

Site Purpose:

This web site is meant to provide information for clients considering renal transplantation in their cats and is not meant to be an all-encompassing thesis on chronic renal failure or feline kidney transplantation. It is strongly suggested, if you decide that a kidney transplant for your cat is of interest to you, that you contact the University of Wisconsin School of Veterinary Medicine or your veterinarian for more information.

History of feline renal transplantation at the University of Wisconsin School of Veterinary Medicine:

Our program in renal transplantation was successfully initiated in 1995 by Dr. Jonathan McNulty. Dr. McNulty received his training at the University of Wisconsin Department of Surgery- Division of Transplantation under the tutelage of Dr. Folkert O. Belzer. Dr. McNulty joined the faculty of the School of Veterinary Medicine Department of Surgical Sciences in 1991 and extended his research training in transplantation science to development of a clinical transplant program for cats. Since that time we have had the opportunity to help a number of clients with pets with chronic renal failure. We hope that this web site will assist you in evaluating if a transplant is the correct choice for you and your pet.

GENERAL INFORMATION

What is chronic renal failure?

Chronic renal failure (CRF) is a gradual loss of function of the kidneys over time which continues until the residual kidney function is insufficient to support life. Chronic renal failure may occur from a variety of causes but the endpoint, terminal renal failure, is the same. Chronic renal failure is frequently diagnosed in clinical veterinary practice in cats. Management of this disease is directed at long-term maintenance of the patient knowing that the patient will ultimately die from renal failure. Kidney transplantation, which is being performed with increasing frequency in cats, is one therapy that may restore renal function and improve the animal's quality of life. However, consideration of a kidney transplant requires a considerable commitment from a cat owner due to the financial investment and effort required to maintain these patients after surgery.

Chronic renal failure is generally considered a geriatric disease. However, the age of cats diagnosed with chronic renal failure may vary from 9 months or less to extreme old age. In very young animals, chronic renal failure may often occur in association with congenital or inherited renal diseases.

The diagnosis of renal failure is usually based on laboratory tests which demonstrate elevated concentrations of waste products in the blood that the kidney would normally filter out and excrete in the urine. These lab tests include elevated blood urea nitrogen (BUN) and serum creatinine concentrations along with an inadequate urine-concentrating ability (dilute urine specific gravity). The chronic nature of the disease is established by historical evidence that the condition has been present for months to years or through further testing to document secondary changes, such as anemia, that eventually develop in the chronic renal failure patient.

Regardless of the cause, it must be recognized that chronic renal failure is an irreversible and progressive disease. Even if the agents responsible for the initial renal insult can be identified and eliminated, kidneys with chronic failure will continue to progressively deteriorate. There is no curative medical treatment for chronic renal failure. Maintenance treatments that are available to the practicing veterinarian are directed at reducing the clinical signs associated with renal failure and slowing the progression of renal dysfunction as much as possible. These treatments may include dietary therapy, fluid administration, management of anemia, modification of calcium and phosphorus, and management of hypertension. Depending on how far along in the progression of CRF your individual cat may be, aggressive medical management (i.e. nonsurgical) may prolong its life from months to several years. However, it is important to try to make an accurate assessment of where your cat is in this process and not just be hopeful that you will obtain a maximum duration of survival out of medical

management. Waiting too long to decide on a transplant will reduce the chances of success considerably.

Kidney transplantation is the only potentially curative treatment for chronic renal failure. Cats receiving transplanted kidneys have been known to survive as long as 6 years or more after surgery. The implanted kidney functions normally and should provide a much improved quality of life for the transplant recipient. However, alleviation of chronic renal failure and elimination of the associated disease and maintenance therapy is achieved in trade for therapy directed at maintaining the transplanted kidney. Transplant patients will require daily lifelong medication to prevent rejection.

When should a kidney transplant be performed?

Clearly, a transplant is needed when a cat has chronic renal failure. However, it is thought that it may be advantageous to try to time the transplantation procedure to obtain maximum benefits for the kidney recipient since some successful grafts may be lost several years after transplant. The rationale for this approach is based on the fact that some kidneys will fail about 3 years after transplant due to chronic rejection. This is NOT THE CURRENT APPROACH TO TRANSPLANTATION AT THE UNIVERSITY OF WISCONSIN (see section below on approach to timing of the transplant at the University of Wisconsin) but is included here since this approach may be considered by some transplant surgeons.

During the post-transplantation period, acute rejection of the transplant is prevented by administration of immunosuppressive drugs. However, long-term survivors may experience **chronic rejection** which is not responsive to these immunosuppressive drugs. This type of rejection results in slowly developing graft vascular disease. Graft vascular disease causes gradual blockage of the renal arteries and reduces blood flow to the transplanted kidney which will cause a slow loss of function. Thus, in some animals the transplanted kidney may stop functioning after about three years. ***The incidence of chronic rejection in the feline kidney transplant population is not known.***

Decompensated renal failure, in simplest terms, is the point in progressive renal failure where the cat is unable to maintain its normal body condition even with adequate supportive care. In the early phases of renal failure, the cat is able to tolerate the elevated amounts of waste products in its blood and does pretty well. You may not even know the cat is ill. This is considered a compensated state of renal failure. When weight loss increases and the cat needs more and more aggressive supportive therapy then we consider it to be in a decompensated state. Eventually, this becomes an uncontrolled toxic condition (uremia).

It is common knowledge that cats with chronic renal failure may be maintained for months to years on conservative medical management. Therefore, it can be

extremely difficult to predict when a cat would develop decompensated renal failure. Different animals appear to have varying tolerances to waste products which accumulate in the blood during renal failure. Serum creatinines (the best simple measure of kidney filtration function) may vary considerably before clinical signs of uremia (overt illness) are present. However, elevation of serum creatinine, when combined with observation of other physical changes such as weight loss, may suggest when to consider a transplant. Cats that are dependent on subcutaneous fluids for maintenance should have a transplant as soon as practicable. These cats have little reserve and may develop a terminal uremic crisis.

Another indication that a cat is progressing to decompensated renal failure may be the incidence of uremic crises. During the progression of renal disease, animals will commonly have several acute exacerbations of their chronic renal failure. This is when the cat becomes ill (usually becomes inappetent with possible vomiting, dehydration, malaise, lethargy, etc.) and requires intravenous fluid therapy to get back to being able to maintain itself again. Initially, these uremic crises may be resolved with intensive IV fluid management but subsequent episodes will become more difficult to reverse. A patient with chronic renal failure that has had one or two uremic crises but is still able to maintain itself should be critically evaluated for transplantation.

One very important indicator that transplant should not be delayed is weight loss which is progressive in spite of adequate dietary therapy and management of the patient. Weight loss that is unresponsive to intensified management, especially dietary management, in the chronic renal failure patient signals the change from a compensated to decompensated condition. Weight loss of 20% or more of normal body weight has been considered to carry a significantly reduced prognosis for success of the transplant surgery. Thus, a transplant should be performed as soon as progressive weight loss is identified.

Some final criteria that may be used to identify a decompensated state of renal failure is the inability of the cat to maintain certain normal metabolic processes. A good example of this is the development of anemia or the loss of the ability to maintain the levels of calcium or phosphorus within reasonable concentration ranges in the blood.

These factors may assist in identifying when your cat has gone into a state of decompensated chronic renal failure. This is a time of considerably increased risk for your cat. ***Our experience at the University of Wisconsin with waiting for patients to develop identifiable decompensated renal failure (in an attempt to delay the surgery as long as possible) has not been satisfactory.***

Thus, our recommendation on timing of the kidney transplant at the University of Wisconsin is not to wait until decompensated renal failure occurs but to use identifiable measurements of advanced chronic renal failure as our criteria to go

ahead with the surgery. These criteria are listed in the section on APPROACH TO TIMING OF FELINE KIDNEY TRANSPLANTS AT THE UNIVERSITY OF WISCONSIN.

APPROACH TO TIMING OF FELINE KIDNEY TRANSPLANTS AT THE UNIVERSITY OF WISCONSIN

Our approach to feline kidney transplantation at the University of Wisconsin School of Veterinary Medicine is to try to do the surgery earlier rather than later in the course of the renal disease. Our experience with delaying surgery until identification of decompensated renal failure, using weight loss as a criteria, has been unsatisfactory. As an extreme example, one potential transplant cat was lost during this waiting period from a terminal uremic crisis even though it was steadily regaining weight on a prescription renal failure diet. This is unusual, however, it does point out that predicting when a cat in chronic renal failure will terminally decompensate cannot be accurately predicted for an individual patient.

We will perform a kidney transplant on a cat with chronic renal failure if:

1. the cat has had an appropriate diagnosis of chronic renal failure; and either:
 - a. the serum creatinine values are sufficiently elevated so that postoperative function of the transplanted kidney can be assessed;
 - or
 - b. the patient exhibits signs of decompensation.

In practical terms, this means we would prefer to transplant cats with serum creatinine values of 4.0 mg/dl or higher. However, cats with serum creatinine values less than 4.0 mg/dl would be considered if they had difficulty in maintaining themselves (food, hydration), were dependent on subcutaneous fluids, or had developed a significant secondary problem related to the kidney failure (anemia is one of the most common and earliest sequelae to occur). Most cats presented for transplant exceed these guidelines by a wide margin.

Cats that have mildly elevated serum creatinines (less than 3.5 mg/dl) and other general sequelae that could be related to chronic renal failure, such as ill health or poor quality of life, may indeed benefit from a kidney transplant. However, many of these patients are ill because of undiscovered or misdiagnosed diseases that are unrelated to chronic renal failure. A cat with clinical signs (general illness) that are not consistent with the level of kidney failure indicated by serum creatinine or other measurements (ie. the creatinine is too low to be consistent with its condition), needs to be evaluated very carefully before a transplant is to be considered.

As with any general guidelines, individual circumstances may dictate altering this approach for specific patients. If you have questions it is best to call and ask.

It is important to remember: Kidney transplantation is not an emergency treatment to attempt salvage of the critically ill patient. Patients presented for transplant in the terminal phase of renal failure have a poor prognosis for success or even survival through the surgery. It can take some time to organize the work-up, obtain and evaluate

a kidney donor and prepare the recipient for surgery. A week is generally a minimum. It can take longer depending on donor availability and matching with the recipient. A patient presented in a terminal condition often does not survive until the surgery can be arranged. It behooves the owner of a cat with chronic renal failure to plan ahead.

For information on selection criteria for appropriate candidates for kidney transplantation, go to [SELECTION OF CANDIDATES FOR KIDNEY TRANSPLANTATION AT THE UNIVERSITY OF WISCONSIN](#).

SELECTION OF CANDIDATES FOR KIDNEY TRANSPLANTATION AT THE UNIVERSITY OF WISCONSIN

The best transplant candidate is the patient that is outwardly healthy. These patients are able to adequately maintain their own food and water intake. Certainly, cats that require subcutaneous fluids or an indwelling stomach tube for their continued survival should have their transplant as soon as possible. In general terms, candidates for transplantation should be screened and determined to be free of infectious or other organ diseases (see section on RECIPIENT TESTING FOR FELINE RENAL TRANSPLANT AT THE UNIVERSITY OF WISCONSIN for actual tests that should be run before coming to the UW for transplant). Kidney transplantation would not be performed on patients with significant heart disease, diabetes, liver failure, active bacterial urinary tract infection, certain cancers or viral infections such as FIV, FIP or FeLV. Similarly, diseases such as oxaluria, cardiac problems, hypertension, inflammatory bowel disease or amyloidosis increase the chances of a poor outcome after surgery or a shortened lifespan for the transplanted kidney and may eliminate a candidate from consideration. See RISK FACTORS FOR SELECTED RENAL TRANSPLANT CANDIDATES for a discussion of some of these problems.

As part of the process in deciding if your cat is a transplant candidate, you will also need to consider a number of issues impacting you as the owner of such a patient. For a select list of these questions and other issues as presented from the cat owner's perspective, see our LINKS section. A good list of such issues is presented in the Feline Chronic Renal Failure website at <http://www.best.com/~lynxpt/transf.htm>.

RECIPIENT TESTING FOR FELINE RENAL TRANSPLANT AT THE UNIVERSITY OF WISCONSIN

Included below is a listing of tests that we require for patients prior to kidney transplantation (you may want to copy this list and take it to your veterinarian). Since many of our clients come from a great distance, our recommendation is to have your veterinarian run as many of these tests as possible. Any testing which your veterinarian cannot perform can be done at the UW School of Veterinary Medicine at your first appointment. In general, we will not repeat the tests run by your veterinarian if they were done recently (within a few weeks) other than preoperative blood work needed for anesthetic and acute postoperative management.

Once the tests are complete, have your veterinarian call us to discuss the results. These results may also be FAXED (608-265-1098) to the General Surgery Service at the UW-VMTH with the header "ATTN: Renal Transplant Candidate". We may request more testing or decide on a time frame when the surgery should be considered.

1. CBC (complete blood count) including WBC count and differential
2. Serum chemistry panel
3. Urinalysis and culture (urine obtained by cystocentesis): evaluate for specific gravity, evidence of infection, crystal type if possible, etc.
4. Feline virus testing (FeLV, FIV, FIP)
5. Cardiac evaluation (auscultation, chest radiograph and electrocardiogram; may require echocardiogram if abnormalities are detected or a murmur is present)
6. Abdominal radiographs- examine urinary tract for mineralization, stones, kidney size or other abnormalities
7. Thyroid panel- not needed in young animals
8. Blood pressure measurement (doppler ultrasound is fine)
9. Blood type- We determine recipient blood type because our donor cats (domestic short hair cats) uniformly have type A blood. If the recipient has type B or type AB blood, it is unlikely that we will be able to find a kidney donor cat for the surgery. Fortunately, these blood types are infrequently encountered in the U.S. They are seen more frequently in certain exotic purebreds. If your cat has either B or AB blood type you will have to find a donor cat for the surgery, possibly through purebred cat breeders.
10. Kidney evaluation- In general, if the kidneys are small in size, we do not require a kidney biopsy prior to transplantation because the anesthesia and biopsy procedure carry the risk of inducing enough loss in residual kidney function to precipitate a terminal uremic crisis. However, if the kidneys are normal size to enlarged (or have unidentified isolated abnormalities) on either radiographs or ultrasound, they should be biopsied since the cat may have a condition, such as renal lymphoma, which would disqualify them as a transplant candidate.
11. Dental evaluation. If your cat passes the testing regimen listed above and is a candidate for a renal transplant, then his dental health should be evaluated. If there is significant dental calculus or any signs of gum or tooth root infections, this should be taken care of prior to presentation for transplantation. Infected teeth or gums are a potential source for bacteria to enter the circulation and could infect the transplanted kidney with disastrous consequences. Teeth cleaning is well known to cause a release of bacteria into the blood stream so we would prefer that this initial teeth cleaning be done before the transplant in the presence of appropriate antibiotics. After surgery, an appropriate regimen of routine dental hygiene should be followed.
12. Blood cross-match with a donor cat. Even though cats may have the same blood type, we have found that there are recipient cats that are not compatible with a particular donor cat on a cross-match due to antibodies against the donor being present in the blood of the recipient. We have found this in cats that have not had a previous transfusion or any reason to have been exposed to a donor cat's particular antigens. Thus, a cross-match is an essential test in identifying a donor cat (blood type alone is not adequate). This test is performed after all other tests have been successfully passed. For information on how donor cats are selected, [click here](#).

After a donor has been successfully matched with the transplant candidate, the recipient will make an appointment for surgery as soon as possible. The recipient will arrive at our hospital a minimum of a few days prior to the surgery to allow appropriate preoperative preparation.

SELECTION OF A DONOR FOR KIDNEY HARVEST

The kidney donor should be healthy and free of any infectious or organic disease. Removal of one kidney in an otherwise healthy animal will not result in any kidney related health problems. The remaining kidney in the donor will enlarge and eventually achieve about 75% of the total function of the two kidneys present prior to the organ donation. This is far in excess of the threshold of function required for survival (about 25% is a minimal tolerable level).

The donor may be provided by the client or we will obtain the kidney donor. If we obtain the kidney donor, the client must adopt that cat after the surgery. We have been very pleased with our source of donor cats in terms of the cat's winning personalities and degree of socialization. To date, we have had no problems integrating these animals into the client's households and our clients have overall been very happy with the donor cats in their homes as new and joyful pets.

We often have concerns voiced about the recipient cat accepting a new cat into the household. Our experience has been that the cats will work it out and establish their personal boundaries and that this has not been overly stressful for the recipient cat. We have one transplant patient that would never socialize with any other cat in the household but now sleeps together only with the donor cat! Some degree of socializing may be needed when the recipient comes home. However, the donor cats are usually very young, thus, they tend to be pretty adaptable and don't get territorial in the time they are in the client's home before the recipient returns home.

The recipient and donor blood are crossmatched to determine blood compatibility (see RECIPIENT TESTING FOR FELINE RENAL TRANSPLANT AT THE UNIVERSITY OF WISCONSIN). We have found some recipients (even males without previous transfusions) to have preformed antibodies to the donor cat blood so this step is mandatory. No other tissue typing is performed.

Preoperative screening of the donor includes complete blood count, serum chemistry panel, urinalysis, and viral testing. An excretory urogram (a dye study to look at the kidney vessels and function) is sometimes done to assure that both donor kidneys are healthy and well vascularized.

When the donor cat is ready we have the recipient cat brought to our hospital for PREOPERATIVE PREPARATION.

PREOPERATIVE PREPARATION OF THE RECIPIENT

The transplant candidate is admitted to the hospital two to three days (or more if needed) before surgery for presurgical preparation. Prior to transplantation, the recipient is given fluids and placed on a low protein kidney diet. Anemia is corrected just prior to surgery with transfusions and erythropoietin therapy. A stomach tube may be surgically placed in some cats to feed the anorexic patient. However, it must be understood that attempts to "build-up" the debilitated patient in chronic renal failure will have limited success at best. Do not delay seeking surgery while trying to build up the patient. Patients should preferably be referred for transplantation before generalized physical debilitation is present.

Cyclosporine A and prednisolone immunosuppressive therapy will be started 24 to 48 hours prior to surgery. These drugs are administered twice a day, with eventual adjustments in the dosages, for the remainder of the patients life (see section on immunosuppressive therapy).

The day before surgery the recipient will have appropriate catheters placed that will be used after surgery for administration of fluids and for taking blood samples. In addition, most patients receive a blood transfusion at this time. The following day the patient will have surgery. This is most often done at our hospital on a Tuesday or a Thursday due to scheduling needs of our operating theatres and equipment. For a description of the surgical procedure see the section on SURGERY AND POSTOPERATIVE CARE.

SURGERY AND POSTOPERATIVE CARE

The kidney is transplanted into the abdomen. The native kidneys are not removed so the cat usually ends up with 3 kidneys. Occasionally, one or both native kidneys may be removed to try to prevent problems related to these kidneys after surgery. This may be done if a kidney is clearly completely non-functional or if it has stones that may become a nidus for infection some time after surgery. Totally non-functional kidneys are removed because they may still act as a cause of elevated blood pressure and cause problems related to hypertension.

The surgery is a complex challenging procedure that is usually done in a chronically-ill patient. Thus, there are many possible acute complications which can occur either during or after surgery. These may include anesthetic problems, delayed function or primary nonfunction of the implanted kidney, arterial or venous thrombosis (clots), leakage of urine at the ureteral implant site, shock, heart failure, paralysis, fatal infection, seizures, pulmonary embolism and death.

The blood vessels of the transplanted kidney are attached to the aorta and vena cava in the abdomen behind the position of the native kidneys. To gain some perspective on this procedure, the suture that is used is finer than a human hair. The ureter is attached to the bladder so that urine will drain into its proper place.

In the relatively low-risk patient with minimal weight loss or debilitation, the survival rate would be expected to be about 90% or better (see UW-SVM Specific Information for more details). Survival rates will decrease as the patient becomes more debilitated. A successful feline transplant program would be expected to have an overall 70-85% "survival to discharge from the hospital" rate.

Longer term complications primarily involve acute graft rejection and the potential for infections. As mentioned above, chronic graft rejection may result in recurrence of renal failure in some cats after several years. Rejection is monitored by weekly examinations for the first month after transplantation. Maintenance of a good appetite and low serum creatinines are assessed along with urine specific gravity when urine can be obtained by free catch, red cell counts (PCV), and cyclosporine A blood levels. After the first 4 weeks the interval between exams may be gradually extended to one month or more.

Rejection of the transplanted kidney is most common in the first month and will be accompanied by malaise, vomiting, and depression and is confirmed by laboratory blood testing. Rejection must be recognized and treated immediately to prevent destruction of the transplanted kidney. Treatment of rejection requires immediate hospitalization with fluid therapy and intravenous cyclosporine A and steroid therapy. When the rejection episode is controlled, oral cyclosporine A treatment is reinstated at a higher dose level.

Although the risk of rejection is highest in the first month, it must be remembered that rejection is a life-long risk. Thus, the owner should observe the recipient with this in mind and if there is any question that rejection may be occurring, the recipient should be

tested immediately to rule out such a possibility. As the owners of these patients become acquainted with how their cats are doing after surgery, it becomes obvious to them when things are not going well and the cat needs to be examined and have blood testing done.

Postoperative monitoring and care of the transplant patient is most intense, in terms of blood testing and monitoring, the first few months after surgery. Gradually, the intervals between blood tests will get longer until testing is done every 1-3 months.

CARE AND MONITORING OF THE TRANSPLANT PATIENT

(For more specifics on the process of obtaining and managing a transplant through the UW-VMTH, see SPECIFIC ISSUES RELATING TO FELINE KIDNEY TRANSPLANTATION AT THE UNIVERSITY OF WISCONSIN)

After discharge from the hospital you will need to be observant of your cat's general health and have periodic monitoring of its blood performed. Early detection of problems in the postoperative period, especially for signs of rejection, can be instrumental in successfully reversing the rejection episode and salvaging the transplanted kidney.

Observation. The first signs of a rejection episode will most likely be a behavioral change in your cat. Loss of appetite, depressed attitude, malaise, loss of energy, vomiting, etc. may indicate a rejection episode. It is possible that early rejection may be picked up on a routine monitoring visit by an increase in serum creatinine or decreased urine specific gravity. However, ***it is more likely that you will observe a change*** that should be brought to the attention of your veterinarian (see rejection section below).

Monitoring. Measurements of the cat's weight, serum creatinine, BUN (blood urea nitrogen), PCV (packed cell volume), total protein, urine specific gravity (free catch urine only unless there is a need for a urine culture) and cyclosporine A trough level in the blood need to be done periodically to be sure that all is going well. In particular, it is important that the cyclosporine A level is closely monitored. As cats get healthier due to their transplant they seem to become more able to metabolize cyclosporine A (probably their liver is getting healthier too) and the blood levels can drop. Monitoring is done daily while the cat is in the hospital. After discharge it is usually done weekly for a month. Then the intervals are increased to biweekly and then monthly. Eventually, depending on the individual cat the monitoring may be done every 2-3 months. ***It is vital that the blood tests are drawn just before the next dose of cyclosporine to get an accurate assessment of the drug levels.***

Immunosuppressive Drug Dosing. The antirejection drugs are given either once or twice a day. These are cyclosporine A (customized dose to obtain blood trough levels of 500 ng/ml as measured by HPLC) and prednisolone (0.25 mg/kg twice a day) and are given by mouth. After one month the prednisolone is changed to once a day at 0.25 mg/kg and the cyclosporine A decreased to achieve 12-hour blood levels about 250 ng/ml. See the section on Immunosuppressive Therapy for more detailed information.

Rejection episodes. Rejection needs to be rapidly identified to prevent loss of the kidney. Rejection is often first noticed as a general malaise, loss of appetite and loss of vigor in the recipient. The recipient should be immediately tested for serum creatinine levels and blood cyclosporine trough levels. A high creatinine combined with a low cyclosporine is considered *de facto* evidence of rejection. Occasionally a kidney biopsy may be needed to confirm the diagnosis. Since it

takes some time to get cyclosporine levels done and we prefer not to lose this time in starting anti-rejection treatment, we will usually give anti-rejection medications if we suspect rejection is present and use response to this therapy as another diagnostic aid in identifying rejection. Serum creatinines will usually drop within 24 hours if rejection was present. Other causes of elevated creatinine can be cyclosporine toxicity or ureteral scarring and stricture. Thus, it may be necessary to examine the kidney by ultrasound to be sure that the problem is not an obstructed ureter. The cat is then administered fluids intravenously to promote urine production.

The further along a transplant patient survives from the time of surgery, the less risk certain problems present to them. See POSTOPERATIVE MILESTONES IN THE PROGRESS AND MANAGEMENT OF THE TRANSPLANT RECIPIENT for a synopsis of these risks.

Taking your cat home. Although the cat is on immunosuppressive drugs, it should be able to mingle with other cats (as long as they don't have known infectious diseases). It will be at a slightly increased risk for infections but this increased risk is not great enough to take undue precautions in managing your cat. Your cat will not require any special diet once it is home and is maintaining itself with a creatinine in the normal range. Your cat should get its normal vaccinations and otherwise be treated normally.

Enjoy your cat. If all has gone well your cat should be healthier, more active, have a good appetite and generally a much improved quality of life. Feline transplant patients have had survivals up to 6 years and more to date (early UC-Davis patients). Our longest survivor is out 4.5 years (as of February 2001) and still going strong. We still don't know what the maximum time limit is yet.

IMMUNOSUPPRESSIVE THERAPY FOR THE FELINE TRANSPLANT PATIENT

All transplant patients must be on lifelong immunosuppressive drug therapy to prevent rejection of the transplanted kidney. Although it is true that rare case in cats and humans are able to maintain their grafts without such drugs, it must be recognized that such cases are rare and you should assume your cat is not one of those cases. Taking your cat off immunosuppressive drugs is extremely risky and will almost always result in destruction of the transplanted kidney.

There are two immunosuppressive drug regimens used at the UW-VMTH. **The standard regimen** involves oral cyclosporine and prednisolone given twice a day (prednisolone is changed to once a day after the first month). We try to achieve blood trough levels (levels measured in the blood just before the next dose is given) of 500 ng/ml in the first month and then 250 ng/ml after that. Trough levels will vary. Levels below 200 ng/ml begin to put the patient at risk for rejection (levels around 100 ng/ml are a high risk for rejection).

Higher levels than our target trough levels present several potential problems. Cyclosporine can be toxic to the kidneys. This is especially true in humans. Most cats are not susceptible to cyclosporine nephrotoxicity. However, there are cats that will have increases in serum creatinine if the cyclosporine levels go above 700-800 ng/ml or more. This toxicity has always been reversible in our experience when the cyclosporine levels are reduced. There are also patients that have systemic effects of cyclosporine toxicity. This most commonly presents as loss of appetite, malaise, vomiting, or diarrhea. It can look like rejection but the serum creatinine levels will not be elevated.

A **triple-agent once-a-day immunosuppressive regimen** is also available. This involves giving cyclosporine, ketoconazole and prednisolone once a day. Ketoconazole prolongs the time cyclosporine A remains in the blood and can allow once a day dosing in many cats. Ketoconazole may also be used to reduce the dose of cyclosporine A when given twice a day if a patient requires inordinately high doses of cyclosporine to maintain their blood levels. This adjunct may be useful to reduce the costs of medication, when medicating a patient is very difficult and so it is desirable to reduce the frequency of pill administration or if the lifestyle of the owner dictates that a once-a-day regimen is needed.

This regimen is not used if:

- a. the patient presents with elevated liver enzymes.
- b. the patient is very sensitive to cyclosporine (either gets easily toxic or achieves very high blood levels on relatively low doses of cyclosporine).

Approximately half of our patients end up on this once-a-day regimen. We have had patients that have been on it for up to 3 years. Patients are withdrawn from this regimen if they have:

- a. persistent elevations in liver enzymes
- b. evidence of weight loss without any obvious medical reasons for this to occur

c. difficulty with regulating cyclosporine levels (ie. they are persistently too high)
This regimen is advantageous for many clients but needs to be closely monitored.

Monitoring is done at the 24 hour time point (before the next dose) rather than at 12 hours as is done with the twice a day regimen. Cats that poorly tolerate this regimen are placed on the conventional twice-a-day therapy with cyclosporine and prednisolone.

RISK FACTORS FOR SELECTED RENAL TRANSPLANT CANDIDATES

We are frequently presented with patients that have various health problems in addition to chronic renal failure. Often these problems will disqualify the candidate for a transplant. However, diseases which are treatable and for which survival with such treatment can be expected to be several years or more are still acceptable candidates for transplant. In these cases we will place the candidate on therapy and assess the response before committing to a transplant procedure. Some commonly presented problems are listed below.

1. Heart disease. **Mild** heart disease or cardiomyopathy will not rule out a candidate. However, we will place these patients on therapy and assess their response prior to moving ahead. A heart murmur alone will not rule out a candidate. Often these murmurs are related to anemia of chronic renal disease and won't affect the outcomes. However, all cats with murmurs are evaluated by echocardiography to assess heart muscle and valve function. **Advanced** heart disease will disqualify a cat from transplant.
2. Hypertension. Hypertension will predispose the patient to a number of serious complications during and after surgery. Hypertension will not rule out a patient for transplant ***if it is controllable*** with medical management.
3. Oxaluria. Oxalate stones and tubular oxalate deposits are a common cause of renal failure. It is known that oxalosis presents an increased risk of premature loss of the transplanted kidney. In extreme cases, this may shorten the graft life to only several months. However, the average overall effect of oxalosis on feline kidney transplant patients is not known. Thus, oxalosis does not rule out a transplant at the UW-VMTH at this time. However, the owner of such a cat must recognize that their cat is at increased risk for graft loss and that the level of risk (ie. % of patients) for early graft loss is not known. All cats transplanted with oxalosis will need to be on dietary and medical management to reduce the chances of a problem with oxalate deposits as much as possible.

SPECIFIC ISSUES RELATING TO FELINE KIDNEY TRANSPLANTATION AT THE UNIVERSITY OF WISCONSIN

In addition to the general information presented elsewhere in this website, this section will address some common questions presented to us by both owners of cats with chronic renal failure and by referring veterinarians.

WHAT IS THE COST OF A FELINE KIDNEY TRANSPLANT AT THE UNIVERSITY OF WISCONSIN?

Due to the continually rising nature of the cost of medical supplies and care as well as the fact that no two patients follow the same course of recovery in the hospital, it is difficult to provide specific costs of this procedure. I am unable to list a price for this procedure on a web page which may not be updated frequently enough to keep pace with rising costs. Serious inquiries about kidney transplantation should be made at the contacts listed below and an estimate of current prices can be given to you. The University of Wisconsin Veterinary Medical Teaching Hospital prices its care by computerized itemization of materials used and services performed. As such, costs will be somewhat dependent on the course of events during the patient's hospital stay and development of complications, if any.

The other primary consideration in the cost of the procedure is the cost of maintaining the cat. Immunosuppressive drugs are expensive. For most cats, annual drug costs will be between about \$500 to \$1500. The actual cost of these drugs depends on the drug regimen used and the amount of drug an individual cat requires to attain the target blood levels. There is also the need for laboratory blood testing and clinic visits. These will be most frequent in the first year and are fewer thereafter so the costs associated with this monitoring will decrease somewhat over time.

WILL MY CAT BE EXCLUDED AS A TRANSPLANT CANDIDATE BASED ON HIS EXTREMELY ELEVATED SERUM CREATININE LEVELS OR ADVANCED AGE?

At the University of Wisconsin, we set no upper limits on the renal function-related blood values (ie. serum creatinine) that define a renal transplant candidate. In addition, since some cats live to be extremely old, it is impossible to know how long any individual cat may live after transplantation. For this reason, we do not limit the AGE at which a cat may receive a transplant but use only the animal's health status to decide if a cat should be excluded as a candidate for a kidney transplant. However, it has to be recognized that a very elderly cat is more likely to develop other diseases associated with old age and thus is at greater risk for having a shortened life span after transplantation compared to a younger animal.

HOW LONG WILL MY CAT BE IN THE HOSPITAL?

The average hospital stay after a transplant is 3 to 4 weeks. Most of this time is spent monitoring cyclosporine A blood levels and adjusting the drug dosages. As

the levels become stable enough to monitor once-a-week, the cat is discharged. The donor cat can go home 1-2 days after the surgery.

WHAT IS THE SUCCESS RATE OF FELINE KIDNEY TRANSPLANTS AT THE UNIVERSITY OF WISCONSIN?

Currently, our overall success rate (survival until discharge) is about 85% (as of 2/1/2001)

HOW LONG WILL MY CAT SURVIVE WITH A TRANSPLANT?

This, of course, is impossible to know without a crystal ball. However, our longest survivor to date (2/1/2001) has been 4.5 years and is still going. We have many that have survived for 3 years. Very few of our patients die of renal failure. They will most often die due to disease unrelated to the kidney transplant. Since our program has not been active much longer than this it is hard to say what our maximum or even average survivals will be. UC Davis, which has been performing transplants longer than the UW, has reported survivals of 6 years or more.

SHOULD MY CAT BE ON ERYTHROPOIETIN THERAPY FOR ANEMIA PRIOR TO TRANSPLANTATION?

The erythropoietin that is used in cats is a human recombinant product. As such, it is foreign to cats and a few cats can develop antibodies to the product, rendering it useless. Since this drug may be of value in the postoperative period, our recommendation is to delay erythropoietin therapy until the cat is significantly anemic (PCV in the mid-teens). We prefer to perform the transplant surgery not too long after erythropoietin therapy has begun to have a beneficial effect. It is best to strictly avoid blood transfusions altogether before the cat comes to us for transplant.

HOW DOES THE PROCESS OF OBTAINING A TRANSPLANT WORK AT THE UNIVERSITY OF WISCONSIN?

It is easiest to consider the process in each of its steps. First, a diagnosis of chronic renal failure is made. If you are considering a transplant, your cat is then worked up by your veterinarian as described in the section on Recipient Testing. After obtaining these results, either you or your veterinarian calls the UW VMTH and contacts the General Surgery Service at the University of Wisconsin Veterinary Medical Teaching Hospital for consultation. At that time, we determine if further testing is needed or if we can start the donor cat search. Donor cats will then be identified and blood will be sent to the UW for crossmatching. You will be notified and will send a fresh blood sample from the recipient cat by overnight mail to the UW to arrive the same day as the donor blood. If a compatible crossmatch is obtained, we will purchase the donor, have it shipped to UW and work it up for any health problems. We then call you to bring your cat in. Based on the clients personal scheduling needs, the recipient cat is often brought in on a Saturday or Sunday. Your cat is then examined, admitted and a deposit is left with the clinic reception desk. Your cat would then start drug pretreatment on

Sun., receive a transfusion if needed on Mon. and have the transplant performed on Tues.

WHO DO I CONTACT AT THE UNIVERSITY OF WISCONSIN REGARDING FELINE KIDNEY TRANSPLANTATION?

For further information you can contact the UW-VMTH clinic reception desk at 608-263-7600 and leave a message for the General Surgery Service. Much of our initial contact and assistance with information or evaluation of your cat's workup is done through our surgery residents. You may also contact Dr. McNulty at mcanultj@svm.vetmed.wisc.edu

POSTOPERATIVE MILESTONES IN THE PROGRESS AND MANAGEMENT OF THE TRANSPLANT RECIPIENT

1. Early phase (first week) problems will most often relate to the potential for failure of the transplanted kidney due to complications. Some kidneys may have a delay up to 10 days in the onset of function (delayed graft function). It is during this period that the cat may encounter acute life-threatening problems. These are more likely in the debilitated cat. A cat that is doing well after surgery will usually be in the hospital 3-4 weeks. Usually the latter half of the stay just involves blood sampling which is required daily until we have determined that the cyclosporine A blood levels have stabilized. Sutures are removed 7-10 days after surgery so this may occur while the cat is still in the hospital.
2. Ureteral problems. If stricture, or narrowing by scarring, of the ureter is going to occur it will become apparent usually within 10 days to 6 weeks after surgery. This is assessed by an ultrasound examination and measurement of serum creatinines after the transplant. Significant blockage of the ureter, as indicated by dilation of the ureter, would require a second surgery for revision of the opening of the ureter into the bladder. The ureter may also leak at its point of attachment. This is one of the most problematic areas in the surgery. Urine leakage would require additional surgery for revision of the ureter implant.
3. Rejection can occur at any time after surgery and is a threat for the remainder of the cats life. The risk of rejection is greatest in the first month after surgery. During this time, cyclosporine A levels are maintained at a trough level of 500 ng/ml when measured just before the next dose of cyclosporine. If all is well by the first month, then the dose is adjusted to attain trough levels of 250 ng/ml. Adjustment of cyclosporine dosages is customized to each individual patient by measurement of blood cyclosporine concentrations using HPLC.
4. Anemia is managed by erythropoietin injections 2-3 times a week. This is continued until the kidney assumes its role in production of this hormone. The time for needing erythropoietin may vary from days to months. In general, if the PCV is 25 or better we will forego erythropoietin treatments.