

Protein Blocker Might Keep Dogs with Spinal Cord Injuries Walking

By Susan Chaney

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In just a few years, dogs with spinal cord injuries may have better mobility than most do today, thanks to a years-long collaboration and a grant from the U.S. Department of Defense.

In the early 2000s, Linda Noble-Haeusslein, Ph.D., a professor in the University of California, San Francisco, Department of Neurological Surgery and Department of Physical Therapy and Rehabilitation, teamed up with “one of the world experts,” Zena Werb, Ph.D., to study how one protein might be leading to the secondary responses that actually damage healthy tissue and lead to immobility after naturally occurring spinal cord injuries.

The duo was able to show that the protein, matrix metalloproteinase-9, has a particularly negative effect when a mouse has a herniated vertebral disk.

As a disk degenerates, the protective covering around it deteriorates as well, Noble-Haeusslein explains. “The disk is rapidly released from the covering around it and hits the spinal cord. It happens in the low part of the back, which interferes with hind-end function.” That’s the “initial insult,” as it’s known in neurological circles.

That insult is followed by release of matrix metalloproteinase-9. “I don’t think the general public realizes that the deficits you see with spinal cord injuries are not due to just the initial insult,” Noble-Haeusslein says. It’s secondary cell damage – caused by the spread of the matrix through the cord – that extends the damage.

An academic veterinarian at Texas A&M had been testing dogs coming in for spinal cord injury treatment and found that they had elevated levels of the matrix. He contacted Noble-Haeusslein to see if he could get some of the broad spectrum metalloproteinase blocker to use on some dogs, she says. “But the [National Institutes of Health] liked the idea of trying out the efficacy of this drug in the dog. If we’re right, these dogs should be better, so [the NIH] funded the purchase of the drug for a study.”

Although that study of about 120 dogs is complete, the results are not yet available, as the data is “in the hands of the statistician,” Noble-Haeusslein says.

Without intervention, the “primary injury, a mechanical insult that causes shearing and tearing,” leads to some “neurological deficit,” Noble-Haeusslein says. “They might walk funny, or they may need equipment, something like a wheelchair.”

Despite the recent completion of the first canine study, the U.S. Department of Defense is now supporting three years of study on dogs going to Texas A&M for treatment of spinal cord injuries, under the oversight of Jonathan Levine, D.V.M., an ACVIM diplomate and assistant professor in neurology at the university’s college of veterinary medicine in College Station.

He and his fellow researchers will study about 90 dogs until October 2014. The dogs are young to middle-aged with canine thoracolumbar intervertebral disk herniation, a spontaneous disease similar to acute spinal cord injury in humans. Dachshunds represent about half of the cases that are treated at Texas A&M.

“Because these injuries happen naturally, they are more diverse,” Levine explained upon receiving news of the grant. “Affected dogs are out in the environment, they’re not all the same breed, the injuries don’t happen the same way. So the diversity probably gives a little advantage exploring theories into the possible treatment of dogs and humans with SCI.”

The DOD funded the research because it may be useful in treating troops with spinal cord injuries, according to the university. It costs anywhere from \$729,000 to \$3.2 million to treat and care for a person with such an injury over his or her lifetime.

The dogs will receive one injection up to three days after the injury. “Ideally, the sooner the dogs are started on the treatment, the better,” Noble-Haeusslein says. “The main force of the protein is coming from a white blood cell called a neutracell. They start infiltrating the cord within the first three hours of the injury and peak at 12 to 18 hours,” she says.

Most scientists believe the first several days are key, she says. “After that you’re involved in wound healing. You want to block the acute injury response without blocking the healing response.”

Dogs taking part in the study are examined six weeks after the injection, Levine says, to assess the result of the treatment.

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