

The scientific picture on BSE: incomplete, but frightening

by Jonathan Tennenbaum

Judging from its characteristics and probable origins, bovine spongiform encephalopathy belongs to a fairly well-defined family of transmissible diseases in humans and animals, whose chief manifestation is a progressive, invariably fatal destruction of brain tissue. The term “spongiform” refers to a peculiar, sponge-like quality of the brain lesions produced by these diseases.

Until the first discovery of spongiform encephalopathy of cattle, in Great Britain in 1985, this family of diseases had attracted attention mainly in two guises: first, a widespread illness in sheep, called scrapie, which had been known as a major problem in flocks of sheep in Europe since at least the middle of the eighteenth century; and second, a group of hitherto extremely rare brain diseases of humans, including especially Creutzfeldt-Jakob disease (CJD), Gerstmann-Straussler-Scheinker disease (GSS), and kuru. In both cases it had proven very difficult to determine the causes and mode of propagation of these diseases.

In the case of scrapie, it can often happen, that only a single animal in a herd is affected; genetically transmitted factors are assumed to play an important role. Major outbreaks of scrapie in the past often correlate with a prehistory of excessive inbreeding, or of breeding practices aimed at rapidly expanding the numbers of animals in periods of “high market demand.”

Nevertheless, it was demonstrated in the 1930s, that scrapie can be artificially transmitted, by injecting small amounts of brain tissue from diseased animals, directly into the nervous system of healthy animals. Later it was demonstrated that CJD, too, possesses some sort of transmissible agent. D. Carleton Gajdusek and others succeeded in transferring Creutzfeldt-Jakob disease to chimpanzees, through injection of brain tissue extracts from human CJD victims. The chimpanzee disease could subsequently be retransmitted among chimpanzees, by the same means.

Such experiments also demonstrated, that the typical latency or incubation period for scrapie and other transmissible encephalopathies—the time from initial infection until the first appearance of symptoms—can be extraordinarily long. In cases of accidental hospital transmission of CJD, by transplants or contaminated surgical instruments, the incubation period can extend to 30 years! For this reason, scrapie and CJD were provisionally termed “slow virus” diseases, placing

them in the same category with maedi-visna (a viral infection of sheep), and HIV-associated AIDS in humans today. Both the maedi-visna and HIV viruses can cause progressive brain disease, among other manifestations. There are important differences, however.

Unusual features of scrapie

While searching for a virus as suspected infectious agent of scrapie in the 1950s, D.R. Wilson, I.H. Pattison, and others discovered several surprising and disturbing facts, which have significant implications for the problem of BSE today.

Firstly, it was found, that brain extracts of diseased sheep remained infectious even after treatment by various of the methods used to sterilize instruments, medical preparations, and food products. This extraordinary degree of resistance to heat, chemicals, and even intense ultraviolet light, suggested the possibility, that these diseases might be connected with an infectious agent of a fundamentally new type. This conclusion gained some support through the finding, that infected animals display no detectable immune reaction to the agent transmitting the disease. (Indeed, according to one of the leading hypotheses being pursued today, the infective agent of scrapie and related diseases is not an ordinary virus at all, but a mere protein—a naturally occurring protein, whose characteristics have been modified by a change in its spatial conformation.)

Secondly, in 1961 Pattison and Millson published the results of experiments, showing that scrapie could be transmitted to sheep by the oral route, through ingestion of as little as 100 ml of scrapie-contaminated brain emulsion. Other experiments have shown, that the transmissible agents of scrapie are not only concentrated in the brain, but can also be present in other organs of the body, albeit generally in very much smaller concentrations.

Thirdly, scrapie was shown to be transmissible to other animals, initially including goats and mice, thereby producing a fatal, degenerative brain disease analogous to that in sheep. These and later experiments of cross-species injection, pointed to the existence of a so-called species barrier, which, however, is not absolute, but depends on such things as the dosage of infectious material and the method chosen to introduce it (by injection or otherwise).

These results, obtained in Great Britain during the 1950s and 1960s, together with the results of related research in

other countries, would obviously cause one to be wary of the practice of “recycling” sheep remains in the form of feed supplement, unless the treatment process involved were sure to deactivate the scrapie agent. Nevertheless, quite the opposite attitude prevailed in British practice, especially from late 1970s on.

When the first cases of BSE appeared in the mid-1980s, the striking similarity with scrapie was immediately noticed. The obvious hypothesis suggested itself—an hypothesis widely, but not universally, embraced among researchers today—namely, that BSE was initially the result of a species-barrier “passage” of the scrapie agent, via “recycling” into feed supplement for cattle.

Quite apart from the hypothesis about a possible “species jump” origin, there was every reason to expect (as has been confirmed by subsequent investigations), that BSE shares many common biological features with scrapie, including the existence of a transmissible agent, the high degree of resistance of that agent to normal sterilization procedures, and the possibility of transmission via the oral route. Hence, it should not have been difficult to guess, what would result from the practice of recycling the cadavers of BSE-afflicted cattle, including their brain tissue, to healthy cattle, via rendering methods which fail to deactivate scrapie-like agents. In view of the scientific results quoted above, permitting such recycling of cattle remains can only be described as an extreme form of criminal negligence. This “cannibalistic” practice almost certainly was the main factor in the rapid, epidemic-like spread of BSE after 1985.

Is there a danger to human beings?

This leaves open the critical question, whether there is a significant danger to human beings, from the consumption of meat and other products from BSE-infected cattle. An apparently strong argument against such a danger, is suggested by the observation, that human beings have been eating the meat of sheep a very long time, and have doubtless been exposed countless times to scrapie via the oral route. Scrapie has often been rampant among sheep herds in Europe, and normal cooking can hardly be assumed to have deactivated the scrapie agent in all cases. Despite this, there is hardly a trace of a correlation between lamb consumption and the incidence of Creutzfeldt-Jakob and other forms of spongiform encephalopathy in humans. The latter incidence remains exceedingly small—generally of the order of one case per million population per year. This would seem to point to the existence of a very large “species barrier” protecting human beings from infection by scrapie.

On the other hand, the reassurance offered by this argument rests on the assumption, that the potentials of transmission of BSE are practically identical to those of scrapie. Unfortunately, recent research points to some significant differences.

As noted above, scrapie can readily be transmitted to

healthy sheep by oral administration of suspensions of brain tissues from scrapie-affected sheep. However, transmission of scrapie to other species, by the oral route, has proven much more difficult. A different picture is emerging for BSE. A recent issue of the *British Veterinary Record* reports experiments, in which a spongiform encephalopathy was induced in scrapie-resistant sheep by oral consumption of the equivalent of 0.5 grams of brain tissue from BSE-infected cattle. Mice have been successfully infected from BSE in a similar way. Furthermore, following the outbreak of BSE in British cattle, spongiform encephalopathies began appearing in England for the first time in cats (68 cases as of August 1995) and in a variety of zoo animals (21 cases), in which this type of disease had not previously been observed. Evidence points to the conclusion, that these are cases of oral transmission via BSE-contaminated beef products.

These data, while not all fully corroborated, do suggest that the infective agent of BSE is more easily transmitted to other species, than that of scrapie.

To this must be added the reported appearance, in England in recent years, of at least 10 cases of a form of Creutzfeldt-Jakob disease apparently never observed before. In contrast to the usual form of sporadic CJD, which mainly infects elderly and middle-aged persons, this variant form has struck young patients (mean age, 26.3 years), and causes a clearly different pattern of brain lesions. Although by no means proven, the possibility must clearly be considered, that the new form of CJD has been caused by a transmission to humans, of the agent of BSE. Clearly, BSE-contaminated material must be rigorously excluded from human consumption.

Mad politicians—more dangerous than mad cows!

As frightening as the BSE outbreak and its possible effects on human health might be, there is every reason to believe that the BSE problem itself can be brought under control. Indeed, measures taken from 1988 on, including especially the prohibition of further “recycling” of sheep and cattle remains into cattle feed, have already produced a drastic fall in the rate of new BSE cases, beginning 1993. Even if significant numbers of people were to eventually develop CJD-type illness as a result of BSE exposure—a “worst-case” hypothesis—it would seem highly unlikely that this would lead to a sustained epidemic involving direct transmission from person to person. In all known diseases of this type, including scrapie, BSE, and CJD, such “horizontal transmission” is exceedingly rare, under normal circumstances.

Unfortunately, we are not living under “normal circumstances.” The main danger we face is not from this or that disease, but from the epidemic of criminal negligence, which made such things as BSE possible. If the policies of Thatcherism are tolerated much longer, then BSE could be a mild taste of things to come.