Organ Procurement

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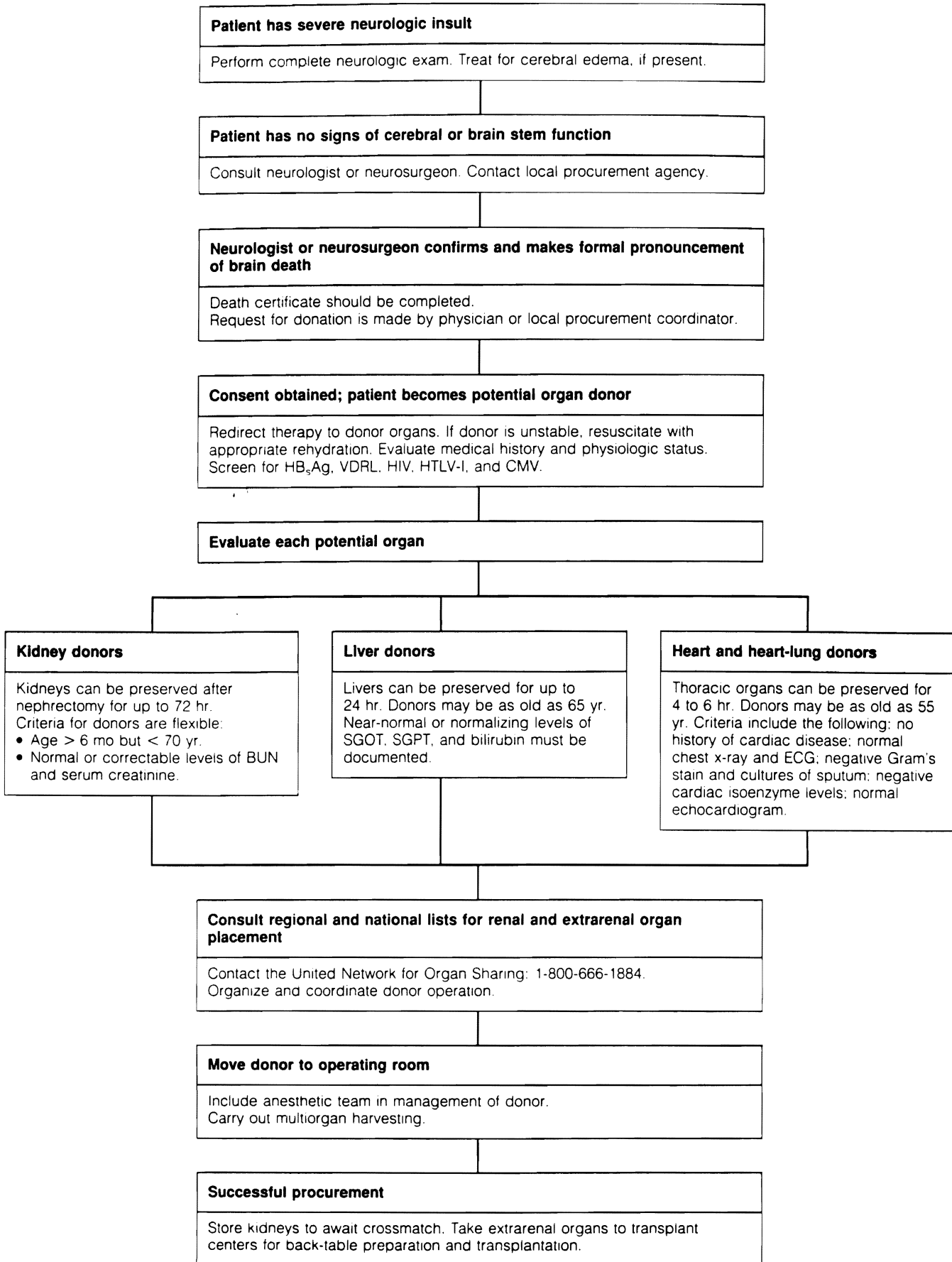# Approach to the Potential Organ Donor

Patient has severe neurologic insult

Perform complete neurologic exam. Treat for cerebral edema, if present.

Patient has no signs of cerebral or brain stem function

Consult neurologist or neurosurgeon. Contact local procurement agency.

Neurologist or neurosurgeon confirms and makes formal pronouncement of brain death

Death certificate should be completed.
Request for donation is made by physician or local procurement coordinator.

Consent obtained; patient becomes potential organ donor

Redirect therapy to donor organs. If donor is unstable, resuscitate with appropriate rehydration. Evaluate medical history and physiologic status. Screen for $HB_s Ag$, VDRL, HIV, HTLV-I, and CMV.

Evaluate each potential organ

Kidney donors

Kidneys can be preserved after nephrectomy for up to 72 hr. Criteria for donors are flexible:
- Age > 6 mo but < 70 yr.
- Normal or correctable levels of BUN and serum creatinine.

Liver donors

Livers can be preserved for up to 24 hr. Donors may be as old as 65 yr. Near-normal or normalizing levels of SGOT, SGPT, and bilirubin must be documented.

Heart and heart-lung donors

Thoracic organs can be preserved for 4 to 6 hr. Donors may be as old as 55 yr. Criteria include the following: no history of cardiac disease; normal chest x-ray and ECG; negative Gram's stain and cultures of sputum; negative cardiac isoenzyme levels; normal echocardiogram.

Consult regional and national lists for renal and extrarenal organ placement

Contact the United Network for Organ Sharing: 1-800-666-1884.
Organize and coordinate donor operation.

Move donor to operating room

Include anesthetic team in management of donor.
Carry out multiorgan harvesting.

Successful procurement

Store kidneys to await crossmatch. Take extrarenal organs to transplant centers for back-table preparation and transplantation.

1 ORGAN PROCUREMENT
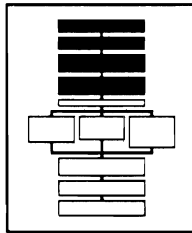
Approach to the Potential Organ Donor

Preliminary Steps

When a patient presents with severe neurologic insult, initial efforts should be directed at saving the injured patient by minimizing cerebral swelling and possible brain herniation [see IV Trauma, 2 Trauma to the Central Nervous System]. Often, this is best accomplished by strict fluid restriction and the administration of diuretics and mannitol. However, one of the key advances in clinical organ transplantation has been improved identification and early referral of potential organ donors. Any patient who has suffered severe brain damage should be considered for organ donation. Causes of such damage include external trauma, motor vehicle accidents, falls, assaults, spontaneous intracerebral hemorrhages, drownings, hangings, primary brain tumors, drug overdoses, and sudden infant death syndrome.

A neurologist, a neurosurgeon, or both should be consulted early in the evaluation of a patient with a severe neurologic insult. Such consultation will be important in an eventual diagnosis of brain death, which can be made on clinical criteria alone[1] but is often confirmed by means of electroencephalography,[2] occasionally a cerebral flow scan,[3] or both. Clinical criteria of brain death include deep coma, lack of spontaneous movement, a positive apnea test, and no response to painful stimuli. In addition, cranial nerve reflexes, such as the oculocephalic (doll's eyes) and the oculovestibular (caloric), should be absent. Brain-dead patients have fixed, dilated pupils and do not have protective corneal reflexes. Spinal reflexes may still be present because they do not involve the higher centers of the brain or the brain stem.[4,5] If the patient has stable cardiovascular function, the clinical criteria of brain death usually are documented twice within an interval of six to 12 hours before a final declaration of death is made [see I Emergency Care, 9 Coma, Seizures, and Brain Death].

As soon as the possibility of donation is established, the local organ procurement agency should be contacted. (The telephone numbers of these agencies are available in most intensive care units.) The procurement coordinator then evaluates the patient's potential for organ donation, assists in the administrative details necessary for declaration of death, and acts as intermediary between the hospital and the donor's family.

When brain death is confirmed, the attending physician or neurologist should make a pronouncement in the patient's chart and complete the death certificate. The physician or procurement coordinator may then formally request consent for donation from the family, making sure that the family members completely understand each of the two distinct issues involved, namely, the diagnosis of brain death and the process of organ procurement.

### Donor Evaluation and Management

After the declaration of brain death, efforts must be redirected toward protecting the organs to be transplanted rather than the now dead brain. Usually, such therapy entails aggressive rehydration. In addition, the procurement coordinator must clearly establish the adequacy of each organ to be used, according to well-recognized sets of standard criteria (see below). A detailed medical history must be obtained that includes the cause of the brain damage as well as the donor's age, height, weight, and blood type. Assessment of acute physiologic status can be made by measuring blood pressure, central venous pressure (CVP), urine output, and arterial blood gases. Serologic analysis must be done for syphilis (VDRL), hepatitis B surface antigen (HB_sAg), and cytomegalovirus,[6] as well as for human immunodeficiency virus (HIV)[7] and human T cell lymphotropic virus type I (HTLV-I); otherwise, recipients may be infected with these deadly organisms.

The criteria for renal donation are the most flexible. A kidney donor can be between six months and 70 years of age. Levels of serum creatinine and blood urea nitrogen (BUN) should be normal, although elevations may be caused by dehydration or other adverse but reversible acute states. If dehydration is responsible, BUN and creatinine levels should fall after adequate fluid replacement.

Kidneys can be preserved after nephrectomy for up to 72 hours. Thus, there may be time for tissue typing and matching before kidneys are sent to recipients in distant cities. However, the chances that a kidney will function immediately in the recipient diminish greatly with storage for more than 24 hours.

With newer preservation solutions, the liver may now be safely preserved for up to 24 hours. Time constraints are more rigid for the thoracic organs, however, and they should be transplanted within six hours after removal from the donor.

There is no consensus on the upper age limit for donors of extrarenal organs. Although an arbitrary limit of 40 to 45 years of age had been used to exclude donors, many recent reports have shown that livers as well as hearts can be successfully transplanted from donors older than 50 years and sometimes from those older than 60 years.[8]
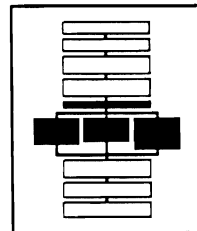
If the liver is under consideration for donation, normal or near-normal serum aspartate aminotransferase (AST, formerly termed SGOT), serum alanine aminotransferase (ALT, formerly termed SGPT), and bilirubin levels must be documented. A history of hepatitis or alcoholism is a warning sign but not necessarily a contraindication to liver transplantation.

Heart and heart-lung donors must have no history of cardiac disease and should have a normal chest x-ray, electrocardiogram, and physical examination. The partial pressure of oxygen in arterial blood (P_aO_2) of heart-lung donors should be 350 mm Hg during ventilation with a fraction of inspired oxygen (F_IO_2) of 1. Sputum cultures and Gram's stains should be negative. In trauma cases, tests of cardiac isoenzymes should also yield negative results.

ABO blood group and organ size are important factors in placing extrarenal organs. Ideally, a liver donor should be slightly smaller than the proposed recipient, but large variations on this generalization may occur, according to the size of the recipient liver that is to be removed. Size is a special concern in pediatric liver transplantation. Because small baby donor organs are scarce, some centers have begun to reduce the size of adult organs by performing right hepatic lobectomies or right hepatic trisegmentectomies and implanting the left lobe itself or the left lateral segment.[9-11] In addition, to maximize the donor potential, a number of procedures have been done in which the liver has actually been split and the right lobe and the left lobe or the left lateral segment have been implanted in separate recipients. These practices address both the restrictions of size and the scarcity of pediatric organ donors.

In heart transplantation, the donor organ usually should be slightly larger than that of the recipient because cardiomegaly is a common finding in the recipient. The height, weight, and chest circumference of the heart-lung recipient must closely match those of the donor. The donor team is responsible for accumulating the information on which wise recipient selection can be based.

During the evaluation, the donor must be maintained in a stable physiologic state.[12] Basic monitoring should include an arterial line for blood pressure monitoring and blood gas surveillance, a central venous pressure monitor, and an indwelling urinary catheter to measure urine output. Because the basic physiologic situation rarely, if ever, improves in brain-dead patients, the interval between pronouncement of death and procurement surgery should be kept as short as possible. If a donor is unstable, aggressive therapy must be directed at maintaining adequate circulation, ventilation, and diuresis. If the donor is dehydrated from earlier efforts to prevent cerebral edema, rapid repletion is required with crystalloid solutions, colloid solutions, or both.

One relatively simple guide to fluid therapy is to maintain the central venous pressure between 10 and 12 cm H_2O if a normal systemic blood pressure can be achieved. However, brain death is sometimes associated with severe neurogenic shock and peripheral vasodilatation. In such cases, the peripheral vascular resistance will not support a normal systemic blood pressure, no matter how well the heart is loaded. In these patients, vasopressors, such as dopamine, should be added to restore normal blood pressure. Norepinephrine bitartrate (Levophed) and metaraminol bitartrate (Aramine) should be avoided because they produce severe visceral and renal vasoconstriction and may injure the organs to be transplanted.

Respiratory care of the potential donor is the same as that of any ventilator-dependent patient in an intensive care setting. Chest x-rays should be obtained at least once a day. Frequent endotracheal suctioning must be done, good pulmonary toilet must be maintained at all times, and arterial blood gases must be monitored frequently. Oxygen saturation should be maintained at no less than 95 percent by adjusting the F_IO_2 settings on the ventilator [see II Care in the ICU, 5 Use of the Mechanical Ventilator]. Levels of positive end-expiratory pressure (PEEP) greater than 5 cm H_2O are not recommended, because the higher levels increase intrathoracic and right atrial pressures, which in turn may cause hepatic parenchymal congestion and preclude the use of the liver.

A stable brain-dead donor should produce urine at a rate of at least 1 ml/kg/hr. The most common cause of oliguria is hypovolemia. If the CVP is low, further fluid resuscitation is in order. In some instances, however, oliguria may be the result of acute heart failure that is secondary to excessive fluid resuscitation, and osmotic and loop diuretics, such as mannitol and furosemide, will be needed.

When trauma to the brain is severe, pituitary function often fails. The resulting absence of antidiuretic hormone causes diabetes insipidus, and a large volume diuresis ensues, which can lead to severe volume depletion and donor instability. Most cases of diabetes insipidus can be handled simply by replacing the urine output intravenously with half-normal saline. Serum electrolytes must be monitored frequently during such treatment because hypernatremia can easily be produced. If fluid replacement cannot keep up with the diuresis, intravenous vasopressin may be given, but only with great caution, because the resulting vasoconstriction can cause severe end-organ ischemia.

Coordination of Donor and Recipient Activities
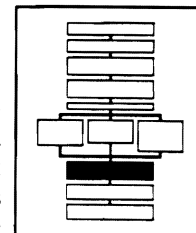
After the donor has been identified, studied, and stabilized, the procurement team contacts regional transplant programs about their needs for renal and extrarenal organs and inquires about needs in other parts of the country. A national computer registry of potential recipients of renal and extrarenal organs is maintained by the United Network for Organ Sharing (UNOS). (The 24-hour UNOS number is 1-800-666-1884.)

Potential recipients of extrarenal organs are categorized according to ABO blood group, weight, acceptable weight range of the donor, distance the recipient team is willing to travel for procurement, length of time the patient has been on the transplant list, and medical urgency status. Sharing of all organs is based on the principle that organs should be allocated first within the local area, then within a specific geographic region, and finally nationally if no suitable recipients can be found locally or within the region. There are two exceptions to this rule: one for livers and one for kidneys. According to UNOS, a so-called STAT liver recipient is a patient who is thought to have no more than 24 hours to live unless a transplant is performed. In this situation, a liver may be offered to the STAT recipient first; local and regional primacy are superseded. For kidneys, when there is a six-antigen match (i.e., a perfect histocompatibility match between a donor and a recipient on all six HLA-A, HLA-B, and HLA-DR antigens) or when there is at least

phenotypic identity between a donor and a prospective recipient, the kidney must be offered to the matched recipient regardless of geographic location.

Within each of these geographic distributions, whether it is local, regional, or national, organs are shared according to computerized point systems, which are based on a variety of parameters that are slightly different for each organ concerned. A potential kidney recipient may accumulate points for time on the waiting list, the degree of histocompatibility match between donor and recipient, and the degree of previous antibody sensitization. There is no allocation of points for medical urgency in kidney recipients. The variables in the point system for liver recipients include blood type compatibility, time on the waiting list, and medical urgency on a scale of 1 to 4, with 1 being the least urgent and 4 being the most urgent. Points are assigned to liver recipients for a variety of logistic factors as well, such as the distance a recipient or donor is from the transplant center. Finally, distribution of thoracic organs is based on principles similar to those governing distribution of livers. However, there are only two categories of medical urgency in heart and heart-lung recipients. A status 1 recipient is a critically ill patient in the intensive care unit receiving either pressor or mechanical heart support. Status 2 includes all other patients who are waiting either at home or in the hospital but outside of an ICU.

Once recipients for extrarenal organs have been identified, the local procurement team must coordinate the arrival of the participating recovery teams, schedule the operating room for donor surgery, and maintain the stability of the donor. With the recent proliferation of experienced extrarenal transplant centers throughout the United States, it is becoming more common for donor operations for extrarenal organs, especially the liver, to be performed by expert local procurement teams.[13] In the past, the recipient institution was required to send a donor team to retrieve the liver. This change has improved the coordination of the retrieval process, reduced the transportation costs associated with long-distance procurements, and helped to ease the burden on the recipient team.

With cooperation from all participants, including promptness, the different procurement teams will arrive as the donor is transported to the operating room. Before actual operation, the renal and extrarenal procurement teams should coordinate their techniques and preferences to avoid unseemly conflicts during a multiple-organ harvest.

The Donor Operation

When the donor is brought to the operating room, the anesthetic team begins to participate in donor management. If spinal reflexes persist in the donor, a muscle relaxant such as pancuronium bromide should be administered.

The operation for multiple-organ procurement must proceed in such a way that the kidneys, pancreas, liver, heart, heart and lung, or various combinations of these or other organs can be removed without any of them being jeopardized. The basic principle of the procedure is to carry out preliminary dissection of the great vessels of the abdomen and chest. The aorta is isolated at preplanned levels to allow cross-clamping, so that the organs to be removed can be core-cooled in situ with cold
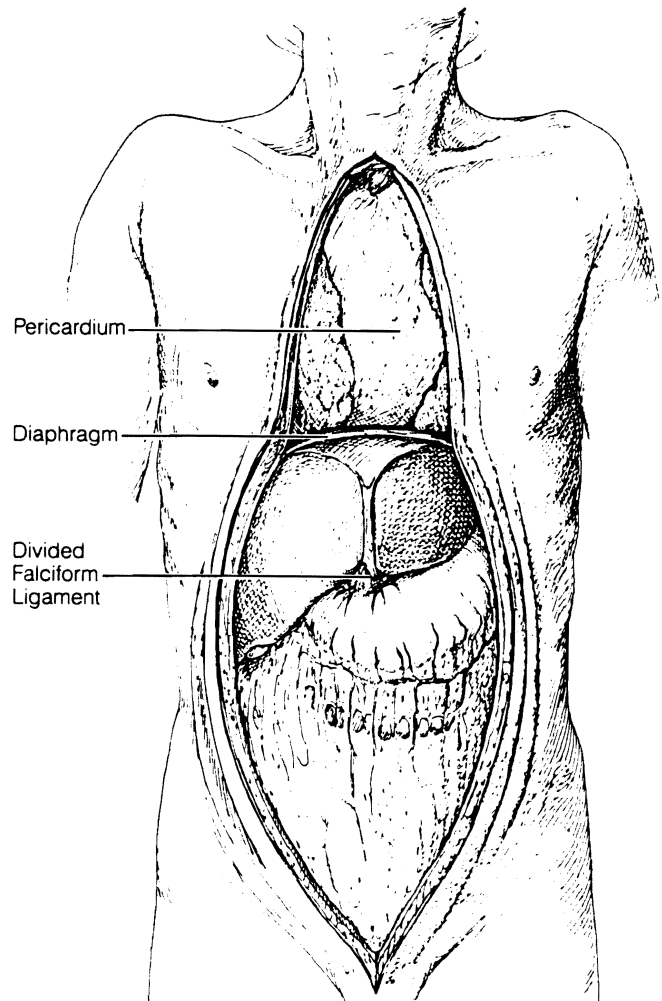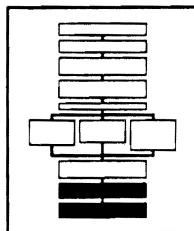

Figure 1   The incision used for multiple-organ procurement is made from the suprasternal notch to the pubis, as illustrated here.

intra-aortic and intraportal infusions (see below).[14] Thus, warm ischemia will be avoided in the donor organs. This technique has been adopted as an international standard. The most refined version of this procedure,[15] commonly known as the rapid-flush technique, can be completed in less than an hour, from beginning to end.

To start, a complete midline incision is made from the suprasternal notch to the pubis [see Figure 1]. If a heart team is on hand for cardiectomy, the pericardium is opened and the heart is inspected. Very minimal dissection is required to prepare the heart for removal. The superior vena cava and the aorta are encircled with tapes to allow eventual occlusion of the inflow and outflow tracts. The heart team can complete its preliminary work in 10 to 15 minutes.

The abdominal team, which consists of hepatic and renal surgeons, then proceeds. The left triangular ligament of the liver is incised, the esophagus is held to the left with a finger, and a longitudinal incision is made in the diaphragmatic crura, between the retrohepatic inferior vena cava and the esophagus [see Figure 2]. The aorta is encircled with a tape at this level.
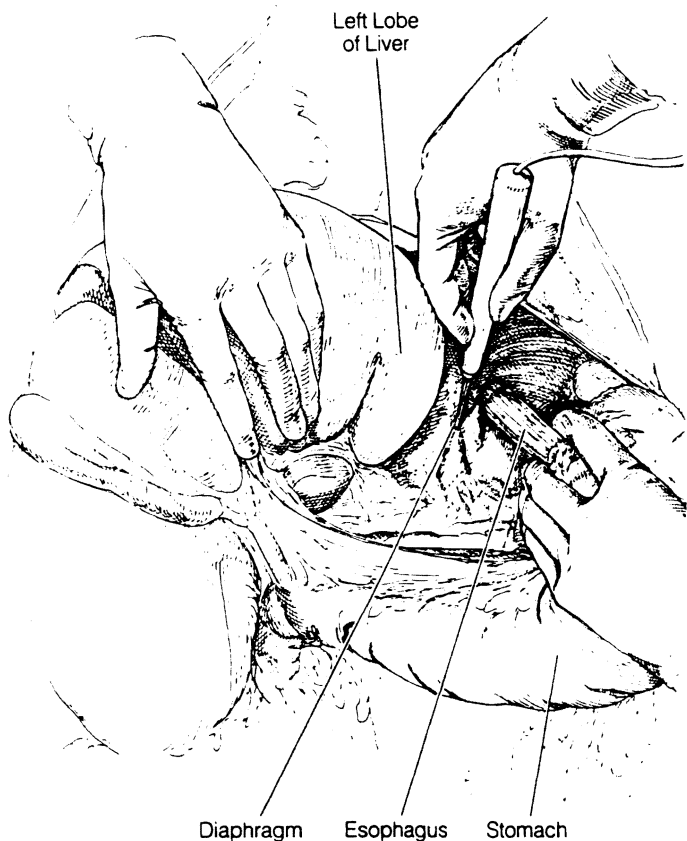
Figure 2 The crura are divided between the esophagus and the vena cava to facilitate exposure and encirclement of aorta at the diaphragm.

inserted into the IMV and advanced superiorly for approximately 5 cm in adults and for lesser distances in children so that the tip is in or just entering the portal vein. In the classical procedure, the splenic vein is isolated and ligated and a cannula is advanced to the bifurcation of the splenic and portal veins. Finally, after systemic heparinization, the distal aorta is ligated and the aortic perfusion cannula is inserted [see Figure 3].

With the abdominal and cardiac teams coordinated, effective circulation is terminated by cross-clamping the aorta at the predetermined levels [see Figure 4]. The cardiac team then proceeds with removal of the heart or heart-lung as expeditiously as possible. The heart is core-cooled with a potassium-rich cardioplegic solution infused via a cannula inserted into the ascending aorta. Blanching of the heart and cardiac arrest from
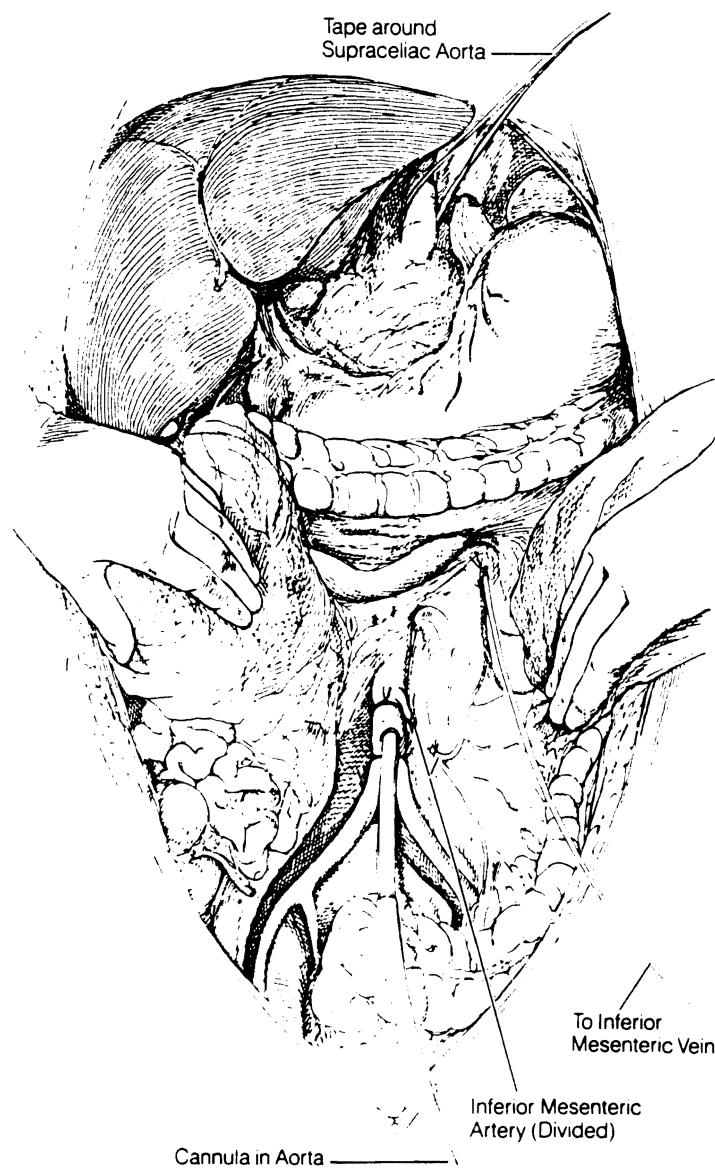
At this point, the abdominal team's decision on how to proceed is based on the physiologic status of the donor. If the donor is hemodynamically unstable and efforts at stabilization have failed, the rapid-flush technique should be used: all dissection is accomplished after circulatory arrest and in situ core cooling of the organs. In hemodynamically stable donors, however, many teams, depending on their experience, prefer to perform varying amounts of dissection of the hepatic hilar structures (including the hepatic arterial supply, the common bile duct, and the portal vein) before in situ flushing, especially when use of the pancreas is being considered. In addition, renal surgeons commonly free up the ureters from the bladder to the ureteropelvic junction and perform variable dissections of the renal veins and arteries. During lengthy preliminary dissections, however, undetected periods of ischemia may occur as individual vessels of the kidneys, pancreas, or liver are occluded during skeletonization. Lengthy dissection can be most dangerous in unstable donors. Periods of ischemia produced during these long dissections probably cause a higher incidence of liver graft failure in liver-pancreas procurements.

When the dissection is completed, the abdominal team turns its attention to the more distal aorta, ligating and dividing the inferior mesenteric artery and encircling the aorta at this level [see Figure 3]. If the rapid-flush technique is used, the inferior mesenteric vein (IMV) is isolated and ligated. A cannula is

Figure 3 The inferior mesenteric artery is ligated and divided. Catheters are inserted into the inferior mesenteric vein and into the distal aorta.
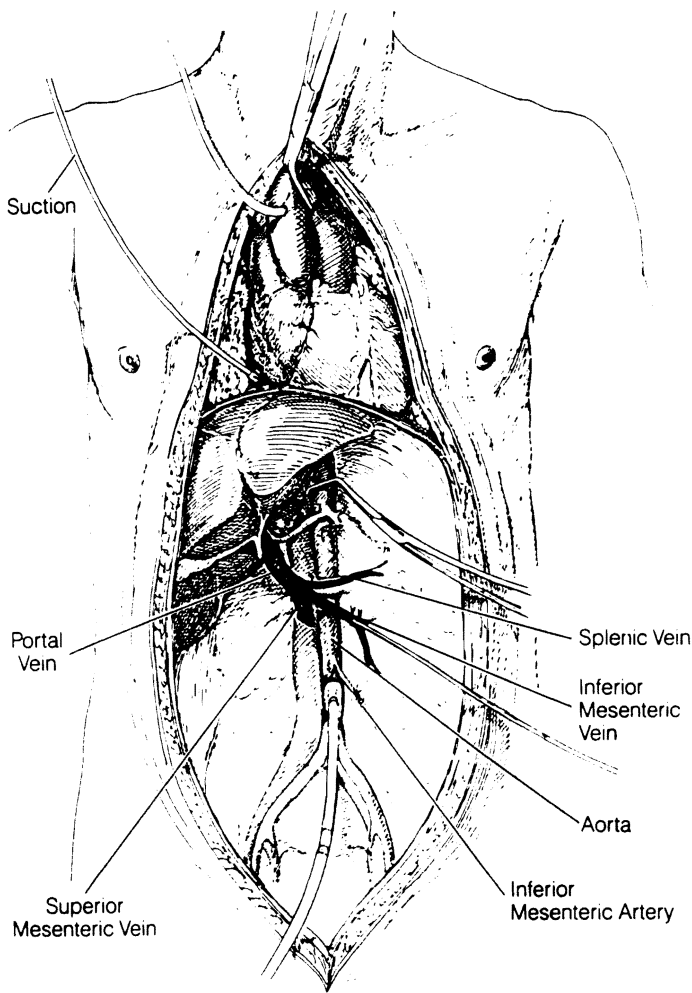
Figure 4 The aorta is cross-clamped at the diaphragmatic level at the time of rapid infusion.

the cardioplegic infusion occur within a few seconds. At the same time, the systemic venous inflow is discontinued by bleeding the inferior vena cava into the pericardium. However, if the cardiac surgeons insist on cross-clamping the inferior vena cava within the pericardium, the vena cava must be vented into the lower abdomen to prevent venous hypertension.

Most cardiac teams require five to 10 minutes from the onset of the cardioplegic infusion to remove the heart. However, as soon as the heart team has discontinued effective circulation by occluding vena caval inflow or by cross-clamping the ascending aorta, the previously encircled aorta is cross-clamped at the diaphragmatic level [*see Figure 4*]. Infusion with cold fluid is begun through both the inferior mesenteric (portal) cannula and the terminal aortic cannula. Thus, the liver is blanching and cooling while the cardiac team is completing removal of the heart. The liver is not dissected further until it becomes palpably cold and free of blood. The kidneys participate in the perfusion and cooling process.

After the liver is cold and the heart has been removed, the liver is removed in a bloodless field while the cold infusion is continued. Above the liver, a patch of diaphragm is removed around the lumen of the suprahepatic inferior vena cava [*see Figure 5*]. The surgeon must now complete the hepatic hilar dissection by cutting or ligating the remaining branches of the celiac axis as far as possible from the parent trunk [*see Figure 5*]. By doing so, and especially by dividing the gastroduodenal artery, he or she uncovers the portal vein. The portal vein is followed inferiorly to the junction of the superior mesenteric and splenic veins, which are cut [*see Figure 6*]. The area posterior to the portal vein must be inspected carefully because it is here that an aberrant right hepatic artery originating from the superior mesenteric artery is most commonly found [*see Figure 6*]. The originating vessel (or vessels, in the case of an aberrant right hepatic artery) is traced to its aortic origin and removed with a Carrel patch [*see Figure 7*]. The liver is excised and placed in a sterile, empty sack immersed in a basin of ice-slush solution.
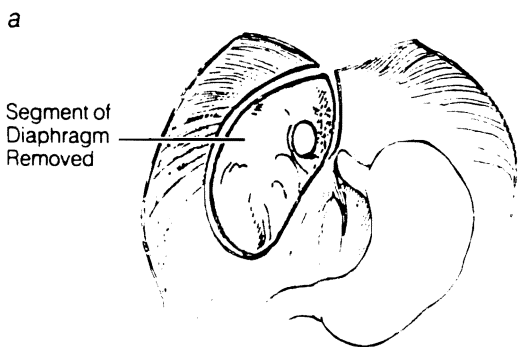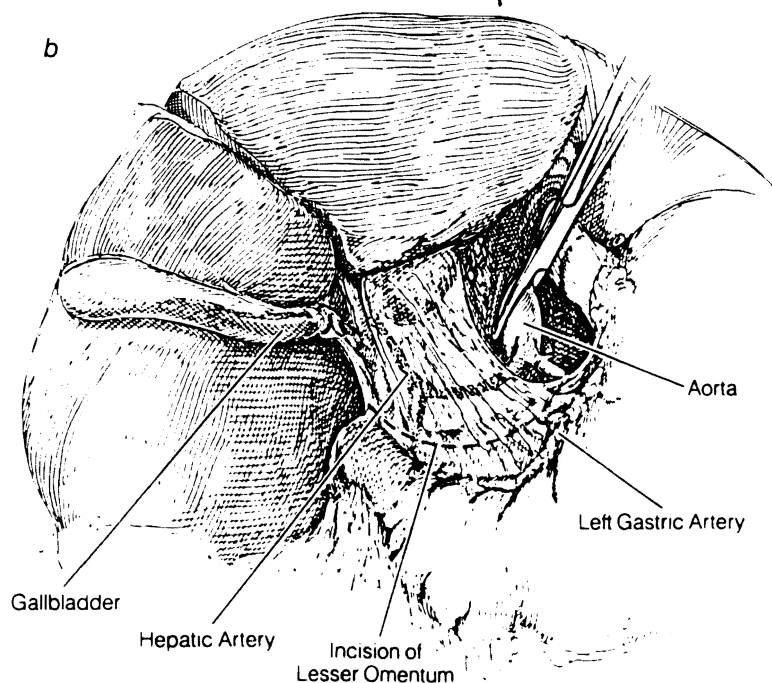

Figure 5 A patch of diaphragm surrounding the suprahepatic inferior vena cava is removed with the liver (*a*). The approach to the hepatic hilar structures is made in a bloodless field (*b*).
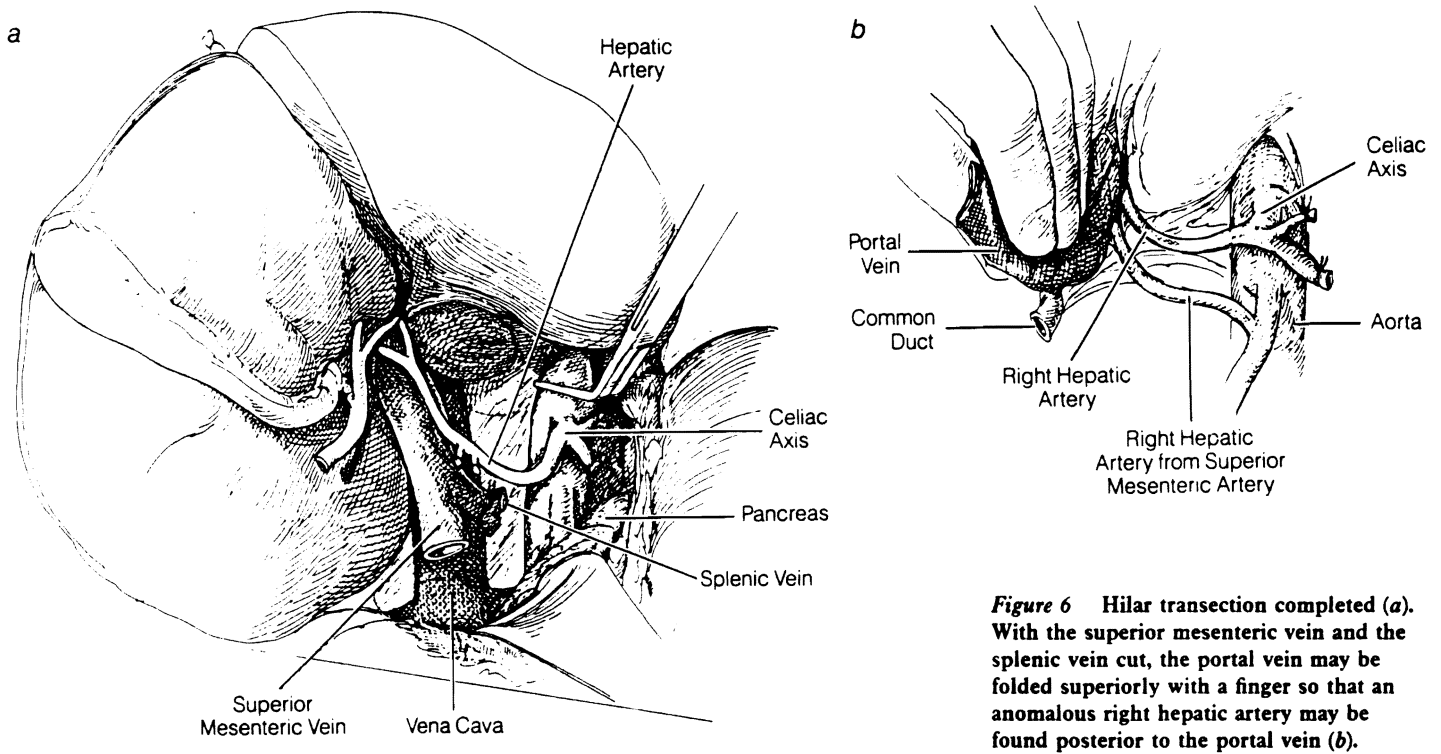
Figure 6   Hilar transection completed (*a*).
With the superior mesenteric vein and the
splenic vein cut, the portal vein may be
folded superiorly with a finger so that an
anomalous right hepatic artery may be
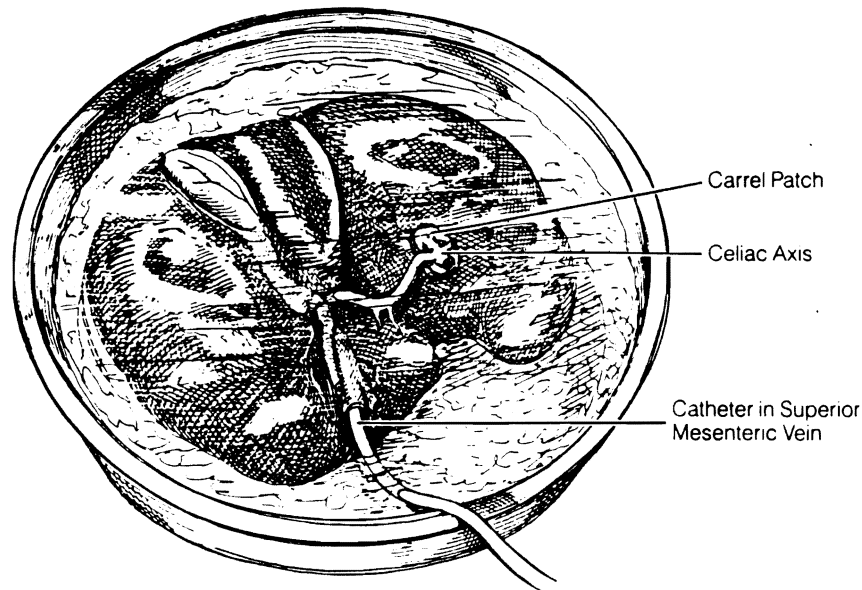found posterior to the portal vein (*b*).

Figure 7   The aortic Carrel patch and the portal cannula used to
infuse chilled preservation solution are shown in this illustration of
an excised liver in an ice basin.

Through a small infusion cannula placed in either the superior mesenteric or the splenic vein, the liver is then perfused with approximately 1.0 to 1.5 L of University of Wisconsin (UW) preservation solution.[16] The organ is subsequently packed in the effluent that remains in the sack and kept refrigerated in a standard ice chest.

The organ is transported to the recipient hospital, where it is cleaned and prepared for transplantation in a formal back table procedure that takes approximately 30 minutes.

Removal of the cold and bloodless liver requires 15 to 30 minutes, but during most of this time, effective cold perfusion of the kidneys in situ continues through the aortic cannula. With the liver out of the field, the two kidneys can be removed en bloc; this process takes an additional five to 10 minutes. Removal is best accomplished from below upward [see Figure 8]. After the kidneys are removed, they are immersed in an ice bath
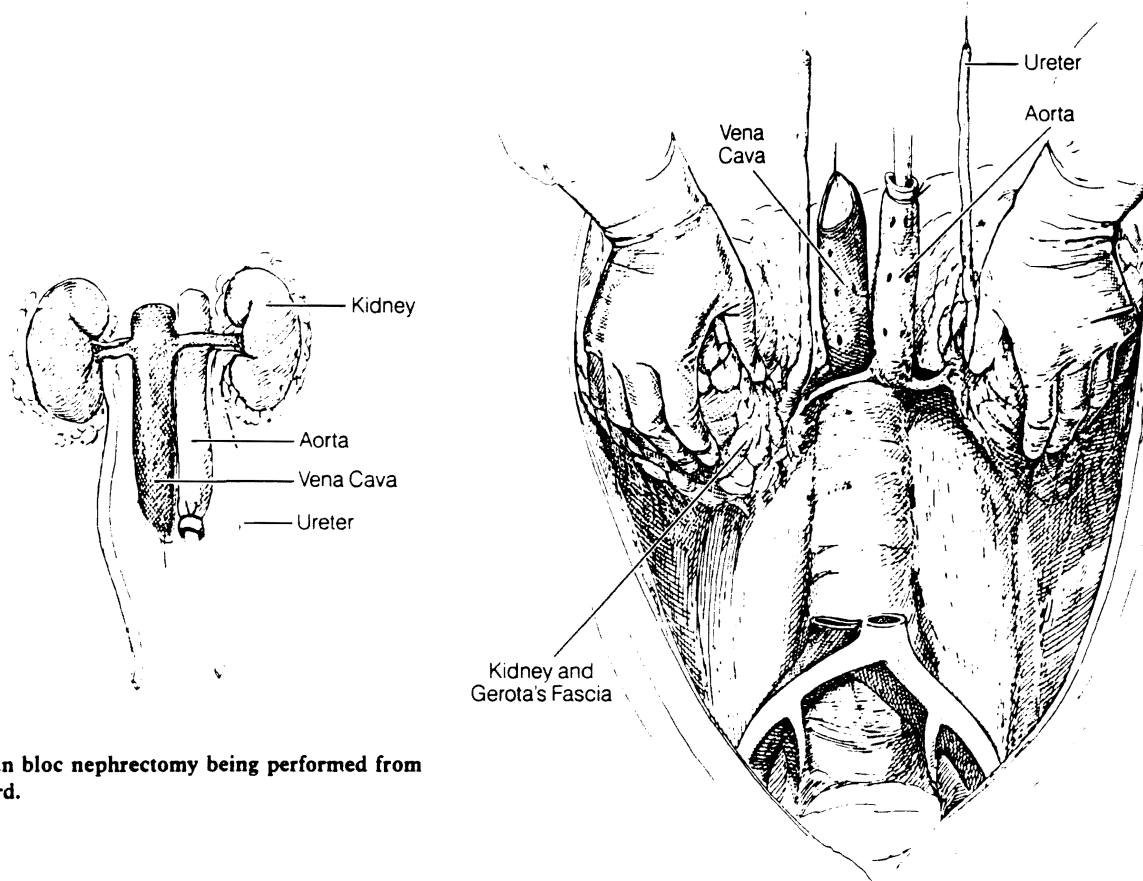
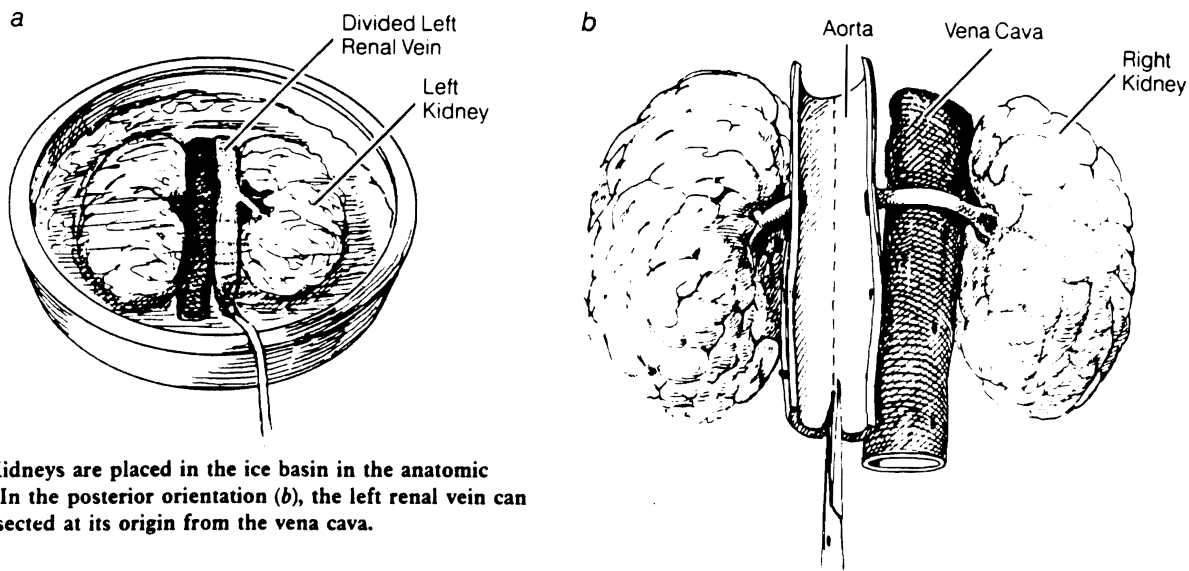*Figure 8* En bloc nephrectomy being performed from below upward.

Figure 9 Kidneys are placed in the ice basin in the anatomic position (*a*). In the posterior orientation (*b*), the left renal vein can be seen transected at its origin from the vena cava.

and reperfused with preservation solution either individually or through the aorta. If the kidneys are to be separated, the left renal vein is transected flush at the point where it enters the inferior vena cava [*see Figure 9*]. The kidneys are then turned over so that the posterior wall of the aorta is accessible. Inserting one blade of a scissors into the aortic lumen, the surgeon incises the posterior wall of the aorta at the midline. A perfect guide to the line of aortic incision is the row of lumbar arteries. Then,

having an internal view of the renal arterial branches passing laterally, the surgeon incises the anterior wall of the aorta longitudinally from the inside. If continuous perfusion is planned for later preservation of the organs, aortic flaps can be fashioned during separation of the kidneys and used for closure so that cannulas need not be placed directly into the renal arteries. Final dissection of the kidneys is performed on a back table at the recipient hospital.
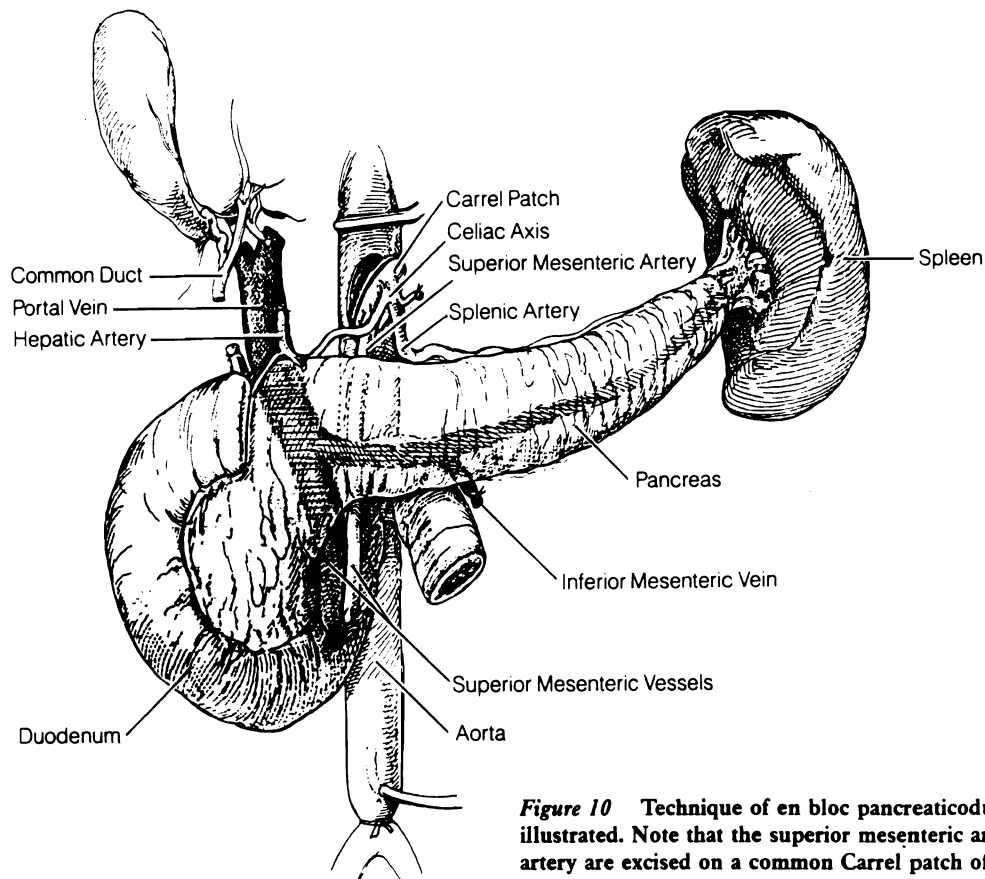
Common Duct
Portal Vein
Hepatic Artery

Carrel Patch
Celiac Axis
Superior Mesenteric Artery
Splenic Artery

Spleen

Pancreas

Inferior Mesenteric Vein

Superior Mesenteric Vessels

Duodenum

Aorta

Figure 10   Technique of en bloc pancreaticoduodenectomy is illustrated. Note that the superior mesenteric artery and celiac artery are excised on a common Carrel patch of aorta.

Total or segmental pancreatectomy can be part of the multiple-organ procurement procedure [see Figure 10]. The technique differs in details but not in principle from that of the procedures described (see above). The dissection is almost always accomplished before in situ flushing and may require between one and a half and three and a half hours to complete. If the whole pancreas is to be transplanted, a Carrel patch, including the celiac axis and the superior mesenteric artery, can be taken from the abdominal aorta [see Figure 10]. This procedure ensures better vascularization of the pancreas graft, and the natural superior-to-inferior pancreaticoduodenal arterial anastomoses are vascularized from both directions.

Although it was previously thought that simultaneous whole organ pancreas and liver recovery could not be done (because both procedures called for retention of the celiac axis and the portal vein), safe techniques have now been established for dividing the vasculature of these organs. With the use of free iliac vein and arterial grafts, successful transplantations of liver and pancreas from a single donor have been accomplished.[17] It is now UNOS policy to encourage utilization of both organs from appropriate donors, although many liver teams approach these donors with trepidation because of the lengthy dissection and associated risks of graft nonfunction. For most diabetics, pancreas transplantation is still somewhat of a luxury because of the option of insulin administration, whereas for patients who require liver transplantation, no alternate form of treatment exists. Therefore, if an anomaly · exists in the donor that precludes successful procurement of both the liver and the pancreas, the liver team must take priority.

With the improved technique that makes possible the use of the liver and the whole pancreas, the liver retains almost all of the portal vein, and the short portal vein of the pancreatic specimen is lengthened with an iliac vein graft from the donor [see Figure 11]. The donor celiac axis, proximal hepatic artery, and superior mesenteric artery stay with the pancreas. The hepatic artery retained with the liver is lengthened with a free iliac artery graft. Obviously, many variations of this technique are possible with the use of free iliac artery and vein grafts.

The arteries and veins of a multiple-organ donor can be put to many other uses. After all the organs have been removed and packaged, segments of the remaining iliac arteries and veins are routinely removed [see Figure 12] and placed in a cold tissue culture solution for refrigeration. The thoracic aorta and pulmonary artery may also be harvested under special circumstances. Vascular grafts can be lifesaving in the event of unexpected technical problems in hepatic recipients, approximately 25 percent of whom require portal vein or hepatic arterial homografts. Vascular grafts are also often employed for reconstruction of renal vessels or for other purposes, including potential pancreas vessel reconstruction.
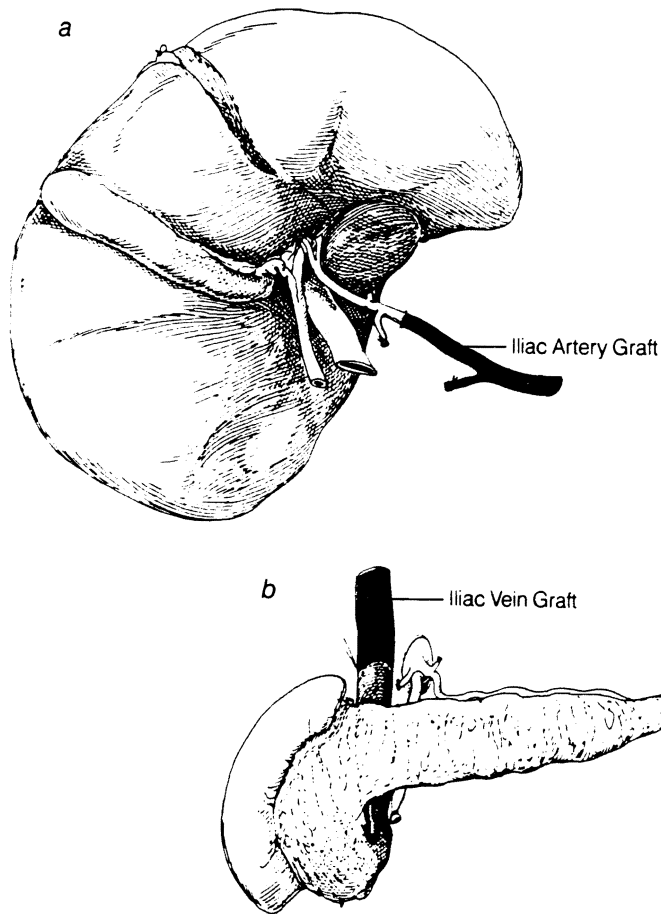
Figure 11   The addition of an iliac artery graft to the hepatic artery and an iliac vein graft to the portal vein of the pancreas graft allows the use of both organs from a single donor.
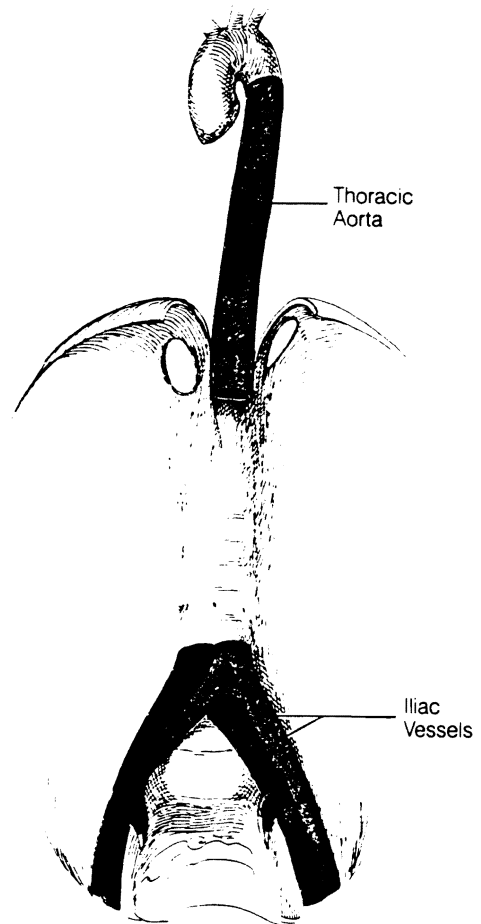

Figure 12   After organs have been removed and packaged, segments of iliac arteries, veins, and thoracic aorta are routinely removed, as illustrated here.

Discussion

Principles and Limitations of Current Methods of Organ Preservation

Despite its importance and despite recent advances, organ preservation remains the least developed component of transplantation technology. Preservation techniques begin with the intraoperative infusion of cold fluids; the paramount objective is to avoid warm ischemia. Cooling of organs by intravascular infusions of chilled lactated Ringer's solution at the time of circulatory arrest was first introduced into the laboratory for experimental liver transplantation more than a quarter of a century ago. The procedure was promptly applied clinically to the preservation of kidneys and other organs. Such cooling lengthens the duration of organ viability and allows subsequent application of more sophisticated preservation measures.

Lactated Ringer's solution is low in potassium and nearly isotonic. In 1969, researchers documented that chilled solutions with an electrolyte composition similar to that in cells, such as Collin's solution, extended the permissible time limit of cold renal ischemia beyond that achievable with isotonic solutions.[18]

The same effect was demonstrated in livers.[19] Cardiac surgeons have cooled the heart with various cardioplegic solutions having potassium concentrations of 20 mEq/L or greater.

From 1969 to 1987, these high-potassium preservation solutions were the only means available for inexpensive cold-storage preservation of transplanted organs. In 1987, the University of Wisconsin solution was introduced.[16] This solution immediately extended safe preservation times for the liver and pancreas and provided improved function as well. The allowable cold ischemia time for the liver increased from eight to 24 hours or longer, and pancreas preservation was increased to 12 hours with excellent postoperative function. UW solution is a complex multiconstituent solution, the components of which address a number of theoretical issues in organ preservation. Although the exact function of each constituent in the solution is unknown, it is felt that the parenchymal cells of the liver, pancreas, and kidney are impermeable to the large anion in the solution, lactobionic acid, and that this prevents the cellular swelling that can complicate all forms of hypothermic preservation. UW

solution receives its oncotic support from the complex starch hydroxyethyl starch rather than from dextrose or the other complex sugars used in the older solutions. Finally, there are a variety of components, including glutathione, raffinose, and allopurinol, that act as free radical scavengers and help prevent reperfusion injury.[20] UW solution is now internationally accepted as a universal flush and preservation solution, although preference for it over isotonic saline as a flush solution is controversial. Its application to cardiac and cardiopulmonary preservation is being studied extensively in the laboratory but has not been studied on a large-scale clinical basis. One of the most profound impacts of UW solution has been felt by liver transplant surgeons, who can now temporally separate the complex donor and recipient operations and perform them in an unrushed, meticulous fashion without jeopardizing organ function.

Highly sophisticated and costly techniques for continuous perfusion of these organs exist, but they have been widely used only for kidney grafts. The continuous perfusion technique for kidneys as originally described used an asanguineous and oncotically controlled fluid.[21] The method has proved to be a good one but has not markedly improved the quality of renal preservation in the first 48 hours over that provided by the simpler infusion-and-slush method. In the future, better continuous perfusion techniques may extend preservation time for all organs.

Even with this new solution, it is still essential to appreciate how unpredictable the outcome of a transplantation can be with any of the currently available preservation techniques. The unknown extent to which the donor has suffered organ ischemia caused by the processes of injury and dying contributes to this unpredictability. All experienced transplant surgeons have been dismayed to observe that homografts retrieved from seemingly ideal donors occasionally do not function, whereas organs obtained under seemingly adverse conditions may function perfectly. One study has documented this phenomonon particularly well for liver transplants[22]; no correlation could be found between liver recipient outcome and the use of ideal versus less than ideal donors. What is urgently needed is a simple, discriminating predictive technique for assessing organ viability before the ruthless biologic test of actual transplantation is performed.

Medical, Ethical, and Legal Considerations

THE RETRIEVAL TEAM

Because the stakes are so high in terms of recipient survival, the technical elements of the organ procurement operation must be constantly reassessed. Much attention is now given to the specific training of the donor, or retrieval, surgeon. When kidneys were the only organs transplanted, transplant centers often assigned organ retrieval to local surgeons whose experience was limited to only the occasional case. Frequently, the penalty for this practice was a prolonged period of acute tubular necrosis in the transplanted kidney, with the attendant risks and mortality. The enormously increased sophistication of today's multiple-procurement procedures make this approach undesirable and probably indefensible from the medicolegal standpoint. In addition, it is important to emphasize that surgeons should not delegate to nonphysicians the actual task of excising organs for transplantation from cadaver donors. Today, most transplant centers tend to delegate organ procurement operations to highly trained surgeons with a specific interest and training in transplantation surgery and organ preservation. Only in this way has it been possible for teams from different institutions to retrieve organs from common donors and to work harmoniously and effectively together. This development reflects the maturation of the field of transplantation.

THE ROLES OF GOVERNMENT AND THE PRIVATE SECTOR

Less than two decades ago, organ harvesting was an uncommon, hurried, poorly standardized surgical exercise in which kidneys (or, rarely, other organs) were rapidly excised from a donor whose heart had just stopped beating.[1] The establishment of irreversible neurologic injury, or brain death, as actual death[23] has made it possible for surgeons to procure organs from heart-beating cadavers in a well-organized manner. Legislation sanctioning the concept of brain death has been passed in 44 states, and judicial precedent exists in the other six.[24]

Despite these developments, skepticism, fear, and anxiety regarding the concept of brain death persist.[25] Brain death must be clearly and fully explained to the relatives of a potential donor to allay the common fear that lifesaving measures may be prematurely terminated to gain rapid access to organs for transplantation. This is never the case. The physician in charge of the initial care of the donor is responsible for determining and making the pronouncement of brain death, with the collaboration of experts in the neurosciences. He or she in no way participates in the donation and harvesting procedures. Conversely, the transplant surgeons cannot participate in the determination of death.

The Uniform Anatomical Gifts Act (UAGA), passed by Congress in 1973, has been adopted in some form in all 50 states.[26] This act states that organ donation is a voluntary gift made by either the donor or the family. The UAGA does not include the concept of presumed consent, whereby organs may be removed automatically unless the next of kin objects. Presumed consent has been practiced in many European countries with some success, and strong ethical arguments have been advanced in its favor.[27] The concept of presumed consent has not gained a foothold in American transplantation.

Despite passage of brain-death legislation and of the UAGA, there is still an acute shortage of cadaveric renal and extrarenal organs, which has been aggravated by the burgeoning success of transplantation. Several factors contribute to this shortage. Some physicians do not wish to face the failure implicit in the death of their patients, or they do not want to burden a grieving family further by requesting donation, or they are aware of certain religious taboos about organ donation, or they have an unrealistic fear of legal recriminations.

The Surgeon General of the United States has made several recommendations for solving these problems, including systematic public education and education of physicians, nurses, and paramedical personnel; recruiting support from the religious community; and sharper delineation of the exact conditions to be met for a pronouncement of brain death.[28] Another strategy for increasing organ donation has been to encourage the signing of donor cards and other forms of living wills.[29]

The organ shortage has prompted a new kind of legislative initiative called required request. Required-request laws have been passed in almost half the states. These laws mandate that each hospital systematically approach the families of all patients who die under circumstances that might make solid organ

donation possible. With such laws, physicians and hospital staff are protected from charges of callousness for asking a grieving family for donation, they are relieved of the fear of legal recrimination, and they can work within an organized administrative channel. If the required-request laws do not increase the supply of organs, further legislation mandating the application of presumed consent may be considered.

Of special interest with regard to the organ shortage are the problems that exist for small children. To address this problem, the use of anencephalic babies as organ donors has been proposed, but such use is a heatedly debated issue.[30-32] Although anencephalic babies clearly have no hope for survival, they cannot be considered brain dead by currently accepted criteria, because they have a functioning brain stem at birth. They are not eligible to become organ donors until their brain stem activity ceases, but by that time, their organs have usually deteriorated. It has been suggested that anencephalic babies be considered a special exception to the classically defined criteria for brain death, to allow this potentially large supply of pediatric organs to become available.

In 1984, Congress enacted legislation authorizing a task force to study issues in organ procurement and distribution and provided for the creation and funding of an Organ Procurement and Transplant Network (OPTN). In 1986, the federal government awarded the OPTN contract to the United Network for Organ Sharing. Under the terms of the contract, UNOS operates a computer-matching system designed to aid in systematic placement of renal and extrarenal organs and to ensure equitable allocation of organs throughout the country. In addition, UNOS is to keep careful data on all harvested organs to analyze and define patterns of organ procurement in the United States so that resources for future development can be better allocated. In the distribution of extrarenal organs, UNOS acts in an advisory capacity to the organ procurement agency managing a specific donor by supplying a prioritized list of acceptable recipients.

It is interesting to speculate how this system will change in the future, as more surgeons are trained in extrarenal organ procurement, as regional centers proliferate, as involvement of personnel at the new centers increases, and as additional demands for equitable allocation of organs are made on the distribution network. As more powerful immunosuppression and preservation techniques are developed and tissue typing and matching become better understood, smaller organ procurement regions in the country may coalesce into larger and more centralized territories to increase the pool of potential local recipients and decrease the time that an organ must be stored before placement. Cold ischemia time would be shortened, and survival might improve. The urgency that still results from present-day organ preservation techniques places a real strain on any organ distribution and sharing system covering a large region.

In parallel with the rapidly growing success of organ transplantation, there has been an increase in federal and state government interest in regulating transplantation medicine. We agree that the government should collaborate with the transplantation community in developing new health policies; however, overregulation could stifle the orderly growth and progress of transplantation. Attempts to limit transplantation of extrarenal organs to existing centers may hinder rather than foster progress in the field and should be resisted. The emphasis should be on constructive collaboration, not on domination of what must primarily remain an effort by transplant surgeons. For example, media coverage of transplantation has led the public to believe it is a fully established science, ready for mass clinical application. This gross misunderstanding of the complexity of the problems involved has generated ambitious proposals for national organ retrieval and sharing legislation that ignore the fact that it will be at least 10 years before organ preservation technology is sophisticated enough to meet the goals the government is setting.

There is also a danger that public misconceptions about transplantation medicine will result in government efforts to regulate the criteria for patient treatment. Political guidelines must not be allowed a role in judging a candidate's suitability for transplantation. Physicians cannot ethically accept any but strict medical criteria in selecting organ recipients.[33,34]

Since the early 1960s, knowledge in the field of transplantation medicine has grown almost exponentially. The tremendous potential of this field continues to depend on broad research aimed at solving a wide variety of problems in the laboratory and at the bedside as well as on resolution of the issues and controversies that transplantation has generated for the public and the medical community.

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