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Doubts about BSE being an Orally Transmitted Infectious Disease

An Alternate Hypothesis Concerning the Origin of the BSE Epidemic in the UK and the Rare Cases of BSE Suspects in Continental Europe

by

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The BSE dilemma started in 1976 when the virologist GAJDUSEK claimed that all spongiforme encephalopathies (SE) are infectious diseases due to a virus transmitted by food. His alleged proof was the Kuru disease in Papua-Newguinea, which, he said, was caused by cannibalistic rituals (which nobody has ever observed), and a putative transmission of the disease by intracerebral injection of Kuru brain material into the brain of mice.

In 1982, the neuropathologist PRUSINER investigated the characteristic plaques in brains of SE patients, showing that they consist of a normal membrane protein which has the tendency to aggregate. In SE patients, this protein is mutated resulting an increased tendency to form aggregates. Thus, at least the human forms of SE are genetic diseases.

Although PRUSINER disproved the viral hypothesis of GAJDUSEK, he was caught by the dogma of infection. Since brain of deceased SE patients injected into the brain of mice caused SE symptoms, he argued that it contains an infectious agent. The aggregated protein would induce the aggregation of normal proteins. He called this material a *proteinaceous infectious agent*, abbreviated "*PRION*" (not "*PROIN*"*, because that's not so snappy*).

GAJDUSEK, PRUSINER and many others who demonstrated infection by means of intracerebral injection apparently did not ask how the immune system reacts to foreign proteins and how it could be involved in the development of neurological and histological symptoms.

In conclusion, the notion of spongiforme encephalopathies being infectious diseases which are transmitted orally appears to stand on a weak base: First, the infectiosity is based on intracerebral injections which can be interpreted as an autoimmune response, second, the oral transmission is based on the rumour of cannibalistic rituals.

On the other hand, PRUSINER's data and former observations (e.g. PARRY 1962: „S*crapie is a genetic disease which can be controlled by proper breeding protocols") suggest that spongiforme encephalopathies are genetic diseases*. They are either inherited

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from gonadal mutations or acquired by somatic mutations. The inherited SE is extremely rare (e.g. familial CJD in humans), but sometimes frequent in inbreeding populations (e.g. scrapie in Scottish sheep herds). The incidence of acquired SE in humans, CJD, is 1 per 1 million per year. Moreover, the acquired SE in cattle is certainly not a new disease. *Mad cows, mucca pazza, vache folle, hierlewirbelige Kühe* have been a quite familiar phenomenon in the past when cows became older than nowadays. According to the records, such cows have been observed at a rate of about 1 per 10 thousand or less. It was considered an age-related, not an infectious disease.

Beginning in 1986, *mad cows* were more frequently observed in England. The monthly numbers rose from 100 in 1987 to 3000 in 1993 and then slowly declined. The epidemic spread from South to North, but the highest incidence was always in the Southeast, where it remained confined to certain counties. By histological investigation the signs of SE were found, like those in the brain of scrapie sheep. Veterinarians who believed in GAJDUSEK's dogma and PRUSINER's idea of infection immediately declared the cows as being infected by scrapie sheep Prions in the meat meal – without any proof. Nevertheless, the meat meal was banned in 1988.

A controlled field experiment of feeding cattle was not performed. Instead, numerous laboratory experiments, mostly with mice in the absence of appropriate controls, were presented as a rather questionable piece of evidence. The decline of the epidemic, 5 years after the meat meal ban, is no proof of the *prion-in-meat-meal hypothesis*, since at least one third of the British BSE cattle was born after the ban.

Thus, it was (and still is) mere speculation that an infectious agent is transmitted from sheep to cattle by feeding and that it will be transmitted from cattle to humans resulting in serious health hazards.

In the light of published observations (e.g. that BSE was heterogenously distributed and restricted to certain counties, e.g. that BSE occured in less than 20% of the herds, e.g. that offsprings of BSE mothers got more frequently BSE, e.g. that the genotype pattern in affected and not-affected herds appeared to be different) and consistent with PRUSINER's data an alternate hypothesis is plausible: **The British BSE epidemic is due to a genetic defect which had been accumulated in the gene pool of some herds by excessive inbreeding.** Cattle with a strong genetic disposition will be more sensitive to environmental factors (e.g. intoxication by insecticides, copper deficiency, autoimmune diseases) and will sicken with BSE sooner than those without such a disposition.

A likely candidate of an environmental factor could be the exposure of cattle to feedstuffs containing bacteria showing molecular mimicry between bacterial proteins and bovine tissue. Analysis of molecular sequence databases shows that the ubiquiteous *Acinetobacter* shares sequences with a peptide of bovine myelin and the prion protein, as was recently reported by the immunologist EBRINGER, London. Thus, antibodies against *Acinetobacter* could enhance the tendency of mutated prion proteins to aggregate. According to EBRINGER, BSE could be an autoimmune disease like, for example, ankylosing spondylitis (M. Bechterw) or rheumatoid arthritis which are observed predominantly with

patients (1) showing a certain genotype pattern, who (2) are exposed to certain bacteria (*Streptococcus*, *Klebsiella* or *Proteus*).

British BSE cows (between 4 and 5 years of age) were clearly sick, diagnosed on the basis of neurological disorders. The incidence in the most affected herds was 1 to 10. On the other hand, **the so called BSE cows in continental Europe** were mostly diagnosed on the basis of a post mortem test. It indicates the existence of some proteinaceous aggregates in the brain which are hardly digestible by a bacterial enzyme, but not the disease itself. These cows **are BSE suspects solely by testing**. They might have got BSE some years later if they hadn't been slaughtered at this relatively young age. In Germany. the incidence is one suspected case per 16.000 tests performed. Most likely, it reflects the mutational rate of the gene of the respective protein in an early embryonic state. Regional differences (e.g. higher rates in Southern Bavaria) might be due to differences in the overall mutational burden.

Those who conceived the *prion-in-meat-meal hypotheses* were convinced that, if prions cross the species barrier between sheep and cattle (by eating the rendered carcasses of scrapie sheep) they will also cross the barrier between cattle and men (by eating products of BSE cattle). A human epidemic was predicted to take off in the early nineties. Thousands of *beefeaters* would contract the Creutzfeldt-Jacob disease. The news media exaggerated this mere speculation which provoked hysterical reactions of European consumers.

Finally, in 1994, a young patient with neurological symptoms died; the post mortem diagnosis was CJD. Because the pattern of symptoms differed from that of older CJD patients, he was declared as the first BSE related case of the expected epidemic. The disease was named **new variant CJD** (*nvCJD*), but its novelty is questionable, since the clinical and neurohistological symptoms are consistent with the first desription of SE in humans; it was the case of a 23 years old patient which had been published by the German neurologist CREUZFELDT in 1920.

Meanwhile, 130 cases of nvCJD were diagnosed in Great Britain, one per 4 millions per year. Most likely they would have been tagged previosly with different diagnoses, as the British epidemiologist VENTERS wrote recently („*nvCJD – the epidemic that never was*"). Extremely rare diseases are usually misdiagnosed, as he said, unless they are in the center of general interest (and anxious expectation). A reliable proof of any connection with BSE is missing, although several scientists (mostly those who receive research money for BSE studies) permanently declare the opposite – and kindle public hysteria again and again.

Publications concerning doubts about BSE being an infectious disease:

1997: Zur Infektiosität der spongiformen Enzephalopathien: Phänomene und Spekulationen, aber keine Beweise. – Arzt und Umwelt: 105 – 112.

2002: 25 Thesen gegen die Behauptung, BSE und vCJK seien oral übertragbare Infektionskrankheiten und BSE gefährde die menschliche Gesundheit. – Deutsche Medizinische Wochenschrift **127**: 341 – 343.

2003: La vera storia della mucca pazza. – Il Secondo Rinascimento **75**: 261 -290.