# New test detects early stage of wasting disease in cattle

March 20 2017

Researchers at the National Institute for Mathematical and Biological Synthesis (NIMBioS) at the University of Tennessee, Knoxville, have identified a more sensitive test for detecting the early stages of paratuberculosis, a fatal disease that plagues dairy herds and causes an estimated annual loss of up to $250 million to the US dairy industry.

Current methods of testing for the presence of the bacteria that cause the disease often misdiagnose animals in the early stages of the disease, which has no cure. Infected animals produce less milk, have fertility problems, and must be culled. In the U.S. it is estimated that 20 percent of dairy herds and 8 percent of the beef herds contain at least one animal infected with the disease, and that 68 percent of farms are contaminated with the pathogen that causes paratuberculosis.

Transmission occurs by ingestion of manure-contaminated food and pastures or by colostrum passed from an infected dam to a calf. The disease usually manifests two to three years after the initial infection, but in some cases, can take up to 10 years before it becomes apparent. During this time, infected animals shed the bacteria, putting the health of the entire herd at risk.

Currently, detection of the pathogen, such as fecal culture test, is the gold standard for diagnosing animals that are shedding the bacteria and for characterizing the stage of the disease, especially in advanced stages.

However, the research, published today in Nature's *Scientific Reports*,

found that the fecal test could not reliably predict persistent infections or early stages. Detection of diseased animals in the subclinical stage of infection is difficult because these animals typically excrete the bacteria in low numbers and have not yet developed antibodies to the bacteria that could be detected.

"Shedding and potential transmission could occur well before a fecal test yields positive results, so what's needed are other disease predictors, especially at the early stages of infection," said lead author Gesham Magombedze, who conducted the research while at postdoctoral fellow at NIMBioS. Magombedze is now an assistant professor and an assistant investigator at the Baylor Research Institute in Dallas, Texas.

Using a suite of mathematical models and statistical simulations, the researchers determined that a test based on a type of immune cells called macrophages produces more reliable diagnoses.

"The macrophage based assay could be a better marker in the diagnoses of paratuberculosis infections, especially in slow or non-progressing infections and also in cases that progress to advance diseases rapidly," Magombedze said.

The immune response against the pathogen is complex and not currently well understood. Current tests that use immune responses are used most effectively to predict disease outcome or disease status at advanced stages, the researchers said.

The researchers recommended that specifically designed experiments be conducted to test the use of the new macrophage based assay.

"Controlling paratuberculosis is important not only from an agricultural perspective, but also in terms of public health, as the pathogen has been a suspected cause of Crohn's disease in humans," said co-author

Shigetoshi Eda.

Research has suggested an association between the bacterium in paratuberculosis to Crohn's disease in humans, a serious inflammatory bowel disease that affects the lining of the digestive tract. However, there is some controversy as to whether the link is causal.

**More information:** Magombedze G, Shiri T, Eda S., Stabel JR. 2017. Inferring biomarkers for Mycobacterium avium subsp. paratuberculosis infection and disease progression in cattle using experimental data. *Scientific Reports*.

Provided by National Institute for Mathematical and Biological Synthesis