

New Leptospirosis Discovery!

Changes seen in pathogen's ability to survive outside a host.

JAMES FOSSE (D838-1)



Veterinary medical officer David Alt processes *Leptospira* cultures for plasmid preparation. The plasmids will contain fragments of *Leptospira* DNA and help scientists assemble its genomic sequence.

The bacterial species that commonly causes leptospirosis in cattle has lost much of its ability to survive in water.

This change, discovered by scientists at ARS's National Animal Disease Center (NADC), in Ames, Iowa, and at Monash University in Melbourne, Australia, is likely affecting the ability of this microbe, *Leptospira borgpetersenii* serovar Hardjo, to spread through the environment.

Leptospirosis is among the most widespread of zoonotic diseases, which are infections transmitted naturally from domestic or wild animals to people.

L. borgpetersenii is one of two leptospiral species associated with most cases of bovine leptospirosis worldwide, and it is responsible for most cases in North American cattle. The other species is *L. interrogans*.

“Our results suggest that *L. borgpetersenii* is now spread mainly, if not

solely, through close contact with infected animals,” says NADC microbiologist Richard Zuerner. “The research also shows that *L. interrogans* is still able to spread easily through contaminated water.”

What's the Difference?

Zuerner says that, before this study, evidence was lacking that *L. borgpetersenii* and *L. interrogans* differed in ways that would affect their survival in the environment. “Now we have a foundation for studying how the disease-transmission processes of both species differ,” he says. “It's a step toward better disease-control strategies that may include changes in farm management and vaccine design.”

There's great demand for better control of leptospirosis, in large part because current vaccines effectively guard only against infection by the serovars, or subgroups, that are used in making them. “This provides limited cross protection,” says Zuerner. “A benefit of obtaining the *L. borgpetersenii* genome sequence is that we can use it to identify proteins that may be incorporated into new, more effective vaccines.”

Leptospirosis is broadly distributed in wildlife and persists in livestock. Each serovar appears to be adapted to a particular animal species in which it causes problems with pregnancy and fertility but usually doesn't cause severe disease. For example, serovar Hardjo is less likely to cause severe infections in adult cattle—its normal maintenance host—but it can cause abortion, stillbirth, or weakened offspring.

“In contrast, when *Leptospira* infect humans, the disease ranges from mild, flulike symptoms to a potentially lethal infection resulting from pulmonary hemorrhage or organ failure,” says Zuerner.

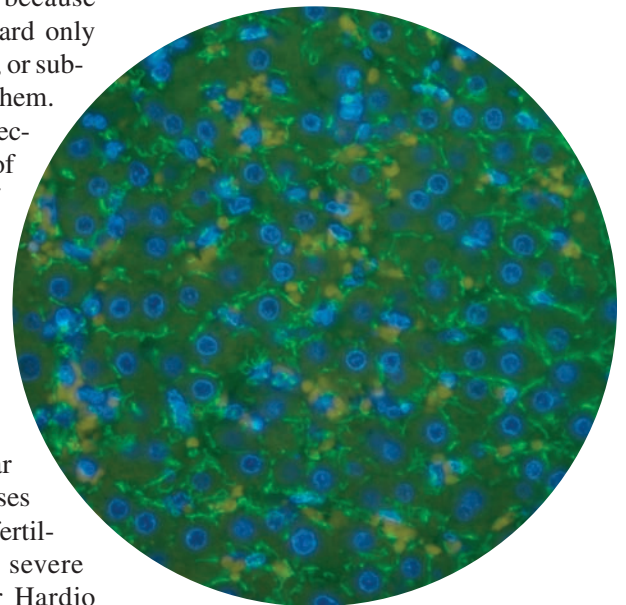
People and animals are commonly infected with *Leptospira* by exposure through water contaminated with urine from infected animals. Direct contact

with body fluids or tissue from infected animals is another common way to contract the disease.

Sequencing Opens the Door

The recent finding was the result of genomic sequencing studies of *L. borgpetersenii* conducted at NADC by Zuerner and veterinary medical officer David Alt, at Monash by scientists Ben Adler and Dieter Bulach, and at the University of Queensland's Australian Genome Research Facility under the direction of Elizabeth Kuczek. Zuerner and Bulach analyzed the data with support from Torsten Seemann, a research

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Corkscrew-shaped *Leptospira borgpetersenii* serovar Hardjo appear bright green. The bright-blue areas are nuclei of hamster liver cells. Red blood cells present in the tissue are light orange.

fellow at the Victorian Bioinformatics Consortium at Monash.

In the report describing their discovery, the researchers explained that the *L. borgpetersenii* genome is decaying.

“The species carries a large number of defective genes as compared to *L. interrogans*,” says Zuerner. “This loss of functional genes is thought to impair both the bacterium’s ability to sense changes in the environment and its capacity to acquire nutrients and survive outside a mammalian host. We concluded that *L. borgpetersenii* is evolving toward dependence on a strict host-to-host transmission cycle.”

In contrast, Zuerner says, most other *Leptospira* species can be transmitted through surface water. “This is a contributing factor to epidemics in human populations that coincide with heavy flooding, especially in underdeveloped countries with inadequate wastewater control,” he says.

Zuerner explains that while *L. interrogans* strains are also found in livestock, they’re often associated with disease occurring during seasonal flooding from chronically infected rats.

He says the initial steps involved in the evolutionary process leading to host dependence are unclear, but identifying them is important.

“If we can characterize the changes that lead to this reliance, it should help identify early events that lead to host dependence among a large variety of other bacterial pathogens,” says Zuerner.

The microbiologist, who works in NADC’s Bacterial Diseases of Livestock Research Unit, is a seasoned leptospirosis researcher. A decade ago, he developed new tests that precisely identify *Leptospira* strains from different host-animal species. That key advancement made it possible to pinpoint the source of infections from a variety of animal species.

An Outbreak in Sea Lions

In 2004, Zuerner worked with many scientists spread along the Pacific Coast

to investigate the deaths of more than 300 sea lions. NADC studies ultimately showed that the animals were infected with *L. interrogans* serovar Pomona.

“That was a notable outbreak because it killed a significant number of marine mammals, including endangered or protected species,” says Zuerner. “It also helped show how animal migration may spread leptospirosis.”

Zuerner says that the new findings with *L. borgpetersenii* may eventually have application outside of leptospirosis.

“Presumably, the mechanism that impaired its ability to survive outside the host and started it on its path toward host dependence is shared by other bacterial genera,” he says.

“It seems that an early step in the process of becoming dependent on a host

for survival is the disruption of sensory functions. If bacteria can’t differentiate between being in the host and being in water, it’s likely they’ll be ill-prepared for the challenges of living in a nutrient-deficient environment.”—By **Luis Pons**, formerly with ARS.

This research is part of Animal Health, an ARS national program (#103) described on the World Wide Web at www.nps.ars.usda.gov.

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In preparation for sequencing *Leptospira*’s genome, technician Rick Hornsby loads a 96-well plate into a machine known as a “colony picker.”