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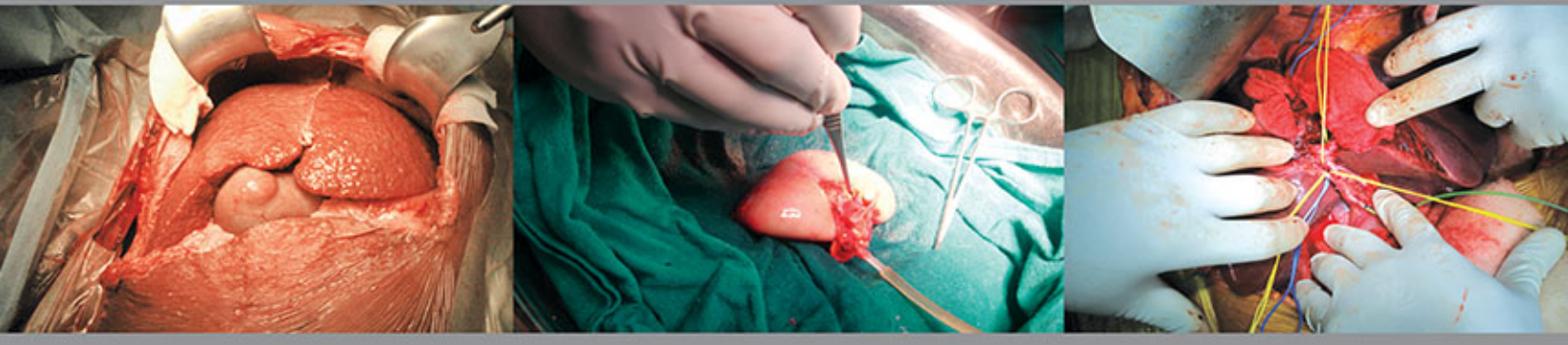
Anesthesia *for* Transplant Surgery

Jayashree Sood • Vijay Vohra



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2 CHAPTER Ethics in Human Organ Transplantation

Amitabh Dutta

Organ transplantation in human subjects became a reality in around the mid-twentieth century. The proven ability of an organ transplant to positively impact longevity has fuelled unprecedented growth of transplantation science. Currently, organ transplantation has evoluted into a truly globalized entity owing to growing awareness, newer safe techniques (anesthesia, surgery, post-transplantation care, rehabilitation), development of infrastructural healthcare resources, presence of proactive formative regulatory guidelines (local, state) and most importantly, the availability of willing donors. With the result, organ transplantation, over the past three decades, has been a notable aspect of medical advancement that has saved innumerable lives and improved quality of life of many. However, there have been issue-based impediments to the relative growth and uniform dissemination of organ transplantation as an accepted independent system. The specific hurdles in regard to above stated include, scarce donor resource (live, cadaveric), the controversy surrounding absolute diagnosis of brain death, conflict of interest (financial, legal, social, psychological), associated specific organ transplant-related implications for the recipient, priorities (social, community, national) and intricacies of human rights issues (right to safe transplantation, right to donate an organ, right to receive an organ). These issues, which otherwise were seemingly abstract outliers hitherto, are threateningly complex whenever an overlap, conflict, or decision-making encroaches the domain of actual process of transplantation.

The current organ transplantation science is elaborate, contentious and has contradictions that mandate debate. Interestingly, the debate matter is not specifically related to the technicality involving the organ transplantation itself, but the more generic and contextual influences that relate organ transplantation science to the general public at large. Ethics, a complex conglomerate of value-based factors (veracity, fidelity, duty, religious/cultural teachings, etc.) seems to be the most significant element that critically impacts, controls and streamlines the contemporary transplantation metrics.

HISTORICAL OVERVIEW

Human organ transplantation began with a series of pioneering experimental studies by a French surgeon, Alexis Carrel (Nobel Laureate, 1912) at the beginning of this century.[1] Surgical transplantation of human organs from donors (living person/deceased) to the sick recipients started around the Second World War. In the late 20th century, with the establishment of safe and effective organ transplantation techniques, introduction of the anti-rejection agent cyclosporine (FDA, 1983), and arousal of public interest vis-à-vis longevity potential the transplantation process offered, the frequency of organ transplantation witnessed an accelerative development. The explosive arrival of structured ethics (Nuremberg Code, 1946) following the Nuremberg War trials (1946) changed the way the patients got treated. Interestingly, the specialty of 'Ethics' kept an exclusive parallel pace with the transplantation science throughout the latter half of the last century (Table 2.1). It veered incisively into the science of human organ transplantation primarily because of the progressive scarcity[2] of the donor organ secondary to enormous growth of sick individuals who were willing-and-waiting for the prospective organ transplantation.

ETHICS AND TRANSPLANTATION

The three facets of the ethics tripod that umbrellas the modern-day transplantation science stems from the need of an individual (the organ recipient), the inter-individual understanding (organ donor ↔ recipient) and the societal/social expectations (public control, community benefit, state regulations/guidelines). The first facet emanates from a super-conscious human process namely, *Altruism*; the second originates from the age-old family/society-driven morality, i.e. '*duty-towards-others*' (*Deontology*, 'Duty Ethics'); the last one involves a community-specific ethical philosophy, known as *Utilitarianism ('greatest good for greatest number of individuals')*. Although in the strictest ethical sense, the

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Table 2.1: Organ transplantation and ethics milestones

Organ Transplantation	*Ethics Milestones*
	1946-The Nuremberg Code
	1948-UDHR
1954-First organ transplant (kidney)	
1962-First cadaveric kidney transplant	
1963-First lung transplant	
	1964-DoH-WMA
1967-First liver transplant	
1968-First heart transplant	
	1978-Belmonte report
	1980-ICMR guidelines
1981-First heart-lung transplant	
1983-FDA approves cyclosporin	
	1991- CIOMS

UDHR, Universal declaration of human rights; DoH-WMA, Declaration of Helsinki–World Medical Association; FDA, Food and Drug Administration; CIOMS, Council for International Organizations of Medical Sciences; ICMR, Indian Council of Medical Research.

three facets of the tripods remain separated to maintain a fine balance, there are variable overlaps depending on the abstract situation(s). The broad-fronted principles of modern-day medical ethics (given below) has lent a structured and operational facelift to the above stated basis of conceptual western ethics. An explorative ethical discussion is therefore warranted whenever an organ transplant procedure is activated in order to specifically balance the aspects related to socio-cultural sensitivity, human ergonomics, legal/regulatory oversight, and above all, financial considerations. Introduced in the year 1979, the famous four principles of Beauchamp and Childress have been in the forefront in catalyzing the understanding between high-level moral concepts and the low-level common morality.[3]

1. Principle of autonomy *(informed consent)*
2. Principle of beneficence *(the patient must get the benefit, risk: benefit ratio)*
3. Principle of Non-maleficence ***(Do no harm,*** *risk: benefit ratio)*
4. Principle of justice *(comparative/distributive)*

The recently introduced principle of *totality of responsibility* (ICMR, 2006, *collective responsibility*) has a holistic stance, which entails professional and moral responsibility for due observance of all the principles.[4]

The ethical governance of human organ transplantation, therefore, is a key to problem solving, decision-making, regulation formulation, and overall success of the organ transplantation procedure. However, the ethical optimization of organ transplantation system may give rise to new case-to-case subtle intra-ethics conflicts (e.g. 'deontology' versus 'utilitarianism'), which demands precision approach that is both inclusive and objective.

The 'Donation-Allocation-Transplantation' (DAT) Protocol

Almost every organ transplantation procedure involves an elaborate expanse that encompasses far greater and more significant zones than the transplantation surgery itself. It probably begins with the 'pre-transplant period' followed by the actual 'operative transplantation phase'. The 'post-transplantation phase' including the 'follow-ups' and 'out-come analyses', completes the range.

ETHICS OF ORGAN DONATION

Altruism and Living Organ Donation

Altruism, an unselfish concern for the welfare of others, or 'selflessness', plays a crucial role in related and the unrelated living organ donations. It forms the basis of motivation that propels the donor to go ahead with organ donation despite knowing the adverse implications of a major surgical intervention and the life after that. Only after the altruistic instincts get makeover of what is called '*Altruistic realization*', the donation can take place. There are subtle ethical conflicts that arise within and between the prospective donor-recipient pair. The catalyst for the altruistic realization to decision for organ donation is influenced by literacy, socio-economic status, need-dependence, cultural/religious aspects, and most importantly, the money-related intricacies. In a recent cross-cultural study, a group of French and Canadian transplant physicians deduced that altruism plays a central yet enigmatic role in promotion of organ donation.[5] In addition, they reiterated that although there is always a cost associated with altruism, it should not be that great enough that it involves sacrificing ones' life. As the evolutionary changes impact human population and individuals, there is a definitive surge in the knowledge among the literates and operational wisdom among semi/illiterates. Richard Dawkins, an eminent evolutionary biologist and author *('The Selfish Gene', 'The God Delusion')*, speculates that with the availability of common knowledge and overriding distractions the humans are confronted with, the belief in god and religion will recede and would continue to be on the decline. With the result,

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the altruistic instincts as well as related realization will have vanishing erosion. The living organ donations, which although are more altruistic than ever, seems be interspersed with disturbing financial undertones.

The recent decline in the number of altruistic living related organ donors might have to do with the above. However, a new type of altruistic living donors is available, i.e. living altruistic donors (LAD) or the non-directed donors (NDD). They come forward on their own to the organ procurement agencies and offer their organ. They typically remain anonymous as well as are not seemingly interested to know as to who got the organ they donated.

In light of the above we may have to confront different shades of altruism (Flow chart 2.1)[6-10] that dictates and lends pre-regulatory approval to the most significant event in organ transplantation system, i.e. an organ donation.

Cadaveric Organ Donation

Since the first 'cadaveric' organ transplant (kidney) happened in the year 1962, it remained the major contributor of organs for transplantation until the beginning of the 21st century when the living organ donation outnumbered the cadaveric organ donation.[11] The primary source of cadaveric organ donors is brain-dead individuals or the recently deceased persons. The significant aspect of the cadaveric donation is that one cadaveric donor can provide different organs (liver, kidneys, cornea, heart, lungs) for different recipients on the wait list. Upon availability of a cadaveric donor, it is a mammoth coordinative exercise to call up and allocate the respective organs to the needy waiting recipients. The process of collective allocation involves certain ethical conflicts that require critical attention.

The three ethical issues pertinent to the cadaveric (*Latin*: *Cadaver*, 'a dead body') organ donation/transplantation are:

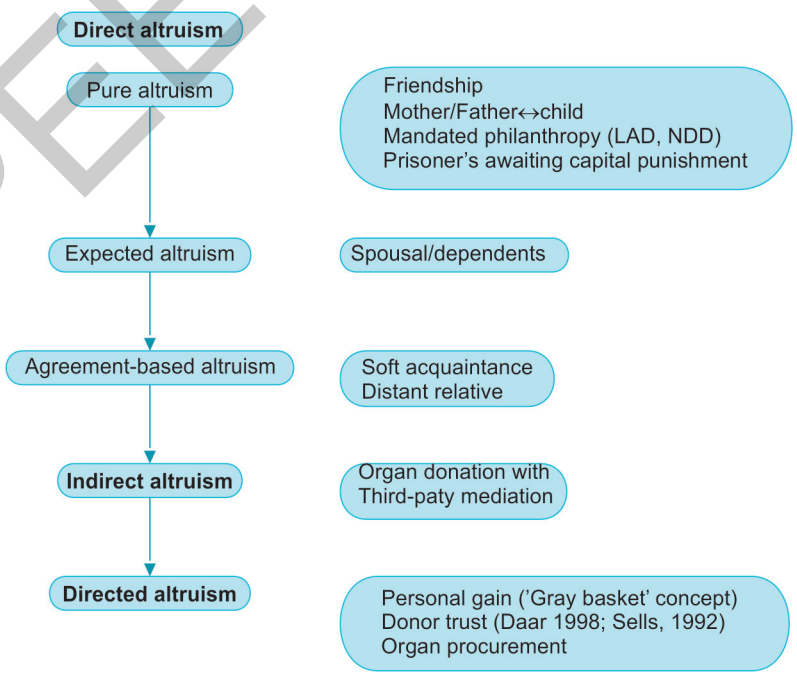
1. The definition of 'death'
2. Advance directives
3. Transplantation-related factors that may adversely affect the risk: benefit ratio
   (Organ (type, size, blood type), distance/time gap from transplant center, waiting list).

The definition and legal quantification of '*death*' is a

Table 2.2: Definition of death

Socio cultural	Kind of dead
Medical death	Brain/cortical death, irreversible loss of function of entire brain (Harvard Medical School Consensus, 1968)
Legal death	Irreversible loss of function of the entire brain as well as the brainstem (US Presidents' Commission, 1981)

Flow chart 2.1: Shades of altruism



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must before one can proceed with organ procurement and transplantation (Table 2.2). In the same regard, it is very important that the family member, close relatives, or legal guardian takes the responsibility of the informed consent admissible under such circumstances vis-à-vis institutional/state regulatory requirements. In case the patient had secured '*advanced directives*', i.e. the 'medical will' for the future course of medical treatment when he/she no longer can be part of the decision-making process for self, legal experts control the procurement of organ.[12] If advanced directives support organ donation, one can go ahead following supplementary family consent. In the absence of advanced directives, the family solely controls the decision to donate.

The institutional/state policy takes its own recourse (*Automatic enforcement*) in the absence of advanced directives and/or when the family/relatives cannot be traced.[13]

As per the WHO draft guidelines for human organ transplantation, there are two consent systems that regulates cadaveric organ retrievals, including. (i) The 'opting in'(explicit consent) consent wherein the deceased persons have had expressed (before death) their desire to donate their organs after their death, or a family member approves the organ removal, particularly in the absence of advanced directives of the deceased person, and (ii) The 'opting out' (presumed consent) consent, which presumes that organs may be removed for transplantation from the bodies of deceased persons until unless their advanced directive suggests objections and/or in absence of such directives, when the close family members actively informed the transplantation team of expressed verbal objections of the deceased person when living.

The persons who wish to be cadaveric organ donors after life can register themselves with local transplant centers. They get a donor card that expresses their organ donation preferences. In Minnesota (USA), it is legally binding to have ones' donation preferences in the driving licenses.[14] With ethical deliberations, new organ donation advocacy systems are in place that takes the responsibility of ethical explanation of cadaveric donation to the family members and facilitate organ donation in a timely manner.

ETHICS IN ORGAN ALLOCATION

After donor availability is secured, the difficult question arises, as to how and whom to allocate the organ for transplantation. Although there are number of ways to allocate organ(s) to the prospective recipients, the allocation decisions are more often than not, conflicting and can be contested.[15] Ethics-based allocations seem to be a unifying process within the standard approach wait-list, the socio-cultural structure of the contemporary local society and, the state regulations (Fig. 2.1). The allocation can be '*duty*'-centric or a '*justice*' (distributive)-oriented process (Flow chart 2.2).[16-18] While the former is more individualistic (related living organ donor) the latter caters to the need specifics/dynamics of a larger society/state and covers living anonymous donation (LAD) by a non-directed donor (NDD) and cadaveric organ donations.[19]

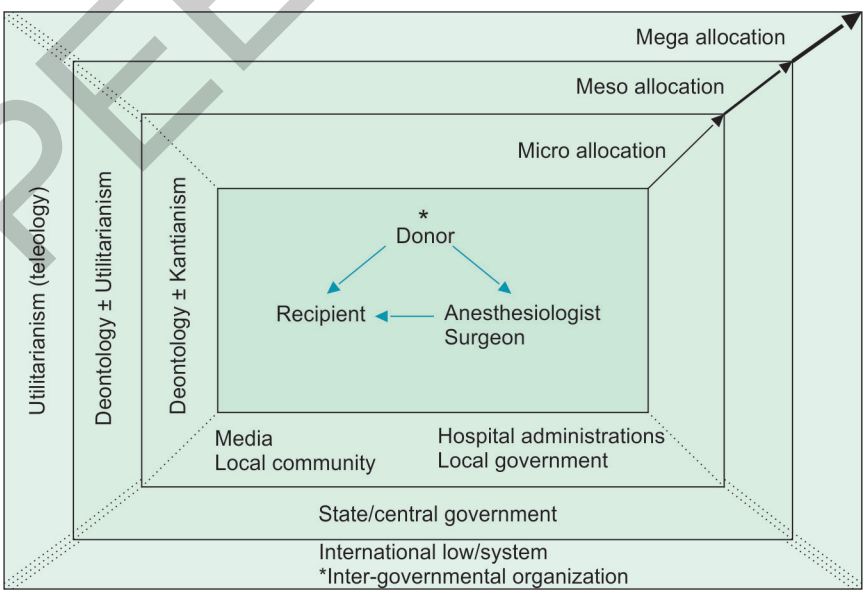

Fig. 2.1: Allocation principles for organ transplantation

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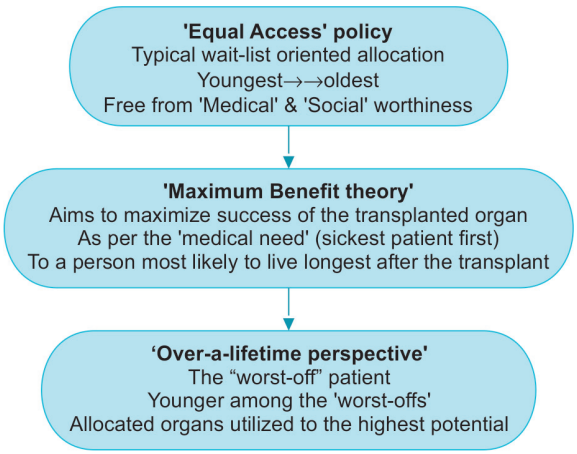
Flow chart 2.2: Distributive Justice in organ allocation



After the ethics-driven allocation of organs to be transplanted is considered, it enters a final rigorous selection trail (Fig. 2.1). The final selection fine-tunes the organ allocation and acts as a socio-scientific bridge between the ethics-directed organ allocation and the social expectations. In the United States, United Network for Organ Sharing (UNOS)[20] has proposed criteria to be considered by organ donation/procurement centers for deliberation on organ allocation and reaching a decision. The criteria include:

1. Medical need for the transplantation
2. Transplant success in terms of number of life-years gained
3. Length of time on the wait list.

In short, ethically, policies need to be aimed at both increasing organ donations and empowering a system that allocates them in the fairest way possible.[21]

ETHICAL ISSUES RELATED TO ORGAN TRANSPLANT PROCEDURE

Domino Transplantation

The 'domino' or the 'double' transplant is a possibility when two 'donor-recipient' sets who are non-matching (ABO incompatibility) within the pair agrees to a cross-matching within them to overcome the incompatibility and facilitate transplantation. The general ethical concern is that it requires participatory agreement and 'informed consent' of all the four (2 donors + 2 recipients) individuals. In addition, there are specific ethical conflicts/dilemma that can mar the above stated double donor-recipient cross-match, including:

1. *Conflict-of-Interest:* (financial, relational)
2. *Donor organ function gradient:* between the two donors (donor specifics (age, co-morbid illness))
3. *Disclosure compliance*: after the first transplantation has started, the donor waiting to donate may refuse donation once he/she gets the current knowledge that the transplant has got affected. This may be secondary to maleficent intention, acute inability to hold altruistic realization to donate the organ, or under duress of financial compulsion. In view of the above, the domino transplant should start together or the current details be kept under the wraps till the second donor gets anesthetized.

Split Transplants

Split transplants are 'splitting of one organ to (e.g. liver) into portions such that it suffices for more than one prospective recipient'. The ethical issue that haunts the split transplants is the risk of a donor portion proving inadequate thereby enhancing risk of transplant failure for the recipients.

Retransplantation

Re-transplantation has evoked intriguing ethical issues because of the obvious imperatives it threatens to draw every single time a retransplantation is considered. In terms of distributive justice, since retransplant recipients at similar level of urgency do significantly worse than primary transplant recipients,[22] a difference that increases with each successive transplant, we need to tread with extreme caution and objective considerations to ensure that the retransplantation will maximize the utility of the retransplanted organ. Irrespective of every requisite procedure in place, the society views every retransplant with reservations and construes the recipient to be a wealthy and powerful personality. Typically society is at its reactive best when a liver retransplant is effected upon a recipient who is considered for transplantation for organ system failure caused by negative lifestyle choices/behavior (e.g. an alcoholic who re-initiated alcohol after the first transplant).[23, 24]

SPECIFIC ETHICAL ISSUES IN THE CONTEMPORARY ORGAN TRANSPLANTATION SCIENCE

Commerce of Organ Transplantation

Financial incentivization of the living organ donation process is currently the most difficult issue the medical bioethicist has to face, deliberate and give a solution.[25] Primarily, the ethicists around the globe have a consensus opinion that commerce (buying/selling) of human organs is an immoral and disrespectful practice.[26] The most likely affected will be the economically weaker sections of the society. In one way,

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they may be lured into selling their organs, and in the other, they will never be in a position to buy one for themselves if and when needed. The economic disparity and the money getting utilized as an organ-buying tool have grave implications on donor safety and the ultimate success of the transplantation process. As per John Dossetor, in the contemporary social systems, buying-n-selling human organs will continue to be reflected in negative light.[27]

Whilst the financial implications of organ transplantation proceed seems all but natural, it becomes troublesome when the economic prospects displace the intricacies involving organ transplantation from the center-fold only to render it a 'driven' rather a 'need' based medical intervention. It possibly stems from state policy that actually allows for regulated/controlled 'medical tourism' wherein organ transplantation is considered an attractive entity both for the healthcare provider (financial gain, fame) and the patients (availability of transplant option, cheaper than their own country). The corrupt practice that undermines the ethical homeostasis of the organ transplantation system is more complicated than one can comprehend. Typically, transition from 'tourism' to 'trading' and from 'trading' to 'trafficking' remains non-descript and opaque. A new ethical problem has emanated from overactive, ambitious and motivated organ transplant coordinators who continually 'track' the donor-recipient pair during the pre-transplant preparation phase. When the transplant scheduling is imminent, the pair gets 'jacked' off by them with some or the other lure (financial [cheaper alternative, incentives], promise of greater expertize, long-term care, etc.). Intriguingly, although this phenomenon seems to be in the common knowledge, it is deliberately under-investigated owing to stakeholders' conflict-of-interest. It is very possible that the '*tracking-jacking*' may cut across city/state boundaries unless an effective identification and block mechanism gets in place.

Alternative Organ Sources for Transplantation

Xenotransplantation

Following the positive impact of the immunosuppressant drug cyclosporine on the uptake of the transplanted organ, the demand for donor organ increased dramatically. In the last two decades of the 20th century, with an anticipated actuarial increase for the demand of donor organs in foresight, the possibility of using animal organs for human transplantation became an intensive study matter. In the year 1986, first xenotransplantation was carried out successfully. However, it drew reactions from bioethicists as well as animal ethicists from around the world. The major ethical issues[28] related to xenotransplantation may include, (i) Exploitation of a healthy living animal, and (ii) The possibility that one or the other species of animal may be targeted and pushed toward extinction, and (iii) Risk to the recipient as well as the whole human species form possible transfer of animal bacteria/viruses to the humans.[29]

Animals are vertebrates, who, like the humans, have a body system that gives rise to adverse consequences when subjected to intervention. The Bentham's advocacy of humane treatment of animals (1780), arrogating rights to animals (Singer, 1975),[30] and the speciesism concept (Regan, 1983)[31] are all in direct conflict with the Kantian deontologists who do not consider animals as moral agents. The Council for Interntional Organizations of Medical Sciences (CIOMS) has formed international guiding principles that propagate the efforts aimed to be critical about every xenotransplantation and that the medical community should look forward to transplantation science that is based on the alternatives to animal use.

Artificial Organs

The first artificial heart transplant (1980) was closely followed by the world. Ethically, the stilted risk: benefit ratio for the transplant recipient, conflict-of-interest related to the procedure itself (surgeons' inclination, related research) and the financial implications (manufacture of artificial organ), has long been a matter of debate. In addition, for the risk involved, and possibility of repeat transplant due to transplanted artificial organ dysfunction, artificial organ transplant may prove to be cost-ineffective.

Stem Cells

Stem cells are next big thing in organ transplantation and the way to overcome organ donor shortage in the future. Stem cells are the ones who have natural ability to form different specialized cells in the human body. Currently, stem cells can be found in human adults. But the most consistent and effective stem cells can be retrieved from a growing human embryo. The ethical conflict is that the practice of using embryo for stem-cells lines may promote termination of pregnancy.

Savior Sibling

A savior sibling is a child who is born to provide an organ or cell transplant to a sibling that is affected with a fatal disease, such as cancer or Fanconi anemia that can best be treated by hematopoietic stem cell transplantation.

Ethical considerations related to a savior sibling selection involve the following:

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1. Commodification of the donor child
2. Possible exploitation of the donor child.

REGULATORY/LEGAL ASPECTS OF ORGAN TRANSPLANTATION

"As Biomedicine and Biotechnology catch the investments of Governments all over the world the need for ethical scrutiny, policy advice and possibly, new regulatory and governance structures is widely recognized."

Alastair Y Campbell, Professor in Medical Ethics

International Efforts

Early Regulations/Laws

The United States made early inroads into legalities of human organ transplantation that facilitated the formation of regulations worldwide in time to come. They came out with following enactments:

The *Anatomical Gift Act (1972)* established 'Uniform organ donor card', which empowered anyone over the age of eighteen years to make decisions regarding their organ donation preferences.[32]

National Organ Transplant Act (NOTA) (1984)-brought the formation of United Network for Organ Sharing (UNOS). It was established to maintain a list of people awaiting organ transplant. UNOS suggested:

1. Financial compensation for organ procurement organizations
2. Prohibition of sale of organs for transplantation.

The WHO Guiding Principles: Based on the 40th World Health Assembly (1987) resolution proposal: "*to study, in collaboration with other organizations concerned, the possibility of developing appropriate guiding principles for human organ transplants*", and its adoption in the 42nd World Health Assembly (1989), the World Health Organization (WHO) came out with 'guiding principles on human organ transplantation'. These guiding principles (Table 2.3) are intended to provide an orderly, ethical, and acceptable framework for regulating the acquisition and transplantation of human organs for therapeutic purposes.[33] The term "human organ" includes organs and tissues but does not relate to human reproduction, and accordingly does not extend to reproductive tissues, namely ova, sperm, ovaries, testicles or embryos. In addition, it does not deal with blood/blood constituents for transfusion purposes.

National Endeavors

The Human Organ Transplantation Act (HOTA), India, 1994 (revised in 2007)

The 'Transplantation of Human Organ Act' (1994), in essence, proposed three important legislative elements:

1. To accept brain death as also a definition of death
2. To stop commercial dealing in organs
3. To define the 'near relative' (father, mother, brother, sister, son, daughter and wife) who could donate organs without permission from the government.

Table 2.3: WHO guiding principles on human organ transplantation

WHO Guiding Principles (WGP)	*Ethics/Transplant Element in Question*	*Sub-details*
WGP-1	Autonomy	▪ Lawful Informed Consent must be secured
WGP-2	Conflict-of-Interest	▪ Transplant physicians determining 'death' for cadaveric donations must not be involved in actual transplantation procedure
WGP-3	Organ donation	▪ Guidelines to promote living organ donations and improve cadaveric organ procurement.
WGP-4	Living organ donation	▪ To establish 'free informed consent' ▪ Minors should be exempted from living organ donations
WGP-5	Commerce related to organ donation	▪ Prohibition of Human organ trafficking ▪ Allows admissible expenditure incurred in transplantation
WGP-6	Advertisement and organ donation	▪ Allows for advertisements for living altruistic donation ▪ Prohibition of advertisement as a profit-sharing tool
WGP-7	Duty of organ transplant physicians	▪ Advises the transplantation physicians to refrain from transplantation if there is knowledge that financial irregularities have taken place
WGP-8	Entrepreneurial practices in organ transplantation	▪ Aims to restrict/abolish entrepreneurial practices for organ 'recovery' as well as 'implantation'
WGP-9	Distributive justice	▪ Supports 'Justice' and the medical need as a basis for transplantation over financial/other considerations

WHO, World Health Organization

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THOA was adopted by all the states and Union Territories except for Jammu and Kashmir and Andhra Pradesh, which have their own organ-regulation legislations.

The revised 'Transplantation of Human Organ Act' (THOA) (2007) has amendment in place for that has expanded the definition of 'near relative' to include grandparents, grandchildren, uncles and aunts. Also, not-so-close relatives who have stayed with the patient can donate organs, provided there are no commercial dealings.

Organ Procurement and Distribution Centers

Under a new plan, Union Ministry of Health, India has proposed organ procurement and distribution centers at the national (National Organ Procurement and Distribution Organization (NOPDO)) and the state (State Organ Procurement and Distribution Organization (SOPDO)) level. Their primary aim is to:

- Increase availability of organs from cadaver donors
- Build capacity for retrieval of organs and transplantation and
- Roll out post-transplant services to both recipients and living donors.

In addition to the above efforts, Ministry of Health plans to initiate an *Organ Donor Register*.

A *National Organ Transplantation Program* is also under consideration.

RECENT ENDEAVORS

An Organ Retrieval Banking Organization (ORBO) is now established at AIIMS, New Delhi, with the sole aim to facilitate organ donation that would help save or improve the quality of life of the awaiting organt transplant recipients. A National Organ and Tissue Transplant Organization (NOTTO) is being set up at Safdurjung Hospital, New Delhi, and is expected to be functional by April 2013.

CLINICAL PEARLS

- Ethics in organ transplantation has gained the rightful significance that protects donor's autonomy, generates a just organ allocation system, brings down the awkward commercial implications related to organ transplantation, settles unnatural conflict of interest(s), paves way for the future research, and most importantly, it builds a socio-scientific bridge that hinges on mutual trust and cooperation.

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