

JANUARY 10, 2002

## Researchers Assess Risk of Mad Cow Disease in Sheep

Although a great deal of uncertainty exists about whether bovine spongiform encephalopathy (BSE), also known as mad cow disease, can be transmitted from cattle to sheep, researchers have developed a mathematical model to assess the health risks of humans contracting BSE from sheep. The model also takes into consideration the effects protective measures would have on transmission of BSE from cattle to sheep.

The newly developed model indicates that if BSE infects sheep in Great Britain, the current health risk to humans, although low, is likely to be greater than that of contracting BSE from cattle – largely reflecting the more stringent control measures in place that protect against cattle BSE. The researchers said, however, that any risk could be greatly reduced by regulations that limit the age at which sheep are slaughtered and further restrictions on the use of animal products in feed.

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Howard Hughes Medical Institute international research scholar Neil M. Ferguson and colleagues at the Imperial College of Science, Technology and Medicine in London published the model and discussed their interpretation of the initial results in an online article in the January 10, 2002, *Nature*.

According to Ferguson, sheep have been infected with BSE in the laboratory by feeding them brain material from infected cattle. However, a recently completed attempt to detect the disease in the sheep flock failed due to contamination. Nevertheless, given the possibility that sheep might transmit the disease, he and his colleagues had been commissioned by the British government Food Standards Agency to develop a model to guide research

and policy-making.

“I should emphasize that we weren’t asked to evaluate the probability that BSE has gotten into the sheep flock — although with the current basis of knowledge there’s no reason to rule out that possibility,” said Ferguson. “Rather, we were commissioned to develop a risk assessment of the potential consequences should infectivity of the sheep flock exist.”

The scientists’ model aimed to explore three major elements – how many sheep might have been infected through consumption of tissue from infected cattle; the likelihood of spread of the disease through sheep flocks; and how the age of the infected sheep might affect the risk to humans of contracting the human version of BSE, called variant Creutzfeldt-Jakob disease (vCJD).

Central to the model, said Ferguson, is an infectiousness profile of BSE in sheep that was developed based on data from other researchers who studied scrapie, a disease similar to BSE that affects sheep. The infectiousness profile postulates that infectivity depends on the age of the sheep and the tissue involved.

“A critical issue is that infectivity really begins to grow to significant levels in the animals about twelve months after infection,” said Ferguson. “Thus, if animals are under twelve months old when they are slaughtered – which is the case for most sheep – then they pose less of a risk to humans.”

Ferguson and his colleagues tested their model by running it using three representative scenarios ranging from optimistic to worst-case. In the most optimistic scenario, the disease would not spread beyond a flock, and in the worst-case scenario, the disease would spread to become a self-sustaining epidemic.

“Our analysis indicates that, on the basis of even the very limited current data, we can just about rule out a very large epidemic of BSE in sheep,” said Ferguson. “We believe that this means that any historical exposure of the human population to BSE infectivity from sheep was perhaps a hundred times lower than the scale of the epidemic in the cattle population.”

Although the risk of infection from sheep might be low, Ferguson said it would be higher than the current risk of infection from cattle, because of the stringent measures taken to protect the population from infection from cattle. He emphasized that two protective measures could greatly reduce even that low risk.

“Since younger sheep would have only recently been infected, they would have a much lower burden of infectious material in their tissues than older animals,” said Ferguson. “Thus, regulations requiring slaughter of animals when young would reduce the risk of infection,” said Ferguson.

“Secondly, a total ban on the use of all internal organs in feed products would reduce the risk even further, with a total reduction from both steps of up to 90 percent,” he said.

Ferguson cautioned, however, that a cost-benefit analysis of these protective measures would have to be taken into account before they were implemented. He emphasized that for the model to be useful in the future, the researchers will have to depend heavily on accurate, large-scale screening of sheep flocks to determine whether BSE infection does indeed exist.

“Also, much research needs to be done on how infectivity develops through time and how BSE or scrapie might transmit from animal to animal,” he said. “We know it happens, but we know very little about the detailed mechanics of transmission.”

Regarding the estimated health risk to humans of contracting vCJD from cattle, Ferguson emphasized that the uncertainty remains quite broad. Human deaths over the next 80 years caused by BSE from cattle could range from 50 deaths to 50,000, concluded the scientists. Adding the potential deaths from sheep under the worst-case scenario would increase mortality to 150,000 over that period.

“However, this worst-case scenario is the only one in which including sheep has more than a negligible effect,” said Ferguson. “And that scenario is unlikely and very pessimistic, although it can’t be excluded.”

The current model represents only a foundation for future efforts, Ferguson said. “This model represents a first pass, and the aim of this effort was largely to put the methodological framework in place,” he said. “We hope to refine these measures considerably and make the risk estimates more precise as we feed in results from screening studies and new experimental findings about the disease.”