Organ donation and transplantation

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Organ Donation and Transplantation

by

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ORGAN TRANSPLANTATION

Although modern science and technology has made transplantation of organs more successful now than in the past, sadly, many people each year die waiting for donor organs.

There are a variety of reasons why not everyone who needs an organ can receive one, even when it is available. Pre-existing medical problems, risk of rejection, advanced age, and high cost of the procedure itself are only a few reasons that keep the dying patient waiting. However, the most common cause of the long wait is organ availability.

What limits the availability of these organs? Basically, people fear becoming donors, if they do make that decision, often they fail to communicate that wish to their families. The consent of the family at the time of the donors demise contributes to this scarcity.

Ravaging diseases people encounter will certainly be fatal to many without an organ replacement. Diabetes is one of the most severe diseases, it virtually attacks, the entire body. Kidney failure is another, it keeps a patient on dialysis to filter out the toxins from their blood, the only way of surviving while awaiting a donor organ. Everyone on dialysis is a also a candidate.

Other barriers exist, such as waiting for the proper donor. Both donor and recipient have to match compatibly in tissue typing and blood type. Even with the aid of computers to do the matching, risk of rejections still remains a reality. Only an organ from an identical twin assures an exact match.

Despite the odds, survivability of recipients have made great strides over the decades. Immunosuppressant drugs have made that a reality. Yet, the sad truth remains, many will die waiting, unless there are more organ donors to save their lives.
Transplants are more successful now, but many die waiting.
### NOMENCLATURE BASED ON RELATIONSHIP BETWEEN DONOR AND RECIPIENT

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>Autograft</td>
<td>Donor and recipient are the same individual</td>
</tr>
<tr>
<td>(Autogenic graft)</td>
<td></td>
</tr>
<tr>
<td>(Autogenous graft)</td>
<td></td>
</tr>
<tr>
<td>Isograft</td>
<td>Donor and recipient of same species and identical genotype</td>
</tr>
<tr>
<td>(Isogenic graft)</td>
<td></td>
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<tr>
<td>(Syngeneic graft)</td>
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<tr>
<td>Allograft</td>
<td>Donor and recipient of same species but different genotype</td>
</tr>
<tr>
<td>(Allogenic graft)</td>
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</tr>
<tr>
<td>(Homograft)</td>
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<tr>
<td>Xenograft</td>
<td>Donor and recipient of different species</td>
</tr>
<tr>
<td>(Xenogenic graft)</td>
<td></td>
</tr>
<tr>
<td>(Heterograft)</td>
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### NOMENCLATURE BASED ON ANATOMICAL POSITION OF GRAFT

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>Orthotopic graft</td>
<td>Transplanted tissue or organ placed in an anatomically normal site for that particular tissue or organ.</td>
</tr>
<tr>
<td>Heterotopic graft</td>
<td>Transplanted tissue or organ placed in an anatomically abnormal site for that particular tissue or organ.</td>
</tr>
<tr>
<td>Accessory heterotopic graft</td>
<td></td>
</tr>
<tr>
<td>Auxiliary heterotopic graft</td>
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</tbody>
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### NOMENCLATURE BASED ON TECHNIQUE OF GRAFTING

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free graft</td>
<td>Transplanted tissue is completely detached from the donor and there are no vascular anastomosis between graft and recipient created by the surgeon.</td>
</tr>
<tr>
<td>Pedicle graft</td>
<td>Graft is initially attached to its site of origin by a vascular pedicle which is subsequently severed when the graft has developed vascular connections at the new site.</td>
</tr>
<tr>
<td>Graft with vascular anastomoses</td>
<td>Graft is completely detached from donor and vascular anastomoses between graft and recipient are created by the surgeon at the time of transplantation.</td>
</tr>
</tbody>
</table>
ATTITUDES TOWARD ORGAN DONATION AND TRANSPLANTATION

In order to understand the reactions to medical procedures after death, it is necessary to reach a deeper understanding of the factors that influence the attitudes toward organ donations and other procedures with the deceased body.

In 1994, a survey was taken from 400 inhabitants of a city in the middle of Sweden. The survey was concerned with attitudes toward transplantation issues. From the interviews, motive complexes were analyzed and interpreted. The motives were divided into these complexes:
(1) Illusion of lingering life. (2) Protections of the value of the individual; (3) Distrust, anxiety and alienations; (4) Respecting the limits set by Nature or God; (5) Altruism; and (6) Rationality.

The individuals that were determined as not willing to donate their own organs were either reacting out of death anxiety defenses, or had a special outlook on life, one that included emphasis on the idea of what was natural. The adverse reactions of the positive group dealt with more initial reactions such as those which were weakened upon confrontation with the subject, or altruistic and fact-stressing arguments.

The Motive Categories

1. Uneasiness at the thought of cutting the dead body. These reactions included attitudes which applied to autopsy. The thought of the body being damaged and destroyed.

2. Anxiety about not keeping the dead body intact. The desire to keep the dead body whole, i.e; that nothing is being removed from it, and a feeling of invasion of private property.
3. *Discomfort with donations of certain organs.* The expression that certain organs were more important than others especially the eyes, or heart, therefore making them more difficult to donate than others. They were expressed as having symbolic meaning.

4. *Difficulty with cutting into children.* The fact that ones own children are felt to be part of oneself, and not yet fully developed, made this particularly difficult as the child’s organs were viewed as being precious possessions.

5. *Fear of destruction.* These feelings were associated with being deprived of human characteristics. Concerns about what becomes of the body after death, either with decomposure or consumed by fire are also brought into this category.

6. *Uneasiness with exposure.* Opposition to the knowledge that the body would be uncovered, exposed to the view of others and revealed.

7. *Fear of disrespect for the dead person.* The main consensus of opinion was to leave the dead alone and let the body rest in peace, incisions and operations on a corpse were in fact disrespectful and disgraceful. It was considered important in this case to view the body as an individual, not just an object providing organs.

8. *Anxiety about offending the family.* This conception was mostly concerned with the consideration of the feelings of the family, the difficulty in the knowledge of a member being cut up and his or her organs being removed.

9. *Discomfort with changes in appearance.* It was important here about thinking how the dead body would appear after the organ removal or autopsy, particularly a fear that the deceased would not be recognized as the person he or she once was.

10. *Apprehension about the funeral.* It was important that the ceremony not be delayed, marking the end of life in a traditional form, and in no way of being offensive.

11. *Fear of obstacle to rebirth.* Advocates fear giving away their organs they would need in the next life, or knowledge that the body would be destroyed by cremation or decomposition, feeling the body must remain intact as it was in the moment of death if there was to be a resurrection involved.
12. **Dislike of having one's organ surviving in another's body or having another's organ living on in one's own body.**
The insecurity some felt as the feeling of imaging one's organ living on even though the person was dead. Concern was to be sure of one's whole body dying at the same time.

13. **Discomfort at giving useless organs.** This was associated with a feeling of shame, that one's organs would not be suitable for another's survival.

14. **Problems with the concept of death.** This category was faced with three types of concerns: (a) A negative view of brain-related death, i.e., organs must not be taken from a person with a still beating heart. (b) Concern with the brain dead person still having pain sensations as well as fragments of consciousness remaining. (c) The view that diagnostic methods used to pronounce death are not adequate or people are being pronounced dead prematurely in order to get hold of their organs. Mostly there was fear of pain during the procedure and even hope for possible survival if one had not been chosen as a donor.

15. **Distrust of the doctors.** The notion that the individual wishes are not being respected, rules being violated, and doctors who are too career oriented exceeding their ethical limits.

Various explanations were offered as to the question why it was important that a corpse be respected in a way that the person maybe never was. One explanation was centered on the fear of the dead seeking revenge, or harm from the dead if something is done to cause their disapproval. For example, giving away their organs against their will. Another more common reaction was the need to protect the individual's worth, this seemed to be connected with the fear of being obliterated as an individual, and the need to protect their worth in society, principally it was the idea with the illusion of symbolic survival.

Perhaps a more common explanation to these opinions is the thought that during life the body and the self is experienced as being inseparable, and this unity does not end abruptly when death occurs. The importance of the funeral act and the burial are significant to this idea. These rites focus on the deceased and his or her life. The belief in a disconnection from God or a divine power reflect the helplessness, insecurity and alienation some people feel will happen once they become transplant donors.
Why do some people feel transplant surgery does not respect the limits set by Nature or God? Many persons feel they will not be themselves any longer, and if they donate their organs they will become part of another persons personality in some way. Another view is there needs to be a limit for the manipulations of mankind and transplantation exceeds this limit. Man loses control over himself when he chooses to rule over the natural forces, he in fact has no right to prolong life. However, persons who make this statement do accept other kinds of advanced medical care such as coronary by-pass surgery and pace-makers. Although this seems illogical in reasoning, when viewing the difference between transplantation surgery and other kinds of medical intervention, there seems to be a special conception of what is natural and what is not.

Very few people in the negative motive complexes mentioned that transplantation can help people to survive or be given a better quality of life. Only a few not willing to donate saw it as an altruistic act. By contrast, people in the positive motive complex groups were not only willing to donate their bodies for dissection but expressed appreciation for those who would. Saving lives was their chief motive, with total indifference to what would happen to the dead body. They also saw the process as a sort of reciprocity for themselves in receiving help if they were ever in need. The rationality behind the opinions formulated in the positive group emphasized actual circumstances and facts concerned with their reaction. These facts concluded: Dead persons cannot be hurt by procedures after death, they do not feel or need anything. Sick and suffering people can be saved by transplanted organs.

When comparing all the attitudes people had as a basis for the procedures after death, they felt the dead do not feel or need anything. By contrast, sick and suffering people can be saved by transplanted organs. When comparing all the attitudes people had as a basis for the total value system or philosophy of life. People who had the highest moral standards also had the most difficulty in their decisions. In individuals who were undecided, lack of factual information played a big role in the influence of their opinions. Among these people there was a genuine causal relationship between knowledge of transplantation issues and the signing of a donor card.

According to this study, there are certain misunderstandings of facts that make people hesitant toward organ transplantation, mostly it is incorrect information about death criteria. Persons in the negative group consisted of people with increased death anxiety defenses, or with a special kind of life philosophy. In these people there was little hope that they would be influenced by
knowledge of the correct facts concerning death. When evaluating decisions made by people whose beliefs and motives took a strong stand concerning procedures with the dead body, it was indicative of their misconceptions and discomfort in thinking of the dead body being cut up. Their assumptions came from the fear of being declared dead too soon, also that the organs would not be suitable as transplants, religious beliefs were also a strong issue.

There is a need to better explore reactions connected with destruction. It is probable that the motives in different age groups would also have different reactions. A strong relationship between attitudes that were negative and age were found to suggest a cohort phenomenon or effect of people’s different positions in the life cycle.

Better understanding regarding the concepts of death are necessary in hope to influence attitudes involved in organ transplantation and inspire interest in donation.
In America, Alexis Carrel was the first to experiment in early transplantation by the transference of organs in animals. Carrel together with Emerick Ullmann performed "en masse" transplantation by removing both kidneys, aorta, and vena cava, taking the ureters with the kidneys for use in anastomosis.

Between 1900 and 1930, in this country and abroad, workers like Carrel and Ullmann were performing this type of experiment. Kidneys were most often used because of their simple vascular supply. The ureters functioned within minutes and gave an index to work with. Although Carrel recognized the transferred kidneys functioned normally, put out urine and maintained life, he was unaware what was causing their loss. The concept of rejection was not yet understood.

The realization of rejection taking place was thought to be due to a process quite distinct from infarction (ie., loss of arterial blood supply) infection, or inflammation. Initially, the term rejection indicated a process by which the host was not accepting of the new organ. It was not long before it was understood that there might be some relationship involving the immunologic process by which an organism combats invading bacterial infection.

In the mid 1920's Emile Holman, a surgeon of the Hopkins, Harvard, and Stanford, carried out an experiment grafting skin from a mother onto her badly burned child. The child not only rejected the mothers skin, he developed a severe necrotizing inflammation of his own skin. This suggested shared antigens between the child and his mother and the development of an autoimmune disease as the cause of the necrotic dermatitis. Although the implications were evident, attempts to study them further were not possible until early in 1951 when the group of David Hume, George Thorn, and Gustave Dammin at the Peter Bent Brigham Hospital in Boston got together to experiment with the grafting process. One important aspect of the groups experience was their collaborative scientific work involving medicine, surgery, pathology, radiology and immunology.
It was the forecast of the group collaboration which marked the efforts of many institutions during the coming decades.

**Skin Grafts**

Actually the earliest record of autogenous pedicle grafts, used to restore mutilations of the nose, ear and lip were found in the Sanskrit of India, the *Sushruta Samhita*, dated circa A.D. 450, which dates back several centuries before the Christian era. Sushruta described the techniques of rhinoplasty and other plastic procedures in his work which appeared to have evolved in response to the social pressures encountered by the stigmata left by mutilations carried out in punishment for crimes committed.

At the middle of the fifth century B.C., prior to Sushruta, Hippocratic physicians gave similar emphasis of training and education in the development of surgery and manipulative skills. However, Hippocrates was a practical man who observed, judged, and developed procedures in theory, but there is no evidence that he used free skin grafts, although he was evidently familiar with the methods of repairing defects. The descendants of Hippocrates did however, understand and employ repair of defects involving the nose, ear, lips and other body parts by means of skin flaps. This documented technique is compiled in the *De Medicina* (A.D. 14-37) and reflects the practices of the Greek School of medicine at Alexandria during the latter part of the fourth and early part of the third centuries B.C.

The practice of skin transplantation methods were also know to Galen (A.D. 131-201) and the tradition carried on by the Alexandrines, then latter followed by Byzantine encyclopaedists (ca. 325-200 B.C.)

**Transplantation of Organs**

Considered the father of experimental surgery, John Hunter (1728-1793) applied the principles of comparative anatomy thereby establishing the precedent for future concepts in grafting and transplantation. Most of Hunters treatises were on the growth and development of the teeth. His first transplantation experiment involved a successful replacement of a premolar. The success he said, was “founded on a disposition in all living substances to unite when brought into contact with one another.”

Hunter established certain principles for transplantation, what he called” the
living Principle" of a part. He proposed in this theory: that the transplant need to be capable of being maintained and supported by the tissues long enough to permit revascularization. The blood he believed contained a living substance from which all else was derived. Unfortunately, he also believed that all blood was the same and could easily be transferred from one living animal into another. Among his many experiments, he successfully transplanted the spur of a cock into its comb, in an attempt to determine the influence of sex upon transplants. This type of experiment encouraged his successors to initiate hormone research.

Hunters experiments with early organ transplants also influenced the most significant research of Charles-Edouard Brown-Séquard (1847-1894). Brown-Séquard received the Lacaze Prize in 1881 for his experiments on irrigation of dying tissues by blood, suggesting that several limbs might be sewn back on. Brown-Séquard went so far in his experiments that they were considered macabre. An example was one in which he perfused the head of a freshly guillotined young man with defibrinated blood in order to demonstrated how the muscles would respond to stimulation. Variants of Hunters work were carried on by Brown-Séquard in his grafting of tails of rats and cats into cocks combs.

Brown-Séquard further extended his grafting experiments by transplanting testes of guinea pigs into old dogs. He was so excited with the prospect of his rejuvenation experiments on dogs, he attempted to rejuvenate himself with self-injected extracts of testes. He measured his success by recording the strength of the flexors of his arm.

Advances in Grafting and Transplantation

One of the major deterrents to the success of grafting was infection. Early in the 20th century, Lister and the development of asepsis made a great number of grafting procedures possible without infection. However another primary problem was the complications of hemorrhage, thrombosis, and stenosis. Developing an effective technique of vascular anastomosis to eliminate the complications was not available until late 1946.

It was not until 1945, that the pathologist Leo Loeb formulated the fundamental concept that tissue and organ transplantability was essentially a search for biological identity. Loeb theorized that surgical failure in transplantation was due to blood group agglutinable substances differing from that of organs and tissues.

In 1930, Peter Goner identified the first histocompatibility antigen,
determining that isoantigenic factors are genetically present in grafted tissue and absent in the host and are capable of eliciting a response resulting in the destruction of the graft.

The advent of World War II enabled Peter Medawar to give direction to the principles of new immunology in research and transplantation. His experiments with war wounds proposed a general theory of the nature of immunity and "self-recognition". In 1965 Medawar wrote that "the success of renal homografts in clinical practice, however meager it may be, is so very much greater than people working in the laboratories had dared to hope."

Medawar, after surveying this progress later said, "we now see what will one day be looked back upon as the first stirrings of the science of somatic cellular genetics...work in which immunology of transplantation is almost certain to occupy a central position."
Chapter 3

IMMUNOLOGY: THE NORMAL IMMUNE RESPONSE

Tissue Typing Procedures

Before an organ can be transplanted, the most suitable donor possible needs to be matched to the recipient in need of the allograft. Various tests are carried out prior to the procedure, but the most important are determining the red cell bloodgroups, ABO, and the human leucocyte antigens HLA.

Human Leucocyte Antigen (HLA)

Originally these antigens were detected on leucocytes, but are actually present on all cells of the body. Compatibility of these antigens between donor and recipient is of major importance to the survival of allografts. These antigens represent part of the major histocompatibility system (MHS) and are homologous in all mammals.

ABO Blood Grouping

Compatibility of the ABO blood group antigens of donor and recipient is necessary for organ allografts. If a kidney is transplanted into an ABO incompatible recipient, the antibody in the recipient combines with the appropriate A and or B antigen on the cells of the donor kidney and will trigger an accelerated or hyperacute rejection.

Cytotoxic Antibody Testing

Since the fluctuation of the antibody is unpredictable, study of the serum of the recipient is necessary in a profile of their cytotoxic antibodies. This examination
studies the production of cytotoxic anti-HLA antibody stimulated by foreign HLA antigens encountered. Serum samples taken at regular intervals are tested in the cytotoxic test against a panel of lymphocytes of individuals who have been characterized and possess representatives of all the common HLA antigens. This allows for the fluctuation in anti-HLA antibody specificity to be monitored and enables an antibody profile to be constructed for the patient.

Tests Using Donor Cells Before Transplantation

The procedures for HLA testing differ somewhat according to whether the donor is a living relative or a cadaver. In living related donors, it is necessary to type the whole family for the HLA-A, B and O antigens to enable haplotypes to be deduced. The donor of choice is an HLA-identical sibling, however, in some cases one haplo-type similar, one haplotype different (haplo-identical) donors are accepted. These are usually siblings, parents or offspring or the recipient.

In cadaver donors, problems may arise in lymphocyte typing. Lymphocytes should be alive. Lymphocytes obtained from a donor who has been on a ventilator for a long period may be moribund (dead) and contaminated. To produce reliable results, dexamethasome is frequently administered to potential donors with head injuries.

Crossmatch Tests

Crossmatch between the serum of the recipient and the lymphocytes of the donor are screened within this test to show if any cytotoxic antibody is present.

Histocompatibility Matching

Histocompatibility antigens are the products of histocompatibility genes. An antigen from one individual induces a recognition and immunological response when presented to another member of a species who differ. Such differences are shown to cause graft rejection.

The genetic makeup in man has led to the conclusion that one genetic system controls strong transplantation antigens, this system is called HL-A. Other genetic systems also exist, such as the ABO system. The less antigenic the graft, the less the host will react against it. When donor and recipient are identical twins and there is no antigenic difference, the tissue is accepted without
immunosuppressive agents.

When the donor and the recipient are siblings or when a parent donor is used, there is greater likelihood for antigen sharing between the donor and the recipient than when a cadaver or unrelated donor is used.

The immune response to histocompatibility antigens or cells of transplanted organs trigger the rejection response. The immune system is composed of lymphocytes, cells of monocytes and macrophages and specialized epithelial cells. These cells are organized into the spleen, lymph nodes, tonsils, thymus and bone marrow. Lymphocytes and macrophages contribute to the recirculating cells found in the blood and lymph. The thymus is essential for the development of cellular immunity. All cells that were once dependent upon the thymus for their development are called T cells. T cells represent the immunocompetent cell population responsible for cellular immunity development. T cells are migratory and must move to the periphery in order to interact with foreign antigens.

T cells are also heterogenous, offering many clones of cells each differing from one another in structure of its antigen receptor and response. T cells mediate important regulatory functions, they help or suppress immune responses, including antibody production. Other T cells act as direct destructive agents to cells bearing antigens (killer functions).

In addition, there are lymphocytes that mediate certain cytotoxic responses. These include the natural killer (NK) cells, which recognize systems that are different from those of T or B lymphocytes. The role of cytotoxic T cells in allograft rejection is well founded.
Antigen-antibody response of transplanted heart:

1. Foreign antigens on the cells of the newly transplanted organ.
2. Foreign antigens are released from the transplanted tissue and move into the lymph node.
3. Memory T cells intercept the foreign antigen and respond.
4. Killer T cells are produced and released to fight against the foreign antigen.
5. Killer T cells attack the cells of the transplanted heart.
Chapter 4

PATHOLOGY OF GRAFT REJECTION

There is no doubt that allograft rejection is a specific immune response provoked by antigenic components in the foreign tissue. The function of the graft depends on many things other than non-specific factors, the most important single factor in evaluating rejection is host recognition of grafted tissue as foreign and the antigenic similarities and differences between donor and recipient. The specific factors include preservation and quality of the donor organ, general condition of the recipient and his original illness, and the possible development of infection. All the above factors are important to distinguish alterations that can be attributed to factors that are non-specific from those due to immunological graft rejection.

In recent years successful survival of grafts has been due to improvements in preservation techniques, technical facilities, tissue typing techniques, and better understanding of the use of immunosuppressive drugs.

The rejection reaction is thought to have three phases: the *afferent arc* from allograft to donor lymphatic tissue, the *central lymphoid tissue response*, and the *efferent arc* from the lymphatic tissues to the graft. The *afferent arc* consists of recognition of foreign antigenic determinants by recipient cells and transfer of this information to lymphoid tissues. Documentation suggests that the histocompatibility antigens are released from the surfaces of graft cells into intercellular spaces then to lymphatic and blood vessels. The antigenic matter may be in molecular form or cellular fragments and be transported into the lymphatic system of the host through the circulation or after being phagocytized by host macrophages. When the antigenic matter is released it suggests that sensitization of responsive cells could occur at a distance from the graft. There is also evidence that in-graft sensitization also occurs and lymphoid cells pick up the antigenic stimuli peripherally. These occurrences may exist as contact is made with specialized passenger leucocytes of the donor organ which present graft antigens directly to the host lymphocytes.
The transportation by which the foreign antigens travel varies. Afferent lymphatic channels are significant in transporting histocompatibility antigens from the graft to the lymph nodes. Although it is clear that afferent lymphatic are essential for the rapid destruction of allografts, the graft is not exempt from immunological attack in their absence.

There is a definite difference between skin and organ allografts when evaluating likelihood of rejection. This depends on several factors, the most apparent is the size of the organ, such as the kidney. Because the kidney is large it is able to release an effective dose of antigen into the blood, especially if it is damaged either before or after transplantation. The kidney also has a rapid blood flow which is restored immediately after the procedure, this factor provides the opportunity for a vast number of host lymphocytes to react with antigen as they travel through the vascular system of the graft.

In the central lymphoid tissue response, the involved lymphoid tissue becomes enlarged with expanding areas of paracortical T cells. The cells become enlarged with prominent nuclei and nucleoli and develop increased amounts of RNA in their cytoplasm. The cells are called blast cells, lymphoblasts, activated lymphocytes and immunoblasts.

The efferent arc phase of allograft rejection has both cellular and antibody-mediated (humoral) components. Similar to a delayed type hypersensitivity, the efferent arc phase shows that allograft immunity is transferable with lymphoid cells from sensitized recipients in studies with animals. Further emphasis is given to the realization that anti-lymphocyte globulin, which is cytotoxic to T lymphocytes, is especially effective in suppressing delayed type hypersensitivity reactions and allograft reaction, but appreciably less for antibody-mediated responses.

Humoral immunity plays a major role in immediate allograft rejection, especially in patients sensitized by multiple pregnancies or blood transfusions, and in ABO incompatible transplantation. The effects of antibodies formed after transplantation is not clear, some contribute to rejection and others do not. Both pre and post transplant development of allograft antibodies can lead to successful graft survival.

Rejection of Kidney Allografts

Although most acute rejection episodes occur within the first two months following transplantation, episodes of acute rejection both clinical and morphological, can occur months or years after transplantation. Generally, the older the graft,
the more likelihood of chronic changes underlying the symptoms.

Typically in rejection of transplanted kidneys, there is usually fever present along with proteinuria and oligouria with a fall in creatinine. The kidney will also become large and tender. Renal blood flow is often reduced.

If acute rejection is controlled and suppressed with treatment, chronic changes become more apparent. The distinction between acute and chronic rejection is unclear. Other changes in addition to proteinuria include a progressive fall in creatinine clearance and a rise in serum creatinine, hypertension may also be a concurrent finding.

Rejection of Liver Allografts

The typical pattern in early rejection of hepatic allografts is apparent when mononuclear cells infiltrate the portal areas. As a result, the infiltrate increases and mononuclear cells adhere to Kupffer cells and endothelial cells which line the sinusoid of the liver. There also may be degeneration and necrosis of liver cells in the central zones of the lobules and patches of necrosis in the periportal areas. Often findings include intrahepatic cholestasis with bile ductules that contain inspissated bile. The patient has fever, jaundice, and an increase in serum trasaminase and alkaline phosphatase levels. Often distinction from infection or biliary obstruction can be difficult and both may be present.

Livers that have survived by means of immunosuppressive therapy have shown various amounts of fibrous tissue that bridge portal ones and portal to central zones. The arteries frequently have stenotic lesions typical of chronic vascular rejection. Hyperacute rejection is hardly ever seen in immunosuppressed hepatic allograft recipients, even in the presence of circulating antibody focused against donor antigen.

Rejection of Cardiac Allografts

Signs of impaired graft functions can vary. Interstitial edema and cellular infiltration leading to a decrease in myocardial contractility result in impaired heart sounds. In severe rejection, signs of low cardiac output, pericardial effusion and congestive heart failure can be evident with ECG abnormalities and arrhythmias. With severe rejection there is increased endothelial damage, rupture of capillaries and venules producing areas of hemorrhage, and individual myocardial fibre necrosis. In addition occlusive vascular disease is a common occurrence in long term cardiac allografts.
In 1984, the federal government funded a network for organ procurement and transplantations, this network was established under The National Organ Transplant Act Of 1984. The organization itself is called The United Network For Organ Sharing (UNOS) UNOS is a private, non-profit organization that monitors the activities and provides service to transplant centers and organ procurement organizations (OPOS) around the nation. UNOS is also responsible for collecting the data from transplant centers on the recipients of organ transplants. Candidates awaiting organ transplants are placed on a central waiting list maintained by UNOS.

At any give time, there are more than 25,000 persons on the waiting list, and far fewer actual organ donors. Each OPO provides services related to organ procurement, they consist of methods of referral, evaluation and surgical recovery. In addition this system offers donor identification, management and consent, recovery of organs, allocation, and follow-up. It is the OPO that works with the hospital staff in determining donation potential. An organ recovery specialist seeks consent from the next of kin, and manages the donor organ after consent has been granted. The OPO is billed for charges relating to the donation and to the donor’s family. The OPO will then bill the cost to the transplant centers which receive the organs for transplantation.

The role and establishment of The UNOS network

When Congress passed the National Organ Transplant Act in October of 1984, a Task Force for Organ Procurement and Transplantation was instituted to conduct an investigation on the medical, legal, ethical, and social aspects involved with procurement and transplantation. The Task force concluded that the demand for organs far exceeded the limited supply and was due to a lack of consistency, standardization, and regulation within the system of procurement.
Recommendations were then made by the Task Force in order to establish uniform standards and uniform Determination of a Death Act legislation which would be implemented in all states. The National Transplant Act also provided for federally funded networks that functioned as private non-profit organizations. These networks were composed of representations from the organ procurement organizations (OPOs), transplant centers, voluntary health organizations, and the general public. The contract was awarded to the United Network for Organ Sharing (UNOS) in 1987 and served as the network necessary for organ procurement and transplantation proceedings.

**Transplant Centers**

The activities and service provided to transplant centers and OPOs are regulated and monitored by UNOS. UNOS also establishes the criteria for evaluating medical staff qualifications of hospitals in the United States that want to perform kidney, heart, heart-pancreas, and liver transplantations. UNOS also must approve the hospital prior to the commencement of all transplantations. There are separate memberships granted for each individual transplant procedure, monitored by a quality assurance committee within UNOS.

Patients in need of transplants are referred to the transplant centers by their private physician or transplant surgeon. The hospitals transplant coordinator then determines an individual's eligibility based on an intensive medical and psychosocial evaluation. Acceptance into a program is based on the extent of damage to the failing organ system and the patient's overall health. The individual's emotional and psychological status are also considered, as well as their ability to appreciate the commitment involved in receiving a transplanted organ. The accepted recipients agree to a substantial change in their lifestyle, adherence to an intense immunosuppressive program, regular clinic visits, routine biopsies to evaluate immune status, and coping with the potential adverse effects of the many medications they will be on. The individual must then make a continued commitment to his own personal health and rehabilitation through the transplant program. The decision to accept or reject a candidate into the program is made by the hospitals transplant committee, composed of specialists involved in patient management prior to the transplantation and postoperatively.

The UNOS Organ Center operates 24 hours a day to provide access to the computerized waiting list and contains the names of all the candidates to match donors with the most suitable recipients. The only transplant procedure not
regulated by UNOS is individuals who are able to receive kidney transplants from living, related donors. However, UNOS does collect data forms submitted by the transplant centers. These forms contain information of patient and graft survival, immunosuppressive regimens, and the functional status of each patient. In addition to the data collection, UNOS compiles this information and relays it to the Department of Health and Human Services.

The system of organ procurement

Over the four past decades, there have been a list of more than 25,000 persons awaiting organ transplants at any given time depending on the geographic region and date of the study. In 1991, there were fewer than 5000 actual organ donors. This scarcity of donors necessitated state and federal governments to pass a legislation to encourage donation and remove legal barriers to the process. This legislation was instituted as early as 1968 by the Uniform Anatomical Gift Act, which allows an individual to make a decision regarding donation of their organs prior to their death. By signing a donor card, an individual may specify certain organs to donate. However, regardless of whether or not the donor card is signed, the decedent’s legal next of kin is required to give consent for donation. In order to ensure the donation occurs, the next of kin must act as surrogate. Unfortunately, the individual’s wishes are not frequently known or expressed to the family and the family is left to make a decision based on their understanding of what they feel their loved one might have wanted. Another legislation passed in 1986 requires all hospitals to ensure protection of the individuals right to donate organs and tissues. It also establishes the policies and procedures for the identification of potential donors, and ensure the option of donation be offered to the ideal next of kin at the time of the potential donor’s death.

The eight basic components of the donation process

The actual organ donation process consists of eight basic components which are: donor identification, referral, evaluation, consent, management, recovery of organs, allocation, and follow-up.

Identification. Potential donors are most often victims of severe head trauma, cerebrovascular events, or incidents of drowning or unsuccessful resuscitation after cardiac arrest. In each of these instances the brain has sustained an injury that causes its complete and irreversible cessation of function, resulting in
death of the patient. Brain death is defined by the 1980 federal uniform Determination of Death Act as no less final than the cessation of the heart beat. Brain dead patients have cardiovascular functions preformed by the aid of a mechanical ventilator to assist in perfusion and oxygenation of the heart, lungs, kidneys, liver, and pancreas. Patients who undergo primary cardiac arrest (cardiac death) can only donate tissue. The most common tissue for donation are heart valves, bone, skin, and corne'a's.

**Referral.** The initial referral of a potential donor to the local OPO is made by a physician or nurse. The recovery coordinator then investigates each referral and the potential for donation. The coordinator is a specialist kept up to date with criteria for donor eligibility and is a member of the heath care team. They also assist the hospital staff in the management and care of the patient and donor.

**Evaluation.** This evaluation occurs by telephone to the hospital. Data about medical history, extent of injuries, and any information about social history are reviewed careful. Recommendations are made on the findings, either to proceed with the consent process or to define medically unsuitability for donation potential.

**Consent.** Once the family has acknowledged the death, the option of donation is presented to them by a member of the transplant team. Concerns the family may have about funeral arrangements and surgical procedures that may change the outward appearance of the deceased are addressed by the team. The family is assured that the donation will not cost them anything, all expenses incurred while the patient was alive are billed to the responsible party, all costs incurred after the time of death are billed directly to the OPO. The family is also assured that the identity of the donor is kept confidential, as does that of the recipient. If the family expresses a desire to donate only for transplantation it is documented on the consent form, however, it is possible to place the organs for research if they cannot be transplanted. The elements on the consent form must be documented to make it legal. The family must specify the exact organs and/or tissues to be donated. All potential donors must be tested for infectious diseases. The order of legal priority to give consent for donation goes first to the spouse, then to the adult child, the parent, sibling, legal guardian, and any person authorized to dispose of the body. If death falls under the jurisdiction of the medical examiners office, additional approval is needed to proceed and that is obtained by the OPO coordinator from that office.

**Management.** Once all consent forms are signed, the coordinator of the OPO writes all orders for the care of the donor. Management of the donor is a
process that may last from 2 to 12 hours or longer and usually involves all the hospital departments. The medical team is trained to care for the body as a system that houses organs which will be given to others. These organs are made to be functioning optimally prior to their removal. Often, the addition of antimicrobials or a broad-spectrum antimicrobial such as cephalosporin is administered. Testing for infectious diseases such as cytomegalovirus, hepatitis, syphilis, and HIV are preformed to assure there are no contraindications to donation.

**Recovery of the organs.** In the operating room at the donor hospital, surgical staff and the visiting transplant teams participate in the harvesting process. Drugs to maintain blood pressure, oxygenation, and adequate urine output throughout the procedure are utilized. Once the body is properly prepared, the organs are each removed individually. Clamping of the aorta and flushing of all the organs with a cold preservation solution are done simultaneously. These solutions maintain the normal cellular osmotic gradient and arrest cellular metabolism. The heart and lungs can be preserved for 4-6 hours, the pancreas up to 8 hours, the liver up to 24 hours, and the kidneys up to 48 hours. The heart and lungs are the first organs removed, followed by the pancreas, liver and kidneys. Tissue donation which includes heart valves, skin, bone, or cornea's, take place after the organs are procured.

**Allocation.** Based on the variables of the donor's age, weight, height, sex, and blood type, each organ is matched according to the national list of potential recipients. The candidates are screened according to their blood group and body size and are allocated according to medical urgency and time on the list. Patients who are local have priority to receive extrarenal organs from local donors. If there are no matches locally then the organs are sent through UNOS to the most suitable candidate in another region. In order to increase the success of transplantation, patients are who listed at transplant centers closer to the donor hospital take priority over those who are located farther away. Information about the donor is shared with the candidate's transplant surgeon. It is the decision of the transplant surgeon to accept or reject the organ. If the organ is accepted, the recovery teams will travel to the donor hospital for retrieval. The local team is responsible for procuring the organ and sending it to the transplanting center. Since the extrarenal organs deteriorate rapidly on a cellular level, they are transplanted immediately.

Kidney allocation begins immediately after the completion of the surgical recovery due to a most important consideration in kidney allografts, the matching of human leukocytic antigens (HLA) in the donor and the recipient. HLA matching
is used only in the allocation system for kidneys. Compatibility profiles are done prior to allocation for the recipients, according to how well their antigens match those of the donor. Prioritization of kidney allocations are dependent on a point system according to how well the antigens match those of the donor, the greater the number of matching antigens the more points given to the candidate for allocation.

**Follow-up.** Several types of follow-up occur once the donation process is completed. Hospital personnel involved in the donation process are provided general information from the OPO as to the disposition of the donor organs and tissues. Special thanks are sent to the donor family, and they are given information about the outcome of their gift. Support programs for donor families are offered by many OPOs to assist the families through the grief process and to resolve any unmet needs or problems occurred in the donation experience.
Chapter 6

THE DONATION PROCESS

The first step involved in the donation process is referral and identification of a potential donor to the OPO. This identification usually occurs in the emergency or intensive care unit of the hospital. The criteria for selection of a potential donor is kept broad to avoid any possibility of excluding a candidate. Because of the increasing number of candidates, donor criteria are constantly changing. This change is mainly due to improved recovery and preservation techniques, and new immunosuppressive medication procedures. Calls are made to the local OPO for consultation regarding donor suitability to ensure that all families are offered the opportunity to consider the option of donation. This referral takes place as soon as the patient's prognosis is considered terminal and irreversible. The OPO is in operation 24 hours a day, seven days a week to respond to all inquiries and potential donations.

When referring a potential donor to the OPO, basic information as to the patient's name, age, sex and race are needed as well as the status of brain death determination. In addition to these details, the family knowledge and acceptance of the situation need to be understood. If brain death declaration is imminent, it is stressed that a referral to an OPO does not mean a commitment to approach the family regarding donation. The attending physician of the patient must approve and grant permission before the donation coordinator may approach the family. Early referral is important to prevent the situation in which the family chooses the option of donation only to learn later that the option no longer exists for it.

The Role of the Critical Care Nurse

The Critical Care Nurse is the major link between the patient and the family in regard to the donation process. They are usually first to identify the potential for donation and influence attitudes about donating in the critical care setting. In most cases the family will not identify the patient as a potential donor. The necessity of the nurse to offer the family the option is a crucial factor when the family
does not have the state of mind when they are grieving to consider the option. The Critical Care Nurse also participates in assessing of potential donors, provides care in order to maintain and optimize function of organs, and provides support to the family both factual and emotional. Because the nurses have a close relationship with the family, they are in the best position to have a positive effect on the family in making an informed decision about the option of donation.

**Donor Eligibility Screening**

The donation coordinator has the first responsibility in determining a patient’s suitability for donation and begins the initial screening either at the donor hospital or by telephone. The evaluation includes an assessment of the admitting diagnosis, and a past medical history which includes previous hospitalization, surgeries, and current medication. To determine medical suitability, each organ system is reviewed separately. This assessment includes current hemodynamic status and vasopressor history, cardiac function, urine output, ventilation status, arterial blood gases, and a review of laboratory data.

Before the family indicates a willingness to consider donation, a corroborating medical history of potential high-risk is assessed by the donation coordinator. Once the family grants permission, serologic studies are performed to rule out transmissible disease. The tests include human immunodeficiency virus antibody, HTLV I and II antibody, hepatitis B core antibody, hepatitis C antibody, syphilis and cytomegalovirus. Blood samples are obtained prior to any transfusions in an ideal situation.

**Determination of Brain Death**

In the past the determining factor for when death occurred was based on respiration, or lack of. However, it was discovered that respiration could be restored if cardiac function was maintained. In the late 1950’s, the forthcoming of cardiopulmonary resuscitation brought an understanding that cardiac and respiratory function could be restored but left organs more sensitive to oxygen deprivation, such as the brain, in a nonfunctional state. Scientists began to question the traditional definition of death with this new knowledge. What was once thought of as an indicator of death by cardiac cessation was justified by the fact that it inevitably lead to brain death and destruction. The concept of brain death was introduced when heart death was merely a useful index.
In 1968, the problem of brain death received questionable attention when Pope Pius XII called the means of sustaining life as *extraordinary*. He announced that for patients who were in an irreversible coma situation, any efforts to preserve life should not be unduly prolonged. This statement recognized that circumstances exist where death is inevitable. As a result, and ad hoc committee was formed by the Harvard Medical School to study the issue of brain death, thus establishing the first criteria used for its determination.

Guidelines were established in 1981 by the President's Commission for the Study of Bioethics in Medicine published criteria in determining death based on complete loss of brain stem function. A special task force on Brain Death in Children set further guidelines on brain death in pediatric patients. Since children under 5 years of age have increased resistance to brain injury and may recover even after exhibiting an apparent loss of brain function over longer periods of time then adults, extended observation was deemed necessary in these patients.

The President's Commission recommends a waiting period of 6 hours between examinations, “when the mechanism of injury is known”, but advocates a 24 hour waiting period in patients with anoxic brain injury. Test such as the electroencephalogram or cerebral perfusion scan is not required in these patients but is recommended. In patients where the waiting period is less than 24 hours, conditions may prevail that invalidate the usual criteria for brain death such as drug or metabolic intoxication, hypothermia, shock, and physical immaturity. In addition, Central nervous system depressants such as barbiturates, sedatives, and hypnotics may produce clinical cessation of brain function. Toxicologic drug screening must be performed when a history of drug abuse is suspected, as patients may completely recover from the effects of drug intoxication and may not exhibit observable signs of brain function.

Hypothermia is a condition that lowers cerebral metabolism and depresses brain function to a point that resemble brain death, It is frequently associated with neurologic injury and the patient must to brought back to homeostatic control before a diagnosis of brain death can be made. Patients in shock in these circumstances have diminished cerebral blood flow which renders the clinical examination unreliable.

A mandatory finding for the diagnosis of brain death is apnea (cessation of breathing). In this instance an accurate assessment of the patient's respiratory drive is made using the apnea test as an important indicator. Arterial blood gases and normal hemodynamic status are necessary for an accurate apnea test.

The final determination of brain death is made by a licensed physician who is
not a member of the organ recovery or transplant team, and this determination much be in accordance with accepted medical criteria. Pronouncement of death is declared when the chart includes a note stating that the patient meets all criteria for brain death with the specific date and time. The note must be signed by the attending physician declaring death. Once the patient is declared legally dead, the possibility of organ donation is considered.

**Considering the Option of Donation**

In order for the option of donation to be successful the family must understand the process. It is a great concern that the family’s suffering not be compounded by this approach. All effort is made by the health care professional to protect families from further pain and suffering, in this attempt many providers of health care may fail to offer the option of donation. As a prerequisite for helping a family through the donation process, healthcare professionals need to evaluate their own feelings about death and donation or organs. Approaching the family with the option of donation begins with helping the family realize this option is offering to rather than taking from a family in grief. The conversation is a major step to the recognition of their loss, the initial response in the grieving process. Timing is critical and the family has to have time to understand the hopelessness of the clinical situation. Sensitivity to the family is vital and information about what brain death is and that it is terminal must be clearly understood before the option of donation is offered.

Often many families may misinterpret references made during a donation discussion in regard to the death of the patient in terms of brain death. Confusion occurs when the family believes that the death of the brain is different from the death of the person. Therefore, distinction between the clinical diagnosis of brain death and the actual legal declaration of death based on the diagnosis must be clearly understood. After sufficient time is allowed for the family to accept the inevitability of death, they are more inclined to perceive donation as an opportunity to create something meaningful and positive out of tragedy.

Training of the donation team is vital in dealing with grief and the donation process so the family does not mistakenly identify those providing care for the patient as agents for another patient who will benefit from a transplant. The Critical Care Nurse assists by enabling family members to spend time with the patient outside the normal hours so they can say everything that they may have always wanted to tell the loved one in private. Family members are also allowed to participate in the care of their love one with simple matters as assisting with a bed
bath or combing the patient's hair. The sensitivity of the hospital staff during this time helps to alleviate any guilt or resentment toward the hospital personnel. The families are further assured that the donor's body will be treated with respect and dignity during the donation process. Any questions regarding disfigurement, funeral arrangements, or cost of the donation process is handled by the donation coordinator. There is no cost incurred by the donor family for participation in the donation process.
STEPS IN THE ORGAN DONATION PROCESS

* Injury or disease resulting in irreversible loss of brain and brain stem function
* Identification of brain injured patient as potential organ donor
* Referral to local organ procurement organization
* Initial donor eligibility screening by telephone
* Determination of brain death
* Offering the family the option of donation
* Detailed donor evaluation
* Donor management
* Organ allocation
* Organ recovery surgery
* Organ preservation
* Organ transplantation
* Donor family follow-up and bereavement support
* Post donation follow-up with hospital staff
CLINICAL CRITERIA FOR BRAIN DEATH

* Irreversibility of coma established with known cause sufficient to account for loss of all neurologic function.

* Unresponsiveness to external stimuli.

* Absence of spontaneous respiration in the presence of hypercarbia.

* Absence of reflex activity, unless of spinal cord origin.

* Absence of cephalic reflexes which include no pupillary response to light, no eye movement with ice water calorics or doll’s eye maneuver, and no gag, cough, or corneal reflex.

* Exclusion of metabolic factors such as drug overdose, shock, hypothermia, or electrolyte imbalance.
DONOR EVALUATION

In order to optimize suitability for transplantation, each organ must be evaluated individually. This procedure ensures optimal function of each organ recovered while maximizing the number of organs harvested. After the initial evaluation of any potential donor, an accurate bedscale weight and measurement of height is taken. For HLA testing and crossmatching, an dissection of lymph nodes are made from the inguinal area. This will provide a proper crossmatch between donor and potential candidates.

Renal Evaluation

The first step is to rule out a past history of renal disease, severe renal injury, prolonged uncontrolled hypertension, family history of renal disease, prior surgery of the kidneys, ureter or bladder, and other renal problems such as hematuria, pyuria, proteinuria, or renal calculi. Baseline information concerning blood urea nitrogen (BUN), peak and terminal creatinine tests about renal function are obtained from the donors admission records. The patient's urine is analyzed for volume and status. The flank and pelvic areas are evaluated for signs of retroperitoneal hematomas or scars. If a peritoneal lavage or exploratory laparotomy have been performed, the results are reviewed. To determine the presence of proteinuria, casts, blood, or bacteria, a recent urinalysis and culture are obtained.

Cardiac Evaluation

As with all organs, the heart evaluation begins with reviewing the patient's medical record to rule out a past medical history. With the heart the history is reviewed to rule out evidence of cardiac disease, pronounced history of cardiac trauma, rheumatic fever, family history of cardiac disease, or previous cardiac procedures. Events prior to hospital admission and throughout are important to document for
hemodynamic measurements. An prolonged periods of hypotension or bradycardia are critically assessed. In addition, the patient is evaluated for episodes of abnormal cardiac rate or rhythm. Any previous cardiac arrest or resuscitation effort are thoroughly evaluated, as well as any chest injuries, cardiac contusion, thoracic or thoracoabdominal injuries. Ideal donor heart evaluation focuses on present heart function with normal cardiac function, however, mild abnormalities may be present. Tests such as a 12 lead electrocardiogram are required to determine the presence of either an old or recent myocardial infarction. In heart donors over the age of 45, a coronary angiography is performed to assess the presence and extent of coronary artery atherosclerotic disease. To evaluate valvular function, ventricular wall motion, chamber size, and estimate ejection fraction, a two dimensional echocardiogram is required. If heart function is found to be normal following clinical evaluation, a recent history of cardiac arrest or hypotension does not preclude heart transplantation.

**Heart-Lung and Lung Evaluation**

Because of the tendency for brain death and donors who are intubated, pulmonary infections, atelectasis and other abnormalities may be present making suitable donors for heart-lung or lung transplantation scarce. Careful attention is therefore given to pulmonary functions, avoidance of high-inspired oxygen levels, and excessive resusitation with fluids in potential donor patients. Family history is assessed for documentation of chronic cough, wheezing, pallor, asthma, cyanosis, or cardiac or pulmonary disease. Also noted are a past or present history of tobacco use of exposure to occupational hazardous materials. In order to document any episodes of prolonged hypotension, cardiac arrest, hypoxia, and acid-base shifts, an evaluation of hemodynamic test results are required. A reviewed or any previous surgery of the chest must be included, especially thoracic or cardiac surgery. To measure the lung fields, a chest radiography is performed. Other tests include an oxygen challenge test to measure the fraction rate of inspired oxygen on expiratory pressure and arterial blood gases. A gram stain and culture are obtained to discover the possible presence of polymorphonuclear leucocytes and bacteria. The anatomy of the lungs and character of secretions are evaluated via bronchoscopy. A complete cardiac is essential in any potential heart-lung donor and includes the detailed work-up specified for solely cardiac organ donors. However, abnormal cardiac evaluation does not rule out the potential for single or double lung transplantation.
Liver Evaluation

In reviewing a patient’s medical history for liver donation, an investigation of chronic alcohol abuse, significant gastrointestinal disease or previous abdominal surgery, hepatomegaly, or active blood clotting disorders as well as documented liver disease in the patient or in their family history is carefully explored. Assessment of hemodynamic status, hypotension, or cardiopulmonary arrest since the time of insult or injury are well documented. Liver functional tests results are performed and normal results are preferred, however, slight fluctuations in the values may be acceptable. Trauma to the liver is a probable rule-out but is evaluated on a case by case basis.

Pancreas Evaluation

The patient’s medical history for pancreas donor evaluation is reviewed for evidence of jaundice, gastrointestinal or pancreatic disease, chronic alcohol abuse, and family history of diabetes mellitus. Tests performed as a routine part of the evaluation include analysis of serial serum glucose and amylase.
Chapter 8

ORGAN SHARING: AN ANSWER TO THE SHORTAGE OF ORGAN DONORS

The demand for transplantable organs far exceeds the short supply. To further complicate the shortage, less than one-fourth of potential organ donors will actually yield an organ that is usable. Although the results of studies toward donation have indicated strong support for the concept of transplantation, efforts to improve the rate of recovery are necessary.

From 1988 through July 1990, a study was performed to assess the potential for organ donation in Kentucky. The study complied data to establish the number and location of potential donors in counties that were outside the area of organ procurement service. All medically suitable donors referred to the procurement agency were discovered from an ongoing death audit. Particular focus was placed on the process of approaching the family and the outcome of receiving signed consent. Aspects of medical care were correlated with the timing of the family preparation, education and approach for donation. In each aspect of the request it was noted as to time of occurrence and the person who performed the task. The failure to obtain permission for donation was again determined to be the main reason for failure.

Based on timing of request for organ donation in relation with brain death, each scenario was analyzed and classified according to two groups. When there was a clear indication that the family understood and accepted brain death before the discussion of organ donation occurred it was considered a decoupled situation. Whereas in those instances in which there was no separation between the explanation of brain death and request for donation, the criteria was consistent with the death notice and donation request occurring simultaneously and was then classified as being coupled.

According to the results of this study, in 1988; 23,263 deaths occurred in patients more than 65 years of age and 3,420 occurred outside a hospital facility. The remaining number of deaths occurring in the hospital were excluded based on the presence of established contraindication for organ donation. Thus, the potential pool of donors represented almost 3 percent of all hospital deaths which
occurred in patients under 65 years of age. Of these one hundred and thirty donors only 38 yielded a usable organ.

In each instance, demographic characteristics had causes of death of the donor under consideration. Most donors were male and white. All age, race, gender and education levels were equally represented in the potential screening. Trauma was the leading cause of death in most of the potential donors. Objection of the family was listed as the reason for not donating on 92 occasions in patients who had received aggressive resuscitative efforts but succumbed within the first few hours after arriving to the hospital. Most failures were however attributed to the physician not identifying brain death soon enough, and not allowing the family to be approached; or not referring a family to the organ procurement agency after brain death occurred. In these instances, delay of the referral made donor stability unacceptable due to rapid deterioration of the organs.

Most often it is the physician who is the person most likely to initiate the discussion regarding donation. Many successful requests were however, the result of the nursing service. In many instances, the consent for donation was denied by the family. Although legislation in Kentucky showed a broad public awareness and support for organ donation, the number actual of donations was low enough to mandate hospitals to establish procedures which ensured families of the option to donate when medically indicated. However, even when legislation showed in favor of improving the donation process, it did not assure the understanding of those in the health care system in how to best manage the request process. This apparently was the one principal factor as to why the percentages of donation in the state were so low.

In summary, the data showed that clear separation of the notification of brain death and the request process had a positive influence on donation. When request was made to a family that had accepted brain death, a donation resulted in half of the instances. When there was not clear acceptance of death, the results were to the contrary. The positive results of separating the brain death occurrence from the request process was noted even when the families who had initiated the request were removed from the comparison. Overall, the number of donors procured in the Kentucky service area improved, this was attributable in large to the visibility of this study within the major donor hospitals and emphasis on the decoupling of the request process. Subsequent review of the donor request process in 155 consecutive potential donors identified one factor that was the most important for positive donation results; the family must have time to understand and accept brain death before any request for donation to increase the
Increasing the number of organ donations.

Most European countries use "presumed consent" in their health care system. It presumes that people consent to donating their organs unless they have specifically objected before their death. Organs may be removed without prior consent of the next of kin. The United States by comparison uses the system of "required request," which states that the hospitals and doctors must inform patients or their families about the option of organ donation.

Although presumed consent in European countries increased procurement rates, the effectiveness of the system is in question in a recent trend toward opting for in-legislation and away from presumed consent. In California and England, some organizations and regions have achieved higher donation rates than the national average. In Canada, their system is much like the United States system of required request, their donor rates vary among provinces and region within provinces.

What is being done to increase the donor rate? Some countries have considered offering incentives to the donor family, some of which include financial compensation. Other strategies have included legislative amendments for required request and presumed consent. Other strategies particularly in the clinical setting now include the recruitment of living donors for lung, liver and bowel transplants in limited instances. Cadaveric donation as a means to recover organs from older donors, "non-heart beating", and donors with diabetes, hypertension or hypotension are considered in this new expanded criteria. What limits the number of donors in intensive care units is the practice of withdrawing ventilator support from patients when further treatment would be futile or prolonging life support until multiorgan failure occurs.

Changes in clinical settings could increase the number of available organs. Kidneys could be recovered from trauma patients who die soon after being admitted to the hospital for example. Organs in non-heart beating patients could be preserved in a perfusion technique employed shortly after pronouncement of death. The next of kin could then be requested to donate their relative's kidneys or tissues. In a study of this concept done in Illinois, all next of kin gave consent to donate. In many instances, families who decide to terminate life support, the organs could be removed immediately when the patient is pronounced dead. Another strategy to increase the donor pool is elective ventilation. A patient dying
as a result of a cerebrovascular accident could be given ventilation upon respiratory arrest in an effort to preserve the organs until consent for donation could be obtained.

Incentives

In a survey conducted by The United Network for Organ Sharing (UNOS), incentives as a means to increase organ donation were suggested. Half of those surveyed agreed that the incentives should be tried. The first choice in this survey was the voluntary method to donate organs in people after death via a donor card. This method would guarantee preferential status on a waiting list for a transplant should they need it. Other options on the survey which included cash incentives, were directed as financial compensation for the families for funeral expenses or to a charity the family specified, or limited life-insurance policies for the surviving relatives. The proposed financial compensation being a onetime payment of $1000 or $2000. Supporters of this compensation method suggested that donor families are not motivated by profit and hospitals are not buying the organs but were, "rewarding the act."

A regulated system of compensation to families does suggest that the organ retrieval rate would increase. After all, the system is not entirely altruistic now, Physicians, surgeons, allied health care professional, hospitals and pharmaceutical companies gain financially from organ donation. Why should we insist on altruism when only the donor family is expected to be altruistic? The Alternative Methods Subcommittee of UNOS does however plan to study rewarded gifting in terms of reimbursing funeral expenses and the preferred-status system.

According to The Canada Market Research for MORE Program of Ontario, Toronto: “Preferred-status” system is not considered an ideal choice due to the fact that many who want to donate after death fail to sign a donor card. Even when their intent is made known, the next of kin still have to be approached for consent. In addition, organ allocation may change, because preferential transplants would be given to those who have a previously signed a donor card. Potential heart and liver recipients who do not have an alternative treatment such as dialysis would have to wait longer. Some believe that access to transplantation would be changed if people do not know that they must sign a donor card for preferred status. If this situation were to occur then ethical principles such as non-discrimination and distributive justice would be jeopardized. Furthermore, some feel that family
compensation would undermine the ethical basis of the altruistic system. Concern is made that families would not give consent to donate if they can trade organs, i.e.: fostering the business principle of selling to the highest bidder...

The intent behind compensation or rewarded gifting is people's reluctance to donate. High refusal rates reflect the mistrust of the health care system. Supporters of rewarded gifting see family refusal to consent as a major barrier. By contrast, proponents of donor compensation in other surveys (established by UNOS), insist that the extent to which donor-family compensation is morally objectionable has been overestimated. Supporters further concur that the entire donation process involves payment for services rendered to every individual apart from the donor or the family, and payment of this nature is not considered to be morally objectionable. Therefore, the argument exists that donor-family compensation would likely encourage more people to become donors, and concern about the lack of altruism when financial compensation is considered is unfounded. It is also believed that why allow thousands of people to die each each waiting for suitable organs when compensation could lead to increased donation? However, since there is no proof that compensation would lead to increase in donation, this is speculative, as is the assumption that people would be morally outraged by the proposal.

Because compensation is legally prohibited by law, and presumed-consent would require legislation to be enacted, in the United States, support for a well-conceived nationally funded and advocated system of equitable distribution of organs is favored. This system would guarantee against exploitation, and benefit the privileged and underprivileged equally. Because financial compensation is prohibited by law in the USA, the system would include alternative methods of compensation such as assistance in payment of funeral expenses, cash award to the donors estate, or to their choice of charity, and a limited low cost life insurance policy redeemable on the donation of organs by the deceased policy-holder. The benefit of this “non-financial” compensation would be a “preferred-status”, and would guarantee the donor or preferential position on a waiting list should they need an organ transplant. This preferred status would be dispensed in the form of “extra points” on the UNOS points system but would not override medical urgency. When responders of a UNOS survey were asked to rank the various forms of compensation; preferred status was the top ranked option, followed by a $2000 payment to the donor family for funeral expenses.

If preferred status legislation were introduced in the United States, the implementation of this strategy could be done through the UNOS database.
In the general guidelines for recipient selection, each patient is assessed individually as a transplant candidate. There are a number of considerations that are taken into account in the selection process. The patient should have a reasonable life expectancy and be able to undertake the surgical intervention of the transplant procedure.

Risk factors that would affect a successful outcome for the patient and the transplanted kidney include contraindications which are *absolute* or *relative* (significant). *Absolute contraindications* include: incurable malignancy and infection, informed patient refusal, and refractory noncompliance. In patients with uncured malignancy or infection, there is an extremely high probability that these conditions will be intensified by immunosuppressive medication, therefore making transplantation improvident.

Because some patients have psychiatric disease or mental incapacity and will be unable to comprehend the problems or comply with the requirements necessary for care of a successful transplantation, the potential benefits and risks involved are thoroughly appraised and for many this procedure will not be an option.

Relative contraindication include those factors or conditions that would prove to be a significant increased risk, and only under unusual circumstances would these patients be considered as suitable candidates. The patient is considered acceptable if the relative conditions are remediable, such as coronary bypass surgery, aortoiliac reconstruction, or construction of ileal or colonic conduit. Age however is not considered remediable, therefore patients over age 65 are rarely transplanted due to the cumulative effects of the aging process and poor tolerance of immunosuppression; these patients are an operative risk.

An aging patient also has a high incidence of vascular disease which further makes them unsuitable. Risk factors have a potentially adverse effect on outcome. Some of these factors decrease the likelihood of graft success, many also have a negative effect on patient survival.
Absolute Contraindications

Incurable malignancy and infection
informed patient refusal
refractory noncompliance

Relative Contraindications

Unusable lower urinary tract
Chronic cardiac failure
Aortoiliac disease
Age >65 years
Chronic pulmonary disease
Renal disease with high recurrence rate

Significant Risk Factors

Age: <5 years, >45 years
Systemic disease leading to renal failure:
   Diabetes
   Amyloidosis
   Fabry's
   Systemic lupus erythematosus
   Scleroderma
Previous Gastrointestinal Disease:
   Liver Disease
   Pancreatitis
   Peptic ulcer disease
   Diverticulitis
Obesity and malnutrition
Renal disease with moderate risk of recurrence
Prior malignancy
When considering age, patients at both ends of the acceptable age range have a decreased rate of success in transplantation. Recipients younger than 5 years of age have poor graft survival due to an increase in vascular problems, donor selection, and rejection. However, transplantation in the pediatric patient does have advantage by permitting for more normal growth and development as well as psychological benefits. In the older recipient, much of the detrimental effect accrues from increased patient mortality rather than from unsuccessful grafting.

Each of the diseases which have systemic disease as the cause of renal failure also have non-renal manifestations that intensify the operative and long-term risks. *Diabetic* patients have increased risk factors secondary to cardiovascular complication, poor wound healing, and decreased resistance to infection. In patients with both primary and secondary *amyloidosis* the heart, liver, gastrointestinal tract, spleen and kidneys are affected. These patients have a higher than average post-transplantation mortality rate due to heart failure secondary to cardiac amyloid deposition; however, most of these patients will die of sepsis.

*Fabry’s* disease results in the accumulation of glycosphingolipid in all the tissues, including heart and kidneys. It is a metabolic defect which causes poor wound healing, and sepsis. High mortality rates from this disease make transplantation doubtful as a viable option.

Transplantation is withheld in patients with *Systemic Lupus Erythematosus* until the condition is latent and anti-DNA titer are absent. Occasional reactivation of systemic symptoms and renal recurrence have been noted in transplantation of patients with this disease. *Scleroderma* is a multisystem disease however, mortality and success rate are considered acceptable in many reported cases.

Pre-existing *Gastrointestinal Disease* represents an increased risk especially in *liver disease*. Advanced cirrhosis is a contraindication to renal transplantation. Pretransplant hepatitis B increases the magnitude of the risk. Long-term survival rate is decreased, partially owing to increased incidence of hepatic failure and infection. Significant factors in *pancreatitis*, such as gallstones, hyperparathyroidism, and alcohol intake play a role in recurrence following transplantation and these patients frequently have a poor prognosis.

A past history of *Peptic Ulcer Disease* is a contraindication to transplantation and require careful evaluation. Recurrence of the disease in post-transplantation patients carries significant increase in mortality. Diverticulitis in the transplanted patient is also accompanied by a high mortality and morbidity rate.
If the patient has the involved colon resected prior to being considered, the rate of successful grafting is greatly increased.

Both obesity and malnutrition have an injurious effect on wound healing and increase the potential for infection. Efforts are made prior to transplantation to correct these conditions in order to minimize the risks.

Immunologic High Responders are identified either by the presence of a broad antibody reactivity to the screening lymphocyte panel or by the early rejection of a previous allograft. Graft survival in these patients is poor.

Most forms of renal disease except for congenital abnormalities have a tendency to recur in the transplanted allograft. There are two primary reasons disease recurs, first many patients have inadequate histologic documentation of their original disease and prediction of recurrence in the graft may be difficult. Second, there may be disease present in the donor organ prior to transplantation. Ischemic injury, drug toxicity, and glomerulonephritis compound the histologic interpretation in donor biopsies.

Prior malignancy that has been treated and cured, still imposes an increased risk because of the potential of immunosuppression to affect the host-tumor interaction, permitting recurrence of metastasis.

Each patient must be individually evaluated as a potential transplant recipient. Attempts are made to identify those factors that will determine the operative, technical, and immunosuppressive risks. Once determined, the risks must be balanced against the likelihood of success of and the advantages of a successful renal transplant.
Chapter 10

LIVER TRANSPLANTATION

The indications for liver transplantation differ in adults and children. Each are grouped and considered separately according to the disease. The most common indications for liver transplantation in adults have been chronic active hepatitis, primary biliary cirrhosis, sclerosing cholangitis, inborn errors of metabolism, and primary liver tumors. In children the principle indications for transplantation include: Biliary atresia, postnecrotic cirrhosis, and inborn errors of metabolism.

B-virus antigen carriers transplanted for postnecrotic cirrhosis have a high incidence of recurrent hepatitis after transplantation. In infants, transplantation is complicated by a high incidence of hepatic artery thrombosis. Although liver transplantation across ABO blood groups is usually successful, results have been best between ABO compatible donor-recipient pairs.

When considering a patient for transplantation for primary liver cancer, it was the hope that this particular disease would be especially favorable for transplantation, since portal hypertension and its complications are usually not present. However, although early patient survival has been excellent, long term patient survival has been poor because of the high rate of recurrence of the tumors in immunosuppressed patients. It is found that the immunosuppression necessary to prevent graft rejection may accelerate the growth of extrahepatic nests of malignant cells unrecognizable at the time of transplantation. Efforts to improve survival have included conventional chemotherapy and radiotherapy in combination with total hepatic resection and transplantation, but results were still poor.

Cirrhosis is the most common indication for liver transplantation in adults. Most of these patients have chronic active hepatitis, few present with cryptogenic cirrhosis of Laennec's cirrhosis. Survival for cirrhotic patients over 40 years old is poor, this apparently relates to the coexistence of other risk factors present in these patients rather than the effect of age itself. For example, there is a significant incidence or hepatitis recurrence in b-virus carriers. Alcoholic patients have always been categorized in the high risk group, since their medical condition is often poor and the tendency to return to their former habits is a constant concern.
Primary biliary cirrhosis (PBC) is the second leading indication for transplantation in adults. This disease is uncommon and most often affects late middle-aged women. The cause is unknown but considered to be an autoimmune disorder. Since there is no effective medical therapy for this disorder, a sudden increase in the rate of serum bilirubin, progression of osteoporosis, or complications of portal hypertension, variceal bleeding, encephalopathy, and intractable ascites are indications for transplantation. There have been no reported deaths or confirmed recurrences of this disease one year post transplantation.

Sclerosing cholangitis is usually associated with other diseases, especially inflammatory bowel disease. Increased risk of carcinoma of the bile duct often coexists with this disease. Survival rate has been improving and risk of late recurrence of the disease or of bile duct cancer after transplantation is not yet known.

Inborn errors of metabolism include alpha-antitrypsin deficiency, Wilson's disease, hemochromatosis, tyrosinemia, and cystic fibrosis. Survival in this group of patients has been reported with good results except for patients who present in advanced stages of hepatic encephalopathy with acute hepatic decompensation from Wilson's disease. The mortality rate in this instance is 50%.

Indications for transplantation in children

Biliary atresia is the most common indication for liver transplantation in children. Most of these children have had previous operations, usually portoenterostomies (Kasai Procedure) and portosystemic venous shunts, often with little if any benefit. Transplantation is the only hope of long term survival in the child with biliary atresia.

The second most common indication for liver transplantation in children has been inborn errors of metabolism. Survival after liver replacement in these children has been excellent. There are other indications for transplantation in adults and children most have been done for cirrhosis, familial cholestasis, and neonatal hepatitis.

Selection of recipients for transplantation

Most patients are evaluated and referred to the transplant center with an established diagnosis and poor prognosis without transplantation.
A major gastrointestinal bleed, a history of recurrent bouts of encephalopathy, progressive neuropathy, refractory ascites, a recent precipitous deterioration in liver function, poor hepatic synthetic function, rapid progression of bone disease, and severe wasting are indications for early transplantation.

To assess surgical risk, a general evaluation of pulmonary, renal, and cardiac function is performed. Portal vein patency is evaluated by ultrasound. In selection of the donor, ultrasound measurements of the liver size are important as well as the patient's weight, height, and ABO blood group.

Cyclosporine has improved the patient survival rate and expanded the indications for liver transplantation. Years ago, liver transplantation was limited to patients younger than 55 years, however, survival of patients older than 50 years in cyclosporine treated patients as been just as good as survival for patients between 18 and 49 years of age.

Predictability of successful transplantation is based on preoperative risk factors and is difficult to access. Patients in deep coma for example, rarely survive unless their condition can be improved to the point that they are awake and off the respirator when taken to surgery. Nonetheless, even patients in acute hepatic failure and coma have survived if transplanted expediently. Since survival is unpredictable, patients for transplantation are routinely selected based on liver size, ABO blood group, and medical urgency. Only patients in deep, irreversible, subacute, or chronic coma have little chance of survival.
Chapter 11

PANCREAS TRANSPLANTATION

Pancreas transplantation is restricted to patients with secondary complications of diabetes. The procedure is performed to provide insulin replacement therapy in Type 1 diabetes mellitus, a disease in which the beta cells within the islets of Langerhans are destroyed by an autoimmune process.

There are more than one million insulin-dependent Type 1 diabetic patients in the United States. The majority of the cases are in children. Diabetes mellitus is the fourth leading cause of death by disease, the leading cause of blindness, and the cause of 25% of all cases of renal failure. Diabetic persons are four to seven times more likely to require an amputation and twice as likely to die of heart disease than the rest of the general population.

Either the whole pancreas or a segment can be transplanted. Because Diabetes mellitus is an autoimmune disease which results in destruction of the beta cells, recurrence of the disease in the graft has been reported. In general, however, immunosuppression prevents this occurrence.

Recipient selection and criteria for pancreas transplantation

Ideally, pancreas transplantation should be performed before the secondary complications of diabetes are prominent. However, almost all transplantations have been performed in patients who already display symptoms of nephropathy, retinopathy, or neuropathy.

The effects of immunosuppression necessary to prevent rejection of these particular complications is uncertain, as a result, most pancreas transplants are performed in diabetic patients with end-stage diabetic nephropathy who are undergoing or have had a kidney transplant, and in whom immunosuppressive therapy is necessary. Because of this selection process, most pancreas transplant patients have had such advanced complications that reversal or stabilization of the lesion may not be possible. However, patients who do not need kidney transplants are also considered as candidates, particularly those with preproliferative
retinopathy and at a great risk for loss of vision.

All patients considered for pancreas transplantation undergo an evaluation that includes the test listed below (from the University of Minnesota). These tests are repeated at yearly intervals after transplantation to document graft function and assess the course of secondary complications. Most important in the evaluation process is assessment of the cardiovascular system, since coronary artery disease may be present without angina in diabetic recipients with neuropathy, a high incidence of myocardial infarctions have been reported in some pancreas recipients.

Due to the side-effects of immunosuppression, pancreas transplantation has been almost exclusively limited to adult recipients over the age of 18 years.

CRITERIA FOR PANCREAS TRANSPLANTS

* At least some evidence of secondary complications (e.g., preproliferative or background retinopathy, albuminuria).
* Progressive complications, but not so far advanced as to be in a self-perpetuating stage independent of the metabolic state.
* Complications that predictably are, or will be, more serious than potential side-effects of chronic immunosuppression.
* Imperfect metabolic control on exogenous insulin.

PRE AND POST PANCREAS TRANSPLANT EVALUATION

* 24 hour metabolic profile
* Glucose tolerance tests
* Urine and serum C-peptide Stimulation with islet hormone secretogogues
* Insulin withdrawal (if no history of ketosis)
* Glycosylated Hb and islet cell antibodies
* Neurologic evaluation:
  Clinical exam, nerve conduction, autonomic tests, and quantitation of sensory loss.
* Ophthalmologic evaluation:
  Visual acuity, retinal photography, fluorescein angiography.
* Renal evaluation:
  Serum creatinine, creatinine clearance, glomerular filtration rate, renal
  blood flow, sieving curve, fractional protein clearance, provocative
  urinary albumin excretion, kidney biopsy.
* Cardiovascular evaluation:
  Stress EKG or thallium stress test, coronary arteriogram if stress test
  positive or history of angina or myocardial infarct.
* Camptodactyly (soft tissue) and joint evaluation:
  Clinical exam, goniometry, hand prints, tracking, skin collagen
  quantitation.
* Psychiatric evaluation.

Pancreas transplants can be performed simultaneously with or after a kidney
transplant. Most prefer to perform simultaneous procedures utilizing transplants
from the same donor. This approach allows monitoring of the kidney for rejection,
leading to earlier diagnosis and treatment of pancreas graft rejection.

Pancreas donor selection

Two types of donors are considered in the selection process, cadaver or related
pancreas donors. Almost any brain-dead cadaver that is a suitable match for use
as kidney donor is also suitable for use as a pancreas donor if there is no prior
history of diabetes. However, brain dead cadavers that may not be acceptable
as kidney donors due to a history of kidney disease but may be suitable as
donors for pancreas and other organ transplants.

Whole or segmental pancreas grafts can be obtained from each cadaver
donor, regardless of what other organs are also procured. The same methods for
use of related donors for kidney transplants are also applied to the use of related
donors for segmental pancreas transplants. A portion of the body and tail of the
pancreas can be removed from a living donor, based on a vascular pedicle of the
splenic vessels. The spleen of the donor can survive on collateral circulation,
and the remainder of the body, head, and uncinate process of the pancreas is
sufficient to maintain normoglycemia in the donor.

Most pancreas transplants from living-related donors have necessary criteria
that the prospective living-related donors must meet before being evaluated, these
criteria are listed on the following page. Living-related donor grafts have decreased
propensity to be rejected therefore have a higher rate of successful survival.
CRITERIA FOR SELECTION OF LIVING-RELATED PANCREAS DONORS

A. Pre-evaluation Criteria
   * Recipient and donor discordant for diabetes for at least 10 years.
   * Donor at least 10 years older than age of onset of diabetes in recipient.
   * In cases of sibling donation, no family members other than the proband are diabetic.

B. Post-evaluation Criteria
   * Normal oral glucose tolerance test result by criteria of Fajans and Conn and of the Natural Diabetes Data Study Group.
   * Delta insulin > 90 μ U/ml for sum of 0-, 60-, 120-, and 180-minute values during cortisone-stimulated OGTT minus sum during standard OGTT according to technique of Fajans and Conn.
   * No islet cell antibodies.
   * Other metabolic parameters normal.
CARDIAC TRANSPLANTATION

For patients with end-stage cardiovascular disease, cardiac transplantation is now an accepted alternative. Considerations for cardiac transplants include: left ventricular ejection fractions of less than 20%, and either ischemic or idiopathic cardiomyopathy.

**Absolute contraindications** include: active infection, recent pulmonary infarction, or elevation in pulmonary vascular resistance.

**Relative contraindications** are: diabetes mellitus, renal or hepatic dysfunction, peripheral vascular disease, and hyperlipidemia.

Donor selection is based on no prior history of heart disease or cardiac trauma, ABO blood group compatibility, and younger than 35 years of age. A donor of smaller size than the recipient is taken into consideration if there is urgency for transplantation.

Survival rates are currently one to five years- 80 to 50%. Mortality causes include infection, rejection, graft arteriosclerosis, and malignancy. The major cause of patient mortality after the first year is graft arteriosclerosis, this pathogenesis is believed to have an immunologic basis and remains an unsolved problem.

**Recipient considerations**

Although any patient with end-stage cardiac disease can be considered as a potential candidate for cardiac transplantation, successful outcome is based on many criteria.

Candidates usually have a left ventricular ejection fraction of less than 20%. In addition to either idiopathic or ischemic cardiomyopathy. Only a small percentage of transplant patients are considered with a history of previous congenital heart defect or rheumatic valvular disease.

Patients with cardiac cachexia (wasting), massive edema, ascites, infections, and renal insufficiency are considered special risks. Since the immunosuppressive regimen necessary for successful grafting will alter recipient immune response,
active infection would be difficult to eradicate, thus, patients with active infection and significantly elevated pulmonary vascular resistance may be excluded from consideration.

Age has been a prominent factor in predicting the outcome of a successful transplant. In the younger age groups <55 years, complications are better tolerated and more easily treated. The average age of cardiac transplant recipients is 38 years.

Diabetes mellitus is a major relative contraindication to cardiac transplantation. Patients with diabetes that is controlled by diet or medication have an increased likelihood for development of infection. Pulmonary infarction is another contraindication. The sites of infection often become repositories for fungal infection in the cardiac transplant recipient.

Other considerations which are assessed for adverse outcome are dysfunction in other organ systems and peripheral vascular disease. The presence of any form of peripheral vascular disease has the potential for altering the long-term outlook. Hyperlipidemia accelerates graft coronary artery atherosclerosis and is considered an adverse factor.

Recipient selection is a process that must include psychosocial factors in assessing candidacy. The patient’s ability to withstand the psychologic impact of transplantation and the regimen of medication necessary post-operatively is an important consideration in making this determination.

CONTRAINDICATIONS TO CARDIAC TRANSPLANTATION

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative *</th>
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<tbody>
<tr>
<td>1 Active infection</td>
<td>1 Diabetes mellitus</td>
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<tr>
<td>2 Recent pulmonary infarct</td>
<td>2 Renal or hepatic dysfunction</td>
</tr>
<tr>
<td>3 Pulmonary vascular resistance</td>
<td>3 Peripheral vascular disease</td>
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<td></td>
<td>4 Hyperlipidemia</td>
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<td></td>
<td>5 History of poor medical compliance</td>
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* Factors that alone or in combination may adversely affect survival.
LUNG TRANSPLANTATION

Lung transplantation has been achieved in both single lung transplantation, bilateral lung transplantation, and combined heart-lung transplants. Patients who have received some form of lung transplant have a reasonable expectation for long-term survival and improved quality of life, however, to date there have been no long-term successful lung transplants. Despite the recent advances, many problems continue to prevent use of lung transplantation as a means of relieving end-stage pulmonary disease.

Single lung transplants are effective in the treatment of bilateral chronic lung diseases. In some cases of severe pulmonary insufficiency one lung is left in place so it may ultimately recover. Use of a single lung can immediately relieve some forms of severe pulmonary hypertension and carry the entire cardiac output. Patients without pulmonary function in their remaining lung can survive solely on the function of their single lung transplant.

Any procedure involving transplantation of both lungs requires a donor with two healthy lungs and is relatively a rare occurrence.

In patients with terminal acute or chronic lung disease accompanied by advanced cardiac disease, combined auto transplants of the heart and lungs are considered as the procedure of choice. Studies show normal cardiopulmonary function lasts up to 2 years post operatively. The combined procedure has remarkable advantages in its relative technical simplicity. Improved healing of the tracheal anastomosis, elimination of all diseased lung tissue, and the maximal amount of functioning pulmonary parenchyma is achieved with this method.
CONCLUSION

Since the writing of this document some disturbing concerns related to transplantation have been expressed by the American public. These concerns were made in regard to a few major celebrities such as: baseball star Mickey Mantle, actor Larry Hagman, and singers Jim Nabors and David Crosby, whom have all acquired preferential status in transplantation of donor livers. These celebrities are over 65 years and chronic alcoholics. They are all in the high risk group for successful survival rate. This information has raised questions and public awareness concerning a privileged advantage involved in the decision making process of recipient selection by the health care system.

As a writer doing research I cannot pretend to know the nature of the legal issues that arise out of these disputes, my intent here is to simply clarify the reasons for the donor shortage situation. If in so doing I have uncovered any questionable practices, I apologize, with the hope that as a result of this paper these issues that have been controversial and under public scrutiny will ultimately become resolved.

It was my hope to increase donor participation in this thesis not to dissuade it. However, the fact remains, certain criteria for recipient selection need to be standardized without exception before the organ shortage can be remedied. Several suggestions as to financial compensation and reciprocal donor contracts have been indicated throughout this documentation. There are solutions... Unfortunately, there does not seem to be a present solution for the inadequacy of the American Health Care System to provide for all equally.

Until there is a time when the future looks promising for those who do need a transplant, many will still die waiting...

Lila Pummer-Verté
REFERENCES


REFERENCES


