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New DNA-Based Test for Inherited Disease in Schipperkes

Collaboration Between Vet School and School of Social Work Takes Off

By Katherine Kruger

At first glance, a collaboration between a School of Veterinary Medicine and a School of Social Work may seem unlikely, perhaps even unnecessary. Not so at Penn, where one of the Vet School's multidisciplinary research centers – the Center for the Interaction of Animals and Society (CIAS) – focuses its attention on the study of human-animal relationships. In fact, collaboration between the two schools was first established almost 20 years ago. Now, **Dr. James A. Serpell**, director of the CIAS, wants to enhance this link because of the unique knowledge and skills that social workers can bring to the study of human-animal interactions.

It's been just over a year since Symme Trachtenberg, MSW, LSW, director of Community Education at The Children's Hospital of Philadelphia (CHOP), signed-on to be the liaison between the two schools, and the relationship is already in full bloom. As of this printing, there are five collaborators from the School of Social Work who are actively contributing to the work of the CIAS.

Current projects underway include the creation of an educational program called, "Kids Caring for Pets," that teaches children about the responsibilities of adopting and caring for pets. This program – developed by Ryan Veterinary Hospital staff members **Dr. Stephen Mehler**, intern; **Sally Powell**, Critical Care/ES nursing supervisor; and **Alison Seward**, behavior technician – is currently being piloted at the new Sadie Alexander University of Pennsylvania Partnership School and other schools in West Philadelphia. Since November, the Kids Caring for Pets Program has visited four schools and done ten presentations. Hundreds of children have participated, and preliminary data suggest that the program is having a positive impact on students' understanding of what it takes to keep pets happy and healthy.

The social work group is also collaborating with CHOP to evaluate its animal visitation program, known as PAW Partners. This program, which provides opportunities for children and their families to interact with visiting animals, has been well received and is highly successful, and the social work group hopes to take a more objective look at its benefits. Dr. Kinney and Ms. Levinthal are studying the link between child abuse and animal abuse. They are also using diagnosis codes from the

Vet School's patient database to map clusters of companion animal disease within the city. This information will be used to target educational and community outreach efforts.

If you would like additional information on the collaboration between the Schools of Veterinary Medicine and Social Work, or you know of a school that would like to host the "Kids Caring for Pets" educational program, please contact Ms. Kathy Kruger at 215-746-0096, or kkruger@vet.upenn.edu. Alternatively, you can learn more about the work of the CIAS by visiting: www.vet.upenn.edu/ResearchCenters/CIAS/



A fourth-grade student at Samuel B. Huey Elementary School listens to Lulu's heart with Sally Powell, Critical Care/ES nursing supervisor.

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Researchers at the School have developed a new DNA-based test for an inherited disease in the schipperke, a breed of dog. The disease, mucopolysaccharidosis type IIIB (MPS IIIB, also known as Sanfilippo syndrome, type IIIB), is an autosomal recessive disease that is classified as a lysosomal storage disease. Other better-known lysosomal storage diseases that occur in humans include Tay-Sachs disease and Gaucher disease.

This is the first time that MPS IIIB has been diagnosed in any companion animal. The symptoms of MPS IIIB in the schipperke are caused by serious and progressive damage to the brain and include tremors, stumbling, and falling. Symptoms in the dog first appear at two to three years of age. The brain disease progresses until the dogs are no longer able to stand, walk, eat, drink, or eliminate without assistance, and owners have had to elect euthanasia for their pets one to two years after the onset of symptoms.

This DNA-based test is the latest in over a dozen different mutation-specific DNA-based tests for inherited disorders offered or developed by the researchers in the Section of Medical Genetics at the School.

The initial schipperke case came to the attention of Penn researchers in late 1998, when **Dr. Urs Giger** and colleagues in the Section of Medical Genetics at the School identified MPS IIIB in a dog in samples that had been submitted for analysis to the School's metabolic genet-

ic screening laboratory. Since then other dogs have also been studied in the breed. The identification of the mutation and development of the test was performed by **Dr. N. Matthew Ellinwood**, a post-doctoral fellow in comparative medical genetics. The DNA testing of schipperkes for the MPS IIIB mutation will be conducted through the School's Josephine Deubler Genetic Disease Testing Laboratory.

"As devastating as this disease is, we are fortunate that we can help eradicate the condition through testing that identifies animals that are affected or are carriers," says Ellinwood. "This allows breeders to eliminate affected animals from their breeding program and mate carriers only to animals that do not carry the disease. Eventually the schipperke breeders, using this test, will be able to eliminate this disease in the breed."

"Unfortunately, the mutations in humans are so rare, and so varied, that it is not practical to test people routinely, nor are there routine and effective ways to screen newborns children for the disease.

"One of the most devastating things is that in some families the eldest child in a family, diagnosed at 3-5 years of age, may have younger siblings who also have the disease but have not yet started to have symptoms, so that parents will confront more than one devastating diagnosis. Finding effective ways to treat this

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Laparoscopy to Enhance Chance of Pregnancy in Goats and Sheep

by Regina Turner, V.M.D., Ph.D., V39

New Bolton Center has acquired a laparoscope for the use in embryo transfer and insemination of sheep and goats. **Dr. Regina Turner**, assistant professor of reproduction at New Bolton Center, explains the benefits of the new instrument.

Laparoscopic artificial insemination in sheep and goats currently is the preferred method for breeding these small ruminants with frozen-thawed semen. Using the laparoscope, semen is deposited directly into the uterine horn, thus placing the sperm in close proximity to the site of fertilization. This increases the chances for pregnancy, particularly when dealing with small numbers of sperm (as is the case with frozen semen).

Before an animal can undergo this procedure, her estrous cycle must be synchronized with hormones. This allows ovulation to be very exactly timed. At around the time of ovulation, the procedure is performed. The ewe may or may not be sedated and a local anes-

thetic is injected at the surgical site. The ewe then is suspended by her hind legs in a specially-designed cradle. This position helps to insure that the rumen and intestines are not in the way of the surgery. A small incision (usually less than a centimeter) is made through the animal's body wall and into her abdomen. The laparoscope is inserted through the cut. The uterus and ovaries generally are easy to see through the laparoscope. Once the reproductive tract has been identified, a second, similar incision is made into the abdomen and a small insemination instrument containing the semen is passed through the cut. The surgeon then can watch through the laparoscope and guide the insemination instrument to the uterus where a small needle at the end of the insemination instrument is used to puncture into the uterus. Semen then is injected directly into the uterine lumen. The instruments are withdrawn and the small holes are closed with one suture each. In the hands of an experienced surgeon, the entire procedure can take less than 10 minutes. Most

ewes stand as soon as they are released from the cradle and suffer no after effects. As with any surgical technique, there can be complications. But these are rare and usually are minor.

Pregnancy rates vary depending on the breed, the season and the semen quality. Highly fertile ewes under excellent management and bred in season can experience pregnancy rates as high as 80%, although more typical ranges are from 40 to 70% in season. These kinds of pregnancy rates make this procedure very practical for valuable animals and open up the possibility of using imported frozen semen from some of the most valuable males in the world.

Another assisted reproductive technique that is gaining in popularity with small ruminant breeders is embryo transfer. Embryo transfer greatly increases the potential number of offspring that a single, valuable female can produce in a year. This can be of great economic benefit to producers and also can help propagate valuable genetics on the female side. For this procedure, the donor animal's estrous cycle and the estrous cycle of a group of recipient (surrogate) females are synchronized hormonally. Additionally, the donor animal is given hormones that make her ovulate a very large number of eggs (sometimes more than 10 each cycle).

The donor is bred either naturally or laparoscopically at a set time. Several days after the breeding, the donor ewe is placed under anesthesia. A surgical incision is made in her abdomen and her uterus is exteriorized. A small incision is made in the uterus and a tube is threaded into the uterine lumen. Flush media is injected through the catheter and collected. Hopefully, this media rinses the embryos out of the uterus. The media is searched under a microscope and embryos are identified. The incision is sutured closed and the ewe recovers from the anesthetic. Any resulting embryos can be frozen for long term storage or they can be immediately transferred into a synchronized recipient.

For the actual embryo transfer, the recipient ewe is sedated and an appropriate number of embryos are placed into her uterus with the help of the laparoscope. The recipient ewe then carries the pregnancy for the donor ewe. As many as 15 embryos can be recovered from a single flush, although more typically the number ranges between 5 and 10. Actual success rates depend on the breed, the time of year, the quality of the semen and the management of the donor and recipient animals.

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rare disorder are going to be challenging and we hope that by studying the disease in the dog, we will be able to make the progress that these children and families hope for."

Dr. Ellinwood, who has judged working hunting dogs, presented his findings at the beginning of April to a meeting of schipperke enthusiasts at this year's annual National Specialty Show of the Schipperke Club of America, in Dallas, Texas. "I am really very pleased to be able to have a part in helping to improve the health of these dogs, by allowing the breeders to use the power of a DNA test to end forever a terrible disease." Unfortunately, children with this rare disease and their families still wait for developments in research that may bring promise of an effective treatment. Helping to eliminate this disease from this dog breed was the 'easy part,' says Ellinwood.

The researchers benefited from the knowledge gained in the field of human medicine and genetics. It took human medical science over thirty years to understand the genetic basis of this disease, from the time the syndrome was

first identified in 1963, until 1996, when DNA mutations could be identified in people. Using this knowledge the researchers at Penn were able to identify the mutation in the schipperkes in a relatively short period of time.

The research on the disease-causing mutation in the schipperkes was funded by a grant from the National MPS Society awarded to **Dr. Mark Haskins**, professor of pathology, in an effort to make progress in understanding MPS IIIB and to help in developing treatments for children with this disease. The incidence of MPS IIIB in the human population is approximately one in every 73,000 live births. The condition in children first appears as delayed development in early childhood, and progresses through childhood with severe mental deterioration leading to dementia. The disease is ultimately fatal, with most children dying in their teenage years. At the present time, there is no treatment that has been proven effective. To learn more about this and similar diseases in children, visit the National MPS Society's web site at <www.mpsociety.org>.