, hepatotoxicity, fever</td>
<td>Same</td>
</tr>
</tbody>
</table>
Risk to Healthcare Providers

• Average risk of HIV transmission: 0.3%
• Effective prophylaxis with HAART initiated within 2 hours after exposure with 28 day treatment
• Average risk of HCV transmission: 1.8%

VIRUSES DON'T GIVE A F**K ABOUT GLAMOR BOYS.
Public perception on offering transplantation to HIV+ recipients may lead to diminished support for donation

- Public perception will be molded by the willingness of physicians to accept transplantation as a viable modality for treatment of end-stage organ disease in HIV-infected patients. An unprejudiced re-examination of the success of these transplants is warranted.

- “Based on ethical grounds, HIV status should not be considered a contraindication to receiving an organ transplant.” Helpern and Caplan (NEJM, 2002)
Summary

- There has been an explosion in the number of patients with HIV across the globe and end-stage organ dysfunction in these patients has been an increasingly common clinical problem.
- Early trials of solid-organ transplantation in HIV+ patients yielded mixed results.
- With the development and widespread implementation of HAART, there has been a substantial improvement in the morbidity and mortality associated with HIV infection.
- Results of recent trials of both liver and kidney transplantation in HIV+ patients have been encouraging.
- Further investigation is necessary to optimize outcomes in HIV+ patients undergoing transplantation.