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# ROTTWEILER Update

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## JUVENILE-ONSET LARYNGEAL PARALYSIS AND POLYNEUROPATHY

An Inherited Disease with a DNA Genetic Test

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# BREEDERS SHOULD TEST FOR JUVENILE-ONSET LARYNGEAL PARALYSIS AND POLYNEUROPATHY

An emergency care veterinarian, Wendy Haumaier, DVM, specializes in helping foster and care for rescued Rottweilers that have medical issues. When she got “Rosie,” an 8-month-old puppy taken in by the Rottweiler rescue organization Kodi’s Club Rescue of New York in November 2018, she began dealing with clinical signs that stumped her.

dic Foundation for Animals. Rosie’s DNA was sent to the University of Missouri Small Animal Molecular Genetics Lab, which confirmed a diagnosis of JLPP.

Knowing that JLPP is a progressive, fatal neurological condition, Dr. Haumaier began doing range-of-motion exercises and physical therapy on a water treadmill to help strengthen Rosie’s weak rear legs. The playful puppy also had begun showing signs of hypermetria, a high-stepping gait in the front legs. Rosie loved the wheelchair cart that Dr. Haumaier got to take her to the park.

The laryngeal muscles of the voice box, or larynx, that normally close when a dog eats or drinks were no longer functioning correctly. The nerves of the muscles had become weak or essentially paralyzed causing food and water to regurgitate into the windpipe, or trachea, and lungs.

Rosie began having difficulty swallowing food, and Dr. Haumaier once had to perform the Heimlich maneuver to keep her from suffocating when food was stuck in her windpipe. This was followed



“Rosie had a wobbly, stilted walk and would fall if she moved too fast,” says Dr. Haumaier of Pleasant Valley, New York. “She also had signs of microphthalmia, meaning her eye globes were unusually small. She was a happy, spirited puppy and very pretty.”

Four days after getting Rosie, Dr. Haumaier took her to a veterinary neurologist at Upstate Veterinary Specialists in Latham, New York, who suspected the condition was genetic. Dr. Haumaier ordered a test kit for juvenile-onset laryngeal paralysis and polyneuropathy (JLPP) from the website of the Orthope-

*A sweet, playful Rottweiler puppy, “Rosie” was born with the neurological disease JLPP. A wheelchair cart helped support her weak rear legs and allowed her to enjoy walks in the park.*

## EARLY SIGNS OF JLPP IN ROTTWEILERS\*

- Laryngeal paralysis noted by difficulty swallowing that can result in choking or pneumonia
- Respiratory distress such as difficulty breathing when excited or during and after exercise
- General weakness and loss of coordination affecting muscle movement, causing gait abnormality, bark sound changes, and abnormal eye movements

\*Signs may appear from 3 to 4 months of age

## JLPP: A DISEASE OF MANY NAMES

The fatal neurological disease that affects young Rottweilers known today as juvenile-onset laryngeal paralysis and polyneuropathy (JLPP) has a checkered past. Not always known as JLPP, the progressive disorder was named according to the clinical signs observed by veterinary neurologists studying affected dogs.

Veterinary neurologist Dennis O'Brien, DVM, PhD, of the University of Missouri College of Veterinary Medicine, who helped identify the *RAB3GAP1* gene mutation for the autosomal recessive condition in Rottweilers and Black Russian Terriers, likens the inconsistent naming to the parable of the blind men and the elephant. "These blind men came across an elephant and gave varied descriptions based on the different parts of the elephant's body they touched. Often research is like the parable in that how we view a disease depends on what aspect of it we come across when we first see it," he says.

In the late 1990s, Dr. O'Brien along with researchers at the University of California-Davis and Utrecht University in Belgium had begun seeing young Rottweilers with spinocerebellar ataxia, or coordination problems. Post-mortem examinations of these dogs showed degeneration of their cerebellum, the part of the brain responsible for coordination, characterized by vacuolation, or fluid-filled sacs, essentially holes, in brain cells. [Lead investigator Gregg Kortz, DVM, DACVIM \(Neurology\), then at the University of California-Davis, referred to the](#)

[condition as neuronal vacuolation and spinocerebellar degeneration \(NVSD\).](#)

Years later, the first cases of affected Black Russian Terriers began to appear. "The thing that struck us were the prominent signs of a juvenile-onset laryngeal paralysis, a condition that can obstruct the airway causing suffocation, and progressive weakness due to problems with the nerves, known as polyneuropathy, so the disease became known as JLPP," says Dr. O'Brien. "We later noted that the dogs also had cataracts, which is very unusual in young dogs. When we performed a post-mortem examination on an affected dog, we also found the vacuoles seen in Rottweilers. When [these findings were published in 2015, we called the disease in Black Russian Terriers polyneuropathy with ocular abnormalities and neuronal vacuolation \(POANV\).](#) However, since the disease was already known as JLPP, that name stuck."

About the same time, other veterinary neurologists noted that Rottweilers with NVSD also developed laryngeal paralysis, progressive weakness and cataracts. "[Once we had the mutation in Black Russian Terriers, we were able to test Rottweilers to see if the same mutation was causing the Rottweiler disease,](#)" Dr. O'Brien says. "These additional features of the disease in Rottweilers were consistent with POANV described in Black Russian Terriers. Since affected Black Russian Terriers were referred to as having JLPP, the same held true for Rottweilers."

by megaesophagus, a condition in which an enlarged esophagus can cause aspiration pneumonia when food and water regurgitate into the lungs. Dr. Haumaier had begun feeding Rose from a Bailey chair, so she was sitting upright to reduce the risk of regurgitation.

"Rosie's condition was suddenly progressing fast," says Dr. Haumaier. "She was now experiencing regurgitation episodes from one to six times a day and could not swallow properly. After one of these episodes, I took her to a veterinary hospital, and then she was transferred to a specialty veterinary clinic. She had declined to a point she could not be

saved. This happened so quickly, in about two months."

## FOUNDER MUTATION LINK

In the late 1990s, veterinary neurologists in the U.S. and Europe began seeing Rottweiler puppies around 3 to 8 months of age with signs of JLPP, though at the time the disease was not identified. Tipping them off that it was a hereditary condition were the clinical signs of laryngeal paralysis and cataracts, conditions more common in older dogs.

These puppies were clumsy and had difficulty climbing stairs. The condition affected all their legs, though the rear legs were more involved.

Breathing difficulties were common, especially with exercise and excitement. Their owners reported first noticing general weakness and

ataxia, or lack of voluntary coordination of muscles, when the puppies were around 6 weeks of age.

In all the dogs, the severity of the disease progressed quickly, and the puppies were euthanized by 17 weeks of age. Although the cause was not known, it was apparent that this disease was different than other neurological conditions in young Rottweilers.

Nearly 20 years later, an autosomal recessive gene mutation was discovered for a similar juvenile-onset disease in Black Russian Terriers. "Once we had the mutation in Black Russian Terriers, we were able to test Rottweilers to see if it was the same mutation," says Dennis O'Brien, DVM, PhD, the Chancellor's Chair in Comparative Neurology at the University of Missouri College of Veterinary Medicine, who worked on the gene mutation in both breeds. "It proved to be the same mutation."

Affected dogs inherit copies of the *RAB3GAP1* gene mutation from their sire and dam, and carrier dogs are heterozygous or have only one copy of the *RAB3GAP1* gene mutation. A deletion in the *RAB3GAP1* gene affects a protein involved in membrane trafficking and causes JLPP in Rottweilers and Black Russian Terriers. The discovery of the mutation allowed for the development of a DNA test to aid in diagnosing JLPP and identifying carriers.

"It is likely the same founder mutation event was the source of the *RAB3GAP1* gene mutation in both breeds," Dr. O'Brien says. "When Stalin (Soviet Communist leader Joseph Stalin) wanted to create a guard dog capable of standing Russian winters in the 1930s, a heavy-coated Russian breed was crossed with Standard Schnauzers and Rottweilers to produce the Black Russian Terrier. The mutation was probably in Rottweilers, then got passed on to Black Russian Terriers."

A more severe neurological syndrome called Warburg Micro syn-



## A PROMISE TO 'SINNBAD'

A life-changing four and a half months living with and caring for a Rottweiler pup named “SinnBad,” who had a funny, wobbly walk and sweet, loving temperament, was not near enough time for Rottweiler lover Suzi Faulkner of Mooresville, North Carolina.

“I thought SinnBad had a hip problem,” Faulkner says. “My veterinarian had no idea what the problem was, even after running lots of tests, including magnetic resonance imaging.”

A rescue puppy, SinnBad came through Atlantic Rottweiler Rescue And Friends, a rescue organization in which Faulkner serves as president, in 2018 when he was abandoned. The rescue raised \$4,000 to fund SinnBad’s health care, only to eventually learn a \$65 genetic test for juvenile-onset laryngeal paralysis and polyneuropathy (JLPP) would have confirmed the puppy’s diagnosis and named the mysterious condition.

“I was bound and determined SinnBad would be the puppy who would beat JLPP,” says Faulkner. “The truth is you can’t beat JLPP. The best you can do is try to ensure that affected dogs live a quality life in the short amount of time they have.”

Since SinnBad, Faulkner has cared for four JLPP pups. Her longest survivor is “Remi,” now 18 months



“Remi,” now 18 months old, has JLPP.

old. One pup, named “Logan,” came to Faulkner severely affected, living only three weeks before succumbing to JLPP.

“I made a promise to SinnBad that I would never let his message die and that I would never leave behind a JLPP puppy in a shelter. I would try to give them the best possible life,” Faulkner says. “That message is to

test Rottweilers for JLPP before breeding to put an end to affected dogs being born.”



A JLPP puppy, “SinnBad” had such an impact on foster parent Suzi Faulkner that she became an advocate helping to educate others about the disease. A brochure, right, that she developed encourages breeders to test for the genetic disease.

Faulkner’s commitment to the cause led to her starting a Facebook page, “SinnBad’s Unknown Path with JLPP,” to chronicle her journey with him. Since SinnBad died, she continues the page, now with 2,400 followers. Its diary format is scripted with daily updates of Faulkner’s life with JLPP puppies. Videos and photos endear the loveable Rottie puppies to all.

Faulkner also developed an informational brochure, “SinnBadd Spread The News: JLPP Knowledge Is Power, Test - Just Do It!” The brochure is on the Facebook page, and Faulkner emails the digital file to anyone interested.

“I get a lot of breeders who ask for information because they have not heard of JLPP,” she says. “Many of them add the information to their breeder packet they give to puppy buyers.”

A disease that will never have a cure, JLPP can only be stopped by genetic testing and smart breeding practices. “I have had Rottweilers 23 years, and I absolutely love them,” Faulkner says. “My mission in life is to make breeders want to test their sires and dams and then their litters for this disease.”



drome occurs in children having the *RAB3GAP1* gene mutation. “Affected children have severe developmental delays and seizures, ocular abnormalities including congenital cataracts, and neuropathy,” Dr. O’Brien says.

## A DISEASE OF PUPPIES

A disease that occurs in young Rottweilers, JLPP affects neurological signaling that travels from the brain through nerves. In puppies born with JLPP, the vagus nerve, the longest and most complex

cranial nerve, fails to develop normally. In a normal dog, the vagus nerve signals the muscles of the voice box, creating the sound of a bark when the vocal folds vibrate as air moves over them and assisting breathing by pulling the vocal

folds aside so air can move easily into the lungs. The vagus nerve also helps to close the larynx when the dog swallows to prevent choking on food or water.

When the nerves are unable to convey messages properly, the

## BREEDING IMPLICATIONS FOR JLPP IN ROTTWEILERS

Owners or veterinarians who notice Rottweiler puppies around 3 to 4 months of age that appear generally weak and show signs of incoordination, such as gait abnormality, unusual changes in bark sounds and abnormal eye movements, should consider testing for juvenile-onset laryngeal paralysis and polyneuropathy (JLPP).

An autosomal recessive condition in which affected dogs inherit a copy of the *RAB3GAP1* gene mutation from the sire and dam, JLPP is a fatal condition with dogs typically dying months after being diagnosed as the disease progresses in severity. [JLPP is designated an optional health test for Rottweilers and is not required for them to receive Canine Health Information Center \(CHIC\) health clearance.](#) However, the American Rottweiler Club requires members to test for this disease prior to breeding. At least one parent must be clear by DNA testing or clear by parentage. Testing results must be registered with the Orthopedic Foundation for Animals (OFA) and posted on the OFA website.

[OFA provides information on its website about ordering the JLPP test](#) that is processed at the University of Missouri Small Animal Molecular Genetics Lab. OFA testing of 3,484 Rottweilers showed 84.5 percent tested normal, 15.1 percent tested carrier, and 0.4 percent tested affected.

“While these testing results do not necessarily represent the frequencies in the entire Rottweiler

breed, it shows that the mutation is not rare,” says Jerold Bell, DVM, adjunct professor of genetics at Cummings School of Veterinary Medicine at Tufts University and a genetic advisor to national parent breed clubs.

“The fact that Black Russian Terriers carry the exact same mutation indicates that it occurred in a dog ancestral to the formation of both breeds, and the mutation is therefore dispersed in the Rottweiler gene pool,” he says.

Breeders who produce affected dogs are advised not to eliminate the breeding of carriers, as this could narrow the gene pool and reduce desirable genetic diversity in the breed. “Narrowing the gene pool by not breeding carriers may inadvertently increase the incidence of other hereditary problems lurking in the bloodlines of Rottweilers that are free of the JLPP mutation,” Dr. Bell says.

Genetic testing of breeding stock combined with selective breeding provide the best approaches to ensure that two JLPP carriers are never bred together and no affected puppies are produced. “Quality carriers can be bred to non-carrier dogs and then you would replace the carrier parent with a quality non-carrier offspring,” says Dr. Bell. “In this way, breeding lines — and breed genetic diversity — are not abandoned, and testable disease liability genes can be lost in one generation.”

### GENOTYPE RESULTS FOR JLPP (AUTOSOMAL RECESSIVE INHERITANCE)

P/P Positive/Positive	Affected dogs have two copies of the mutation that causes the condition and will develop the disease.
P/N Positive/Negative	Carrier dogs have one copy of the normal gene and one copy of the mutant gene. They will not develop the disease but will pass a mutant gene on to about half of their offspring.
N/N Negative/Negative	Clear dogs have no copies of the mutant gene responsible for the condition and will neither develop the condition nor pass it on to their offspring. Clear dogs can be bred to a dog with any test result without the risk of producing affected offspring.

## ROTTWEILER BREEDERS & OWNERS CAN SUPPORT BREED HEALTH RESEARCH

The Rottweiler Health Foundation urges Rottweiler breeders and owners to become a member of the Foundation and help support research of breed health concerns. Founded in 1997, the Foundation is a non-profit organization that focuses on identifying and helping to advance understanding of diseases, defects and health conditions in Rottweilers. An annual membership fee of \$50 along with charitable donations, fundraising efforts and memorial contributions help to support and promote breed health research. A charter member of the AKC Canine Health Foundation, the Rottweiler Health Foundation has helped fund several studies in recent years, including research of tick-borne diseases, looking at the cellular processes of inflammation, developing a next-generation sequencing diagnostic platform and defining how ticks locate dogs to prevent disease; hemangiosarcoma, focusing on targeted P13K therapies and a novel mechanism to regulate cancer growth; and enhanced testing to help diagnosis the zoonotic bacterial disease bartonellosis.



muscles become weak or paralyzed. The vagus nerve is often affected first, explaining why laryngeal paralysis is generally the first sign of JLPP. The vocal folds cannot be pulled out of the way as the dog breathes. Instead, they vibrate noisily and can obstruct the flow of air into the lungs. When a dog regurgitates food or water, this can result in aspiration pneumonia.

The second longest nerve in the body, the sciatic nerve, is typically affected next. This accounts for why dogs dogs have difficulty getting up and wobble as they walk. Usually the rear legs are affected first, followed by the front legs.

Treatment for JLPP is limited. The breathing problems caused by laryngeal paralysis can be improved with surgery, but the progressive disease eventually wins over. Weakness and coordination problems become more severe, and dogs can develop problems swallowing. While a rare condition, eventually all dogs have to be euthanized.

Dr. Haumaier had hope that a total laryngectomy and tracheostomy, which reroutes the opening of the windpipe to the front of the neck away from the esophagus, a procedure performed in humans with throat cancer, could possibly help Rosie. “This might have helped Rosie by taking away the risk of aspiration pneumonia by closing off her airway, but it would not have reversed the other complications,” she says.

Reflecting on JLPP, Dr. Haumaier says, “I am thankful there is so much attention to this little-known disease. It’s good that the genetics are known, so hopefully breeders will make testing part of their program. Rosie was an inspiration. I hope her story can help to save others.” ■

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

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