Carrier status matters in foot-and-mouth disease

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Foot-and-mouth disease virus (FMDV) is believed to be one of the most contagious pathogens of animals in its acute form; however, there is still controversy over whether it is transmissible from asymptomatic, long-term carriers. Despite the lack of evidence for transmission by direct contact with FMDV carrier cattle, there is demonstrable contagion associated with these animals, according to a new study published in the journal *mSphere*. The findings impact the way countries manage foot-and-mouth disease (FMD), a viral disease of livestock with substantial impact on agricultural production and subsistence farming on a global scale.

"An outstanding question in the FMD research world is 'do carrier animals ever transmit the virus?' There is this conventional wisdom that they do not matter. We performed this study to see if, under slightly contrived conditions, we can show that carriers will transmit foot-and-mouth disease to naïve-unexposed animals, and the answer was 'yes'," said Jonathan Arzt, Veterinary Medical Officer at the Foreign Animal Disease Research Unit, United States Department of Agriculture/Agricultural Research Service (USDA/ARS) Plum Island Animal Disease Center, Orient Pt, New York. "Before this study, we questioned the legitimacy of the concept that there is a threat from these animals, but now we have a better vision that it is true."

Control and eradication of FMD have been complicated by the existence of a persistent, subclinical, phase of infection in ruminants. To prevent the spread of FMD and minimize trade impacts, countries that are FMD-

free, such as North America, Europe, and Australia, euthanize these so-called carrier animals, even though the benefit of killing them is unclear.

In the new study, the investigators from USDA/ARS and the Technical University of Denmark (DTU-Vet) exposed susceptible cattle and pigs to oropharyngeal fluid or tissues harvested from persistently infected cattle. These inoculated cattle developed clinical FMD of similar severity as animals that had been infected with a high-titer inoculum. In contrast, pigs exposed via intra-oropharyngeal inoculation of the same fluid, or by ingestion of the infected tissues harvested from the same cohort of persistently infected cattle, did not develop FMD.

The new research demonstrates that countries that are FMD-free need to continue to cull carrier animals until better products are developed to justify "vaccinate-to-live" strategies. "There is this perception by countries that carrier animals have residual contagion, and if we don't go around and euthanize all these animals, the disease is going to spread," said Carolina Stenfeldt, DVM, Ph.D., a visiting scientist at the USDA's Foreign Animal Disease Research Unit, who conceived the new study. "Unfortunately, this study confirms that is at least, in part, true. I would rather be giving the world evidence that we don't have to euthanize those animals, but the reality is right now if we don't, then we are missing FMDV."

The study suggests that FMDV carriers may be relevant to the epidemiology of this disease in FMD-endemic regions, which includes Asia and Africa, despite the prevalent conventional wisdom that carriers do not matter in the field. "This is the first study that unambiguously demonstrates FMDV contagion in carrier cattle," said Dr. Arzt. "Clearly, we need better vaccines and products that are going to prevent the carrier state."

The 2001 FMD outbreak in the United Kingdom and continental Europe

affected approximately 10 million animals and cost an estimated $14 billion.

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