Variant of mad cow disease may be transmitted by blood transfusions, according to animal study

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Blood transfusions are a valuable treatment mechanism in modern medicine, but can come with the risk of donor disease transmission. Researchers are continually studying the biology of blood products to understand how certain diseases are transmitted in an effort to reduce this risk during blood transfusions. According to a study in sheep prepublished online in *Blood,* the official journal of the American Society of Hematology, the risk of transmitting bovine spongiform encephalopathy (BSE, commonly known as "mad cow disease") by blood transfusion is surprisingly high.

BSE is one of a group of rare neurodegenerative disorders called transmissible spongiform encephalopathies (TSEs), and there is no reliable non-invasive test for detecting infection before the onset of clinical disease. In addition to BSE, these diseases include scrapie, a closely related disease in sheep, and Creutzfeld-Jakob disease (CJD) in humans, which causes neurological symptoms such as unsteadiness and involuntary movements that develop as the illness progresses, rendering late-stage sufferers completely immobile at the time of death.

A new variant of CJD (termed vCJD) was recognized in the United Kingdom in the mid-1990s, apparently as a result of the transmission of BSE to humans. Because the symptoms of this disease can take many years to appear, it was not known how many people might have been infected, and without a reliable test for identifying these individuals,

clinicians were very concerned that the infection could be transmitted between people by blood transfusion or contaminated surgical and dental instruments. As a result, costly control measures were introduced as a precautionary measure to reduce the risk of disease transmission, although at the time it was unclear whether there really was a significant risk or whether the control measures would be effective. This sheep study sought to better understand how readily TSEs could be transmitted by blood transfusion in order to help develop more targeted controls.

"It is vitally important that we better understand the mechanisms of disease transmission during blood transfusions so we can develop the most effective control measures and minimize human-to-human infections," said Dr. Fiona Houston, now a Faculty of Veterinary Medicine, University of Glasgow, UK, and lead author of the study.

The nine-year study conducted at the University of Edinburgh compared rates of disease transmission by examining blood transfusions from sheep infected with BSE or scrapie; the BSE donors were experimentally infected, while the scrapie donors had naturally acquired the disease. While scrapie is not thought to transmit to humans, it was included as an infection acquired under field conditions, which could possibly give different results than those obtained from experimentally infected animals. Because of the similarity in size of sheep and humans, the team was able to collect and transfuse volumes of blood equivalent to those taken from human blood donors.

The outcome of the experiment showed that both BSE and scrapie could be effectively transmitted between sheep by blood transfusion. Importantly, the team noted that transmission could occur when blood was collected from donors before they developed signs of disease, but was more likely when they were in the later stages of infection. Of the 22 sheep who received infected blood from the BSE donor group, five showed signs of TSEs and three others showed evidence of infection

without clinical signs, yielding an overall transmission rate of 36 percent. Of the 21 infected scrapie recipients, nine developed clinical scrapie, yielding an overall transmission rate of 43 percent.

Investigators noted that the results were consistent with what is known about the four recorded cases of vCJD acquired by blood transfusion in humans. In addition to the stage of infection in the donor, factors such as genetic variation in disease susceptibility and the blood component transfused may influence the transmission rate by transfusion in both sheep and humans.

"The study shows that, for sheep infected with BSE or scrapie, transmission rates via blood transfusion can be high, particularly when donors are in the later stages of infection. This suggests that blood transfusion represents an efficient route of transmission for these diseases," said Dr. Houston. "Since the results are consistent with what we know about human transmission, the work helps justify the control measures put in place to safeguard human blood supplies. It also shows that blood from BSE- and scrapie-infected sheep could be used effectively in non-human experiments to answer important questions, such as which blood components are most heavily infected, and to develop much-needed diagnostic tests."

Source: American Society of Hematology