



# DOG Update

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## RESEARCH INSIGHTS

Supraspinatus Tendinopathy, Kennel Cough & Pain Sensitivity

# SUPRASPINATUS TENDINOPATHY, KENNEL COUGH & PAIN

## ARE FOCUS OF CANINE RESEARCH

Here is a look at recent research that is helping to advance care for dogs. One study is evaluating the best regenerative medicine approach to treating a common shoulder injury in dogs. Another is using an airway cell-culture model to study a novel treatment for kennel cough. Meanwhile, behaviorists are studying whether dog breeds from Chihuahua to Great Dane have different pain sensitivity levels.

### **EVALUATING STEM-CELL THERAPY IN TREATING SUPRASPINATUS TENDINOPATHY**

One of the most common sporting injuries in dogs is supraspinatus tendinopathy — an injury akin to a rotator cuff tear in people. Lameness in a front leg is the most common sign of a partial or complete tear of the tendon supporting the supraspinatus muscle in the



shoulder. Repetitive activities such as agility, flyball, herding, and field trials involving outstretched forelimbs, quick turns, and jump-turn combinations put a dog at risk by causing stress to the shoulder muscle.

A challenging condition to diagnose, supraspinatus tendinopathy may lead to chronic lameness and pain due to the tearing of the tendon fibers and resulting inflammation. Untreated disease can cause mineralization and calcification of the tendon that ultimately reduces function of the joint and surrounding muscle tissue. Treatment with rest, nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy do not alleviate the condition long term. Surgery for chronic cases involves removing the calcification on the tendon.

Regenerative medicine using platelet-rich plasma (PRP), adipose stem cells (ASC) and stromal vascular fraction (SVF) provides alternative therapies for supraspinatus tendinopathy as well as other joint diseases. An investigation underway at The Ohio State University in collaboration with Virginia-Maryland College of Veterinary Medicine aims to learn the most effective regenerative medicine treatment for this type of tendon injury in dogs. Funded by the [AKC Canine Health Foundation](#), the research is considered a landmark clinical trial as it is the first evidence-based study looking at these novel treatments for supraspinatus tendinopathy.

“We have found that PRP and stem-cell therapies accelerate and promote healing through tissue regeneration and reduced scarring,” says lead investigator Jennifer G. Barrett, DVM, PhD, DACVS, DACVSMR, the Theodora Ayer Randolph professor of equine surgery at Virginia-Maryland College of Veterinary Medicine. “Dogs become comfortable, and those with partial tears in the supraspinatus tendon tend to heal completely rather than to completely tear the tendon as often happens when dogs are not treated.”

Having followed dogs treated for this condition for many years retrospectively, Dr. Barrett has begun a collaboration with Nina R. Kieves, DVM, DACVS, DACVSMR, assistant professor of small-animal orthopedic surgery at The Ohio State University. Dr. Kieves



performs the clinical assessment and treatments, and Dr. Barrett provides the regenerative therapies. For the stem-cell procedure, Dr. Kieves provides a half-inch cube of adipose (fat) tissue — essentially the size of a sugar cube — and blood samples for extracting stem cells from dogs being treated for supraspinatus tendinopathy.

Dogs are randomly assigned to one of three treatment groups, each having 20 dogs. The treatment groups are described below:

- Stromal vascular fraction group, a fast-turnaround method in which

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roughly 10,000 stem cells are extracted from the adipose tissue and quickly returned for treatment.

- Stem cell with PRP group in which 1 to 5 million stem cells are produced to aid therapy. The PRP, which contains growth factors that aid healing, is extracted from a dog’s own blood.
- Blind control group in which dogs receive blood serum injections. This group is eligible for regenerative medicine therapy following the completion of their progress evaluation.

“We hope that this research study will show which of two regenerative therapies is best for treating this difficult injury in dogs,” Dr. Barrett says. “We are happy that all dogs treated in the study will have access to stem-cell therapy at the conclusion of the trial if it proves to be most effective.”

**DEVELOPING A MODEL TO EVALUATE POTENTIAL NEW THERAPY FOR KENNEL COUGH**

Owners who train their dogs in group settings and participate in sports where there are lots of dogs have likely experi-

enced canine kennel cough. A honking sound, strong cough, runny nose, lethargy, and loss of appetite are telltale signs of canine infectious respiratory disease (CIRD) complex caused by various viral and bacterial pathogens.

Easily spread through airborne droplets and direct contact with a contagious dog or contaminated object, kennel cough can quickly affect all dogs in a kennel or those living closely together. Most dogs recover without treatment in 10 to 14 days. Preventive vaccines are available for the *Bordetella bronchiseptica* bacterium, a common cause of kennel cough with signs ranging from mild upper-respiratory illness to severe bronchopneumonia, as well as some of the viral causes. Antibiotic treatment may ease the clinical signs of infected dogs with bacterial infections, but they do not work for viral infections.

“While there are vaccines, they vary in efficacy and sometimes fail to induce a sufficient immune response to slow or stop infection,” says Gisela Soboll Hussey, DVM, PhD, associate professor of pathology and diagnostic investigation at Michigan State University. “We are



developing a canine airway cell-culture model to study the viral pathogens that contribute to kennel cough and to evaluate the efficacy of a modified interferon lambda as a new therapy.”

Funded by [Morris Animal Foundation](#), and the Office for Research and Graduate Studies and the Department of Pathobiology and Diagnostic Investigation at the College of Veterinary Medicine at Michigan State University, the research focuses on prevention strategies using interferons, which are proteins found naturally in the body that have an important role in fighting infectious diseases. “We are hopeful this will provide an emergency therapeutic or an adjunct therapy to use with vaccines to effectively reduce or control CIRDC infections,” Dr. Hussey says.

[Nine bacterial and viral pathogens are linked to CIRDC.](#) Besides *Bordetella bronchiseptica*, they include the bacterium, *Mycoplasma cynos*, found in dogs with pneumonia, and *Streptococcus equi* subsp. *zooepidemicus*, which can cause mild upper-respiratory disease and subclinical infections. Neither has a vaccine treatment.

[Viral pathogens that can cause CIRDC](#) and for which there are vaccine treatments are: adenovirus-2, which can cause a harsh cough and mild upper-respiratory signs; distemper virus, producing respiratory signs combined with lethargy, ocular discharge and fever; influenza virus, ranging from subclinical to severe disease with secondary bacterial infection; and parainfluenza virus, a highly contagious, upper-respiratory illness. Viral pathogens for which there are no vaccine treatments are herpesvirus-1, which causes subclinical or mild respiratory signs in adult dogs and severe disease in neonates, and respiratory coronavirus, which ranges from subclinical to mild upper-respiratory signs.

Long-term immune protection from viruses involves a strong interferon defense. “By using interferons directly as a treatment, there may be an advantage for immediate protection and also for stimulating better vaccine immunity,” Dr. Soboll Hussey says. “Interferons may function like a broad-spectrum antiviral that helps protect dogs against multiple viral groups. This is what we hope to find out.”

## UNDERSTANDING PERCEPTIONS ABOUT DOG BREEDS’ SENSITIVITY TO PAIN

Theoretically, all dogs should have similar pain thresholds, but according to over 90 percent of respondents, half of which were veterinarians, of an online survey, there are differences among dog breeds. Small-breed dogs, such as Chihuahua and Maltese, were rated as being less tolerant of pain than some of their larger cohorts, such as Doberman Pinscher and Rottweiler.

The survey findings, published March 17, 2020, in [PLOS One](#), piqued interest by the investigators to continue studying beliefs about how dog breeds differ in their sensitivity to pain. The [AKC Canine Health Foundation](#) is funding the follow-up research underway at North Carolina State University.

Lead investigators Margaret Gruen, DVM, MVPH, PhD, DACVB, assistant professor of behavioral medicine, and Duncan Lascelles, BVSc, PhD, DECVS, DACVS, professor of translational pain research and management, are working to learn if perceptions about dog breeds’ varied pain thresholds are scientifically grounded. Rachel Cunningham, DVM, a postdoctoral research associate who is now a surgical intern at Michigan State University, and Rachel Park, a graduate student in the Comparative Biomedical Sciences program, conducted the study.

“Our null hypothesis is that dogs regardless of their breed have similar pain thresholds,” Dr. Gruen says. “The risk of ungrounded, preconceived beliefs about dog breeds’ pain tolerance is that it could negatively impact clinical treatments and result in unnecessary pain for dogs believed to have low pain sensitivity.”

The current study comprises 147 dogs representing 10 breeds. Included are Chihuahua, Maltese, Jack Russell Terrier, Boston Terrier, Golden Retriever, Labrador Retriever, Border Collie, Siberian Husky, American Staffordshire Terrier, and German Shepherd Dog.

“We screened dogs by performing physical and orthopedic examinations to ensure they are free of conditions causing chronic pain, as this can change their neurobiology and lower their pain thresholds,” Dr. Gruen says. “Owners

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Gisela Soboll Hussey, DVM, PhD, associate professor of pathobiology and diagnostic investigation, Michigan State University

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completed the [Canine Behavioral Assessment & Research Questionnaire \(C-BARQ\)](#), which gathers information about their dogs' personalities, breeding, overall health, and behavior."

Quantitative sensory testing in which the investigators examined the threshold at which dogs would withdraw their paws from pressure or heat provided scientific insights. "Imagine that I slowly push my finger into you until you say, 'Hey, stop doing that,'" explains Dr. Gruen. "That's basically what we did but in a more sophisticated way."

Bonnie Giles of Chesterfield, South Carolina, enrolled her two Golden Retrievers, "Willow," 11 years old, and "Eve," 8 years old, in the study. "It is interesting that there may be different pain tolerances among dog breeds," Giles says. "Both my dogs are really calm, as they are retired breeding moms for service dogs. Willow was a certified therapy dog. I've been through C-sections (cesarean sections) and minor veterinary procedures with them. In my opinion, they always seem unfazed by pain."

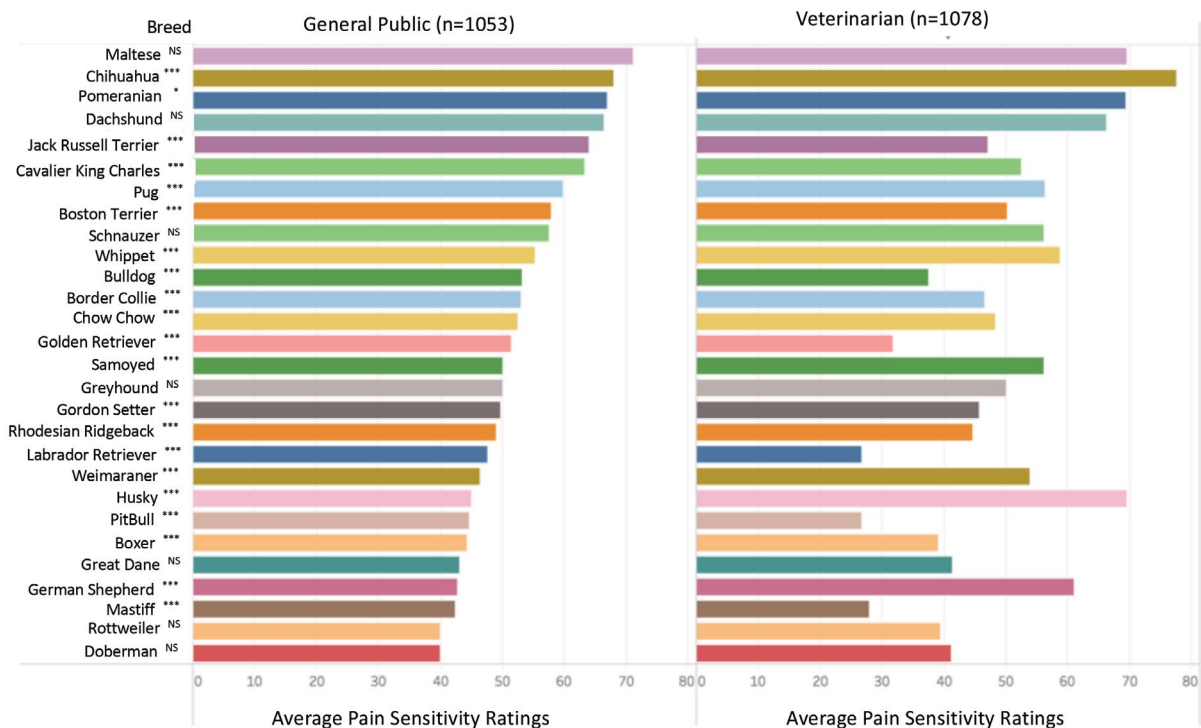
The results of the study are expected to be published in 2022. Not revealing their discoveries, Dr. Gruen says, "If there are breed differences in pain sensitivity, future work will look at understanding genetic associations and how to advance understanding of effectively treating pain in a breed-specific manner."

"If there are no differences among breeds related to pain sensitivity, then it is important to understand our perceptions of breed differences to ensure dogs of every breed receive appropriate pain management and to understand where these beliefs came from."

The notion that human perceptions influence how dog breeds' pain sensitivity is interpreted aligns with the generalized group characterization hypothesis summarized in the *PLOS One* article on the survey results. "This hypothesis predicts that people will rate dogs of different breeds as having different pain sensitivity based on group traits like physical appearance and social behavior stereotypes," says Dr. Gruen.

The online survey included 2,131 responses, of which 1,078 came from

### AVERAGE PAIN SENSITIVITY RATINGS BY THE GENERAL PUBLIC & VETERINARIANS



Respondents to an online survey rated pain sensitivity for pictures of dogs not described by their breed names, ranging from 0 for not sensitive at all to 100 for most sensitive imaginable.

COURTESY OF DR. MARGARET GRUEN/NORTH CAROLINA STATE UNIVERSITY



veterinarians. Pictures of 28 dog breeds representing a wide range of sizes, body and head shapes, and coat types/lengths were shown though breed names were not identified. Respondents rated their beliefs about the pictured breeds' pain sensitivity on a scale from 0 to 100, with 0 being not sensitive at all and 100 being the most sensitive imaginable.

"Ratings by the general public were driven mostly by size, with smaller dogs rated as more sensitive to pain and larger, heavier dogs rated as less sensitive," Dr. Gruen says. "Dogs on breed-specific legislation lists that are considered dangerous were generally rated as less sensitive to pain. These findings support the prediction that people rate pain sensitivity in dogs differently for different breeds based on their appearance and common group stereotypes."

While dog size appeared to influence veterinarians' ratings, it was not as strong a relationship as seen with ratings by the general public. "Veterinarians tended to rate the dogs based on commonly held beliefs about different dog breeds," she says. "For example, two large breeds, German Shepherd Dog and Siberian

Husky, were rated among the most sensitive to pain by veterinarians."

When deciding on individual factors believed to influence pain sensitivity and response to pain in dogs, the general public was somewhat evenly distributed among: a breed's skin thickness, 41 percent; environment raised, 40.1 percent; genetics, 39 percent; and temperament, 35.6 percent. Most veterinarians attributed pain sensitivity to temperament, 80.9 percent; followed by genetics, 33.3 percent; environment, 29.5 percent; and skin thickness, 9.3 percent.

As to Giles' belief that her Golden Retrievers are largely unfazed by pain, the online survey reinforced her interpretation. The general public rated Golden Retrievers around 51 percent on the 1 to 100 scale, indicating the breed has an average threshold for pain. Veterinarians rated Goldens around 32 percent, giving the breed a rating that reflects low sensitivity to pain.

"Ultimately, we think there is strong evidence that people rate pain sensitivity based on breed-specific stereotypes or phenotypic traits and dog breed archetypes," reflects Dr. Gruen. "Further investigation is needed to more fully comprehend the impact." ■

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