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Multiple Organ Procurement

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Solid-organ transplantation (heart, lung, liver, kidney, pancreas, and intestine) has become a successful and widely accepted treatment for a variety of conditions. However, the shortage of cadaveric organs is hindering the larger use of this therapeutic option. In spite of the progressive evolution of public and professional understanding and acceptance of organ donation during the past 30 years, only a little more than 25% of potential brain-dead organ donors actually donate.[1-3] As of October 31, 1997, 55,789 transplant candidates were registered on the national organ waiting list compiled and managed by the United Network for Organ Sharing (UNOS), the agency that coordinates organ allocation in the United States.[4] This statistic represents a 580% increase from the 9,632 patients who were waiting in December 1986, whereas the supply of organ donors underwent only a moderate increase between 1988 and 1996 (from 4,083 to 5,417)[5-7] (Fig. 177-1).

It is estimated that every day seven potential organ recipients in the United States die before a suitable organ is found.[8] Consequently, although the need has increased dramatically, we observe with mounting concern the persistent wastage of available organs and the death of potential recipients. These are both mainly related to an unwillingness to donate or a lack of awareness regarding donation, as well as delays or failure by the medical staff to consider organ donation.[3] Other forces at work also have significantly decreased organ availability for the sicker patients, such as a policy implemented by UNOS in 1991 that substantially changed previous allocation criteria.[9] As a result of this, an even more limited number of organs are available for the most severely ill patients, and some advocate their outright exclusion from transplant candidacy in favor of the elective cases.[10, 11]

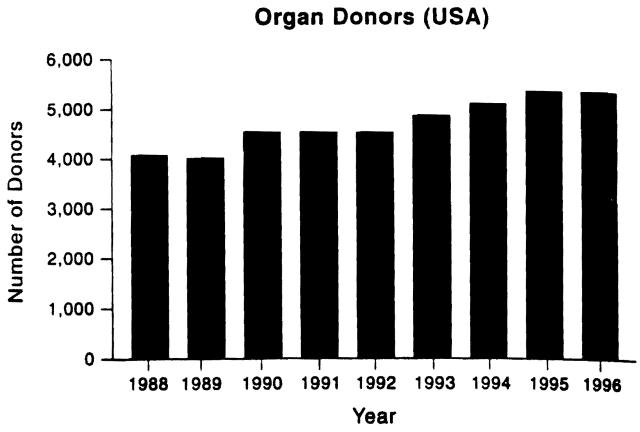

Figure 177–1. Organ donor supply in the United States from 1988 through 1996.

Many routes have been explored in an attempt to remedy this situation, including the development of artificial organs,[12] utilization of living donors even for extrarenal organs,[13-15] xenotransplantation,[16-18] and non-heart-beating donors.[19] However, a more immediate impact on organ shortage could be achieved by improving our current mechanisms for organ recovery and the management of potential donors.

ORGAN RECOVERY

Standardized criteria for the determination of brain death were defined by the Ad Hoc Committee of the Harvard Medical School[20] and have been the subject of a more recent report.[21] The concept of brain death and the management of the brain-dead donor are discussed in detail in Chapter 174.

Once a potential organ donor is identified, the multiple organ procurement process should be triggered. This starts by contacting the local organ procurement organization (OPO) as soon as the irreversibility of brain injury has been established. As of July 1, 1997, there were 54 OPOs and 280 transplant centers in the United States. These represent the largest organ procurement and transplant network in the world. Most intensive care units (ICUs) have the telephone number of the local agency available. However, the telephone number and location of area OPOs can be obtained from UNOS, which has a 24-hour telephone hot line (800-355-SHARE).

These OPOs, originally set up to organize the recovery of kidneys, now also coordinate the complex logistics of multiple organ recovery and their distribution within a predetermined geographic area. They are also responsible for the payment of all charges incurred during the process of organ donation, ensuring that donor families are not billed for any of them. Once contacted, the local OPO sends a procurement coordinator to the referring hospital. These coordinators perform a number of administrative and technical functions, covering every aspect of the donation process. On receiving a referral, they perform an evaluation and discuss organ donation with the potential donor's family, making sure the relatives have a complete and satisfactory explanation of the diagnosis of brain

death and a clear understanding of the organ procurement process.

Families should be informed separately but as soon as possible after the irreversibility of the lethal brain damage has been established and should be given a clear explanation of the prognosis. This measure will give them time to accept the patient's death and allow them to deal with their grief. It is important to respect this phase, because it has been demonstrated that consent for donation increases from 18% to 60% if the family is allowed to absorb the concept of brain death first and if the issue of organ donation is brought up later.[4] Religious beliefs about human life, the dead body, and life after death are important considerations for those involved in organ donation and transplantation. No major religion specifically prohibits organ donation, although in some situations there may be restrictions. Table 177-1 summarizes some of the major religious and cultural beliefs associated with organ donation and transplantation.[22] Families may feel the need to discuss the matter with a church representative before making a decision.

If the family decides to donate, a consent for donation form is supplied by the hospital or by the procurement coordinator, and it is completed and signed by the next of kin. In addition, the coordinator ensures that all medicolegal requirements are met, from adequate documentation of brain death in the chart to securing permission from the coroner when necessary. Medical staff privileges for the recovery teams are also arranged. Hospitals differ in their policies for granting such privileges. Some hospitals do not consider the organ procurement a surgical procedure because a determination of brain death has been made. In this circumstance, temporary privileges are not required for outside surgeons.

At the same time, the procurement coordinator assumes control of three main activities:

- Donor evaluation
- Coordination of donor and recipient matching
- Donor operation and organ preservation and shipment to the recipient's hospital

The role of the coordinator in each of these is critical, because the most important issue in organ procurement, once the decision to proceed has been made, is to have someone who "directs traffic," maintaining clear lines of communication between the members of the different teams involved. A lack of communication at this point can disrupt donor care and compromise organ stability. Therefore, the needs and protocols of the individual teams should be discussed in detail before any donor surgery begins. If possible, the logistic arrangements between teams should be expedited so that no time constraints are placed on the host team. On the other hand, the host team must be tolerant because different organs often have to be flown to distant parts of the country, and some recipient surgery may be quite complex and time-consuming. To facilitate matters, the host team should make available basic information on the donor to expedite the evaluation by the visiting teams (Fig. 177-2).

DONOR EVALUATION AND MANAGEMENT

There are few absolute contraindications to organ donation, and they can be grouped into three broad categories:

1. Severe trauma.
2. Malignancy outside the central nervous system (CNS).
3. Active infections.

Trauma refers only to major injury to the organ itself and does not preclude donation of those organs not affected. Even in the case of a major trauma, however, the final decision to use or discard the organ should be made only after surgical examination of the donor and careful examination of the organ's anatomy. In the case of a liver trauma, for example, many organs can be saved if the donor team is experienced in liver surgery. Minor, and even major, parenchymal lesions can be repaired in situ, and the vascular anatomy can be precisely determined during the final preparation of the organ. Techniques of transplantation of liver segments have been

TABLE 177–1. Major Religious and Cultural Beliefs Associated with Organ Donation and Transplantation

Group	Donation	Transplantation
Amish	Reluctant if transplant outcome uncertain	Acceptable for the well-being of the candidate
Baha'i	Acceptable	Acceptable
Baptist	Individual decision	Acceptable
Buddhist	Individual decision	Buddha's teachings on the middle path (i.e., the avoidance of extremes) could be applicable to this
Christian Science	Individual decision	Individual decision
Episcopal	Encouraged	Encouraged
Evangelical Covenant	Encouraged	Encouraged
Greek Orthodox	Acceptable (although not for research)	Acceptable for the well-being of the candidate
Gypsies	Against	Against
Hinduism	Individual decision	Individual decision
Islam	Acceptable (organs of Moslem donors must be transplanted immediately, and not stored in organ banks)	Acceptable
Jehovah's Witness	Individual decision (not encouraged)	May be considered acceptable (organs should be completely drained of blood before transplantation)
Judaism	Generally encouraged	Encouraged
Latter-day Saints (Mormon Church)	Individual decision	Individual decision
Protestant denominations	Individual decision	Acceptable
Society of Friends (Quakers)	Individual decision	Individual decision
Roman Catholic	Encouraged	Acceptable
Unitarian Universalist	Acceptable	Acceptable
United Methodist	Encouraged	Acceptable

Donor Information | **Donor ID#** | **UNOS ID#**

Name _____ Admitting Date: _____ Referral Date: _____

Age: _____ Sex: _____ Race: _____ Recovery Date: _____ Clamp Time: _____ AM PM

Date of Birth: _____ Hospital: _____

Next of Kin: _____ City/State: _____

Relationship: _____ Referred By: _____

Address: _____ Phone #: _____

_____ Program: _____

_____ Program 24 hr #: _____

Next of Kin Phone: _____ Attending: _____

Consulting: _____

Medical Records No.: _____

Pronouncement Date: _____ Time: _____

Consent For: _____

_____

Cause of Death: _____

Past Medical History: (Complete history please)

Heart Disease: (Y/N) _____

Liver Disease: (Y/N) _____

Renal Disease: (Y/N) _____

Diabetes: (Y/N) _____

Neurological: (Y/N) _____

Cancer: (Y/N) _____

Lung Disease: (Y/N) _____

Arthritis or Joint Disease: (Y/N) _____

Recent Flu-like Symptoms: (Y/N) _____

Unexplained Weight Loss: (Y/N) _____

Toxic Exposure: (Y/N) _____

Drug Use: Prescribed or Other: (Y/N) _____

Alcohol Abuse: (Y/N) _____

Smoker: (Y/N) _____

Blood Transfusion History: (x 2 yrs.) (Y/N) _____

Previous Surgery: (Y/N) _____

Immunization or Vaccinated: (x 6 mo.) (Y/N) _____

Travel outside U.S.A. since 1977: (Y/N) _____

Homosexual or Bisexual: (Y/N) _____

Received pit-hGh: (Y/N) _____

Recent Infections: (Y/N) (if yes give treatment) _____

_____

G.I. Disorders: (Y/N) _____

Hematologic Disorders: (Y/N) _____

Under Physician's Care: (Y/N) _____

Physician, Phone #, Address: _____

Donor Information **Donor ID#**

ABO: _____ HLA: _____ DR: _____ LE Type: _____ WT: _____ HT: _____

Chest Cir: _____ Girth: _____ RC/BRR: _____ LC/BLR: _____

Hospital History (Include E.R., V/S, Arrests, O.R. Procedures, Injuries, Infection, ect.)

_____

_____

_____

EKG, Echo & Cardiac Consult:

_____

_____

Chemistries					Urinalysis				ABG'S & Lytes			
Date					Date				Date			
BUN					Color				pH			
Creat.					Appear.				PO2			
T. Bil.					pH				PCO2			
D. Bil.					Sp. Grav.				O2 Sat.			
SGOT					Glucose				FIO2			
SGPT					Protein				PEEP			
LDH					Blood				VT			
GGT					RBC				Rate			
Amylase					WBC				Na +			
CPK					Epith.				K +			
Glucose					Casts				Cl -			
Hgb/Hct.					Bact.				Ca ++			
PT												
PTT												
Plat.												
WBC												

Blood Pressure (Note B/P< 90.Time)	Urine Output (Note Anuria/Oliguria)	Med. During ADM
		Blood & Blood Products

Serology

Date	Time	Test	Pre	Post Result	Local/Import	Reported By	Reported To
		RPR/VDRL					
		HBs Ag					
		HAA					
		HIV					
		HTLV-I					
		CMV					
		HCV					

Cultures (Blood, Urine, Sputum) Date, Results

_____

_____

Figure 177–2. Donor data sheet used by the Western Pennsylvania Organ Procurement Organization, CORE (Center for Organ Recovery and Education). (Courtesy of Brian Broznick.)

described and successfully used, particularly in pediatric patients. These techniques may be used to rescue a liver partially damaged by trauma.

Malignancy, other than primary CNS tumors, is an absolute contraindication to organ donation.

The presence of active *infections* is an exclusionary criterion that deserves close attention. Systemic sepsis, active tuberculosis, viral encephalitis, and Guillain-Barré syndrome are contraindications to organ donation, as well as active hepatitis or the presence of the hepatitis B surface antigen. Past infection with the hepatitis B virus (HBV), as evidenced by the presence of antibodies, was not considered a contraindication to organ donation until recently. Early in 1995, a study showed the transmission of hepatitis B in eight of 13 liver recipients (negative for HBV infection before the liver transplant) transplanted with livers from hepatitis B core antibody-positive donors.[23] Our policy at the Pittsburgh Transplantation Institute is to use these donors only for hepatitis B core antibody-positive recipients.

Whether organs should be used if the donor has hepatitis C antibodies has been the subject of controversy in the past few years, as there is evidence of hepatitis C virus (HCV) transmission after transplantation.[24] However, the organ shortage is so severe that the use of HCV antibody-positive donors must be seriously considered, at least for life-saving organs such as the liver, heart, and lungs.[25] Obviously, for active disease to be ruled out, a prospective HCV antibody-positive donor absolutely requires a frozen section examination of the liver before implantation.

The human immunodeficiency virus (HIV) has greatly affected the field of transplantation. After the screening enzyme immunoassay became available in March 1985, a number of positive kidney, heart, and liver recipients were quickly reported.[26] However, the extent of the problem was clearly defined only after a large study of 1043 transplant patients was completed at the University of Pittsburgh. It was found that, overall, 1.7% were positive for HIV, with the incidence in liver transplant patients being 2.6%. Only a third of these patients were positive before the transplantation, as determined by testing stored pretransplant sera.[27] Donors who test positive for HIV antibody are now automatically rejected.

Prospective donors should also have a Venereal Disease Research Laboratory (VDRL) test as well as cytomegalovirus (CMV) titers, determined as soon as possible. The significance of a positive VDRL test is difficult to ascertain, but it is our practice to treat recipients of VDRL-positive donors with a course of benzathine penicillin. The CMV status of the donor has prognostic significance regarding the incidence and severity of subsequent CMV infections. Recipients of organs harvested from seronegative donors have a lesser chance of developing a CMV infection, regardless of their own serologic status.[28, 29] Epstein-Barr virus and varicella-zoster virus (VZV) are not part of the routine donor viral screening. The only situation in which these viruses become relevant is when the donor has active disease related to them (infectious mononucleosis or systemic VZV infection). In these cases, organ donation should not be considered.

Donors with infections under control or those affecting organs not specifically considered for donation (i.e., an abdominal organ donor suffering from pneumonia) may still be suitable. Children who die as a result of bacterial meningitis related to *Haemophilus influenzae* or *Neisseria meningitidis* can still be considered for donation if the organism and its sensitivity are known beforehand.

Prolonged organ ischemia related to severe hypotension or cardiac arrest might represent a contraindication to donation. However, it is the policy of the Pittsburgh Transplantation Institute to critically evaluate all donors, including those with cardiac arrest and prolonged cardiopulmonary resuscitation (CPR). In fact, many of these donors have been found acceptable by post-CPR physiologic and biochemical criteria, and their organs have been successfully transplanted.[19, 30]

Other patients who may not be acceptable as donors are those with a long-standing history of diabetes mellitus, hypertension, and cardiac or peripheral vascular disease. Again, however, the donor and organ viability should be assessed on a case by case basis. A patient who is not acceptable as a heart or lung donor might still be an excellent abdominal organ donor. Sometimes the suitability of individual organs can be assessed only after direct examination by the donor surgeon at the time of procurement.

The donor's age deserves special mention. The chronologic age is less important than the physiologic age in assessment. For some organs, age may not be an important limiting factor.[31-32] We have successfully used livers from donors as old as 75 years. In 1985, Popper[33] dedicated an extensive review to the aging of the liver. According to his study, the liver's great functional reserve, its regenerative capacity, and its large blood supply are the key factors in its delayed aging compared with other organs. Based on these considerations, it has long been thought that the liver is less affected than other organs by senescence.[31, 32] However, the demonstration that satisfactory livers can be obtained from donors well into the seventh decade of life or beyond was followed by a flurry of confirmatory reports, countered by descriptions of degraded results using geriatric livers.

Less has been written about the effect of the donor's sex on outcome of liver transplantation. Extensive literature, summarized by Neugarten and Silbiger,[34] shows poorer results with kidney allografts from female donors.

We have examined the effects of donor age and sex on the outcome of a consecutive series of 462 liver transplants, which included the use of 54 donors aged 60 years or older. Nine other donor variables and eight recipient variables were also analyzed, with the endpoint of the analysis being *graft failure* (defined as either patient death or retransplantation). Graft failure was significantly associated with donor age and donor sex. The effect of donor age was evident only when the donors were aged 45 years or older. Livers from female donors yielded significantly poorer results, with the 2-year graft survival of the female to male combination being 55%, female to female 64%, male to male 72%, and male to female 78%.[35]

We believe that older female donors (≥60 years) are questionable for liver procurement because in them the adverse effects of age and gender are at least additive. Because of the current organ shortage crisis, we believe that these livers should still be used, but under circumstances that are adjudicated on a case by case basis. For example, many liver transplant centers in North America and in Europe exclude from recipient candidacy patients who are HIV-positive, HBV carriers with evidence of deoxyribonucleic acid (DNA) replication, and others with risk factors that predictably degrade patient and graft survival. These patient categories would certainly be better helped by receiving geriatric female livers rather than being automatically excluded from transplantation. Table 177-2 shows the age guidelines for individual organs used in our institution. In general, it is rare to find a suitable heart or lung allograft from donors older than 60 years of age because of the increased incidence of coronary artery disease and chronic pulmonary disease.

In summary, given the enormous need for organs and the few criteria that absolutely disqualify a potential donor, the local OPO should be contacted in virtually every case. Figure 177-2 shows the data collection form used by the Center for Organ Recovery and Education, which is the organ procure-

TABLE 177–2. Age Guidelines for Organ and Tissue Donation Used at the Pittsburgh Transplantation Institute

Organ/Tissue	Age (yr)
Heart	≤60 yr*
Heart-lung	≤60 yr*
Lung	≤60 yr*
Kidney	1 month–75 yr*
Liver	≤75 yr*
Pancreas	≤65 yr*
Intestine†	
Bone	15–65 yr
Bone marrow	≤75 yr
Cornea	1–65 yr
Skin	15–65 yr
Heart valve	≤55 yr

*Donors beyond these age limits could be accepted on the basis of the individual organ function. Female donors aged 60 years or older are questionable for liver procurement because in them the adverse effects of age and gender are at least additive.

†No age limits have been set for intestinal donors. Intestines should be available from most organ donors and are always evaluated on an individual basis.

ment agency for western Pennsylvania, southern New York, and West Virginia. These data should be promptly faxed to those involved in the evaluation process.

Individual Organ Assessment: Abdominal Organs

The criteria used to determine the suitability of kidneys are very flexible. As shown in Table 177-2, a kidney donor can be between 1 month and 75 years of age. Serum creatinine and blood urea nitrogen (BUN) are used as markers of donor renal function and should be normal. Obviously, donors with chronic renal disease are not considered for kidney donation. However, patients with transient creatinine and BUN elevations related to dehydration, hypotension, or both are not excluded from kidney donation if the BUN and creatinine fall after appropriate volume correction.

Attempts at predicting liver allograft function after transplantation based on donor information have met with little success. The diverse literature devoted to the topic is testimony to our lack of a clear understanding, one that can translate into well-informed decision making during donor evaluation.[45, 45-46] As a rule, the donor should have normal or near-normal serum aspartate transaminase (AST), serum alanine transaminase (ALT), bilirubin, and prothrombin time, but we have successfully used livers from donors with AST and ALT that were 10 times greater than the upper limit of normal. The important parameter is not an isolated AST or ALT value, but the trend established since the ICU admission.[47] The bilirubin can be elevated as a result of massive blood transfusions used during the resuscitation of a shocked patient. A history of hepatitis or alcoholism is certainly a warning sign but does not preclude the use of the liver. In general, in the case of a marginal liver donor, the intraoperative assessment by the donor surgeon is the best single piece of information.

There is only one absolute exclusion criterion in the evaluation of a pancreas donor: a history of diabetes mellitus. Amylase elevations have been seen in as many as 39% of pancreas donors without any evidence of pancreatitis, and thus isolated hyperamylasemia does not contraindicate the use of the pancreas.[48] The serum glucose may be falsely elevated in donors receiving steroid therapy or as a result of decreased circulating insulin.[49]

Intestinal transplantation is emerging as a valuable modality for the treatment of patients with intestinal failure. Early in 1993, UNOS formed a subcommittee responsible for systematizing the listing of recipients, helping identify suitable donors, and establishing guidelines for the equitable allocation of intestinal grafts at both the local and national levels. Because of the time constraints, it is impossible to perform a functional assessment of the donor bowel. Relatively young age, hemodynamic stability, and donor-recipient size match are the critical parameters used in evaluating an intestinal donor.[50] At our institution, preference was initially given to infant and juvenile donors with stable hemodynamics. However, the age range has gradually expanded, providing the donor is stable and receiving minimal vasopressor support (≤10 $\mu g/kg^{-1}/min^{-1}$ of dopamine). Size matching is always given special consideration. The majority of intestinal transplant recipients have undergone extensive intestinal resections, leading to a significant reduction in the size of the abdominal cavity. Therefore, donors are chosen who weigh 15% to 40% less in body weight than the selected recipients.[50]

Individual Organ Assessment: Thoracic Organs

Aside from a negative history of cardiac disease and a normal chest x-ray film, the donor should have a normal heart physical examination and 12-lead electrocardiogram. However, a number of electrocardiographic changes may be detected in brain-dead patients, which do not preclude thoracic organ donation.[51, 52] A brain-dead patient who is able to maintain a systolic blood pressure greater than 90 mm Hg with a dopamine requirement less than 10 $\mu g/kg^{-1}/min^{-1}$ is considered a suitable candidate for heart donation.[53, 54] Cardiac isoenzymes are recommended in the case of chest trauma, to rule out myocardial contusion, and when the potential donor has suffered a cardiac arrest or prolonged hypotension. In male donors older than 35 years of age, the incidence of coronary artery disease increases, especially with risk factors such as hypercholesterolemia, a family history of heart disease, and a history of smoking. Coronary angiography may be helpful in the evaluation of high-risk and older donors, but it is not routinely required and most hospitals find the logistics of performing it prohibitive. Therefore, a decision must be made based on a cardiologic consultation, evaluating the history, electrocardiogram, and echocardiogram.

As is the case for the liver, and because of the severe shortage, it is prudent, even in high-risk donors, for the heart to be examined on the operating table following sternotomy. Visualizing and palpating the coronary arteries provides a significant amount of information with respect to the incidence of coronary artery disease. If plaques are felt along the left main coronary artery or left anterior descending artery, the heart, in most cases, is not suitable for transplantation. In extreme cases of a sick recipient, however, the transplantation team may decide to use this heart. Isolated cases of coronary artery bypass being performed at the time of transplantation have been reported. Reports exist of cases of isolated mild coronary artery disease in which the donor allograft functions well, with no increase in early mortality.

Transesophageal echocardiography has been demonstrated to be an important adjuvant in the evaluation of a potential cardiac donor. Severe cardiac hypertrophy, valvular defects, and global myocardial dysfunction or segmental wall abnormalities have been diagnosed in what appeared to be otherwise reasonable cardiac donors. At this time, limited information is available about the use of such hearts. In most cases, it is prudent to avoid the use of a heart with demonstrated wall-motion abnormalities.[55] In general, minor changes in the electrocardiogram or echocardiogram, localized infection,[56]

transitory hypotension, brief cardiac arrest, and thoracic trauma do not contraindicate heart donation. The importance of donor-recipient weight mismatch greater than 20% is critical only in the face of high pulmonary vascular resistance. In carefully selected donors, survival after transplantation with a donor between 40 and 55 years of age is no different than that observed in the case of younger donors.[57] As the limits for donor selection are extended, it becomes more evident that it is safe to extend donor age up to 55 to 60 years and ischemic time longer than 4 to 5 hours.[58-60]

The presence or absence of cardiac or cardiopulmonary arrest in itself is not a contraindication to the use of a heart for transplantation. Especially in the pediatric population, it has been found that even in donors who have undergone extended CPR (up to 125 min), as long as cardiac function at the time of cardiectomy is normal, there does not appear to be an increased risk for performance of the heart or survival of the recipient after transplantation.

All of the selection criteria mentioned in the case of a heart donor also apply to heart-lung or isolated single or double lung donors. In addition, a donor is not acceptable for lung or heart-lung donation when there is a history of heavy smoking, chronic lung disease, or pulmonary aspiration. The height, weight, and chest circumference of the heart-lung donor should closely match those of the recipient. A number of physiologic parameters can be used when assessing a lung donor, including the partial pressure of arterial oxygen/fraction of inspired oxygen (Pao_2/FIO_2) ratio ($\geq$250 mm Hg) and peak airway pressure ($<$30 cm H_2O with 15 mL/kg of tidal volume and 5 cm H_2O of positive end-expiratory pressure [PEEP]).[61-63] Aspiration pneumonia is frequent in the brain-dead patient, and thus the character of the sputum is a critical piece of information. The role of bronchoscopy is still being debated; it is considered mandatory by some authors,[64] whereas others believe it is indicated only when there is a question of foreign-body aspiration or to obtain sputum for Gram's stain and culture.[9] Bronchoscopy, however, provides important culture information to guide appropriate antibiotic therapy after transplantation. If frank purulence is noted on bronchoscopy, the lungs are not suitable. However, one lung may be salvaged for transplantation from a set in which one appears to be more infected than the other.

COORDINATION OF DONOR AND RECIPIENT MATCHING

Once the coordinator finishes the donor evaluation, there are still many hours of intense work before completing the process. After obtaining the appropriate consent, therapeutic efforts should be geared to protect the donated organs until the actual retrieval is accomplished. Their integrity should be maintained by optimal organ perfusion, avoidance of further damage, and subsequent removal and preservation with minimal ischemic injury. Care of the donor during organ procurement, therefore, requires a continuation of the intensive care that was provided before brain death was declared, followed by a precise surgical procurement procedure. Whereas in the 1970s and early 1980s donor management mainly, if not exclusively, addressed kidney function, the patient now must always be approached as a multiple donor, and this can present a real challenge to the physician managing the case.

The physician should keep the patient hemodynamically stable with optimal organ perfusion and oxygenation. This is not easy because of the loss of many body reflexes and the dramatic changes in the hormonal milieu.[65] Several studies have shown a significant reduction of cortisol,[66] insulin,[66] and thyroid hormones.[51, 66-70] About 50% to 70% of brain-dead patients suffer from diabetes insipidus.[71, 72] A number of protocols that call for the use of hormones such as triiodothyronine, cortisol, or insulin during donor management have given conflicting results.[49, 52, 67, 69, 70, 73]

The details of donor management are provided in Chapter 174 and are not repeated here. We stress only a few points we believe are important. Adequate perfusion should always be maintained while keeping the use of vasoactive drugs to a minimum. This may require the administration of several liters of fluid to obtain adequate filling pressures. Replacement therapy with fresh frozen plasma, platelets, and cryoprecipitate may be used if a serious bleeding diathesis is present. However, even if fibrinolysis is suspected, ϵ-aminocaproic acid should be avoided because it can induce microvascular thrombosis in the donor organs.

During this phase, the procurement coordinator asks local transplantation programs about their needs for organs. Under the current system, local programs have first priority, and only when organs are not used locally are inquiries made at the regional and national levels. An exception to this rule is when a prospective kidney recipient who resides in another region is found to have a so-called six-antigen match. These kidneys have to be sent away, with the receiving transplantation center "paying back" at a later date. Organ allocation is a very complicated and controversial subject, and what system should be used is presently being debated.[10] As of this writing, amendments to the National Organ Transplant Act (NOTA) are being discussed in Congress, and it is not clear what changes will be implemented.

A point system for renal transplantation was developed in Pittsburgh in 1985. Credit points were given to renal transplant candidates for time waiting, quality of antigen match, degree of immunologic sensitization, medical urgency, and logistic considerations of getting the donor organ and the recipient together within the time limitations of safe organ preservation. The system began in western Pennsylvania on January 1, 1986.[9] Although initially adopted by UNOS on November 1, 1987, the point system never went into effect at the national level because of difficulties encountered in reconciling it with a myriad of local interests. A similar point system was developed for liver transplantation, having been in place in Pittsburgh since January 1987. Our experience with organ allocation based on point systems, in which organs go to those who have been waiting longer or are sicker, has been most favorable.[10, 11] Graft and patient survivals have not suffered by giving organs to sicker or older patients. At the same time, our observations provide some assurance that the concepts of equitable access and efficient use of a scarce societal resource are not mutually exclusive.

Although human leukocyte antigen (HLA) matching is not a critical issue for extrarenal organs, we routinely perform HLA typing on all extrarenal organs, a practice at variance with what most other institutions do in the United States. Although it is expensive, we consider it important because it allows us to determine the presence of microchimerism in the recipient, information that may be extremely useful in the future when deciding how to manage the immunosuppression.[74]

When the recipients for all the abdominal and thoracic organs are identified, an operating room (OR) time in the donor hospital is arranged. The procurement coordinator contacts the recipient institutions to arrange for the simultaneous arrival of all the harvesting teams. Kidneys have been procured by local teams for many years and shipped if they were not used locally. Today, a similar practice is being adopted in the United States for other organs, particularly livers.[75]

The intestinal donor should receive intravenous ampicillin and cefotaxime at the appropriate doses when first evaluated and every 6 hours after that. The last dose is given in the OR at the time of harvesting. Polyethylene glycol-electrolyte

solution (GoLYTELY) is administered through the nasogastric tube to flush the intestine. The total amount ranges from 250 to 2000 mL, depending on the recipient's body size (250 mL in the infant and 2000 mL in the adult), and the administration rate is 10 to 30 mL/min. After the intestinal flushing, an antibiotic mixture that includes polymixin E (100 mg), tobramycin (80 mg), and amphotericin B (500 mg) is given through the nasogastric tube every 4 hours until procurement. In pediatric donors, the doses are halved, whereas infants receive only one fourth of the dose. Newborns receive no intestinal preparation. If preharvest flushing cannot be performed, this is done after procurement, using cold lactated Ringer's solution. Polymixin B or kanamycin can be substituted for polymyxin E, if the latter is not available at the donor hospital.

MULTIPLE DONOR OPERATION

Anesthesia

The donor operation can be time-consuming, and the role of the anesthesiologist is very important, especially if we compare the multiple organ procurement that is now usually performed with those carried out in the past, when the kidneys were often the only organs removed. A complete review of the anesthetic aspects of organ donation was recently published,[76] and we will restrict ourselves to its salient points.

The goal of medical management during organ procurement is to avoid ischemic organ damage by optimizing organ perfusion. Therefore, care of the donor is a continuation of the intensive care that was provided before brain death (see Chapter 174). The most important issue is the clear communication between the members of the procurement team because the surgical procedure and procurement protocol may differ depending on the procurement team and the specific organ. For the preoperative evaluation of the donor, the anesthesiologist should review the medical and surgical histories, including the cause of brain death, condition and supportive measures of vital organs, drug allergies, and medications. Cardiopulmonary function is assessed by means of the hemodynamic profile, requirement of inotropic support, efficiency of gas exchange, degree of ventilatory support, chest radiograph, electrocardiogram, arterial blood gas tensions, and acid-base state. Renal function is evaluated by urine output, BUN, and serum levels of creatinine and electrolytes. Hepatic function is evaluated by AST, ALT, and bilirubin, and pancreatic function is evaluated by blood glucose level and serum amylase. Hemoglobin concentration and the blood type of the donor are identified to prepare blood products. In addition, the validity of brain-death certification, consent from family members, and permission from the coroner are verified. The transition from the ICU to the OR is a crucial period, and the donor is continuously monitored, ventilated, and treated.

Intraoperative care of the donor is essentially similar to that of other critically ill patients undergoing major surgery, although management of pathophysiologic changes unique to the donor should be clearly understood. In general, equipment and medications routinely available for general anesthesia are satisfactory for the management of donors. However, a volume ventilator may be needed for donors requiring high levels of PEEP or airway pressure. The OR should be kept warm, and a warming blanket and blood warmer are necessary to prevent hypothermia. A large volume of crystalloids and colloid solutions (e.g., 5% albumin, plasma protein fraction, or hetastarch) and five units of packed red blood cells should be prepared. The electrocardiogram is monitored, preferably using lead V_5, to detect arrhythmias or myocardial ischemia, particularly in heart donors. Blood pressure is monitored by an indwelling catheter in the radial artery or brachial artery. The femoral artery cannulation is avoided because the aorta will be cross-clamped. Central venous pressure (CVP) monitoring is essential,[77] and a pulmonary arterial catheter is useful in unstable donors. Two-dimensional transesophageal echocardiography may be used to assess preload and cardiac contractility in unstable heart donors. Urine output and body temperature are monitored, and all or some of the following laboratory tests may be needed: hemoglobin and hematocrit, arterial blood gas tensions and acid-base state, serum electrolytes, ionized calcium, lactate, and blood glucose level.

General anesthetic agents are required to blunt sympathetic response that occurs during surgery.[78] This so-called mass reflex is caused by neurogenic vasoconstriction and stimulation of the adrenal medulla by the spinal reflex arc and manifests as tachycardia hypertension, perspiration, and involuntary movements. These movements, also known as the *Lazarus sign,* which includes arm and hand movements toward the body, can be disturbing to those involved in the organ recovery, and muscle relaxants should be administered ahead of time.

Isoflurane is the agent of choice because the degree of myocardial depression is less than with other inhalation agents. Halothane is avoided in liver donors because hepatotoxicity may be a concern in the presence of potential hepatic ischemia. Enflurane is avoided in kidney donors because it increases the blood level of inorganic fluoride. Short-acting narcotics, such as fentanyl (5 to 10 μg/kg), may be used in hemodynamically unstable donors. In addition, muscle relaxants (pancuronium bromide, 0.05 to 0.1 mg/kg, or vecuronium bromide, 0.05 to 0.1 mg/kg) are required to provide satisfactory abdominal muscle relaxation and to abolish involuntary movements. Other pharmacologic interventions include systemic heparinization (300 to 500 U/kg) before cannulation of the aorta, mannitol (0.25 to 0.5 g/kg), and furosemide (40 mg) to induce diuresis before division of the renal pedicle and prevent ischemia-induced acute tubular necrosis.[79-81] Alpha-adrenergic receptor blockers, such as phenoxybenzamine, may be used to promote renal vasodilation and prevent vasospasm.[82] However, these blockers are not recommended in multiple organ procurement because their effects on other organs are unknown. Prophylactic administration of antibiotics such as broad-spectrum cephalosporins is recommended by some centers,[83, 84] although its efficacy is controversial.[47, 85]

Specific goals of ventilatory care are to maintain a Pao_2 between 70 and 100 mm Hg, an oxygen saturation of arterial hemoglobin greater than 95%, and a partial pressure of arterial carbon dioxide within the range of 35 to 45 mm Hg to avoid pulmonary complications. In hypothermic donors, a mild respiratory alkalosis (pH 7.4 to 7.5) may be preferred to improve tissue perfusion.[86, 87] This goal frequently is achieved by ventilating with a tidal volume of 10 to 15 mL/kg, a respiratory rate of fewer than 20 breaths/min, FIO_2 of 30% to 40%, and a low level of PEEP (<5 cm H_2O). However, when pulmonary complications interfere with gas exchange, the tidal volume is increased up to 20 mL/kg, the respiratory rate is increased up to 20 breaths/min, and the PEEP is increased up to 10 cm H_2O. In general, an increase in FIO_2 is preferred to an excessive tidal volume and high PEEP to maintain venous return and splanchnic blood flow.

The goal of circulatory care is to preserve perfusion of all organs that are to be procured by maintaining systolic blood pressure between 100 and 120 mm Hg, with a CVP less than 10 cm H_2O and minimal vasopressor support.[51, 88, 89] Hypotension (systolic blood pressure < 80 mm Hg or mean arterial pressure < 40 mm Hg) is associated with an increased incidence of acute tubular necrosis and nonfunction of the donor kidneys[90, 91] as well as poor function of the liver.[92] However, maintaining a satisfactory blood pressure is difficult

to achieve at times because of altered circulatory physiology in the brain-dead donors. Preload frequently is decreased because of blood loss, vasomotor paralysis, diuretic therapy, or diabetes insipidus. Tachycardia, bradycardia, and arrhythmias caused by massive sympathetic discharge are not unusual, and myocardial contractility frequently is impaired by myocytolysis, coronary spasm, and reduction of myocardial energy storage.[93] Afterload may be increased by excessive sympathetic tone or decreased by vasomotor paralysis.

Intravascular volume is adjusted with the guidance of the CVP (<10 cm H_2O). Fluid deficit is corrected with the infusion of a balanced electrolyte solution (e.g., lactated Ringer's solution) or a colloid solution (5% albumin or hetastarch).[94] Urine output and insensible losses are replaced by a hypotonic solution with glucose (e.g., 5% dextrose in 0.45% sodium chloride [NaCl], 1 mL/kg^{-1}/hour^{-1}). Adjustment of intravascular volume may decrease the need for vasopressors in many cases,[95] but acute volume expansion may increase myocardial oxygen consumption, congestive heart failure, arrhythmias, and the need for inotropic support because the compliance of the heart is decreased in most donors.[91] Excessive urine output (>200 to 250 mL/hour) is replaced by a hypotonic electrolyte solution with supplementation of potassium chloride (KCl, 20 mmol/L). When hypotension persists even after adequate volume replacement, vasopressors may be required. Dopamine (2 to 5 μg/kg^{-1}/min^{-1} and up to 10 μg/kg^{-1}/min^{-1}) is the first choice to improve cardiac contractility. Other inotropes include dobutamine (2 to 10 μg/kg^{-1}/min^{-1}) and isoproterenol (0.1 to 1 μg/kg^{-1}/min^{-1}), but these drugs may dilate peripheral vascular beds, decreasing blood pressure. Alpha-vasopressors (phenylephrine, norepinephrine bitartrate, or metaraminol bitartrate) are avoided because they may decrease splanchnic and coronary blood flow.[96, 97] In addition, the oxygen-carrying capacity to the peripheral tissues is improved by transfusion of packed red blood cells (1 to 3 U) to maintain the hematocrit between 25% and 30%.[98]

Severe cases of tachycardia and hypertension caused by the mass reflex may be controlled by the administration of general anesthetics, a beta antagonist, such as labetalol or esmolol, or a calcium channel blocker, such as verapamil.[99] Occasionally, an α-blocker, such as hydralazine or sodium nitroprusside, may be given to reduce afterload. Supraventricular or ventricular arrhythmias are treated with conventional antiarrhythmic drugs. Circulatory arrest, which occurs in 10% of potential donors and in 66% of referred donors,[99] is treated according to conventional circulatory resuscitative measures. If bradycardia is a concern, a direct-acting agent, such as isoproterenol or epinephrine, is used because donors are unresponsive to centrally acting chronotropic drugs, such as atropine.

Progressive hypothermia, which is seen in up to 86% of donors because of the loss of hypothalamic function.[51] results in sinus bradycardia, atrioventricular dissociation, and ventricular arrhythmias. At a temperature lower than 28°C, prolonged PR and QT intervals and wide QRS complexes are replaced by T-wave inversion, ST-segment depression, and a rise of ventricular fibrillation. Other effects of hypothermia are a leftward shift in the hemoglobin-oxygen dissociation curve, an increase in blood viscosity, a decrease in splanchnic blood flow and glomerular filtration, hyperglycemia, and metabolic and respiratory acidosis. Body temperature is kept within the normal range (>35°C) by increasing the room temperature, infusing all fluids through a blood warmer, and using a warming blanket and a heated humidifier in the inspiratory limb of the ventilation circuit.

Adequate diuresis (>0.5 mL/kg^{-1}/hour^{-1}, preferably 1 to 1.5 mL/kg^{-1}/hour^{-1}) is important because urine output is an indirect indication of preload and a prognostic indicator for renal graft and hepatic function.[100] The administration of fluid or dopamine may be effective in maintaining adequate renal perfusion and diuresis. However, a high dose of dopamine (>10 μg/kg^{-1}/min^{-1}) may lead to acute tubular necrosis and nonfunction of the renal graft.[90] For persistent oliguria, furosemide (1 to 2 mg/kg) and mannitol (0.5 g/kg) may be administered. Diabetes insipidus, caused by a nonfunctioning pituitary gland, results in polyuria, hypovolemia, and electrolyte imbalance. Excessive urine output is replaced with a hypotonic solution (0.45% NaCl with KCl, 20 mmol/L), and supplemental antidiuretic hormone is administered to maintain urine output in the range of 100 to 250 mL/hour. The synthetic analog of vasopressin, desmopressin acetate (DDAVP), is preferred (0.5 to 1 U/hour) because of its long duration of action and a low pressor/antidiuretic effect ratio.[101] However, the pressor activity in excessive doses of DDAVP may increase the risk of acute tubular necrosis[102] and reduce hepatic blood flow.[103] DDAVP increases the sensitivity to catecholamines,[103] and catecholamine doses should be reduced when DDAVP is given to the donor. Hyperglycemia is a complication of diabetes insipidus and is treated by an infusion of insulin (5 to 10 U).

Metabolic acidosis caused by inadequate tissue perfusion may be compounded by respiratory acidosis. Because of potential myocardial depression, metabolic acidosis is corrected by administration of sodium bicarbonate. When hypernatremia is a concern, tromethamine, or *tris*(hydroxymethyl) aminomethane (THAM) may be used instead of sodium bicarbonate:

$$0.3 \text{ mol THAM (mL)} = \text{body weight (kg)} \times \text{base deficit (mmol/L)}$$

Electrolyte imbalances (hypernatremia, hypokalemia, hypocalcemia, hypophosphatemia, and hypomagnesemia) caused by fluid shifts and diabetes insipidus may result in arrhythmias and myocardial dysfunction. Hypernatremia and hypokalemia are treated by administration of a hyponatremic solution (0.45% NaCl) and KCl (20 mmol/L). Ionized hypocalcemia caused by large blood transfusions is corrected by the administration of calcium chloride or calcium gluconate to preserve cardiac contractility. Hypomagnesemia is treated with magnesium sulfate (50 mg/kg), also to preserve myocardial contractility[104] Glucose metabolism is relatively well maintained, although hyperglycemia may occur as the result of a decreased level of insulin and as a complication of diabetes insipidus. Serum levels of triiodothyronine, insulin, and cortisol are low in animal models, and the administration of triiodothyronine improves hemodynamic stability by maintaining myocardial stores of energy and glycogen; however, the beneficial role of triiodothyronine is unclear in clinical settings.[52, 68]

Coagulopathy may occur in organ donors. Dilutional coagulopathy is caused by the shift of intravascular volume, consumption coagulopathy may result from the release of tissue thromboplastin from injured tissues and the ischemic organs, and fibrinolysis results from intravascular coagulation or the release of tissue plasminogen activator from the ischemic tissues. Disseminated intravascular coagulation (DIC) has been reported in 80% of donors with head injury,[105] but its clinical significance is unknown. Coagulation abnormalities are treated conservatively.

Once cardioplegia is induced, no further supportive care is necessary. After cross-clamping of the aorta (the time is recorded by the procurement coordinator) (Fig. 177-3), mechanical ventilation and monitoring are discontinued and all cannulas are removed. The organs are swiftly removed in the following sequence: heart, lungs, liver, pancreas, intestine, and kidneys. No supportive care is needed for procurement of corneas or bones because these tissues tolerate a prolonged ischemia without significant injury.

Recovery Data

Donor ID# _____

Surgeons Renal: _____ Assisting: _____

Hepatic: _____

Cardiac: _____

Heart/Lung: _____

Pancreas: _____

Coordinators/Technicians (Tissue): _____

In O.R. _____ AM PM Incision _____ AM PM Depart O.R. (0) _____ AM PM Depart O.R. (T) _____ AM PM

Condition During Surgery (include: Blood Pressure, Urine Output, Complications, Comments)

Operating Room Drugs (include dosage and time)

Methylprednisolone: _____ Mannitol: _____ Furosemide: _____

Heparin: _____ Vasodilator: _____ Blood Products _____

Antibiotics: _____ Others: _____

Nephrectomy Data

En Bloc: Y/N In Situ: Y/N

Flush Sol'n: _____ Vol: _____

Final Flush (Sol'n Vol): _____

Storage Sol'n: _____

	R	L
Art Clamp:		
Flush Start		
Flush End:		
Warm Ischemia Time		
Clamps Off:		
Cold Ischemia Time		

Hepatectomy Data

Precool Start _____

Sol'n/Vol: _____

Portal Flush Start: _____

Sol'n/Vol: _____

Aortic Flush Start: _____

Sol'n/Vol: _____

Final Flush (Sol'n/Vol) _____

Clamps Off: _____

Cold Ischemia Time _____

Anatomy: _____

Cardiectomy Data

Infusion Start: _____

Sol'n/Vol. _____

Clamps Off: _____

Cold Ischemia Time _____

Heart Lung Data

Infusion Start (R) _____

Sol'nVol: _____

Infusion Start (L) _____

Sol'n/Vol: _____

Clamps Off: _____

Cold Ischemia Time _____

Single or Double Lung Data

Infusion Start: _____

Sol'n/Vol. _____

Clamps Off: _____

Cold Ischemia Time _____

Pancreas Data

Infusion Start: _____

Sol'n/Vol. _____

Final Flush; (Sol'n/Vol) _____

Clamps Off: _____

Cold Ischemia Time _____

Anatomy _____

Renal Anatomy

R  _____

L  _____

Biopsy Results: _____

Organs and Tissues Recovered (Check appropriate box and circle "T" for Transplant, "R" for Research)

☐ **R-KI** T/R ☐ **L-KI** T/R ☐ **LI** T/R ☐ **LU** T/R ☐ **PA** T/R ☐ **HR** T/R ☐ **HV** T/R ☐ **MV** T/R ☐ **Bones** T/R

☐ **BM** T/R ☐ **Veins** T/R ☐ **Skin** T/R ☐ **Cornea** T/R ☐ **INT** T/R ☐ **Other** T/R

Figure 177–3. Intraoperative data collection sheet used by the Western Pennsylvania Organ Procurement Organization, CORE (Center for Organ Recovery and Education). (Courtesy of Brian Broznick.)

Donor Operation

Before starting a multiple procurement, the different surgical teams must discuss the techniques and sequence they want to adopt. A detailed discussion of the surgical procedure is critical because, after aortic cross-clamping, time is of the essence. Everything should proceed as smoothly and expeditiously as possible to minimize organ damage. The basic principle of any donor operation is the core cooling of the organs to be removed. Cooling of a solid organ at the time of donor circulatory arrest was described for experimental liver transplantation nearly 40 years ago.[106] Cooling was then promptly applied to kidney preservation in clinical transplantation,[107] and it still represents the single most important aspect of any organ preservation technique. The first solution used was chilled lactated Ringer's solution, replaced in the late 1960s by the so-called Collins' solution, characterized by an electrolyte composition close to the intracellular one.[108] This solution was successfully used for about 20 years until the introduction of the University of Wisconsin solution,[109, 110] which extended the duration of organ viability. The easiest way to achieve almost immediate internal core cooling of the donor organs is by in situ infusion of the preservation solution, chilled to 4°C, at the time of the circulatory arrest. The remaining technical aspects of organ retrieval are secondary to this critical maneuver.

The surgical procedure for multiple cadaveric organ procurement has undergone a progressive evolution. In 1984, when procurement of extrarenal organs was becoming more common, the Pittsburgh group[111] published a technique that required a meticulous in vivo dissection of the donor organs and extensive manipulation of the abdominal viscera. A subsequent refinement of this technique was introduced in 1986.[112] This improved technique is used today and is basically characterized by a "no-touch en bloc removal" of the core cooled solid organs. The technical details of this operation lie outside the scope of this chapter, and we will only describe the major points.

A complete midline incision is performed from the suprasternal notch to the pubis (Fig. 177-4) (see Color Plate). As soon as the thoracic and abdominal organs are visualized, the procurement coordinator collects the first information on the appearance of the donor organs and relays it to the local OPO so that it can be made available to the recipient teams. The aorta is then exposed and encircled either immediately above or below the diaphragm (Fig. 177-5) (see Color Plate). The inferior mesenteric vein is encircled and cannulated for infusion of the cold portal perfusate. The aorta is then dissected for 2 cm at the level of the origin of the inferior mesenteric artery, which is tied and divided. The aorta is encircled at this level and prepared for cannulation. Figure 177-6 shows the donor inferior mesenteric vein and the infrarenal aorta cannulated for the cold perfusate (see Color Plate). The common bile duct is tied distally and transected close to the upper margin of the duodenum, and the gallbladder is incised and washed free of bile to prevent autolysis of the mucosa of the biliary tract.

The arterial anatomy of the liver should be carefully examined for possible anomalies. Prior knowledge of any anomaly is helpful in preventing mistakes during organ removal. At this point, the basic initial dissection is completed (Fig. 177-7) (see Color Plate) and the thoracic team prepares the chest organs for removal. The pleural spaces are opened widely after initial mediastinal dissection. Very little initial dissection is done around the inferior and superior vena cava and aorta other than to place sutures for the expected cannulation of the aorta for cardioplegia or the main pulmonary artery if the lungs are being harvested as well. The lungs are quickly examined through the pleural spaces, and little dissection is required thereafter. It should be noted that the donor's heart has continued beating spontaneously and maintained circulation of all organs.

As soon as the thoracic team completes its dissection, 300 to 500 U/kg of heparin is given intravenously, and the aorta is cannulated after ligating it distal to the inferior mesenteric artery (see Fig. 177-6). The thoracic team then occludes the superior vena cava, and the aorta is simultaneously clamped proximal to the innominate artery and just above or below the diaphragm (Fig. 177-8) (see Color Plate). The cold infusion is started, the inferior vena cava is vented, and the heart is separately perfused with cold cardioplegic solution. The heart is removed first. If the lungs are being harvested simultaneously, cold flush is started through the pulmonary artery, venting the solution through the left atrial appendage.

Once cardioplegic solution has been administered, the aorta is transected, and the rest of the lung perfusion solution is allowed to drain through the open aorta. Mediastinal dissection is then carried out, removing the lungs and heart en bloc if the block is to be used for a heart-lung transplant. The more common situation is one in which the heart is harvested by one group and the lungs are used for separate transplants. In this situation, once the cardioplegia and lung perfusion have

Figure 177–4. Intraoperative photograph showing the total midline incision used for multiple procurement. (See Color Plate.) (Courtesy of Andreis Stieber, MD.)

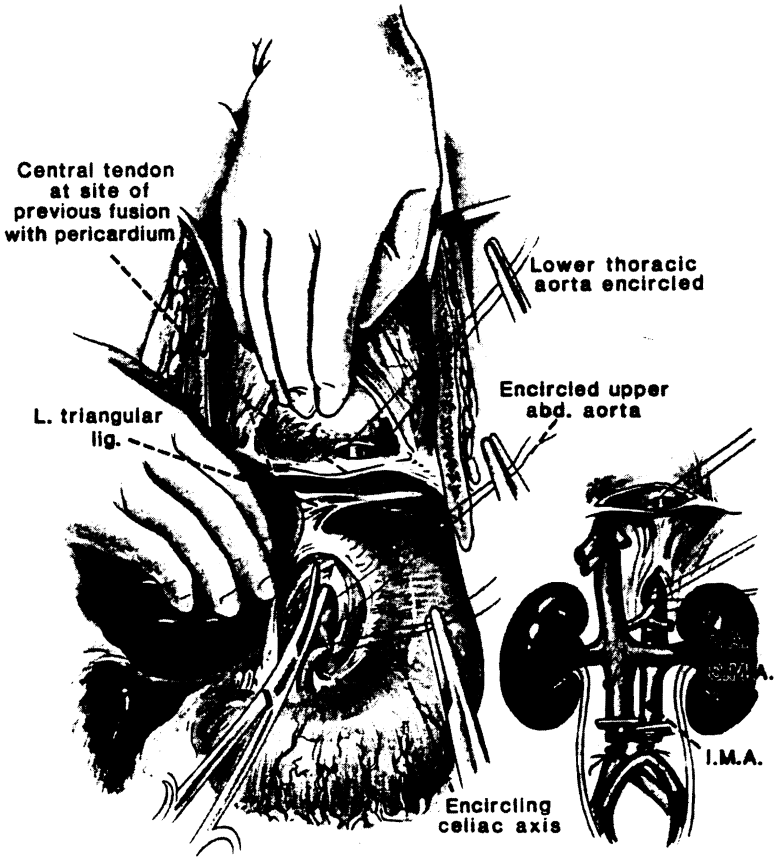

Figure 177–5. The aorta is dissected and encircled just above (or, alternatively, just below) the diaphragm. L. triangular lig. = left triangular ligament; encircled upper abd. aorta = encircled upper abdominal aorta; C.A. = celiac axis; S.M.A. = superior mesenteric artery; I.M.A. = inferior mesenteric artery. (See Color Plate.)

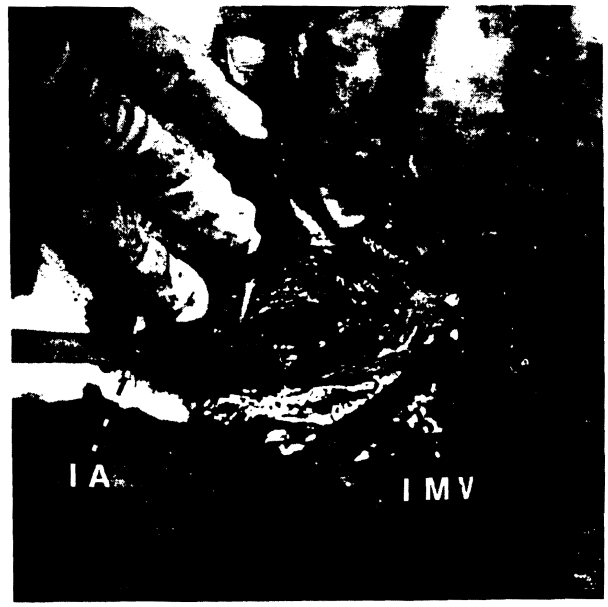

Figure 177–6. Intraoperative photograph showing cannulas for cold perfusion inserted into the dissected donor inferior mesenteric vein (IMV) and the infrarenal aorta (IA). (See Color Plate.) (Courtesy of Andreis Stieber, MD.)

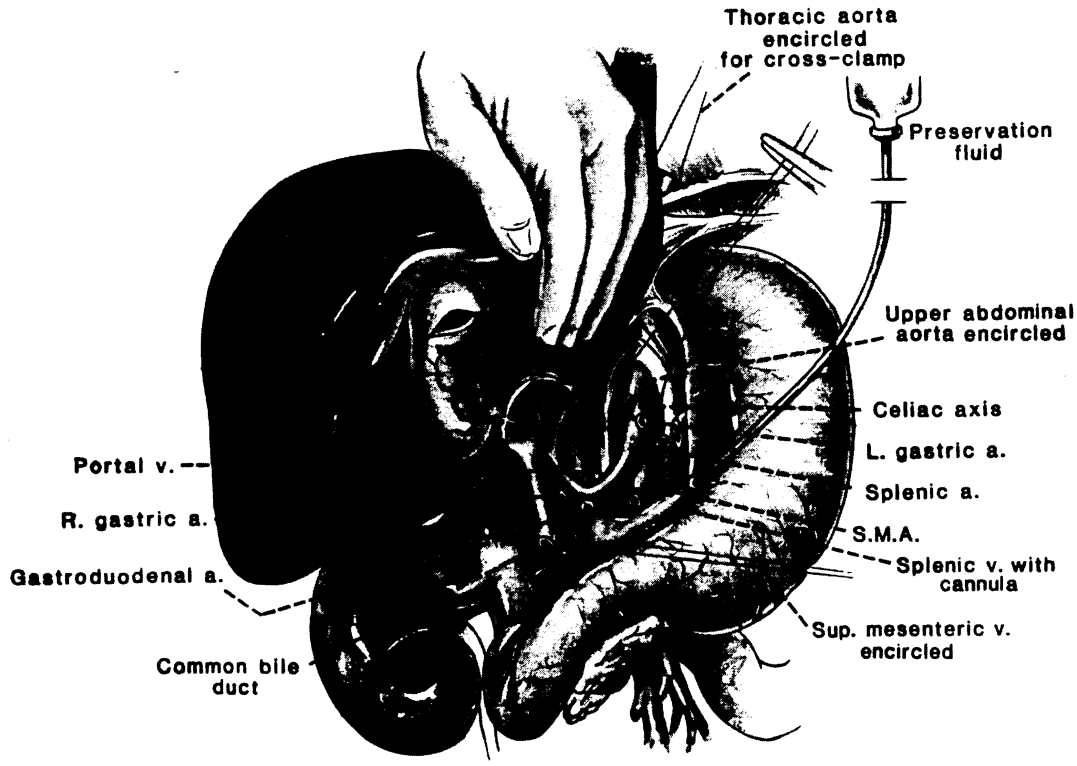

Figure 177–7. Liver hilar dissection, transection of the common bile duct, and incision of the gallbladder fundus to prevent autolysis of the mucosa of the biliary tract. In this drawing, the splenic vein is cannulated; however, the inferior mesenteric vein can be cannulated alternatively, as shown in Figure 177-6. Portal v. = portal vein; R. gastric a. = right gastric artery; Gastroduodenal a. = gastroduodenal artery; L. gastric a. = left gastric artery; Splenic a. = splenic artery; S.M.A. = superior mesenteric artery; Splenic v. with cannula = splenic vein with cannula; Sup. mesenteric v. encircled = superior mesenteric vein encircled. (See Color Plate.)

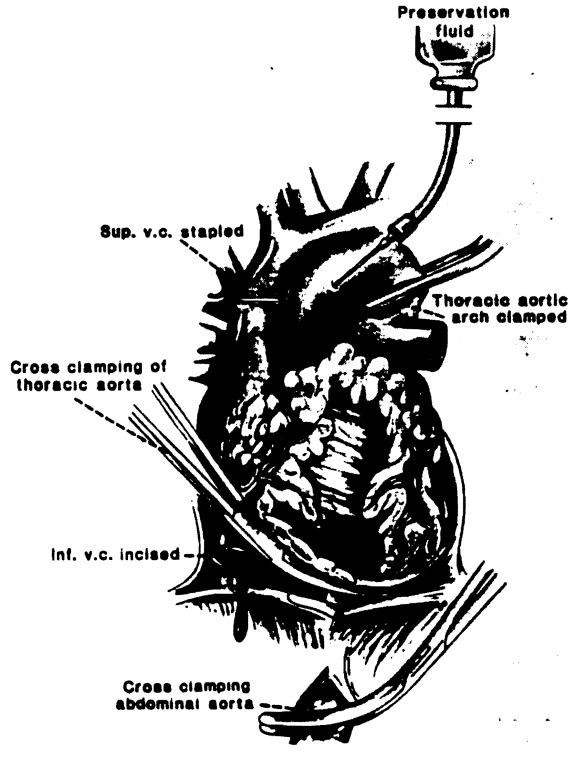

Figure 177–8. Occlusion of the superior vena cava inflow and simultaneous clamping of the aorta proximal to the innominate artery. The aorta is also simultaneously clamped just above or below the diaphragm. Cardioplegic solution infused through the ascending aorta is allowed to run only in the heart. Sup. v.c. stapled = superior vena cava stapled; Inf. v.c. incised = inferior vena cava incised. (See Color Plate.)

been completed, the heart is carefully dissected by the two teams, ensuring that enough pulmonary artery and left atrial cuff remain on the heart and the lungs, making them both available for transplantation. After the heart has been removed, the lung team can then proceed with extraction of the lungs.

During this phase, the abdominal organs are untouched while they are exsanguinated and the cold perfusion is continued. After removal of the thoracic organs, the abdominal team proceeds with the final dissection and removal of the liver, pancreas, intestine, and kidneys. The technical steps have been outlined elsewhere by us[50, 111-114] and others.[115-117] After the organ recovery, long segments of the iliac arteries and veins, inferior vena cava, and aorta[118] (and carotid arteries in children) should always be removed and stored under hypothermic conditions. This ensures the ability to deal with all possible vascular problems that might be encountered during the recipient operations.[118-123]

With the development of the intestinal and multivisceral transplant program at the University of Pittsburgh (see Chapter 184), a technique was developed for the removal of essentially the entire abdominal visceral bloc (Fig. 177-9) (see Color Plate).[50, 124] Anatomic considerations are fundamental during intestinal and multivisceral procurement because recipients require different types of intestinal transplantation (isolated small bowel, liver and small bowel, true multivisceral, and so on) based on different diseases and needs.[124] These procurement techniques do not interfere with those of other organs. In our first 35 intestinal donor operations, there were 62 kidneys, 35 livers, 18 hearts, and 3 lungs procured simultaneously.[50]

Figure 177–9. En bloc harvesting of liver and small bowel from a pediatric donor. (See Color Plate.)

At the end of the operation, the procurement coordinator completes the form shown in Figure 177-3. These data and the other basic donor information collected earlier in the donor procurement process (Fig. 177-2) are of critical importance in the selection of the recipient and the outcome of the transplantation. The risk factors associated with an unfavorable outcome, at least in some organs, may be identified by the information readily available at the time of the multiple organ procurement. This knowledge can help us stratify prospective donor-recipient combinations according to their predicted risk of failure, providing insight as to the probable outcome of individual patients and the factors that determine it. It can also be used to describe study populations, stratified according to their risk, and allow uniform comparison of outcomes.

In Pittsburgh, we have completed an analysis determining that the outcome of a liver transplantation can be predicted at the time of the surgery. This may be achieved by using information obtained as part of a routine pretransplant recipient and donor work-up, which is always available at the time of organ allocation.[125] Because of the interaction of two different biologic systems—the donor and the recipient—the outcome of an organ transplantation is a complex phenomenon. Therefore, the various aspects of multiple donor organ procurement discussed in this chapter should be carefully considered in each potential procurement scenario as fundamental to the success of the transplantation procedure.

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Principles of Immunosuppression

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Recent advances in molecular biology and immunology have unraveled mechanisms of antigen-presenting cell (APC) and T cell interactions. This includes elucidation of molecular mechanisms involved in the activation and turning off of T cells and interleukin-2 (IL-2) gene transcription and translation. Studies leading to novel ways of inhibiting T cell activation have focused on various subunits (α, β, and γ) of the IL-2 receptor. This has led to an explosion of trials of these agents in combinations with more conventional immunosuppressive drugs.

BASIC PRINCIPLES

Optimal immunosuppression consists of drug therapy that enables graft acceptance while suppressing systemic immunity as little as possible and producing the least systemic toxicity. Immunosuppression predisposes to infection and malignancy, in addition to other side effects that are inherent risks with all the currently available immunosuppressants. Blood level monitoring and titration of immunosuppression are limited to only a few immunosuppressive agents, and in practice too much or too little immunosuppression almost invariably becomes apparent only in retrospect. Surrogate biologic assays, such as suppression of the mixed lymphocyte reaction, are either impractical or do not have proven clinical correlates.

The timing, dosing, and selection of immunosuppressive agents differ much. Current protocols use multiple drugs, each directed at a discrete site in the T cell-activation cascade.[1] Most immunosuppressive regimens are combinations of drugs, often with different modes of action and toxicity. This approach allows giving smaller doses of each drug. Transplantation immunosuppression can be (1) *pharmacologic*, consisting of drugs like corticosteroids, cytokine suppressive agents, antiproliferative agents, and cytotoxic agents or (2) *biologic*, consisting of monoclonal and polyclonal antilymphocyte antibodies and anti-cytokine receptor antibodies.[2] Newer agents are being introduced.

Tacrolimus (Tac) or cyclosporine (CyA) with steroids forms the backbone of most immunosuppressive regimens being used today. An antiproliferative agent or an antilymphocyte antibody, or both, may be added. When acute cellular rejection occurs, it is common to treat it with large doses of steroids or antilymphocyte antibodies, or both.

In general, the early postoperative period calls for the greatest degree of immunosuppression. As time goes on, many patients can maintain graft function with smaller quantities of immunosuppressive agents. Some patients can tolerate complete withdrawal of therapy without exhibiting rejection[3]; however, this is best done as a protocol-based strategy with patients under strict supervision.

OVERVIEW OF TRANSPLANT IMMUNOBIOLOGY

Lymphocytes are preprogrammed as they develop in the thymus to recognize foreign antigen. Antigen specificity is determined by an antigen-binding unit on the T cell surface, the T cell receptor (TCR). The specificity and diversity of the binding site of the TCR derive from its amino acid composition and the variations in this composition from T cell to T cell. The gene sequence that codes for the TCR rearranges during development, so each T cell ends up with a different TCR-binding specificity. Because the gene rearrangements are completely random, a huge library of binding sites capable of recognizing both *self* and *foreign* molecules is generated. Thymocytes with TCRs that bind to self molecules (and thus potentiate the development of autoimmunity) are subsequently destroyed, by mechanisms that are poorly understood.

Lymphocytes recirculate at a rate of 1% to 2% per hour, migrating through all tissues of the body. Recirculation routes are not random. Specialized cell-surface "homing" molecules on T lymphocytes mediate attachment to specific endothelial molecules in targeted tissues. Once inside tissue, antigen-presenting cells (APCs), such as macrophages, make intimate contact with the lymphocytes and present foreign antigen that has been processed in the cells by the APCs. The APCs phagocytose foreign proteins and cleave foreign protein enzymatically into small peptides of eight to 12 amino acids length. These peptides are loaded onto a class of specialized carrier molecules known as the *major histocompatibility complex* (MHC). MHC molecules carry the peptide fragments to the cell surface, where they are displayed to T cells.

The TCR is a cell-surface molecule. The TCR associates with "accessory" molecules, including CD3 and either CD4 or CD8. The TCR-CD3 complex interacts with the peptide fragment in the binding groove of the MHC molecule of the APC, and this complex is stabilized by the CD4 or CD8 molecule of the T cell. This interaction produces the signal that initiates activation of the T cell, leading to proliferation of that T cell clone, which recognizes the particular antigen fragments of foreign protein. The basis for MHC-restricted antigen recognition is the requirement for antigen presentation by APCs bearing an MHC molecule specific to the host.

Antigen-directed proliferation of T cell clones is absolutely