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Strength in Numbers

One veterinary radiation oncologist, two immunologists and thousands upon thousands of specialized immune cells are joining forces to develop a new cancer immunotherapy that has the potential to help dogs diagnosed with oral melanoma.

Clinicians at the Western College of Veterinary Medicine often use a combination of surgery, chemotherapy and radiation therapy to treat oral melanoma in dogs. But even with that "triple whammy" of therapies, the chances of a full cure are very slim, says veterinary radiation oncologist Dr. Monique Mayer.

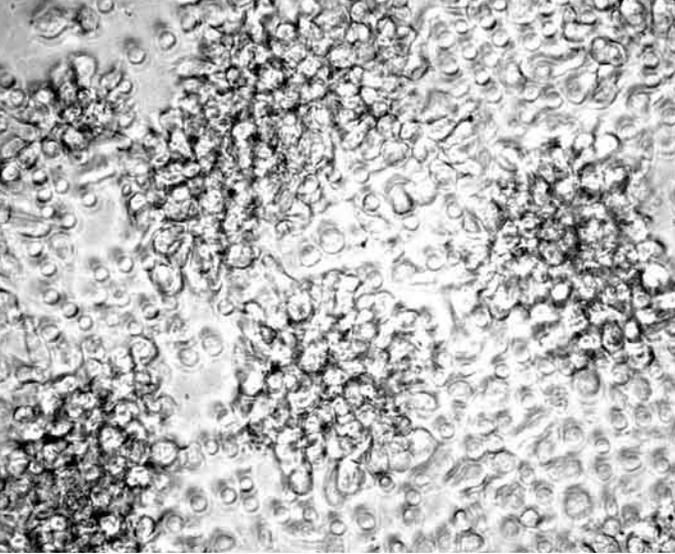
"It's a highly metastatic type of cancer that's very difficult to cure with standard treatment. And even if we get rid of the tumour in the mouth, there's a high rate of spread to other parts of the body — especially to the lungs," says Mayer, an assistant professor in WCVN's Department of Small Animal Clinical Sciences who operates the College's busy pet radiation therapy program.

"What we're trying to do is to find a way to kill the tumour cells that have spread somewhere else so they don't come back."

One possibility is dendritic cell vaccines — a new immunotherapy that has shown promise in treating various types of human cancer including breast cancer and prostate cancer. Dendritic cells are potent, antigen-processing cells

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ABOVE (left to right): Drs. John Gordon, Hui Huang and Monique Mayer.



“Other therapies are more effective at removing or reducing the size of the tumour. But our ultimate goal is that the dendritic cells will help to stimulate the immune system and kill off the tumour cells that have spread.”

LEFT: This microscopic image shows clusters of dendritic cells after six days of growth in the laboratory.

that initiate primary immune responses by stimulating T cells and other lymphocytes. Their precursors (the substance from which dendritic cells are formed) can be found in bone marrow and peripheral blood.

OUT-OF-BODY EXPERIENCE

With financial support from the Companion Animal Health Fund, a team of WCVN researchers including Mayer and immunologists Drs. John Gordon and Hui Huang now plan to produce dendritic cell vaccines for dogs diagnosed with oral melanoma using processes similar to those developed for human cancer patients.

Several factors make canine oral melanoma an ideal target for testing this new dendritic cell immunotherapy, points out Gordon. Researchers have ready access to the actual tumour without doing major surgery, plus it's a type of cancer that has proven to be very resistant to other therapies.

Gordon describes melanoma as an “immunologically silent tumour” that has the ability to actively suppress a patient's immune response. “These tumour cells secrete various *cytokines* (or immune response-regulating mediators) that can render dendritic cells tolerant of the diseased cells. By removing the tumour from the body and stimulating the dendritic cells *ex vivo* with radiation-crippled tumour cells, we're able to activate the dendritic cells in a way that should potentially induce a tumour-specific immune response.”

As a first step, the scientists will purify dendritic cell precursors from blood collected from five canine cancer patients at WCVN's Veterinary Teaching Hospital. Next, they'll use dendritic cell stimulants to reproduce large quantities of the immune cells in the lab. Finally, before these mature dendritic cells are re-injected into each patient, the researchers will expose them to each dog's tumour cells in such a way that the dendritic cells are “turned on” and primed to stimulate the immune system's response against the specific cancer cells.

“We'll extract the patients' blood before they begin any other cancer treatment, and then once the dendritic cell precursors are purified, we'll reproduce them in the lab until we have enough for the patient's first dose of the vaccine. Altogether, we'll give them six treatments with two weeks in between each dose,” explains Mayer.

She adds that the research team will measure the length of time that each dog lives disease-free or survives to evaluate the vaccine's effectiveness.

“Human patients have lived longer and lived disease-free for a longer period of time with the vaccine, but in dogs, not enough research has been done to ensure that this treatment really makes a difference,” says Mayer, stressing that the immunotherapy isn't a replacement for standard oncology treatments.

“Other therapies are more effective at removing or reducing the size of the tumour. But our ultimate goal is that the dendritic cells will help to stimulate the immune system and kill off the tumour cells that have spread.”

RESEARCH COMES FULL CIRCLE

Gordon, a professor in WCVN's Department of Veterinary Microbiology, was the first to suggest the idea of dendritic cell vaccines after listening to a presentation by Mayer during one of the College's “research coffees.” The weekly event is designed to encourage scientists of all disciplines to share research ideas and to explore new collaborations.

“I'm lucky to be working with Dr. Gordon on this project because he's been part of similar studies in human medicine, and he knows people who have worked with similar research protocols,” says Mayer. “I wouldn't be able to pull together all of the resources needed for this study without him.”

Dendritic cells are familiar research subjects for Gordon who has used a reciprocal approach — immunosuppressive dendritic cell therapy — to eliminate asthma in severely asthmatic laboratory animals. His research team has also shown that this process can be recapitulated *ex vivo* using dendritic cells generated from allergic people to reduce the allergic reactivity of their immune cells.

The process of generating large numbers of dendritic cells in the lab is similar, but Gordon's work with the immune cells to treat asthma is the “mirror opposite” of this new cancer therapy. “We're trying to shut down or suppress a pre-existing immune response in asthma patients whereas with cancer patients, we're trying to stimulate a response against a tumour in a functionally naïve host,” explains Gordon.

Still, shifting the research focus from asthma to cancer isn't a huge leap. In fact, what compelled Gordon to look at dendritic cell therapy for asthma was what he knew about the tricky traits of cancer cells.

As he explains, some tumour cells like melanoma can trick a host's immune system by secreting a cytokine called *interleukin-10* (IL-10) that turns off the dendritic cells' immune-stimulating activities. “With that knowledge, we hypothesized that we could shut down the expression of the asthmatic response in a patient by giving allergen-presenting, IL-10-treated dendritic cells to that patient,” says Gordon. “Basically, our research has come full circle. We're now back to looking at it from the other side.”

NEXT STEP: CLINICAL TRIAL?

Besides Gordon and Mayer, another key person involved in the canine study is Dr. Hui Huang. Before joining Gordon's laboratory to pursue a PhD degree, Huang worked alongside the Saskatoon Cancer Centre's Dr. Jim Xiang — an immunologist whose research focuses on the development of dendritic cell vaccines for human patients. Xiang's research has now progressed to the point where he is testing the efficacy of dendritic cell vaccines in human patients through a clinical trial.

“Dr. Huang is a talented young immunologist who worked in Dr. Xiang's lab on tumour immunization in mouse model systems for quite some time, so he's a very good link to have between the two labs. His experience in developing dendritic cell vaccines for human medicine will also be very valuable on this particular project,” says Gordon, who has collaborated with Xiang and Huang on several dendritic cell-linked studies.

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PET PROJECTS

SURGICAL OPTION FOR ORAL RECONSTRUCTION: Surgical specialists at WCVM have investigated several different “skin flaps” to repair wounds caused by trauma or the removal of cancerous tumours in the past two decades. This latest study, co-authored by Drs. Jim Dundas, David Fowler, Cindy Shmon and J.B. Clapson, tested the use of an extended *pedicle* (entry point of flap’s blood supply) flap based on the *superficial cervical artery* (SCA) to close defects inside dogs’ mouths.

The superficial cervical skin flap is a lengthy piece of skin and tissue that’s cut and rotated from the patient’s neck and front shoulder region. A single artery vein (the superficial artery and vein) supplies blood to the skin region in this flap — an attribute that makes it ideal for reconstructive surgery. Surgeons have used the flap to reconstruct large defects in dogs’ heads, but before this study, it had never been tried in oral reconstruction cases.

Dundas, who was the Companion Animal Health Fund’s research fellow and completed a surgical residency at WCVM in 2004, initially worked with 13 canine cadavers to fine tune the surgical technique. Then, Dundas conducted the reconstructive surgery on three research dogs. In all cases, the surgical specialist implanted the skin flap in stages so he could evaluate the flap performance *in vivo*.

In the first stage, he prepared the flap for implantation into the oral cavity. Next, the flap was fully developed to include the one degree, two degrees and partial three degrees *angiosome* (three-dimensional block of tissue supplied by a single-source artery) of one SCA pedicle. Dundas transposed the flap by a bridging incision and through the *parapharyngeal* tunnel (a potential space lateral to the upper pharynx), and used the flap to reconstruct a partial-thickness defect created in the palate.

Based on the study’s results, Dundas and his co-authors conclude that the extended SCA pattern flap may be adapted for closure of oral defects. A loss of pliability (due to skin loss and staging) limited the rostral reach of the flaps, but the flaps survived well in the harsh, oral environment. Dundas and his colleagues also recommended that the flaps may be modified to reconstruct full-thickness palatal defects in dogs.

Dundas JM, Fowler JD, Shmon CL, Clapson JB. “Modification of the superficial cervical axial pattern skin flap for oral reconstruction.” Veterinary Surgery. 2005; 34(3): 206-213.

VACCINE continued

If the pilot project’s results are promising, the team plans to apply for additional research funding so they can conduct a larger study involving more canine patients. Ultimately, those efforts could help to put dendritic cell vaccines on the list of therapy options for oral melanoma that are available at WCVM’s teaching hospital — and no one would welcome that addition more than Mayer.

“It’s the most common oral tumour that we treat and one of the most frustrating. We can treat a dog with oral melanoma that has no metastasis — and yet, the cancer continues to spread even after the dog has received multiple therapies,” says Mayer. “It’s one of the cancer types where we need to do more work so we can have better outcomes in these cases.”

Gordon acknowledges that the research will give scientists new insights into dendritic cell immunizations — but what’s more crucial is that the study holds the potential of generating a better way to treat a highly pathogenic type of cancer and to extend the survival rates of dogs diagnosed with oral melanoma.

“Here’s the bottom line: can we do something for these patients? That’s the real motivation behind this research.” **V**

If you have a dog or a patient that has been diagnosed with oral melanoma and may be a potential candidate for this study, please contact Dr. Monique Mayer (monique.mayer@usask.ca), Dr. Candace Grier (candace.grier@usask.ca) or contact WCVM’s pet radiation therapy program at 306-966-1894.



What do you know about wills and charitable giving?

By Joanne Wurmlinger, CFRE

Want to leave your legacy? Plan a charitable gift through your estate today and have the satisfaction of knowing that you will be making a difference in the years to come.

Besides the benefits of outlining your wishes about your children, the disposition of your assets and other legal concerns, there are many tax and income advantages to planning your estate now. And remember: anyone can make a planned gift — for any amount.

Test your knowledge of wills and charitable giving by answering true or false to the following questions. You can compare your responses to the correct ones on the back cover.

- A married couple only needs one will.
- You can donate to your favourite charity and receive guaranteed income for life.
- Once you have a will, you never need to change it.
- If you want to leave your home to a charity, you can donate it now, obtain an immediate tax benefit and continue to live in it until you pass away.
- You can provide for your favourite charity through your estate without reducing the amount that you would like to leave for your family and friends.
- Charities can be named as beneficiaries of your life insurance policy, your Registered Retirement Savings Plan (RRSP) or your Registered Retirement Income Fund (RRIF).
- Cash is the only way to make a gift to your favourite charity.
- You must claim all of your charitable donations in the year that you make the gifts.



A New Wave of Companion Animal Research

This spring, the Companion Animal Health Fund (CAHF) is funneling nearly \$78,000 into eight pet health-related research projects that will be conducted by a pool of researchers at the Western College of Veterinary Medicine over the next two years. In this latest tide of studies, scientists are investigating a wide range of issues that have the potential to bring a fresh wave of benefits to Western Canada's companion animals: new diagnostic and therapy tools for oncology patients, a new treatment for a bacterial infection in cats, new insights into the genetics of a retinal disease, a better understanding of a marker for acute inflammation, and more in-depth knowledge of two common orthopedic problems in dogs. Watch for further introductions and updates in future issues of *Vet Topics*.

Can dendritic cell vaccines effectively treat canine oral melanoma?

Drs. Monique Mayer, John Gordon and Hui Huang

WCVN scientists are testing the potential of *dendritic cell vaccinations* to treat malignant canine oral melanoma — a highly *metastatic* (spreadable) type of cancer that's difficult to treat even with multiple therapies.

Dendritic cells are special antigen-presenting white blood cells that initiate a body's primary immune response to disease. Based on techniques developed in human research, the WCVN team will extract immature dendritic cells from a cancer patient's blood, then encourage the cells to grow and multiply in the laboratory. Before vaccinating each patient with its own dendritic cells, researchers will expose the cells to the dog's own tumour cells — stimulating an immune response.

If the vaccine slows down the development of metastatic disease and increases the overall survival rate of the pilot study's five patients, researchers will develop a clinical trial to test the vaccine's efficacy in more dogs.

Does gabapentin relieve neuropathic pain in bone cancer patients?

Dr. Monique Mayer, Dr. Candace Grier, Erica Collen and Tara Shymko of WCVN, and Dr. Susan LaRue of Colorado State University

Researchers from WCVN and Colorado State University are investigating the addition of the drug *gabapentin* to treat bone pain in canine patients undergoing palliative therapy for appendicular osteosarcoma.

Veterinarians use radiation therapy, opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) to treat the pain associated with this type of primary bone cancer, but these therapies may not effectively treat neuropathic pain caused by peripheral nerve damage. Gabapentin, which is used to treat epilepsy and neuropathic pain in humans, may increase the level of pain relief and patients' quality of life.

During the next 18 months, researchers will conduct a clinical trial to assess pain and quality of life scores in dogs that receive palliative radiation therapy and gabapentin, as well as those patients that receive radiation therapy with no gabapentin.

Is PCR analysis effective for diagnosing lymphosarcoma in dogs?

Drs. Kathi Ellis, Beverly Kidney, Marion Jackson, Elisabeth Snead and Monique Mayer

A group of WCVN scientists are working on a more efficient, less invasive way to diagnose lymphosarcoma in dogs. The team will test whether PCR (polymerase chain reaction) analysis of DNA from a cytology slide containing canine lymph node and tissue cells can help veterinarians determine the *phenotype* of lymphosarcoma and confirm diagnosis by detecting clonality (phenotype is the expression of a specific trait based on genetic and environmental influences). If this method is successful, it may eliminate the need for obtaining invasive biopsies for further testing.

Determining the phenotype (B cell versus T cell) involved in individual lymphosarcoma cases is extremely valuable in establishing a diagnosis, prognosis and a therapy plan. Through this study, researchers will determine whether PCR is effective in determining the phenotype of the cancer, whether it can be used to differentiate reactive and neoplastic lymphocytes in lymphoid tissue, and whether PCR analysis using DNA from a dog's peripheral blood is more sensitive than microscopic examination of a blood film for cancerous lymphocytes. As well, the team will also look at whether PCR is effective in detecting relapsed or residual disease in canine patients.

Is a human CRP assay useful for studying acute pancreatitis and atherosclerosis in dogs?

Drs. Valerie Wong, Marion Jackson and Beverly Kidney

C-reactive protein is an acute phase protein in many species and a very sensitive marker of acute inflammation in dogs. However, the current

method for measuring canine CRP is very time consuming and labour intensive — making it difficult for veterinarians to conduct routine screening of CRP levels as in human medicine. In this study, researchers in WCV's Department of Veterinary Pathology hope to validate an automated human assay and provide a more efficient method for measuring CRP in dogs. As well, the WCV research team will investigate the usefulness of CRP level as a prognostic indicator for acute pancreatitis in dogs.

Scientists will also measure CRP levels in serum samples from healthy miniature schnauzer dogs — a breed that's predisposed to *atherosclerosis* (thickened blood vessel walls due to fatty deposits). While this condition is common in humans, it's rarely diagnosed in dogs. Human medical research has shown that CRP may not be just a marker for atherosclerosis but a mediator of this condition. Once WCV scientists have established baseline CRP levels in miniature schnauzer dogs, this work could lead to future studies evaluating the association between CRP levels and the higher risk of atherosclerosis in this breed.

What genetic mutation causes retinal dysplasia in miniature schnauzers?

Drs. Lynn Sandmeyer, Bruce Grabn, George Forsyth and Bianca Bauer

WCV scientists are continuing to investigate the genetic mutation responsible for inducing retinal dysplasia in miniature schnauzer dogs, a common inherited disorder that often causes blindness in the breed.

In preliminary studies, the WCV team found abnormalities of mitochondrial morphology and reduced levels of a molecular marker called *mitochondrial Tfam transcription factor* in affected miniature schnauzers. Mitochondrial transcription factors are energy-producing proteins that control when genes are switched on or off.

The next step is to identify the genetic mutation that causes retinal dysplasia in this breed of dogs. Specifically, the researchers will examine the role of Tfam and two associated mitochondrial transcription factors in the disease's development by using DNA sequencing of these potential candidate genes.

Finally, the team plans to apply its discovery of another molecular marker (decreased Tfam) and a morphologic marker called altered mitochondrial morphology to specific dogs of other breeds that develop retinal dysplasia. Through this stage in the study, scientists can determine whether the molecular and morphologic abnormalities identified in miniature schnauzers are unique to the breed, or if other breeds suffering from retinal dysplasia have similar changes.

What causes patellar tendon stress after TPLO surgery?

Drs. Cindy Shmon, Matt Johnson, and Kathleen Linn of WCV; Dr. Michael Kowaleski of Ohio State University; and Glen Watson of the College of Engineering, U of S

Tibial plateau levelling osteotomy (TPLO) is a relatively new surgical procedure for treating cranial cruciate ligament rupture, one of the most common orthopedic problems in dogs. The TPLO procedure is reported to improve long-term function and dramatically slows the progression of degenerative joint disease in large breed dogs. However, nearly 80 per cent of dogs that undergo TPLO surgery develop patellar tendinopathy or abnormal thickening of the patellar tendon (the tendon connecting the knee to the tibia). This often causes prolonged pain and lameness.

In this study, scientists will use a biomechanical testing model on the hind limbs of canine cadavers to measure the change in stress on the patellar tendon in association with two different positions of the osteotomy (the surgical levelling of the tibial plateau). Based on their results, they can determine what aspects of the TPLO procedure ultimately cause patellar tendon stress.

Are canine Achilles tendon injuries linked to a lack of blood supply?

Drs. Cindy Shmon, Peter Gilbert and Kathleen Linn

In this project, a team of WCV researchers will evaluate whether a lack of blood supply to parts of the canine Achilles tendon plays a role in chronic tendon injuries — a common, progressive problem that can result in complete rupture of the tendon.

Human medical research has shown that certain regions of the Achilles tendon are *avascular* (without a blood supply) which explains why tendon rupture is more prone in these areas. Based on these findings, WCV scientists will evaluate the blood supply in the hind limbs of canine cadavers and determine if — like humans — there are areas of poor blood supply within the canine Achilles tendon.

By gaining a more detailed understanding of the tendon's blood supply and its area of attachment on the *calcaneus* (heel bone), surgical specialists can manage early injuries more effectively and modify repair techniques to preserve and enhance the blood supply to the repaired tendon.

How prevalent is hemotropic *Mycoplasma* infection in local cats?

Drs. Elisabeth Snead, Belle Marie Nibblett, Sue Taylor, Klaas Post, Marion Jackson and Cheryl Waldner

In this two-part study, WCV researchers are investigating the prevalence of two species of hemotropic *Mycoplasma* in two local feline populations, then evaluating the treatment of subclinical infection with a new antibiotic therapy. Formerly classified as *Haemobartonella*, hemotropic *Mycoplasma* are extracellular parasites of red blood cells that cause anemia in cats. In fact, up to 15 per cent of healthy cats may be subclinically infected with two bacteria species: *Mycoplasma haemofelis* and *Mycoplasma haemominutum*.

First, researchers will conduct an epidemiologic study to determine the prevalence of hemotropic *Mycoplasma* infections in two distinct populations: cats from the Saskatoon SPCA, and healthy housecats undergoing spay and neuter procedures at the WCV Veterinary Teaching Hospital. The research team will use PCR (polymerase chain reaction) and other tests to quantify the amount of bacteria present, to identify the strain of bacteria and to search for anemia indicators. In the study's second stage, scientists will evaluate the efficacy of two antibiotics — azithromycin and doxycycline — for the treatment of subclinical hemotropic *Mycoplasma* infections. **V**





Blood Lactate Level Watch

“Will my dog live?” When veterinarians need to respond to an anxious owner’s questions about whether a critically ill dog will live or die, treatment decisions could depend on the accuracy of their answer. With so much at stake, clinicians need accurate prognostic tools that can help them weigh the odds of survival and give pet owners a realistic idea of what can be done.

Based on the results of a Western College of Veterinary Medicine (WCV) study, serial measurement of blood lactate levels is one useful tool for calculating a dog’s chances of survival, confirms Dr. Connie Stevenson, a graduate student in WCV’s Department of Veterinary Pathology and the study’s main investigator.

As Stevenson explains, lactate is a byproduct of *anaerobic glycolysis* (glucose breakdown), and rising blood lactate measurements can often be the first sign of an animal’s worsening state even when there are no other indicators. In healthy dogs, normal blood lactate ranges from 0.3 to 2.5 millimoles (mmol) per litre. But if a dog’s blood lactate concentration increases, it may indicate that the perfusion of blood in a dog’s tissues isn’t optimal and that parts of its body aren’t getting enough oxygen.

In the WCV investigation, Stevenson says dogs whose blood lactate levels didn’t return to reference limits within six hours of treatment were 16 times more likely to die than dogs whose lactate levels did return to reference limits within that time span.

“These findings are significant and confirm what our research team had projected going into this project. Our results were also similar to those in human medical research which is encouraging,” says Stevenson, whose co-investigators at the College were Drs. Beverly Kidney, Tanya Duke, Elisabeth Snead, Raul Mainar-Jaime and Marion Jackson.

The scientists received financial support from WCV’s Companion Animal Health Fund as well as from the Ludwig, Olga and Constance Kaye Canine Research Trust Fund to complete their blood lactate-related investigations.

The study involved 80 sick dogs — ranging in age from two months to 16 years — that were admitted to WCV’s Veterinary Teaching Hospital and required intravenous (IV) fluid therapy. Clinicians took blood samples before IV fluid therapy was initiated, then repeated the sampling process six hours later. Less than 15 minutes after each sample was taken, blood lactate levels were measured on WCV’s blood gas analyzer.

The American Society of Anesthesiologists’ physical status scoring system was applied to categorize each patient’s level of illness. The scoring was done blindly, without knowledge of the blood lactate level. Besides severity of illness, the team collected information about each patient’s age, size and gender. But even when these other factors were taken into account, Stevenson says dogs with blood lactate concentrations of more than 2.3 mmol per litre at six hours were more likely not to survive.

As well, the study’s findings also strengthened the argument for taking serial blood lactate measurements. While lactate concentrations at “zero hour” (before IV fluid therapy) were similar in survivors and non-survivors, the levels were significantly different in those two groups when the research team measured blood lactate at six hours.

Excitement, agitation or exercise can cause a temporary increase in a dog’s lactate concentration. But because these non-disease-related increases would be less likely to persist, serial blood lactate measurement would give clinicians a much truer picture of a patient’s response to therapy and the severity of illness in a systemically ill dog, says Stevenson.

You can read more about this CAHF-supported project in the Summer 2005 issue of *Vet Topics*. Visit www.cabf.usask.ca to view archived issues.

When Lactate Goes Up, Analyzer’s Accuracy Goes Down

By Jessica Eissfeldt

Hand-held blood lactate analyzers are convenient, affordable and portable — but they may have their limits when it comes to accuracy, reports WCV researchers.

In a year-long study, the research team set out to determine the accuracy of the Accutrend® (formerly known as AccuSport®) hand-held blood lactate analyzer — a device that was initially developed to measure blood lactate levels in human athletes training for elite sports.

The machine caught the interest of veterinarians — especially those who work with emergency and critical care patients — because it’s portable and relatively inexpensive (about \$200) in comparison to large blood gas analyzers, the veterinary profession’s “gold standard” for measuring blood lactate levels.

To test accuracy, scientists compared blood lactate concentration readings from the hand-held analyzer and from the College’s blood gas

analyzer. Altogether, the team compared 274 samples from 100 healthy dogs and 107 systemically ill dogs at WCV’s Veterinary Teaching Hospital. Researchers also used the samples from the 100 healthy dogs to establish a reference interval for the Accutrend® machine.

The research team found that the Accutrend® machine’s accuracy was moderate in comparison to the blood gas analyzer, and that the hand-held device had a significantly higher reference interval.

The blood lactate levels that registered best with the Accutrend® were those that were 4.0 millimoles (mmol) per litre or less (blood lactate levels range from 0.3 to 2.5 mmol per litre in normal, healthy dogs). “The device didn’t perform well at levels above 4.0 mmol per litre: its readings were higher than the readings from the blood gas machine,” explains graduate student Dr. Connie Stevenson who conducted the CAHF-supported study with Drs. Beverly Kidney, Tanya Duke, Elisabeth Snead and Marion Jackson. *continued . . .*



There's Veterinary Medicine in Her Blood

By Jessica Eissfeldt

With three generations of veterinarians in her family tree, Dr. Connie Stevenson's career selection was a natural. "My great-grandfather and my grandfather and my uncles were veterinarians. It's something that I grew up with, and it's always been in the family."

Her Bachelor of Science degree in biochemistry from Simon Fraser University was also a major motivator and piqued her interest in clinical pathology during her undergraduate veterinary degree at the Western College of Veterinary Medicine.

After graduating from WCV in 1996, Stevenson spent eight years in a small animal practice in B.C. before deciding to return to WCV in 2004 to pursue a Master of Veterinary Science degree in clinical pathology.

"My favourite part is clinical chemistry: I love to see the way diseases affect measured metabolites in the body. I also enjoy the diagnostic part of things: interpreting hematology and chemistry results and cytology and surgical histopathology samples," describes Stevenson.

Thanks to those interests, she soon found herself involved in the investigations of canine blood lactate levels and the usefulness of a hand-held device for measuring the levels.

"When I was in private practice, I wasn't aware of blood lactate levels because I didn't have an Accutrend® unit or other means to measure blood

lactate concentrations, so that's what I liked about the research: it gave me the chance to see if I could provide veterinarians with useful information about these hand-held units."

Besides testing the accuracy of the hand-held analyzer, Stevenson wanted to evaluate blood lactate levels in ill dogs to determine if this measurement was useful in predicting patients' outcomes in critical situations. She developed the research plan, wrote the research grant proposal for the Companion Animal Health Fund, conducted the research and wrote two scientific papers based on the study's results.

Out of the entire process, what was Stevenson's favourite part? Analyzing the data: "It was very interesting working with statisticians to see information come to light."

Her keenness earned Stevenson the distinction of being one of this year's two CAHF Fellows — a title that Dr. Marion Jackson believes her graduate student earned through hard work. "Dr. Stevenson is a fine representative for the Fund, having dedicated her professional life to helping companion animals — initially through clinical practice and now by becoming skilled, clinical pathologist and by completing a very practical, applied research project."

Now in the third and final year of her graduate program, Stevenson will gain additional experience in diagnostic clinical pathology and surgical pathology in the teaching hospital. She'll also be preparing for the American College of Veterinary Pathologists' board examinations — a significant achievement and an important credential for a diagnostic clinical pathologist.

According to Jackson, Stevenson is well suited to a career as a clinical pathologist: "She's mature, dedicated, organized, conscientious and stays calm even in the hectic environment of a busy lab. She is also academically superb."

Once Stevenson becomes a board-certified clinical pathologist, she doubts that she'll return to private practice. Her experience in the field gave her valuable insight into veterinarians' perspectives and concerns, but Stevenson thinks that she can be of more help to veterinarians and animals — large or small — by fulfilling her role in clinical pathology.

It's a new twist to an old family practice — but there's no doubt that Stevenson is upholding an honoured tradition for another generation. **V**

Jessica Eissfeldt is a Saskatchewan-based writer who holds a degree in English and news editorial journalism from Oklahoma State University.

ANALYZER continued

She adds that the team didn't have enough samples from dogs with very high blood lactate levels to fully evaluate the machine: only 11 of the dogs involved in the study had blood lactate levels higher than 4.0 mmol per litre.

As Stevenson reports, the study's results illustrate the importance of proper assessment of instruments for diagnostic use in veterinary medicine and reveal the danger of adopting data generated from different machines.

For example, a lactate concentration of 3.0 mmol per litre on the blood gas analyzer indicates that the perfusion of blood and oxygen through a dog's tissues isn't optimal. However, this reading on the Accutrend® machine would still be within the reference interval. Those types of differences could affect patient management and prognosis, says Stevenson.

Despite the need for further investigation of the hand-held device at high blood lactate concentrations, Stevenson still believes the Accutrend® machine works well for measurements in the reference interval. "If veterinarians want an option for reading lactate concentrations, they can use it knowing that its readings of higher concentrations aren't necessarily accurate. Overall, however, the hand-held analyzers do have merit."

It's a diagnosis that no cat owner ever wants to hear. *Feline aortic thromboembolism* (FATE) is one of the most common — and deadly — complications of feline heart disease. Up to 50 per cent of cats suffering from *hypertrophic cardiomyopathy* (thickening of the heart muscle) develop FATE, and most animals diagnosed with this frustrating condition must be euthanized or die outright. For those cats that survive, the likelihood of a second attack is high and current methods of treatment have limited effectiveness, says Dr. Cheryl Vargo, a veterinary internal medicine resident in the Western College of Veterinary Medicine's Department of Small Animal Clinical Sciences.

"Some cats that recover from the initial episode do have an acceptable quality of life. But recurrence is common and the long-term prognosis is guarded to poor — especially for cats who are already in heart failure."

When veterinarians see cats affected with FATE, they most often see animals in pain with pale or bluish foot pads, with no femoral pulse and hind limb paralysis. These clinical signs occur when a clot, which usually forms in the left atrium of a cat's heart, breaks loose and travels through the animal's blood stream. The clot typically lodges in the "Y" or saddle where the *aorta* (the body's main blood vessel) divides — obstructing blood flow to the cat's hind limbs.

Since the goal is to prevent the growth of the clot and future clot formation, veterinarians usually treat FATE-affected cats with anticoagulant (anti-clotting) medication. *Unfractionated heparin* is an effective antithrombotic agent, but it requires intensive monitoring and carries a high risk of hemorrhage.

An alternative is a related compound called *low molecular weight heparin*. LMWH products like dalteparin are safer, easier to monitor, carry a lower risk of hemorrhage and are more predictable in terms of dosage than unfractionated heparin in human patients. Unfortunately, little research has been done until now to determine dosage and efficacy in cats, explains Vargo.

"Veterinarians have been using LMWH products to treat FATE, but they have used dosages extrapolated from human studies and results have been far from satisfactory. Some research has been done in this area involving dogs, but there's almost nothing with cats — even though cats are much more likely to suffer from thromboembolism than dogs," Vargo explains.

This frustrating lack of information was one factor that prompted Vargo, along with Drs. Sue Taylor and Anthony Carr of WCV's Department of Small Animal Clinical Sciences, to undertake a study that evaluated the effect of administering low molecular weight heparin on coagulation parameters in cats. The project was one of the Companion Animal Health Fund's annual research grants in 2005.

The research team administered dalteparin (a LMWH product) to eight healthy adult cats over a period of one week with each animal receiving a commonly recommended "standard" dose (100 IU per kilogram) twice a day for seven days. Because dalteparin inhibits a clotting factor called *Xa*, the scientists monitored **anti-Xa activity in the cats before and after dalteparin administration**. The team took more blood samples at four, six, eight and 12 hours after the first dose on day one, then repeated the sampling intervals after the final dose of dalteparin was given on the study's last day.

All of the blood samples were tested for anti-Xa activity and antithrombin III concentrations at Cornell University in Ithaca, N.Y. — the only North American laboratory that conducts Xa assays. Several other tests — platelet



Study Strives to Change Cats' Fate

By Roberta Pattison

counts, prothrombin time (PT) and partial thromboplastin time (PTT) — were conducted at WCV. Besides the sampling, the researchers regularly checked the cats for signs of anemia, bleeding or other illnesses.

The study's results were significant and a little surprising, acknowledges Vargo. Only four of the eight cats developed anti-Xa activity in the therapeutic range. In those four animals, anti-Xa activity peaked at four hours after dosing, then returned to baseline measurements by six hours. The dalteparin therapy affected no other coagulation parameter, and no cats experienced clinical bleeding during the study. Based on those results, Vargo explains that the effect of dalteparin wasn't uniform among the study's cats, and that doses of 100 IU per kilogram didn't achieve or sustain an anticoagulant effect in any of the animals — an indication that veterinary clinicians may need to rethink their dosing recommendations. Future research might look at an increase in the dose, an increase in the frequency of administration (perhaps to three times per day) — or both.

In June, Vargo presented the study's findings at the 2006 American College of Veterinary Internal Medicine (ACVIM) Scientific Forum in Louisville, Ky. Her research abstract garnered interest from a number of the forum participants — including former WCV resident Dr. Marilyn Dunn. Now an associate

Tenacious Resident Earns CAHF Honour

By Roberta Pattison

professor at the University of Montréal's faculté de médecine vétérinaire, Dunn has conducted similar research in dogs and offered some insight into this therapeutic challenge: "Dr. Dunn suggested that not only Xa but other clotting factors should be assessed. She also suspects the peak comes earlier than four hours," says Vargo, who is now preparing the WCVM study's findings for publication.

Meanwhile, clinicians continue to deal with the challenges of treating FATE in their feline patients — a frequent, devastating problem that still needs a great deal of research to determine the best therapy. One hindrance is money: "Although ours was a relatively small study, it was still expensive," points out Vargo. "Even with the small number of cats and the relatively short study period, many blood samples had to be collected, processed, frozen and shipped by courier to Cornell University. None of that comes cheaply."

But it's only through these types of investigations that scientists will ultimately track down an effective way to treat FATE — and provide veterinarians with the tools they need to save the lives of people's beloved pets. For cat owners and companion animal veterinarians everywhere, that makes it money well spent. **V**

Roberta Pattison is a freelance writer who is a regular contributor to the national publication Dogs in Canada. Recently retired from grain farming, she still lives on her farm near Delisle, Saskatchewan.



When small animal resident Dr. Cheryl Vargo talks about why she undertook a study to test an alternative method of treating cats with aortic thromboembolism (or FATE), her voice resonates with enthusiasm for her work as well as empathy for her patients and their owners.

"This problem has such a high incidence and poor prognosis. It's so frustrating. Cats die before you can do anything to help them," says Vargo, who is in her third and final year of her small animal residency and her Master of Veterinary Science degree programs at the Western College of Veterinary Medicine (WCVM).

Vargo's enthusiastic energy and commitment to her job are two of the reasons why her residency supervisor, Dr. Sue Taylor, nominated the graduate student for the Companion Animal Health Fund's annual research fellowship. This spring, Vargo became one of the two CAHF fellows for 2006-07 — an honour that pays for half of her annual salary.

"Dr. Vargo works very hard, both in the clinic and in her research. She has great enthusiasm and is deeply interested in her cases. She designed the FATE project from the ground up and did all the work despite her huge clinic work load," says Taylor, one of Vargo's co-investigators on the FATE project.

It wasn't an easy study to organize. For example, the team had originally planned to use in-dwelling catheters to collect the frequent blood samples from the study's cats. But the catheters plugged up after a day or two of use, and Vargo had to start over and use the more stressful and labour-intensive option of drawing individual blood samples. "Cats aren't easy to work with, especially these ones — we're not talking about pets here. But she persevered," says Taylor.

The WCVM professor adds that one of the big reasons why this particular project appealed to Vargo was because of its practicality: "It wasn't just research for its own sake. Cats seen by veterinarians every day in general practice will very likely benefit from the knowledge gained from this study's results."

Tracking down Dr. Cheryl Vargo to learn more about her background isn't a simple task: she's a very busy person. Originally from Ontario, Vargo attended the University of Winnipeg as well as the University of Manitoba before coming to WCVM. After receiving her Doctor of Veterinary Medicine degree in 1999, Vargo spent four years at a small animal practice in Thunder Bay, Ont., before heading south to Greensboro, N.C., for a small animal internship. In 2004, it was back to Saskatoon and WCVM for a veterinary internal medicine residency program. "I can't say enough about the wonderful program here, about the people and the mentoring that I've received. It's been a great experience," Vargo affirms. "And it's certainly an honour to have been chosen for the fellowship."

Vargo wrote and passed her first board examination for the American College of Veterinary Internal Medicine on May 30 and will write the final one for board certification status next year. She has greatly enjoyed her research work, but her immediate plans after completing her residency include working in a specialty referral practice where she can pursue her particular interest of endocrine and gastrointestinal diseases in cats and dogs.

"Will I rule out a return to academic research? No. I can certainly see myself coming back to it one day," says Vargo. Whatever the future holds for her, rest assured that this young veterinarian will be doing her best to make life easier for people's pets in whatever way she can.

Our Contributors

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The Fund's Year in Review

The Companion Animal Health Fund's statement of revenue, expenditures and fund balances for the year ended, December 31, 2005

EXPENDABLE	2005	2004
Revenue		
Donations		
Private	\$92,105.49	\$82,810.48
Organizations	7,739.50	9,359.10
Memorial and special (estate)	0.00	6,583.50
Note card sales	1,056.05	1,121.42
Silent auction	0.00	106.00
	100,901.04	99,980.50

Expenditures		
Fellowship program	33,928.93	33,731.02
Grants in aid of research	59,141.46	98,169.24
Cost recovery from previous grants	(5,283.35)	(36,681.79)
Extension and fund raising	14,031.19	20,915.76
Vet Topics	7,736.94	9,370.62
	109,555.17	125,504.85

Surplus (deficiency) of revenues over expenditures	(8,654.13)	(25,524.35)
Balance, beginning of year	40,981.37	66,505.72
Balance, end of year	\$32,327.24	\$40,981.37

RESTRICTED	2005	2004
Balance, beginning of year	\$374,100.49	\$352,212.03
Interest income	12,453.82	21,888.46
Transfer from (to) unrestricted	0.00	0.00
Balance, end of year	\$386,554.31	\$374,100.49

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Bits & Bites



HOSPITAL ON THE RISE: Crews are making steady progress on the two-storey addition to WCVM's Veterinary Teaching Hospital. Scheduled for completion this winter, the addition includes a new reception area and more space for treatment, teaching, administration and client support. Donate to the VTH Expansion Campaign by using the enclosed tear out card, visiting www.wcvm.com/supportus, or contacting Joanne Wurmlinger (306-966-7450 or joanne.wurmlinger@usask.ca).

MAGRANE LECTURER: In June, veterinary ophthalmologist Dr. Bruce Grahn spent a week at the University of Wisconsin-Madison as an invited faculty member at the William Magrane Basic Science Course in Veterinary and Comparative Ophthalmology.

Organized by the American College of Veterinary Ophthalmologists (ACVO), the four-week, in-depth "Eye Camp" is held every second year. The course, which covers the basic and clinical sciences of veterinary ophthalmology, is a requirement for all North American veterinary ophthalmology residents and is also open to international students.

Grahn was one of six professors who taught ocular pathology during the camp's final four days when students complete a short course on the histologic basis of ocular disease. The topics of Grahn's lectures were the pathology of glaucoma in animals and the pathology of uveitis in animals.

HOME AWAY FROM HOME: Every month, dogs and cats diagnosed with cancer leave their homes across Western Canada and come to WCVM for radiation therapy. They need daily treatments for an average of four weeks, so most

owners from other cities or provinces must leave their pets behind at the College's Veterinary Teaching Hospital.

It's a stressful time for everyone — but there's one way that Saskatoon and local area residents can help. The College's pet radiation therapy program needs foster families who can give its four-legged patients a temporary home during their stay in Saskatoon, a daily ride to and from the radiation therapy centre, and plenty of TLC.

Cancer patients receive excellent care in the veterinary teaching hospital, but veterinary radiation oncologist Dr. Monique Mayer acknowledges that a month-long stay in the clinic's kennels can be physically and emotionally draining for the pets.

"It's not a home environment where they can relax and feel normal," says Mayer. "Our foster families make a really big difference for the pets as well as their families — just the satisfaction of knowing that their pets are well taken care of is a big load off of their minds."

For more information, call 306-966-1894 or 306-966-1257, or send an email message to tara.shymko@usask.ca.

What do you know about wills and charitable giving?

Answers to the quiz on page 3

1. **FALSE.** Each partner in the marriage should have his or her own will.
2. **TRUE.** You may purchase a charitable gift annuity through your favourite charity, receive a receipt for income tax purposes for a portion of the annuity amount, and receive guaranteed income payments for life.
3. **FALSE.** Marriage, new children, grown children, and legislation are but a few examples of changes that could prompt a new will. Even if you don't experience major life changes, professionals advise people to review their wills every few years.
4. **TRUE.** You may establish a trust and make an irrevocable transfer of your property to your favourite charity. You will receive an official receipt for income tax purposes and be granted the use of the property until your passing — or until another predetermined time.
5. **TRUE.** You can make a provision for your favourite charity without reducing the amount that you would have been able to give to your family. You can use leveraged annuities and insurance products to bring your after tax estate balance back to the level it would have been at without having made the charitable gift.
6. **TRUE.** You may specify the charity as beneficiary on your insurance policy, RRIF or RRSP. Simply contact your broker or financial institution to file the request. Your estate will still receive an official receipt for income tax purposes. Or, you may transfer ownership of your new or paid-up insurance policy and receive a receipt now for the cash surrender value and ongoing premiums.
7. **FALSE.** Gifts of securities, real estate, valuable collections and insurance are some other examples of gifts that you may make. Giving gifts of securities provides additional tax incentives over giving cash.
8. **FALSE.** You may carry forward the gift to any return in the next five years.

For confidential, no-obligation information on charitable giving and the Companion Animal Health Fund, contact:

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Note: Donors should consult their professional advisor on matters relating to estate and financial planning.