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Is mad cow disease caused by a bacteria?

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Summary Transmissible spongioform enchephalopathies (TSE's), include bovine spongiform encephalopathy (also called BSE or "mad cow disease"), Creutzfeldt–Jakob disease (CJD) in humans, and scrapie in sheep. They remain a mystery, their cause hotly debated. But between 1994 and 1996, 12 people in England came down with CJD, the human form of mad cow, and all had eaten beef from suspect cows. Current mad cow diagnosis lies solely in the detection of late appearing "prions", an acronym for hypothesized, gene-less, misfolded proteins, somehow claimed to cause the disease. Yet laboratory preparations of prions contain other things, which could include unidentified bacteria or viruses. Furthermore, the rigors of prion purification alone, might, in and of themselves, have killed the causative virus or bacteria. Therefore, even if samples appear to infect animals, it is impossible to prove that prions are causative. Manuelidis found viral-like particles, which even when separated from prions, were responsible for spongiform STE's. Subsequently, Lasmezas's study showed that 55% of mice injected with cattle BSE, and who came down with disease, had no detectable prions. Still, incredibly, prions, are held as existing TSE dogma and Heino Dringer, who did pioneer work on their nature, candidly predicts "it will turn out that the prion concept is wrong." Many animals that die of spongiform TSE's never show evidence of misfolded proteins, and Dr. Frank Bastian, of Tulane, an authority, thinks the disorder is caused by the bacterial DNA he found in this group of diseases. Recently, Roels and Walravens isolated *Mycobacterium bovis* it from the brain of a cow with the clinical and histopathological signs of mad cow. Moreover, epidemiologic maps of the origins and peak incidence of BSE in the UK, suggestively match those of England's areas of highest bovine tuberculosis, the Southwest, where Britain's mad cow epidemic began. The neurotaxic potential for cow tuberculosis was shown in pre-1960 England, where one quarter of all tuberculous meningitis victims suffered from *Mycobacterium bovis* infection. And Harley's study showed pathology identical to "mad cow" from systemic *M. bovis* in cattle, causing a tuberculous spongiform encephalitis. In addition to *M. bovis*, *Mycobacterium avium* subspecies *paratuberculosis* (fowl tuberculosis) causes Johne's disease, a problem known and neglected in cattle and sheep for almost a century, and rapidly emerging as the disease of the new millennium. Not only has *M. paratuberculosis* been found in human Crohn's disease, but both Crohn's and Johne's both cross-react with the antigens of cattle paratuberculosis. Furthermore, central neurologic manifestations of Crohn's disease are not unknown. There is no known disease which better fits into what is occurring in Mad Cow and the spongiform enchephalopathies than bovine tuberculosis and its blood–brain barrier penetrating, virus-like, cell-wall-deficient forms. It is for these reasons that future research needs to be aimed in this direction.

The origin of the existing theory

The theory surrounding neurologist Stanley Prusiner's "prions", coined for proteins that were

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infectious, was under a rightful cloud of suspicion from its onset. Working on obscure diseases thought to be caused by slow viruses, he would in effect rename them, and by April, 1982 had announced that the real culprit behind such diseases as scrapie in sheep, kuru in cannibals, Creutzfeldt—Jakob disease (CJD) in humans, and chronic wasting disease in deer and elk was either a virus, not yet isolated, or some rogue infectious protein-only "prion", which unlike anything yet known could multiply, and infect, without genes.

Biologists in the 1930s had incorrectly said that viruses were only proteins and that 'slow viruses' might be gene-less had been proposed by and discarded in Britain as early as 1967. Prion advocates, salvaging from the experience, put forth that prions were way smaller than other viruses without the capacity to carry genes. The biology of scrapie, however, because of its many strains alone, called for an agent with genes [75].

By 1984, National Institute of Health's Rohwer showed that prions were the size of small viruses, with plenty of room for genetic material [2]. In the same study Rohwer attacked the prion supposition that prions were immortal, citing agents of potential damage (ibid).

Early prion workers used a test called the incubation-time assay to judge purification, utilized cautiously in England since the 1960s. A modification cut the time to score this assay from a year to a couple of months. Rohwer commented that this test was enormously less accurate than traditional methods and that purifications using it could be off by a factor of from 100 to 1000. Such knowledge kept the viral or virus-like bacterial theories alive.

The finding that prions were proteins normally found in the body, including the brain of healthy controls, seemed to contradict the best evidence that they were infectious. The theory survived by finding a difference. Prions from healthy animals were "cellular" protein, those from scrapie were "scrapie" protein. Scrapie protein aggregated into rods while cellular protein did not. Another "critical clue" [76]: scrapie protein survived proteinase while "cellular" did not. This still did not mean however that some virus or bacteria did not cause the change to begin with *M. bovis*, for example, both by virtue of its cell-wall-deficient, virus-like forms, and that it shares methyllysines with other mycobacteria is also protease-resistant [77]. The amyloid proteins in Alzheimer's, not currently linked to prions, are also protease resistant [78].

Healthy "cellular" prions remain a mystery, but they need not be. Prions are amyloid and it was common knowledge before prions that there is a soluble serum protein component (SAP) of amyloid in healthy blood, its purpose also unknown [74]. What is clear is that the role of deposited amyloid fibrils, once formed, is to disrupt, destroy, and compromise, whether in mad cow, JCD, Scrapie, Alzheimer's or any of the other degenerative disorder.

Prion theorists further elaborated that although proteins normally fold into three-dimensional states, protein prions sometimes 'misfolded', assuming an incorrect, infectious state, which subsequently changed cellular protein into itself, setting off an infectious chain reaction. And since the damage done by prion protein seemed similar to the malfunctioning proteins of Alzheimer's disease, and even Parkinson's, these too might be caused by prions.

Critics point out that despite the vast expenditure [3] on research geared to verify that prions caused spongiform encephalopathies, to this point prions have not been established fully as the cause of any disease. Furthermore, it remained unclear how prions destroy brain tissue. In the meanwhile, experts pointed out that investigators have not proven that protein-only prions, even amplified over 100-fold and from infected brain — have increased infectivity, perhaps the best kept secret of prion researchers [4,5].

Both CJD and scrapie can be transmitted without prions [6]. Also, Brain material from which the prion and its antibodies have been removed can still infect animals. Prions have been found in completely unrelated disease processes, such as Kawsaski syndrome and inclusion body myositis. Finally, there were many strains of "prion" diseases, and no credible theory as to how these strains exist without genetic material. Aguzzi points out that abnormal prions have exactly the same amino acid structure as nonpathogenic prions, found in everyone. How could prion proteins, then be claimed to do what they are claimed to do? [7].

By all logical estimates, the death-knell to the prion hypothesis should have occurred with Lasmezas's 1997 interspecies transmission of bovine spongiform encephalopathy (BSE) in which more than half of injected mice had no detectable prions [6]. If this was not enough, then there was Manuelidis's 2002 [8] study on infectious neurons (microglia) with low prion levels in otherwise highly infectious material, which supported the concept that pathologic prions were the result of infection rather than being the actual infectious agent. To Manuelidis this was likely to be a virus, although she admitted the fundamental mystery remained. In fact, to many dissenters, some other, not as yet identified pathogen such as a virus or bacteria

caused "prions" to misfold thus damaging the brain.

Virus or a viral-like bacteria

The initial slow virus concept for the causal agent of TSE arose simply because the agent was filterable. By the mid-1990s, Manuelidis found viral-like particles which even when separated from proteinacious prions were responsible for transmitting infection [9].

In 1928, Eleanor Alexander-Jackson, discovering unusual and to that point unrecognized forms of the human and bovine TB bacillus, marveled at their many forms, including the tiny particles which the German Hans Much saw in 1908 and soon became known as Much's granules [10]. In 1910 Fontes proved Much's granules, as a sub-classification of Kleinberger's cell-wall-deficient "L-forms" were filterable and therefore also often mistaken for viruses. In fact, in certain circles, the variable acid-fast granules were called 'the TB virus' [11].

Much, for almost 30 years. studied the typical and atypical forms of tuberculosis watching the tiny nonacid-fast granules named after him convert thru a diptheroid stage into classic acid fast rods and fibrils [10].

L-forms, the connecting link between viruses and bacteria, where first described by Klieneberger-Nobel [12] at England's Lister Institute for which they were named. L-Forms were "cell-wall deficient" because they either had a disruption of or lack of a rigid bacterial cell wall. This allowed them the plasticity to assume many forms (pleomorphic) — some of them viral-like, but all of them different from their classical parent and poorly demonstrated by ordinary staining [12]. Of all the bacteria, L-forms predominate and are crucial to the survival of tuberculosis and the *mycobacterium*, whose cell-wall deficient forms escape destruction by the body's immune system. Because of their small size and configuration bacterial L-forms have, at different times, been called 'viruses', 'retroviruses' or 'C-particles'.

Mellon and Fisher warned that filterable forms of *M. avium*, *M. bovis* and *M. tuberculosis* could easily be mistaken for viruses. Mellon stated that the granular, prion-like forms of TB, found in its bovine and avian strains, prevalent in the very animals susceptible to BSE, including cattle and sheep, all originated from Much's granules [13]. Such viral forms of mycobacteria like *M. bovis* could by themselves produce disease. And since they were filterable, they could easily penetrate the blood—brain barrier [14]. Filterable, viral form of TB or TB in cattle have been recovered as an ultra virus in all body fluids, including urine and in the spinal fluid in central nervous system infection. This is similar to the granules Gabizon found in "prions" in the urine [15].

Xalabarder of Barcelona noted L-forms of bovine tuberculosis even in the blood of people simply vaccinated against TB with BCG, a diluted *M. bovis* vaccine [16]. He emphasized that L-Forms of the mycobacteria were remarkably different from L-forms of other species in their resistance to physical and chemical agents [17]. Similar to prions, mycobacterial CWD forms escape destruction by the body's immune system, and are seemingly imperishable (ibid). Xalabarder noted that these L-forms contain proteins, both RNA and DNA but do not stain well by ordinary mycobacteria dyes. Klieneberger-Nobel adds that L-forms consists of the formation of very small forms, poor in ribonucleic acid (ibid). Yet no matter how small and enucleated, some of these L-forms will revert back to virulent mycobacteria. In the case of cattle this has led to a 10,000—15,000 year history of sometimes fatal interaction between *M. bovis*, the cow, and man.

Like Klieneberger, Dr. Virginia Livingston compared the filterable forms of her tuberculosis-like germ to 'L-mycoplasma' or 'mycoplasmic-like forms', because without intact cell walls they were often mistaken for the bacteria mycoplasma, which has no cell wall [18]. The differentiation between Mycoplasma and cell wall deficient bacteria, in general, is difficult at best [19], and L-forms of TB-like bacteria are already on record as having been mistaken for mycoplasma-like forms [20]. One of these bacteria is *Spiroplasma*.

To Dr. Frank Bastian, professor of neuropathology at Tulane University, morphological and immunologic evidence all pointed to a bacterial cause for TSE. His finding DNA in TSE tissues clearly indicated the association of a bacteria with the disease [21].

Bastian collected evidence suggesting that a cell-wall-deficient, spiral-shaped bacteria (can also occur as a coccoid or filamentous form), called *Spiroplasma*, a mycoplasma, picked-up by both its DNA and on electron microscopy is involved in brains infected with Creutzfeldt—Jakob but not in controls [21]. Bastion also found this particular mycoplasma, only discovered in 1976, in another spongiform encephalopathy, scrapie in sheep. The *Spiroplasma* implied, however, *Spiroplasma mirium*, is for the most part hosted in rabbit ticks and before his research caused cataract and disease in

suckling mice only. And *Spiroplasmas*, in their short, less than 30 year history, had *always been* associated with an insect host at some point, though several primary isolations have been made from plants.

Whether *Spiroplasma* causes the abnormal proteins in TSE or is a consequence of TSE itself requires further experimentation [21,72].

An unnoticed epidemiologic finding

While various theories continued to swarm around the cause of TSE's, the best epidemiologic maps of the peak incidence and prevalence of BSE or mad cow disease, done in the UK, it turns out, suggestively matched those of the highest prevalence of England's bovine tuberculosis in cattle, with a predominant distribution in the Southwest (see Figs. 1 and 2) extending to counties further north [22,23], the very area where BSE in the UK began.

An idea of the prevalence of cow tuberculosis in England during the nineteenth century can be gained by the following: in 1890, Queen Victoria ordered that the dairy cows at the Home Farm at Winsor be tuberculin tested. Thirty-five of forty were found tuberculin positive and tuberculous lesions were found in all of these positive reactors. And yet the premises "in which these cows were kept were probably the best in the kingdom..." [24]. It is claimed that in England, supposedly next to BSE, bovine TB is the most serious animal disease that its Ministry of Agriculture has to cope with and in 1934 at least 40% of British cows were infected with TB [25], accounting for 6% English deaths from

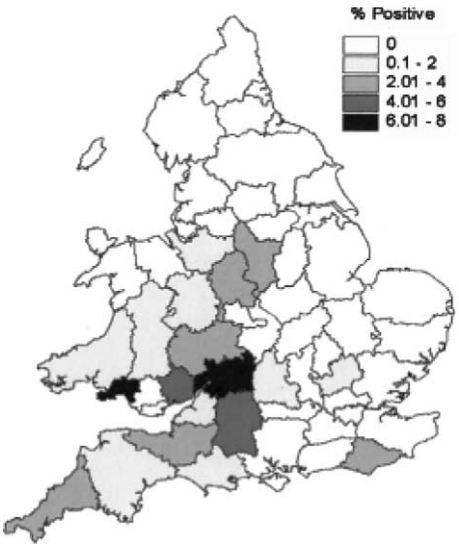

Figure 1 Bovine tuberculosis in UK 1999.

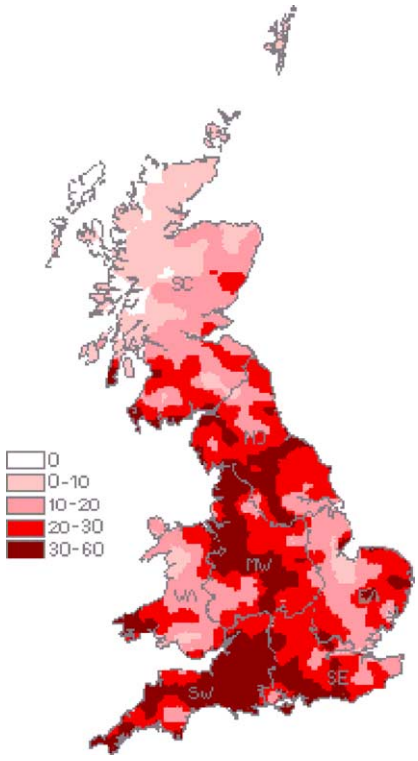

Figure 2 BSE-positive cattle in UK 1997.

tuberculosis in the 1930s and 1940s. Despite the fact that mandatory cow tuberculin skin testing was introduced in 1960, data for the year 2000 in Great Britain show a national herd incidence of 2.8%, with an exponential increase in cases in the southwest of England over the past 10 years [26]. Furthermore, there is small but significant reservoir of humans who ate beef and milk products prior to 1960 and can reactivate previous *M. bovis* infection, sometimes with CNS manifestations [27].

In his 1932 historical overview, Webb speculates that man was first introduced to tuberculosis when he began domesticating cattle around 5000 B.C. [28]. Thus one could surmise that human tuberculosis originated by transfer of *M. bovis*, which has the potential to infect humans, into the human body, where it adapted as the tubercle bacillus (ibid).

Garnier though, using deletion analysis, recently questioned this, placing human *M. tuberculosis* as having come first, and, having infected cows at the time of cattle domestication 10,000—15,000 years ago [26]. At any rate, prior to that, the tuberculous bacilli, always soil born, first infested and then infected an assortment of mammals, both ruminants and primates.

Modern genetics has verified that DNA between human (*M. tuberculosis*) and cow (*M. bovis*) tuberculosis are almost identical, indicating they are

virtually the same species [29]. Even in culture plates their appearance is similar.

The mycobacteria emerge in mad cow disease

By 1975, a new problem had arisen in the wildlife of southwest England, the cradle of BSE. Bovine strains of mycobacterium were isolated from the badger *Meles meles*. An entirely new development in a country where the bovine form of the disease had been supposedly eradicated since 1960, it was viewed with grave concern by public health authorities. Not only was it not clear how the badgers of southwest England, in intimate contact with the cattle their, had acquired bovine tuberculosis but it was then found that not a single badger from other areas harbored the disease [81].

Furthermore, it soon became obvious that the cattle found to harbor TB, either *M. bovis* or *M. avium* (fowl TB) were consistently and markedly underestimated, with many "healthy" animals harboring the disease [30—34]. There were many reasons for this. TB lesions, were virtually to be found in any organ or body cavity of diseased animals yet traditionally only a handful of organ systems were checked before slaughter. Also in the early stages of the disease, lesions were hard to find, even during post-mortem examination. Therefore Francis's observation that "the possibility of danger to public health from the flesh of tuberculous cattle, although very small, can never be absolutely denied" is only partially correct [35]. Carnivores may acquire *M. bovis* through the alimentary tract by eating infected meat [36,73]. Man is no exception. Adding to the problem is that despite clear FDA recommendations for cooking meat [37], certain consumers prefer to eat their meat rare to medium-rare.

The power of oral consumption of virulent mycobacteria into the alimentary tract was unfortunately shown in the German Lubeck tragedy, in which inadvertent mycobacterial contamination of otherwise watered-down bovine tuberculosis was protectively administered for infant immunization. Out of 251 newborns, 72 died and 100% had alimentary lesions, primarily in the small intestine [38].

That tuberculosis and the mycobacterium can cause the progressive ataxia found in Mad Cow 'downers' has been adequately cited, in both man and cattle [39—41]. Moreover, that *M. bovis*, cow tuberculosis, can cause the clinical signs and histopathology of "mad cow" in cattle is also on record [42]. Otter [40] studied ataxia and weight loss secondary to *M. bovis* in deer. No other TB organism has as great a host range as bovine TB, which can infect all warm-blooded vertebrates (animals with a backbone).

Mycobacterium bovis, a relatively common cause of TB meningitis in pre-pasteurization times, cannot only cause meningitis and encephalitis in humans [27,43,44] but in cattle as well [45]. The US Department of Agriculture's fact sheet on bovine tuberculosis clearly and specifically states that in diagnosing the disease, lesions must be looked for in the nervous system of cattle. Hartley's study showed pathology identical to "mad cow" from systemic *M. bovis* in cattle, causing a tuberculous spongiform necrotizing encephalitis without recovery from the CNS of classical forms of TB (ibid). The neurotaxic potential for cow tuberculosis is best attested to by that, in England, prior to 1960, one quarter of all tuberculous meningitis victims suffered from *M. bovis* infection [46]. Wilkins, doing an epidemiological survey found bovine tuberculosis associated with lifelong residency in the UK and attributed its low incidence among tuberculosis isolates to a low tendency for *M. bovis* to reactivate [71].

Once the most prevalent infectious disease of cattle in the US, bovine TB caused more losses among US farm animals in the early part of this century than all other infectious diseases combined [47]. And *M. bovis* still causes worldwide annual losses to agriculture of $3 billion dollars. In his Nobel Prize address of 1901 Von Behring stated "As you know, tuberculosis in cattle is one of the most damaging infectious diseases to affect agriculture" [26]. But the problem was more extensive than even Von Behring realized. Enter *Mycobacterium avium* complex or MAC.

Fowl tuberculosis: a major plight in the cattle industry

Mycobacterium avium causes tuberculosis in chickens and other fowls but can also infect an extensive range of different animal species including cattle, sheep, deer and man. The *M. avium* complex (MAC) includes closely related *M. avium*, *M. intracellular* and *M. avium* subsp. *paratuberculosis* or paratuberculosis. Paratuberculosis, extremely slow growing, causes Johne's disease in domestic and wild ruminants, a problem known and neglected in cattle and sheep for almost a century. Johne's disease caused by *M. paratuberculosis* is rapidly emerging as the disease of the new

millennium. Recent European epidemiological studies indicate an alarming increase of paratuberculosis in cattle and sheep, and the USDA reports that between 20% and 40% of US dairy herds are infected [48]. This, as well as its role in Crohn's disease in humans has shifted attention front and forward [49].The evidence to support *M. paratuberculosis* infection as a cause of Crohn's disease is mounting rapidly [50].

Not only has *M. paratuberculosis* been found in Crohn's disease by five investigative groups in different countries, but Crohn's patients and Johne's diseased cattle have antibodies which cross-react with the antigens of paratuberculosis [19]. All paratuberculosis isolated from Crohn's have been of the bovine subtype, found in cattle [51]. Cattle and sheep can infect one another with paratuberculosis [52]. Deer are also susceptible.

Since paratuberculosis is not classified as a human pathogen, the beef from cattle infected with it is not prevented from entering the food chain [53]. Paratuberculosis causes a disease in cattle that is similar to Crohn's in humans in that both attack the terminal illium. Crohn's disease is no small problem, and the number of Americans suffering from it is between 400,000 and 1,000,000 (Scientific facts about Mycobacterium paratuberculosis and Crohn's disease Source: http://members.aol.com/ParaTBweb/crohn.htm).

Paratuberculosis is highly heat resistant [54], and may not be killed by standard techniques for cooking beef [55], even more so than *M. bovis*. It is estimated that from 5% to 20% of all cattle in the US alone, are infected with paratuberculosis, bringing estimated losses to $1.5 billion annually, [56], but the problem is worldwide. And Rosisiter found it in up to 34% of dairy cows [57], the very same cattle frequently used for the production of the ground beef that enters the food chain [58].

Amyloid: the common denominator in all spongioform encephalopathies

"It is an astounding finding, because we never would have dreamed that amyloid and prions are the same", proclaimed Stanley Prusiner [1].

In the past amyloid was usually the deposition that took place due in the course of chronic inflammatory disease, mainly tuberculosis, the usual precipitating cause. The very term "amyloidosis", coined by Virchow, was a misnomer, assuming that the infiltrative material had chemical similarities to the starch (or amylum) of plants, which it did not. Nevertheless, by force of use and habit, the word stuck.

Hass's study proved a direct correlation between amyloid deposition and the mycobacteria by injecting *M. bovis* into rabbits and following *M. tuberculosis* in humans. He concluded that the only infectious disease which served as an apparent cause of amyloidosis was tuberculosis [59]. All 21 human subjects with amyloid in Hass's investigation had chronic pulmonary tuberculosis. In a 50-year study based upon autopsy, Schwartz saw amyloidosis, primary and secondary, in the brain and elsewhere as a by-product of underlying infectious tuberculosis, either reactivating itself or being reactivated by a host of traumatic, chemical, biologic or physical insults [60]. Microscopically, in the brain, Schwartz found plaques and amyloid degeneration of nerve fibrils.

When Schwartz injected 22 guinea pigs with *M. tuberculosis*, all but four came down with amyloidosis. His uninfected controls, with the exception of one showed no amyloid. He thereby confirmed Hass, who's large series of rabbits showed that three out of four inoculated with bovine tuberculosis had amyloid disease within 15 months [59]. Hass's amyloid uniformly showed a principal protein fraction as well as a minor fraction whose physical behavior also implied another protein.

The amyloid issue had surfaced previously when in 1978, Researcher Pat Merz, in breakthrough work, identified tiny fibrils in the brains of scrapie infected mice not present in well controls. Prion purists refused to admit that their prion rods were related to Merz's find, citing her entities as longer fibrils and claiming that Merz stated plainly that her scrapie associated fibrils (or SAF) were not amyloid and therefore could not be prion rods, the term Prusiner used for amyloid fibrils. Actually Merz said that her Scrapie associated filaments were amyloid-like on more than one occasion and workers in the field suggested that the two entities in Merz and Prusiner's papers were identical [1]. Delgado saw such fibrils in either case as typical features of amyloid [62].

Meanwhile, by 1994, de Beer, studying the relationship between a major rise of serum amyloid and having tuberculosis, saw a rapid descent in amyloid in patients treated with anti-tubercular drugs [63].

As an offshoot of de Beer's work, Tomiyama dissolved β-amyloid plaque with rifampin, a first line drug in the treatment of TB, and one of the few agents, to this day, that is able to dissolve amyloid plaque [64].

Conclusion

The TSE's are chronic wasting diseases and virtually every aspect and finding of the currently held "prion" theory for TSE's, and then some can be found in the literature of Bovine tuberculosis, a known disease going back 10,000—15,000 years. *M. bovis* extracts have long been known to shorten the incubation period of scrapie, purportedly as an immune "stimulator" [72]. In addition bovine TB's blood—brain penetrating L-forms can simulate viral elements found in the TSE's [9] and have, on at least one occasion been mistaken for mycoplasmic-like forms [20], such as *Spirolemma*. In addition prions [74] protease resistance is shared by both bovine tuberculosis cell-wall deficient forms [17] and the fact that it produces protease-resistant methyllysines [77]. In the UK, the highest area of bovine TB, the Southwest, was the very area which both spawned and contained the highest rate of BSE in cattle [22,23]. *M. bovis* causes the clinical and histopathology of "mad cow" in cattle [42]. And tuberculosis and the mycobacterium can cause the progressive ataxia found in mad cow "downers" both in man and cattle [39—41]. Although no other form of TB has a greater host range than bovine TB, which includes man and all the other warm-blooded vertebrates subject to the TSE's, it is extremely hard to isolate and Hartley's study of mad cow from systemic *M. bovis* showed a tuberculous spongioform encephalitis without recovery of classical CNS mycobacteria [45]. That bovine tuberculosis can be transmitted thru ingesting contaminated meat cannot be denied [35], and its neurotaxic potential showed clearly in an England prior to 1960, where 25% of all tuberculous meningitis victims suffered from *M. bovis* [46]. And that both forms of bovine tuberculosis, *M. bovis* and *M. avium* subsp. *paratuberculosis* (also referred to as paratuberculosis) are consistently and markedly underestimated in the meat that we eat has been extensively brought up [30—34,53]. Paratuberculosis, extremely slow growing, causes Johne's disease, a rapidly emerging, known and neglected, malady in cattle and sheep for almost a century. The evidence to support cattle paratuberculosis as the cause of human Crohn's disease is mounting rapidly [19,50,51], and Rossiter found in up to 34% of dairy cows, the very same cattle frequently used to produce the ground beef that enters the food [57]. Central neurologic manifestations of Crohn's disease are not unknown [79].

The detection of 14-3-3 protein, in the cerebrospinal fluid, originally thought to be a highly reliable indicator for "prion" diseases, also appears in CNS tuberculosis [69] and the very fabric of the TSE's and prion diseases, amyloid has been implicated and re-implicated as being caused by bovine and human tuberculosis [59,60]. The well-known resistance of the edible muscle tissue, favored by man, in cattle to tuberculosis once even brought up the possibility of using muscle grafts for surgical salvage in pulmonary tuberculosis [70].

Creutzfeldt—Jakob only kills somewhat over 200 Americans per year, though this number is questionable after a study in which Alzheimer's was misdiagnosed in up to 13% of patients actually suffering from Creutzfeldt—Jakob disease [61]. This relatively low incidence fits in with evidence that man is less susceptible to bovine tuberculosis then other animal species. In guinea pigs, a single bovine bacillus may suffice to establish progressive infection [65]. And Villemin documented that none of his rabbits inoculated with human tuberculosis presented a disease so "rapidly and completely generalized as that obtained by inoculation with the tubercle of the cow.....” [66]. Rich, however, argued that there was no satisfactory evidence that humans possess a higher native resistance to bovine rather then human tubercle bacilli [67]. In 1917, 5% of US cattle were infected with *M. bovis*, and approximately 25% of human TB fatalities originated from cattle [68].

Virginia Livingston [80] quotes Ellen G White's 1905 *Ministry of Healing* regarding the topic. Incredibly, White, almost 100 years ago:

> "Flesh was never the best food; but its use is now doubly objectionable since disease in animals is so rapidly increasing. Those who use flesh foods little know what they are eating. Often if they could see the animals when living and know the quality of the meat they eat, they would turn from it with loathing. People are continually eating flesh that is filled with tuberculosis and cancerous germs. Tuberculosis, cancer and other fatal diseases are thus communicated."

Today the greatest hindrance to finding a cure for TSE's lies in the very theory they have become embedded in. Santana's oft quoted "he who does not remember the past is condemned to relive it in the future" seems clear here. Early twentieth century recognition of the spread of cow tuberculosis was obvious and at one time American milk contained the words: "tuberculin tested," an epitaph to the up to 30% of human cases of pre-pasteurization tuberculosis. It is almost certain that Crohn's disease is a form of bovine tuberculosis. How long will it then take before the transmissible

spongioform encephalopathies are also recognized as being the result of this disease?

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