

Two Boxer dogs, one slightly behind the other, are sitting in a field of dry, brown leaves. They have a brown and white coat and are looking off to the side. The background is a soft-focus green field.

 PURINA
PRO PLAN

Boxer Update

A NESTLÉ PURINA PUBLICATION DEDICATED TO BOXER ENTHUSIASTS

VOLUME 16 | SPRING 2018

UNDERSTANDING **KIDNEY DISEASE**

Study Is 1st to Evaluate
U.S. Boxers

NEW STUDY TO EXAMINE CHRONIC KIDNEY DISEASE IN AMERICAN BOXER DOGS

“This study will help us determine if there is a pattern of inheritance that might lead to the detection of a gene mutation.”

Jessica Hokamp, DVM, PhD, DACVP,
assistant professor of clinical pathology,
The Ohio State University

A newly funded study has just begun at The Ohio State University to better understand the causes of chronic kidney disease in Boxers. Among the goals of the researchers leading the study is to advance genetic discovery should the disease prove to have a heritable origin traceable through Boxer families.

“We will retrospectively examine archived medical records and tissue samples and prospectively examine tissues submitted to our biopsy service to discover the main causes and prevalence of kidney disease in Boxers,” says Jessica Hokamp, DVM, PhD, DACVP, assistant professor of clinical pathology and lead investigator. “We cannot assume every Boxer has the same kidney disease.”

The [two-year study, which is funded by the AKC Canine Health Foundation](#) with support from the [American Boxer Charitable Foundation \(ABCF\)](#), is the first study to focus on kidney disease in U.S. Boxers. Dr. Hokamp, along with fellow lead investigator Rachel Cianciolo, VMD, PhD, DACVP, clinical assistant professor, will tap into the International Veterinary Renal Pathology Service (IVRPS) housed at Ohio State to characterize the disease.

“We hypothesize that purebred Boxers in the U.S. may have several causes of kidney disease,” Dr. Hokamp says. “Once we identify a predominant cause, we will prospectively analyze samples from families of purebred Boxers to see if certain

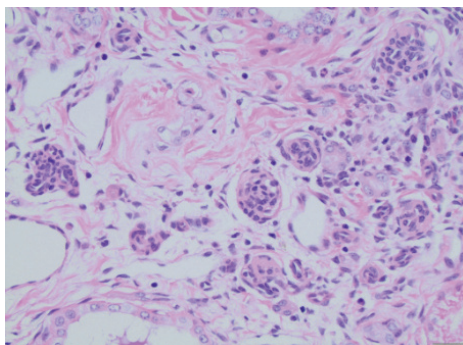
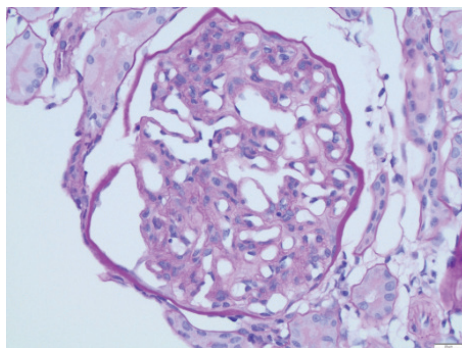
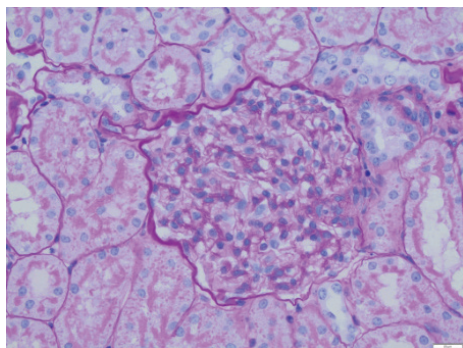
types of kidney disease follow a heritable pattern. This study will help us determine if there is a pattern of inheritance that might lead to the detection of a gene mutation.”

A collaboration between Ohio State and Texas A&M universities, IVRPS provides histologic, ultra-



structural and immunohistologic examinations of kidneys to assist veterinarians, especially nephrologists and specialists, in evaluating patients for kidney disease. Dr. Cianciolo, co-director of IVRPS, says about 45 Boxers have been evaluated thus far through the database.

“The most common cause of kidney disease in those 45 Boxers was immune-mediated glomerulonephritis, an inflammatory disease of the glomeruli, which are small bundles



Histology renal images show, clockwise from top left: normal kidney from a non-Boxer dog, Boxer with immune complex mediated glomerulonephritis, and a Boxer with renal maldevelopment, a form of juvenile nephropathy.

Images provided by Dr. Jessica Hokamp/The Ohio State University

of tiny vessels in the kidneys. The immune-mediated disease impairs the kidneys from filtering waste products and excess water from the bloodstream to make urine,” Dr. Cianciolo says. “The second most common cause was maldevelopment of the kidneys.”

Joyce Campbell, DVM, an ABCF trustee, says, “Reports of renal disease in Boxers have been pushing to the forefront for a few years now, so it is wonderful to have the AKC Canine Health Foundation fund this study. ABCF is proud to support the research, and we are optimistic that our Boxer community will benefit from new knowledge that will come from this.”

INCIDENCE & GENETICS IN EUROPEAN BOXERS

Although the prevalence rate of kidney disease in U.S. Boxers is not known, [a Swedish study published in *Veterinary Record*](#) in 2015 rated Boxers as having the third highest incidence of kidney disease and the fourth highest incidence of kidney-related mortality. The median age of diagnosis in Swedish Boxers

was 5.9 years, with females making up 45 cases and males 26 cases from nearly 2,000 dogs.

Put into perspective, the study indicated an incidence rate among all breeds of 1.6 percent per 1,000 dogs that lived to age 10. Considered the first epidemiological study to estimate the incidence of kidney disease in dogs, the report was based on an evaluation of insurance data from 1995 to 2006 in Sweden, where about 77 percent of dogs are insured.

In the U.K., Steynmere Boxer breeder and geneticist Bruce Cattanaach, PhD, DSc, FRS, says, “I am confident there are many causes of kidney failure that are not inherited, but there also is an inherited kidney disease in Boxers. Our pedigree evidence suggests that these so-called different inherited causes are most likely one and the same, as cases of renal dysplasia can be found in the same litters as the more loosely described juvenile kidney disease or chronic kidney disease.

“It runs in families with inbreeding and/or known producers of juvenile

SIGNS OF KIDNEY DISEASE

Boxers are among the breeds considered predisposed to kidney disease. If you recognize your dog having these clinical signs of kidney disease, you should follow up with your veterinarian.

- Increased drinking
- Increased urination
- Vomiting
- Weight loss
- Anorexia

“We believe we know the chromosome on which the gene for juvenile kidney disease lies.”

Bruce Cattanach, PhD, DSc, FRS,
Steynmere Boxer breeder and geneticist

kidney disease on either side of the pedigree, suggesting an autosomal recessive type of inheritance,” he says. “However, the incidence is lower than a simple recessive gene mutation, meaning other factors or a low penetrance could be involved.”

The emeritus visiting scientist at the Medical Research Council Harwell in Oxfordshire collaborates



with Professor William Amos, an evolutionary geneticist at the University of Cambridge. Together, they have collected DNA samples from 1,000 Boxers and their relatives worldwide. Using microsatellite markers, Professor Amos has found two markers on one chromosome that partly co-segregate with the disease, with preliminary analysis suggesting linkage on this chromosome.

“We believe we know the chromosome on which the gene for juvenile kidney disease lies,” Dr. Cattanach says. “Candidate genes located in this region are being tested one by one, however, it will be some time before a peer-reviewed publication will be ready to share.”

A CHALLENGING DISEASE TO RECOGNIZE

Kidneys play a vital role in canine health. Besides removing waste products and excess fluid from the body through urine, the kidneys balance the body’s fluids, release hormones that regulate blood pressure and control the production of red blood cells. When the kidneys do not function properly, toxins build up in the blood and a dog can become ill and possibly even die.

Kidney disease in dogs can be challenging to recognize. Unless owners are aware of a dog’s predisposition to kidney disease, they are likely to miss clinical signs. These may include increased drinking and urination, vomiting, weight loss, and anorexia, which can be mistaken for other health conditions.

“While we are getting better at recognizing clinical and pathological changes that occur in the early stages of kidney disease, in some cases a large amount of renal function might be lost before kidney disease is diagnosed,” Dr. Hokamp says.

A widely used measure for determining how well the kidneys are working is measurement of serum creatinine concentration. Creatinine is a waste product from the normal breakdown of muscle tissue that filters through the kidneys and is excreted in urine. When kidney disease develops and waste filtration is altered, creatinine increases in the blood.

“Additional tests to determine kidney function and damage would be helpful, particularly for early detection of renal disease when therapy is most effective,” says Dr. Hokamp. “Serum creatinine can be a relatively sensitive marker of declining renal function if changes are monitored closely within an individual patient with stable muscle mass, rather than relying on reference intervals, but it has its limitations, so

OWNERS OF BOXERS CAN TAKE PART IN KIDNEY DISEASE STUDY

Owners of Boxers diagnosed with kidney disease, as well as their close relatives, are eligible to participate in a study underway at The Ohio State University to learn more about renal disease in the breed. The two-year study, titled [Characterization of Renal Disease in American Boxer Dogs](#), is funded by the AKC Canine Health Foundation with support from the American Boxer Charitable Foundation.

If approved to participate in the study, owners should take their Boxers to their primary-care veterinarian or specialty veterinary clinic for the collection of blood and urine samples for diagnostic testing and genetic analysis. The study covers the cost of a renal biopsy, urinalysis, serum chemistry, urine protein gel electrophoresis, and DNA isolation, an estimated \$850 value. The owner pays for the clinical evaluation, CBC (complete blood count) analysis before biopsy, and the biopsy procedure to obtain the tissues.

For information about participating, please contact lead investigator Dr. Jessica Hokamp at Ohio State by sending an email to hokamp.1@osu.edu. You also may call the veterinary clinical trials office at 614-247-8706 or by sending an email to CVM-ClinicalTrials@osu.edu.

other tests to assess kidney function and the presence of damage are helpful in the early diagnosis of kidney disease and in monitoring of disease progression.

“Commonly used tests in addition to serum creatinine and SDMA (symmetric dimethylarginine, a renal biomarker specific to kidney function) include BUN (blood urea nitrogen), full serum chemistry analysis, CBC (complete blood count), and urinalysis. Additionally, researchers continue to evaluate other tests to help diagnose kidney disease earlier than currently possible and to potentially help diagnose difficult causes of kidney disease.”

In early-stage disease, a kidney biopsy might help diagnose the inciting cause of disease. By the time a dog is in end-stage kidney failure, the kidneys might be too damaged to determine the cause. Additionally, biopsy samples might not contain enough diagnostic tissue to determine the cause of disease, leading to an inconclusive test.

In young dogs, renal disease may be congenital, inherited and/or acquired. Canine kidneys normally develop in the womb and during the first weeks of life. In some dogs, the kidneys don't develop normally, and their underdeveloped kidneys are not able to filter urine normally. They also may suffer from a reflux condition in which urine flows backward from the bladder into the kidneys, introducing infectious organisms into the kidney and causing further secondary damage.

A retrospective [Norwegian study of seven young Boxer dogs with end-stage kidney lesions published in *Veterinary Pathology*](#) in 2008 reported that chronic kidney failure with end-stage kidney lesions in these juvenile, adolescent and young adult dogs is often congenital and often inherited. So-called canine juvenile nephropathies may have many causes, but both the well-defined hereditary nephropathies and the less well-understood juvenile nephropathies manifest as small, underdeveloped kidneys.

This study concluded that end-stage kidney disease in this small study of young Boxers closely resembled reflux nephropathy, a condition originally described in humans as juvenile malignant nephrosclerosis, and subsequently known as the Ask-Upmark kidney. In children and adolescent humans, it is characterized by abnormally small unilateral or bilateral kidneys with so-called segmental hypoplasia and one or more grooves on the capsular surface of the kidneys.

STUDY'S POTENTIAL FOR FAR-REACHING IMPLICATIONS

Although little is known about renal disease in U.S. Boxers, the Ohio State study offers promise that more knowledge may soon be coming. “Better characterization of kidney disease in Boxers might allow future studies to isolate the responsible mutations and develop a DNA test if a heritable pattern of disease is detected,” Dr. Hokamp says. “It also will allow affected dogs in the U.S. to be compared to the European dogs.”

Importantly, the study could have far-reaching implications. “The goal of this research as well as related future studies is to try and reduce kidney disease in dogs,” she adds. “If we determine that some causes of kidney disease in Boxers are due to a heritable genetic mutation, Boxer breeders will be able to find out if their dogs have the mutation. This will allow them to perform informed and careful breeding such that the disease is not perpetuated, ultimately decreasing the disease in the breed.” ■

Purina thanks Dr. Joyce Campbell, chair of the American Boxer Club Health and Research Committee and a trustee of the American Boxer Charitable Foundation, for helping us to identify this topic for the *Boxer Update*.

PPCP PROGRAM RAISES MORE THAN \$7 MILLION SINCE 2002

A healthy payday is coming to the 193 parent clubs that participated in the 2017 Purina Parent Club Partnership (PPCP) program. Purina is disbursing the 2017 PPCP earnings of \$455,085 this spring, with half going directly to the participating parent clubs and half to the clubs' fund at the AKC Canine Health Foundation (CHF).

Since it began in 2002, the PPCP program has raised more than \$7 million for canine health research.

The American Boxer Club (ABC) will receive cumulative PPCP earnings of \$7,522 based on its members' participation in PPCP in 2017. Half of the earnings will go to the parent club, and half will be sent directly to the club's fund at CHF. A charter member club, ABC has earned \$146,459 since the program began.

This year, when clubs use their PPCP funds at CHF to support a CHF research program of their choice, the AKC will match up to \$250,000 to CHF research programs through the **CHOICE** (Canine Health Opportunity to Impact CarE) matching-gift initiative.

[LEARN ABOUT PPCP](#)



Ann Viklund of Purina, right, presents the 2017 PPCP earnings to Dr. Charles Garvin, chair, and Dr. Diane Brown, CEO, of the AKC Canine Health Foundation. An equal amount is being distributed directly to the participating parent clubs.



PURINA PRO PLAN INTRODUCES FOCUS SMALL BREED SENSITIVE SKIN & STOMACH SALMON & RICE FORMULA

Purina Pro Plan recently launched FOCUS Small Breed Sensitive Skin & Stomach Salmon & Rice Formula, made especially for small-breed adult dogs weighing 20 pounds or less. Formulated with natural prebiotic fiber to promote digestive health, this complete and balanced food also is high in protein, with salmon as the No. 1 ingredient, to meet the needs of highly active small dogs. This food includes antioxidants to help support immune system health, omega-6 fatty acids and zinc to nourish the skin and promote healthy coat, and omega-3 fatty acids to support healthy joints and mobility. It is made without corn, wheat or soy, has no artificial colors or flavors, and no poultry byproduct meal.

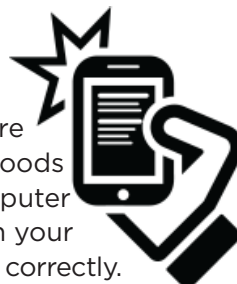
[LEARN MORE](#)

LOOKING TO REPRINT?

Boxer Update articles may be reprinted provided the article is used in its entirety and in a positive manner. To request permission to reprint an article, please contact the editor at: barbara.fawver@purina.nestle.com. Reprints should include the following attribution: Used with permission from the *Boxer Update*, Nestlé Purina PetCare.

PURINA PRO CLUB INTRODUCES RECEIPT SUBMISSION

Purina Pro Club is on a fast track to help members get their Purina Points into their accounts sooner. A new receipt submission program allows you to take a picture of your receipt from purchases of eligible Purina dog foods on your smartphone or scan the receipt into your computer and submit it online. Your Purina Points will show up in your account by the end of the day in most cases if uploaded correctly. Note that July 31, 2018, is the last date to mail in weight circles. Once you start submitting receipts, you will not be able to submit any more weight circles. To get started, click on the link below that will take you to helpful tools — instructions and a video — and then log on to your Pro Club account, register and begin submitting receipts.



[GO TO HELPFUL TOOLS](#)