BOVINE SPONGIFORM ENCEPHALOPATHY

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The epidemic of Bovine Spongiform Encephalopathy (BSE) which has affected British cattle since the mid 1980s is now abating. This is a direct result of the ban on feeding ruminant derived protein to cattle which was introduced in 1988, the delayed effect being simply a reflection of the long incubation period of the disease. There is an apparent lack of lateral or maternal transmission, and this appears to afford the opportunity to achieve total eradication eventually .However, this will depend upon enforcing scrupulous measures to ensure that meat and bone meal is excluded consistently from cattle diet.

The transmissible degenerative encephalopathies (TDE) form a group of unusual, fatal neurological diseases of animals and humans caused by unconventional but uncharacterized transmissible agents. The only histopathological changes which can be observed are confined to the CNS, in which there are degenerative, but not inflammatory lesions. Because vacuolar changes are found frequently in neurons, the diseases are often described as transmissible spongiform encephalopathies, but spongiform change is not a consistent feature, and TDE is a more accurate description.

BSE is a transmissible, neurodegenerative, fatal brain disease of cattle. BSE first came to the attention of the scientific community in November 1986 with the appearance in cattle of a newly-recognised form of neurological disease in the United Kingdom (UK). It is believed to be the bovine equivalent of Scrapie disease in sheep and Creutzfeldt-Jacob disease in humans. Mad cow disease is the layman's name for BSE.

Epidemiological evidence indicates that the primary cause of BSE was probably the use of commercial cattle feed concentrates which contained meat and bone meal derived from sheep presumed to have been infected with Scrapie. By June1990, there were some 14,000 confirmed cases out of an estimated population of 10 million cattle in Great Britain. Since 1986, almost 200,000 cases of BSE in cattle have been identified in Great Britain. The epidemic peaked in 1992-93 at almost 1,000 cases per week. The epidemiological tracing and DNA evidence proves that the BSE positive cow slaughtered in state of Washington on ninth December, 2003 was born in a dairy farm in Calmar, Alberta, Canada on ninth April, 1997. She was moved to US in September 2001 along with 80 other cattle from that dairy.

TSE of other species

- Chronic wasting disease of mule deer
- Transmissible mink encephalopathy
- Exotic ungulate encephalopathy
- Large cat spongiform encephalopathy
- Feline spongiform encephalopathy
- Zoo primate spongiform encephalopathy
- Scrapie

TSE of human beings

- Creutzfeldt- Jacob disease-first described by Jacob in 1921
- Gerstmann-Straussler Scheinker Syndrome(GSSS)
- Kuru

Etiology

BSE is not caused by a bacterium or virus (it contains no nucleic acid) The disease appears to be caused by an unconventional infectious agent, called prions. The causative agent is found to be abnormal conformation form (PrPSc) of a normally occurring protein (PrP). PrP is the abbreviation used to identify the normal 'prion' protein. The agent is extremely resistant to heat and normal sterilization processes. PrPSc does not evoke a detectable immune response or inflammatory reaction in host animal. PrP is present on nerve cell membranes. Most cases were reported in the Holstein Friesian breed, although all cattle are susceptible to the disease. Onset of clinical symptoms observed in cattle as young as 1 y 10 m, and precipitated by stress, oestrus and calving. The course is 2 weeks to 14 months and resulting in death or humane destruction within 4 months. The agent has been found in brain tissue, spinal cord and in the retina of the eye. They are also seen in the small intestine, bone marrow &dorsal root ganglia, but not in muscle and milk. Affected countries include Ireland, Switzerland, France, Scotland, Holland, Denmark etc.

Pathogenesis

In most experimental models of Scrapie, after peripheral non-neural routes of infection, replication of the agent can first be detected in lympho-reticular system (LRS) tissue. When the route of introduction of agent into the body is localized, initial involvement will be in LRS tissue draining the infection site. Thereafter, there is a striking amplification of the agent in the LRS and spread by lymphatic/haematogenous routes, giving widespread dissemination in the LRS. This precedes replication in the CNS, but is not the means by which infection reaches the CNS. There is now substantial evidence from experimental

models of Scrapie that involvement of the CNS is by peripheral nervous system (PNS) pathways. In some models employing oral exposure, the earliest localized LRS replication is in the gut associated lymphoid tissue (GALT) and autonomic PNS routing to the CNS has been implicated.

The way that a deranged PrP protein 'prion' causes spongiform changes to the grey matter is easy to be understood. The normal cell containing PrP protein can be destroyed by a process where the prion converts the normal cellular protein to more prions, something along the line of "a bad protein converting a good protein to be bad". When a cell is parasitized by a prion converting a normal protein to deranged protein, the cell creates more normal protein to make up for the protein lost in the process. The process continues and large quantities of prions are released to go to other normal cells, parasitize them and begin the process all over again. Normal brain tissue is destroyed. 'Holes' appear in the grey matter where cells have died and the pathology resulting from this process is called a "spongiform encephalopathy". Infection is dose dependant, but the required dose for BSE transmission to cattle is small. An oral dose of 500 mg to 1 g of infected brain appears sufficient.

Specified Risk Materials

Specified risk materials are tissues in BSE infected cattle that contain the agent which may transmit the disease. The infective agent is concentrated in brain and spinal cord. Cattle younger than 30 months do not contain the infective agent, in these tissues.

The feed ban refers to the Bovine Offal (Prohibition) Regulations1989 which prohibit the use of "specified bovine offal" {brain, spinal cord, thymus, tonsils, spleen and intestine (duodenum to rectum)} in ruminant feeding stuffs. These specified bovine offals (SBO) now termed specified risk materials (SRM) were also banned in human food in 1989 (1990 in Scotland).

While BSE is a cattle disease, the human disease called variant Creutzfeldt -Jacob disease (vCJD) has been associated with the consumption of products derived from BSE infected cattle. Cattle tissues identified as specified risk materials are not generally consumed as food. How ever, during processing, SRM could be unintentionally included in meat products destined for human consumption.

Clinical signs

BSE is so named because brain tissue sections of infected cattle appear spongy and infiltrated with amyloid (starch like) plaques when examined under a microscope. Cattle affected by BSE experience a progressive degeneration of the nervous system.

Affected animals may display

- Changes in temperament such as nervousness, aggression
- Abnormal posture
- In co-ordination and difficulty in standing
- Decreased milk production
- Loss of body weight despite continued appetite
- Excessive licking
- High stepping
- Death.

BSE elicits no immune or inflammatory reaction. It aff primarily mature cattle.

Disease in man

Kuru and Creutzfeldt-Jacob disease are thought to be different spongiform encephalopathies in man. In Kuru, the progressive neurological disease of human being becomes infectious. It was first seen in tribes of Papua Guinea. These diseases are caused by different variants of pri Gerstmann-Straussler Scheinker syndrome is a fatal fam insomnia. CJD occurs at the rate of 1 in 1 million people. types of CJD are classical and variant CJD. Classical is see much older patients (onset at about 64 years) and begins psychic disorders and the average course is six mon Electroencephalogram in CJD will be typical. Variant CJ seen in much younger persons than classical CJD per (average age is 28 years). It begins with serious psychic diso and there will be problems with senses (eye, ear, and nose), muscular inco-ordination, muscle spasms, mental confusion The course of disease is 13 months. There will be large qua of prion accumulation in brain surrounded by vacuoles. CJ a hereditary predisposition. A small percentage of case iatrogenic. CJD can also be transmitted to humans as a resu treatment with natural growth hormone. Replacement of na growth hormone by recombinant growth hormone has allev this risk.

Necropsy findings

- No abnormalities in gross pathology and diag depends upon histological findings
- Pathognomonic lesion is bilaterally symmetric cytoplasmic vacuolation of neurons and grey n neutrophil.
- Occurrence of vacuolation in the solitary tract and tract of trigeminal nerve in the medulla oblongata basis of the statutory diagnosis of disease in Great Bi
- Scrapie associated fibrils can be visualized by EM.

Diagnosis

- Histopathological studies
- Western Blotting and immunocytochemistry
- Immunocapillary electrophoresis using blood o animal is currently used for the diagnosis of prec Scrapie.

- Adapted sandwich ELISA
- Urine test in live animals with detection of disease specific physiological or metabolic markers
- Mouse inoculation tests

Differential Diagnosis

- Hypomagnesemia
- Nervous acetonemia
- Rabies
- Lead poisoning
- Polioencephalomalacia
- Neurogenic toxins

Treatment

- For cattle with BSE, there is not likely ever a treatment. Slaughter will continue to be the end game.
- In case of human beings, those drugs which stabilize the protein throughout the body may be useful for treatment, preventing formation of abnormal PrP protein.
- As it is not immunogenic, vaccine production is not practical.

Prevention and control

WHO suggested some recommendations to reduce the exposure to the BSE agent.

1) All countries must prohibit the use of ruminant tissues in ruminant feed and must exclude tissues that are likely to contain the BSE agent from any animal or human food chain
2) All countries are encouraged to conduct risk assessment to determine if they are at risk for BSE in sheep and goats.
3) No infectivity has yet been detected in skeletal muscle tissue. Reassurance can be provided by removal of visible nervous and lymphatic tissue from meat.
4) Milk and milk products are considered safe.
5) Human and animal vaccines prepared from bovine materials may carry the risk of contamination of animal TSE agents. If absolutely necessary, bovine materials should be obtained from countries which have a surveillance system for BSE in place and which report either zero or only sporadic cases of BSE.
6) To prevent BSE from entering the US, there is restriction of importation of live ruminants and ruminant products from countries where BSE is known to exist. Other products derived from ruminants, such as fetal bovine serum, bone meal, meat cum bone meal, blood meal, offals, fat and glands also can not be imported into US from these countries, except under a special permit for scientific research purposes.

In Great Britain, carcasses of animals aged more than 30 months must be deboned in licensed plants under supervision of British Meat Hygiene service. They must be rendered and incinerated. Prion's infectivity is destroyed by one molar NaOH at 55°C or chlorine bleach at the rate of 20000ppm.

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Award for Dr. W. J. Cherian

The Dr. G. Nirmalan Trust that has instituted a Best Veterinarian Award for the outstanding Veterinarian of the year has conferred the honour on Dr. W. J. Cherian, Deputy Director in the District Animal Husbandary Office, Ernakulam.

Honour for Dr. K. G. Suma

The reviewing meet of the Indian Association of Lady Veterinarians held at Tamil Nadu Veterinary and Animal Sciences University at Madras, Dr. K. G. Suma, Thrissur as the National Vice President and Dr. Devatha as the Executive committee member.

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extensively bound to plasma proteins in treated animals and might result in persisting residues in meat. Anthelmintics like thiabendazole, benzimidazole, oxybendazole are extensively metabolized in mammals after administration and the metabolites predominate in plasma, tissues and excreta. The main toxic effect is teratogenicity. As residues of benzimidazole compounds can occur in meat and meat products, it is necessary to observe withdrawal time for meat and milk. The unbound drugs or metabolites of these compounds are most likely to be associated with toxic effects.

The way to manage chemical residues is not by banning products but by judicious use and robust surveillance. Public health veterinarians will have to take effective measures by observing the suspicious anti mortem and post mortem lesions during meat inspection and observation of withdrawal periods before slaughter to minimize the risks of these residues.

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