

The BSE Inquiry / Statement No. 18
Scheduled to give evidence on 30/03/98

STATEMENT OF JOHN WILLIAMS:

18th March 1998

1. My name is David John Williams. I have worked as a professional medical translator with my own business since 1973, specialising in medicine and biological sciences.
2. I grew up on a farm in South Wales. This is one of the reasons for my interest in BSE and TSEs in general. As parliamentary candidate for the Ashford constituency in Kent, I was confronted with the issue of potential groundwater contamination from the effluent of Thruxted Mill rendering plant. This was the subject of a planning inquiry held in Canterbury in February 1997, which I attended in its entirety, and at which I cross-examined scientific witnesses on behalf of local residents.
3. Prior to the planning inquiry, I had felt that passage of BSE prions into the groundwater was unlikely. My previous scepticism with regard to the risk of groundwater contamination was dispelled by the detailed testimony of the scientific witnesses speaking on behalf of the rendering plant proprietors and the Environment Agency (EA). In particular their replies to cross-examination by Dr. Alan Colchester and myself at the planning inquiry gave rise to my concern that there might indeed be a real risk.
4. I subsequently investigated in theoretical terms on the basis of the EA testimony in conjunction with other scientific data the likelihood that BSE prions could have passed into the groundwater (and therefore might be responsible for the "Ashford Cluster" of vCJD cases). Professional experience accumulated over 25 years in Heidelberg in the evaluation and presentation of empirical medical research equipped me to examine critically the experimental and theoretical indications for a "common source" origin of the British BSE epidemic.
5. The generally accepted explanation in the scientific literature was that the widespread distribution of BSE cases throughout the United Kingdom (although this distribution was by no means even) in the months following November 1986 resulted from scrapie crossing the sheep/cattle species barrier in consequence of changes in methods of rendering (specifically, the abandonment of solvent extraction of tallow) at the beginning of the 1980s^{1,2}. This "scrapie hypothesis" has been additionally called in question by a recently published paper reporting no deactivating effect of the one solvent (n-heptane) investigated on scrapie infectivity³. However, the latter experiments need

amplification by testing other solvents and TSE strains before any firm conclusions can be drawn.

6. The most frequently cited evidence in support of the scrapie theory is circumstantial: namely that the size of the British sheep flock (currently ca. 28 million) relative to that of the cattle herd (ca. 11 million) is incomparably larger in Britain than in almost any other country in the world. Consequently, the exposure of British cattle to sheep rendering products was greater than anywhere else in the world. However, the Swiss “mini-epidemic“ (ca. 0.7% of the UK incidence) has occurred in a country with more than four times as many cattle as sheep. Moreover, it is remarkable that ovine BSE does not seem to have been manifested in the course of the cattle epidemic despite the extensive use of concentrates to supplement sheep rations in the winter in large parts of Britain. This is even more surprising in view of the known particular susceptibility of sheep to prion diseases (there are more than 20 strains of naturally occurring scrapie). Experimental infection of sheep with BSE also produces a disease distinct from any known form of scrapie.

Why does it matter whether or not BSE originated in cattle?

7. Greater scientific and political attention would have focused on the potential transmissibility of BSE to humans as a matter for urgent investigation if the "scrapie theory" had not been relatively uncritically accepted in the crucial initial years (and indeed up to the present). Enforcement and policing of stringent preventative measurements would otherwise have been accorded a higher priority from the beginning.
8. The scrapie hypothesis unfortunately misled many Government scientists into inferring a negligible risk that BSE could be transmitted to humans. Scrapie-infected sheep tissues have been consumed by humans for centuries without ill effects. BSE has proved to be radically different from scrapie, not least in this respect. The lesion profiles of BSE and vCJD are very similar (in fact, almost identical), and diverge conspicuously from the strains of scrapie investigated so far. This in itself raises questions as to whether the putative scrapie origin of BSE was ever tenable.

Origin of BSE

9. There are numerous unresolved questions concerning the origin of the BSE prion:
 - a) Did the BSE prion arise by mutation and selection from an as yet unidentified strain of sheep scrapie which crossed the species barrier to cattle?
 - b) If so, why have sheep not developed ovine BSE on any noticeable scale?
 - c) Did BSE arise in cattle, either from an endemic avirulent prion infection or by mutation of bovine prion protein?

d) Was there a single original focus of the epidemic? If so, is there any way of establishing where this was located?

BSE and vCJD - The Kent/Hampshire Connection

10. The paper that was made available to the Inquiry and which has been submitted for publication in a scientific journal addresses the following core issues:
 1. How can the higher percentage of dairy herds affected with at least one confirmed case of BSE in Hampshire and some adjacent counties as compared to Kent be explained if BSE originated as result of the Smarden spill? (Part I)
 2. Is there a link between the operation of the Thruxted Mill rendering plant and the conspicuously raised incidence of vCJD in the vicinity of Ashford? (Part II)
11. Part I formulates a scientific hypothesis challenging the hitherto accepted view that BSE originated from sheep scrapie. It postulates an autochthonous origin of BSE in cattle in connection with the 1963 Smarden spill.

The Smarden Spill

12. The mutagenic chemical methyl bromide (one component of the “Smarden spill“) was capable of inducing a nucleotide base substitution (giving rise for example to a cytosine-to-thymine transition via 5-methylcytosine) in the prion protein gene of a single animal (cow or bull) analogous to the mutations in the human prion protein gene that generate Gerstmann-Sträußler-Scheinker syndrome (GSS). Alternatively, proto-PrP^{BSE} could also have been generated by a post-translational modification in the three-dimensional structure of existing prion proteins resulting from a non-mutagenic effect of amino acid alkylation by methyl bromide.
13. Had the carcass of the animal in which BSE putatively originated as a result of the Smarden spill not been rendered and had the meat and bone meal produced not been incorporated into cattle feed, the initial generation of BSE in a single animal (if this is indeed what happened) could not have given rise to the British BSE epidemic.
14. Whatever the origin of the “proto-PrP^{BSE}“ template (unless it is generated regularly or is indeed part of an endemic reservoir), it has long since been replaced as a molecular species by the BSE prion, of which the primary peptide sequence and three-dimensional structure are contingent on the host prion protein. The latter is the indispensable substrate for BSE prion replication (principle of allelic nonequivalence), even if unidentified intron-located nucleic acid also plays a role
15. In consequence of “allelic nonequivalence“ (which is essentially a corollary of the prion hypothesis), it will in practice probably never be possible to reconstruct the primary amino acid sequence of the prion mutation or post-translational modification of prion protein by methyl bromide which gave rise

to BSE (if this was indeed the mechanism of its origin). However, the phenotype homology between the lesion profile of BSE passaged in a number of species and that of cattle BSE as well as the great similarity of this "BSE signature" and the lesion profile of vCJD in humans indicate that altered prions are a necessary and determining factor in the transmission of a specific prion phenotype in BSE-related diseases.

Thruxted Mill and vCJD in Ashford

16. The potential role of the Thruxted Mill rendering plant in causing the Ashford cluster of vCJD cases was the subject of a theoretical paper originally written in the summer of 1997. This has now become Part II of the paper currently submitted for publication and made available to the BSE Inquiry.
17. Thruxted Mill currently disposes of ca. 100,000 cattle carcasses per year from the British Government's over thirty months scheme (OTMS). This is about one-seventh of the cattle over thirty months old currently being slaughtered annually in Great Britain (contrary to popular belief, the number of carcasses to be disposed of is not decreasing, and will not decrease until the policy is abandoned). In addition, some 2000 tonnes of specified bovine material (SBM) is being processed per year at Thruxted. The Environment Agency (EA) invested a very substantial amount of public money in an effort to prove that the proposed discharge of effluent will be entirely harmless to man and beast.
18. The EA's assertion at the Thruxted planning inquiry that the precautionary principle does not apply in the case of Thruxted Mill in view of the low risk entailed by its effluent discharge is entirely unfounded. The source data presented by the EA at the Thruxted Inquiry derive in part from its assumptions concerning the segregation of infectivity to the various products of rendering. The EA also stipulates a minimum particle size of 10^{13} molecules for human infection and assumes there is a 2500-fold reduction of infectivity by rendering, filtration and biological treatment prior to discharge. In fact, the minimum particle size may be at least 10^{12} times lower. The reduction in the input levels of BSE infectivity prior to discharge will also be very substantially less than implied in the EA source data, and may indeed be minimal. The EA assumes that biological treatment of the rendering effluent will reduce or eliminate BSE infectivity. This is probably the exact opposite of what is actually likely to happen.
19. In his proof of evidence at the Thruxted Inquiry, Mr Young asserted that "effective filtering of clumps of material is likely". As already mentioned, infectious prions are known to pass through 400 nm filters (i.e. less than half a micron). Micropore filtration would therefore seem to have inherent limitations given the size of prion particles under consideration.
20. Micropore filtration in the chalk can hardly be relied upon to remove all or even most of the prion aggregates "liberated" by biological treatment of the effluent. The unsaturated chalk matrix is composed predominantly of micro-

fossil debris with pore-throat diameters of 0.1 to one micron. The mean pore size in the upper chalk is 0.65 μm , that in the middle chalk 0.53 μm (range 0.1 to 1.0 μm)⁵.

21. Without relevant tests on site, the presence of fissures in the chalk cannot be ruled out. If present, they would allow the 85 metres of unsaturated chalk between the discharge site and the aquifer to be traversed in a matter of days or indeed hours.
22. In respect of adsorption, according to Baxter and Clark virus adsorption by soils is reduced when the flow increases above some "break-point" and that therefore the flow rate may be the most important single factor affecting virus removal efficiency.⁶
23. Once the unsaturated chalk layer has been traversed, the Environment Agency assumes a travel time within the aquifer to the boreholes at Godmersham and Chilham of two to twenty years.
24. The question of a "fast-track" discharge via a well within the curtilage of Thruxted Mill may have been in use both prior to and after the discharge consent for the surface soakaway in "Bluebell Wood" was issued in 1985 is of particular relevance in relation to accelerated passage of infectivity through the unsaturated layer above the aquifer.
25. The effects of attenuation, dilution and hydrodynamic dispersion between the discharge point and the boreholes would, under favourable circumstances, reduce the number of infectious doses reaching the drinking water very substantially, though the extent of the reduction is difficult to quantify. At all events, it appears problematical to assume (as does the EA) that their attenuation in the unsaturated zone of the chalk is necessarily comparable to that of viruses. This is in view of the specific aggregation characteristics of infectious prions, and the effect of aggregation on their infectivity.

Fate of prions in rendering

26. Considering the nature of the rendering process, it is entirely implausible to suppose as does the EA Proof of Evidence that prions released from specified bovine material (SBM) and corresponding tissues in cull cattle will be distributed evenly between meat and bone meal (MBM) and suspended solids (SS). Fat/water emulsions may be expected to raise very substantially the proportion of prions segregating to the water-based product (rendering "condensate") containing the SS. The review article by Gabizon and Prusiner on "prion liposomes" shows that infectious prion aggregates are highly soluble in lipid droplets⁷. Gabizon et al. reported a 100-fold increase of scrapie infectivity when rod-shaped prion amyloids were dissociated into liposomes⁸. The SS will also contain proteins. Given the very much larger particle size of the MBM fraction relative to that of the SS, the latter will have a much larger

surface area (well over 1000 times greater) than that of the MBM, so their aggregation affinity for prions will be correspondingly greater.

27. The mouse brain bioassay is in any case subject to major methodological deficiencies, not least those deriving from the sample processing procedure. This bioassay entails injecting a distilled-water supernatant resulting from centrifuging a suspension of macerated or ground tissue.

Risk of infection from rendering effluent discharge above an aquifer

28. The risk of infection via drinking water crucially depends on the size of the human infectious dose. The individual risk of infection (infections per person per year) calculated by the EA's Centre for Integrated Environmental Risk Assessment in conjunction with the independent consultants Det Norske Veritas (CIERA/DNV risk support unit) as resulting from the proposed effluent disposal is 3.8×10^{-9} (95% confidence limit). A mere 1000-fold increase would entail a risk level which is higher than the "one in a million" incremental risk of death criterion generally regarded as negligible by the Health and Safety Executive. The actual risk level is likely to be higher by a factor of at least one thousand million-fold the EA figure.
29. The size of the minimum dose required and consequently the risk of human infection will be crucially affected by the susceptibility of the individual human beings supplied with drinking water from the Chilham and Godmersham boreholes. 62% of human beings exposed to an infectious dose may be unsusceptible for genetic reasons. Moreover, the risk of infecting cattle would be substantially greater than that of infecting humans because of the absence of a species barrier or a known genetic component in bovine susceptibility to BSE. Neither the risk to cattle nor to humans supplied with drinking water from the Chilham and Godmersham boreholes is acceptable.
30. The potential danger to public water supplies emanating from the past and future discharge of effluent from the Thruxted rendering plant into the chalk above the aquifer supplying some 140,000 people around Ashford with drinking water raises serious questions concerning the reliability of the Environment Agency's risk assessment and point to a theoretical possibility that Ashford's drinking water has been contaminated with BSE prions for many years. While the Thruxted planning inquiry was mainly concerned with future effluent discharge, I feel that the graver question of what happened in the past (when the number of cattle infected with BSE was very substantially greater) must be addressed by the Government as a matter of urgency. If BSE did indeed originate in Kent, then it is possible that significant amounts of BSE infectivity have been entering the aquifer for more than 20 years.

What indications are there for an origin of BSE in Kent?

31. According to Bradley and Wilesmith (1993)⁴, only five English counties (all adjacent) had an incidence of more than 60% of their dairy herds with at least

one confirmed case of BSE between November 1986 and 30 July 1993: Hampshire, West Sussex, Wiltshire, Avon and Dorset. With the exception of Cambridgeshire and Lincolnshire, all other counties south of a line from the Severn to Humber estuaries plus Lancashire and Cheshire had an incidence of more than 45% dairy herds with confirmed BSE in the same periods. The whole of Scotland plus Cumbria and West Yorkshire had an incidence of less than 30% dairy herds with confirmed BSE in the same period.

32. Postulating an origin of BSE in Kent would therefore have entailed problems given the published epidemiological data which may be interpreted to indicate an epicentre of the epidemic somewhere in Hampshire. Eyewitness reports from Kent, Sussex and Hampshire obtained by the Kentish Express newspaper (much of which has not yet been published, but which will be made available to the Inquiry) do however corroborate a Thruxted/Fareham or Kent/Hampshire connection.
33. According to information provided to the Kentish Express newspaper by the current mill manager David Richardson, the greaves from Thruxted Mill were not processed to MBM from 1978 to 1982, being sent instead to a sister company at Fareham (Midland Meat Products). In the event that the Smarden hypothesis is correct, the gradual build-up of BSE infectivity which could have occurred in Kent cattle herds from the late 1960s to 1978 would have been diverted in part to Midland Meat Products in Fareham and the other full renderers taking Thruxted greaves. The effects of such a diversion can be quantified only indirectly on the basis of epidemiological data, since Sheppey Glue and Fertiliser continued to produce MBM during this period. The "Kent-Hampshire connection" is significant in providing an explanation for the dissemination of BSE along the south coast of England.

Time scale of the BSE epidemic in the early years prior to its detection

34. In the event that the Smarden hypothesis is correct (BSE arose in consequence of a mutation induced in a single cow or bull caused by methyl bromide in 1963 or in one of the immediately preceding years), and the animal concerned survived long enough to incubate the disease (this might have required its living for at least eight years after the initial mutation occurred), then it could have transmitted BSE via meat and bone meal from about 1971 onwards. In contrast to the putative protracted first incubation period, the cycle of transmission subsequent to the first incubation would be the approximately four years of the current latency period, that is to say two transmission cycles could have occurred by about 1978.
35. Assuming that the information supplied to the Kentish Express in November 1997 is correct, the BSE infectivity deriving from the second transmission cycle (ending in about 1978) would not have passed primarily into meat and bone meal in the rations of cattle in Kent. Instead, it would have been disseminated primarily from the rendering plant in Fareham which reportedly received most of the Thruxted greaves in the period 1978-82.

36. To corroborate or refute the Swarden hypothesis, specific raw data on BSE incidence from 1986 to 1992 initially promised by CVL at the beginning of February but not yet forthcoming are absolutely indispensable.
37. Clarifying the circumstances surrounding the putative third transmission cycle (ca. 1978 to 1981/82) will be exceedingly difficult, and will probably have to rely exclusively on anecdotal and circumstantial evidence.

Acknowledgement

38. I have discussed scientific questions relating to TSEs and the hypotheses contained in the paper BSE and vCJD - The Kent/Hampshire Connection with Dr. Alan Colchester, Professor Alan Dickinson, Dr. James Hope (Compton Laboratory) and various TSE specialists abroad, including Dr. Paul Brown and Dr. Robert Rohwer (NIH) as well as Professor Klaus Beyreuther, Molecular Biology Centre, University of Heidelberg. Responsibility for its content is entirely my own.
39. Media enquiries concerning the content of this statement can be made on tel. no. 07771 622076; copies of the full paper can be requested and dispatched by E-mail (biomed-translations@t-online.de).

Signed

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