Kidney transplants

By Francine Robinet-Leduc, R.N.

Kidney transplantation involves transplanting a kidney from a living related donor or human cadaver to a recipient who has end-stage-renal-disease, and who requires dialysis in order to maintain life. In the information that follows, I have researched such areas as the pre-operative transplant recipient, immunosuppression and infection prevention.

Kidney transplantation is a form of treatment for kidney failure. Other forms of treatment include hemodialysis (HD), and continuous ambulatory peritoneal dialysis (CAPD)

Dialysis

The diffusion of accumulated uremic toxins across a semipermeable membrane, passing from the side of higher concentration in blood to that of lower concentration in dialysis fluid (dialysate), is known as dialysis. Dialysis is used in renal failure to remove toxic substances and body wastes normally excreted by healthy kidneys. The purpose of dialysis is to maintain the life and well being of the patient. Methods of therapy include hemodialysis and peritoneal dialysis. Both methods replace the essential function of the kidney.

Transplants vs. dialysis

With a successful kidney transplant, dialysis treatments would not be required. Constant removal of wastes and excess water, and the regulating of hormones would successfully occur (dialysis cannot regulate hormones). Other advantages are that renal transplantation would improve the physical health of the recipient, permit freedom from certain dietary restrictions, and would allow the recipient to experience a better quality of life with increased energy level due to absence of anemia.

Disadvantages

The risk of rejecting the transplanted kidney is to be considered as well as the risk of infection due to decreased resistance from the administration of anti-rejection medication. There would be frequent post-operative visits to the doctor and possible hospitalization for treatment of rejection episodes, and possibility of side effects due to the anti-rejection medication. Anxiety caused by fear of losing the function of the transplanted kidney is another disadvantage of kidney transplantation.

Candidates for transplantation

There is virtually no age limit in dialysis treatment for individuals with end-stage-renal-disease. The age range in which transplantation has been performed continues to lengthen. The usual age for a kidney transplantation ranges approximately between four and 65 years. Beyond this range, transplantations are usually not done, or are considered individually. Patient survival declines with increasing age.

There are several factors to consider when determining who should have a kidney transplant. The younger the recipient, the greater the chance for success. The individual's general health is to be assessed, as well as the original disease, and the person's ability to care for himself/herself.

Dialysis patients with severe chronic pulmonary disease, a known cancer within three years of surgery, advanced or non-correctible cardiac disease, or anyone with a known active infection are all considered unsuitable candidates. Other contraindications to transplantation are: severe congenital urinary tract abnormalities, coagulation disorders, mental retardation, psychosocial problems such as psychosis, alcoholism, and drug addiction.

Additional general assessments

A. Psychological study: To assess the individual's ability to deal with hospitalization and stress, and the ability to comply with a medication regimen and long term medical follow-up post-transplant.

B. Gastrointestinal evaluation: Diagnostic studies are done to rule out peptic ulcers. Upper gastro-intestinal haemorrhage and perforation of a peptic ulcer are dangerous complications to renal transplantation with a high mortalty rate; steroid therapy is thought to be important contributory factor. If a peptic ulcer is present, it may require surgical correction prior to transplant.

C. Infection evaluation: The respiratory and urinary tract should be investigated for infection. If infection is present, it must be eradicated before a transplant is possible. A skin test for T.B. is done to determine possible exposure to the bacillus. Immunosuppression could exacerbate an activation of T.B.

D. Urological assessment: Evaluation of the lower urinary tract is performed to rule out a neurogenic bladder, and to assess the ability of the bladder to accommodate normal urine output. Conditions requiring pre-transplant urological assessment include: bladder neck obstruction, ureterovesical and ureteropelvic strictures. In these cases, investigation usually starts with a voiding cysto-urethrogram. This will give information on bladder size and efficiency of emptying, and the presence of reflux.

Next, a cystoscopy may be done to inspect the bladder mucosa. At this time a retrograde pyelogram may be carried out. Urodynamic studies can be done as well: a cystometrogram (to provide evidence of bladder function and sensation), and an electromyography of the urethral sphincter. A decision can be made at this time as to whether or not urological surgery is required prior to the renal transplant.

E. Liver function assessment: Liver function studies are carried out to define the hepatitis status of the individual. Medications administered for kidney transplantation are potentially hepatotoxic; therefore, determining the degree of liver function present is of importance. The state of the hepatitis carrier is an adverse factor but not a contraindication to a transplantation. The individual assessed as being suitable and who has received all the necessary preparations can be considered for a kidney transplant.

Prior to any type of kidney transplant, several tests and treatments must be completed:

a) Blood tests

In order to minimize rejection and improve the chances of survival of a transplanted kidney, efforts are made to match as closely as possible the blood types and tissue types of the donor and recipient.

First, the blood is tested for ABO or blood type compatibility. Second, a tissue typing is done to identify the protein antigens that are specific to each individual. These antigens are the human leukocyte antigens (HLA), so called because they are easily identifiable on leukocytes. The more compatible HLAs the donor and recipient share, the less likely that tissue rejection will occur.

A third test that is done is cross-matching. This involves mixing the intended recipient's serum with lymphocytes from the potential donor. A positive reaction would show destruction of the donor's cells by antibodies in the recipient's serum, thus eliminating the possibility of using the kidney from that particular donor. The probability of survival of a transplanted kidney is greatest when the donor is a sibling who is HLA identical to the recipient.

b) Blood transfusions

In some centres, individuals being placed on the transplant list are expected to have blood transfusions before the kidney transplantation. It is believed that blood transfusions help protect the transplant recipient against rejection. In the research carried out, it has been found that at the Ottawa Civic Hospital 70-75% of recipients have successful kidney transplants with transfusions and 50-55% success without transfusions.

Selection of the kidney donor

When the decision is made that a renal transplantation is an option for the ESRD patient, a decision about the type of transplant to be performed must be made. There are two types of kidney donors: (1) living related donors and, (2) cadever donors.

The use of a living related donor for K.T. involves transplantation of a kidney from one of the patient's immediate family to the patient (mother,

father, brother, sister, son or daughter). When K.Ts. are done using living donors, it increases graft survival rates compared to cadaveric transplantation.

The operation can be specifically planned, thus allowing time for recipient preparation. The use of living donors allows the chronic inability of cadaveric donation to fulfill the increasing demand for organ transplants. (Keown, et al., 1986, p. 522).

The donor should be of an acceptable age, normally between the ages of 18 and 60 years, and should have no significant medical history. Hypertension and diabetes contraindicate donation. The living donor must be in excellent physical health, highly motivated, with the normal emotional responses necessary to be able to donate their kidney. A psychological evaluation is often recommended. The donor has a blood test to determine ABO compatibility which is essential between donor and recipient.

Then, the donor has a second blood test to determine if genetic similarities exist between donor and recipient, which would make the transplant more likely to work. This is called HLA tissue typing.

Other tests are done to ensure that no health hazards occur by donating a kidney, and to confirm normal renal function with no evidence of disease.

An intravenous pyelogram and voiding cysto-urethrogram are performed to show the kidney and urinary structure and to eliminate vesicoureteric reflex. If it is a requirement that the renal vasculature be visualized, an angiogram is performed. If tests are completely normal, the donor can serve as a low risk donor.

When there is no suitable living related donor available for patients with ESR failure, a cadaveric donor is utilized. The use of a cadaver donor involves transplantation of a kidney from a person who has died from brain trauma, or some other sudden, terminal event that occurs in a previously healthy person. The success rate of cadaveric donors is inferior to that of living related donors. The results are acceptable as the majority of cadaver recipients have long-term rehabilitation free of chronic dialysis therapy.

The blood group of the donor must be compatible with the recipient, and to ensure as much as possible that the potential kidney is compatible, a number of other blood tests are performed.

Due to present methods of preservation of the kidney (up to 72 hours), opportunities are available to carry out tests to evaluate the physiological condition of the cadaveric kidney and for determining histocompatibility between the recipient and donor-even after the kidney is removed from the cadaver.

The cadaveric donor should not exceed 65 years of age. He or she should have no evidence of previous hypertension, diabetes mellitus, previous renal disease, malignancy, generalized viral or bacterial infection and normal BUN creatinine.

After the kidney is procurred, it is preserved under cold conditions (4 - 6°C) to allow return of function of the kidney after revascularization. The kidney is maintained at cold temperatures, either with a saline flush solution or pulsatile perfusion, which allows prolonged storage of the organ (up to 72 hours).

Transporting a cadaveric kidney

If a kidney is going to another centre, the following should accompany the kidney in the transportation container:

Figure 1:
Transportation contents of a cadaveric kidney

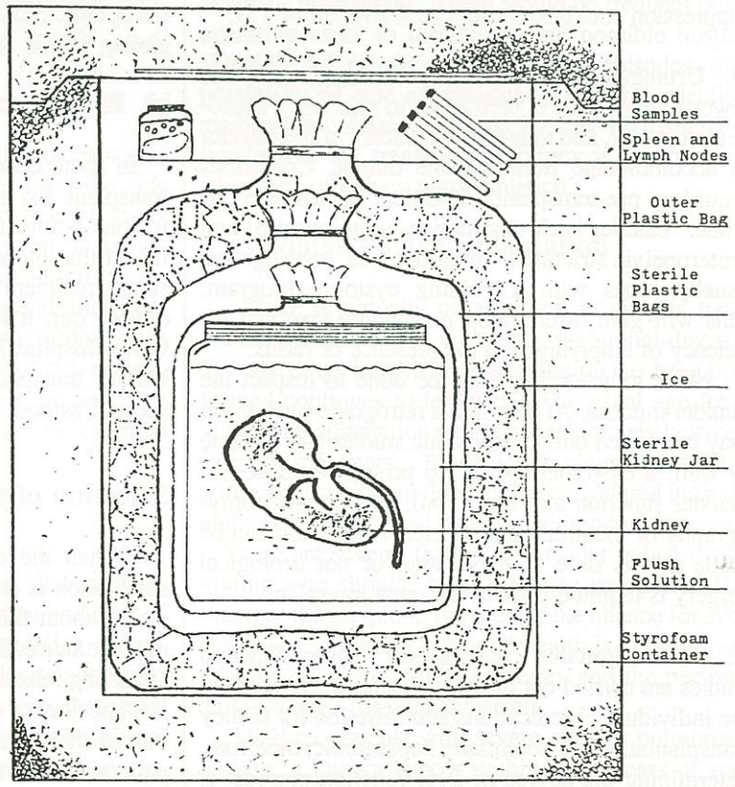
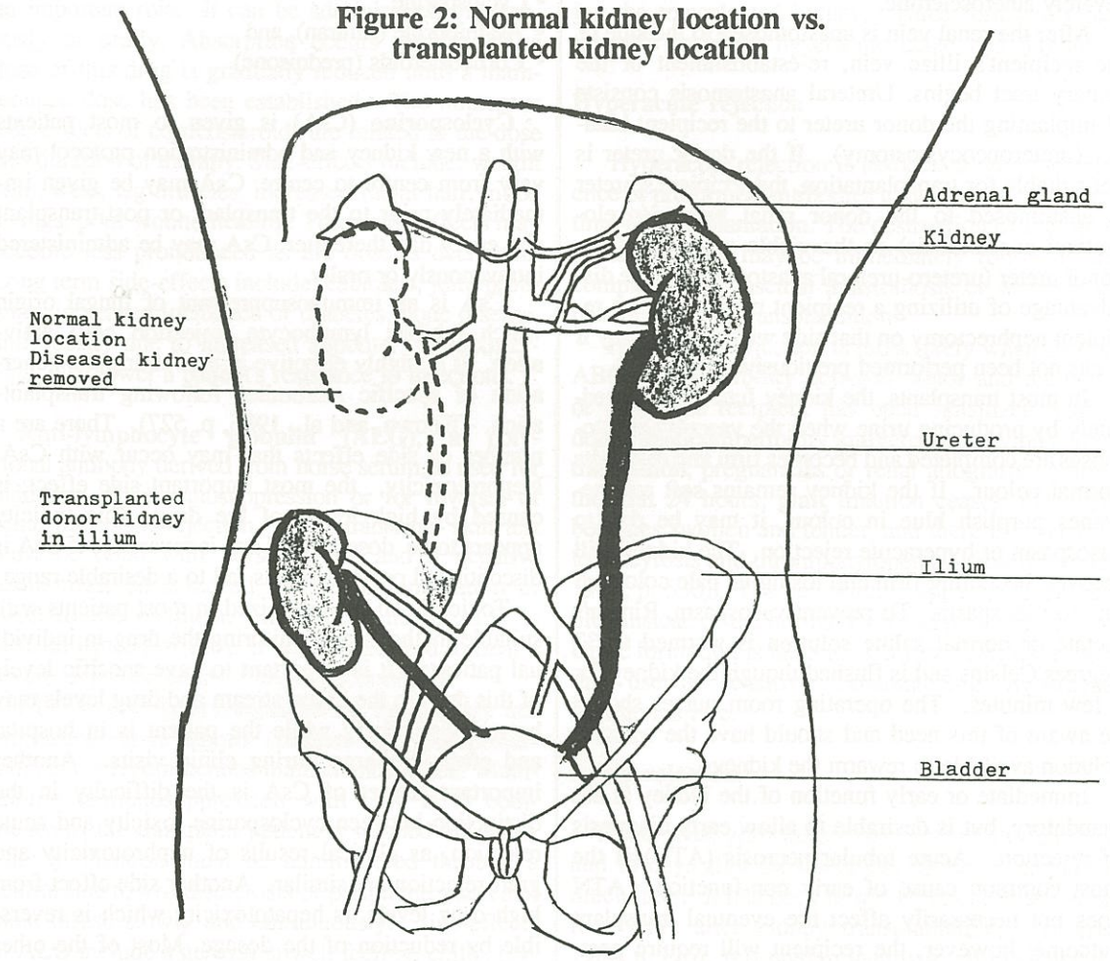


Figure 2: Normal kidney location vs. transplanted kidney location



- blood (4, 10cc tubes)
- lymph nodes (minimum of three in a McCoy's medium or normal saline)
- spleen (some centers include the whole spleen and others may require two samples to be transported in a McCoy's medium or normal saline)

The kidney is placed in a sterile jar containing perfusate and the lid is screwed on. The sterile kidney jar is then placed in two sterile plastic bags and then placed in a third sterile plastic bag. Ice is inserted in the outer plastic bag covering all areas of the inner plastic bags to allow preservation of the kidney. The spleen and several lymph nodes, needed for cross matching, are placed in a sterile jar and blood samples are included in the transportation for testing ABO compatibility between donor and recipient.

The combination of kidney, spleen and lymph nodes, and blood vials are then placed in a styrofoam container which is properly labelled and is then ready for shipping **(Figure 1, preceding page).** Deterioration of the kidney begins once it is removed from the body. Therefore it is essential that transportation be completed as quickly as possible.

Renal transplantation

The site favored for the transplanted kidney is the right iliac fossa (right or the left kidney can be utilized) because it allows for easier access to the recipient blood vessels. The iliac vein on the left side tends to be somewhat deeper, and the sigmoid colon may make the exposure somewhat more difficult. The right or left iliac fossa is selected because there is good blood supply. The implanted kidney will be protected by the hip bone, and the kidney can be easily felt by the physician. It is also the easiest position from which to connect ureter to bladder.

The three anastomoses in renal transplantation are the renal artery, the renal vein, and the ureteral anastomosis. The donor renal artery is anstomosed end-to-end to the hypogastric artery. The renal artery may be anastomosed end-to-side to the iliac artery, in cases where the hypogastric artery is too small or

severely atherosclerotic.

After the renal vein is anastomosed to the side of the recipient's illiac vein, re-establishment of the urinary tract begins. Ureteral anastomosis consists of implanting the donor ureter to the recipient bladder (ureteroneocystostomy). If the donor ureter is not suitable for transplantation, the recipient's ureter is anstomosed to the donor renal pelvis (pyeloureteral anastomosis) or the viable segment of the donor ureter (uretero-ureteral anastomosis). The disadvantage of utilizing a recipient ureter is that a recipient nephrectomy on that side will be necessary if it has not been performed previously. **(Figure 2)**

In most transplants, the kidney functions immediately by producing urine when the vascular anastomoses are completed and becomes firm and regain its normal colour. If the kidney remains soft and becomes purplish blue in colour, it may be due to vasospasm or hyperacute rejection. The kidney will recover, becoming firm and losing its pale colour, if due to vasospasm. To prevent vasospasm, Ringer's lactate or normal saline solution is warmed to 37 degrees Celsius and is flushed though the kidney for a few minutes. The operating room nurses should be aware of this need and should have the warmed solution available to rewarm the kidney.

Immediate or early function of the kidney is not mandatory, but is desirable to allow early diagnosis of rejection. Acute tubular necrosis (ATN) is the most common cause of early non-function. ATN does not necessarily affect the eventual transplant outcome; however, the recipient will require post-transplant dialysis. The frequency of ATN is influenced by over-prolonged or inadequate preservation, and by suffering a prolonged degree of warm ischaemia during retrieval of the donor kidney.

Anti-rejection medication

The chief limiting element of a kidney transplantation is the system's immunologic response that leads to rejection of the transplanted kidney. The recipient's system recognizes the transplanted kidney as a foreign tissue and attempts to destroy it. The survival of the transplanted kidney depends on the methods used to suppress the immunologic reaction. To overcome or minimize the body's defense mechanism, immunosuppressive drugs are given.

There are a number of drugs that can be administerd in order to help prevent rejection of the transplanted kidney. These drugs are sometimes used in combination with one another. The individual must take drugs for the life of the kidney. The commonly administered drugs used to prevent rejection during kidney transplants are as follows:

- Cyclosporine
- Asathioprine (Imuran), and
- Corticosteroids (prednisone)

Cyclosporine (CsA) is given to most patients with a new kidney and administration protocol may vary from centre to centre. CsA may be given immediately prior to the transplant or post-transplant and every day thereafter. CsA may be administered intravenously or orally.

CsA is an immunosuppressant of fungal origin which inhibits lymphocyte (rejection cell) activation. It is highly effective in preventing the generation of specific antibodies following transplantation. (Keown, and al., 1985, p. 527). There are a number of side effects that may occur with CsA. Nephrotoxicity, the most important side effect, is caused by high levels of the drug. This toxicity appears to be dose-related and is reversible if CsA is discontinued or when levels fall to a desirable range.

Toxicity can be minimized in most patients with suitable methods of monitoring the drug in individual patients. It is important to have specific levels of this drug in the blood stream and drug levels may be measured daily while the patient is in hospital and after discharge during clinic visits. Another important aspect of CsA is the difficulty in the distinction between cyclosporine toxicity and acute rejection, as clinical results of nephrotoxicity and graft rejection are similar. Another side effect from high drug levels, is hepatotoxicity which is reversible by reduction of the dosage. Most of the other side effects cause minimal problems in most patients, such as fine hair growth on the upper body, a decreased appetite, increased sex drive, slight gum enlargement and mild tremors.

Asathioprine (Imuran) is an immunosuppressant which inhibits lymphocyte proliferation. It suppresses the production of white blood cells which are active in the process of rejection. It can also suppress the production of other cells formed in the bone marrow such as platelets which are responsible for blood clotting. This bone marrow suppression is an adverse side-effect of this drug.

Another adverse side effect is hepatitis and, occasionally, hair loss. A complete blood cell count may be done daily, when the recipient is in the hospital or during clinic visits upon discharge. To keep blood counts within safe limits, the dose of the drug is adjusted as necessary.

Corticosteroids (Prednisone) is also very effective in suppressing the process of rejection. The powerful anti-inflammatory action of this drug plays an important role. It can be administered intravenously or orally. Absorption occurs rapidly. The dose of this drug is gradually reduced until a maintenance dose has been established. The numerous side-effects of corticosteroids are related to the dose and duration of therapy. Side-effects include: weight pain, weak leg muscles, increased facial hair, mood swings, poor wound healing. These side effects may become less pronounced as the dose is decreased. Long term side-effects include: cataracts, joint problems, increased incidence of diabetes, bone disease, and obesity due to increased appetite. Corticosteroids also lower a patient's resistance to infections.

Anti-lymphocyte globulin (ALG), a polyclonal antibody derived from horse serum, is used for induction of immunosuppression or for reversal of acute transplant rejection. An intradermal skin test must be done with horse serum, and a negative result must be achieved for the administration of ALG to the recipient. In some centres, ALG is utilized instead of CsA. If ALG is utilized to treat a severe rejection crises, CsA is discontinued.

ALG is usually accompanied by the primary immunosuppressive agents (Imuran and Corticosteroids) in the recommended maintenance doses. Maintaining immunosuppression with CsA is to commence as the transplant patient is weaned off ALG. This medication must be administered through a central line to avoid sclerosis of peripheral veins and must infuse slowly and continuously. Side-effects of ALG include a general unwell feeling, chills, fever, joint discomfort, and a decrease in platelets.

All of the medications used in renal transplantation to prevent rejection of the new kidney interfere in some way with the body's normal defense mechanisms. A very delicate balance must be maintained in their administration in order to avoid tipping the scales in the direction of rejection of the kidney on one side and a fatal infection on the other.

Rejection in renal transplantation

Following a kidney transplant, the recipient must be assessed for signs and symptoms of threatened graft rejection: oliguria, edema, fever, increased blood pressure, weight pain, and swelling or tenderness over the graft.

Rejection is the immune reaction of the recipient to foreign tissue cells (antigens) after kidney transplantation, with the production of antibodies. These antibodies are capable of inhibiting metabolism of the cells within the new kidney. Eventually they cause the destruction of these new cells, thus destroying the transplanted kidney. Three forms of rejection are classified: hyperacute, acute, and chronic.

Hyperacute rejection

Hyperacute rejection is associated with the presence of preformed antibodies to donor antigens at the time of transplantation. The destruction of the transplanted kidney may be immediately following the completion of vascular anastomosis or within minutes or hours of transplantation.

Hyperacute rejection is most likely when there is ABO incompatibility between donor and recipient, or when the recipient has been sensitized against donor histocompatibility antigens by previous blood transfusion, pregnancies or renal allografts. Within the first 24 hours, graft function ceases, the organ becomes swollen and tender, and there is fever with leukocytosis and thrombocytopenia. (Keown, et al., 1986, p. 530). The new kidney appears flaccid and blue instead of the normal firm and pink appearance. Urine formation is lacking. Currently, with the routine use of sensitive crossmatching, hyperacute rejection is rare.

Acute rejection

Acute renal graft failure may occur between three and 14 days after the transplant, though it can occur much later. It has been observed to occur as late as five years after kidney transplantation. (Morris, 1984, p. 126). It is predominantly a cell-mediated reaction where sensitized lymphocytes attack foreign tissue. Clinically, a sudden sharp deterioration in renal function occurs, accompanied by fever, pain, swelling, graft tenderness, leukocytosis, and thrombocytopenia.

Chronic rejection

Chronic rejection, generally occurs more than six month post-transplant, and may occur as early as three weeks after renal transplantation. There is gradually a progressive loss of function of the transplanted kidney with less severe symptoms than in the acute form. The progressive deterioration in graft function (over a period of months to years) is accompanied by hypertension and mild proteinuria. Clinically, the kidney does not appear tender or enlarged, and there is no fever leukocytosis, or thrombocytopenia.

Repeated insults from acute rejection episodes, lead to the gradual deterioration and eventual loss of renal graft function. If the kidney remains in situ

with deterioration or complete loss of function, the fibrosis occurs and the kidney becomes shrunken and shrivelled. The possibilities of graft function after renal transplantation may occur as follows:

- the kidney starts functioning immediately, and there are no problems; no rejection;
- the kidney does not work, and will never function, therefore the kidney is removed;
- the kidney undergoes rejection, is treated and begins to function;
- the kidney rejects, is treated and does not begin to function;
- the kidney functions, undergoes rejection, is treated with the administration of specific immunosuppressive agents when rejection occurs; kidney begins to function, then rejects...

Dialysis may be required when the kidney does not function immediately or if the recipient experiences rejection; this does not mean the kidney will not respond to treatment.

When a patient rejects a first renal transplant within the first year, transplant nephrectomy is usually necessary. Rejected foreign tissue left in situ will produce a symptom of fever, allograft tenderness, generalized malaise, cachexia (malnutrition, wasting away), and weight loss. Transplants that undergo chronic rejection, if well tolerated, may be left in place. Retransplantation a second or third time can be attempted if the first transplant fails.

Infectious complications

The success of renal transplantation depends on the achievement of sufficient immunosuppression to avoid rejection; but immunosuppressive agents reduce the body's resistance to infections. The problem of infection contributes substantially to the morbidity and mortality in transplant recipients.

The recipient is constantly monitored for infection post-transplant since the recipient is susceptible to faulty healing and infection due to both immunosuppressive therapy and complications of renal failure. A distinction must be made between infection and rejection since impaired renal function and fever are evidence of both infection and rejection.

Prevention of infection is essential. Therefore the patient should be screened for latent infection before transplantation. Complications of the operation itself are the underlying cause of many early infections of the wound and urinary tract. The use of wound drains is controversial since drainage is an excellent culture medium for bacteria. However, if used, it should be a closed system.

Throughout the surgical technique, sterility is essential to help prevent post-operative infection. The administration of prophylactic antibiotics given at the time of surgery has contributed to a marked decrease in post-transplant infection. Strict reverse isolation may be carried out with health team members wearing masks for the first 48 hours in the intensive care unit. When the recipient returns to the surgical area, protective isolation should be maintained by the use of a private room, and prevention of patient contact with infected individuals.

Septicemia in renal transplant patients is responsible for a significant number of the deaths. Clinical manifestations of septicemia include shaking, chills, fever, tachycardia, tachypnea, and leukocytosis. Daily blood cultures should be performed and antibiotics given immediately if the patient develops a fever.

Conclusion

Successful transplantation depends upon careful preparation of the recipient and donor, the surgical technique, and the optimal manipulation of the immune response to prevent graft rejection. With advances in organ preservation, histocompatibility, immunosuppression, and patient management, there is a higher likelihood of successful renal transplants with reduced patient mortality.

An HLA-identical sibling is the ideal choice for a kidney transplantation. The rejection of a transplanted kidney remains a matter of concern to the patient, the patient's family, and the supporting health care team for many months. The fears of kidney rejection and the complications of immunosuppressive therapy place great psychological stresses on the patient. Kidney transplantation remains the preferred way of treating most patients with end-stage-renal disease. ■

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About the author

Francine Robinet-Leduc, a recent graduate of the Post-Graduate Operating Room Technique and Management Program at the Hotel Dieu Hospital, Kingston, Ontario, received her nursing diploma from St. Lawrence College of Applied Arts and Technology, Cornwall, Ontario. Currently she is a staff nurse in the O.R. at the Ottawa Civic Hospital.

The next frontier in medicine: bioartificial organs

Using the principles of organ transplantation to replace worn-out or end-stage body parts has been successful - to a degree. The shortage of compatible donor parts from living or cadaveric sources will not keep up with the demand. However, the solution, predict the experts in the field, is to combine organ transplant principles with prosthetic engineering.

"In the next 50 years, medicine will take advantage of what nature has invented and put it together with what we can do by engineering design to produce bioartificial organs," says Dr. Pierre Galletti of Brown University in Dallas, Texas.

Already researchers are attempting to treat diabetes with islet of Langerhans, he said. Other researchers are experimentally growing tissue on artificial meshes or tubes to produce new skin, nerves, esophagi and vascular structures.

While organ transplantation is often successful, donor organs are in short supply, he said. Prostheses such as the artificial heart and other organs are only at the beginning of a long evolution.

Meanwhile, bioartificial organs may allow replacement of a portion of an organ, provided specific hormones and chemicals are used to actually rebuild a lost structure, he said.

The concept of an artificial pancreas has sparked the interest of researchers throughout the world as a possible means of producing insulin for diabetics without daily injections, he said. The concept is to use pancreatic tissue islets encapsulated in a small plastic membrane that has selective permeability.

Four diabetic patients in a Chinese-Canadian research effort have already been given these transplants (plastic membranes and human fetal islets). All were able to reduce their insulin dosage from between 10% and 25%.

The same principle might be used to provide dopamine to Parkinson's patients, Dr. Galletti said.

Besides the use of bioartificial endocrine organs is the use of scaffolds and normal cells to grow tubular structures of the body such as an esophagus or blood vessels. "By directing the body's own healing process, in the future, medical science might be able to regrow structures by forming a scaffold for directed growth... If the body is helped and directed, conceivably certain parts could be generated in an orderly fashion."

He predicted that in the next 35 years, medical science will continue to combine the positive aspects of transplantation with the concept of prosthetic devices to form new artificial organs. "I think the future is in combining the aspects of the two."

Bubonic plague awaits grave diggers

There have been a number of plagues since the beginning of history, and although they are a distant scourge of the past, except for isolated areas, authorities in Ireland have issued a grave warning to archaeologists and, especially, unauthorized diggers at certain Middle Age sites, to be wary of exposure to the medieval aftermath of the largest plague of them all, the Black Death of the 14th century.

It seems that there is a burial ground located in County Tipperary, Ireland. Tresspassers have been known to dig in the area. Historical records indicate that victims of that Plague, which killed 25 million people in Europe alone, were buried there.

"It is not unknown for the Black Death germ (bacillus Yersinia pestis) to survive in graves used during the Great Plague," said a spokesman for the Office of Public Works in Ireland, which is responsible for the burial site. "Archiologists working on similar sites often receive protective injections," the spokesman said.