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Mad cow-like diseases linked by bacteria

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WASHINGTON, June 25 (UPI) — For more than 20 years, one scientist has ignored the conventional thinking among researchers that mad cow disease and similar disorders are caused by abnormal proteins and instead has pursued an alternative view that the culprit is a tiny, rare bacteria.

Dr. Frank Bastian, a pathologist at Tulane University in New Orleans, has encountered controversy over the years and seen his hypothesis roundly dismissed by nearly all other researchers working in this field. Nevertheless, he has stubbornly persisted in collecting data to support his hypothesis.

Now, Bastian may have uncovered the first molecular evidence of a link between chronic wasting disease — a mad-cow-like illness that afflicts deer — and scrapie, the sheep equivalent.

The finding, which has not been corroborated, could help answer the long-standing question of the origin of chronic wasting disease, which seemed to have come out of nowhere in the 1960s and has been spreading ever since across deer and elk herds in the midwestern United States and into Canada.

Bastian said his discovery also could force a paradigm shift in thinking about the cause of these disorders and perhaps open the door to treatments and vaccines for their human versions: Creutzfeldt Jakob disease and variant CJD, the latter of which has been linked to the consumption of mad-cow-infected meat.

"If I'm right on this ... we should have a vaccine, we should have a therapy," Bastian, medical director of the CJD Diagnostic Center at Tulane, told United Press International.

To date, there is no therapy to prevent or cure either CJD, vCJD or the other, mad-cow-like disorders, which are always fatal and are known collectively as transmissible spongiform encephalopathies, or TSEs.

In a study published in the August issue of the journal *Experimental and Molecular Pathology*, Bastian reported evidence of bacteria called *Spiroplasma mirum* in deer brains afflicted with chronic wasting disease, sheep brains afflicted with scrapie, and human brains afflicted with CJD. There was no trace of the bacteria detected in corresponding brains that were not diseased.

Comparing the results from the different species, Bastian found that some *Spiroplasma* strains seen in scrapie–infected sheep brains matched strains found in deer brains infected with CWD.

As Bastian and his co–authors wrote in the journal, the findings imply "the CWD epidemic may have originated from scrapie infection."

Bastian cautioned, however, that the link is not yet proven. "At this stage, we don't know for certain — but it's surely suggestive," he said.

Before Bastian's bacteria hypothesis can progress to therapies, it first must pass a barrage of resistance from other TSE scientists, most of whom have accepted the prevailing hypothesis that misfolded proteins called prions are the causative agent.

One scientist, who did not wish to be identified but who is considered one of the world's foremost experts on TSEs, told UPI, "If I were you, I would stay away entirely from anything having to do with *Spiroplasma*."

The scientist's caution stemmed from an unpublished study that took place approximately five years ago. At the time, Bastian allegedly was unable to distinguish infected scrapie brains from normal brains by testing for the *Spiroplasma* bacteria.

Bastian disputed that assessment, however, and said he correctly identified infections in 80 percent of the samples.

Despite Bastian's contention, the negative view of the study — which was conducted in Dr. Robert Rohwer's lab at the Veterans Administration hospital in Baltimore — has circulated among TSE scientists and perhaps has overshadowed the data Bastian has accumulated since then in support of his bacteria hypothesis.

Asked to comment on Bastian's recent research, Rohwer brought up the unpublished study and told UPI, "We saw no evidence of any bacteriological contamination of these brains."

Rohwer added, "I really question the quality of his research, and I think it's unfortunate that Dr. Bastian continues to ignore his own data. He's not convinced, but I certainly am, that there's nothing to his story."

Bastian claimed that Rohwer's lab technician found evidence of the bacteria in one of the samples, but Rohwer did not mention this when he later made a presentation to National Institutes of Health officials dismissing the bacteria hypothesis.

Bastian said shortly after the test Rohwer was awarded a \$2 million NIH grant while Bastian did not receive any funding.

"I think (Rohwer is) totally dishonest," Bastian said, charging that Rohwer attempted to dismiss his hypothesis to get a grant from the NIH.

"If Rohwer has anything to say about that study, he should publish the data rather than making unsupported statements," he said.

Bastian also noted his latest study lends credence to the presence of the bacteria in diseased brains. Spiroplasma DNA was detected in eight of 10 scrapie samples, six of seven CWD samples and two of two CJD samples, he said.

Another reason Bastian's idea meets such heavy resistance is Spiroplasma bacteria as a group were only relatively recently discovered. The organisms, which are small even by bacteria standards, escaped detection until the 1970s when they were first recognized as being the cause of a few plant and insect diseases.

Spiroplasma mirum, the agent involved in Bastian's hypothesis, is carried by rabbit ticks and is known to cause cataract disease in suckling mice.

Although his hypothesis is controversial, Bastian is not without his supporters.

"I've been following his work for a while and I think he's onto something," said Dr. Jeanne Drisko, a clinical assistant professor of alternative medicine at the University of Kansas Medical Center in Kansas City.

Drisko also noted that in 2001, NIH awarded Bastian a three–year grant, which means it was reviewed and approved by experts in the field.

"That's not an easy thing to do," so it is an indication there is some evidence to support his idea, she told UPI.

In addition, Bastian's studies, including his latest research, have been published in peer–reviewed scientific journals.

"My impression is no one has looked at (Bastian's Spiroplasma hypothesis) carefully," Drisko said. "It's almost a knee–jerk response. There's been so many people saying there's no evidence of this, so instead of looking at the quality of the evidence he's providing, they simply dismiss it."

Several researchers contacted by UPI to review Bastian's latest article either dismissed the bacteria idea outright or did not comment.

Other scientists gave Bastian's new data a positive review but remained skeptical about his overall hypothesis, which was not surprising because the prion hypothesis is nearly dogma among experts in this field.

There is little evidence, however, supporting the central tenet of the prion view: that misfolded prions have the capability to infect cells and cause the brain destruction typically seen in TSEs.

Dr. Adriano Aguzzi, a pathology professor at the University Hospital in Zurich, Switzerland, pointed out in an article in the *Journal of Experimental Medicine* last year that much of the evidence surrounding prions is contradicted by other studies. As Aguzzi put it, the prion has been "reported to do almost everything, including the opposite of everything."

Under Bastian's concept, *Spiroplasma* bacteria use the normal prions, which occur on the outer surface of cells, to help them gain entry. The misfolding of the prions actually occurs on the inside of the cells and is merely a result of the infection, not the cause.

Bastian's idea was bolstered recently by a study done by Japanese researchers. In a 2003 report in the *Journal of Experimental Medicine*, they discovered another bacteria called *Brucella* depends on the normal prion protein to cause the disease brucellosis, which strikes both livestock and humans.

Bastian also showed — in research published in the *American Journal of Pathology* in 1984 — that *Spiroplasma* are capable of producing in suckling rats the type of brain destruction seen in TSEs.

Still, other researchers were not willing to accept the bacteria as the cause and said that has not been demonstrated yet.

"Although this (latest) work shows an association of the presence of *Spiroplasma* DNA, this work does not demonstrate causality," said Beth Williams, a veterinarian at the University of Wyoming in Laramie, who is credited as the first scientist to identify chronic wasting disease as a TSE disorder.

"Thus, it is not a logical extension, in my opinion, of these data to say" that scrapie may have given rise to CWD, Williams told UPI. "But I believe in keeping an open mind."

Linda Detwiler, a former U.S. Department of Agriculture veterinarian and expert on scrapie and other TSEs, said Bastian's data suggesting a link between CWD and scrapie is interesting because researchers still do not have any solid answers for how CWD emerged.

"He may be onto something," Detwiler told UPI, but she cautioned that further confirmation of Bastian's data is needed before this hypothesis was accepted.

Detwiler's hesitation stems from a study Bastian did with the USDA a couple of years ago, in which he was unable to identify correctly whether sheep brain samples were or were not infected with scrapie.

She was not ready to dismiss his hypothesis completely, though, and said his latest results were intriguing.

"I would hope this would spur somebody to relook at this," she said.

In his defense, Bastian said he correctly identified two out of five scrapie infected brains in the USDA study using a less sensitive technique called polymerase chain reaction. When using a more sensitive method called DNA sequencing, he said he finds evidence of the bacteria in nearly all the infected brain samples he examines, but not in any of the non–infected brains.

He concedes evidence showing the bacteria causes these diseases still needs to be collected and plans to conduct future studies with mice lacking the prion gene to help support his hypothesis. If his idea is correct, the mice should not become infected by the Spiroplasma.

One missing factor that would improve therapy for CJD and vCJD is a test that can detect infection before symptoms occur, he said. Research is planned to develop a test that can detect the abnormal prions in blood, but if Bastian's idea is correct, it would be too late, because by then the brain already would have begun degenerating. Bastian said he knows of no one working on a test to detect Spiroplasma in the blood.

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