

TOPIC #2: Prions as Infectious Agents

Background:

Bovine spongiform encephalopathy (BSE) or “mad cow disease” was linked to a variant of Creutzfeldt-Jakob disease (CJD) in humans. This association had major implications in the United Kingdom where there have been over 160,000 cases of BSE. Sporadic cases of BSE may also occur in the United States, but firm evidence for this is still lacking. Both BSE and CJD are believed to be transmissible spongiform encephalopathies (TSE). This group of infectious agents are extremely resistant to inactivation and are thought to consist only of a normal host protein (“prion”) which has been post-translationally altered. Although some investigators still believe that TSEs could be caused by a conventional virus, most scientists now believe that prions which lack either DNA or RNA can cause this type of disease. It is now believed that most of the cattle with BSE were infected by the consumption of animal feed that was contaminated with the carcasses of sheep infected with a scrapie agent (a TSE of sheep). There is very compelling evidence that the infectious agent responsible for BSE can be transmitted to humans by the consumption of contaminated beef and dairy products.

Discuss the background and the major issues surrounding this BSE. How good is the link between BSE and CJD? What is the scientific evidence that suggests that a TSE either can or cannot be transmitted from one species to another? What evidence is currently available to suggest that BSE may already have been transmitted to the human population in the UK? Discuss what steps should be taken to prevent the future transmission of BSE (or scrapie) to humans in the UK and in the United States.

Starter References:

Taylor, D.M. (2002). Current perspectives on bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease. *Clinical Microbiology & Infection*. **8**:332-339.

Collee, J.G. and Bradley, R. (1997) BSE: a decade on - Part I. *The Lancet* **349**: 636-641.

Collee, J.G. and Bradley, R. (1997) BSE: a decade on - Part II. *The Lancet* **349**: 715-721.

Additional References:

Prusiner, S.B. (1996) Prions. Selected pages from Chapter 37 in *Fundamental Virology*, Third Edition, edited by B.N. Fields, D.M. Knipe and P.M. Howley, et al.

Legname, G. et al., (2004). Synthetic Mammalian Prions. *Science* **350**: 673-675.

Review Points

Because of the nature of small group discussions, we expect (and hope) that each group will cover slightly different aspects of each topic. In order to make sure that key aspects of each topic are covered by all groups, please make sure that the discussions in your group includes the following points. It is from these points that exam questions will be drawn.

Topic #2 Prions as Infectious Agents

- Be sure to understand the “infectious nature” of the prion in transmitting disease and how it acts catalytically to re-fold normal proteins to an altered form.
- What is the difference between CJD and nvCJD?
- Even though Koch’s postulates have not been formally satisfied (in humans) linking consumption of BSE tainted meat to nvCJD, the epidemiological link is compelling and is supported by some diagnostic data.
- There does exist clear data showing that spongiform encephalopathies can be transmitted across species lines, BUT in general these routes of transmission are much less efficient than intra-species transmission.
- There has been a lot of concern about the safety of the blood supply. Be sure the group discussion touches on the fact that the mode of transmission of nvCJD is not clear: beef muscle does not seem to contain much prion material at all, and the transmission would be most likely due to meat tainted with CNS material.
- Make sure the group touches on the known human diseases that are linked to prions (CJD and Kuru).