The ability to perform renal transplantation as a treatment in cats has been attributed to a number of factors including the:

- Development of microsurgical techniques in veterinary practice
- Ability to use an allograft from an unrelated donor
- Application of the drug cyclosporine for immunosuppressive therapy.

It is estimated that between 400 to 500 cases of feline renal transplantation have been performed at a few limited centers around the country (Table). In a study comparing survival time of cats that had undergone a renal transplant to a control population of cats treated medically, renal transplantation appeared to prolong survival time and quality of life compared with the medical management of the disease.

Although there is not a retrospective study encompassing all of the cases that have been performed to date, both published and unpublished information from different centers suggests that survival to discharge and long-term survival are improving. This is likely related to:

- More stringent case selection
- Surgical experience
- The clinician’s ability to better recognize early, and treat successfully, both peri-operative as well as long-term complications.

Renal transplantation continues to remain a viable treatment option for cats with early decompensated chronic kidney disease or irreversible acute renal failure.
INDICATIONS
The most common histopathologic diagnosis (identified from native kidney biopsy samples) of cats needing a renal transplant is chronic interstitial nephritis. Other conditions that have resulted in renal transplants in the cat include:

- Polycystic kidney disease
- Oxalate nephrosis
- Membranous glomerulonephropathy
- Ethylene glycol & lily toxicity
- Renal fibrosis
- Amyloidosis
- Pyelonephritis
- Renal dysplasia.

Because of the potential long-term effect on the allograft, it is unclear whether patients with pyelonephritis or amyloidosis are appropriate candidates for the procedure.

RECIPIENT SELECTION
The best time to intervene with surgery is not completely known in this patient population. Surgical intervention has been recommended in cats with early decompensated chronic kidney disease or irreversible acute renal failure.99 Indications of decompensation include continued weight loss, worsening of the anemia, and azotemia in the face of medical therapy. It is important to note that some clinically stable candidates can rapidly deteriorate and die without prior evidence of decompensation.

Evaluating Potential Candidates
Both physical and biochemical parameters need to be carefully evaluated when determining a cat’s candidacy for renal transplantation. Current evaluation at our facility involves:

- Laboratory tests: Complete blood count, serum biochemistry profile, blood type and crossmatch, and thyroid evaluation
- Urinary tract evaluation: Urinalysis, urine culture, and urine protein:creatinine ratio
- Abdominal evaluation: Abdominal radiographs and ultrasound
- Cardiovascular disease evaluation: Thoracic radiography, electrocardiography, echocardiography, and blood pressure measurement
- Screening for infectious disease: FeLV, FIV, Toxoplasma titer (IgG, and IgM).

Based on historical experience, cats that are FeLV positive or have an active FIV infection, patients with recurrent urinary tract infections that have failed a cyclosporine challenge (see Why a Cyclosporine Challenge?), and those with underlying neoplasia are declined as candidates for the procedure.

Risk & Survival Factors
Limited information exists regarding risk factors associated with morbidity and mortality in these patients.

WHY A CYCLOSPORINE CHALLENGE?
A cyclosporine challenge is performed prior to renal transplantation to help determine if a patient is harboring an infection that may be detrimental to the patient, resulting in morbidity and mortality after renal transplantation and immunosuppression.

To perform a cyclosporine challenge, the patient is started on oral cyclosporine (2–5 mg/kg depending on patient’s appetite) at a dose necessary to obtain therapeutic levels (300–500 ng/mL). Once therapeutic levels are obtained, the patient is kept on the medication for ~2 weeks. During that time, the patient is evaluated for any recurrence of infection.
The degree of anemia, azotemia, urine specific gravity, and age do not determine a suitable patient for transplantation, although azotemia has been identified with complications.

The degree of azotemia prior to surgery was found to be a risk factor in 1 study. In a second study, the level of azotemia significantly increased the risk of neurologic complications in the perioperative period, but was not related to long-term survival.

In 3 separate studies, age was identified as a factor associated with survival following discharge. Preoperative blood pressure, duration of anesthesia, and weight have also been shown to influence overall survival.

Objective information is still needed for a number of gray areas, including cats with echocardiographic abnormalities, hyperthyroidism, diabetes, inflammatory bowel disease, and upper respiratory infections. Additionally, questions regarding the appropriate nutritional status for these patients comes up repeatedly.

POTENTIAL DONOR EVALUATION

Kidney donors are young (1–3 years of age) and in excellent health. Standard screening includes:

- Complete blood count and serum biochemistry profile
- Urinalysis and culture
- FeLV and FIV testing and Toxoplasma titer (IgG and IgM).

To determine compatibility, a blood type and red cell crossmatch are performed between the feline kidney donor and recipient. Although rare, incompatible crossmatch tests between AB compatible donor and recipient pairs have been identified. Additionally, we

AN IMPERATIVE INCLUSION: IMMUNOSUPPRESSION

Current immunosuppression in the cat includes a combination of the calcineurin inhibitor— cyclosporine (Neoral, pfizer.com)—and the glucocorticoid—prednisolone. These drugs are used together for their synergistic effects.

Cyclosporine
- At our facility, cyclosporine is begun 24 to 96 H prior to transplantation at a dose of 1 to 4 mg/kg PO Q 12 H, depending on the patient's appetite.
- A 12-hour whole-blood trough concentration is obtained the day prior to surgery to adjust the oral dose for surgery. Ideally, through the use of high-pressure liquid chromatography, a target 12-hour trough concentration of 300 to 500 ng/mL prior to surgery is the goal.
- This level is maintained for approximately 2 to 3 months and then tapered to approximately 250 ng/mL for maintenance therapy.

Prednisolone
- Prednisolone is administered beginning the morning of surgery.
- It is started at a dose of 0.5 to 1 mg/kg PO Q 12 H for the first 3 months; then tapered to Q 24 H.

Azathioprine
- It is important to note that protocols for both cyclosporine and prednisolone vary between transplantation facilities. If renal function starts to deteriorate in the first weeks to months following transplantation, azathioprine (0.3 mg/kg Q 72 H) may be added to the immunosuppressive protocol. Cats receiving azathioprine should have their white blood cell count monitored regularly.

Ketoconazole
- Another option for immunosuppression currently in clinical use is a protocol for once-a-day administration of ketoconazole:
  - Ketoconazole, 10 mg/kg PO Q 24 H, is administered in addition to the cyclosporine and prednisolone.
  - Once ketoconazole is added to the immunosuppressive protocol, cyclosporine and prednisolone are administered once a day and cyclosporine doses are adjusted into the therapeutic range by measuring 24 H whole blood trough levels.
  - If signs of hepatotoxicity are identified, ketoconazole administration should be discontinued.

Currently, we perform computed tomography (CT) angiography to evaluate the renal vasculature and parenchyma for abnormalities (Figure 1). This technique has allowed us to identify patients unsuitable for donation prior to surgery, including patients with renal infarcts as well as those with multiple renal arteries. Although, in my experience, renal donation does not appear to affect normal life expectancy, long-term monitoring is recommended.

**TRANSPANT SURGERY**

**Preoperative Care**

Preoperative care will vary depending on the stability of the patient.

- **Hemodialysis** may be necessary in some cases in order to stabilize the patient prior to surgery.
- **Intravenous fluid therapy** of a balanced electrolyte solution (1.5–2× daily maintenance requirements) is administered to most patients. However, underlying cardiac disease may preclude this rate of fluid therapy due to development of pulmonary edema and pleural effusion.
- **Whole blood transfusions or packed red cells** may be used to correct anemia (depending on the stability of the cat) prior to or at the time of surgery. The first unit that is administered is a unit that had been previously collected from the crossmatch compatible donor cat. It has been suggested that the administration of a unit of blood from the donor cat may decrease the incidence of allograft rejection.
- **Hormonal therapy**, including darbopoietin or erythropoietin, can be administered if a delay in the transplant procedure is expected. This therapy can greatly reduce the need for blood products at time of surgery. Although uncommon, antibodies to erythropoietin have been identified in cats and owners should be cautioned that this could result in significant morbidity and increase in cost during the postoperative period. The current risk with darbopoietin is unknown at this time, but thought to be less than with erythropoietin.

- **Calcium channel blocker amlodipine** (Norvasc, Pfizer.com) may be indicated (0.625 mg/cat PO Q 24 H) if the cat is hypertensive.
- **Gastrointestinal protectants** and phosphate binders are given if deemed necessary; a nasogastric or esophagostomy tube may be placed prior to surgery if the cat is anorectic.

![Figure 2. Image of the surgical setup for the transplant procedure; in our facility, the donor and recipient surgeries are performed simultaneously](image)

![Figure 3. Isolation of the donor renal artery (A) and vein (B) for nephrectomy](image)
Insights Into Feline Kidney Transplants

Immunosuppression

Immunosuppression is begun in our facility 24 to 96 hours prior to transplantation. See An Imperative Inclusion: Immunosuppression (page 38) for a complete discussion on this critical aspect of transplantation.

Surgery

Currently, at our facility, 3 surgeons are involved with each transplant procedure: 2 surgeons to perform the procedure on the donor and recipient and a third surgeon to close the donor following nephrectomy (Figure 2, page 39).

Donor Surgery

The donor is brought into the surgical suite approximately 45 minutes prior to the recipient to allow preparation of the donor kidney for the nephrectomy.

1. The left and right kidneys are examined for a vascular pedicle that consists of a single artery. The left kidney is preferred because it provides a longer vein than the right kidney (Figure 3, page 39). The renal artery and vein are cleared of as much fat and adventitia as possible.

2. The ureter is dissected free to the point where it joins the bladder. The nephrectomy will be performed when the recipient is prepared to receive the kidney.

3. At the time of the original incision, the donor is given a dose of mannitol (0.25 g/kg IV). Fifteen minutes prior to nephrectomy, an additional dose (1 g/kg IV) is given to the donor cat.

4. Mannitol is used to reduce the incidence and duration of acute tubular necrosis that can occur during warm ischemia.

Recipient Surgery

The majority of the recipient surgery is performed using an operating microscope.

1. In the current surgical procedure, the renal artery is anastomosed end-to-side to the caudal aorta (proximal to the caudal mesenteric artery), and the renal vein is anastomosed end-to-side to the caudal vena cava (Figure 4).

2. Partial occlusion clamps are used to obstruct blood flow in both vessels. Using templates made from the donor vessels, windows are created that match the size of the renal artery and vein, respectively. Nylon suture (8-0) is used for the arterial anastomosis and silk (7-0) for the venous anastomosis. Suture size and type may vary depending on the facility performing the procedure.

Client Education

It is important for clients to understand that they are embarking on a commitment that exists for the lifetime of their cats. In addition, while renal transplantation is a treatment option for cats in renal failure, it is not a cure.

Candidacy: Not every cat is a candidate for the procedure and an owner needs to be informed that his or her cat may be turned down for treatment if the cat fails any aspect of the screening process.

Risks: The owner needs to be aware of risks that can occur in the immediate perioperative period and months to years following surgery. A veterinary hospital that can provide 24-hour care must be identified as well as a veterinarian who is willing to care for a renal transplant recipient.

Medical Therapy: Although medical therapy, including subcutaneous fluid therapy, low protein diets, phosphate binders, hormonal therapy, antihypertensive medication, and gastrointestinal protectants can often be discontinued following transplantation, clients need to realize that their pets will need to be on immunosuppressive therapy for life.

Cost: Additionally, the owner must be made aware of both short- and long-term costs, including the cost of the transplant procedure and additional costs once the cat leaves the transplant facility, such as repeated veterinary visits, treatment of potential complications, and lifelong medical therapy.

Donor Adoption: Finally, one of the most important aspects of any transplant program is donor adoption. The client must be willing to provide a lifelong home for the donor animal regardless of the outcome of the transplant procedure.

Figure 4. Image of the native and allograft kidney. The native kidney can be seen on the left adjacent to the gloved finger. The suture in the native kidney marks the location of a renal biopsy. The allograft is on the right. The native kidneys are usually left in situ to act as a reserve if graft function is delayed.
3. Once the vascular anastomosis is finished, a ureteroneocystotomy is performed using a technique to appose ureteral and bladder mucosa. Three techniques have been described and are currently being performed at different centers around the country. At our facility, an intravesicular mucosal apposition technique is used. Two extravascular techniques have also been described, including a technique in which the entire ureter and ureteral papilla from the donor is harvested.

4. Prior to closure, 1 of the native kidneys is biopsied and the allograft is pexied to the abdominal wall using 6 interrupted sutures of 5-0 prolene to prevent torsion and avulsion. The native kidneys are not removed at this time since they can act as a reserve if graft function is delayed. If warranted, the native kidneys can be removed at a later date.

**Postoperative Care**
- The recipient is administered a balanced electrolyte solution until water and food are accepted.
- Blood analysis, including a packed cell volume, total protein, renal panel, and blood cyclosporine level are checked every 2 to 4 days.
- Broad spectrum antibiotics are administered.
- Voided urine is collected and assessed daily.
- Central venous pressure is measured continuously until fluid balance stabilizes and the patient can be weaned from fluid therapy.
- During the first 48 hours, blood pressure is monitored every 1 to 2 hours for the development of hypertension.
  - If the systolic blood pressure is ≥ than 180 mm Hg, hydralazine (2.5 mg SC for an approximately 4-kg cat) is administered.
  - If the cat is refractory to hydralazine, acepromazine (0.005 mg/kg IV) has been used.

**COMPLICATIONS**

**Peri-Operative Complications**

Typically, azotemia resolves within the first 24 to 72 H following surgery. If improvement in renal function does not occur or improvement is initially identified but then worsens, an ultrasonographic examination of the allograft is recommended:
- The allograft should be evaluated for adequate blood flow as well as any signs of a ureteral obstruction including hydronephrosis and/or hydroureter. If repeat ultrasonographic evaluations reveal worsening hydronephrosis, then a ureteral obstruction should be suspected and the cat taken back to surgery.
- If graft perfusion has ceased, torsion of the allograft or thrombosis of the renal artery with vascular obstruction may have occurred. If no sign of urine flow obstruction is present and graft perfusion is adequate then delayed graft function should be considered.

Following discharge, the cat should be examined weekly until cyclosporine levels have stabilized (typically 6–8 weeks). During each examination, renal function and urine should also be evaluated. The intervals between veterinary visits are increased once the cat stabilizes (4×/year in stable patients).

**Long-Term Complications**

Long-term complications that still challenge us include those associated with the allograft and complications secondary to chronic immunosuppressive therapy.

**Renal Complications**

Renal complications following transplantation include:
- Acute and chronic rejection
- Calcium oxalate nephrosis

*Figure 6. Gastrointestinal lymphosarcoma in a cat (A) 4 years following renal transplantation with metastasis to the renal allograft (B); note the 2 native polycystic kidneys in B*
Insights into Feline Kidney transplants

Today's Veterinary Practice

**Immunosuppressive Complications**
Complications secondary to chronic immunosuppressive therapy include:
- Development of infections (including opportunistic infections)
- Diabetes mellitus
- Neoplasia.

Toxoplasma gondii seropositive cats remain acceptable candidates for transplantation, but should receive lifelong prophylactic chemotherapeutics to prevent fatal infections. The prevalence of malignant neoplasia in cats following renal transplantation has been reported from 9.5% to 24%, with lymphoma being the most common type reported (Figure 5, page 41).

**CONCLUSION**
Renal transplantation has become a life-saving measure for cats with renal failure.

Based on published and unpublished reports of cats having undergone renal transplantation, 70% to 92% were discharged from the hospital and median survival times ranged from 360 to 613 days.6,19 Current information suggests that survival times following discharge are improving.6,19

Continued clinical experience in the management of both short- and long-term complications, as well as the ability to identify specific risk factors both pre- and postoperatively will hopefully continue to improve long-term outcome in these patients.

CT = computed tomography; FeLV = feline leukemia virus; FIV = feline immunodeficiency virus; IgG = immunoglobulin G; IgM = immunoglobulin M

**References**