



A Team Approach to Tackling Osteosarcoma

Dear Friends:

Our mission at the Center for Companion Animal Health is to improve the health and well-being of all animals by supporting research and building programs that achieve these goals. I have served as director of the CCAH for more than two years, and continue to be impressed and inspired by the quality and impact of the research being done to improve animal health, and end disease and suffering. I am equally humbled and grateful for all the support we have received and continue to receive from our supporters. Without you, we could not accomplish any of this.

We recently redesigned our website to better share with you our current activities and on-going studies. The site now includes more information on our groundbreaking research, and we invite you to take a look (<http://www.vetmed.ucdavis.edu/ccah/>). We will continue to update the site and would love to hear what you think—and what other content you'd like to see.

In this issue, we share the latest research by our nutrition group, which found that many vegetarian diets for cats and dogs are contaminated by meat. We also share the latest breakthroughs from Dr. Niels Pedersen, who remains hard at work after “retirement” to make advancements in the diagnosis and treatment of autoimmune diseases in poodles. Our shelter medicine program continues to save lives and celebrated a huge milestone in the fight to save 1 million cats. Additionally, we tell

the story of how our cancer group takes a team approach to tackling osteosarcoma—a deadly bone cancer in dogs that also affects cats, people and other animal species. It is only by taking a long-range, multifaceted approach that we can hope to cure tough cancers such as this one.

As always, your interest in our work and your support of our continued research are what make breakthroughs possible. Thank you for being part of our team.

My best,

Michael Kent, MAS, DVM
 Director, Center for Companion Animal Health

Also in this issue:

- Study Finds Meat in Vegetarian Pet Food 2
- Saving a Million Cats, One at a Time 3
- DNA Test Helps Standard Poodles..... 4
- Companion Animal Memorial Fund Honor Roll..... 5
- A Team Approach to Tackling Osteosarcoma 6

CCAH-Funded Study Finds Meat in Vegetarian Pet Food

Truth in pet food labeling is a growing concern these days. In our last newsletter, we reported on a study by researchers in the UC Davis veterinary hospital's Nutrition Support Service that found significant errors and omissions in the information shared on the labels of many brands of vegetarian pet food. Only a third of the no-meat diets the research team examined were compliant with pet food labeling laws.

Now that same team has discovered another problem with this subset of diets, finding traces of the one ingredient you would never expect in a vegetarian food product—meat. Donations to the CCAH helped fund this study—the first to examine vegetarian pet food diets for the presence of mammalian DNA.

The research team, comprising veterinary resident Dr. Kayo Kanakubo and nutrition faculty members Drs. Andrea Fascetti and Jennifer Larsen, studied 14 pet foods for cats or dogs—canned and dry, marketed as vegan or vegetarian. Through the school's Veterinary Genetics Laboratory, which has sensitive tests that can pick up even trace amounts of mammalian DNA, the team tested these diets for the presence of 11 different animal species, including cow, deer, goat, horse and rabbit.

Half of the diets tested positive for the presence of cow, pig or sheep, Dr. Larsen says. For six of the seven meat-positive diets, the result was repeatable when the lab tested samples from a different lot number of the same food. All six of the dry diets tested positive for meat, versus just one of the canned diets. The results of the study were recently published in the *Journal of Animal Physiology and Animal Nutrition*.

“The presence of mammalian DNA in the products tested in the current study may violate not only federal regulations, but also owners' trust in choosing vegetarian or vegan pet diets,” the study states.

Veterinarians sometimes use non-meat diets to manage certain medical conditions such as liver disease, while owners might have a philosophical or ethical drive to use plant-sourced diets. However, Dr. Larsen cautions against over-interpreting the study's results.

“The test that we used is really, really sensitive,” she explains. “Just because we found the DNA does not mean that the diets



Donations to the CCAH helped fund the first study to examine vegetarian pet food diets for the presence of mammalian DNA.

“Half of the diets tested positive for the presence of cow, pig or sheep.”

– Dr. Jennifer Larsen

were intentionally adulterated. It could just simply be cross-contamination with trace amounts of meat-based ingredients that happened during storage or processing. We're not able to determine how much was in there and whether it was included on purpose. In addition, we don't know if the amounts present are clinically relevant to individual veterinary patients.”

For pet owners who want to feed vegetarian diets to their animals, Dr. Larsen recommends they use commercially available veterinary therapeutic diets.

“When companies make veterinary therapeutic diets, the level of quality control is a little bit higher,” she says. “We are confident regarding the manufacturing, safety, and efficacy of those products.”

Saving a Million Cats, One at a Time

Dr. Kate Hurley has cats on the brain. Lots and lots of cats. Perhaps her passion dates from grade school when she would dress in ears and a tail, despite the fact that it was neither Halloween nor dress-up day. Or perhaps it's because she went on to become the world's first shelter medicine resident at UC Davis. Or maybe her drive comes from Chumley, an overweight orange tabby with a neurological disorder that rules Hurley's house and heart.



Thanks to Maddie's Fund, an ear-tipped cat (a universal signal that a free roaming feline has been spayed or neutered) proudly sits in Times Square inviting shelters across North America to join the Million Cat Challenge.

Whatever the reason, Hurley's determination to improve the welfare and save the lives of cats has never waned. In 2014, together with co-founder Dr. Julie Levy of the University of Florida and sponsored by Maddie's Fund, a California-based family foundation dedicated to improving the welfare of homeless animals, Hurley launched the Million Cat Challenge with the visionary goal of saving the lives of 1 million cats in five years by approaching the way we shelter cats and dogs differently.

"What was missing from the sheltering landscape was a plan that was cat specific," recalls Hurley, who leads the Koret Shelter Medicine Program—the first academic program designed to improve the operations of shelters across the globe. "We intuitively know these two species are very different, but our sheltering strategies often lump cats and dogs together. Year after year we've celebrated the climbing lifesaving rate for dogs. Meanwhile, in many communities, a cat still has less than a 50 percent chance of leaving the shelter alive. We had to do something about that."

With over 50 years' experience between the two, shelter medicine pioneers Levy and Hurley drafted five key initiatives that could be utilized by any shelter with the desire to do better by the cats in their care. The programs were designed to reduce admissions, optimize shelter operations, reduce barriers to adoption and, when appropriate, sterilize, vaccinate and return cats to their place of origin rather than euthanize.

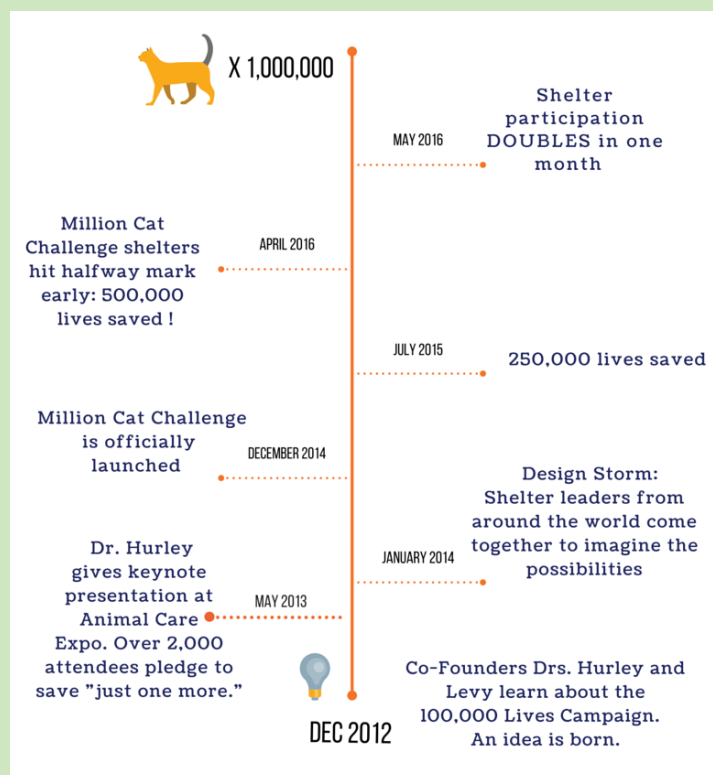
Today, the Challenge and its initiatives are empowering shelters large and small, those that are well-funded as well as those operating on a hope and a prayer, to make change in their communities by providing proven, practical options rather than euthanasia. What began as a shelter campaign has grown into a full-blown cat crusade. Supported by leading animal welfare organizations such as Maddie's Fund, Best Friends Animal

Society, ASPCA and the Humane Society of the United States, the Challenge now has over 900 North American shelters participating and has grown into the world's largest feline-lifesaving initiative. On April 4, 2016, participating shelters passed the halfway mark, saving 500,000 cats earlier than expected.

The best part, reports the cat-saving duo, is the peer-to-peer support that has transpired as the Challenge has grown. Shelters are

working together, sharing resources and strategies.

"There is the Challenge campaign, which we designed," Dr. Julie Levy says. "And then there is the shelter community that makes up the Challenge. In our wildest dreams, we couldn't have guessed the impact that starting the conversation and creating a platform for shelters to connect would have. The Challenge is so much bigger than the two of us. It belongs to the shelters that participate. The power of shelters supporting each other to embrace the five initiatives leaves us both completely awestruck."



Groundbreaking DNA Test Helps Restore Breed-Wide Health in Standard Poodles

Standard poodles are known for their soft wavy coats, friendliness, and sparkling intelligence. But in recent years, the breed has also become known for its propensity to develop a host of devastating autoimmune diseases—especially sebaceous adenitis, a difficult-to-treat disorder that causes major hair loss; and Addison’s disease, a potentially life-threatening condition that destroys the adrenal gland.

Rise in Autoimmune Diseases

Decades ago, Dr. Niels Pedersen, a distinguished professor at the UC Davis School of Veterinary Medicine and a renowned expert on infectious and immunologic diseases in dogs and cats, began noticing a rise in autoimmune diseases, especially among purebred dogs and in certain breeds more than others. The suspected culprit: a narrowing of genetic diversity caused by inbreeding.

“The more inbred the breed, the more autoimmune disease it seemed to suffer,” Dr. Pedersen explains.

But the genetic basis of these autoimmune diseases had never been established. What was needed was a genome-wide test that could confirm that these diseases were both heritable and largely concentrated among inbred dogs.

Dr. Pedersen wasn’t the only one clamoring for such a test. Poodle breeder and expert Natalie Green Tessier of Buffalo, NY, had observed the same rise in autoimmune disease in the breed. In 2005, she started an email list comprising nearly 90 poodle breeders, all of them sharing health data privately on their dogs.

“We were starting to see dogs crash at 10 months old with Addison’s,” Tessier says. “You’d have three or more different autoimmune diseases in one litter. Everyone was starting to know that there was a problem.”



Dr. Niels Pedersen and his research associate Hongwei Liu with some of the subjects of the Standard Poodle Project that has helped develop a DNA test for various autoimmune diseases in the breed.

Standard Poodle Project

Eventually Tessier’s email list grew into the Standard Poodle Project—a group dedicated to the genetic health and well being of the breed—and a public poodle health registry was launched. Lynn Brucker, another prominent poodle lover and keeper of breed history and pedigrees, was also a strong supporter of the effort.

While it was common knowledge among conscientious breeders that standard poodles were dangerously inbred, there was no way of knowing which individual dogs lacked diversity in their DNA and were therefore most likely to develop autoimmune disease and other health issues.

“We needed help,” Tessier explains. “We were looking for a genome-wide test that could confirm for us if a dog was diverse or not.”

Through a series of lucky emails and phone calls, Dr. Pedersen and Tessier joined forces in 2014 to make that test happen. The first step was to collect DNA samples from a large pool of poodles in order to build baseline data for the breed. Dr. Pedersen sent Tessier enough DNA swabs for 30 dogs, hoping that most would be returned. Instead, Tessier and her network deluged the UC Davis Veterinary Genetics Laboratory with DNA samples—760 in total, from dogs representing a diversity of lineages, including the more rare pedigrees.

“He didn’t realize how active we are,” laughs Tessier.

A broad community of poodle breeders and experts helped fund the testing as well, thanks to Tessier’s active outreach to different poodle clubs and the creation of an online fundraiser. Their donations to the CCAH helped support the research costs, ultimately, inspiring the *Poodle Club of America Foundation* to come in as a major funder of the project.

– continued on page 6

Thank You



Companion Animal Memorial Fund Honor Roll

(January, 2015 – March, 2016)

We gratefully acknowledge veterinary clinics and practitioners who made heartfelt tributes to beloved pets through a gift to the Companion Animal Memorial Fund. This fund helps to support clinical research to better identify, diagnose, treat and prevent animal diseases and conditions—including cancer, genetics, nutrition, infectious diseases, endocrinology, immunology, anesthesiology and internal medicine. The following supporters contributed \$500 or more to the memorial fund, from January 2015 to March 2016.

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A Team Approach to Tackling Osteosarcoma

Some cancers are so complex and mysterious that it takes tremendous time and research to even begin to unravel them. To gain insight into these diseases, UC Davis veterinary researchers don't conduct just one study at a time. Instead, they collectively "attack" these diseases on all fronts, launching a flurry of studies designed to uncover more about how they work and how they might be stopped.

"We take a multifaceted approach," explains veterinary oncologist and CCAH director Dr. Michael Kent. "We look into the causes of these diseases, try to figure out the cellular mechanisms, and run clinical trials that help test our hypotheses and come up with new treatments."

This approach enables researchers to uncover valuable knowledge far faster than they could otherwise. Our veterinarians use multiple tactics to study osteosarcoma (OSA) for example—a



debilitating yet common bone cancer affecting mainly large-breed dogs. Osteosarcoma is diagnosed in more than 8,000-10,000 dogs in the United States each year, yet it continues to be among the most difficult canine cancers to manage. OSA tends to spread rapidly and the prognosis can be poor, even with aggressive treatment. The school's veterinary hospital sees about 100 new cases each year.

"Simply put, it's a devastating disease," Dr. Kent says.

Creating Breakthroughs

However, the team approach to osteosarcoma research is creating breakthroughs in what is known about the disease and its possible

— continued on page 7

◀ This image created from a CT scan shows the location of an osteosarcoma in a dog's leg.

DNA Test (continued from page 4)

Research Breakthrough

The diversity test results were illuminating. The DNA results, matched against the vast and detailed pedigree and health data collected for years by poodle expert Lynn Brucker, clearly showed that the more inbred an individual poodle was, the more prone it was to autoimmune disease. The findings led to several groundbreaking scientific papers that helped establish the connection between inbreeding and autoimmune disease. Critically, the results also showed that the poodle breed is still genetically diverse as a whole—but that most of that diversity is concentrated in a minority of dogs and not well distributed across the breed. This means breeders can, over time, actually correct the current genetic imbalance.

Tessier and her colleagues were thrilled.

"It's the first real breakthrough we've had in 12 years in looking for help with these diseases," she says. "Before you couldn't test for a susceptibility to these diseases or predict which dogs would develop them. Now we can see where the risks are higher and where they are not."

Available DNA Test

The DNA test is now available to all poodle breeders through the Veterinary Genetics Laboratory. Indeed, poodle breeders are already using the test results to help select mates to produce more genetically diverse offspring, which over time will result in a much healthier breed.

Dr. Pedersen and the Veterinary Genetics Laboratory hope to enroll more breeds in genetic diversity testing in the near future. They also hope that other breeders will use the results to help reestablish genetic diversity in their breeds, just as their poodle counterparts are now doing.

"Poodle breeders have taken hold of the concept of improving diversity by using both DNA and pedigrees better than any of the groups that we've worked with," Dr. Pedersen says. "We picked them as collaborators because we knew they would lead the way for other breeds."

To read an interview with Dr. Niels Pedersen about his work on the genetic basis of autoimmune disorders in dogs, including standard poodles, please visit the CCAH website. www.vetmed.ucdavis.edu/go/ccah-news

Osteosarcoma (continued from page 6)

causes. One recent UC Davis study, led by veterinary oncologist Dr. Robert Rebhun and funded by donations to the CCAH, explored the theory that high levels of fluoride in everyday tap water may be associated with osteosarcoma development. Joining forces with the university's Department of Civil and Environmental Engineering and the veterinary school's Department of Population Health and Reproduction, Dr. Rebhun and his team mapped OSA cases against regional water node maps and ultimately found no link between fluoridated water and the disease.

“Our findings indicate that water fluoridation likely has little to do with naturally occurring osteosarcoma in our pet population, and that the optimally fluoridated water that humans consume everyday from our tap also appears to be safe for dogs,” explains Dr. Rebhun, who has led or participated in nearly 20 research studies related to OSA in dogs. “Disproving the fluoride theory gives pet owners one less thing to worry about. It also allows us to focus on other areas of research regarding possible causes and treatments.”

Other CCAH-funded studies are advancing what is known about how osteosarcoma works at the cellular level, while still others are creating new understanding of which treatments work best against the disease. For example, while OSA has been prevalent for decades, there is still no consensus in the veterinary community about which chemotherapy protocols are most effective at slowing its progress.

Shedding New Light

But a recent study by veterinary oncologist Dr. Katherine Skorupski—the first-ever clinical trial to directly compare two chemotherapy protocols for canine OSA—has shed critical new light on this issue. Dr. Skorupski and her team compared treatment with the chemotherapy drug carboplatin with treatment involving alternate doses of carboplatin and another chemotherapy drug called doxorubicin. Importantly, they found that dogs receiving carboplatin alone remained disease-free far longer than dogs that received the two drugs.

“Already, these findings have influenced the choice of chemotherapy regimen recommended by veterinarians for dogs with this devastating cancer,” Dr. Skorupski says.

Meanwhile, several more potentially groundbreaking OSA studies are underway, including one looking at an antibiotic that might inhibit the disease, and another exploring ways to help control pain and the disease's spread by injecting OSA tumors with a dog's own natural killer cells. Very little of this research would be possible without biobanking—that is, collecting and storing tissue samples from animals with OSA and other diseases that researchers need to study.

“Biobanking is absolutely critical to our efforts to stay on the forefront of veterinary cancer research,” explains Dr. Rebhun, adding that owner permission is always sought before collecting these samples. “If we want to test the importance of a protein in 100 osteosarcoma patient samples, we can now perform this study in about a month. Without biobanking, it would take a year or more before we would be able to reach the same conclusions.”

The knowledge gained by UC Davis researchers about osteosarcoma is leading to much-needed advances in the understanding and treatment of the disease.

“Over the last few decades we've pushed average survival time from three months to a year, and now we're trying to make that next big jump.”

— Dr. Michael Kent

“Over the last few decades we've pushed average survival time from three months to a year, and now we're trying to make that next big jump,” Dr. Kent says.

Helping Dogs and People

Importantly, these advances are having an impact on human medicine as well. Osteosarcoma is one of many cancers found in both dogs and humans, making it possible for dogs to be a model for studying the human form of the disease. For example, one recent study showed that the protein BM11, known to be involved in the growth of OSA tumors in humans, may also play a role in canine OSA. Figuring out how to inhibit that protein may improve chemotherapy responses in dogs and people alike.

While knowledge about OSA and how to fight it grows every day thanks to these efforts and our donor partners, any cancer researcher will tell you that there remains a long way to go.

“Osteosarcoma is still a big black box, but we've got to figure it out,” Dr. Kent says. “And the way to do that is to continue working at it constantly and from every angle.”

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Center for Companion Animal Health
c/o Office of the Dean—Development
School of Veterinary Medicine
University of California
One Shields Avenue
Davis, CA 95616-8734

Bailey's Lasting Legacy

Bailey was a 2-year-old apricot-colored ball of fluff when he first came to the UC Davis veterinary hospital in June 2002. While vacationing in Arizona, he contracted Valley Fever, a life-threatening fungal infection. Bailey was separated from his human and animal family throughout an intensive course of intravenous therapy. Halfway through his three-week hospitalization, he was finally stable enough for a visit with his owner and his favorite canine companion, Pippin. The outpouring of joy that I witnessed during their reunion is something I will never forget.



Bailey left a lasting legacy at the UC Davis veterinary hospital when his owners became loyal supporters of research in respiratory medicine.

necessary for respiratory endoscopy broke, Bailey's owner replaced it with state-of-the-art equipment that remains in constant use.

Bailey returned to our hospital in February 2013, suffering from early cataract formation. In October of that year, he was diagnosed with diabetes and started receiving insulin injections. With continued care—and a lot of love—Bailey enjoyed a few more years of good health. But in December 2015, it was time to give up the fight. He spent his last days watching for turtles on the beach in Hawaii (photo). Bailey leaves behind

a forever memory in his owner's heart and a lasting legacy of support for the veterinary hospital.

— Lynelle Johnson
Bailey's doctor at the UC Davis
School of Veterinary Medicine

In gratitude for the care that Bailey received, his owner became a loyal supporter of research in respiratory medicine at the veterinary hospital. Dozens of research projects were made possible through his financial support and encouragement. When a key piece of equipment

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The CCAH is dedicated to advancing studies in veterinary medicine—encompassing new ways to prevent, diagnose and treat diseases including cancers, genetic and immune disorders, infectious diseases, kidney and heart diseases, and nutritional disorders in companion animals. We welcome visitors to come and learn more about our mission and programs. To schedule a visit, please call (530) 752-7295.

Center for Companion Animal Health

Business Office: (530) 752-7295 Fax: (530) 752-7701

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