

BEAGLES ARE AMONG BREEDS PRONE TO

STEROID-RESPONSIVE MENINGITIS-ARTERITIS

Originally known as "Beagle pain syndrome," SRMA was first recognized in Beagles exhibiting signs of pain, lameness and fever.

Given his handsome looks and outgoing charm, "JR" (GCH Pun Kotzky Jolly Roger Of Sunbriar CD BN RA CA TKI), a 15-inch tricolor male Beagle, easily finished his show championship title. When he was 2 ½ years old, JR earned an invitation to the Top 20 competition at the 2015 National Beagle Club (NBC) National Specialty.



"JR," a 15-inch tricolor male Beagle, pictured with owner Susan Sprout, was successfully treated for SRMA.

Months before the National, JR started to limp in his right rear leg and seemed "out of sorts," recalls owner Brett Sprout of Alliance, Ohio. Soon he recovered and resumed his winning ways only to become suddenly lame again, this time favoring his right front leg.

"The veterinarian thought that JR had an orthopedic problem affecting his legs," Sprout says. "He took X-rays of JR's legs and had a specialist examine him. They posted JR's radiographs on VetRad, a teleradiology internet site for

veterinarians, hoping someone would offer clinical suggestions. No one provided feedback."

Meanwhile, JR's limping continued to come and go. "One day he would seem all right, and then the lameness would return," says Sprout.

Sadly, JR missed the 2015 National Specialty because he was too lame to compete and seemed to be in pain. "We were beginning to think JR was on a path leading to a bad end," Sprout says. "It appeared that he was not enjoying life."

Sprout and his wife, Susan, attended the National Specialty that year at Purina Farms in Gray Summit, Missouri, without JR. Querying fellow Beagle owners about JR's mysterious condition, Sprout wasn't getting anywhere — until he talked to Darlene Stewart, chair of the NBC Health and Genetics Committee. That conversation may have saved JR's life.

"Darlene homed in on a likely cause of the problem, and the more we talked, it seemed more and more plausible," Sprout says. "As she described 'Beagle pain syndrome,' an inflammatory neurological disorder in dogs now known as steroid-responsive meningitis-arteritis (SRMA), it seemed that this could be the diagnosis. As it turns out, Beagles are among the breeds predisposed to developing this condition."

When the Sprouts returned home, they shared the information with JR's veterinarian. After confirming that SRMA was a likely cause of JR's pain, the veterinarian began

treatment with a corticosteroid, prednisone. Within a day, JR was better.

"We were concerned that JR's pain was becoming unbearable and we might have to euthanize him, but after treatment he became a new dog," Sprout says.

Stewart (AlaDars) of Theodore, Alabama, was no stranger to SRMA. Nearly two decades earlier, her 14-month-old 15-inch tan-and-white female Beagle, "Sandi" (CH AlaDars Sandwitch), started moving hesitantly as if in pain in her shoulders or neck. The veterinarian began treating her with steroids for a perceived disc disorder. Sandi responded well, so the cycle of treating her with steroids for intermittent pain continued for many years.

At age 8, Sandi suffered a severe bout of pain and was so unresponsive to treatment that euthanasia seemed the only choice. Desperate for answers, Stewart scoured the veterinary literature and found an obscure article describing signs that fit Sandi perfectly. Her veterinarian followed the suggested treatment, and Sandi improved within a day.

"She never had another severe episode, but at the first sign of her 'headache look' I would start her on prednisone for about a week,"



"Sandi," a 15-inch tan-and-white female Beagle, enlightened owner Darlene Stewart about SRMA when she was diagnosed at age 8 after years of suffering from the neurological condition.

CLINICAL SIGNS OF STEROID-RESPONSIVE MENINGITIS-ARTERITIS IN DOGS*

- Neck pain
- Lethargy
- · Reluctance to rise or walk
- Stiff gait
- Decreased appetite
- Kyphotic posture
- Tremors
- Diarrhea
- Vomiting
- Inappropriate urination

*Source: Lau J, Nettifee JA, Early PJ, et al. Clinical Characteristics, Breed Differences, and Quality of Life in North American Dogs with Acute Steroid-Responsive Meningitis-Arteritis. *Journal of Veterinary Internal Medicine*. 2019;33(4):1719-1727.



Stewart says. "Sandi lived to be 16 and ultimately died of cancer."

Through the years, Stewart has heard many stories of Beagles experiencing clinical signs and pain similar to Sandi. The typical scenario is a young hound that suddenly develops acute neck pain and lethargy that may progress to whole body pain and often includes lameness and fever. Veterinarians initially presume a dog has suffered an injury or may diagnose disc disease or bacterial infection. Chronic cases may develop other neurological deficits, such as incoordination or weakness of the limbs.

The disorder originally was known as Beagle pain syndrome because it was first recognized in Beagles exhibiting signs of pain, lameness and fever. An article published in 1989 in *Toxicological Pathology* on these dogs reported that veterinarians at Cornell University suspected this was an unusual syndrome in Beagles and that cases as far back as 1973 seemed to match

"Clinical signs of SMRA are resolved in most dogs with treatment, but relapses may occur as treatment is tapered or discontinued. Little is known about what triggers it."

Karen Muñana, DVM, MS, DACVIM (Neurology), North Carolina State University

Beagle pain syndrome. In the 1990s, several large-scale studies reported on the syndrome occurring in various breeds. Once such study was published in 1994 in the *Journal of Small Animal Practice*.

The good news is that the pain and other clinical signs of the disease resolve with treatment. Antibiotics and rest are not effective in treating dogs with SRMA. Rather, it is the anti-inflammatory benefits of corticosteroids that help to resolve the clinical signs of SRMA. Not a lot is understood about the cause of SRMA, but it is believed to be an immune-mediated condition.

A NEUROLOGICAL DISEASE

"Steroid-responsive meningitisarteritis is a common inflammatory disease of the nervous system of dogs involving the meninges, or membranes that cover the brain and spinal cord, and associated arteries," says Karen Muñana, DVM, MS, DACVIM (Neurology), professor of neurology at North Carolina State University. "Clinical signs are resolved in most dogs with treatment, but relapses may occur as treatment is tapered or discontinued. Little is known about what triggers SRMA."

A recently completed study at North Carolina State University evaluated clinical and treatment differences among breeds of dog with acute SRMA and surveyed owners to learn about the quality of life of affected dogs. The research, led by neurology resident Jeanie Lau, BVSc, working with mentor Dr. Muñana, was funded through the AKC (American Kennel Club) Canine Health Foundation Clinician-Scientist Fellowship program.

"The AKC Canine Health Foundation was excited to support this important research, and we are thankful to the breeders who participated in the study," says Dr. Diane Brown, CEO of the AKC Canine

Health Foundation. "We are interested in further supporting investigations into this disorder of young dogs and raising awareness among breeders and the veterinary community."

"Our retrospective study included 61 dogs," Dr. Lau says. "We sent an online survey to the owners of 29 dogs identified through an AKC Canine Health Foundation survey and 32 dogs treated at the North Carolina State Veterinary Hospital. Among the questions, we asked owners to rate their dog's quality of life during treatment, during clinical resolution and since being diagnosed with SRMA."

The first study of SRMA in dogs in the U.S., the research was published online in the June 7, 2019, issue of the Journal of Veterinary Internal Medicine. The study provided insightful information that included identifying two breeds not previously recognized as being susceptible to SRMA -Golden Retrievers and Wirehaired Pointing Griffons. A review of the medical records of affected dogs looked at their age, breed, sex, neuter status, body weight, length of time between clinical signs and treatment, duration of treatment with corticosteroids, and results of additional diagnostic tests.

All dogs in the study experienced lethargy and neck pain. Many also had decreased appetite and were reluctant to rise or walk and had a stiff gait. Some dogs had a crouched posture or tremors. About three-quarters of the dogs had fever, and 38 percent of dogs had a temperature greater than 104 degrees Fahrenheit.

The study charted four outcomes:
1) clinical resolution, 2) relapse,
3) clinical remission, or 4) death
for reasons unrelated to SRMA.
A relapse was defined as recurrent
clinical signs that resolve completely
after treatment with an increased
dosage of corticosteroids and the
addition of a second immunomodulatory drug or both. Clin-

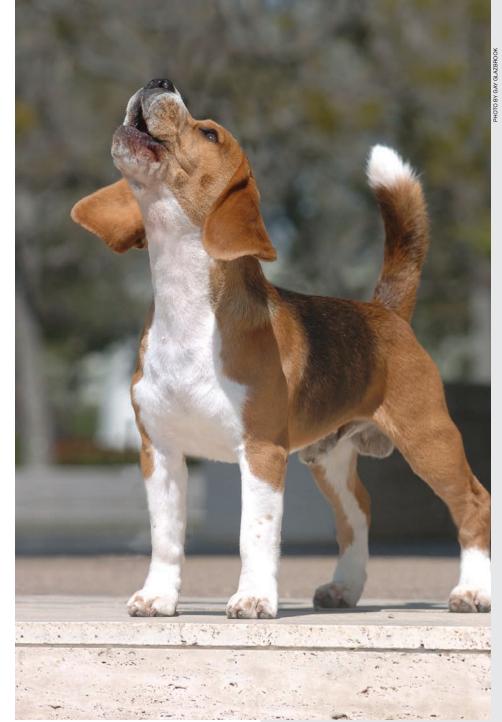
ical remission was the absence of clinical signs after beginning corticosteroid treatment, and clinical resolution was the absence of clinical signs after completing corticosteroid treatment.

"We asked owners to rate their dogs' quality of life on a scale of one to 10, with one being poor and 10 being excellent," Dr. Lau says. "The mean quality of life for dogs during treatment was significantly worse than during clinical resolution and since being diagnosed with SRMA. This was associated with the severity of prednisone's adverse effects. When we asked owners to assess the severity of their dogs' neck pain at onset, around 77 percent noted improvement of clinical signs within one to two days of starting prednisone."

Among the negative effects owners noted about continued use of prednisone were: polydipsia (excessive thirst), polyuria (excessive urination), polyphagia (excessive hunger), panting, weight gain, thinning of hair coat, restlessness, sleeping more than usual, inappropriate urination, "pot belly" appearance, development of non-dermatological infections, diarrhea, dermatitis, and vomiting.

"Any breed can develop SRMA, though a predisposition was previously recognized in several breeds," Dr. Muñana says.

Breeds previously considered predisposed include: Beagle, Bernese Mountain Dog, Border Collie, Boxer, English Springer Spaniel, Jack Russell Terrier, Nova Scotia Duck Tolling Retriever, Weimaraner, and Whippet. The two newly recognized breeds prone to SRMA were highly represented in the study. Golden Retrievers had the highest incidence with 12 dogs affected, and Wirehaired Pointing Griffons had the third-highest incidence with nine dogs affected.



Other breeds with a high prevalence were: Bernese Mountain Dogs with 10 dogs affected, Boxers with nine dogs affected, and Beagles with six dogs affected.

"Our findings suggest that Golden Retrievers and Wirehaired Pointing Griffons should be included among breeds recognized to develop SRMA," says Dr. Muñana. "Golden Retrievers were included in a previous study of SRMA, but Wirehaired Pointing Griffons had not been previously described with SRMA.

"Further, we saw that the Wirehaired Pointing Griffon had a



SRMA typically affects dogs from 6 to 18 months of age. The long-term prognosis for young dogs with acute SRMA is fair to good.

significantly higher number of prednisone-related adverse effects compared to other breeds. This is likely because they were treated with substantially higher prednisone dosages when compared to Beagles, Bernese Mountain Dogs and Golden Retrievers. It also could be due to the difference in their lifestyle as a hunting breed or could reflect an increased genetic susceptibility to corticosteroid-related adverse effects."

DIAGNOSING SRMA

SRMA typically affects dogs from 6 to 18 months of age. The median age at which dogs in the North Carolina State study were diagnosed was 8.5 months, with 95 percent of dogs being under 2 years of age. The study com-

prised 34 males, 18 intact and 16 neutered, and 27 females, six intact and 21 spayed.

"Diagnosis is based on increased numbers of neutrophils, a type of white blood cell, in the cerebrospinal fluid (CSF) of affected dogs and exclusion of other infectious diseases combined with a positive response to corticosteroids," Dr. Muñana says. "Some neurologists use magnetic resonance imaging (MRI) to rule out clinically similar conditions, such as intervertebral disc disease, though an MRI is a costly procedure and is not required to diagnose SRMA, particularly in a young dog with signs typical of SRMA."

A newer noninvasive, more affordable test involves measuring the level of C-reactive protein (CRP), a substance produced by the liver in response to inflammation in the blood serum indicating systemic infection. In affected dogs, the CRP level is elevated parallel to that of neutrophils in CSF.

"CSF analysis is useful for an initial diagnosis followed by CRP analysis to monitor a dog's response to therapy," Dr. Muñana says. "Since therapy is associated with side effects, some of which can be quite serious, I do not recommend treatment unless it is supported by a diagnosis."

The most effective treatment for dogs with SRMA is immunosuppressive dosages of corticosteroids given over several months. "Most dogs improve dramatically within one to three days, then continue on daily high doses of prednisolone or prednisone for four to eight weeks, though some dogs may continue treatment for six months to a year," says Dr. Muñana. "During this time, dogs should have regular blood work to ensure they are tolerating the steroid therapy and to monitor CRP levels."

The long-term prognosis for young dogs with acute SRMA is fair to good. Most dogs — at least 80 percent —

respond well to the initial course of steroids. About 10 to 15 percent relapse during treatment, and about 20 to 30 percent relapse in the month following discontinuation of treatment. A few dogs will relapse over a year after treatment ends. Some dogs require lifelong therapy.

Whereas acute cases respond well, chronic SRMA is more challenging to treat, says Dr. Muñana. "Chronic SRMA develops in dogs that are not diagnosed and treated in a timely manner or that have recurring relapses. Chronic cases have fewer CSF abnormalities than dogs with acute SRMA, but the abnormalities are consistent with chronic infection. Their treatment is the same — high-dose immunosuppressive corticosteroids, and a second immunosuppressive drug is usually needed."

"Our research included identifying factors associated with the frequency of relapses and owners' assessments of the severity of relapses in the 29 dogs that relapsed," Dr. Lau says. "Among the variables we studied were the age at onset of clinical signs, prednisone dosage and treatment duration, treatment with a second immunomodulatory drug at initial diagnosis, and duration between onset of clinical signs and initiation of treatment."

Treatment results on prednisone were excellent, with 29 dogs having complete resolution of clinical signs for a median of 37 months. In 25 dogs, remission was achieved, thus they began a tapering schedule to reduce prednisone at follow-up. One dog was euthanized due to developing neurological problems during relapse.

LONG-TERM PROGNOSIS

As with the success JR and Sandi experienced, treatment results show that dogs with SRMA have an excellent prognosis for remission and a fair to good prognosis for

resolution, with remission and resolution rates of 98.4 percent and 54 percent, respectively. "Most dogs experience improvement within 48 hours of beginning treatment," says Dr. Muñana.

Reflecting, Dr. Lau says, "As a retrospective study, this had several limitations including that the accuracy of the completeness of the data collected was dependent on the information available in the dogs' medical records. We also were limited in the numbers of particular breed cases, and this restricted the power of the study."

Many questions remain. "I think the most pressing questions involve determining optimum treatment and the cause of SRMA, including whether there is a genetic basis," Dr. Muñana says. "Our team feels further investigation is warranted to learn the influence of individual breeds on disease severity and its clinical course and how it impacts a dog's quality of life."

Meanwhile, Sprout's hound JR has rebounded and resumed a busy performance career. At the 2017 NBC National Specialty, JR earned High in Trial in obedience with a score of 194, and he made the final cut for Best of Breed. At the 2018 and 2019 Rally National Championships, JR was the highest-scoring Beagle.

"We recently started JR in agility, and he has already earned two Q's out of two attempts," Sprout says proudly. "Plus, he is a bronze Grand Champion. Everything he has achieved has been possible thanks to a conversation with Darlene Stewart at the 2015 National."

Purina appreciates the support of the National Beagle Club, particularly Darlene Stewart, chair of the Health and Genetics Committee, for helping us to identify topics for the *Beagle Update*.

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*Data was collected by Relevation Research via an online survey from August 15-19, 2018. A total of 826 nationally-representative dog owners qualified and completed the survey. Qualified participants were men and women age 18 and older, owned one or more adult dogs, were household members most responsible for taking the dog(s) to a veterinarian, and had taken the dog(s) to a veterinarian in the past 12 months.

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