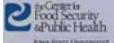


S 1 i d e	<h1>Transmissible Spongiform Encephalopathy</h1> <p><i>TSE</i></p> 	
S 1 i d e 2	<h2>Overview</h2> <ul style="list-style-type: none"> • Organism • History • Epidemiology • Transmission • Disease in Humans • Disease in Animals • Prevention and Control <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>In today's presentation we will cover information regarding the organism that causes transmissible spongiform encephalopathies and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and the clinical and necropsy signs observed. Finally, we will address prevention and control measures for TSEs.</p>
S 1 i d e 3	<h2>TSEs</h2> <ul style="list-style-type: none"> • Group of diseases caused by same infectious agent • Causes same pathology in respective hosts <ul style="list-style-type: none"> – Microscopic sponge like holes in brain • Clinical signs are all neurological in nature <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>TSEs share the same infectious agent and pathology in their respective hosts. Post mortem microscopic evaluation of brains from TSE infected individuals exhibit a generalized appearance of microscopic holes resembling a sponge. Thus was born the term spongiform encephalopathy (encephalon meaning brain and pathos meaning disease of). Clinical signs are predominantly neurological and are similar in all infected hosts.</p>
S 1 i d e 4	<h2>Human TSE's</h2> <ul style="list-style-type: none"> • Kuru • Creutzfeldt-Jakob disease (CJD) <ul style="list-style-type: none"> – Familial, sporadic, iatrogenic • A variant of CJD (vCJD) • Gerstmann-Straussler-Scheinker syndrome (GSS) • Fatal familial insomnia (FFI) <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>These diseases are all examples of human TSE's and they are all caused by the same infectious agent known as a prion. Three of these diseases are familial (genetically inherited) Gerstmann-Straussler-Scheinker syndrome (GSS), fatal familial insomnia (FFI), and familial Creutzfeldt Jakob Disease (CJD). Three of these diseases are acquired, sporadic CJD, Kuru and vCJD, the other form of CJD is iatrogenic.</p>
S 1 i d e 5	<h2>Animal TSE's</h2> <ul style="list-style-type: none"> • Bovine Spongiform Encephalopathy (BSE, "mad cow disease") • Scrapie (sheep) • Chronic wasting disease (CWD) (elk and deer) • Mink Spongiform Encephalopathy (TME) • Feline Spongiform Encephalopathy (FSE) <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>Animals are susceptible to this prion disease as well. Cattle can suffer from bovine spongiform encephalopathy (BSE, or "mad cow disease"), sheep can get infected with scrapie, elk and deer can acquire chronic wasting disease (CWD), and mink and cats have their own TSE's. In addition, there are also several exotic animals that have also been infected. These animals include cheetah, eland, gemsbok, greater kudo, mouflon, mule deer, nyala, ocelot, and puma. These animals were believed to have been infected when fed feed contaminated with BSE contaminated parts.</p>

The Organism



Prion

- Smaller than smallest known virus
- Not yet completely characterized
- Most widely accepted theory
 - Prion = Proteinaceous infectious particle
- Normal Protein
 - PrP^C (C for cellular)
 - Glycoprotein normally found at cell surface inserted in plasma membrane

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Prions are smaller than the smallest known virus and have not yet been completely characterized. The most widely accepted theory is that prions are mutated proteins, although not all scientists accept they are the cause of disease. Professor Stanley Prusiner, the Nobel prize winning scientists who first proposed that prion proteins could cause disease, says that today "a wealth of experimental and clinical data" proves his ideas were right. The idea of a protein-only infectious agent was first proposed by Griffiths in 1967. However, it was only after the co purification of the prion protein with hamster scrapie infectivity that Prusiner was able to distinguish it from a virus. The normal protein is designated as PrP^C the C stands for cellular. The glycoprotein is normally found at the cell surface and is inserted in the plasma membrane.

Normal protein

- Secondary structure dominated by alpha helices
- Easily soluble
- Easily digested by proteases
- Encoded by PRNP gene (in humans)
 - Located on human chromosome 20

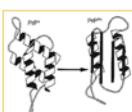


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The secondary structure of the normal protein is dominated by **alpha** helices. There are likely three of these structures. The normal protein is easily soluble and digested by proteases. This gene in humans is designated PRNP and located on our chromosome 20. Image from www.prionics.ch, shows normal cellular prion protein.

Abnormal Protein

- PrP^{Sc} (Sc for scrapie)
 - Same amino acid sequence and primary structure as normal protein
 - Secondary structure dominated by beta conformation
- When PrP^{Sc} contacts PrP^C
 - Converts it to the abnormal form



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The abnormal protein is designated as PrP^{Sc}, the Sc stands for scrapie, a spongiform encephalopathy in sheep. This protein has the same amino acid sequence as the normal protein and the primary structures are identical. The secondary structure is dominated by a **beta** conformation. When the abnormal protein comes in contact with the normal protein (PrP^C) it converts the normal protein to its abnormal form. Diagram depicts normal prion on left, abnormal on right.

Abnormal Protein

- Insoluble in all but strongest solvents
- Highly resistant to digestion by proteases
 - Survives in tissues post-mortem
- Extremely resistant
 - Heat, normal sterilization processes, sunlight
- No detectable immune response

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The abnormal protein is insoluble in all but the strongest solvents and is highly resistant to digestion by proteases. It survives in tissues post-mortem and is not destroyed by various rendering processes. The abnormal form of the protein is extremely resistant to heat, normal sterilization processes and sunlight. It is also very resistant to most disinfectants and is stable at a wide range of pH. The abnormal protein also does not evoke a detectable immune or inflammatory response in its host so the body does not react to it as an invader.

History



History: Kuru

- New Guinea in early 1900's
 - People practicing cannibalism
 - 1957-1968
 - Over 1,100 people died
 - Majority of deaths
 - Women, children and elderly
 - Incubation period >30 days



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An unknown disease appeared in New Guinea in the early 1900's. It occurred in an isolated group known as the South Fore consisting of about 8,000 people. This group practiced a ritualistic form of cannibalism. When a member of the tribe died, the women and children ate the person's brain and the men ate the muscle tissue. The practice was done to take in the spirit of their ancestors and to ingest a rich source of protein which was difficult to get in the area. It is through these acts of cannibalism that Kuru is believed to have been transmitted among the people. The disease has since been defined as a TSE. Women and children were affected at a rate of about 5 times that of men because they ate the most infectious parts of the body. Between 1957 and 1968, over 1,100 of the South Fore died from kuru. Kuru has essentially disappeared since the termination of cannibalism in the 1970's. Sporadic cases of kuru still occur, demonstrating that the incubation period is greater than 30 years. The photo depicts Papuans from the central highlands of Papua New Guinea wearing traditional dress and decoration, which is usually reserved for ceremonial or festive occasions. Source: C. Seghers/Photo Researchers, Inc. "Papuans of Papua New Guinea," Microsoft® Encarta® Encyclopedia 2000. © 1993-1999 Microsoft Corporation.

History: CJD

- Sporadic human encephalopathy
- Worldwide 1-2 cases/million people
- Different forms
 - Spontaneous (85%)
 - Genetic (10-15%)
 - Iatrogenic (<1%)
- Average age of onset 65 years
- Duration of illness, 4.5 months

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Classic Creutzfeldt-Jakob Disease is a sporadic encephalopathy affecting humans that occurs worldwide at a rate of 1-2 cases per million people. It can occur spontaneously, genetically, or iatrogenically. Average age at onset is 65 years which, as we will discuss, is much older than the variant form of CJD. The duration of illness is approximately 4.5 months. The spontaneous form occurs in about 85% of cases, the genetic form occurs in 5-15% of the cases, and the iatrogenic form (passed unintentionally from a medical procedure) occurs in less than one percent of the cases. An example of an iatrogenic infection has occurred during dura mater grafts where a piece of infected brain tissue is grafted into a healthy person's brain. Another example has occurred when previously healthy people have been injected with gonadotropin hormones that were prepared from the pituitary glands of people infected with CJD. This disease is not caused by eating BSE contaminated food products.

History: BSE

- 1986, First confirmed case in United Kingdom (UK)
- 1988, UK bans meat and bone meal from ruminants in cattle feed
- 1989, USDA bans importation of ruminants from countries with BSE
- 1993, Peak of BSE in UK
 - 1,000 new cases reported weekly

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The first confirmed case of BSE occurred in 1986 in the United Kingdom. Following that discovery, in 1988 the UK banned meat and bone meal products rendered from ruminants from inclusion into cattle feed. In 1989, the United States Department of Agriculture (USDA) banned the importation of live ruminants and most ruminant products from countries that were known to have BSE. Major efforts were made to stop the spread of this disease in the UK and continue today. Roughly 5.8 million cattle in the U.K. over thirty months of age have been slaughtered as of June 23, 2003 in continued efforts to stop the spread this devastating disease. The peak incidence of BSE in the UK occurred in January 1993, with more than a 1,000 cases being reported weekly. Since then, the number of new cases has been decreasing at a steady pace (number of cases reported in 1993 was 35,000, in 2002 case number had decreased to 1,144).

History: BSE

- 1997, US & Canada ban ruminant products fed back to ruminants
 - US importation ban extended to all of Europe
- 2001, European Union ordered mandatory tests on cattle
 - Older than 30 months destined for slaughter
- May 2003, BSE diagnosed in 6 yr. old Angus beef cow in Alberta, Canada
 - Herd mates all tested negative
 - Single case in 1993 was cow imported from UK

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History: BSE

- December 2003, BSE diagnosed in 6½ yr old Holstein cow in Washington State
 - Possibly imported from Canada
 - DNA testing being conducted
 - Complications following calving
 - Sent to slaughter
 - Brain tissue sent to NVSL-per FSIS protocol
 - Presumptive positive by NVSL
 - Definitively positive by UK lab

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In 1997, Canada and the FDA of the United States instituted a ban on feeding ruminant meat, bone meal, and other ruminant proteins, back to ruminants. Additionally in 1997, the U.S. extended its ruminant import ban to all of Europe regardless of BSE status. In 2001, the European Union ordered mandatory testing to be done on cattle older than 30 months of age that are destined for slaughter. On May 20, 2003 BSE was diagnosed in an 6 year old angus beef cow in Alberta Canada. Tracebacks were done on 40 herds and 2,700 cattle were slaughtered, all of which were over 24 months of age and all were found to be BSE negative. Although Canada had a prior case of BSE in 1993, it was found in a single cow imported from the UK. This 2003 case is the first case of BSE originating in Canada.

History: vCJD

- Human encephalopathy due to consuming BSE contaminated foods
- 1995, UK: First confirmed case
- Incubation period not known
- Mean age at death
 - 28 years old
- Mean duration of infection
 - 14 months

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Currently, it is thought that people who ingest BSE contaminated food products may develop variant Creutzfeldt Jakob Disease (vCJD). The incubation period for vCJD is unknown because it is a relatively new disease, but it is likely to be many years or decades. Therefore, a person who develops vCJD likely would have consumed an infected product or products many years earlier. In contrast to classic CJD, the variant form (vCJD) in the UK predominantly affects young people with 28 years as the mean age at death. This is much younger than the classic form of CJD. The mean duration of infection is 14.1 months for vCJD, which is much longer than the 4.5 months of illness related to classic CJD.

History: Scrapie

- Sheep and goat disease
- Recognized 250 years ago
 - Great Britain and W. Europe
 - 1947 diagnosed in the U.S.
 - More than 1,000 flocks; mostly Suffolk
 - Scrapie: Ovine Slaughter Surveillance Study (SOSS)
 - Overall national prevalence 0.2%
 - Higher in black-faced sheep

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Scrapie was first recognized in sheep in Great Britain and other countries of Western Europe more than 250 years ago. Since then scrapie has been reported throughout the world. Only two countries are recognized by the United States as being free of scrapie, Australia and New Zealand. The first case of scrapie in the United States was diagnosed in 1947 in a Michigan flock. The flock owner had been importing sheep of British origin through Canada for several years. Scrapie has been diagnosed in more than 1,000 flocks in the United States and has primarily been reported in the Suffolk breed. It also has been diagnosed in Border Leicester, Cheviot, Corriedale, Cotswold, Dorset, Finnsheep, Hampshire, Merino, Montadale, Rambouillet, Shropshire, Southdown, and a number of crossbreeds. The Scrapie: Ovine Slaughter Surveillance Study (SOSS) was a study conducted by the USDA Veterinary Services to estimate the regional and national prevalence of scrapie in mature cull sheep in the U.S. The overall weighted national prevalence was found to be 0.20%; prevalence was far higher in black-faced sheep (0.84%) than in white-faced sheep (0.01%).

History: CWD

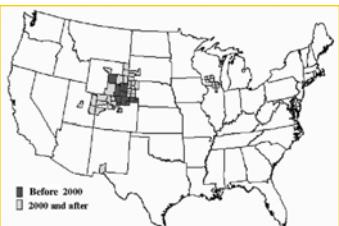
- 1967, Chronic "wasting" syndrome in mule deer
 - Northern Colorado wildlife research facility
- 1978, defined as TSE
- Deer and elk affected
- Not thought to be zoonotic
 - Risk, if any, is low
 - Concern when three hunters died of CJD
 - No correlation found between their deaths and CWD



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First recognized as a clinical "wasting" syndrome in 1967 in mule deer in a wildlife research facility in northern Colorado. Chronic wasting disease was identified as a TSE in 1978 and it affects deer and elk in both captive herds and in free ranging animals. CWD is typified by chronic weight loss leading to death. There is no known relationship between CWD and any other TSE's of animals or people. There has been no documented case of CWD being transferred to humans and it is not thought to be a zoonotic concern. A news story about two Wisconsin men who died from Creutzfeldt-Jakob disease and another who died of a similar brain disease in the 1990s after eating Wisconsin venison and western elk at a Brule River cabin raised concern among hunters about possible effects of chronic wasting disease. The men's brains have been studied by medical experts and there is no evidence that the men's deaths are linked to CWD of deer and elk. Photo is of a mule deer with chronic wasting disease; source muledeernet.org.

History: CWD



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This figure depicts the distribution of CWD by county in the U.S., before 2000 (red) and after 2000 (yellow). Two epidemics, one in captive deer and elk and the other in a free-ranging population, established the original distribution prior to the year 2000. After this time, the disease began spreading outward from the original distribution as free-ranging herds moved naturally and commercial herds were moved into new areas. The states with infected herds and wildlife include WI, IL, NM, UT, CO, WY, SD, and NE. The disease also has occurred in the Canadian provinces of Saskatchewan and Alberta. Map from CDC website <http://www.cdc.gov/ncidod/EID/vol10no6/03-1082-G.htm>.

History: TME

- First detected U.S. in 1947
 - Minnesota and Wisconsin
- Countries with reported cases of TME
 - U.S., Canada, Finland, Germany, and republics of the former Soviet Union

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Transmissible mink encephalopathy (TME) is a rare illness that affects the central nervous system of ranch-raised mink. It was first detected in the Minnesota and Wisconsin in 1947. Since then, TME outbreaks have been reported in numerous locations worldwide, including the United States, Canada, Finland, Germany, and the republics of the former Soviet Union.

History: FSE

- Domestic and captive wild cats
 - Including tigers, puma, ocelot and cheetah
- Exclusively in the United Kingdom
 - Single case in Norway
- Incidence unknown
 - 81 domestic cats in the UK

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Feline spongiform encephalopathy has been found in domestic cats and captive wild cats, including tigers, a puma, an ocelot and a cheetah. FSE has been found exclusively in the UK, with a single isolated case in a cat in Norway. The overall incidence rate of FSE is unknown.

Transmission



Human Transmission

- Humans consuming cattle products infected with BSE can develop vCJD
 - Brain and spinal tissue
- Dose required not known
- Genetic susceptibility
 - All human cases have been homozygous for methionine at codon 129 of PrP^C.

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The first confirmed case of variant Creutzfeldt Jakob Disease (vCJD) (human form of BSE) was diagnosed in the UK in March 1996. It is widely accepted that (vCJD) occurs by eating cattle products (primarily brain and spinal tissue) infected with BSE. The dose of infected material required to cause the disease is not known at this time. Genetic susceptibility may play a role in the development of vCJD. To date all cases of human infection have been homozygous for methionine at codon 129 of the prion protein gene (PrP^C).

Human Transmission

- Possible modes
 - Transmission from surgical instruments used on tonsils, appendix, or brain tissue
 - Growth hormone injections
 - Vaccines

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Other possible modes of transmission in humans may be possible. Since abnormal prions are extremely resistant, they persist on surgical instruments despite autoclaving and sterilization procedures. Many instruments used in brain surgery are disposable for this reason. Human and veterinary vaccines prepared from bovine materials may also carry the risk of transmission of animal TSE agents. For this reason, the World Health Organization (WHO) recommends that the pharmaceutical industry should ideally avoid the use of bovine materials and materials from other animal species in which TSEs naturally occur. 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. These precautions apply to the manufacture of cosmetics as well.

Human Transmission

- Unlikely modes
 - Blood transmission
 - Consumption of milk and milk products
 - Gelatin products (when manufacturing process is done correctly)

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Acquiring BSE through blood transfusions is an unlikely mode of transmission. However, as a precaution, the FDA and the Red Cross have implemented screening standards for blood donors. Milk and milk products are not thought to contain prions at this time, although continued research is ongoing in this area. A Food Standard Agency funded project will try to determine whether infectious prions can be detected in the milk of cattle experimentally infected with the BSE agent. The final report is expected at the end of 2004. Gelatin products that are largely made of crushed bones and hides of cattle could potentially be a source of prions. However, the manufacturing process for gelatin, when done correctly, will destroy any prions present.

Transmission: Animals

- BSE
 - Cattle feed
 - Sheep carcasses infected with scrapie
 - Cattle carcasses infected with unknown TSE
 - Maternal transmission occurs at very low levels
- Scrapie
 - Spread from ewe to offspring through placenta and placental fluids
 - Genetic susceptibilities

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The exact mechanism responsible for the emergence of BSE in cattle is still under debate. BSE may have occurred by feeding cattle feed that was infected with scrapie products. Another theory is that BSE spontaneously emerged in cattle and that this agent was fed back to cattle through the rendering process and led to widespread dissemination and the epidemic. Changes in rendering operations in the early 1980's particularly the removal of a solvent extraction process that included a steam heat treatment, may or may not have played a role in the appearance of BSE and the subsequent amplification of the agent in the cattle population. After reviewing years of epidemiological data, offspring of clinical BSE cases have an increased risk of developing the disease, but it is still uncertain whether it is true maternal transmission or a genetic susceptibility to acquiring infection from a feed source. As a precaution, retrospective offspring culling of infected dams has occurred since 1997. BSE cases detected in other

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Transmission: Animals

- FSE and exotic zoo animal forms
 - Feed contaminated with BSE infected cattle products
- CWD: Environmental, other?
- TME: Not known at this time
- Number of animals infected experimentally
 - Hamsters, mice, rats, voles, gerbils, some species of monkeys



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countries appear to be a result of importation of live cattle or more significantly contaminated feed from the UK. Scrapie is known to be transferred from ewe to offspring through the placenta and placental fluids. While the interaction between the scrapie agent and host genetics is not fully understood, genetic susceptibility does play a major role in transmission of scrapie.

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Disease in Humans



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Human TSEs

	Variant CJD	Classic CJD
Average age at Onset	26.3 years	65 years
Duration of Illness	14.1 months	4.5 months
Transmission	Eating BSE contaminated products	Sporadic

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It is important to understand the various characteristics between variant CJD and the classic form of CJD. This graph depicts the average age at onset for the various diseases as well as the duration of illness and the mode of transmission.

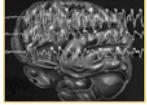
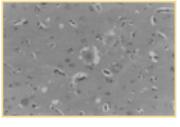
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Clinical Symptoms: vCJD

- Initial symptoms
 - Depression and schizophrenia like psychosis
 - Neurological signs
 - Unsteadiness, difficulty walking, and involuntary muscle movements
- Progression
 - Become completely immobile and mute

vCJD has atypical clinical features (as compared to CJD), with prominent psychiatric or sensory symptoms at the time of clinical presentation. Onset of neurological abnormalities is delayed and include ataxia within weeks or months. Dementia and myoclonus occur later in the illness. Affected persons generally become completely immobile and mute at the end stage of the disease.

S 1 i d e 3 2	<h3>Diagnosis: vCJD</h3> <ul style="list-style-type: none"> U.K. criteria for antemortem diagnosis <ul style="list-style-type: none"> - Neuropsychiatric disorder with duration longer than 6 months - Specific clinical signs - Abnormal EEG - Tonsilar biopsy with detection of prion protein  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	The United Kingdom has established antemortem diagnostic criteria for vCJD and it includes a progressive neuropsychiatric disorder with duration of illness greater than 6 months with no alternative diagnosis or history of iatrogenic exposure. Also, early psychiatric symptoms such as depression, anxiety, apathy, withdrawal and delusions, persistent painful sensory symptoms, ataxia, myoclonus, and dementia. An electroencephalogram (EEG) that rules out sporadic CJD, a positive tonsil biopsy, and spongiform changes in the brain are definitive diagnostic criteria.
S 1 i d e 3 3	<h3>Diagnosis: vCJD</h3> <ul style="list-style-type: none"> Post mortem definitive diagnosis <ul style="list-style-type: none"> - Amyloid plaques surrounded by vacuoles - Prion protein accumulation in cerebellum - Spongiform appearance in gray matter  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	On post mortem exam, examination of the brain should show the following neuropathological features: numerous widespread amyloid plaques surrounded by vacuoles, spongiform changes most often seen in the basal ganglia and thalamus, prion protein accumulation shown by immunocytochemistry, especially in the cerebellum. Image: Large kuru-type plaque surrounded by a zone of spongiform change in a cerebral cortical- biopsy specimen (center). A smaller plaque is also present (right) but spongiform change is sparse. For reference, kuru is a spongiform encephalopathy that affected humans in Papua, New Guinea in the early 1900's. Those people practiced cannibalism as a funeral rite and were afflicted with the same type of brain lesions; hence, kuru-type plaque.
S 1 i d e 3 4	<h3>Treatment: vCJD</h3> <ul style="list-style-type: none"> No effective treatment available <ul style="list-style-type: none"> - Experimental drugs under investigation <ul style="list-style-type: none"> • Quinicrine Symptomatic treatment Supportive care 	There is no known effective treatment for vCJD though there is experimental treatment taking place with Quinicrine. Since this drug effectively crosses the blood-brain barrier there is hope that it will show some effectiveness. Supportive treatment and symptomatic care are recommended.
S 1 i d e 3 5	<h3>TSE's and Animals</h3> 	
S 1 i d e 3 6	<h3>Incubation Period</h3> <ul style="list-style-type: none"> Scrapie: Sheep 2-5 years BSE: Cattle 2-8 years CWD: Deer and elk 18 months TME: Mink 7+ months FSE: Feline unknown, most 4-9 years of age 	Incubation periods differ for different animal groups affected with TSEs. The incubation of scrapie is 2 to 5 years. The incubation period for BSE is 2 to 8 years, it is believed that the incubation in deer and elk affected with CWD is relatively short at about 18 months. The incubation for mink affected with TME is roughly 7 months or more. Incubation period for FSE is unknown but most diagnosed animals are between 4-9 years of age.

S 1 i d e 3 7	<p>Clinical Signs: BSE, Scrapie, CWD</p> <ul style="list-style-type: none"> Initial clinical signs subtle, mainly behavioral <ul style="list-style-type: none"> Increased excitability, nervousness, aggressiveness, and increased sensitivity to noise Pruritus and rubbing <ul style="list-style-type: none"> Sheep  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	The initial clinical signs of TSEs are very subtle and generally include behavioral changes. An infected animal generally shows increased excitability, nervousness and aggressiveness. Infected animals also tend to be agitated by sudden movements and loud noises. Sheep infected with scrapie may show signs of pruritus and rub against fixed objects, apparently to relieve itching. The name scrapie comes from this observation. Image: sheep with scrapie from www.aphis.usda.gov/vs/scrapie.htm
S 1 i d e 3 8	<p>Clinical Signs: BSE, Scrapie, CWD</p> <ul style="list-style-type: none"> Terminal state <ul style="list-style-type: none"> Hypokinesia, hypermetria, falling and general paresis Tremors and muscle fasciculations <ul style="list-style-type: none"> Neck and face Wasting despite good appetite PU/PD in deer and elk  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	During the end phase of the disease most animals have motor control difficulties including hypokinesia, hypermetria and general paresis. The animals can also experience tremors of the neck and face. There is generally a wasting syndrome despite the animals good appetite. In the terminal state of CWD, deer and elk show increased drinking and urination.
S 1 i d e 3 9	<p>Clinical Signs: Mink</p> <ul style="list-style-type: none"> Subtle initial signs <ul style="list-style-type: none"> Nest soiling Dispersal of droppings in cage Progressive signs <ul style="list-style-type: none"> Increased excitability Arching tail Incoordination Chewing tail Clenching jaw  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	Clinical signs of TME can last from 3 days to 6 weeks. Early clinical signs, which can be subtle, include an increase in nest soiling and dispersal of droppings throughout the cage. Mink may step into their food often or may have difficulty eating. As the disease progresses, mink become increasingly excited and may arch their tail over their back. Infected mink may exhibit severe incoordination, may have difficulty walking, and show pronounced jerkiness of hind limbs. In advanced cases, signs include rapid circling, compulsive chewing of the tail, and clenching of the jaw. In the end stage of disease, mink become sleepy and unresponsive. Image: mink.
S 1 i d e 4 0	<p>Clinical Signs: FSE</p> <ul style="list-style-type: none"> Behavioral changes, tremors, ataxia Increased aggression Later stages <ul style="list-style-type: none"> Somnolence Convulsions Excessive salivation Hyper-responsiveness to loud noise Dilated pupils Death in 6-8 weeks  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	The clinical signs of FSE may include behavioral changes, tremors and ataxia. Cats may become aggressive or tend to creep aimlessly around their home and hide. In later stages, somnolence is common and convulsions may occur. Excessive salivation, hyper-responsiveness to loud noises, and dilated pupils have also been seen. Death occurs after 6-8 weeks.
S 1 i d e 4 1	<p>Diagnosis</p> <ul style="list-style-type: none"> Post mortem: detection of prion <ul style="list-style-type: none"> Microscopic examination of brain tissue at necropsy Live animal tests: USDA/APHIS <ul style="list-style-type: none"> Tonsillar biopsy in deer <ul style="list-style-type: none"> Time consuming and expensive 3rd eyelid test in sheep Blood tests  <p>Center for Food Security and Public Health Iowa State University - 2004</p>	The post mortem diagnosis for TSEs is microscopic examination of the brain tissue during necropsy and detection of the prion protein. There is a live animal test developed by the Colorado Division of Wildlife, for CWD in deer but it is lengthy and expensive. The new test works because the mutant proteins that cause CWD concentrate in deer tonsils. The animals are tranquilized and then a piece of tonsil is extracted with a special biopsy tool. New tests to diagnose scrapie in live sheep include collection of lymphoid tissue from the 3 rd eyelid. Other tests being validated include capillary electrophoresis and fluorescent labeled peptides to detect abnormal prion protein in the blood and immunoblotting to detect abnormal prion protein in blood, cerebrospinal fluid or tissues.

S 1 i d e	<h2 style="text-align: center;">Prevention and Control</h2> <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	
4 2	<h3>U.S. Government Precautions</h3> <ul style="list-style-type: none"> • 1989: Import restrictions <ul style="list-style-type: none"> - Live ruminants and ruminant products - From countries known to have BSE • 1997 <ul style="list-style-type: none"> - Import restrictions expanded to include all European countries - FDA "animal feed rule" - Banned most mammalian proteins as food source for ruminants <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>The United States government has a number of stringent safeguards in place to prevent the spread of BSE in the US. In 1989, they banned the importation of live ruminants and restricted many ruminant products from countries where BSE was known to exist, including the U.K. These regulations were expanded to include all of Europe in December of 1997. In August 1997, the FDA instituted regulations to prohibit the use of most mammalian protein, with a few exceptions, in ruminant animal feeds. The "animal feed rule" exempts the following products: blood and blood byproducts, milk products, pure porcine and pure equine products, plate waste, tallow, gelatin and non-mammalian protein (poultry, marine, vegetable).</p>
4 3	<h3>U.S. Government Precautions</h3> <ul style="list-style-type: none"> • Targeted surveillance <ul style="list-style-type: none"> - High risk animals <ul style="list-style-type: none"> ▪ Adult animals with neurological signs ▪ Non-ambulatory "downer" cows ▪ Rabies- negative cattle ▪ Cattle dying on farms - 2003: 20,000 animals tested for BSE <ul style="list-style-type: none"> ▪ 47 times the number required by the OIE - 2004: Enhanced surveillance <ul style="list-style-type: none"> ▪ Test maximum number of animals possible <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>The United States has had a targeted surveillance program for BSE in place since May 1990. BSE is a notifiable disease and the Food Safety Inspection Service (FSIS) along with the Animal and Plant Health Inspection Service (APHIS) coordinate testing of high risk animals, including downer animals (animals that are non-ambulatory at slaughter), animals that die on the farm, older animals and animals exhibiting signs of neurological distress. During fiscal year 2002, the USDA tested 19,990 animals and 20,000 during 2003. Both of these figures are significantly higher than the standards set by the Office International des Epizooties (OIE), the standard setting organization for animal health for 162 member nations. Under the international standard, a BSE-free country like the US would only be required to test 433 head of cattle per year. The 2004 enhanced BSE surveillance program is focusing on testing the maximum number of animals possible that are identified within the high risk population. Random sampling from "normal" populations will also be performed to further safeguard our country from BSE.</p>
5	<h3>Specific Guidelines for Hunters Regarding CWD</h3> <ul style="list-style-type: none"> • Public health officials recommend avoiding human exposure to CWD agent • Harvest only animals that look and behave normally • Do not eat any animal products of sick or infected elk and deer • Do not eat brain, spinal cord, eyes, spleen, tonsils and lymph nodes <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>There are specific guidelines for deer and elk hunters to protect them from possible exposure to CWD. Public health officials recommend that human exposure to the CWD agent be avoided as they continue to research the disease. Harvest only animals that look and behave normally. Do not eat brain, spinal cord, eyes, spleen, tonsils and lymph nodes, do not eat any animal products of sick or infected deer or elk.</p>

Specific Guidelines for Hunters Regarding CWD

- Dress the deer/elk properly
 - Minimize handling of brain and spinal tissues
 - Wear rubber gloves when field dressing
 - Use strong household bleach for cleaning knives and saws
- Any suspicious elk and deer should be reported to health officials
- Testing of elk and deer available in many states

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It is recommended that you dress the deer/elk properly. One should minimize handling of brain and spinal tissues, wear rubber gloves when field dressing and wash hands. Instruments should be cleaned completely after dressing with a strong household bleach solution. Any suspicious elk and deer should be reported to health officials. Testing of elk and deer are available in many states. Contact your state department of natural resources for specific information.

Prevention and Control

- Surveillance for CJD in US
 - CDC
- Blood/plasma donation restrictions
 - Persons who have traveled or resided in the U.K. for 3 or more cumulative months from 1980 to 1996
- FDA Website
www.fda.gov/cber/gdlns/cjdvcjd.pdf



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In response to the threat of BSE, the CDC has activated a surveillance program in the U.S. Additionally, the Red Cross has restricted blood and plasma donations from persons who have traveled or lived for 3 or more cumulative months in the U.K. between the years of 1980 to 1996. Military personnel who resided on bases in Germany, U.K. Belgium and the Netherlands for 6 months or more between 1980 and 1990 should be deferred indefinitely from donations. Other military personnel living on bases in Greece, Turkey, Spain, Portugal, and Italy for 6 months or more between 1980 and 1996 should also be deferred. For more information, please access the FDA website
www.fda.gov/cber/gdlns/cjdvcjd.pdf

Prevention and Control

- Scrapie Flock Certification Program
 - Voluntary
 - Producers-industry-states-APHIS
 - Certify origin in scrapie-free flock
- National Accelerated Scrapie Eradication Program
 - Live animal testing and active slaughter
 - Animal tracing/animal identification
 - Clean-up strategies including genotyping

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Since 1952 the USDA and industry have made numerous attempts to eradicate scrapie through various programs. The two programs in place presently include the Scrapie Flock Certification Program and the National Accelerated Scrapie Eradication program. The Scrapie Flock Certification Program was implemented in 1992 to reduce the incidence and control the spread of scrapie through flock certification. The certification program is a voluntary and cooperative program among producers, industry, states and APHIS. The program provides participating producers with the opportunity to protect their sheep from scrapie and to enhance the marketability of their animals through certifying their origin in scrapie-free flocks. The USDA has also initiated a National Accelerated Scrapie Eradication Program (NASEP). Key concepts of the program include the identification of preclinical infected sheep through live animal testing and active slaughter; effective tracing of infected animals to their flock of origin made possible as a result of new animal identification requirements and clean-up strategies which include genetic testing. When scrapie infected, source and exposed flocks are identified, the sheep are genotyped. Genotype determines its risk for scrapie infection. Sheep with genotype QQ are highly susceptible to scrapie, QR are considered rarely or much less susceptible and sheep with the genotype RR are considered resistant to scrapie. Susceptible genotypes are either removed from the flock or their movement restricted. All 50 states have active scrapie control programs. As of November 30, 2003, there were 59 scrapie infected and source flocks in the United States.

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