No Greater Gift:
New Ethical Debates in Transplantation

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Bioethics and the Law
November 7, 2008
New Ethical Debates in Transplantation

Objectives:

- Understand relevance of “Dead Donor Rule”
- Discuss ethics of novel approaches to increasing donor pool
- Discuss ethics of “creation of savior siblings”
- Explore ethics of cardiac transplantation via DCD
Brief History of Transplantation

- **1954:** First successful renal transplant
  Boston by Joseph Murray, M.D.
  Identical twin transplant in 23 y.o.
  Survived 8 years, fathered children
- **1962:** Use of immunosuppression for renal transplants:
  corticosteroids
  azathioprine (Imuran)
Brief History of Transplantation

- **1967**: First heart transplant
- **1983**: Immunosuppression: cyclosporine
- **1990s**: Immunosuppression:
  - tacrolimus (Prograf)
  - mycophenolate mofetil (CellCept)
  - sirolimus (Rapamune)
Brief History of Transplantation

Current organs:
- Kidney
- Liver
- Heart
- Lung
- Heart/lung
- Pancreas
- Small intestine
Current Transplant Statistics

Waiting lists (10/2008)
- Kidney: 77,623
- Liver: 16,030
- Heart: 2697
- Lung: 2130
- Pancreas: 1590 (Kidney/pancreas: 2256)
- Intestine: 230

www.optn.org
Organ Donors and Transplantations in the United States, 1988-2006

Current Transplant Statistics

January – July 2008

- Total transplants: 16,385
  - Deceased donor: 12,757
  - Living donor: 3,629

- Total donors: 8,326
  - Deceased donor: 4,698
  - Living donor: 3,628
Current Transplant Statistics

- Over 6000 deaths per year awaiting kidneys
- One-year survival after transplant:
  - Living related kidney: 95%
  - Cadaver kidney: 89%
  - Liver: 73-83%
- 15,000 brain-dead potential donors yearly:
  - Only 35-45% become donors
Current Transplant Statistics

Demand for organs surpasses supply

- Under-utilization of brain-dead donors
- Poor rates of donor “preregistration”
- Lack of acceptance of donation by families
- Under-utilization of live donors
- Under-utilization of “other” dead donors
Federal laws and regulations

- Uniform Anatomical Gift Act (1968)

  Allows individual to make irrevocable gift of organs, body parts, body by documentation prior to death
  Cannot be rescinded by next of kin
  Allows next of kin to make donation in absence of documentation by decedent
Federal laws and regulations

- Uniform Determination of Death Act (1980)

- Oklahoma Statute:

  “An individual who has sustained either: 1) irreversible cessation of circulatory and respiratory functions, or 2) irreversible cessation of all functions of the entire brain, including the brain stem is dead. A determination of death must be made in accordance with accepted medical standards; provided all reasonable attempts to restore spontaneous circulatory or respiratory functions shall first be made, prior to such declaration.”

  (OK Law: Title 63, Section 3122)
Federal laws and regulations

- Established national coordinating organization
- 1986: Organ Procurement and Transplantation Network
  Contracts with UNOS (United Network for Organ Sharing)
  Joins 63 OPOs nationwide
Federal laws and regulations

- Oklahoma OPO (Organ Procurement Organization) is LifeShare of Oklahoma

- Six designated transplant centers in OK:
  - Integris Baptist Medical Center
  - OU Medical Center
  - Children’s Hospital of Oklahoma
  - St Anthony Hospital
  - St. Francis Hospital
  - St. John Medical Center
Federal laws and regulations

OPTN “Final Rule”

- Proposed in 1998
- Finalized in 2000
- Controversy related to national vs. local allocation of organs
- Provides that “organs should be distributed over as broad a geographic area as feasible” with some local prioritization allowed.
Ethical principles in transplantation

- Autonomy: right to donate; need for consent
- Beneficence: obligation to provide organs as is possible
- Nonmaleficence: *Primum non nocere*: “Dead donor rule”
- Justice: equity in allocation of organs
Autonomy: Consent issues

- Principle of autonomy: self-consent
- Primacy of patient preference:
  Expressed in: advance directive
donor card
driver’s license
donor registry
- Principle of “first person: decedent’s prior documented consent overrides survivors’ objections.”
Autonomy: Consent issues

- Surviving next of kin may make donation in absence of decedent’s prior donation
- OK hierarchy of decision makers:
  - Spouse
  - Adult son or daughter
  - Either parent
  - Adult brother or sister
  - Guardian of the decedent
  - “Any other person authorized or under obligation to dispose of the body”
- “Shall not accept gift” if there is disagreement
Autonomy: Consent issues

Presumed consent vs. expressed consent:
- Presumption that organs may be procured absent a specific documented refusal
- An “opt-out” strategy
- Used in Spain, Belgium, Italy, Austria
- Increases donations by 25-40%
- Objections: Loss of autonomy
  Taking of property without due process and just compensation
  (violates Fifth Amendment)
Justice: Allocation of organs

Allocation criteria:

- Financial resources
- Age of recipient
- Compliance and lifestyle issues (alcohol, drug, tobacco use)
- Co-morbid illnesses
- Citizenship
- Length of time on list
- Geography
Nonmaleficence: ‘Dead Donor Rule’

Vital organs cannot be removed from a potential donor until/unless the donor is dead.
Nonmaleficence: “Dead Donor Rule”

- First cadaver donors after cardiac death
- Brain-dead as primary donor pool 1970s-1990s
- Development of protocols for “non-heart-beating cadaver” donation in 1990s
Increasing the donor pool

Donation after Cardiac Death (DCD):

Process:
- Decision made to withdraw life support
- Family approached for potential donation
- Conventional terminal care
- Withdrawal of life support in/near OR
- Declaration of death by cardiac (asystole) criteria
- Organ procurement 2 to 5 minutes after asystole
Increasing the donor pool

DCD:

Advantages:

- Increases donor organ pool (kidneys)
- Allows families some solace/meaning to loved one’s death
- Permits timely organ procurement
Increasing the donor pool

DCD:

Ethical concerns:

- Decreases respect for dying patient
- Provides “incentive” to withdraw care
- Potential conflicts of interest among care-providers
- Not addressed in most advance directives
Increasing the donor pool

DCD:

Necessary safeguards:

- Decision to withdraw care made independently and previous to any discussion of organ donation
- Provision of customary terminal care
- Established policy carried out by trained personnel
- **Total** separation between treatment team and transplant team
### Principles Governing Organ Transplantation Involving Deceased Donors

<table>
<thead>
<tr>
<th>Principle</th>
<th>Donation after Brain Death</th>
<th>Donation after Cardiac Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respect the dead donor rule</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Determine death using accepted tests and procedures</td>
<td>Yes, using brain-death tests</td>
<td>Yes, using circulatory-death tests</td>
</tr>
<tr>
<td>Separate death-determination team from organ-procurement team</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Separate decision to refuse life-sustaining therapy from decision to donate</td>
<td>Not applicable</td>
<td>Yes</td>
</tr>
<tr>
<td>Obtain surrogate consent for withdrawal of life-sustaining therapy</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Obtain surrogate consent for organ donation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Provide palliative care during dying</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Provide end-of-life family support</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Properly design and scrupulously follow protocol; document findings</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Increasing the donor pool

Directed Donation

Definition: Gift of donated organ to a specific individual

- Commonly used in living-related donations
- Allows tissue-typing and -matching electively
- Performed altruistically
- May have issues of true voluntariness
Increasing the donor pool

Directed Donation

Problems with unrelated/stranger live-donors:

- Possible covert payments or other influences
- Potential for discrimination
- May by-pass usual allocation criteria
Increasing the donor pool

Directed Donation

Possible abuses:

- Advertising for organs (billboards/internet)
- Organ sharing networks
- On-line organ clearing houses:
  
  MatchingDonors.com
Increasing the donor pool

Directed donation

Organ exchange:

- Pairing unrelated donor-recipient pairs with unrelated tissue-matching donor-recipient pairs
- No payments or incentives provided
An Exchange Performed because of a Cross-Match Incompatibility in One Pair and a Blood-Type Incompatibility in the Other

Increasing the donor pool

Paid Donation

- Proposed by a number of ethicists, economists, policy makers
- Two models: (1) free market capitalism
  (2) set fee payment from network/government
- Arguments for based on utilitarianism and potential donors autonomy/property rights
Increasing the donor pool

Paid donation:

Current OPTN policy:

“It shall be unlawful for any person to knowingly acquire, receive or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce.”
“Creation” of hematopoetic stem cell (HSC) donors

Clinical case:

- 1994: M.N., female infant born with Fanconi’s anemia
- 1996: Parents begin quest for HLA-matched conception through IVF
- 1999: Fifth IVF attempt successful with HLA-matched “healthy” embryo
- 2000: Cord blood stem cells from brother A.N. infused into M.N.
- 2003: M.N. alive and well with XY bone marrow
“Creation” of HSC donors

Clinical scenarios:
Child with: (1) life-threatening congenital condition treatable by HSC transplantation
(2) acquired life-threatening disease potentially curable by HSC transplantation
No HLA-matched donor available
“Creation” of HSC donors

Options for HLA-matched HSC donors:

- Living relative match: < 1 in 4 chance
- Sibling match: 1 in 4 chance (3 in 16)
- Unrelated adult HSC donor from National Marrow Donor Program: 1 in 200-400
- Cord blood from HSC bank: < 1 in 400
- “custom” embryo via IVF + PGD: 100%
“Creation” of HSC donors

Technique: IVF + PGD (preimplantation genetic testing)

- “routine” IVF
- Removal of single cell from blastomere (8-12 cell embryo), 2-3 days post-fertilization
- Amplification of single cell DNA by PCR
- Screen DNA for disease and HLA genes
- Implant selected HLA-matched, “healthy” embryo
- Harvest cord blood for HSC transplant
“Creation” of HSC donors

Legal status:
- **USA**: law prohibits use of abortuses and most embryonic stem cell research; PGD not addressed
- **UK**: regulated through Human Fertilization and Embryo Authority (HFEA)
- **Australia**: regulated by Infertility Regulatory Authority
- **Germany**: PGD prohibited
“Creation” of HSC donors

Ethical issues:

- AMA Code of Ethics: Prenatal diagnosis is “acceptable to prevent, cure, or treat genetic disease:

- Kantian principle: “A person should never be solely used as a means for another person, but always seen as an end to itself.”
“Creation” of HSC donors

Ethical issues:

- Parents have reproductive autonomy & procreative beneficence
- Parental motivation for donor child beyond donor status
- Beneficence toward: ill child
  - family unit
  - donor child
- Nonmaleficence toward donor child –
  Risks: cord blood harvesting: ethical
  bone marrow harvesting: maybe ethical
  solid organ donation: not ethical
“Creation” of HSC donors

Ethical guideline: “principle of post-natal test”:

If donation of tissue/organ from an already living minor child is judged to be ethical, than similar donation from a not-yet-born child is ethical.
Anencephalic infants as donors

Clinical aspects:

- Anencephaly is congenital absence of the cerebral hemispheres, skull and scalp, with brainstem and spinal cord present.
- Permanently lack any consciousness
- Usually without other congenital anomalies
- Most die within first 1 – 7 days after birth
Anencephalic infants as donors

History:

- **1988-89:** Infant heart transplant program at Loma Linda using anencephalic donors
- **1992:** Campos case in Florida: Parents of infant girl born with anencephaly sought unsuccessfully to donate organs. Child died at 10 days.
Anencephalic infants as donors

Legal and ethical barriers:

- Patients are not brain-dead
- Organ use violates Dead Donor Rule and Uniform Determination of Death Act
- AMA Code of Ethics:
  - 1988: Prohibited organ procurement prior to death
  - 1994: Allowed organ procurement prior to death as ethical and called for change in legal definition of death
  - 1995: Reintroduced prohibition of donation prior to death
Anencephalic infants as donors

Ethical approaches:

- Violates Dead Donor Rule
- Concept of “higher brain death”
- Define anencephalic infants as “never living” because of lack of consciousness
- Define anencephalic infants as “brain absent”

Greater issue of relevance of Dead Donor Rule
Infant heart transplant after DCD

Clinical issues:

- About 100 infant heart transplants yearly
- Indications: Severe congenital defects (hypoplastic left heart) Cardiomyopathies
- > 50% 15 year survival
- High mortality awaiting transplantation
Infant heart transplant after DCD

Denver Children's Hospital report:

- Three infants transplanted 2004-2007 with donation from 3 newborns via DCD
- All donors were term infants with severe birth asphyxia and parental decision to withdraw life support
- Cardiac death declared 11.5 to 27.5 minutes after withdrawal of life support
- Heart procurement began 180 seconds (1st case) to 75 seconds after cardiac death
Infant heart transplant after DCD

- All three infants have survived > 18 months post-transplant
- Clinical course comparable to 17 other heart transplant patients in same period
- Nine other potential donors via DCD in same time period without recipients
- Process was approved by Hospital Ethics Committee and by IRB
Infant heart transplant after DCD

Ethical issues:

- Violated Dead Donor Rule:
  Donors did not have “irreversible” loss of cardiac function

- Concern about short interval between asystole and initiation of harvesting”:
  only 75 seconds vs. IOM guideline of 300 seconds (2000) or American College of Critical Care Medicine of 120 seconds (2001)
Infant heart transplant after DCD

Conclusions of ethicists:

- Truog & Miller: “... may be ethical, but reason cannot be that we are convinced that they are really dead.”
  Most important aspect is to obtain truly informed consent from donor family.

- Veatch: violates Dead Donor Rule
  Need to change law (1) to allow donation from non-dead patients or (2) to recognize “total loss of brain functions responsible for consciousness” as basis for death.
Infant heart transplant after DCD

Reopens issue of donation from non-brain dead potential donors:

- Patients with PVS
- Patients with catastrophic brain injury but brainstem function
- Anencephalic infants
A final word:

“In the report by Boucek et al., one conclusion is clear. As a result of their investigational protocol, three babies are now alive; had the procedures not been performed, it is virtually certain that all six babies would be dead.”