Solid Organ Transplantation

Daniel Maluf, MD  
Assistant Professor of Surgery  
VCU School of Medicine

Basic Immunology

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Precursor</th>
<th>Activity (function)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B cell</strong></td>
<td>Lymphoid stem cell (H-7, H-8, H-9)</td>
<td>Plasma cell; immune antibody, humoral immunity. (Total lymphocytes: 25% B cells or 20-40% of WBC)</td>
</tr>
<tr>
<td><strong>T cell</strong></td>
<td>Lymphoid stem cell (H-10)</td>
<td>Thymus cell; cytotoxic T-cells, helper T-cells. (Hand-transplant: altered self-cells; Memory cell: long-term immunity)</td>
</tr>
<tr>
<td><strong>Null cell</strong></td>
<td>Lymphoid stem cell</td>
<td>Natural Killer (NK) cell; anti-tumor and anti-viral cytotoxic activity. (0-20% of lymphocytes in blood)</td>
</tr>
</tbody>
</table>

History of organ transplantation

1954 First successful kidney transplant  
   Dr. Joseph E. Murray, Brigham & Women’s Hospital, Boston, MA

1966 First successful pancreas/kidney transplant  
   Drs. Richard Lillehei, William Kelly, University of Minnesota, Minneapolis, MN

1967 First successful liver transplant  
   Dr. Thomas Starzl, University of Colorado Health Sciences Center, Denver, CO

1968 First isolated pancreas transplant  
   Dr. Richard Lillehei, University of Minnesota, Minneapolis, MN

1968 First successful heart transplant  
   Dr. Norman Shumway, Stanford University Hospital, Stanford, CA

1981 First successful heart-lung transplant  
   Dr. Bruce Reitz, Stanford University Hospital, Stanford, CA

1983 First successful single lung transplant  
   Dr. Joel Cooper, Toronto Lung Transplant Group, Toronto General Hospital, Toronto, Canada

1986 First successful double lung transplant  
   Dr. Joel Cooper, Toronto Lung Transplant Group, Toronto General Hospital, Toronto, Canada

1989 First successful living-related liver transplant  
   Dr. Christoph Broelsch, University of Chicago Medical Center, Chicago, IL

1990 First successful living-related lung transplant  
   Dr. Vaughn A. Stanis, Stanford University Medical Center, Stanford, CA

*Transplant was the first of its kind in the world
Cadaveric Donors, Cadaveric Transplants, and Number on Waiting List

Waiting List Additions 1994-2003: U.S.

Patients waiting for transplantation

Organ Donor and Recovery

Percent of Cadaveric Donors Contributing to Each Organ Type

Source: OPTN data as of 9/5/00; snapshot of OPTN waiting list on the last day of each year.
Recovered and Transplanted Cadaveric Organs

Note: Each liver and pancreas segment is counted as an individual organ in this figure.
Source: OPTN data as of 9/5/00.

Organ Disposition (N=21,213) Cadaveric Donors

Note: Disposition is shown for 21,213 organs which includes liver and pancreas segments.
Source: OPTN data as of 9/5/00.

Need more organs for transplant!!!
Living Donor:

Deceased and Living Donors 1993 - 2003

Using Live-donor Organs: Considerations

Kidney Transplantation

- Outcome superior to cadaveric
- Costs < cadaveric
- Donor psychological benefits
- Donor decision: voluntary

Not Used
9%

Used Research
3%

Transplanted (Shared)
28%

Transplanted (Local)
60%
Kidney Transplantation

- 1997 National Wait Time
  - 1099 days
- 2001 MCVH Wait Time
  - 845 days
- 2001 Length of Stay
  - 7 days

Kidney Transplantation: Etiology

<table>
<thead>
<tr>
<th></th>
<th>Europe</th>
<th>US</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>glomerulonephritis</td>
<td>25</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td>diabetes</td>
<td>12</td>
<td>33</td>
<td>13</td>
</tr>
<tr>
<td>cystic disease</td>
<td>8</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>HTN</td>
<td>10</td>
<td>29</td>
<td>8</td>
</tr>
<tr>
<td>analgesic</td>
<td>2</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>interstitial nephritis</td>
<td>17</td>
<td>?</td>
<td>11</td>
</tr>
<tr>
<td>UNK</td>
<td>2</td>
<td>61</td>
<td>51</td>
</tr>
</tbody>
</table>

Kidney Transplantation: Severity of renal failure

<table>
<thead>
<tr>
<th>GFR (ml/min)</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>30-50</td>
</tr>
<tr>
<td>moderate</td>
<td>10-29</td>
</tr>
<tr>
<td>severe</td>
<td>&lt;10</td>
</tr>
<tr>
<td>end-stage</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

Kidney Transplantation

- Contraindications
  - Active Infection
  - Cancer w/in 5 years
  - Morbid Obesity
  - Active Substance Abuse
  - Severe Coronary Artery or Peripheral Vascular Disease
  - Medical Non-Compliance

Kidney Transplant Operation

- MCV Evaluation: The Listing process
  - history and physical, financial and social support system evaluation
  - blood typing, CXR, EKG, TB, Hep C, Hep B, HIV testing and dental clearance
  - Women must have a pap smear & mammogram
  - Diabetics:VCUG & gallbladder u/s & cardiac clearance
  - Colonoscopy mandatory for age>50
Kidney transplant Operation

**National Data. UNOS.ORG**

<table>
<thead>
<tr>
<th>Blood Type</th>
<th>From Post Transplant</th>
<th># Alive</th>
<th>Survival Rate</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>D</td>
<td>1 Year</td>
<td>17461</td>
<td>65.7</td>
<td>(64.6, 66.8)</td>
</tr>
<tr>
<td>A</td>
<td>1 Year</td>
<td>16796</td>
<td>63.4</td>
<td>(62.1, 64.8)</td>
</tr>
<tr>
<td>B</td>
<td>1 Year</td>
<td>4765</td>
<td>63.7</td>
<td>(62.6, 64.8)</td>
</tr>
<tr>
<td>AB</td>
<td>1 Year</td>
<td>1790</td>
<td>63.8</td>
<td>(62.9, 64.9)</td>
</tr>
<tr>
<td>D</td>
<td>5 Year</td>
<td>37252</td>
<td>68.8</td>
<td>(67.8, 69.7)</td>
</tr>
<tr>
<td>A</td>
<td>5 Year</td>
<td>30383</td>
<td>68.7</td>
<td>(67.6, 69.7)</td>
</tr>
<tr>
<td>B</td>
<td>5 Year</td>
<td>4821</td>
<td>68.7</td>
<td>(67.6, 69.8)</td>
</tr>
<tr>
<td>AB</td>
<td>5 Year</td>
<td>1792</td>
<td>68.7</td>
<td>(67.8, 69.6)</td>
</tr>
<tr>
<td>D</td>
<td>5 Year</td>
<td>13117</td>
<td>66.6</td>
<td>(65.6, 67.6)</td>
</tr>
<tr>
<td>A</td>
<td>5 Year</td>
<td>11560</td>
<td>64.8</td>
<td>(63.8, 65.8)</td>
</tr>
<tr>
<td>B</td>
<td>5 Year</td>
<td>3368</td>
<td>65.2</td>
<td>(64.2, 66.2)</td>
</tr>
<tr>
<td>AB</td>
<td>5 Year</td>
<td>1317</td>
<td>64.8</td>
<td>(63.8, 65.8)</td>
</tr>
</tbody>
</table>

*Kidney Graft Survival One- and Five-Year by Level of HLA Mismatch*

![Graph showing kidney graft survival rates for One-Year and Five-Year by level of HLA mismatch.]

**Renal Transplant Patient Survival VCUHS vs National Average**

![Graph showing renal transplant patient survival comparison between VCUHS and national average.]

**Using Live-donor Organs: Considerations**

- Outcome superior to cadaveric
- Costs < cadaveric
- Donor psychological benefits
- Donor risks: Morbidity, Mortality, Financial—must improvise
- Donor decision voluntary
Living-Donor Liver Transplantation in the U.S.

Kidney Transplantation At VCUHS Living Donor Transplants

Kidney Transplantation: Complication - rejection

Kidney Transplantation: Complication - infection

Post-Transplantation Cancer

Post-Transplantation Cancer (by age)
Incidence of Skin Cancer in Organ Transplant Recipients

- Squamous cell carcinoma – 65-fold
- Squamous cell carcinoma of the lip – 20-fold
- Basal cell carcinoma – 10-fold
- Melanoma – 3.4-fold
- Kaposi’s sarcoma – 8.4-fold
- Other:
  - lung,
  - prostate,
  - colon,
  - PTLD, etc.

Kidney-Pancreas Transplantation

Pancreas Transplantation

- Indications
  - Pancreas alone
    - Retransplant/Graft Failure
    - Diabetes Mellitus – Type I
    - Diabetes Mellitus – Type II Diabetes
      - Chronic Pancreatitis
      - Cystic Fibrosis
    - Pancreas after kidney
    - DM
  - Arterial inflow provided by ‘y graft’
  - Splenic attachment preserved to decrease graft hyperperfusion
  - Spleen is removed and exocrine secretions drained via duodeno-ileostomy or duodeno-cystostomy
Kidney-Pancreas Transplantation

Success rates

<table>
<thead>
<tr>
<th></th>
<th>MCV</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 day</td>
<td>100%</td>
<td>98.4%</td>
</tr>
<tr>
<td>1 year</td>
<td>95.6%</td>
<td>94.5%</td>
</tr>
<tr>
<td>5 years</td>
<td>83.8%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Kidney-Pancreas Transplantation: success rates

<table>
<thead>
<tr>
<th></th>
<th>MCV</th>
<th>National</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 day</td>
<td>Pancreas 90%</td>
<td>Kidney 97.9%</td>
</tr>
<tr>
<td>1 year</td>
<td>Pancreas 82.6%</td>
<td>Kidney 95.7%</td>
</tr>
<tr>
<td>5 years</td>
<td>Pancreas 75.7%</td>
<td>Kidney 90.2%</td>
</tr>
</tbody>
</table>

Kidney-Pancreas Transplantation

- Immunoologic issues
  - ABO incompatibility
  - high PRA
  - African-American descent
  - Hyperacute rejection (preformed antibodies)
  - Accelerated rejection (second set exposure)
  - Acute and chronic rejection
  - Drug toxicity

- Hypertension/pressor agent usage
- Age
- Oliguria

- Preservation issues
  - Prolonged warm ischemia
  - Prolonged cold ischemia
**Kidney-Pancreas Transplantation**

- **Early complications**
  - Vascular thrombosis
    - venous/ arterial
  - Ureteral issues
    - leakage/stenosis
  - Lymphocele
  - Incisional issues

**Kidney-Pancreas Transplantation**

- **Contraindications**
  - Active Infection
  - Cancer w/in 5 years
  - Morbid Obesity/Type II diabetes
  - Active Substance Abuse
  - Severe Coronary Artery or Peripheral Vascular Disease
  - Medical Non-Compliance
  - age >50 years

**Liver Transplantation**

- **Severity, Signs and Symptoms**
  - quality of life issues
    - recurrent cholangitis, intractable ascites or pruritis, severe lethargy or bone disease
  - severe hepatic dysfunction & complications
    - hyperbilirubinemia / jaundice
    - severe coagulopathy
    - marked hypoalbuminemia / ascites
    - variceal hemorrhage
    - spontaneous bacterial peritonitis

**Liver Transplantation**

- **Etiology**
  - Hepatitis C 23%
  - Alcohol 20%
  - Cryptogenic 12%
  - PSC 10%
  - PBC 11%
  - Autoimmune 5%
  - Fulminant failure 5%

**Liver Transplantation**

- **Contraindications**
  - HIV
  - Extrahepatic malignancy
  - Uncontrolled sepsis
  - On going substance abuse
  - Advanced cardiopulmonary disease
  - Severe pulmonary hypertension
  - Noncompliance
Liver Transplantation

- **MCV evaluation**
  - multidisciplinary team assessment
    - surgical (alternative or adjunct procedures)
    - hepatologist (intensive medical management)
    - cardiologist (catheterization/stenting/ P-Thal)
    - pulmonologist (PFT, bubble echo, ABGs)
    - psychologist (organic brain syndromes/dependency)
    - social work (support system analysis)
    - financial (can it be done)

Liver Transplantation

- **Cadaveric liver**
  - National 1997 Wait Time - 439 days
  - MCVH 2000 Wait Time - 178 days
  - Average 2000 Length of Stay - 9 days

Liver Transplantation

- **Success rates**
  - Cadaveric liver patient survivals
    |            | MCV | National |
    |------------|-----|----------|
    | 30 day     | 93.2% | 94%      |
    | 1 year     | 83.8% | 85.6%    |
    | 5 years    | 78.5% | 75.9% (3yr) |

Liver Transplantation

- **Success rates**
  - Cadaveric liver graft survivals
    |            | MCV | National |
    |------------|-----|----------|
    | 30 day     | 89.8% | 90%      |
    | 1 year     | 79.5% | 79.8%    |
    | 5 years    | 73.7% | 68.8% (3yr) |
Liver Transplantation

Liver Transplantation

Liver Transplantation

Liver Transplantation

Liver Transplantation

Liver Transplants by Donor Type
1997-1999

Living Donor Relationship To Recipient
1990, 1995, 1999

Source: Scientific Registry data as of 9/5/00.

Source: OPTN data as of 9/5/00.
Liver Transplantation

- Live donor liver
  - 2000 Wait Time: 108 days
  - Recipient Length of Stay: 10.5 days
  - Donor Length of Stay: 6.5 days

Liver Transplantation

- Live donor liver - Survival 1999-2000
<table>
<thead>
<tr>
<th>Patient</th>
<th>Graft</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 day</td>
<td>95%</td>
</tr>
<tr>
<td>1 year</td>
<td>83%</td>
</tr>
</tbody>
</table>
Liver Transplantation

- Graft loss etiology
  - Sepsis
  - MI
  - CVA
  - Recurrent disease

Liver Transplantation

- Early complications
  - primary graft dysfunction
  - hepatic artery thrombosis
  - bile duct leakage
  - rejection
    - acute cellular
    - chronic
  - infection

Liver Transplant Graft Survival

VCUHS vs National Average

Liver Transplant Patient Survival

VCUHS vs National Average

Source: www.ustransplant.org

Living Donor Liver Transplant At VCUHS Graft Survivals

Living Donor Liver Transplant At VCUHS Patient Survivals

Source: www.ustransplant.org
Solid Organ Transplantation

Daniel Maluf, MD
Assistant Professor of Surgery
VCU School of Medicine