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BSE/TSE TRANSMISSION RESEARCH

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The epidemic of bovine spongiform encephalopathy (BSE) in the United Kingdom which began in 1986, is declining in incidence each year. This is evidenced by the number of new cases diagnosed annually. Though cases have occurred in several other EU countries outside the UK boundaries, the total number of new cases globally have likewise been declining. Surveillance data published illustrates an annual decline beginning in 1993. The association of the variant form of Creutzfeldt-Jakob Disease (vCJD) with BSE in 1996 has resulted in considerable consternation, fear, prediction of epidemic and hypothesis for the transmission of the causative agent both inter and intraspecies. The first onset of illness in the first case of vCJD occurred in 1994. Through the end of 2000, there have been 91 confirmed or probable cases of vCJD, with the number of cases of onsets in 2000 well below any previous years total (three).

As has been referenced so many times the exact nature of the infectious agent is unclear at this time. It is still being debated. Thus the exact mechanism of transmission has defied the ability to meet all of Koch's Postulates traditional to the scientific process of describing cause and effect for given diseases. Studies to describe transmission are complex, extremely expensive and due to the associative long incubation periods are long term projects. North American researchers have not had the opportunity to use the BSE causative agent identified in cattle in the UK as a research tool. The scrapie agent and laboratory animal models have comprised the research base. Such models have likewise been used in the UK to expedite the time lapses and costs for conducting BSE research. The human element of vCJD precludes definite transmission determinations, relying instead on retrospective demographics, social and personal habits associative with the prolonged development of symptoms and extended illnesses and post mortem diagnosis. Laboratory studies have been convincing to establish a BSE/vCJD link by showing that the pathologic agent isolated from BSE-infected cattle and human cases of vCJD have identical, distinctive biological and molecular features. It has not conclusively been

established that any transmission has resulted from the oral consumption of beef. The hypothesis is the most prominent but when described the words of "appears to have been" "probably resulted" "could have occurred" and "perhaps" are the caveats used to detail the possible transmission sources. Muscle has however never been reproductively shown to contain the infectious agent in any form of spongiform encephalopathy.

TSE studies of transmission have been heavily oriented using parenteral inoculations especially intracranial. Experiments that are essential for determining medical and surgical procedures, but care should be used in extrapolating parenteral inoculation research as being applicable to the oral route of exposure. It should also be noted that the primary base of research has been conducted using raw nervous system tissue when in actuality food or feed ingredients are heat processed. Research has shown that heat does not destroy the infective agent but does lower its infectivity by a number of log reduction factors.

ORAL CHALLENGES – BSE TO CHICKENS

Dr. Danny Mathews — The Veterinary Laboratories Agency, Weybridge, UK, has reported (USDA/ARS, BSE Workshop Meeting – March 15, 2001) that studies incorporating intracranial, intraperitoneal and the oral inoculation of BSE infected brain stem into chickens shows no transmission from either inoculation route. Inoculated chickens were taken to a 57-month endpoint with no infectivity in tissues at endpoint. The parenteral challenge consisted of 50 micro ml intracranial and 1 ml intraperitoneal. Male chickens that showed any "motor disturbance" following inoculation were sacrificed and tissues sub-passaged back to chickens looking for any subclinical form of disease. Sub-passage in mice was also attempted and is complete and negative. The oral challenge consisted of 5 grams given by oesphageal tube into the crop at 4, 5, and 6 weeks. Again no infectivity was found in tissues assayed at endpoint.

ORAL CHALLENGES – BSE TO PIGS

The Veterinary Laboratories Agency, Weybridge, UK has reported that pigs receiving an oral challenge of 400 grams of BSE infective brain stem material three different times were sacrificed over a2 to 7 year period with no infectivity in assayed tissues at 2 or 7 years. Titration studies are currently in progress.

ORAL CHALLENGE – SCRAPIE TO CATTLE

Dr. Randal Cutliff, USDA/ARS Ames Iowa and his colleagues inoculated 34 calves in 1992 either intracranial or orally with meat and bone meal and tallow from rendered material derived from scrapie positive sheep. The infected sheep were derived from multiple infected flocks and processed using standard rendering processes. There were no definitive transmission evidence in any of the orally inoculated cattle following an 8-year observation period. The last remaining animal was recently sacrificed. This oral exposure experiment is currently being prepared to be published in a peer reviewed journal manuscript.

ORAL CHALLENGE – CWD TO CATTLE

Dr. Janice Miller, USDA/ARS has reported that studies are in progress that initiated in September 1997 that involves the inoculation of 26 calves (13 intracranial and 13 orally) with CWD (Chronic Wasting Disease) tissues from infected mule deer. Three of each inoculated groups were sacrificed at 24-26 months and all were histopathologic negative for prion protein. All remaining animals (20) are healthy and are to be observed for 3-4 more years.

ORAL CHALLENGE – SCRAPIE TO CATTLE

Dr. Janice Miller, USDA/ARS Ames, Iowa, has also reported on a companion experiment to that of rendered scrapie tissue that involved the inoculation of 34 calves with in rendered scrapie positive brain material either intracranial or orally. Oral inoculation consisted of the administration of 5 ml into 17 calves. All 17 remained unsymptomatic. Eight were sacrificed at 1 year post inoculation and 9 observed for up to 8 years. All were negative for PrP^{sc}. Intracerebal inoculations resulted in 9 animals developing Central Nervous System (CNS) signs and positive reaction to the Western Block test; a test to screen sheep for the presence of scrapie.

SUMMARY

Oral transmission of the TSE agent based on research cannot be compared directly to that of other parenteral inoculations or exposures. It is difficult to evaluate the cause and effect relationships unless exposure route is considered. Research has been limited compared to the importance it commands. The entire subject of the TSE's are complex, have no analogies to any other infective agents or diseases and defy normal research procedures. Studies involving their transmission have been very difficult to conduct, replicate and interpret. This inference is not uncomplimentary to the important work accomplished or in progress but the recognition of the challenge that the TSE complex presents. This document provides research references to illustrate that the transmission of the TSE agents is receiving some attention and the research should merit review. Additionally it illustrates that the oral route provides an enhanced safety factor. This coupled with the fact the US and Canada in the presence of an intensive, scientifically developed and implemented surveillance program has not identified BSE in the North American cattle population knowledge that the cooking process (food preparation and rendering) lowers the risk of oral transmission of the TSE agents below that of research conducted with unprocessed tissues provides an additional layer of assurances. The further assurance that via the regulatory process, certification programs and compliance demands accompanying the "Ruminant to Ruminant" ban places the countries at the lowest potential risk since the first report of BSE.

**The views expressed and the interpretations made are not necessarily those of or endorsed by FPRF. The material is the result of consultation and interpretation with those researchers referenced within the text.*