# Study suggests that early detection is possible for prion diseases

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A fast test to diagnose fatal brain conditions such as mad cow disease in cattle and Creutzfeldt-Jakob disease in humans could be on the horizon, according to a new study from National Institutes of Health scientists. Researchers at NIH's National Institute of Allergy and Infectious Diseases (NIAID) have developed a highly sensitive and rapid new method to detect and measure infectious agents called prions that cause these diseases.

"Although relatively rare in humans and other animals, prion diseases are devastating to those infected and can have huge economic impacts," says Anthony S. Fauci, M.D., director of NIAID. "Scientists have promising concepts for developing therapies for people infected with prion diseases, but treatments only are helpful if it is known who needs them. This detection model could eventually bridge that gap."

Prion diseases are primarily brain-damaging conditions also known as transmissible spongiform encephalopathies. They are difficult to diagnose, untreatable and ultimately fatal. A key physical characteristic of these diseases is dead tissue that leaves sponge-like holes in the brain. Prion diseases include mad cow disease, or bovine spongiform encephalopathy in cattle; scrapie in sheep; Creutzfeldt-Jakob disease in humans; and chronic wasting disease in deer, elk and moose. For more information about NIAID research on prion diseases, visit the NIAID Prion Diseases portal.

Currently available diagnostic tests lack the sensitivity, speed or

quantitative capabilities required for many important applications in medicine, agriculture, wildlife biology and research. Because prion infections can be present for decades before disease symptoms appear, a better test might create the possibility for early treatment to stop the spread of disease and prevent death.

Now, a blending of previous test concepts by the NIAID group has led to the development of a new prion detection method, called real time quaking induced conversion assay, or RT-QuIC. This approach is described in a paper now online in the open-access journal *PLoS Pathogens*. Byron Caughey, Ph.D., led the study at NIAID's Rocky Mountain Laboratories in Hamilton, Mont.

Scientists believe disease-causing prions are abnormal infectious clusters of prion protein molecules. Normally, prion protein molecules are unclustered, harmless and found in every mammal. In a process not fully understood, abnormal infectious clusters develop and can convert normal prion protein molecules into the infectious prion form; these clusters tend to gather in the brain. Ongoing replication allows the disease to spread and damage the brain.

Infectious prions also are found outside the brain, in saliva, blood, breast milk, urine and the nasal and cerebral spinal fluids used in the study. But the concentrations of infectious prions in these bodily fluids are so low that scientists, clinicians and wildlife biologists have not been able to measure them for routine purposes.

The new assay can detect when miniscule amounts of infectious prions initiate the conversion of large amounts of normal prion protein into an abnormal form in test-tube reactions. By comparing the extent to which different samples can be diluted and still initiate conversion, scientists can estimate the relative infectious concentrations in the original samples. In their study, the NIAID scientists used RT-QuIC to detect

prion infections in deer known to have chronic wasting disease and sheep known to have scrapie. In scrapie-infected hamsters, they found surprisingly high levels of prions in nasal fluids, pointing to such fluids as possible sources of contagion in various prion diseases.

Along with optimizing their existing applications in the laboratory, Dr. Caughey and his colleagues are teaming up with a number of other laboratories around the world to extend the practical and scientific applications of RT-QuIC. Related testing approaches might also aid the diagnoses of similar neurodegenerative protein diseases, such as Alzheimer's, Huntington's and Parkinson's diseases.

**More information:** J Wilham et al. Rapid end-point quantitation of prion seeding activity with sensitivity comparable to bioassays. PLoS Pathogens 6(12): e1001217. DOI:10.1371/journal.ppat.1001217 (2010).

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