PURINA PRO PLAN

ROTTWEILER Update

A NESTLÉ PURINA PUBLICATION DEDICATED TO ROTTWEILER ENTHUSIASTS

VOLUME 15 | FALL 2017

RESEARCHERS STUDY

CRUCIATE LIGAMENT RUPTURES IN ROTTWEILERS

CH Esmonds Yield No Yards tore both his cruciate ligaments within one year. An avid swimmer, "Reggie" is completely healed after two surgeries and rehabilitation. One would never know today he had the injuries, says owner Pat Carkoski.

Just like clockwork, exactly one year and a day after tearing his left cruciate ligament, "Reggie," a 7-year-old fast-moving male Rottweiler, whose namesake is NFL Hall of Famer Reggie White, tore his right cruciate ligament.

The injury happened as Reggie (CH Esmonds Yield No Yards) made a sharp turn while chasing his buddy, 8-year-old "Coach" (Select AM/CAN CH Esmonds V T Lombardi Vanstone RE RL2 TT HIC RTD). As Coach trotted on, Reggie limped in pain, while his owners winced in pain, knowing what lies ahead.

After his first cruciate ligament rupture, Reggie had surgery and underwent three months of rehabilitation therapy. His successful recovery earned him fourth in Sweepstakes at the 2016 American Rottweiler Club National Specialty, held in his hometown of Lancaster, Pennsylvania.

Owners Ron and Pat Carkoski estimate they spent around $14,000 for Reggie's surgeries and rehabilitation to stabilize his knees (stifles). "The second time he tore his cruciate ligament, we knew immediately," Pat Carkoski says. "At the veterinary orthopedic clinic, they used a pressure mat that showed he was only putting 5 percent of his weight on the injured leg. Radiographs confirmed the injury, and the next day Reggie had surgery."

Cruciate ligament rupture is the most common cause of hind limb lameness in dogs, says Peter Muir, BVSc, PhD, DACVS, DECVS, the Melita Grunow Family Professor of Companion Animal Health at the University of Wisconsin-Madison.

Dr. Muir has studied cruciate ligament rupture in dogs for nearly two decades. He is committed to developing safe, effective therapies and finding ways to prevent progressive degradation of affected cruciate ligaments. Importantly, he wants to discover how to promote healing in dogs that have torn their cruciate ligaments.

The Rottweiler's high risk for developing painful cruciate ligament rupture is tied to genetics, as the condition is heritable. Sadly, there is no genetic test to identify dogs with a high risk of developing cruciate ligament rupture, thus breeders may breed affected dogs from bloodlines that have gone generations without an incidence of rupture.

Esmond Rottweiler breeder Ann Felske-Jackman of Ontario, Canada, who bred Reggie and Coach, laments about not having a genetic test to screen dogs for risk of cruciate ligament rupture. Although she bred both Rotties, they are from different lines.

"Coach is the result of five generations of his line, and I made careful attention to breed away from this trait during those generations," Felske-Jackman says. "Reggie, however, was the result of the addition of quite a few new ancestors on both sides of the pedigree. In the quest for genetic diversity, desirable and undesirable traits are added. When this happens, affected dogs must be removed from the breeding program."

A disease that occurs in a dog's knee, cruciate ligament rupture usually involves fiber damage to both the cranial (anterior) and caudal (posterior) cruciate ligaments, Dr. Muir explains. It starts like the fraying of a worn rope and progresses to complete failure or rupture of the cruciate ligament. Both the cranial and caudal cruciate ligaments may be damaged, but the disease particularly affects the cranial cruciate ligament.

The ligaments are short bands of tissue that function as joint stabilizers connecting the femur (thighbone) to the tibia (shinbone) so a dog can straighten and bend its leg normally. When a rupture occurs, joint stability is lost and the bones slide across each other causing joint pain. Some dogs eventually develop rupture of both the caudal and cranial cruciate ligaments.

Lameness ranging from mild to severe is the first sign of cruciate ligament rupture. It typically develops gradually, but many owners do not notice mild lameness in the early phase of the disease. Lameness is more severe when the knee joint becomes unstable after the cranial cruciate ligament has completely ruptured. Due to pain, dogs may lean to one side when sitting or hold up a leg when standing.

"Cruciate ligament rupture puts a great burden on owners as surgery is expensive," Dr. Muir says. "U.S. dog owners spend more than $1 billion a year on treatment of this disease. Also, dogs that have one cruciate ligament rupture have a greater than 50 percent chance of developing a second rupture in their other hind limb within a year."

"There will always be undesirable traits, but the things that cause dogs pain and cost owners the most money are the things we first remove from our breeding program," says Felske-Jackman. "With a polygenic condition such as cruciate ligament rupture, it is not easy to breed this out of a line."

The Carkoski family, who has a home on a farm in Wisconsin, learned about the cruciate ligament research of Dr. Muir at the University of Wisconsin-Madison. They were happy to enroll Reggie and his unaffected buddy, Coach, in the study. "It is absolutely critical to try and figure out what is going on with this disease and to identify early dogs with the

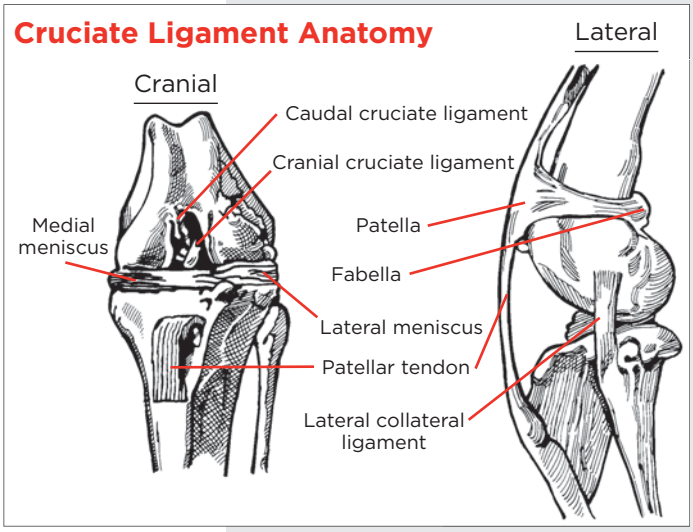
WHY PEOPLE TEAR THEIR ACL & DOGS TEAR THEIR CCL

Anatomy explains why people tear their ACL (anterior cruciate ligament), and dogs tear their CCL (cranial cruciate ligament).

In people, the ACL is one of four ligaments that keeps the knee stable. The ACL controls rotation and forward movement of the tibia relative to the femur at the level of the knee joint. ACL rupture often happens when a person lands on the leg and then quickly pivots or twists the knee in the opposite direction while it is slightly bent.

In dogs, the structure corresponding to the ACL is the CCL, which also is one of four ligaments that stabilize the knee. It forms a cross shape with the caudal cruciate ligament as they work together as stabilizers connecting the femur (thighbone) and tibia (shinbone).

ACL rupture in humans and CCL rupture in dogs are similar because ligament rupture typically develops without a contact injury. Both dogs and people are at risk for developing osteoarthritis with a CCL or ACL rupture. Advances in knowledge about the cruciate ligament rupture disease mechanism in dogs may ultimately expand understanding of human ACL rupture.



propensity to tear their cruciate ligament in order to decrease the risk," Pat Carkoski says.

Due to the prevalence of cruciate ligament rupture in the breed, the Rottweiler Health Foundation continues to support Dr. Muir's work.

A GENOME-WIDE ASSOCIATION STUDY

Multiple factors influence whether a dog develops cruciate ligament rupture. "The underlying process that leads to cruciate ligament degeneration is not completely understood," Dr. Muir says. "We have focused on how knee joint inflammation and alterations in repair and maintenance of the cruciate ligament tissue promote fiber rupture in the cruciate ligaments."

In the current Rottweiler study, Dr. Muir and his team are working to identify genetic variants, or alterations in the DNA nucleotide sequence, that predispose the breed to cruciate ligament rupture through a genome-wide association study using single-nucleotide polymorphism (SNP) markers as well as analysis of whole-genome sequence data. The goal is to link associated genetic variants to biological pathways influencing degeneration of the cruciate ligaments.

The research builds on their earlier genome-wide association study in the Labrador Retriever, another breed predisposed to cruciate ligament rupture. The Labrador study, published in *PLOS One* in April 2017, found 99 regions of association with cruciate ligament rupture, affirming that the disorder is a complex, highly polygenic condition.

"In the Labrador study, cruciate ligament rupture occurred most commonly in middle-aged dogs around 6 years old," says Dr. Muir. "Past studies have found that a loss of sex steroids through neutering of male and female dogs is a risk factor for cruciate ligament rupture. The genetic component of this complex disease likely consists of many genetic variants concentrated differently in different breeds through population bottlenecks and intense selection, thereby explaining the range in disease risk in different breeds. The most important risk factor for initiation of cruciate ligament degeneration and rupture in dogs is genetic background — in other words, breed."

Studying 98 cases and 139 control dogs, the research team undertook an association analysis of genome-wide SNP markers in Labradors. "An accurate genetic test for risk of cruciate ligament rupture in dogs could be used to identify at-risk dogs before rupture occurs," Dr. Muir says. "This information could be used to control environmental variables known to contribute to cruciate ligament rupture risk and also could provide an opportunity to improve patient treatment once a causal gene or pathway with a large effect on disease risk has been identified and targeted therapeutically."

The goal in the new Rottweiler study is to use the locations of genetic variants to gain further insights into the biological processes that cause ligament rupture. This knowledge could ultimately lead to development of ligament-saving treatments.

A progressive condition not usually associated with trauma, cruciate ligament rupture is preceded by chronic inflammation and arthritis

TIPS ON REDUCING RISK OF CRUCIATE LIGAMENT RUPTURE

Experts attribute cruciate ligament rupture to many causes, including a dog's genetic background and environmental risk. Here are tips to help prevent a rupture in your Rottweiler.

Keep your dog active. Inactivity decreases the stimulation of the cruciate ligament, potentially causing atrophy and weakening of the ligament. An active lifestyle helps maintain muscle tone and joint health, as well as optimal weight, and may help reduce the risk of cruciate ligament rupture.

Avoid high-impact activities. Although activity is important, it is helpful to avoid high-impact loading of the knee joint, which could promote fraying of the ligament fibers and eventual development of cruciate ligament rupture. High-energy activities with a lot of turning, pivoting or jumping put high loads on the cruciate ligaments of the knee.

Keep excess weight off your dog. An overweight dog has a greater risk for developing cruciate ligament rupture than healthy, fit dogs. Obesity increases the amount of force applied on the knee joint at each step, causing repetitive loading that may lead to excessive loading of the cruciate ligaments and increased fiber rupture.

Wait to neuter or spay. Consider waiting until dogs are more than 1 year of age or skeletally mature before neutering or spaying. Studies have shown that a loss of sex steroids through neutering of males and spaying of females is a risk factor for cruciate ligament rupture.

in the knee joint. "Our evaluations of affected dogs have shown that knee inflammation and osteoarthritis precede development of joint instability, and this osteoarthritis precedes and promotes fraying of the cruciate ligaments," says Dr. Muir.

"Detailed analyses of affected knees suggest that joint immune responses are activated by a specific protein trigger, or an antigen. This is similar to what happens in people with rheumatoid arthritis or reactive arthritis," he says. "The factors that lead to joint inflammation in cruciate ligament rupture are not completely understood, but genetic background is likely to be important."

THE RECOVERY PROCESS

Most dogs that rupture their cruciate ligament require joint stabilization surgery. This helps them retain good limb function and reduce the progression of osteoarthritis associated with the condition.

The standard surgery to repair a cruciate ligament rupture is TPLO (tibial plateau leveling osteotomy). The procedure involves cutting the tibial plateau to rotate it and thus stop it from sliding across the femur. A surgical plate is then used to keep the osteotomy of the tibia in position until the bone cut has healed. Surgery is expensive, and it can take months of rehabilitation for a dog to fully recover.

Reggie, the Rottweiler, had TPLO surgery following left and right cruciate ligament ruptures, each costing nearly $5,000, though the procedures came with lifetime guarantees. Reggie's four-month recovery after the first surgery included twice-weekly rehabilitation at $80 per visit. Underwater treadmill work at a therapy clinic helped to strengthen the injured leg, and exercises at home focused on increasing his range of motion.

The process was repeated for the second rupture, though Reggie healed more quickly, allowing the rehabilitation process to be shortened by nearly two months. The Carkoskis used a special harness both times to help them lift the 118-pound Reggie when he was not allowed to bear weight on the injured legs as they recovered.

Reflecting on the challenges to not produce dogs that rupture their cruciate ligaments, breeder Felske-Jackman says staying in contact with the owners of dogs she's bred and tracking their offspring to learn about development of the disease is critical. She is not one to shy away from doing what must be done to end a detrimental trait that crops up in her line.

"Twice I've stopped breeding lines due to a higher than average risk of cruciate ligament rupture in the extended family," she says. "It is so important to breed for overall quality, and for me the priorities are health, temperament and longevity. Breeding away from one particular trait requires caution because as you breed away from one trait, you will inevitably add other undesirable traits, effectively replacing one flaw with another."

Meanwhile, Reggie, now 8 years old, has much to look forward to as the Carkoskis prepare to retire to their Wisconsin home. Completely healed from both cruciate ligament stabilizing surgeries, Reggie, who loves to swim, will enjoy the lakes on the farm.

"You would never know today that Reggie ruptured his cruciate ligaments," Pat Carkoski says. "He walks completely normal. Although this was a difficult injury to go through, I am happy we were able to contribute to Dr. Muir's research. Maybe someday soon, we'll understand more about what causes this." ■

Purina thanks Roberta Kelley-Martin, president of the Rottweiler Health Foundation, for helping us to identify this topic for the *Rottweiler Update*.

ROTTWEILER OWNERS CAN TAKE PART IN A GENETIC STUDY OF CRUCIATE LIGAMENT RUPTURE

Owners of Rottweilers of any age that have ruptured their cruciate ligament and those over the age of 8 with no cruciate ligament rupture and no sign of knee arthritis via radiographic screening may be eligible to participate in a study underway at the University of Wisconsin-Madison School of Veterinary Medicine.

A large number of Rottweilers — both affected dogs and healthy controls — are needed for the genome-wide association study. The Rottweiler Health Foundation is helping to fund the study. For information, please contact Dr. Lauren Baker or Dr. Peter Muir.

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