

bellwether

NUMBER 66 | SPRING 2007

THE NEWSMAGAZINE OF THE UNIVERSITY OF PENNSYLVANIA SCHOOL OF VETERINARY MEDICINE

100 PUSHING

Penn Vet's Feline Renal
Transplant Program
Approaches the
Magic Number

inside
Barbaro
Tribute
a legend in motion

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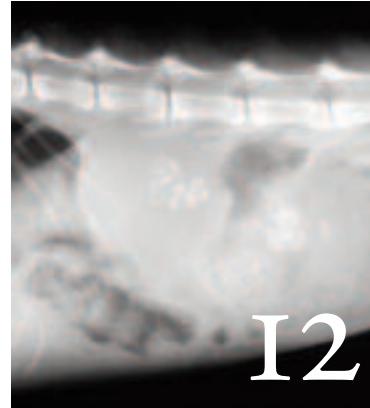
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contents spring 2007



bellwether

features

- 5 EDUCATION NEWS
- 12 KIDNEY TRANSPLANTS FOR CATS
- 28 PENN ANNUAL CONFERENCE

departments

- 3 EDITORIAL NOTES
- 4 DEAN'S MESSAGE
- 8 FACULTY FOCUS
- 20 RESEARCH BRIEFS
- 22 CLASS NOTES
- 26 ALUMNI PROFILE
- 28 SCHOOL EVENTS

about the cover:

In 1998 Penn Vet's Feline Renal Transplant Program was successfully initiated by Dr. Lillian R. Aronson, assistant professor of small animal surgery. Since then, nearly 100 cats have undergone kidney transplants at Penn, and life expectancies of recipients continue to increase. Here we see Dr. Aronson holding her 96th kidney transplant patient, Speedy, who was in for a routine post-surgery checkup. Photo by Lisa Godfrey.

TRANSPLANTED TIME

Extending the Lives of Cats through Kidney Transplant

BY SUSAN I. FINKELSTEIN

You could say Jackie Miller, M.D., knows a little something about kidneys. As a pediatric nephrologist, Dr. Miller diagnosed and managed kidney disease and kidney function in children. She consulted with surgeons in cases involving kidney transplants, and helped manage dialysis procedures. To become a specialist, she had spent the better part of a decade in medical training, particularly studying the development of the kidneys and urinary tracts in children.

As a patient with end-stage renal disease herself, Dr. Miller underwent a kidney transplant 18 years ago, and immunosuppressive medications and regular follow-up visits to her own nephrologist will be part of her routine for the rest of her life.

So it almost came as no surprise, around Christmastime last year, when Jackie's cat Speedy was diagnosed with chronic renal failure—and that a kidney transplant was her best chance for survival. As a client at the Matthew J. Ryan Veterinary Hospital, Jackie (now researching vaccines at GlaxoSmithKline) learned firsthand the process by which veterinary surgeons select, prepare and perform kidney transplants in cats. In keeping with this Miller medical motif, Speedy became the ninety-sixth patient to receive a new kidney through Ryan's Feline Renal Transplant Program (courtesy of donor Hammy). Truly, for Jackie, Penn Vet's trademark—*Many Species, One Medicine*—had come full circle.

Functioning and Failing

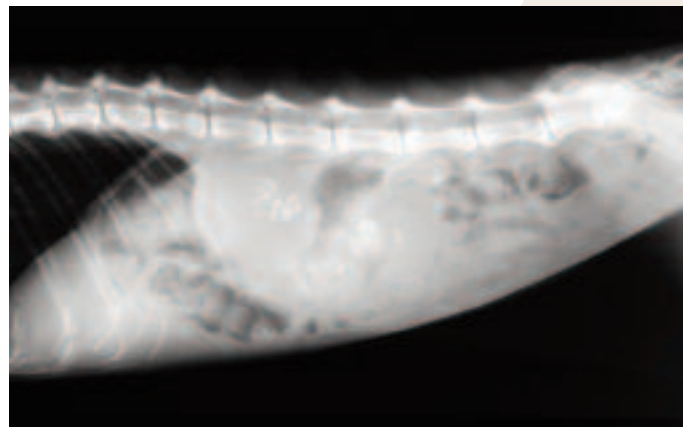
More than 1.2 million people worldwide suffer from end-stage kidney disease, and about seven percent more will be diagnosed every year, according to the National

Kidney Foundation. Just as dismal, the number of kidney failure patients in the United States is predicted to double in the next 10 years, influenced in part by diseases associated with an aging population such as diabetes and high blood pressure.

And as we humans live longer and develop age-related health problems, so too do our pets. Kidneys in both



Dr. Lilly Aronson (left) and Dr. Jackie Miller, respectively holding Hammy (donor) and Speedy (recipient). Sitting for this photo was the first time the two cats had met. Photo by Lisa Godfrey.



Radiograph of a cat with kidney stones

people and animals act as the body's filters to cleanse the blood of waste products. They take in blood, filter it and produce urine for excretion. They also help regulate blood pressure and calcium levels. When the kidneys fail, toxins are released into the body and, if untreated, death occurs.

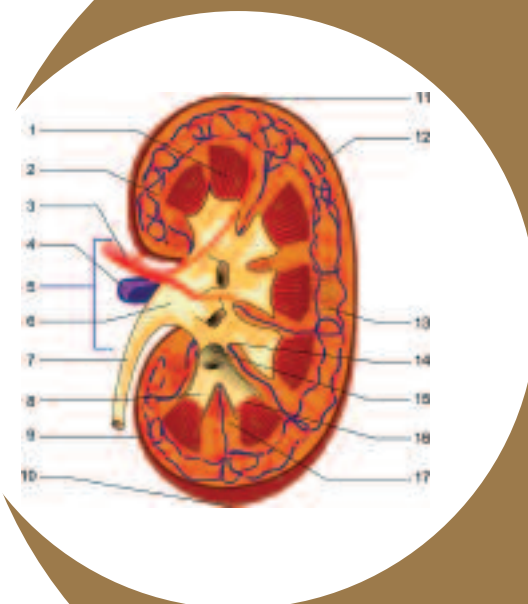
Kidneys can go into two kinds of failure, acute and chronic. Acute renal failure (ARF) is a serious condition usually with a sudden onset and often triggered by a particular event—for cats, ingesting lilies or antifreeze is potentially lethal. ARF commonly is treated with intravenous fluids and other medications and, if the animal survives the initial crisis, much or sometimes all of its normal kidney function can be regained.

Chronic renal failure (CRF) also may appear very suddenly and require intravenous treatment, but unlike ARF it is an ongoing disease in which kidney damage is irreversible; the goal is to keep the remaining function as long as possible. CRF is seen most often in older pets; cats and small dogs may show early signs of kidney failure at 10 to 14 years of age, but large dogs can experience it much earlier. This type of kidney disease can arise from a wide variety of causes, including hereditary/congenital abnormalities, bacterial infections, inflammation of the internal structure of the kidneys, cysts within the kidney, and urinary tract blockages such as kidney stones. Some cases are acute on chronic; for instance, a cat with CRF that acutely obstructs with a kidney stone.

In most cases of renal failure, treatments aimed at alleviating the symptoms are usually the first course of action. No cure exists for chronic renal failure, but for a time it can be managed via intravenous and subcutaneous fluids, changes in diet, medication and hemodialysis. If and when these therapies are ineffective, another option can be considered—and here is where this remarkable story inside the Ryan Veterinary Hospital really begins.

Double Bonus

Penn Vet has a habit of bringing its own back into the fold, and **Dr. Lillian R. Aronson, V'92**, assistant professor of small animal surgery, is no exception. After graduation and an internship at Penn Vet, Dr. Aronson was accepted for a three-year surgical residency and one-year lectureship at the University of California, Davis, where she became interested in kidney transplantation. Under the tutelage of Dr. Clare Gregory, considered a pioneer in the field, she coordinated UC-Davis's renal transplant program



Structures of the mammalian kidney:

1. Renal pyramid
2. Interlobar artery
3. Renal artery
4. Renal vein
5. Renal hilum
6. Renal pelvis
7. Ureter
8. Minor calyx
9. Renal capsule
10. Inferior renal capsule
11. Superior renal capsule
12. Interlobar vein
13. Nephron
14. Minor calyx
15. Major calyx
16. Renal papilla
17. Renal column

until 1996. A year later,

Dr. Aronson moved back to Philadelphia—bringing along her newly acquired expertise—and by 1998 Penn had its own fledgling Feline Renal Transplant Program. Today, Ryan is the only teaching hospital on the East Coast that performs kidney transplants—and Dr. Aronson estimates that the Ryan transplant team will celebrate its one-hundredth transplant, literally, any day now.

Dr. Aronson emphasizes that the program is hardly hers alone, and only possible through the efforts of a consortium of specialists from across veterinary disciplines. “Each case wouldn’t work without a team of people; in anesthesia, surgery, critical care, nurses and other surgeons. Each case really has three surgeons involved—and the whole team makes it go very well and smoothly,” she said.

The transplantation process actually begins very early on, starting with the initial assessment of the cat’s kidney disease, as well as the owner’s willingness to bear the burden of frequent visits, expensive bills and years of administering daily medicine to the animal. (For reasons related to dogs’ immune systems, and the greater expense of medicating a much larger animal every day for potentially years, Ryan’s renal transplant program focuses on cats.) One way Dr. Aronson determines her clients’ suitability for the program is their desire to bring home two cats instead of one; the owners must agree to adopt the donor cat, or the deal is off.

“Part of the screening process happens before I even talk with the clients,” Dr. Aronson explained. “I probably don’t hear from those people who say to their referring vet, ‘Oh, we’re not interested in the donor.’ They absolutely must adopt the donor, or it’s just not going to happen. And we follow the donors for the rest of their lives to make sure they have good homes.”

So who are these donors anyway?

A donor cat can be selected from those in the recipient’s household or, more commonly, from cats currently living at the Ryan Veterinary Hospital that have come from shelters or research colonies. Dr. Aronson is working with the SPCA in York, Pennsylvania, to adopt more cats, potential donors that likely would otherwise be destroyed. It’s a sad fact of today’s animal shelters, one that Dr. Aronson is all too familiar with. “When people go to shelters, they see the cute little kitten and that’s the one they want. They don’t necessarily want the one- or two-year-old cat; those are the ones that often get euthanized, so those are the ones I would love to adopt into our program,” she said. With Ryan’s Feline Renal Transplant Program, for every cat that gets a new lease on life through a kidney transplant, so does another through its rescue from the pound.

Gifts in Kind

Deciding which cats are ideal candidates for kidney transplants—and when to do them—can be a tricky business, but there are some standard guidelines. “Many people ask about the right time to intervene, and that can sometimes be hard to answer,” Dr. Aronson stated. “Probably the best time to intervene is when the patient is starting to fail medical management—losing weight, becoming more

anemic, more azotemic [accumulating waste products in the blood] in the face of medical therapy. Having said that, I have

intervened sooner in some cases, and much later in others. I think a key to success is that no other disease processes are going on.” An animal’s age historically has not been a factor, either: the oldest cat that has been transplanted was 18. Generally, transplantation is not performed as an emergency or “last ditch” effort; transplants performed on inappropriate candidates usually do not have good results. Some patients also may need hemodialysis to stabilize them prior to the transplant.

The donor should be a healthy, young, FeLV/FIV-negative adult cat, preferably the same size or a little larger than the recipient. Donor and recipient should be matched by blood typing. And, of course, tests should confirm that the donor has two normal-shaped healthy kidneys. Unlike the recipient, which requires life-long medications to suppress its immune system so that its new kidney is not rejected, no special, long-term care is necessary for the donor.

“I tell my clients that they’re going to have the same number of kidneys in their house, just distributed differently,” Dr. Aronson joked as she explained that, in the majority of cases, the recipient’s native kidneys are left in as “back-ups” should the donor kidney fail. Most transplanted kidneys are functioning well by 72 hours after surgery—at this point, the recipient’s condition will have dramatically improved. (Re-transplantation is very rare, performed only in situations where a clot has developed in the renal artery or the graft breaks down from its surgical site and twists—both very uncommon conditions.)

The transplant procedure, lasting about four to six hours, involves two surgical teams operating on both cats simultaneously. After removal, the donor’s kidney must be transplanted into the recipient—in the lower abdomen next to the bladder—in less than an hour, to minimize its time without a blood supply. The ureter from the donor’s kidney is attached to the bladder, and the new kidney is connected to the recipient’s blood vessels.

The work is painstaking, requiring an operating microscope to magnify cats’ tiny veins, arteries and ureters. For an idea of scale, the feline renal artery measures only about two millimeters around (less than a tenth of an inch). To stitch it to another artery, Dr. Aronson must use an enormous surgical microscope suspended above the patient, with dual eyepieces for her and her assistant.

The sutures are brought into view, but Dr. Aronson’s eye-hand coordination must be re-established; seen

Oli, the donor (left), and Mr. Moto, the recipient





Surgeons operate at two workstations simultaneously to quickly move the kidney from donor to recipient.

through the eyepiece, the most delicate forceps appear as pliers.

Making Time

In most cases, a kidney transplant buys clients more than a few extra months with their pets: the mean survival time at the Ryan Veterinary Hospital is close to four years, with some cats living eight years or more following transplantation. Presently, almost 94 percent of the cats leave the hospital, and 70 percent are alive one year out. “Anecdotally, if nothing seems to be an issue in the first six months after surgery—whether a rejection episode or problems with infections—and if the owners follow instructions about medications so the cats don’t develop problems like cancer or diabetes, then recipients tend to do well long-term,” explained Dr. Aronson.

When transplanted cats do die, it is most likely not from renal problems; continuous immunosuppression can bring out latent infections or cause tumors to form. “I would say only four or five that I’ve documented [since 1996] have gone back into chronic kidney failure,” Dr. Aronson said. In successful cases, the donor can join its new family after surgery in just a few days; its life

expectancy is no less than that for two-kidneyed cats. The remaining kidney enlarges to provide about 75 percent of the total function of two kidneys. Longer hospitalization is needed for the recipient, but a normal, active life with virtually no restrictions—and a new friend, to boot—can be expected.

“A Potpourri of Knowledge”

Ryan is a university teaching hospital, and as such offers a rich array of cases from which future veterinarians can learn. The students and residents who assist doctors in the Feline Renal Transplant Program are on each case from scrub-in to discharge and beyond. In addition to her duties as surgeon, Dr. Aronson is also an educator. “It’s not like our other surgery cases, where students come in, assist with the case, and then the case is discharged within a few days—students on these cases follow the cats for a long time,” she said. “The transplant cases are often in for at least two weeks, and so there is a good opportunity to learn about renal physiology and the medical aspects of kidney disease. They learn about client communication. They definitely get a good potpourri of knowledge: internal medicine, surgery and, post-operatively, critical care

management.” She also lectures to the third-year elective surgery class and the students’ Feline Club, and almost every year presents at the Penn Annual Conference.

The best teachers drive themselves to be continuous learners, and Dr. Aronson is still finding knowledge in healing animals and educating students. A recent transplant case involved Cleo, an Abyssinian cat with amyloidosis, a rare disease marked by abnormal protein buildup in various organs that can cause permanent damage. “We never had a cat with amyloidosis before,” she explained. “The cat’s creatinine and numbers were all normal, so my thought was that if we just transplant the cat, we might not be fixing the old problem. We really had to take out *both* its kidneys.” Because Cleo’s protein level was so low, fluid had built up in the chest and abdomen, and she was having a lot of difficulty breathing. In addition, she needed her chest tapped multiple times. After consulting with physicians at the Hospital of the University of Pennsylvania, Dr. Aronson’s sense of what should be done was confirmed. But removing two kidneys of an otherwise normal cat was “disconcerting,” and the outcome unsure. Cleo been flown up from Florida, and her owners asked their referring veterinarian to make the trip to Penn—euthanasia solution in his bag—in case the worst happened. Within days after the transplant surgery, both native kidneys having been removed, Cleo’s proteins had normalized completely. To show their appreciation, Cleo’s owners made a gift to the Ryan Veterinary Hospital that helped the renal transplant program purchase a new microscope.

Where Sciences Meet

Experimental kidney transplants in animals were first performed in 1902 at the Vienna Medical School, and in 1954, myriad medical advances had made possible the first kidney transplant operation on identical 23-year-old human twins in Boston. Thirty-three years later—in 1987—kidney transplants for the first time were used to successfully treat end-stage renal disease in cats at UC-Davis. For both animal and human patients, however, problems remained in preventing the recipient’s immune system from treating the new kidney as a foreign body and subsequently rejecting it. Powerful immunosuppressive drugs like cyclosporine and prednisolone have proven effective in staving off rejection, but they impair the ability of the recipient to resist infection—both new diseases and

activated latent ones. “Additionally, these patients are more prone to the development of cancer,” stated Dr. Aronson.

“The most common cause of morbidity and mortality in humans and cats that have received transplants is complications associated with long-term immunosuppression,” she continued. Within six months of beginning transplants at Penn, two of Dr. Aronson’s first 20 recipient cats died of pneumonia after a reactivation of latent toxoplasmosis (caused by the parasite *Toxoplasma gondii*). Dr. Aronson and **Drs. Christopher Hunter**, professor of parasitology, and **Nicola Mason**, assistant professor of medicine, are now collaborating to study newer immunosuppressive therapies *in vitro*. They are looking at some therapies being used in people that are more specific to the transplant site, rather than the systemic immunosuppression that occurs with traditional post-transplant drugs. This way, doctors can prevent organ rejection, while still allowing their patients to respond to potentially life-threatening infections. Published papers of the team’s work conclude that the results of their research should bring about *in vitro* and *in vivo* studies in humans and other animal models.

But today, for people like Dr. Jackie Miller, the intersection of veterinary and human medicines has never been keener—or more personal. As she and Speedy take their respective daily medications, each can be unwittingly benefiting from the knowledge their doctors are gaining not only through research, but also during their post-transplant, long-term recoveries. 🐾



Leo, the first kidney recipient at the Ryan Veterinary Hospital

For more information on the Penn Vet Feline Renal Transplant Program, please visit www.vet.upenn.edu/catkidneytransplant.html.

For more information on the recent pet food recalls, please visit www.vet.upenn.edu/nutrition