



**Bovine Spongiform
Encephalopathy
(BSE)**

**Variant Creutzfeldt-Jacob Disease
(vCJD)**

A Review in Plain Language
of a
Complex and Perplexing
World Health Issue

Prepared by



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Introduction

Humans are said to be distinct from other animals dwelling within nature by virtue of our intelligence. Our abilities to perceive, to remember, to form judgments and to reason are held as characteristics that distinguish humankind from the rest of the animal kingdom. As we use that intelligence to learn more about those “other” animals sharing our habitat, we find evidence that many share those same qualities, to some degree. It’s a phenomenon that has led some philosophers among us to tip humans from their long-held exalted status as lord and master of the world and its creatures. The trend today is to see humans as little more than “Thinking Apes.”¹

Still our ability to think brings with it certain advantages over “fellow animals” with less developed cognitive powers. Our thinking skills allow us to escape from the limits imposed upon how other earthly creatures live their lives. Unlike solitary tigers roaming a set geographical area constantly in search of food or to fend off interlopers invading their terrain, we humans are not tied to a specific plot of habitat. We are adaptable omnivores who can be quite social.

Humans can wander throughout the world and be quite comfortable living in a wide variety of climates, eating from the Earth’s cornucopia of diverse foods, and building homes to accommodate any terrain. If we choose, we can learn to live in harmony with different cultures and a diversity of animals and natural resources. Thanks to our ability to understand who we are, where we are, how others differ from us, what we need to do to survive in their midst, and how to travel the length and width of the world even to cross natural barriers such as Earth’s vast oceans, we enjoy great freedom.

Precisely because we are so defined by our intelligence and because it allows us such latitude in how we spend our individual time on earth, any thing that threatens our intelligence elicits great fear among us. This is why disease or trauma that physically insults our brain, our physical repository of intelligence, is considered an unbearably horrific affliction.

The Transmissible Spongiform Encephalopathies (TSEs) are diseases of the brain that can infect other individuals or species. They produce cavities in brain tissue that resemble the cratering or holes normally associated with sponges. Bovine Spongiform Encephalopathy (BSE) afflicts cattle. BSE can also infect humans. When BSE invades the human brain, the disease receives a new name: variant Creutzfeldt-Jakob Disease (vCJD).

Nobel Laureate Carleton D. Gajdusek first observed the TSE called “kuru” among the ancient cannibal tribes of Papua New Guinea in 1957. The pediatrician was alarmed at the incurable and always fatal disease striking down young and old.ⁱⁱ As a virologist, Dr. Gajdusek was equally disturbed at the lack of medical knowledge about the origin, prevention or cure for the disease.

Perhaps because kuru was considered a disease of an isolated, primitive people word of its existence did not trouble the world’s human population save for fellow medical investigators equally as perplexed as Gajdusek over what was riddling the brains of the highland-dwelling Fore people. In 1985, a TSE hit the British Isles. Suddenly the mysterious disease of the quaint pre-historic Fore had its counterpart among advanced society. The popular reception of such news was twofold: fear followed by an arguably artificially contrived forgetfulness when resumption of familiar ways blocks out the sheer terror of a mysterious disease that strikes without warning and that eats holes in victims’ brains. Barely a week after public disclosure of the most recent discovery in Canada of the TSE common to cattle, Bovine Spongiform Encephalopathy (BSE), polls in the United States and Canada found that two of three consumers had no intention of changing their consumption of beef.ⁱⁱⁱ

The horror of vCJD is that it robs us of our ability to walk, to talk, to see, to swallow, to think, to perceive, to interact with those around us. In short, it takes from us the freedom and traits that make us uniquely human. Therein lays the fear that forces even the remotest thought of such a disease out of our consciousness lest the prospect of imaging ourselves or our loved ones fatally infected by the brain-eroding disease overwhelms our ability to cope emotionally or otherwise with such a scenario.

The unfortunate truth is that the menu of Transmissible Spongiform Encephalopathies including BSE and vCJD are with us. We still do not understand their origin. We do not have full knowledge of how they are spread or whether the disease is lying dormant within us, nor have we effective treatments or cures. Only by better understanding the phenomena can we avoid the mistakes of the past, strive to unravel its mysteries and create an antidote or a prophylactic vaccine, and, if need be, to steel ourselves in the event predictions of epizootic re-manifestation of the disease prove true.

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Today Canada

May 20, 2003 is the date of record when the most recent case of Bovine Spongiform Encephalopathy (BSE) was recorded in Alberta, Canada. The only other diagnosed case of BSE in that country was found in a beef cow imported from Britain in 1987.

The disease with the long name and known by three short, chilling initials was pronounced present in a lone cow in a nation to whom its agricultural heritage is of tremendous economic importance.

The enormity of the discovery of that single case of BSE caused more than 20 nations worldwide to impose import bans on Canadian beef, cattle and beef products including milk, semen, embryos and hides. The global barriers were emergency measures erected to keep Canadian beef from foreign markets in the U.S. and Mexico to the south as well as Japan, Korea, Taiwan, Indonesia, the Philippines and Australia across the Pacific.

The United States is Canada's primary trading partner in beef, livestock and cattle-related products. The two nations' exchange of cattle and beef can be seen as neighboring ranches with a steady stream of live cattle, beef and related products flowing north and south between the two. Compared to the overall inventory of cattle in the U.S.A, Canada might even be likened to a large cattle raising state. As of January 1, 2003, the U.S. cattle population was 96.1 million. Canada was home to 13.4 million.^{iv}

U.S. purchases accounted for 83 percent of the 1.2 million metric tons of beef and veal exported from Canada in 2002. That same year, the U.S. imported 1.7 million head of live Canadian cattle. Between 1999 and 2002, more than 180,000 tons of Canadian cattle feed were imported each year by the U.S.^v The ban on Canadian cattle and associated products was costing Canada some C\$27.5 million or US\$20.2 million a day.^{vi} Exports of beef and cattle to the U.S. alone averaged some C\$3.5 billion annually.^{vii} After May 20th, they averaged none. That same year the U.S. sent 134,220 head of cattle to Canada together with nearly a quarter million pounds of beef and veal.^{viii}

One of the key dates in the most recent Canadian BSE scare is January 31, 2003. On that day, an Alberta Agriculture, Food and Rural Development (AAFRD) meat inspector condemned the carcass of a six-year-old "downer" (an industry term for animals that are non-ambulatory at the time of slaughter) as unfit for human consumption. The animal's head was sent to the Canadian Food Inspection Agency's (CFIA) National Centre for Foreign Animal Disease in Winnipeg. All AAFRD tests

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were completed by May 16th. On May 20th the World Reference Laboratory at Weybridge, United Kingdom produced the final report on the incident.

Prior to the final test findings that the cow did contain BSE, Investigators tracked the carcass to a rendering plant and the remains were processed into poultry feed. Some parts of the animal are thought to have found their way into the contents of dog food made by the Champion Pet Foods Ltd.^{ix} Food, public health, and agricultural safety inspectors around the world sprang into action to ensure that consumers, national cattle and food supplies were not contaminated.

The origins and history of the infected cow, its siblings, off-spring, herd mates and feed supply were traced. Some 2000 tests from cattle located at 25 farms in Saskatchewan (19) and Alberta (6) were conducted. Approximately Canadian 2700 cattle were killed. The BSE-positive cow's entire 150-cow herd was destroyed. An additional 1000 cattle from non-quarantined farms suspected of having been exposed to the same feed given to the infected cow met the same terminal fate.^x

All of the 2000 tests including those on all of the BSE cow's herd mates proved negative for the disease. Still the history of all animals related to the infected cow either by birth or herd proximity or common feed was pursued.

On 3 June 2003, four days after official word confirming BSE in the cow was received, the Canadian Food Inspection Agency notified its trading partners including the United States Department of Agriculture Animal and Plant Health Inspection Service (APHIS). U.S. officials were told that five bulls from one of the "possible" Saskatchewan birth herds of the animal in question were sold to a ranch in Montana. APHIS inspectors learned that during the period from 1999-2002, 24 bulls were taken from the farm identified by CFIA. APHIS believes the five Canadian bulls were part of this group. Twenty-three of the bulls were sent to three stockyards, one in Montana and two in South Dakota. One was slaughtered for personal consumption. The whereabouts of the 23 animals were further traced to slaughterhouses in Nebraska, Minnesota, Texas, South Dakota and Wyoming.^{xi}

The rapid response by nations to word of BSE appearing in a major beef producing country was conditioned by the tragic experience in Great Britain 18 years earlier.

Pulitzer Prize-winning journalist Richard Rhodes articulately recreates the account of English veterinarian, Dr. Colin Whitaker the fateful day, April 25, 1985, when BSE made its dramatic official debut in the United Kingdom.^{xii} Dr. Whitaker was called to treat a "sick" Holstein at the Plurenden Manor dairy farm outside Ashford in central Kent. The normally placid cow was acting out of sorts. It was aggressively knocking into other cows and continually staggered and stumbled on shaky hind legs. Perplexed, the doctor watched as the cow's condition worsened. When it died, the carcass was sent

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to the "knacker's yard," British slang for a rendering plant. Within 18 months, seven more Holsteins from the farm displayed similar symptoms. Soon the affliction was seen

in farms in the counties of Cornwall, Devon and Somerset. With conditions reaching epidemic proportions, the Ministry of Agriculture, Fisheries and Food (MAFF) was called in.

By the end of 1987, investigators had identified telltale, scrapie-associated fibrils (SAFs) in test samples. The stick-like particles of prion protein (PrP) crystals detectible only via an electron microscope and the very noticeable deposits of protein fibers that formed saucer-like “plaques” throughout the brain tissue were proof positive that England was dealing with some variety of spongiform encephalopathy. The MAFF scientists dubbed the disease “bovine spongiform encephalopathy” (BSE). The British press called it “Mad Cow Disease.” In a short while, 420 cases were confirmed in England and Wales. Unfortunately, all of the cases detected proved to be “index” cases, that is, the first to appear in a herd with more certain to follow.^{xiii}

The common method of infection deduced by the legion of biologists working on the issue appeared to be the meat-and-bone meal (MBM) fed largely to British dairy cattle as a dietary supplement to bolster their ability to sustain production of large volumes of milk. The U.K. is not a soybean-producing region (a major source of cattle protein enhancers elsewhere) so it relied on the MBM to feed its dairy cattle. Traditionally, MBM is derived from dead, ill, and downer livestock declared unfit to enter the human food supply.

Researchers tracing the history of the BSE cows backwards determined that two changes in carcass-rendering methods went into effect at roughly the same time as the four-five year incubation period for BSE in livestock. An American-developed system using lower temperatures and cessation of the use of solvent extraction to extract tallow replaced the traditional British techniques.^{xiv}

The British government’s desire to eliminate the risk of accidents caused by use of the flammable solvent combined with industry’s reluctance to purchase expensive equipment mandated by the new government standards for working with the chemical led to the decrease in the use of solvent extraction from 50 percent to ten percent between 1981 and 1982. Consequently the fat content in the meat-and-bone meal rose from less than five percent to about 12 percent. According to Richard Rhodes “Fat protects microorganisms from heat.” Further bolstering the link between rendering techniques and the outbreak of BSE was the fact that Scotland, where the solvent extraction was still in use. Scotland was the last part of the UK to report BSE among its cattle.^{xv}

At the peak of the UK epidemic, January 1993, 1000 new BSE cases were reported each week.^{xvi} From 1985 until 2002, 183,000 cases of BSE were confirmed in UK cattle distributed over 35,000 herds.^{xvii} As tragic as the infection of so many cattle in Great Britain may be, in human terms the UK’s BSE epidemic took a decidedly darker

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turn for humans. The year 1993 saw a new variety of lethal brain disease introduced into the human inventory of infection and death with the illness of 15-year-old English

schoolgirl Victoria Rimmer who lived comatose until she died in 1996. A biopsy displayed the characteristic traits of sponge-like lesions and discs of amyloid plaques combined in this new variant to form a signature pattern that looked like “chrysanthemum blooms.”^{xviii}

This new BSE-associated transmissible spongiform encephalopathy had larger plaques than classic Creutzfeldt - Jakob Disease. The perimeter of each amyloid platelet was dotted with the spongiform holes. Even more troubling was the fact that these physical “insults” to the victim’s brain were not confined to the egg-sized lower brain, the cerebellum, as is characteristic of the then known human TSE’s, Creutzfeldt-Jakob Disease and kuru. They were everywhere. Floral plaques and holes permeated the cerebellum and the cerebrum, the large upper twin-halved brain mass that deals with thinking, memory and the senses. Within a year of Victoria Rimmer’s diagnosis, other British teenagers began showing signs of the newly named “new variant Creutzfeldt-Jakob Disease (vCJD)”. Not until March 20, 1996 did the U.K.’s Spongiform Encephalopathy Advisory Committee (SEAC) announce the presence of the first ten cases identified as new variant CJD.^{xix}

The youthfulness of the vCJD patients was particularly disturbing. According to the U.S. National Center for Infectious Diseases, the median age at death of patients with classic CJD in the U.S. is 68 years old, with cases under 30 exceedingly rare. New variant CJD killed its UK victims at a median age of 28.^{xx}

By April 2, 2002 the U.S. Centers for Disease control reported 125 cases of vCJD throughout the world. One hundred seventeen were from the U.K. Six were French. Ireland and Italy had one victim each. The majority of the 125 cases had histories of spending more than one year in Britain during the period when BSE was epidemic there: 1980-1996. To date every case of vCJD has been linked to time spent or residence in a country where BSE was present in local cattle.^{xxi} As of May 2003, the global tally of vCJD cases has reached 139. The lone case of vCJD in the United States involved a woman who contracted the disease during her residence in the United Kingdom but whose symptoms did not appear until she had moved to the U.S. a number of years later.^{xxii}

Similarly, Canada logged its first and to date only case of vCJD in April 2002. The patient exhibited all of the outward signs of most non-U.K. vCJD victims. He was young, under the age of 50 and was a frequent visitor to Britain during the most intense BSE years. He had eaten a variety of processed meat products while in the U.K. An autopsy confirmed vCJD as did subsequent testing by a CJD expert in the United Kingdom. Health Canada, that country’s public health agency, insured that the hospital where the man was confined identified all individuals exposed to any medical devices used to treat the vCJD patient. None of those individuals were allowed to donate blood

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and any who had done so had their blood, blood components and any other donor blood pooled with theirs destroyed. All were kept under close observation.^{xxiii}

As tragic as the number of human lives lost to date may be, they are quite moderate when juxtaposed with the potential global caseload suggested by some. Worse case scenario predictions from credible scientists suggest that the eventual human death toll related to BSE may run from the hundreds to thousands to millions given the decades long incubation period of vCJD and the potential exposure in Britain and around the world from British cattle and beef exports before preventative public healthy measures were put in place.

Ancient History – Cannibals & the 1950s

To the Fore mountain women of New Guinea burying the bodies of dead kin was a waste of good meat. Fore men enjoyed the finer cuts of pigs and other delicacies taken from Nature by hunting and foraging. Since roughly the turn of the 20th Century, women reserved the flesh of family members, including that of their late husbands, as their special dining treat – meat, brain, internal organs, bones and all – to be shared with their children. Fore culture kept women and men separate with each sex living in their own communal lodge; each eating their own particular diet virtually in secret away from the other. The cultural beliefs of the Fore, that men and women possessed different and very incompatible qualities created an on-going tension between the sexes. It was a primitive dynamic in the sense that men regarded women as simply wild and untamable.

Fore men were believed by Fore women to practice sorcery. When women began to stagger, depend upon walking sticks and eventually lost their ability to swallow, they believed themselves victims of killing witchcraft conjured by the men. Throughout the progressive stages of their lethal journey where their bodies betrayed them, the Fore women were conscious and alert with no signs of dementia. Every afflicted Fore woman and child died from the shivering spell called kuru were dutifully eaten by surviving children, female relatives and acquaintances that is, until Dr. D. Carleton Gajdusek became fascinated with their culture and unique affliction. His first visit to the New Guinea interior was a stop-over lark on his way back to the United States after a research stint in Australia in 1957. It would not be his last.

The intellectually brilliant 34-year-old pediatrician from New York became intrigued and puzzled by the Fore and the kuru that killed their women and children. No signs of infection, disease specific bacteria, or parasites were detectable yet kuru was present in every village. Kuru, he found, was the leading cause of Fore death after wounds inflicted in the continuous life of warfare practiced by the Fore. Kuru looked like brain diseases such as Alzheimer's in modern society but that it also exhibited unique characteristics that surrounded it in a deep troubling and mysterious shadow of medical questions that had no answers. No known treatment from antibiotics to aspirin elicited even the slightest response.

Gajdusek spent his life and won a Nobel Prize in 1976 for his decades of pioneering research into the brain-wasting disease of the ancient people as well as its relationship to counterpart diseases among modern society and its domestic and wild animals.^{xxiv}

With the passion of a detective in pursuit of a mass murderer, Gajdusek systematically began assembling evidence he hoped would lead modern medical science

to the true culprit behind the kuru deaths. Countless specimens of kuru victim body parts were shipped to labs in Australia and the United States. Every aspect of the Fore diet was examined. The obvious suspect was the Fore's consumption of human flesh.

Gajdusek's early collaborative efforts with colleagues in the United States focused on the similarity of damage to the brains and presence of fibrous protein patches called amyloid plaques in juvenile victims to that of elderly Alzheimer's patients. Such plaques were unheard of in children. The medical investigators noticed another unlikely similarity between kuru and the extremely rare condition discovered forty years earlier, Creutzfeldt-Jakob Disease (CJD). But that affliction was regarded as confined to the middle aged, not children. To the best of their then limited knowledge, CJD affected the upper region of the brain. Kuru seemed confined to the lower cerebellum.

The mention of similarities to Creutzfeldt-Jakob Disease and one other, no matter how slim they appeared at the time, would be key to the immense progress flowing from Dr. Gajdusek and his colleagues' work.^{xxv} The "other" was scrapie. The suggestion that scrapie and kuru might be related came from noted veterinary pathologist, William J. Hadlow.^{xxvi}

Scrapie was first discovered in English sheep in 1730. Infected sheep itched to the point that they scraped their wool off, staggered about, went blind and died. Scrapie, Alzheimers and CJD each displayed the presence of plaques. Scrapie, CJD and kuru had another common trait, countless tiny holes throughout their victim's brain matter giving it the look of a sponge.

Dr. Gajdusek's force of personality and thirst for scientific knowledge seized kuru as the impetus for his quest to solve the puzzling mysteries of that and similar brain maladies. As a visiting scientist at the U.S. National Institutes of Health (NIH) National Institute of Neurological Disorders and Stroke, Gajdusek marshaled some of the brightest colleagues around the world to join his quest for groundbreaking studies into transmissibility, identifying markers, and potential causes of the puzzling brain diseases. His ability to apply theory to practical consequences led him by default to be considered the world's expert and oracle on Transmissible Spongiform Encephalopathies. ‘

Whatever their cause, TSE's were transmissible indeed. Gajdusek's colleagues at NIH managed to infect a menagerie of species from mice to primates. The infective agents of the disease were also virtually indestructible. High heat and even radiation left specimens viable and dangerous. Traditional methods of medical device sterilization had no effect. That fact led to transmission and death via the inadvertent introduction from one patient to another by physicians dealing with CJD.^{xxvii}

TSE, CJD, BSE, Scrapes and More

Transmissible Spongiform Encephalopathies (TSE) are rare and fatal diseases that affect the central nervous system of humans and animals. When brain tissue is examined at autopsy, each displays the characteristic of sponge-like holes and the presence of tangles of protein fibers called amyloid plaques. Those plaques are now described in the majority of scientific literature as aggregates of what is called proteinaceous infectious particles or prions.^{xxviii} The scientific shorthand for the normal prion protein is PrPc with the “c” referencing the fact that this protein is normally and benignly found on the surface of specific types of cells. The modified version thought to cause TSE is written PrPsc (for scrapie) also referred to in early TSE literature as Scrapie-associated fibrils (SAF).

TSEs are traditionally divided into two distinct categories: those associated with animals and those whose victims are humans. Among the former are scrapie found in sheep and goats, transmissible mink encephalopathy, feline spongiform encephalopathy in cats, chronic wasting disease in deer and elk, and bovine spongiform encephalopathy (BSE) that afflicts beef and dairy cattle. The latter include Creutzfeldt-Jakob Disease (CJD), Gerstmann-Straussler-Scheinker syndrome (GSS), Fatal familial Insomnia (FFI), kuru, and Alpers Syndrome.

Unlike most known diseases affecting humans and animals alike, TSE has thus far eluded even the most meticulous medical investigator attempting to track down its origin, develop definitive early warning detection systems, or create either vaccines or other effective medical treatments although significant and hope filled progress is being made in these directions. TSE infective matter does not contain detectible or identifiable nucleic acid that provides the genetic information allowing other diseases to be detected at a treatable stage. These diseases also fail to provide a typical immune response; that is, it does not produce anti-bodies traditionally used in diagnostic techniques. Physicians “suspect” the presence of CJD from the typical symptoms. Unfortunately by then the disease appears to have taken hold and all that can be done is establish a watch-and-wait vigil until the disease has run its lethal course.

The U.S. Centers for Disease Control (CDC) indicate that the presence of the 14-3-3 protein in cerebrospinal fluid or electroencephalogram (EEG) patterns is reported to be used to detect the disease. CDC warns however that confirming the presence of the disease requires brain tissue testing via “biopsy or autopsy.”^{xxix}

For all science knows Transmissible Spongiform Encephalopathies (TSEs) may have existed for millennia. On the other hand, recently detected variants such as kuru or variant CJD associated with BSE may be relatively recent varieties created by some unknown mutation. In 1997, Dr. Stanley Prusiner was given the second Nobel Prize

associated with TSE's for his work attempting to explain the TSE phenomena through the prion hypothesis. That international recognition caused the prion theory to become the dominant explanation of TSE to date even though Prusiner's theory and techniques are fraught with controversy. Still, a legion of competitive scientific hypotheses on the origin of TSE, and BSE in specific, exist with the insistence that at some point a viral causality will be proven. This group of scientists remains the most stubborn in clamoring for scientific recognition. At least 32 different theories competing with the prion concept, albeit at a much lesser degree of acceptance, are testament the mystery that still surrounds these afflictions.^{xxx}

Transmissible Spongiform Encephalopathies did not become major public health issues until modern epidemiological investigation techniques and transmission studies were undertaken on a large scale due largely to Dr. Gajdusek's work on kuru. A combination of scientists realizing the scant credible knowledge about spongiform encephalopathies that existed and their emerging awareness through the Gajdusek-directed transmission work at the National Institutes of Health (NIH) of the lethal and highly resilient nature of the disease's unknown infective agent caused a global reevaluation of certain accepted medical and industrial practices. That awareness inadvertently touched off a growing corpus of medical research filled with episode after episode of tragedy and death of animals and humans alike.

Creutzfeldt-Jakob Disease was first diagnosed in 1913. The victim was Bertha Elscher, a maid in a German convent. The outbreak and duration of World War I, kept Dr. Hans Gerhard Creutzfeldt from publishing his paper describing the new disease he discovered until 1920. From that paper, Dr. Alfons Jakob recognized the symptoms as similar to the affliction that killed four of his patients.^{xxxii} The newly identified brain-destroying disease was named for the two physicians.

At least four forms of CJD are known to exist. They are **sporadic, variant, genetic** and **iatrogenic CJD**.

The classic and most common form of CJD is described as a typically sporadic disease, that is, until the revelations made by Gajdusek about the Fore kuru epidemic in the 1950s. Classic or sporadic CJD affects one in a million people. That translates into approximately 50 to 60 deaths per year in the U.K., Australia, Canada, and the U.S. that occur with no obvious relationship to any of the various animal-borne TSEs. The cause is unknown but scientific speculation favors the theory that normal prion proteins (PrPc) spontaneously change to the suspected infective PrPsc form where they aggregate in a way similar to the formation of crystals and begin their wanton destruction of brain tissue.

Typically, CJD patients are older with most between 50 and 75.^{xxxiii} However, the disease does, on occasion, strike younger victims.

Genetic CJD describes a group of even more exceedingly rare TSE mutations. In most cases, genetic CJD is caused by the inheritance of an abnormal gene passed from one generation to the next. In families with a history of the disease, a blood test can detect the presence of the abnormal gene.^{xxxiii} **Gerstmann-Straussler-Scheinker syndrome (GSS), Fatal familial Insomnia (FFI), and Alpers Syndrome** are all forms of genetic CJD. Alpers Syndrome or Alpers Disease affects infants and children.^{xxxiv} Fatal familial insomnia attacks the thalamus in the brain and results in hallucinations, the inability to sleep and coma before death.^{xxxv} GSS strikes middle aged victims in their 40s and 50s and can be both genetic and sporadic.

Iatrogenic CJD is one of the most professionally troubling forms of the disease for the scientific and medical community of men and women dedicated to healing and saving lives. It is the accidental infection of a patient or patients by an attending physician or contaminated instruments or therapies during medical, dental or surgical procedures.^{xxxvi}

Until the transmission studies performed at NIH under Gajdusek's supervision, little was known about the ability of much less the consequences of cross-infecting various species with scrapie, kuru or CJD. As Gajdusek and his colleagues found, spongiform encephalopathies were and are highly transmissible, a quality that quickly sent a panic among the world's human and veterinary health corps and, in particular, chilled the pediatric medical community during the late 1970s and early 1980s.

Human growth hormone extracted from the pituitary glands of cadavers was being injected into children afflicted with pituitary dwarfism. Between the years of 1966 and 1977 pituitaries from nearly a half million cadavers were rendered into growth hormone. Statistically that means any where from 25 to 250 pituitaries from CJD infected cadavers may have been introduced into the mix. The results of the hormone treatment on the physical development of the undersized children were considered all but miraculous for the children and their parents. Hundreds of thousands of children around the world received the treatment. By 1985, the terrible consequences of treatment with contaminated hormones began to manifest themselves. That year the first growth hormone recipient died of CJD. Between 60 and 80 deaths were attributed to the CJD contaminated growth hormone by 1996.^{xxxvii} Human growth hormone is no longer culled from corpses. Now it is genetically synthesized.

Other incidents of physician-introduced (iatrogenic) CJD were traced to the use of the human-derived fertility drug gonadotrophin, membrane and corneal transplantation. Physicians who mistakenly believed that normal procedures for sterilizing medical instruments used to treat CJD patients were free of all infective agents were fatally wrong. Electrodes implanted in the brains of CJD patients and recycled for use with other patients became deadly carriers. Bits of flesh, membranes harvested from CJD cadavers and treated with compounds such as hydrogen peroxide and radiation for inner ear repair or patching the tough outer sheathing or "dura matter" that houses the brain

proved equally lethal. In England, a dentist and two patients died of CJD.^{xxxviii}

As of May 21, 2003, the Centers for Disease Control noted reports of more than 250 cases iatrogenic transmission of CJD worldwide.^{xxxix} Figures for suspected CJD cases and for CJD-related deaths from 1990 to 4 July 2003 in the U.K. are justifiably frightening. Suspected CJD cases total 1730. Total deaths in the U.K. attributed to “definite and probable CJD” listed by that country’s CJD Surveillance Team tally 889. Sporadic CJD accounted for 659. Iatrogenic CJD killed 41. Fatal Familial Insomnia and GSS took 38 and 19 respectively. BSE-related variant CJD proved fatal to 132.^{xl}

In response to the very real danger posed by CJD transmission through medical and other health care related procedures, the World Health Organization (WHO) issued a set of CJD infection control guidelines for healthcare workers.^{xli}

The WHO guidelines were formulated with full knowledge of the current lack within scientific literature of definitive studies on deactivating, neutralizing, or killing the infective agent in CJD. WHO strongly recommends incineration of medical instruments, materials and waste from procedures on suspected or confirmed CJD patients. If disposal of medical instruments is not economically feasible, the guidelines provide recommendations for sterilization of medical instruments including the use of chemicals, high heat, and accepted autoclave techniques. Chemicals such as sodium hydroxide and sodium hypochlorite suggested by WHO for use on instruments used on highly infective tissues such as brain, spinal cord and eyes of CJD patients as well as those involved in lower risk tissues (cerebrospinal fluid, kidneys, liver, lungs, lymph nodes, spleen, and placenta) can be corrosive so care must be taken in their handling and use.

Fear of transmission is so strong, that the guidelines extend to measures for embalmers of the dead as well as precautions for members of the family and loved ones viewing the deceased. WHO warns medical and funeral home personnel against allowing anyone to touch or kiss the face of known or suspected CJD victims who have been autopsied lest infective matter from the brain etc. might be lurking on the corpse’ skin.

Sporadic and genetic CJD are low priorities on the public health radar screens. The focus of public health concern is **variant CJD (vCJD)**, for good reason. It is the form of CJD that has the potential to infect the greatest number of members of the human race with this always-fatal disease. Medical researchers believe vCJD is transmitted to humans by means of infectivity in food processed from BSE-involved cattle.^{xlii}

Bovine Spongiform Encephalopathy (BSE), commonly known as “mad cow disease,” is the first of the animal transmissible spongiform encephalopathies traced to a distinct human TSE. The ubiquitous presence of beef and dairy products throughout society as well as its place of economic importance in national and international commerce, makes the malady particularly troubling not just to cattle, dairy and veal farmers but to consumers and public health officials too.

First diagnosed in Great Britain, BSE is confirmed in native-born cattle in Austria, Belgium, the Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, Luxembourg, Liechtenstein, the Netherlands, Northern Ireland, Poland, Portugal, Slovakia, Slovenia, Spain, and Switzerland with 95 percent of the incidents reported in the United Kingdom. The disease is not known to exist in the United States although other “native” animal TSEs such as **scrapie, transmissible mink encephalopathy, feline spongiform encephalopathy** and **chronic wasting disease** are present. As referenced earlier in this paper, the first incidence of a native-born BSE infected cow was diagnosed in Canada this year.

Many medical investigative fingers point to **scrapie** (pronounced “scrape-ee”) as the precipitating disease transmitted in some way to British cattle that mutated into the distinct form of TSE now found in beef and dairy cattle.

Scrapie was first detected in the U.S. in 1947. Subsequently the disease has been diagnosed in over 1000 domestic flocks. Researchers have puzzled over why BSE did not develop in a cow-dense nation such as the United States if scrapie is the culprit in infecting cattle. One suggestion is that the sheep to cow ratio in Great Britain heavily favors sheep.

Although scrapie has been a recognized disease of sheep and goats in Britain and parts of Western Europe for more than 250 years, it was not believed to affect the health of humans or other animals until the recent Gajdusek work demonstrated its highly transmissible nature. A multitude of theories as to how a TSE such as scrapie or even human CJD infected Britain’s cattle abound each with a degree of plausibility. The idea that scrapie is BSE is discounted by the fact that both are quite different when examined under laboratory conditions. That does not rule out the idea that somehow scrapie mutated into BSE during the course of transmission. Still, scrapie, to date, is viewed by a large number of public health officials and agencies as the most “likely” source for BSE. Details supporting the main theory that scrapie is the key infective agent of British cattle are compelling.

Equally intriguing are some of the side hypotheses regarding this assumed relationship. Among them is the theory espousing the possibility that human CJD that may be the infecting agent shape-shifting back and forth between cattle and humans given the tradition of using rendering plants as repositories for a vast spectrum of waste animal carcasses from a wide variety of sources. Individual theories recounted in the 32 hypotheses reviewed by British pathologist Dr. Stephen Dealler^{xliii} include the surreptitious disposal of a murdered CJD victim’s body into a rendering plant vat; the dumping of body parts of cattle inoculated as part of a transmission experiment with scrapies; the spreading of the ashes of a CJD victim’s body over ground grazed upon by cattle; neurological damage resulting from use of the now banned organophosphorus pesticides; diet imbalance and subsequent increased susceptibility to prion infection due to a lack of selenium brought on by an increase in rape seed (canola) farming or a copper

deficiency; mink bodies infected with transmissible mink encephalopathy tossed into rendering plants and others.

One interesting point emerges from a reading of Dr. Dealler's review of the multitude of theories on the origin of BSE. Dr. Dealler repeats the contention that "organic farms do not get BSE."^{xlv} Therein lays a theoretical host of practices that can and should be examined for potential preventative measures by beef and veal producers.

The most viable theory surrounding the scrapie/BSE relationship has key components including the change in British rendering methods (described earlier) and the prevalence of meat-and-bone meal (MBM) produced by those plants as a nutritional supplement to dairy and beef cattle operations. Whether the original infective agent came from scrapie-infected sheep or from cattle inoculated with scrapie or other TSE material rendered into the high protein meal is a question only biomedical investigators can answer. The facts remain that contaminated matter was in British rendering plants and that the process used to extract the fat, bone and flesh used to make tallow was not capable of killing the infective agents and that infected meat-and-bone meal and tallow contribute to the spread of the disease.

Arguments against the theory that contaminated meat-and-bone meal is the prime infective agent tend to center on the more recent realization that British cows were infected with BSE at an extremely early age (from one month or earlier to seven months) long before most calves in other countries are fed meat-and-bone meal. Dr. Dealler points out that animal husbandry practices in Britain routinely fed the meal to calves far sooner than most.^{xlv} This early feeding of meat-and-bone meal to U.K. calves appears to reinforce the theory that tainted meal is the key culprit in the British BSE epidemic.

An important point in the investigation of the disease' transmittal is the fact that no sign of BSE has been found in embryos taken from infected cows. That suggests not only that BSE is not spread from mother to offspring but also that infection takes place after birth. If the precipitating infective agent is not meat-and-bone meal, the lack of evidence of birth-infection brings the investigation back to the theory that BSE is passed on via some form of feed.^{xlvi}

In 1988-89 the British government ordered all meat-and-bone meal banned from cattle feed. A month after the order went into effect; the numbers of BSE infected cattle in the U.K. dropped. In 1989, the United States banned all imports of British cattle and cattle products. By 1997 that ban extended to all live ruminants (cud-chewing animals including cows, sheep, goats etc.) and most ruminant products from Europe. That year too the U.S. Food and Drug Administration (FDA) prohibited feeding most mammalian proteins to ruminants. As events show, the MBM ban and the decline in BSE reported cases occurring the same year are not necessarily an example of cause-and-effect.

A compelling case is made that British calves were in fact contracting BSE as

early as two weeks after birth, long before they would have been weaned onto solid feed.^{xlvi} This suggests that milk or milk substitute may be the prime suspect in initial BSE infection. Upon pursuing this theory, investigators discovered their focus narrowing on milk substitute fed the newborn calves.

Milk cannot be said to be prion free, only that the scientific evidence to date shows that BSE as well as other TSEs are not likely to be transmitted through milk. Milk from BSE-infected cows was fed to and injected into mice. None contracted any form of transmissible spongiform encephalopathy. Similar studies were conducted with milk from scrapies-infected sheep and mice. Even milk from Fore women with kuru failed to produce the disease after it was injected into mice.^{xlvi}

The majority of natural milk produced by cows is siphoned off for human consumption leaving young cattle in need of a replacement or a “milk substitute.”

Milk substitute fed calves is described as essentially large amounts of protein, fat and sugar. Traditionally the protein is provided from skimmed milk. Fat for British calves was tallow. Prior to 1988, the tallow in milk substitute originated at the same source as the contaminated meat-and-bone meal: the carcasses of slaughtered animals. Early studies attempting to determine the presence of infective prions in tallow failed to impress investigators that any such relationship exists.^{xli} Those conclusions are now dismissed as the result of faulty testing methodology.

The wealth of scientific literature makes a strong case for prion-contaminated tallow. The probability that the tallow added to milk substitute” was contaminated in the same way as meat-and-bone meal is very high. The resilient TSE prions infecting meat-and-bone meal and contaminated tallow are both processed at the same rendering plants with the latter produced via the tallow extraction process that eliminated solvents and used lower cooking temperatures prior to the UK/Europe BSE outbreak.

If, as the British government claims, the addition of tallow to milk substitute was halted in 1988, then yet another variable may be responsible, in whole or part, for the subsequent reduction in BSE cases among British herds. Still the tallow theory appears the most plausible explanation.

Yet another argument for tainted tallow in milk substitute as the most likely contributing factor to the British BSE epidemic comes from Japan.

The first two cases of BSE among Japanese cattle raised on Hokkaido farms were confirmed in the fall of 2001. Suspicion among public health investigators fell on the milk substitute fed the infected calves. The common link between those calves and a third diagnosed with BSE was the milk substitute fed each. Although the milk substitute was produced at a local Japanese factory, the animal fat it contained was imported from the Netherlands where 21 cows were diagnosed with BSE since 1997.¹

The Japanese government acknowledged it had imported BSE tainted meat-and-bone meal from the U.K. until 1996.^{li} Officially Britain ordered a ban on the meal in 1988-89. A 1996 study commissioned by the European Union found that British animal feed mills retained a five percent level of contaminated banned “material” that had lodged in British milling machine nooks and crannies.^{lii}

Given the average four-year incubation period for an infected cow, the appearance of Japan’s first BSE calf four to five years after the last importation of BSE-infected feed can be considered right on time. Between 2001 and 2003, Japan’s total number of BSE-positive cattle rose to seven a reasonable amount when compared to the U.K. figures of 1144 BSE cases for 2002.^{liii} Even Britain’s tally for that year seems mild compared to the 37,000 cases FAO noted it suffered a decade earlier.

The link between milk substitute and BSE infection is cause for the world’s veal industry to take stock of its practices to insure that its products are disease free.

Government public health agencies in BSE-countries such as Great Britain and BSE-free nations such as the United States have declared milk prion free and safe for consumption by humans and animals alike. That is good news for veal growers. But, that industry is far from immune to potential damage from the reality or perceptions of BSE in their meat.

The recent revelations about artificial milk/milk substitute acting as a BSE infective agent presents a very real problem for veal growers if they’ve fed their calves milk substitute containing animal fat from any BSE nation. That reality no longer allows veal growers to avoid public scrutiny and fears over BSE by halting use of animal protein feed or by documenting that their animals were never fed meat-and-bone meal from any country.

A further precaution should be considered. The Japanese government prohibits meat-and-bone meal from BSE nations to be fed to any food animal including farmed fish in order to avoid any chance that the animals or waste from processing those animals might be used to make feed for cattle.

If the veal industry in BSE-free countries or in those nations with histories associated with BSE hopes to maintain consumer confidence and avoid the pall of suspicion borne by beef interests, they must be very scrupulous in assessing potential exposure via any and all feeding practices. Milk substitute and protein meal containing any animal fat, flesh or bone from known BSE countries should be avoided altogether at least for the foreseeable future.

The Beginning of Wisdom – The Little We Know

The reality of what we truly know about Transmissible Spongiform Encephalopathies is that we know very little with complete certainty. At best, we can say that TSEs exist and that they are lethal. Science believes that the prion theory is the best explanation of the deadly phenomena to date, but it leaves open the possibility that another more complete and less controversial hypothesis, such as the unknown viral theory held by many within the scientific community, will prove to hold the complete story of what are now known as “prion diseases.”

Based on the best evidence available to date, scientific knowledge believes that Bovine Spongiform Encephalopathy (BSE) is not transmitted from bull to cow, cow to cow or cow to calf via reproduction, casual acquaintance, or birth. The preponderance of data offers a very strong case that the addition of BSE-contaminated animal waste or cadavers rendered into feed both as meat-and-bone meal and animal fat used in milk substitute is the primary infection vehicle for livestock around the world.^{liv}

Carleton Gajdusek and his colleagues as well as more recent medical investigators who have taken up the quest of those pioneering researchers proved that regardless of what strain of TSE is under examination, whether associated with animals or humans, each is true to its name. Even if the vehicle is as unnatural as direct injection of the infected matter directly to the brain of another individual or species, each is indeed transmissible.

What we know for certain is that we simply don't to this day have answers to all of the questions arising from TSEs whether bovine or its human afflicting variety, vCJD. The Bovine Spongiform Encephalopathy/variant Creutzfeldt-Jakob Disease experience is not so much an example of one disease “crossing” the species barrier as much as it is one of the disease's ability to “jump” a species hurdle as first premised by Dr. Dealler.^{lv}

The medical community's lack of definitive knowledge about BSE and vCJD has led to anxious eyes monitoring every development within “ground zero” of the BSE/vCJD epidemic of the past decade plus: the United Kingdom. Animals and humans alike who are over a certain age are being nervously observed for any sign that the potential exposure they received during the British BSE/vCJD epidemic is developing into an even greater toll as the assumed initial incubation periods pass.

In theory citizens and visitors alike to Great Britain now over five years old have been exposed via British beef or beef-derived products. Those in other countries where contaminated feed and beef was shipped after the UK ban remain at risk. Further, evidence shows that the disease may not manifest itself for as long as 30 years in humans, a fact that is both frustrating and frightening. Theoretically, children under the age of

five in the U.K. and the various known BSE/vCJD-free countries may be the first generation free of the specter of the deadly diseases.^{lvi}

In an attempt to provide some preventative protection for citizens and erect barriers to the potential spread of these diseases many nations have imposed some very commonsense measures including import bans of potentially infected live animals, meat, body parts and feed possibly containing contaminated animal proteins from any nation known to have confirmed cases of BSE. Native cattle are tested routinely.

U.S. measures in place to prevent the introduction of BSE include^{lvii}:

- Restrictions on importation of live ruminants and products from nations where BSE is known to exist (exceptions are allowed for scientific, educational or research purposes).
- The Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA) created a Transmissible Spongiform Encephalopathy Working Group to analyze risks to the U.S., and act as a reference source for accurate information about the diseases.
- Established cooperative information exchange among APHIS, the Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), the Food and Safety and Inspection Service (FSIS) and the National Institutes of Health (NIH).
- Education of veterinary practitioners, veterinary laboratory diagnosticians, industry and producers about clinical signs and pathology of BSE.
- Monitors all cattle allowed into the country before the import ban went into effect.
- Examines tens of thousands of brains of cattle found neurologically ill on farms or taken to veterinary labs or hospitals as well as those of rabies-negative cattle, cattle condemned at the slaughter house, non-ambulatory cattle (“downers”), and adult cattle dying on farms of unknown causes.

In the U.S. even Americans who’ve spent vacations or been temporary residents in the U.K. are forbidden to donate blood.

Recently Canada imposed stricter regulations designed to safeguard its beef and veal industry from potential BSE-involvement. On July 18, 2003, Canada’s Agriculture and Agri-food Minister Lyle Vanclief, together with Health Minister Anne McLellan announced that “specific risk materials (SRM)” – tissue from the brain and spinal cord from animals older than 30 months as well as a small portion of the small intestine of all animals – will be removed from carcasses at the time of slaughter to prevent their being included in the Canadian food supply.^{lviii} The “30-month” rule is based on the scientific belief that cattle younger than that lack infective agents in such tissue.

That new measure prompted Canada’s North American trading partners, the U.S.

and Mexico to make public statements that resumption of trade in Canadian beef and veal would soon take place. Mexico's Ambassador to Canada, Maria Teresa Garcia de Madero, went so far as to state that her nation intended to be the first to renew importation of Canadian beef.^{lix}

Even with the new Canadian measures in place, economic problems for nations such as the U.S. still exist. Japan, still very leery about exposing its people to BSE from contaminated cattle or beef and veal products from a "pass-through" nation, said they would not allow U.S. beef to enter their nation until and unless the U.S. could assure Japan that no Canadian product is present in U.S. beef and veal imports.^{lx}

As mentioned, some nations including Japan have banned meat-and-bone meal for use in all food animals including pigs, chickens and fish as a precaution against any part of those animals being in turn rendered as finishing feed for cattle.

The Food and Agriculture Organization (FAO) of the United Nations recommends every nation to apply recommendations for prevention and control of BSE offered by FAO, the World Health Organization (WHO) and the Office of International Epizootics (OIE).^{lxi} The FAO recommendations include:

- National risk assessments of the presence of BSE including imports of feed, cattle and efficiency of rendering and feed industries.
- Removal of all risk materials including brains, eyes, tonsils, spinal cords, etc. from all beef and sheep carcasses over 12 and 6 months respectively.
- Stringent rendering standards imposed with particular attention to temperature, time and pressure (133 degrees, 20 minutes and 3 bar).
- Strict avoidance of cross-contamination of feed for pigs, poultry, and pets with that of cattle.
- Banning of meat-and-bone meal.
- Testing of all animals showing neurological symptoms as well as surveillance of all animals killed because of disease or accident, all emergency slaughtered cows and random sampling of all cows during routine slaughter.
- BSE infected cows, their offspring and those born in the same year and herd as the BSE-positive cow must be killed and their carcasses incinerated.
- Effective national identification and recordation to enable tracing of animals back to their source.

The growing list of national and international precautions coupled with emerging scientific knowledge should give the cattle, beef and veal industries real hope. The veal industry, for an example, could eliminate virtually any possibility or perception of their product as a vehicle for BSE if a system was in place that guaranteed no meat-and-bone meal or any derivative is used in formula fed to veal calves. That could be accomplished

by returning veal calves to a milk feed formula with vegetarian roughage as well as vegetarian-only fat content in milk substitute. Such a diet would be of great value to the industry and consumers alike in that its “more natural” configuration underscores the reality and public perception that veal raised under those conditions is “BSE-Free.” An “organic” designation would advance that perception even more.

Scientists working on TSEs are offering even more hope in the area of medical prevention and treatment. Pharmaceutical companies such as Aventis are developing new, more sensitive tests for prions that can diagnose the presence of the disease in time, it is hoped, for effective treatment in both humans and animals. Biomedical researchers are seeing real progress in the use of anti-oxidants in providing temporary relief of CJD symptoms.^{lxii} Researchers around the world are using drugs such as Pentosan polysulphate to remove the offending prion proteins (PrPsc) from TSE-involved mice.^{lxiii}

In June 2003, Dr. Neil Cashman at the University of Toronto revealed that he and his colleagues discovered a means of identifying an antibody associated with the abnormal prions responsible for both BSE and vCJD. That news marks the end of a 15-year frustrating quest. If the early indications prove true and the process can be replicated in sheep and cattle, it will allow substantial progress towards developing an effective vaccine. Immunization via such a vaccine could potentially eliminate BSE in much the same way small pox has been brought under control via medical science. Cashman hopes his work will lead to a vaccine for cattle within a year. He cautions that it will be five to ten years before its human counterpart might be available.^{lxiv}

The reality of BSE/vCJD is horrific enough in terms of the strict science involved. Any attempt to inject ideological bias and stir panic or fear among consumers either by groups advocating philosophies centered on doctrinaire non-meat consumption (veganism or vegetarianism) or alternative methods of farming (organic versus conventional) does the public a great disservice.

Unfortunately, the high degree of mystery and lack of knowledge surrounding TSEs lends itself to exploitation by individuals and groups willing to stretch the ethical and moral bounds between advocacy and alarm. Therefore all claims in the media or sourced from groups with histories of bias against the beef, veal or any other aspect of the global food industry should be closely examined for credibility.

Life is by its very essence is not without risk and the lack of absolute assurances of success. Suffering and even death demonstrate the true value of life. The family vacationing by the sea cannot know for certain that the moment they enter the ocean they will not encounter the lethal jaws of a menacing bull shark. Nonetheless they enter and more often than not they and tens of millions of others find enjoyment and life-renewing pleasure.

Similarly, BSE and vCJD do pose very real threats to life and health. However, in

nations free of the disease, the decision to pour a tall ice-cold glass of milk to accompany a plate of fresh from the oven cookies or to dine on a hamburger or fine steak or an elegant dish of thinly sliced veal in mushrooms and Marsala or lemon is one that falls into the same category of choice as the family poised at the ocean's edge.

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